

Metatarsal Strains Are Sufficient to Cause Fatigue Fracture During Cyclic Overloading

C. Milgrom, M.D.[¶]; A. Finestone, M.D.^{¶¶}; N. Sharkey, Ph.D.[†]; A. Hamel, Ph.D.^{††}; V. Mandes, B.S.[§]; D. Burr, Ph.D.^{§§}; A. Arndt, Ph.D.^{**}; I. Ekenman M.D., Ph.D.^{*}

Jerusalem, Israel; Huddinge, Sweden; University Park, PA., USA; Indianapolis, Indiana; Petah Tikvah, Israel

ABSTRACT

Human *in vivo* tibial strains during vigorous walking have not been found to exceed 1200 microstrains. These values are below those found in *ex vivo* studies (>3000 microstrains) to cause cortical bone fatigue failure, suggesting that an intermediate bone remodeling response may be associated with tibial stress fractures. Metatarsal stress fractures, however, often develop before there is time for such a response to occur. Simultaneous *in vivo* axial strains were measured at the mid diaphysis of the second metatarsal and the tibia in two subjects. Peak axial metatarsal compression strains and strain rates were significantly higher than those of the tibia during treadmill walking and jogging both barefoot and with running shoes and during simple calisthenics. During barefoot treadmill walking metatarsal compression strains were greater than 2500 microstrains. During one- and

two-leg vertical jumps and broad jumping, both metatarsal compression and tension strains were >3000 microstrains. Compression and tension strains in the metatarsus unlike those of the tibia may be sufficiently high even during moderate exertional activities to cause fatigue failure of bone secondary to the number of loading cycles without an intermediate bone remodeling response.

Key Words: Stress Fracture; Tibia; Metatarsal; Strains

INTRODUCTION

Stress fractures are considered to result from cyclic overloading of bone. Historically, the first steps in our understanding of the role of bone strain in the etiology of stress fractures began with *ex vivo* testing. It was found that cortical bone fails within 10^3 to 10^5 loading cycles at strain levels of 5,000-10,000 microstrains.⁵ However, when uni-axial tensile strains within the normal physiological range (~1,200-1,500 microstrains) are applied, bone stiffness decreases, but the bone does not fail even after the number of loading cycles equivalent to 1,000 miles of walking.¹⁷

During uphill walking with a backpack, human mid diaphyseal medial tibial compression and tension strains have not been found to reach 1,200 microstrains.^{2,11} Even during fast running they have not been found to exceed 2,500 microstrains in compression and tension.^{12,13} These observations have led to the hypothesis that stress fractures at this commonly affected site may be in many cases mediated by an intermittent bone remodeling response. According to this hypothesis bone reacts to unaccustomedly high strain levels by attempting to strengthen itself.³ The strengthening begins with bone resorption and is followed by new bone formation. It is during the phase of bone resorption when bone is weakened that continued cyclic loading can lead to stress fracture.

The authors observed that the epidemiology of 2nd metatarsal and medial tibial stress fractures is often

Presented in part at the 47th annual meeting of the Orthopaedic Research Society

Corresponding Author:

¶ Prof. C. Milgrom
Dept. of Orthopaedics
Hadassah University Hospital
Ein Kerem, PO Box 12000
Jerusalem, Israel
Phone: 972-2-6776412
Fax: 972-2-6434434
E-mail: milgrom@md2.huji.ac.il

* Senior Physician, Dept. of Orthopaedics, Huddinge University Hospital, Huddinge, Sweden

** Biomechanical Engineer, Dept. of Orthopaedics, Huddinge University Hospital, Huddinge, Sweden

† Associate Professor of Kinesiology, Orthopaedics and Rehabilitation, Center for Locomotion Studies, Pennsylvania State University, University Park, PA, USA

†† Mechanical Engineer, Center for Locomotion Studies, Pennsylvania State University, University Park, PA, USA

§ Mechanical Engineer, Center for Locomotion Studies, Pennsylvania State University, University Park, PA, USA

§§ Professor of Anatomy and Orthopaedics, Dept. of Anatomy and Orthopaedics, University of Indiana School of Medicine, Indianapolis, Indiana

¶¶ Senior Physician, Dept. of Orthopaedics, Rabin Medical Center, Beilinson Campus, Petah Tikvah, Israel

quite different.¹⁵ Military recruits, completely asymptomatic before a march can be found to have fractured their 2nd metatarsal at the end of a march. Medial tibial stress fractures typically have a much slower onset and rarely evolve into frank fracture. The authors hypothesized that second metatarsal strains may far exceed those recorded for the medial cortex of the mid tibia diaphysis, and may be in the range that can cause bone fatigue failure without an intermediate bone remodeling response. It was also hypothesized that shoe gear would have a greater influence on 2nd metatarsal strains than on medial tibial strains.

MATERIALS AND METHODS

Simultaneous measurement of axial tibial and second metatarsal strains were completed at the Huddinge University Hospital, on two members of the research team (A.F. age 40, 78 kilos, with pes planus foot type and C.M. age 54, 82 kilos, with high normal arch type), in March 2000. Both subjects received explanations of the goals, risk and benefits of their participation in the experiment and gave informed consent. The experimental protocol was approved by the Research Ethical Committee of the Karolinska Institute.

Strain Measurement Validation

Strain gauged staples made from 16 x 15 mm bone staples with a 1.0 mm staple bridge thickness (3M Health Care, St. Paul, MN, USA), with two MicroMeasurements strain gauges (Measurements Group Inc, Raleigh, NC,

USA) types EA-06-031DE-350 and EA-06-031EC-350 mounted perpendicular to each other on the underside of the staple were used to measure axial tibial and 2nd metatarsal strains. The application of the staple technique to the tibia was previously validated *in vitro* in three- and four-point bending models^{4,8} and to small animal bones in a four-point bending model.¹ To validate the technique of simultaneously recording tibial and 2nd metatarsal strains using strain gauged staples the dynamic gait simulator described by Sharkey and Hamel was used with one young cadaver lower limb specimen.¹⁸ Strain gauged staples aligned in an axial direction were inserted to a depth of 4 mm into the medial aspect of the mid tibial diaphysis and into the dorsal surface of the mid 2nd metatarsal diaphysis of a freshly thawed cadaver specimen. MicroMeasurements EA-06-031DE-350 strain gauges were bonded to the bone in the area between the legs of each of the two staples. Strain recordings were made from the strain-gauged staples and the strain gauges during five stance cycles. The linear regression analysis of the two measurement techniques for the tibia was $R^2=0.992$ and for the 2nd metatarsal was $R^2=0.999$. Figure 1 compares the average output of the metatarsal and tibial strain gauges with the strain-gauged staples during the course of five stance cycles.

In Vivo Strain Measurements

Strain-gauged staples were inserted in an open surgical procedure in the medial aspect of the mid tibial diaphysis and the dorsal surface of the mid 2nd metatarsal diaphysis. The strain-gauged staple signals were amplified by a strain gauge conditioner (Model 2120A, Measurement Group Inc, Raleigh, NC, USA). Data was sampled at 1,000 Hz and recorded with digital data collection software (Bioware, Kistler, Switzerland).

In vivo strain measurements were made while subjects walked on a treadmill at 5km/hr and jogged on a treadmill at 11 km/hr while wearing Nike Air Max running shoes and while barefoot. Each measurement was made over a one-minute interval after an initial one-minute "warm-up period." One subject (CM) performed four repetitions of a 50 cm broad jump, a vertical jump on one leg to 10 cm, and a two-legged vertical jump to 10 cm while wearing the running shoes.

Table 1a: Peak Metatarsal and Tibial Axial Strains Wearing Running Shoes.

Activity	Compression Strain (ms)		Tension Strain (ms)	
	Metatarsal	Tibial	Metatarsal	Tibial
Treadmill Walk				
Subject 1	934±450	395±45.6	1031±281	259±13.1
Subject 2	1354±42.8	748±31	490±59.8	185±65.8
Treadmill Jog				
Subject 1	1649±217	359±35.9	590±149	639±39.3
Subject 2	1287±53.2	446±82.3	416±20.5	1225±84.4

Table 1b: Peak Metatarsal and Tibial Axial Strain Rates Wearing Running Shoes.

Activity	Compression S.R. (ms/sec)		Tension S.R. (ms/sec)	
	Metatarsal	Tibial	Metatarsal	Tibial
Treadmill Walk				
Subject 1	5766±980	2241±795	8880±2582	2943±767
Subject 2	5742±1500	2164±211	6337±1072	3764±1397
Treadmill Jog				
Subject 1	17290±3514	2028±611	10354±764	6895±2048
Subject 2	16771±4079	3795±1237	2647±765	10020±2378

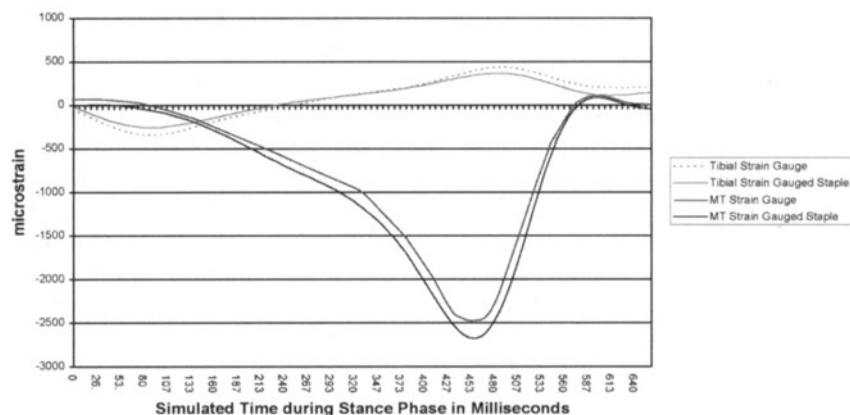


Fig. 1: Simultaneous tibial and metatarsal axial strains calculated from strain gauges and strain gauged staples.

Surgical Protocol

Surgical implantation of the strain-gauged staples was performed on an outpatient basis at the Huddinge University Hospital. Surgical implantation was performed in the morning, and the staples were removed the same day after completion of the experimental protocol.

The left leg was prepared and draped and surgical anesthesia achieved at the sites of tibial and 2nd metatarsal strain-gauged staple insertion with 2.5 ml 1% lidocaine and 2.5 ml of 0.5% of bupercaine. First a 2-cm skin incision was made over the dorsum of the 2nd metatarsal and with the tendons protected, dissection carried down to expose the periosteum. A drill guide was used to drill two holes through the cortex to a depth of 4 mm. Using a specially designed insertion tool the strain gauged staple was inserted into the predrilled holes to a depth of 4 mm (Fig. 2). The tibial strain-gauged staple was similarly inserted through a 2.5-cm skin incision. The surgical wounds were left opened and a gauze dressing placed loosely over each of the staples. At the end of experiment the strain gauged staples were removed and each skin wound closed with two sutures. Prophylactic oral antibiotics were given at the time of staple insertion and removal.



Fig. 2: Lateral radiograph of the foot shows the position of the strain gauged staple in the second metatarsal.

Data Analysis

Data was processed using a custom-written computer program written in Borland C++ for Windows which takes the digitized amplified strain-gauged staple outputs, performs a low-pass filter at 5 Hz, enables baseline correction, and derives the maximum axial tension and compression strains and strain rates. Means were calculated for each of the activities on the basis of four consecutive strides or from four jumps. The major outcome variables were the means of the maximum axial compression and tension strains and strain rates for each of the activities performed. The statistical analysis tests whether the mean of each of the major outcomes for each individual differs for the different

activities using repeated measures analysis of variance, with statistical significance, $p=0.05$.

RESULTS

For both subjects, both of the strain-gauged staples recorded for all of the experimental trials. Neither of the subjects experienced pain or discomfort during the experiment. Postoperatively there was mild swelling at the tibial and metatarsal surgical sites for one week. One subject uneventfully returned to his normal sport activity including running and basketball, one week after surgery. The second subject (A.F.), returned to full activity four weeks after surgery.

The peak axial metatarsal compression and tension strains (Fig. 3) and strain rates (Fig. 4), for both subjects while walking on the treadmill were significantly higher than those of the tibia. During treadmill barefoot jogging, the peak compression strains (Fig. 5), and compression strain rates (Fig. 6), for both subjects were significantly higher than those of the tibia. A peak axial compression strain of 5,766 microstrains was reached for the pes planus subject during treadmill jogging barefoot.

Wearing running shoes during treadmill walking and running significantly lowered the metatarsal, but not the tibial compression strains in both subjects (Table 1), as compared to performing the activity barefoot. The tension strains for both subjects significantly increased during treadmill walking while wearing running shoes. Metatarsal compression and tension strains and strain rates while wearing running shoes for both subjects were significantly higher than those of the tibia for all activities except for tension strain and tension strain rate during treadmill jogging (Tables 1, 2).

During broad jumping and vertical jumps on one and two legs, both tension and compression strains exceeded

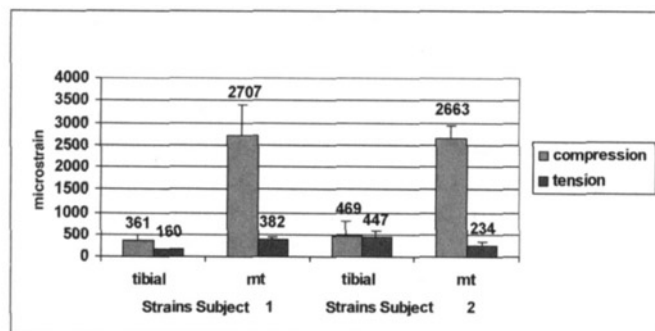


Fig. 3: MT vs. tibial strains during barefoot walking.

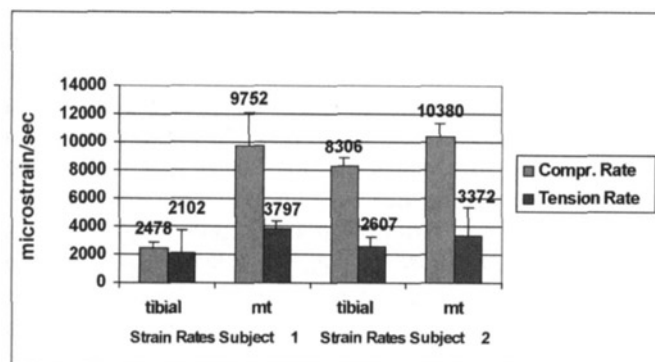


Fig. 4: MT vs. tibial strain rates during barefoot walking.

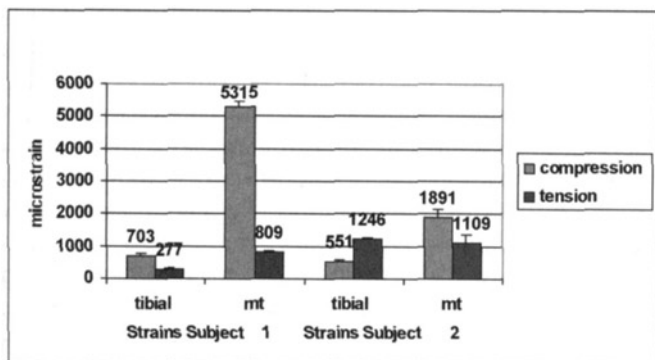


Fig. 5: MT vs. tibial strains during barefoot jogging.

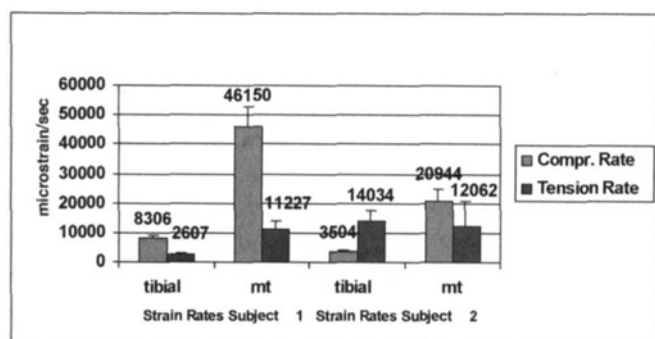


Fig. 6: MT vs. tibial strain rates during barefoot jogging.

3,000 microstrains and were significantly higher than those of the tibia (Figs. 7a, 7b).

DISCUSSION

Epidemiological observations in military recruits have shown that metatarsal stress fractures often occur sooner than a biological remodeling response to increased bone loading would be expected.¹⁵ A military recruit can be completely asymptomatic at the beginning of a long march and at the end be hobbled by pain and found to have a frank metatarsal stress fracture. Devas describes the scenario of a usually sedentary tourist who after a week of intensive vacation walking is hobbled by forefoot pain and found to have a frank metatarsal stress fracture.⁶ Extrapolating from *ex vivo* cortical bone testing, 2nd metatarsal bone strains of 3,000-5,000 microstrains (0.5% deformation) in tension or compression would have to have occurred during the recruit's or the tourist's activity to cause fatigue failure of the bone if there was no intermediate bone remodeling response.

Estimation of human bone strains can be made using finite element models, *in vitro* test models or *in vivo* measurements. Each of these methods has its pros and cons. Finite element models conveniently allow experiments to be done using computer simulation, but to date the models are insufficient to adequately calculate bone strain. One of the best of the human *in vitro* strain measurements models is the dynamic cadaver apparatus described by Sharkey and Hamel.¹⁷ This apparatus uses freshly thawed cadaver below-knee specimens. The physiologic action of the extrinsic foot muscles during stance phase is simulated using force feedback controlled linear actuators interfaced with the tendons of the test specimen. The model mimics the normal kinetics of the foot, ankle and tibia during the stance phase of gait from heel-strike to toe-off. The model is limited in that the velocity of gait is much lower than that of normal walking and no measurements can be made during the swing phase of gait. *In vivo* human strain measurements were initially made using strain gauges bonded directly to the bone.^{2,11} Because of the relative surgical invasiveness of this technique, most subsequent measurements have been made using strain-gauged bone staples.^{9,12,13,14} Recruitment of subjects for *in vivo* measurements is difficult and most experiments have had to rely on subjects from the scientific staff.

The validity of the simultaneous *in vivo* tibial and 2nd metatarsal strains recorded in the current study is dependent upon the validity of the measurements obtained using strain-gauged bone staples. Previous to the current experiment, the use of strain-gauged bone staples to record *in vivo* bone strains has been validated for the tibia *in vitro* in three- and four-point bending models^{4,8} and in small ani-

mal bones in a four-point bending model.¹ In the current experiment the technique of simultaneous tibia and 2nd metatarsal axial strain measurements using strain-gauged bone staples was further validated using the dynamic cadaver model described by Sharkey and Hamel.¹⁷ The linear regression analysis of axial strain measurements of the strain gauge and strain gauged staple for the tibia and 2nd metatarsal was $R^2=0.99$ in a specimen using this model.

Most *in vivo* human bone strain data is from the medial tibial diaphysis.^{2,11,12,13,14} This is both because of surgical considerations and the fact that the medial tibial diaphysis is nowadays the most common site of stress fractures in military recruits and sportspeople. At this site the largest strains observed are in shear rather than in compression or tension. During basketball rebounding tibial tension strains of 3000 microstrains have been recorded.¹³ During free running the largest compression or tension strains reported are less than 2200 microstrains.¹² During walking on level ground tibial compression and tension strains do not exceed 1000 microstrains.^{2,11}

If strain levels are similar in the 2nd metatarsal to those of the tibia than we do not have an adequate explanation for the development of many metatarsal stress fractures. For medial tibial stress fractures which typically take a longer time to develop than metatarsal stress fractures we have an adequate model. The

model assumes that first the tibia is exposed to overloading. It then responds by trying to strengthen itself. As a first step in this process bone is locally reabsorbed before new stronger bone is laid down. If during this absorption phase cyclic overloading continues before strengthening has occurred, microdamage may accumulate and lead to stress fracture.

In this study *in vivo* axial strain measurements were made simultaneously at two sites where stress fractures frequently occur, the dorsal surface of the 2nd metatarsal mid diaphysis and the medial cortex of the mid tibial diaphysis. The strains at these two sites might be expected to differ since the tibia was instrumented at a site on the diaphysis closer to its neutral axis of bending than was the metatarsal. The tibial strains were similar to those previously reported for treadmill walking for the same subjects,^{2,14} but lower than those reported for free jogging at the same speed.² Similarly, it is likely that metatarsal strains during free walking would be higher than those recorded during treadmill walking in this experiment.

The mean peak metatarsal axial compression strains during barefoot treadmill walking in this study for both subjects were slightly larger than 2500 microstrains. This is similar to the 2,500 microstrains recorded in the 2nd metatarsal, during stance phase, in our dynamic cadaver model specimen. Donahue and Sharkey reported mean peak axial strains of 1897 microstrains in their *in vitro* cadaver measurements at the same anatomical site.⁷ For the subject with pes planus in the current study, metatarsal compression strains were larger than 5,000 microstrains in compression during barefoot treadmill jogging. That the plantar arch is an important structure in determining 2nd metatarsal strains is shown in the Donahue and Sharkey *in vitro* experiment.⁷ When they performed a plantar fasciotomy on their cadavers specimens, compression strains increased by 100%, reaching 3,797 microstrains, during simulated normal walking conditions. Gross and Bunch, in a mechanical model of metatarsal stress fracture during distance running, calculated a dorsal compressive strain of 6,662 microstrains for the second metatarsal. This was 6.9 times greater than the estimated value for the first metatarsal.¹⁰ Extrapolating from *ex vivo* cortical bone fatigue experiments the *in vivo* barefoot metatarsal strains found in the present study are high enough to cause stress fracture in the previously mentioned recruit or tourist model without an intermediate remodeling response.⁶

By the age of the subjects in this study, the bones of their feet had adapted to the wearing of shoes. They did very little walking and almost no running without shoes. Wearing running shoes compared to barefoot walking and jogging significantly lowered 2nd metatarsal compression strains. Wearing different types of shoes may

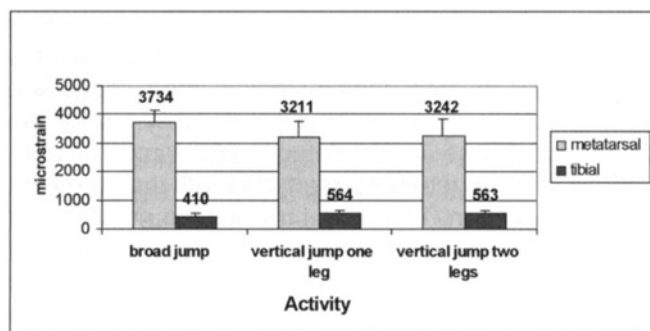


Fig. 7a: Compression strains vs. activity

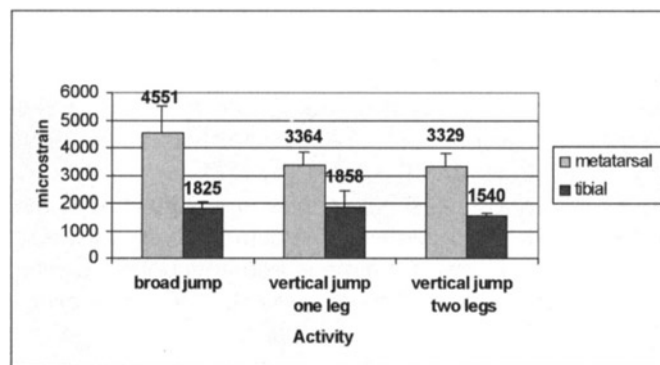


Fig. 7b: Tension strains vs. activity.

be expected to have varying effects on strains. During simple calisthenics in this experiment both metatarsal compression and tension strains were above 3000 microstrains. These calisthenics did not approach maximal subject effort as the vertical jumps were only to a height of 10 cm and the broad jump to a distance of 50 cm. Higher strains can be expected when performing these activities to near maximal distances.

The present experiment evaluates two common stress fracture sites. Although limited to only two subjects, with two different foot types, it indicates that dorsal mid diaphyseal 2nd metatarsal strains are significantly higher than mid diaphyseal anteriomedial tibial strains. It supports the hypothesis that 2nd metatarsal strains may be sufficiently high to cause stress fracture on the basis of cyclic overloading alone, without an intermediate bone remodeling response.

REFERENCES

1. **Arndt, A; Westblad, P; Ekenman I; Halvorsen, K; Lundberg, A:** An in vitro comparison of bone deformation measured with surface and staple mounted strain gauges. *J. Biomech.*, **32**:1359-1363, 1999.
2. **Burr, DB; Milgrom, C; Fyhrie, D; Forwood, M; Nyska, M; Finestone, A; Hoshaw, S; Saia, E; Simkin, A:** In vivo measurement of human tibial strains during vigorous activity. *Bone*, **18**:405-410, 1996.
3. **Burr, DB:** Bone, exercise and stress fracture: *Exerc. Sci. Sport Rev.*, **25**:171-194, 1997.
4. **Buttermen, GR; Janevic, JT; Lewis, JL; Lindquist, CM; Wood, KB; Schendel, MJ:** Description and application of instrumented staples for measuring in vivo bone strain. *J. Biomech.*, **27**:1087-1094, 1994.
5. **Carter, DR; Caler, WE; Spengler, DM; Frankel, VH:** Fatigue behavior of adult cortical bone. The influence of mean strain and strain rate. *Acta Orthop. Scan.*, **52**:481-490, 1981.
6. **Devas, M:** Stress Fractures, Churchill Livingstone, New York 1975.
7. **Donahue, SW; Sharkey, NA:** Strains in the metatarsals during the stance phase of gait: Implication for stress fractures. *J. Bone Joint Surg.*, **81A**:1236-1244, 1999.
8. **Ekenman, I; Halvorsen, K; Westblad, P; Fellander-Tsai, L; Rolf, C:** The reliability and validity of an instrumented staple system for in vivo measurement of local bone deformation – an in vitro study. *Scand. J. Med. Sci. Sport*, **8**:172-176, 1998.
9. **Ekenman, I; Halvorsen, K; Westblad, P; Fellander-Tsai, L; Rolf, C:** Local bone deformation at two predominate sites for stress fracture of the tibia: An in vivo study, *Foot Ankle Int.*, **19**:479-484, 1998.
10. **Gross, TS; Bunch, RP:** A mechanical model of metatarsal stress fracture during distance running. *Am. J. Sport Med.*, **17**:669-674, 1989.
11. **Lanyon, LE; Hampson, GJ; Goodship, AE; Shan, JS:** Bone deformation recorded in vivo from strain gages attached to the human tibial shaft. *Acta Orthop. Scand.*, **46**:256-268, 1975.
12. **Milgrom, C; Finestone, A; Levi, Y; Simkin, A; Ekenman, L; Mendelson, S; Millgram, M; Nyska, M; Benjuya, N; Burr, D:** Do high impact exercises produce higher tibial strains than running? *Brit. J. Sports Med.*, **34**:95-199, 2000.
13. **Milgrom, C; Eldad, A; Nyska, M; Finestone, A:** Using bone's adaptation ability to lower the incidence of stress fractures. *Am. J. Sports Med.*, **28**:245-251, 2000.
14. **Milgrom, C; Finestone, A; Simkin, A; Ekenman, I; Mendelson, S; Millgram, M; Nyska, M; Larrson, E; Burr, D:** In vivo strain measurements to evaluate the tibial bone strengthening potential of exercises. *J. Bone Joint Surg.*, **82B**:591-594, 2000.
15. **Milgrom, C:** The role of strain and strain rates in stress fractures. In Burr D.B and Milgrom C. (ed.), *Musculoskeletal Fatigue and Stress Fractures*, Boca Raton, CRC Press, 2001, 124.
16. **Schaffler, MB; Radin, EL; Burr, DB:** Mechanical and morphological effects of strain rate on fatigue of compact bone. *Bone*, **10**:207-214, 1989.
17. **Sharkey, NA; Hamel AJ:** A dynamic cadaver model of the stance phase of gait: performance, characteristics and kinetic validation. *Clin Biomech*, **28**:420-433, 1998.