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Effect of Fatiguing Exercise on Longitudinal Bone Strain as Related to Stress Fracture in Humans

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Abstract—Muscular fatigue in the training athlete or military recruit has been hypothesized to cause increased bone strain that may contribute to the development of a stress fracture. Under normal circumstances, muscles exert a protective effect by contracting to reduce bending strains on cortical bone surfaces. *In vivo* strain studies in dogs show that muscle fatigue following strenuous exercise elevates bone strain and changes strain distribution. However, a similar experiment has yet to be performed in humans. The purpose of this work was to test the hypothesis in humans that strenuous fatiguing exercise causes an elevation in bone strain. It was also hypothesized that this elevation is greater in younger people than in older people due to the decline in muscle strength and endurance that normally occurs with age. To test these hypotheses, strain in the tibiae of seven human volunteers was measured during walking before and after a period of fatiguing exercise. Neither hypothesis was sustained. *Post-hoc* analysis of the strain data suggests that strain rate increases after fatigue with a greater increase in younger as opposed to older persons. Although not conclusive, this suggests that it is strain rate, rather than strain magnitude, that may be causal for stress fracture. *© 1998 Biomedical Engineering Society.* [S0090-6964(98)01404-0]

Keywords—Stress fracture, Bone strain, Fatigue, Aging.

INTRODUCTION

Mechanical testing of devitalized bone shows that bone will fail within 10^3 to 10^5, loading cycles at strain ranges of 5000–10,000 microstrain, or within 10^6 cycles at 3000 microstrain in uniaxial tension.[2–5] Even during strenuous physical exertion, however, principal strains on the medial aspect of the human tibia, a site known to be at risk for stress fracture, never exceed 2000 microstrain,[1,15] well below the strain known to cause fracture.[2,34] Based on cyclic load to failure studies,[2,3] and linearly extrapolating to the range of strains measured in the human tibia (i.e., 2000 microstrain), stress fractures should not occur at this site for at least 10^6 cycles, if failure is caused solely by the repetitive application of load. This means that a person would have to run at least 1000 miles without any bone remodeling before bone is even remotely likely to fail.[18] Recruits during basic training march approximately 70 miles and run approximately 130 miles over 12 weeks.[13] The majority of stress fractures in military basic training occur between 3 and 7 weeks in the training regime, when approximately 140,000 or fewer loading cycles have been placed on the skeleton.

The relationship between the number of loading cycles and failure in bone at a given strain is not linear.[25] Tensile fatigue tests on primary and Haversian bone conducted at strain and strain rates similar to that measured in the human tibia[32] show that healthy bone does not fail in tension by fatigue even after 37 million loading cycles under strain control.[34] Because stress fractures do occur long before this many loading cycles, other factors besides the number of load cycles must contribute to the pathogenesis. Candidates for additional components are muscular fatigue, loss of coordination, age-related effects, and high impact or high strain rate loading.

There is relatively strong evidence for age-related effects in the incidence of stress fracture. Using self-reports from over 2000 active duty US Army women, the prevalence of stress fracture was 19.6% in women 22–23 years old but only 1.4% for women over the age of 40.[7] Stress fracture incidence between ages 18 and 34 was consistently between 15%–20%, but fell rapidly to about 5% by age 38. While the covariate effects of menstrual history, smoking, ethnic origin and family history were controlled in this study, the change in physical activity among women of these different age groups was not controlled. Therefore, the age effect could have been partly due to reduced physical activity in the older groups. In a large prospective study of 783 male Israeli military recruits between the ages of 17 and 26, Milgrom *et al.*[22] reported that recruits more than 20 years old had only a 2.9% incidence of stress fracture, while those recruits younger than 20 had an incidence of 26%. More-

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over, each year of increased age above 17 years reduced the risk of a stress fracture by 28%.

It is unknown whether bone strain magnitude or rate increase after fatiguing exercise in humans or whether changes in bone strain magnitude or rate after fatigue are age related. The purpose of the current study was to determine in humans whether longitudinal bone strain magnitude changes after fatigue in an age-related way.

METHODS

In vivo strain measurements in the longitudinal direction of the tibia were made on seven male subjects aged 23, 24, 28, 29, 35, 43, and 50 years. All but one of the subjects (24 year old) had successfully completed or were currently in military service. The exceptional individual was a recreational long-distance runner and judged to be an appropriate subject for the study. No attempt was made to find subjects susceptible to stress fracture for logistical reasons. This decision may have resulted in some selection bias in the subjects.

Two 2-mm-diam *k*-wires with 15 mm of thread and trochar tips were inserted under local anesthesia into 1.5-mm-diam predrilled holes to a depth of 6 mm in the antero-medial tibial midshaft. The proximal and distal *k*-wires were placed parallel to each other and perpendicular to the surface of the tibia 19.1 mm apart. Consistent *k*-wire alignment was achieved through the use of drill and wire placement guides. After placement, the *k*-wires were cut so each wire protruded from the skin about 15 mm. All procedures were approved by the Helsinki Committee of the Hadassah University Hospital and informed consent was obtained from all subjects.

Following surgery, the subjects walked at 5 km per hr on a treadmill while prefatigue strains were collected for 20 s. Subjects then participated in a 2 h session of strenuous outdoor exercise that included rapid walking, running up and down hills, and stair climbing. After the outdoor exercise, subjects ran on the treadmill at 11 km per hr until voluntary exhaustion. Strains were measured immediately postfatigue while the subject walked on the treadmill at 5 km per hr.

Strains were measured with a custom displacement transducer (17.4 g) attached between the two *k*-wires. The transducer consisted of a phosphor bronze beam (0.254 mm thick) with two pairs of uniaxial strain gauges (CEA-09-062UW-350), one pair bonded to the top and the other bonded to the bottom surface of the beam. The gauges were wired as a full Wheatstone bridge. The beam was supported by an aluminum block (19.1×19.1×9.53 mm). Bridge voltages were recorded on an FM analog cassette recorder (TEAC HR10) and digitized at 400 Hz (SnapShot, HEM, Troy, MI).

The relationship between beam displacement and longitudinal bone strain was determined from two calibration experiments. The first was placement of the extensometer on a fresh frozen dog tibia *in vitro* with a strain gauge (CEA-13-06UW-350) mounted on the bone between the pins. The extensometer and bone construct was loaded axially in compression in an INSTRON 8501 Servohydraulic loading system with a 0.25 Hz, 1500 N haversine to determine the relationship between the two methods of estimating strain. Extensometer and strain gauge output voltages were collected at 100 Hz using Labtech Notebook (Wilmington, MA). The second calibration experiment involved placement of the extensometer on a composite tibia (Pacific Research Laboratories, Vashon, Washington) with a strain gauge (CEA-06-062UW-350) mounted between the pins. This construct was used to examine the effect of impact loading on the readings of the extensometer. Data were collected at 20,000 Hz using a Nicolet 420 digital oscilloscope (Nicolet Instruments, Madison, WI). Two experiments were performed: (1) The composite tibia was bent by hand as rapidly as possible (>2 Hz) in the anteroposterior direction; (2) the distal end of the composite tibia was manually struck against a solid object covered with a $\frac{1}{2}$ in. layer of packing foam to produce an acceleration in the construct similar to that experienced in field applications.

The period of foot placement was recorded using a footswitch.[9] The footswitch system used thin pressure sensitive switches (Interlink Electronics, Santa Barbara, CA) placed in the shoe to record a signal proportional to the pressure on the sole of the subject's foot. The output of this footswitch was not accurate enough to be used quantitatively, but was representative of the magnitude of force on the instrumented foot, and of the time of heelstrike.

The data were reduced using a low pass Fourier filter written in MATHCAD (Mathsoft, Cambridge, MA) to remove a heelstrike signal. A cutoff frequency of 2 Hz was chosen to reduce the data. This cutoff frequency resulted in the best correlation between the filtered strain signal and the footswitch (pressure) signal (Fig. 1). (The fast Fourier transform used in MATHCAD results in a discrete range of possible cutoff frequencies. All possible cutoff frequencies between approximately 0.5 Hz and 60 Hz were examined.)

Strain ranges for ten cycles of gait were determined and averaged for each subject before and after exercise. (Strain range was used because it is known to be an important determinant of fatigue life for reversed loading.) The change in the strain range between the before and after exercise states was normalized by dividing by the initial strain range to determine the fractional change in the strain range. Linear regressions were made be-

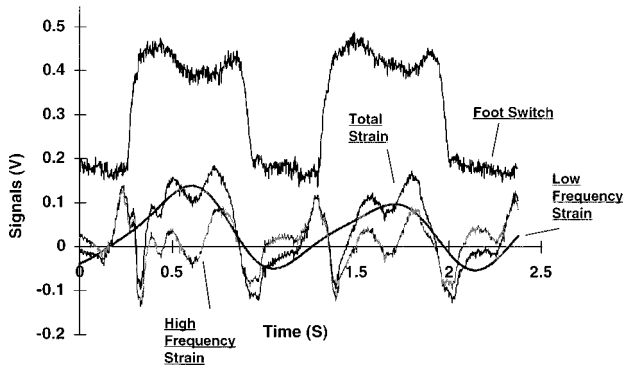

FIGURE 1. Relationship between footswitch signal, unfiltered and filtered strain signals from an *in vivo* data set. Note the correspondence between the filtered (low frequency) strain and the footswitch signal.

tween age and the fractional change in the range of the filtered data and also the fractional change in the range of the unfiltered data with a significance level of $p<0.05$.

RESULTS

The validation experiments for the extensometer mounted on the dog tibia showed an $r^2>0.96$ correlation between the output of the strain gauge and the extensometer. Similarly, the experiment of rapid manual bending of the composite tibia construct had a correlation between the strain gauge and extensometer output of $r^2=0.998$. However, the impact experiment with the composite tibia showed only an $r^2=0.40$ relationship between the unfiltered output of the extensometer and the strain gauge. After Fourier filtering at 3.7 Hz, the relationship between the two data sets was improved to $r^2=0.70$.

For the human experiment, data from the 29-year-old subject was discarded after filtering as it had a correlation between the filtered strain signal and the footswitch signal of $r^2<0.04$. The average correlation and standard deviation of the correlation between the filtered strain signal and the foot switch signal for the remaining six subjects were $r^2=0.49$ and 0.14, respectively.

The regression of fractional strain change against subject age was not statistically significant even when the 43-year-old outlier was excluded (fractional filtered strain range change$=0.009\text{Age}-0.197$, $r^2=0.33$; Fig. 2). The fractional change in the range of the unfiltered data against age was statistically significant at $p<0.05$ (fractional unfiltered strain range change$=-0.0132\text{Age}+0.437$, $r^2=0.49$; Fig. 3).

Subjects younger than 30 years averaged 10 min on the treadmill while those over 35 averaged 5.5 min.

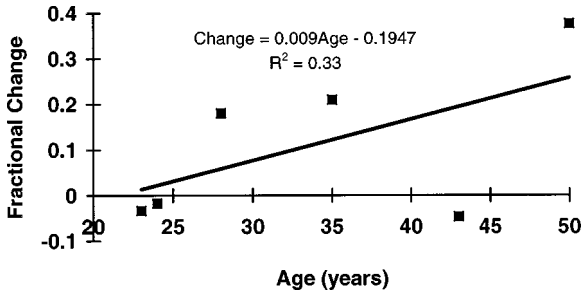

FIGURE 2. The fractional change in filtered strain range following fatiguing exercise increased nonsignificantly with subject age.

DISCUSSION

The purpose of this study was to test the hypothesis in humans whether muscle fatigue increases longitudinal bone strains relative to the prefatigue baseline. This is the primary reason why the fractional changes in strain range between the fatigued and unfatigued state were examined. Also, examination of strain range eliminated artifacts resulting from drift in the strain baseline. This conservative approach was chosen due to the presence of unanticipated artifacts in the data as discussed below. The data obtained in these experiments were quite noisy. However, these results are important because of their relevance to hypotheses about stress fracture etiology because they represent data that can only be collected on human subjects. Due to logistical and financial reasons, there is currently no plan to rerun this particular experiment using another group of human subjects.

The impact shock of heelstrike being transmitted to the strain sensing element created an unanticipated artifact. This transmission was not strongly present in the *in vitro* experiments using the composite tibia system. As the composite tibia was less damped than a real tibia due to the absence of soft tissue, it was expected that the *in vivo* preparations would have only a small heelstrike

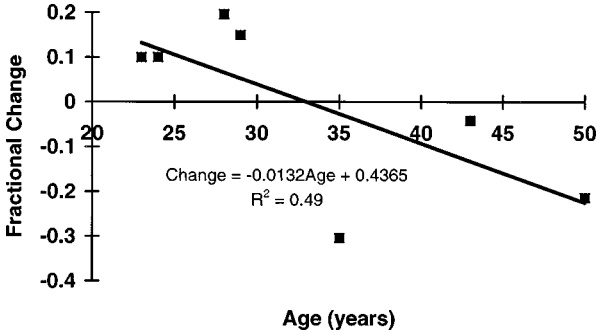

FIGURE 3. The fractional change in unfiltered strain range ("acceleration," see text) decreased significantly with age following fatiguing exercise. This is indicative of increased heelstrike impact in the younger (<35 years) subjects.

artifact. However, this was not found to be the case. The primary cause for this was the *in vivo* pin placement procedure. In the *in vitro* experiments, the pins were drilled completely through the cortex of the preparations, allowing placement of the extensometer within a millimeter of the cortical surface. In the *in vivo* experiment, the surgeon did not screw the pins completely through the cortex of the tibia to avoid compromising the medullary canal, thereby reducing the chance of bone infection. Because the threaded portions of the pins were 15 mm long, the extensometer was placed approximately 10 mm from the cortical surface. This increased distance between the extensometer and the bone surface reduced the stiffness of the system, causing a greater sensitivity to the impact at heelstrike. In essence, the unfiltered strain signal from the extensometer reflected both the acceleration of the sensor and the actual change in distance (strain) between the transcutaneous pins.

To reduce the heelstrike artifact, the data were filtered and the portion of the extensometer signal most correlated with the footswitch signal was obtained. This was reasonable as the strains in a bone are correlated to the load applied to the bone. The footswitch used in this study provided a signal roughly proportional to the load applied to the foot. Therefore, the filtered strain signal that best correlated to the footswitch signal should be the best estimate of the strain available from the data (Fig. 1).

The range of unfiltered data was used as a representation for the peak accelerations occurring in the tibia because the heelstrike artifact was so clearly evident in these data. Using this interpretation, an examination of the relative changes in acceleration of the tibia was performed. The ''acceleration'' results from the present study were consistent with direct measurements by other investigators of peak accelerations before and after fatiguing exercise.[38]

The regressions of fractional change in filtered and unfiltered data against subject age show that: (1) Longitudinal bone strain range appears to have a nonsignificant tendency to increase during walking after fatiguing exercise in older people (>35), but is unchanged in younger people (<35); (2) heelstrike impact (unfiltered signal range or ''acceleration'') is significantly increased in younger persons (<35) and significantly decreased in older persons (>35) after fatiguing exercise. The age trend in the first result is inconsistent with our original hypothesis, so we consider the original hypothesis not to be sustained. The second observation suggests an effect of muscular aging on gait after fatigue. We hypothesize that the loss of muscle strength and endurance with age[16,36] prevents forceful muscle contractions when synergistic control of muscles is lost following fatigue. This reduces impact loading at heelstrike in older persons. Coordinated muscle action is also impaired after fatigue for younger people; however, muscle strength and the ability to create rapid forceful muscle contraction remains. As a result, there will be an increase in impact loading in younger persons due to rapid, forceful, discoordinated, leg action at heelstrike. This difference in postfatigue impact accelerations may be the cause of the difference in stress fracture rates between younger and older individuals.

Accelerations of 5–10 g are regularly produced at heelstrike.[17,26,37] The leg muscles decelerate the limb before heelstrike[11] and reduce strain rate by absorbing impact energy through eccentric contraction during movement.[10,20,26,27,30] This attenuates potentially large ground reaction forces[23,29–31] in approximately 75–100 ms.[21,28] Fatigue may slow muscle reaction or otherwise change the normal mechanisms for attenuating the heelstrike transient. The transfer of mechanical energy between the eccentric and concentric phases of muscle contraction is reduced during muscular fatigue,[8] making the muscle less capable of dissipating impact energy. As a result, muscular fatigue may have a significant effect upon bone loading.[40] As evidence for this thesis, an experimentally induced absence of appropriate muscle contraction in the leg increases the magnitude and rate of application of ground reaction forces at heelstrike.[29–31]

Muscular fatigue in humans leads to a 50% increase in tibial acceleration.[38] This is probably related to (1) a delay in the activation of knee flexors and extensors that would normally attenuate the impact at heelstrike and (2) a fatigue-related increase in muscle contraction time.[35] With muscle fatigue, knee flexion occurs earlier in the gait cycle,[24] reducing stride rate,[6] and increasing the amplitude of the heelstrike impact.[38] Gait changes from fatigue increase peak vertical ground reaction force from 2.35 to 2.97 body weight (about 25%).[24]

High impact activities also are associated with stress fractures. Increased time spent running on hard surfaces is correlated with a higher incidence of stress fractures.[12] Because bone is a viscoelastic material, higher loading rates may increase its elastic modulus and material stress[39] and decrease its fatigue resistance.[14,19,33] However, the actual mechanisms whereby high impact activities increase stress fracture are unknown. The pattern of age dependence in heelstrike impact (unfiltered signal) after fatigue may explain the observation that stress fracture is age related and occurs more frequently in younger people.[22]

The data collected in these experiments were affected by an unforeseen heelstrike transient, but are significant due to their uniqueness as a set of tibial strain measurements for human subjects before and after fatiguing exercise. Our data, in combination with previously published data, support our conclusions that (1) high strain rate caused by rapid deceleration of the tibia at heelstrike rather than strain magnitude is implicated in the etiology

of stress fracture and (2) the age dependence of stress fracture may result from the age dependency of changes in strain rate after fatiguing exercise.

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