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Skeletal loading: implications for injury and treatment

Stacey A. Meardon
Iowa State University

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Skeletal loading: implications for injury and treatment

Stacey A. Meardon

A dissertation submitted to the graduate faculty
in partial fulfillment of the requirements for the degree of
DOCTOR OF PHILOSOPHY

Major: Kinesiology (Biological Basis of Physical Activity)

Program of Study Committee:
Timothy Derrick, Major Professor
    Jason Gillette
    Ann Smiley-Oyen
    Gregory Welk
    Annette O’Connor

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2009
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ABSTRACT

Physical activity is important for the overall health of individuals. Impacts that occur when the foot hits the ground have the potential to be an influential factor in both the etiology of overuse injury and the promotion of bone health. Stress injury to bone is considered the ultimate overuse injury and accounts for the nearly one fourth of injuries in active populations. This dissertation evaluates bone loading in three ways: in vivo strain gage measurement, a combination of experimental and modeling techniques, and tibial accelerometry. Emphasis was placed on the clinical implication of findings from such techniques on the treatment and prevention of bone stress injury. The first study assessed the influence of orthotics on bone strain. The results of this study indicated that bone strain and strain rates were minimized with the use of orthotics. Secondly, the use of custom orthotics was more effective in minimization of strains and strain rates than semi-custom orthotics. The second and third studies used a combination of experimental data and musculoskeletal modeling to estimate combined loading, internal bone forces, moments and stresses. The findings from these studies were 1) the tibia is predominately undergoes in-phase loading of axial and torsional loads 2) gait mechanics can independently influence bone stresses and stress rates in the distal tibia 3) runners with a history of stress fracture demonstrate only moderately elevated internal bone forces and moments in the distal tibia. The final study of this dissertation evaluated injury more globally and assessed variability of stride time output. The patterned behavior of stride time variability was sensitive to fatigue and group differences. The results of these studies add to an ever growing body of knowledge of gait and injury and suggest that the internal loads of bone can be influenced by external support.
and gait mechanics. However, the multifactoral nature of injury cannot be ignored in the study of stress fracture. Additionally, fatigue and injury status play a role in the neuromuscular control system output during running and influence overall gait dynamics.
CHAPTER 1. GENERAL INTRODUCTION

As the merits of exercise for health and wellness have gained public acceptance, running has become an exercise of choice for many. In fact, 35.9 million Americans participated in running as a form of exercise in 2008, an 18% increase from 2007 (National Sporting Goods Association, 2008). Running is convenient and economical. Unfortunately, the risk for overuse injury is well documented in the literature with incidence rates for injury ranging from 19.4% to 79.3% (van Gent et al., 2007). In general, the lower extremity is most commonly injured in runners with stress injuries to bone accounting for approximately 6% to 52% of injuries in athletes (Bennell et al., 1996; Clement, 1974; Hame et al., 2004; James et al., 1978; Lloyd et al., 1986; Taunton et al., 2002). During running, the impacts that occur when the foot hits the ground have the potential to be an influential factor in both the etiology of overuse injury and the promotion of bone strength. Knowledge of optimal patterns of biomechanical loading and physical activity patterns will allow exercise routines to be developed that maximize osteogenic potential and minimize cumulative bone and joint stress.

Injury to bone in active populations creates a challenge to the medical community. First, diagnosis needs to be made, then appropriate treatment needs to be provided and finally changes need to be made to prevent recurrence. In order for changes to be made, we need to understand and address the underlying causes. While sometimes the cause may be obvious, such as a marked increase in training or poor nutrition affecting bone quality, many times it is multifactoral. Factors can be categorized as extrinsic (training, surface, footwear) or
Figure 1. Factors associated with stress fracture

intrinsic (skeletal alignment, muscle imbalance, gait mechanics) (Brukner et al., 1999). Most likely, it is more than one factor that results in injury (Figure 1).

Introduction to the Problem

Stress fractures of the lower extremity plague military recruits and athletes (Barrow & Saha, 1988; Bennell et al., 1996; Brunet et al., 1990; Johnson et al., 1994; Milgrom et al., 1994a; Nattiv, 2000; Nattiv et al., 1997; Shaffer et al., 2006; Taunton et al., 2002). They are serious injuries that result in significant health care costs, lost training time, and interference with job performance and competition. In fact, stress fractures are estimated to cost the U.S. Department of Defense in excess of 10 million dollars a year in medical costs and lost training time (Military Operational Medicine Research Program Fact Sheet, 1999).

Considered an overuse injury, stress fractures occur when repetitive microtrauma to bone outpaces bone repair. The two most common sites for lower extremity stress fracture in
both military and running populations are the tibia and metatarsals (Barrow & Saha, 1988; Beck et al., 1996; Benazzo et al., 1992; Bennell et al., 1996; Nattiv, 2000; Shaffer et al., 2006; Sullivan et al., 1984; Taunton et al., 1981). Studies of stress fracture due to physical activity in recruits and training in athletes became more plentiful in the 1980’s, when reported stress fracture incidence in running populations ranged from 3.4% to 37% (Barrow & Saha, 1988; Collins et al., 1989; Kowal, 1980) and from 2.2% to 21% in military groups (Brudvig et al., 1983; Cowan et al., 1996; Jones et al., 1989; Montgomery et al., 1989).

Subsequent epidemiological research focused on the roles of training parameters, anthropometrics, skeletal alignment, and fitness parameters in the development of stress fracture (Fredericson & Misra, 2007; Lun et al., 2004; Macera et al., 1989; Taunton et al., 2003; Walter et al., 1989; Wen et al., 1989). Meanwhile, biomechanical research has implicated ground reaction forces, moments, and gait mechanics in the cause of stress fracture (Bennell, 1999; Milner et al., 2006a; Milner et al., 2007; Pohl et al., 2007). Despite increased knowledge of risk factors, 30% of runners still report a history of stress fracture (Kelsey et al., 2007) and 12% of military recruits still sustain stress fracture in basic training (Finestone et al., 2008). Thus, despite efforts in the past three decades to identify risk factors associated with stress injury to bone and to institute appropriate interventions, stress fracture incidence remains a significant healthcare challenge, especially in civilian populations.

Dissertation Organization

This dissertation will first introduce the problem, stress injury to bone and then review the epidemiological and biomechanical literature associated with this injury. The following chapters will present four manuscript style studies (related to the main topics listed
in italics below) and close with a global summary of the work presented with suggestion for future research. The four studies are summarized below. Integral to all studies in this dissertation are factors associated with skeletal loading.

*Effects of orthotics on bone strain.* Whereas exact causes of stress fractures are multifactorial, repetitive bone strain of high magnitude and rate results in micro-fracture and can ultimately lead to stress fracture (Burr *et al.*, 1990; Li *et al.*, 1985). Thus, minimizing bone strain and strain rate would seem like a logical goal in preventing stress fracture. In order to design appropriate interventions, an accurate estimate of bone strain is necessary. Bone strain can be measured directly using strain gages applied to bone. This technology provides actual measures of bone strain, the characteristic that, when too great or when applied repetitively, leads to fatigue, microdamage, and ultimately fracture (Burr *et al.*, 1985; Burr *et al.*, 1990; Li *et al.*, 1985).

The second metatarsal, a common area for stress fractures, undergoes a large amount of bone strain in the stance phase of gait due to the large bending moment that occurs during late stance. The strains caused by bending moments are minimized by the plantar fascia and the muscles crossing the plantar surface of the metatarsals (Donahue & Sharkey, 1999; Sharkey *et al.*, 1995; Stokes *et al.*, 1979). Thus, providing external support to the plantar surface of the metatarsals with footwear or orthotics may minimize 2nd met bone strain. The purpose of the first study of this dissertation was to measure the effect of custom and semi-custom orthotics on second metatarsal bone strain using cadaveric gait simulation. It was hypothesized that custom and semi-custom foot orthotics would equally decrease bone strain of the second metatarsal (2nd met). Cadaver specimens, mounted to a dynamic gait simulator, walked over a force platform while force and bone strain data were collected. Peak bone
strains, strain rates and tendon forces during the stance phase for each condition were analyzed using repeated measures analysis of variance and effect sizes. The methodology used in this study measured directly the consequence, bone strain, of loading and provided support for the use of orthotics in 2nd met fractures.

*Crossover running pattern.* Direct measurement of bone strain is time intensive and in most countries is limited to cadaveric tissue. Alternatively, ground reaction forces and moments have been used as surrogate measures for skeletal loading in biomechanics of human running. However, these loads make up a limited portion of the total loading environment. Rather, a model of human running individualized to anthropometrics can be used to estimate bone strain based gait mechanics. Using such a model, the effects of running patterns on tibial bone stress and strain can be estimated.

Gait mechanics have long been implicated in the development of stress fracture in runners. While many studies have assessed the effect of stride length manipulations on lower extremity kinematics and kinetics, relatively few published studies have examined the effect of stride width on gait mechanics. A crossover running pattern is characterized by the foot landing medial to the line of progression during the gait cycle and has previously been associated with gait mechanics commonly reported in persons with a history of tibial stress fracture (Milner *et al.*, 2005; Pohl *et al.*, 2008; Williams & Ziff, 1991). Furthermore, increased forces in the frontal plane are associated with manipulations of step width away from neutral (McClay, 1995) and the free moment, an estimate of torsion, is positively correlated with the degree of crossover in running (Meardon & Derrick, 2008). These factors acting in concert may act to increase the stresses applied to the tibia throughout the stance phase of running; however, this association has not been established.
The purpose of the second study of this dissertation was to evaluate the effect that step width (e.g. the mediolateral distance between the heels during the stance phase of gait) during running has on tibial bone stress. It was hypothesized that tibial stresses would be greater in the narrow step width condition when compared to normal and wide step widths. Synchronized force platform and kinematic data were collected and a combination of experimental and musculoskeletal modeling techniques were used to determine joint contact forces acting on the distal tibia. Centroid moments and forces were calculated at the distal tibia (75% of the distance from the proximal tibia). Peripheral stresses were estimated at 4 locations of the tibia (anterior, lateral, medial, and posterior) and the tibia was modeled as hollow cylinder. Using this standardized model of the tibia, the study design allowed for the assessment of the influence of gait mechanics independent of bone geometry. Clinical insight was gained by evaluation of factors contributing to the stress environment of the tibia, the most commonly injured bone of the lower extremity.

_Gait mechanics and combined loading in injury._ The possibility exists that previous studies have not captured the key biomechanical factors leading to stress injury to bone. Previous research has focused on biomechanical factors of skeletal alignment, ground reaction forces, impact accelerations and free moments as contributory factors for stress fractures in runners (Creaby & Dixon, 2008; Milner _et al._, 2006a; Milner _et al._, 2006b; Milner _et al._, 2007; Pohl _et al._, 2007; Pohl _et al._, 2008). In both prospective and retrospective studies of tibial stress fracture, odds of stress fracture were associated with greater vertical and torsional external loads (Milner _et al._, 2006a; Milner _et al._, 2006b; Pohl _et al._, 2007; Pohl _et al._, 2008). George and Vashishth (2005) found in-phase axial and torsional loads result in greater principal strains, smaller distribution of forces, and a 7-fold decrease in fatigue.
This research suggests that variation in the timing of the application of axial and torsional loads alters fatigue life of bone. Simultaneous axial and torsional loads result in a larger effective load and a concentration of that load. Most likely, it is the cumulative effect of axial and torsional loads that leads to increases stresses applied to the tibia. The association of in-phase loading with stress fracture has not been documented.

Additionally, the previous study of this dissertation suggests that gait mechanics independent of bone influences the stress environment of the tibia. Given the multitude of studies reporting faulty gait kinematics and increased ground reaction force data, runners with stress fracture likely demonstrate increased tibial bone forces and moments, key components of bone stresses. However, internal bone forces and moments have not been studied in runners.

The purpose of this study was to evaluate timing differences of combined loading in persons with and without a history of tibial stress fracture and to assess differences in internal bone forces and moments. It was hypothesized that persons with a history of stress fracture would demonstrate more in-phase patterns of axial and torsional loads and greater internal bone forces and moments in the distal tibia. A model of human running based gait mechanics and individualized to anthropometrics was used to calculate tibial bone forces. Phase lag using cross correlation of axial forces and torsional moments was calculated to characterize the degree of in phase loading. Key forces and moments associated with injury were identified and the multi-factorial nature of stress fracture was highlighted.

Stride time variability. As mentioned in the summary of the combined loading study, a smaller distribution of forces is associated with decreased fatigue life of cortical bone (George & Vashisht, 2005). If one loads their skeletal system the same exact way with
each impact with the ground, distribution of forces throughout bone is diminished and potential for injury may increase. In fact, previous studies of runners indicate that decreased kinematic variability is present in runners with a history of injury (Hamill et al., 1999; Heiderscheit et al., 2002; Miller et al., 2008).

However, a certain degree of consistency in the pattern of stride times, as demonstrated by the persistence of long term correlations, is a hallmark of healthy gait and may in fact be an attractor or stable state that humans seek during locomotion. Biologic stressors, such as speeds away from preferred, have been shown to strengthen the patterns found within stride time variations (i.e. increase the long range correlations). Speeds away from normal are postulated to act as constraints limiting dynamical degrees of freedom and decreasing adaptability (Jordan et al., 2006). But, fatigue studies of reaching tasks and balance have actually shown cycle to cycle fluctuations become more random (i.e. decreased long term correlations) when compared to non-fatigued states resulting in an error correcting strategy. This loss of patterned movement with fatigue seems logical because as we fatigue, errors increase and in order to successfully complete or maintain the task at hand, corrective action needs to be made. The corrections would then serve to actually increase the cycle to cycle variability and decrease stride time correlations.

If one demonstrates persistence of long range correlations at preferred speeds above what is considered normal for healthy gait, flexibility to adapt to the environment may be limited. In the ever changing world around and within us, the ability to adapt is crucial. Individuals who fail to make the correct adaptations, whether to fatigued muscles, surface changes, or changes in footwear, may have increased risk for injury.
The purpose of the final study of this dissertation was to evaluate the effect of a prolonged run on stride time variability in persons with and without a history of injury. Over an exhaustive run, it was hypothesized that variability will decrease and the structure of that variability, as measured with long term correlations, will become less patterned. Secondly, persons with a history of lower extremity injury are hypothesized to have less variability and will be more patterned at the onset of running. Analysis of stride times, captured with accelerometry, over a run on an indoor track to volitional fatigue resulted in enough data to quantify the mean, standard deviation, coefficient of variation, and long range correlation of stride times. Stride time parameters were processed separately for three phases of the run to examine the effect of an exhaustive run; data from the first lap were omitted from analysis. The results of this study suggest that long range correlations were sensitive to group differences and offer insight into the role of injury and fatigue on the output of a multi-dimensional system.

Significance of Research

The completion of this dissertation provides a global perspective on skeletal loading and implications for both the etiology of and the potential intervention for stress injury to bone. Studies presented progress from confined measurement of bone strain, to estimations of bone stresses as influenced by gait mechanics, to the implication these bone stresses have in persons with and without a history of injury, and then finally to the overall coordination of the system. The work presented offers a deeper understanding of the following: 1) how can bone loads be modified by gait mechanics, fatigue and orthotics; 2) how persons with a history of injury differ in their mechanical loading from those without;
and 3) how system organization may ultimately influence bone loading. All of these questions are critical to the advancement of treatment and prevention of injury as well as optimization of bone health. Figure 2 illustrates the overall relationship between the factors related to injury assessed in this dissertation.

![Diagram](image-url)

Figure 2. Hypothesized concept map for dissertation entitled *Skeletal loading: implication for injury and treatment*

References


CHAPTER 2. REVIEW OF LITERATURE

Introduction

Physical activity is essential for health and preservation of the human body and has been reported by the U.S. Department of Health and human services to benefit a number of conditions, including coronary heart disease, colon cancer, diabetes mellitus, osteoporosis, anxiety and depression. In a joint statement in 2007 the American Heart Association and the American College of Sports Medicine recommended that all adults between 18 and 65 years of age, at a minimum, accumulate 30 minutes or more of moderate intensity physical activity 5 days of the week or vigorous activity for 20 minutes 3 days per week (Haskell et al., 2007). In this position statement, a clear dose-relationship between physical activity and health is emphasized.

Unfortunately, one of the few side effects of increased physical activity is musculoskeletal injury. In physically active populations, a clear dose-response between increased physical activity and injury also exists. Increased running volumes have been independently associated with injury (Macera et al., 1989; Marti et al., 1988; Rochcongar et al., 1995). In the Aerobics Center Longitudinal Study, researchers found increased risk of sustaining an activity-related injury with greater impact activity, higher duration of physical activity per week and cardiorespiratory fitness levels (Hootman et al., 2002). In this study, 1856 men (71% of active participants) and 294 women (52% of active participants) reported running for fitness. For men and women respectively, odds of sustaining an injury were 2.38 and 1.68 times that of a sedentary person but were overall not significantly greater than persons who walked for fitness. However, persons who ran 1.25-3.75 hours per week had a
47% increased risk for injury and those who ran more than 3.75 hours per week had a 138% increased risk for injury compared to those who walked for fitness. Thus, a clear dose response between running injury and increased time spent running is present in this study, especially when running on average greater than 45 minutes a day, 5 days a week. Furthermore, men and women with the highest level of fitness experience increased risks of injury, 164% and 52% respectively.

Running injuries in recreational runners are reported to have annual incidence levels of 24-86% (Lun et al., 2004). Stress fractures are among the five most common running injuries, and account for 6-20% of all injuries sustained by runners (Bennell et al., 1996; James et al., 1978; Snyder et al., 2006). The burden of stress fracture in an otherwise healthy active population is being addressed across fields in health care. A recent report from a radiology clinic states that stress fractures encompass 10% of cases in sports medicine clinics (Berger et al., 2007). Other sources report 0.5%- 7.8% of recreational or competitive athletes who visit sports medicine clinics present with stress fractures (Snyder et al., 2006). Stress fractures are perhaps the most serious overuse injury in runners resulting in up to 12 weeks of rest from impact activity, and thus interrupted work and training. Reoccurrence of stress fracture is high (Kelsey et al., 2007) and long term sequelae and complications can arise such as delayed union and non union. Long term implications of running related stress fracture on bone health are unknown. Given that the first three decades are the prime years in which to enhance bone quality, and most stress fractures are reported during this time, a more complete understanding of the multifactoral nature of stress injury to bone would result in the identification of prevention and treatment strategies for the optimization of bone health.
Response to actual bone loading results in a clinical continuum from bone remodeling, accelerated remodeling, stress reaction, stress injury, to ultimately stress fracture. A number of factors influence bone’s response to external loads. Three main areas contribute to lower extremity bone loading: training factors, gait mechanics, and bone properties (mass and geometry). While research has been done extensively in all areas, it is generally accepted that the interaction of these factors ultimately result in stress fracture. Thus, the runner with greater impact forces may be more likely sustain stress fracture when combined with skeletal mal-alignment, detrimental lower extremity kinematics, excessive training, and/or diminished bone quality.

Risk factors for bone stress injuries have been classified into seven categories (Brukner et al., 1999):

- Intrinsic mechanical
- Physiologic factors
- Nutritional factors
- Hormonal factors
- Physical training
- Extrinsic mechanical factors
- Genetics and psychological traits

The above listed factors can interact in such a way to decrease bone strength, elevate bone strain, cause unaccustomed bone strain, or result in inadequate repair of microdamage that leads to a continuum of stress injury (Figure 1). Underlying bone health can be positively or negatively influenced by nutrition, genetics, hormones and bone loading history affecting bone’s ability to tolerate loading. Gait mechanics consist of both intrinsic and extrinsic factors. For example, the magnitude and rate of load applied to bone can be mediated by such factors as footwear, lower extremity alignment, impact attenuation, and fatigue resulting in increased bone strain. Faulty training patterns (volume, intensity, duration, and rest periods)
can lead to unaccustomed bone strain or too little time for recovery allowing for the accumulation of microdamage. Again, it is likely that these factors (gait mechanics, training patterns and bone properties) act in concert to result in stress fracture.

Chapter 2 of this dissertation will provide an overview of the pathophysiology, epidemiology and risk factors associated with stress injury to bone in runners. Additionally, it will introduce gaps in the existing research that need to be studied to further our knowledge of stress injury to bone. This will serve to ultimately increase researchers’ and clinicians’ understanding of factors related to stress injury to bone and provide a basis for future intervention.

**Pathophysiology**

Repetitive impacts are vital for the building and maintenance of bone strength. By adapting to applied loads, bone mass increases in response to physical activity (Morris et al.,...
Additionally, small increases in bone mass result in large increases in bone strength. This is due in part to the fact that new bone formation occurs at the sites of the greatest mechanical loading (Robling et al., 2002). In fact, the importance of physical activity in bone health is recognized by leading organizations such as the American College of Sports Medicine. Current recommendations are for youth to engage in relatively high intensity loading forces, such as jumping and running, at least three times a week and for adults to engage in moderate to high intensity loads three to five times per week (Kohrt et al., 2004).

However, bone can lose strength as a result of repetitive loads due to microscopic crack formation and propagation. In support of this, Schaffler and colleagues (Schaffler et al., 1989, 1990) reported decreased bone stiffness with low magnitude loading at low and high strain rates in bovine bone in vitro. Additionally, response to actual bone loading results in a clinical continuum from bone remodeling, accelerated remodeling, stress reaction, stress injury, to ultimately stress fracture. Using an animal model, both Li et al. (1985) and Burr et al. (1990) describe the presence of microdamage, as evidenced by microcracks, and the progression to stress fracture due to repetitive non-traumatic loads. Thus there appears to be a positive range of loading for bone health and a negative range of loading for injury.

Threshold level of strain needed for accumulation of microdamage is suggested to be 2000 µε (Frost, 1989). If strain is continually applied, microcracks result and can progress to fracture if repair does not occur. Stress fractures can result from high magnitude repetitive loads decreasing structural integrity on bone independent of the remodeling process and prior to attempts of repairs by remodeling. It is this process that is suspected to occur in the causation of second metatarsal stress fracture (Milgrom et al., 2002). However, stress fractures are more commonly thought to occur microdamage if too extensive to be repaired
by normal bone remodeling processes. Modeling is the uncoupled action of osteoblasts (bone building cells) and osteoclasts (cells that break down bone) that occurs primarily before skeletal maturity and functions to change bone size and shape. Bone remodeling is a process that repairs fatigue damage and adjusts bones’ microstructure to the loading environments. It is this coupled action of osteoclasts and osteoblasts that removes portions of older bone and replaces it with newer bone and serves to repair microdamage that could lead to stress fracture. As a result of mechanical stimuli associated with fluid flow within the canilicular network of bone (impacts), osteoclasts form and migrate to the area of stress to remove older or damaged bone. After a time delay, bone formation follows. However, the formation phase is much slower than the resorption phase requiring three months compared to three weeks to come to an end. Thus, a period of time exists between bone resorption and bone formation at which point the bone is weakened due to osteoclastic activity. If repetitive impacts continue to occur at the site of remodeling during this lag, accelerated remodeling occurs with bone resorption outpacing bone formation. It is this process that leads to the accumulation of microdamage and ultimately stress injury to bone.

Stress fracture is the break in the cortical bone typically characterized by localized pain on palpation. Typically, the onset is gradual and associated with progressively increasing pain with activity. Localized swelling and redness may be present and pain may be reproduced with vibration or percussion. Diagnosis is made by a combination of history and testing. Medical testing includes radiographs, computerized axial tomography (CT), scintigraphy (triple phase bone scans), and/or magnetic resonance imaging (MRI). Of these tests, MRI provides better anatomic detail and is sensitive to marrow edema and periosteal reactions (precursors to stress fracture) (Berger et al., 2007). Scintigraphy (bone scan), on the
other hand is not as specific, providing poor anatomic detail, but is very sensitive. Using a grading system that incorporates radiograph findings and MRI or bone scan, stress injuries to bone are classified into four categories (Arendt, 2003; Zwas, 1987). Grade 1 is characterized by negative radiographs and mild to moderate periosteal edema (MRI) and/or small, ill-defined cortical areas of mild increased tracer uptake (bone-scan). Grade 2 stress injuries present with moderate to severe periosteal edema, marrow edema and/or better-defined cortical areas of moderately increased tracer activity. Grade 3 stress injuries also have moderate to severe periosteal edema and marrow edema but have high uptake of tracer in the cortical medullary area of bone present on bone scan. And finally, grade 4 stress injuries present with periosteal edema, marrow edema and a clear fracture line on MRI. On bone-scan, transcortical area of increased tracer uptake is present.

The above grading system suggests a continuum of bone stress in symptomatic individuals that is commonly accepted radiologically and clinically (Berger et al., 2007; Brukner et al., 1999). While several theories on the origin of shin pain in runners exist, recent evidence suggests that medial tibial stress syndrome (MTSS) is a stress reaction of bone to repetitive loading (Gaeta et al., 2005). Medial tibia stress syndrome is an exercise-induced pain along the distal posterior two thirds of the posterior-medial tibia characterized by constant or intermittent pain exacerbated by weight-bearing activities. Gaeta et al. (2005) found that both CT and MRI show evidence of early stress injury to bone in athletes with complaints of tibial bone pain. Furthermore, animal studies of bone microdamage following repetitive loading provide evidence of accelerated remodeling and periosteal reactions prior to incomplete and complete fractures of cortical bone (Li et al., 1985). However, not all evidence of tibial abnormalities found via MRI and CT in humans is associated with pain and
future injury (Bergman et al., 2004; Gaeta et al., 2006). Authors agree that the aforementioned early tibial abnormalities provide evidence of site specific accelerated remodeling. In fact, in a study of 20 asymptomatic and 11 symptomatic distance runners, 100% of symptomatic runners and 16.6% of asymptomatic runners demonstrated cortical osteopenia with high-resolution CT (Gaeta et al., 2006). Thus, while accelerated remodeling leads to a weakening of the bone, it is not a perfect predictor of pain and diagnosis of tibial stress should be based on a combination of history and imaging.

Incidence & Prevalence

Injury occurrence. Epidemiologic studies of stress fracture that report incidence rates are generally retrospective or prospective cohorts or case series designs. Interpretation of studies is influenced by sampling, confounding variables, expression of injury rates and definition of stress fracture. Sampling populations in the area of stress fracture can for the most part be divided into military and civilian populations. In the military population, sample sizes tend to be greater and training levels, footwear, and fitness levels vary from athletic populations. Furthermore, because of the nature of military training, these confounding variables can be more easily measured within a study. Studies of athletes tend to have smaller sample sizes and often are in the form of case control or case series. Because of the variability inherent to this population, less control of confounding variables exists. Furthermore, selection bias may exist when a non-random sample is used; participants willing to participate in studies of stress fracture may have characteristics that differ significantly from those who choose not to enroll. Differences in observation periods may make comparisons among studies difficult as the amount of time spent running can influence
the potential for injury. Consequently, careful consideration needs to be made when interpreting results of military populations and applying them to active populations and vice versa.

Injury occurrence can be expressed many ways. Incidence of stress fracture refers to the number of new cases of stress fracture that occur during a specific time period in the population at risk. Cumulative incidence, a measure of incidence, is calculated by using a time period over which all participants are considered to be at risk. Participant and case cumulative incidence is most commonly reported in the stress fracture literature. Participant incidence refers to the number of participants who sustained a stress fracture out of the number of participants observed; whereas case rates refers to the number of stress fractures observed out of the number of participants observed. A third and probably more accurate way of expressing injury is reporting injury based on exposure.

For the purpose of this dissertation, exposure is defined at running activity and the outcome is the occurrence of stress fracture or stress reaction of bone. Defining and collecting meaningful exposure data for running related stress fracture in runners is difficult (Finch, 2006). However, controlling for the amount as exposure is important. Longer exposure times could very well result in greater incidence of stress fracture. For example, a runner who trains for 3 months does not have the same risk as a runner who trains for 12 months as the training volume differs. Expressing injury in terms of exposure allows for meaningful comparison of injury across studies as well as within studies. Properly reporting exposure results in an incidence rate in which the denominator is the sum of the times that each person in the study was at risk and is often reported in person-years. However, in
running, it may be more appropriate to report in athletic exposures or time spent running versus years as training activity may vary with the season (Rauh et al., 2006).

Finally, definition of stress fracture varies. As discussed further in the next section of this chapter, a clinical continuum of responses to bone loading exists from accelerated remodeling to stress reaction to stress fracture. Some researchers have chosen to only include persons with a stress fracture in their study, where others have included persons with stress fractures and persons with stress reactions in their studies. Additionally, recent work suggests that tibial stress syndrome is a precursor to tibial stress fracture (Gaeta et al., 2005) and may need to be considered in future epidemiological studies. Furthermore, studies differ on diagnostic tools. Specificity and sensitivity of radiographs, bone scan and magnetic resonance imaging (MRI) vary and thus may affect reported incidence or prevalence.

Modified from Brukner et al. (1999), tables 1 and 2 report stress fracture incidences for military and running populations. As evidenced by the tables, stress fracture incidence rates in both populations do not appear to be changing over the last few decades. Incidence rates in military populations range from as low as 0% to 15.1% in recent years. In running populations, participant incidence rates reported in 2008 are as high as 14%-31%. Perhaps even more disconcerting is that work by Rauh and colleagues indicate that in a study of high school cross country runners, 42% experienced lower leg injury and the shin was the most injured body part (Rauh et al., 2006). Unfortunately type of injury was not delineated in the study.

*Site.* Distribution of stress fractures in the military population and running populations are similar. Stress fractures are most common in the lower extremity. In a recent military study, the tibia (25%), metatarsals (22%), pelvis (22%), and femur (20%) are most
Table 1. Selected military studies in which stress fracture incidence has been reported, expressed as case incidence unless otherwise reported. The dotted line indicates a gap in the years reported.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Design</th>
<th>Subjects</th>
<th>Observation Period (weeks)</th>
<th>Diagnosis of stress fracture</th>
<th>Stress-fracture incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protzman 1977</td>
<td>PC</td>
<td>102 - F</td>
<td>8</td>
<td>X-ray</td>
<td>9.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1228 - M</td>
<td></td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>Kowal et al. 1980</td>
<td>PC</td>
<td>327 - F</td>
<td>8</td>
<td>X-ray</td>
<td>21.0</td>
</tr>
<tr>
<td>Brudvig et al. 1983</td>
<td>PC</td>
<td>4422 - F</td>
<td>8</td>
<td>X-ray or bone scan</td>
<td>4.0</td>
</tr>
<tr>
<td>Milgrom et al. 1985</td>
<td>PC</td>
<td>295 - M</td>
<td>8</td>
<td>Bone scan</td>
<td>62.0</td>
</tr>
<tr>
<td>Jones et al. 1989</td>
<td>PC</td>
<td>186 - F</td>
<td>14</td>
<td>not reported</td>
<td>13.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>124 - M</td>
<td></td>
<td></td>
<td>3.2</td>
</tr>
<tr>
<td>Jones et al. 1989</td>
<td>PC</td>
<td>323 - M</td>
<td>8</td>
<td>not reported</td>
<td>2.2</td>
</tr>
<tr>
<td>Montgomery et al. 1989</td>
<td>PC</td>
<td>505 - M</td>
<td>13</td>
<td>Clinical exam</td>
<td>6.3*</td>
</tr>
<tr>
<td>Pester and Smith 1992</td>
<td>PC</td>
<td>33,059 - F</td>
<td>8</td>
<td>X-ray or bone scan</td>
<td>1.1*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>76,237 - M</td>
<td></td>
<td></td>
<td>0.9*</td>
</tr>
<tr>
<td>Taimela et al. 1992</td>
<td>CT</td>
<td>823 - M</td>
<td>8</td>
<td>X-ray</td>
<td>2.7</td>
</tr>
<tr>
<td>Jones et al. 1993</td>
<td>PC</td>
<td>186 - F</td>
<td>12</td>
<td>not stated</td>
<td>12.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>124 - M</td>
<td></td>
<td></td>
<td>2.4</td>
</tr>
<tr>
<td>Jones et al. 1993</td>
<td>PC</td>
<td>303 - M</td>
<td>8</td>
<td>not stated</td>
<td>3.0</td>
</tr>
<tr>
<td>Jordaan and Schwellnus 1994</td>
<td>PC</td>
<td>1261 - M</td>
<td>12</td>
<td>X-ray</td>
<td>1.2</td>
</tr>
<tr>
<td>Milgrom et al. 1994</td>
<td>CT</td>
<td>783 - M</td>
<td>9</td>
<td>X-ray or bone scan</td>
<td>24.0*</td>
</tr>
<tr>
<td>Shwayhat et al. 1994</td>
<td>PC</td>
<td>224 - M</td>
<td>14</td>
<td>not reported</td>
<td>6.7</td>
</tr>
<tr>
<td>Beck et al. 1996</td>
<td>PC</td>
<td>626 - M</td>
<td>25</td>
<td>X-ray</td>
<td>4.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.7</td>
</tr>
<tr>
<td>Cowan et al. 1996</td>
<td>PC</td>
<td>294 - M</td>
<td>12</td>
<td>not stated</td>
<td>5.0*</td>
</tr>
<tr>
<td>Heir and Glomsaker 1996</td>
<td>PC</td>
<td>6488 - M</td>
<td>12</td>
<td>not stated</td>
<td>0.2</td>
</tr>
<tr>
<td>Bijur et al. 1997</td>
<td>PC</td>
<td>85 - F</td>
<td>6 to 10</td>
<td>not stated</td>
<td>15.0*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>473 - M</td>
<td></td>
<td></td>
<td>2.3*</td>
</tr>
<tr>
<td>Rudzki 1997</td>
<td>CT</td>
<td>180 - M</td>
<td>12</td>
<td>not stated</td>
<td>1.1*</td>
</tr>
<tr>
<td>Windfield et al 1997</td>
<td>PC</td>
<td>101 - F</td>
<td>10</td>
<td>X-ray or bone scan</td>
<td>11.5*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7.9*</td>
</tr>
<tr>
<td>Rauh et al. 2006</td>
<td>PC</td>
<td>824 - F</td>
<td>13</td>
<td>bone scan</td>
<td>8</td>
</tr>
<tr>
<td>Shaffer et al. 2006</td>
<td>PC</td>
<td>2962 - F</td>
<td>13</td>
<td>X-ray or bone scan</td>
<td>5.1</td>
</tr>
<tr>
<td>Lappe et al. 2008</td>
<td>PC</td>
<td>5201 - F</td>
<td>8</td>
<td>X-ray or bone scan</td>
<td>5.9*</td>
</tr>
<tr>
<td>Merkel et al. 2008</td>
<td>PC</td>
<td>227 - F</td>
<td>8</td>
<td>X-ray or bone scan</td>
<td>12.0 *</td>
</tr>
<tr>
<td></td>
<td></td>
<td>83 - M</td>
<td></td>
<td></td>
<td>0.0*</td>
</tr>
<tr>
<td>Finestone and Milgrom 2008</td>
<td>PC</td>
<td>308 - M</td>
<td>16</td>
<td>X-ray or bone scan</td>
<td>11.6</td>
</tr>
<tr>
<td>Finestone et al. 2008</td>
<td>PC</td>
<td>99 - F</td>
<td>16</td>
<td>X-ray or bone scan</td>
<td>12.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>36 - M</td>
<td></td>
<td></td>
<td>0.0</td>
</tr>
</tbody>
</table>

Notes: * indicates stress fracture incidence expressed as participant incidence. M = males, F = females, PC = prospective cohort, CT = clinical trial
commonly injured (Shaffer, 2006). In runners, on average across studies, the tibia is the most commonly injured (44%), followed by the navicular (15%), metatarsals (14%), fibula (14%), tarsals (7%), femur (5%), and pelvis (3%) (Kelsey et al., 2007). Interestingly, foot fractures

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study design</th>
<th>Population</th>
<th>Subjects</th>
<th>Data Collection Method</th>
<th>Observation period</th>
<th>Diagnosis of stress fracture</th>
<th>Stress fracture incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barrow and Saha 1988</td>
<td>XS</td>
<td>Collegiate distance runners</td>
<td>240 - F</td>
<td>Questionnaire</td>
<td>Hx</td>
<td>X-ray or bone scan</td>
<td>37</td>
</tr>
<tr>
<td>Collins et al. 1989</td>
<td>XS</td>
<td>Finishers in Seafair triathlon</td>
<td>59 - F, 198 - M</td>
<td>Questionnaire</td>
<td>1 year</td>
<td>not stated</td>
<td>3.4, 3.5</td>
</tr>
<tr>
<td>Brunet et al. 1990</td>
<td>XS</td>
<td>Recreational and competitive runners</td>
<td>375 - F, 1130 - M</td>
<td>Questionnaire</td>
<td>Hx</td>
<td>X-ray or bone scan</td>
<td>13.2, 8.3</td>
</tr>
<tr>
<td>Goldberg and Pecora 1994</td>
<td>CS</td>
<td>Collegiate athletes</td>
<td>486 - F, 217 - M</td>
<td>Review of medical records</td>
<td>3 years</td>
<td>X-ray or bone scan</td>
<td>3.7</td>
</tr>
<tr>
<td>Johnson et al. 1994</td>
<td>PC</td>
<td>Track athletes</td>
<td>45 - F, 62 - M</td>
<td>Monitoring</td>
<td>2 years</td>
<td>X-ray or bone scan</td>
<td>31.1, 9.7</td>
</tr>
<tr>
<td>Bennell et al. 1995</td>
<td>XS</td>
<td>Track and field athletes</td>
<td>53 - F, 65 - M</td>
<td>Questionnaire</td>
<td>Hx</td>
<td>X-ray, bone scan or CT</td>
<td>51.5</td>
</tr>
<tr>
<td>Bennell et al. 1996, 1998</td>
<td>PC</td>
<td>Track and field athletes</td>
<td>46 - F, 49 - M</td>
<td>Monitoring</td>
<td>1 year</td>
<td>Bone scan or CT</td>
<td>21.7, 20.4</td>
</tr>
<tr>
<td>Arendt 2003 CS</td>
<td>Cross country athletes</td>
<td>250 - F, 150 - M</td>
<td>Review of medical records</td>
<td>10 years</td>
<td>X-ray, bone scan or MRI</td>
<td>6.4, 3.9</td>
<td></td>
</tr>
<tr>
<td>Arendt 2003 CS</td>
<td>Track and field athletes</td>
<td>580 - F, 530 - M</td>
<td>Review of medical records</td>
<td>11 years</td>
<td>X-ray, bone scan or MRI</td>
<td>1.6, 0.8</td>
<td></td>
</tr>
<tr>
<td>Kelsey et al. 2007 CS</td>
<td>Cross country athletes</td>
<td>127 - F</td>
<td>Questionnaire</td>
<td>1.85 years</td>
<td>X-ray, bone scan or MRI</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

Notes: * indicates stress fracture incidence expressed as participant incidence. M = males, F = females, XS = cross sectional, CS = case series, PC = prospective cohort. Hx indicates self report of history of stress fracture.
were more frequent in more explosive runners (i.e. sprinters, jumpers, hurdlers) and longer distance runners tended to sustain tibial and femoral stress fractures (Bennell et al., 1996).

Risk Factors

Age. Incidence in military and civilian population varies with age and gender; however, this remains controversial. Typical mean age reported in stress fracture studies is 19 to 30 years. One recent study of 19-26 year old runners reported an increase in stress fracture with decreasing age (incidence rate ratio =1.42, confidence interval = 1.05, 1.92) (Kelsey et al., 2007). Another study that stratified results by age, found younger age groups (<20 years of age) comprised 50% of the persons sustaining stress fractures (Iwamoto & Takeda, 2003). One case series reports that stress fracture incidence in persons >50 years old was 4.2% compared to 11.2% in younger persons (<50 years old) (Matheson et al., 1989). However, assessment of an age effect in civilian populations is difficult due to varying levels of exposure. In military populations, where physical activity across age groups is more similar, stress fracture incidence was greatest for persons aged 29 to 34 (5%) and the least for those 17 to 22 years of age (1.3%). Stress fracture incidence over the age of 35 dropped to 3.4% (Brudvig et al., 1983). Similarly, stress fracture incidence has been found to be inversely proportional to age in military recruits (Milgrom et al., 1994b).

Overall, the association between age and stress fracture remains unclear. Younger bone may not have developed maximal bone strength yet and may be more at risk; but, older bone may have declining bone quality and be more at risk. This has not been explored or discussed at length in the literature. The association of age with stress fracture is most likely
subject specific as subjects may reach peak bone mass at different times and subjects may
have varying level of exposure that is age specific.

*Gender.* As for the existence of a gender bias for stress fracture, the effect seems to
differ in military and civilian populations. It is generally more accepted that female military
recruits are more prone to stress fracture than males. In fact, women had greater than 4x
higher incidence rate of stress fracture when compared to men in 7 out of 10 studies reported
in Table 1 and had greater incidence rates than men in all studies. However, Table 2
illustrates conflicting outcomes of the gender effect in civilian populations. Incidence rates
vary from being nearly the same (Arendt, 2003; Bennell *et al*., 1998; Bennell *et al*., 1996;
Collins *et al*., 1989) to being up to 3x greater in females (Arendt, 2003; Bennell *et al*., 1995;
Johnson *et al*., 1994). Iwamoto and Takeda (2003) in a study of 10,726 patients (6415 males,
3861 females) that sought medical care for sport-related injuries, report no significant
differences in stress fracture incidence between men and women. However, Hame *et
al*.(2004) does report a significantly more stress fractures in female athletes (p=0.001). These
seemingly contradictory findings can be attributed, in part, to study design, lack of power and
variability of physical activity patterns characteristic of civilian population. However, if in
the civilian population level of exposure is taken into consideration, results may be clearer. In
the study by Bennell and colleagues (1996) men sustained 0.54 stress fractures per 1000
training hours and women sustained 0.86 stress fractures per 1000 hours. Hence, when
training volume is taken into consideration, a clinically relevant finding may exist.

*Bone mass.* Underlying bone density, size and shape determines the response of bone
to loading. Mechanical strength and thus the ability to tolerate applied loads is influenced by
nutrition, endocrine status, bone mass and geometry, and loading history. Carter and Hayes
(1976) found that compressive strength of skeletal tissue was approximately equal to the square of the apparent density for a given strain rate. Consequently, a small reduction in density results in a large decrease in strength. In support, Alho et al. (1988) report highly significant positive correlations between femoral bone strength, measured using an axial load, and bone density in cadaveric human femur bones. Thus low bone density could contribute to bone. The role of bone mass, as measured by bone mineral density (BMD) in stress fracture is unclear. Until recently, little prospective evidence exists to support the role of decreased bone mass and stress fracture. Giladi et al. (1991) reports no significant difference between bone density in 91 male recruits and 198 controls in a prospective study of male military recruits; rather tibial bone width was a strong predictor of stress fracture. Crossley (1999) and Bennell (1996) found no differences in BMD in male track and field runners with a history of stress fracture when compared with runners without a history of stress fracture. In a prospective study of 58 female track and field athletes, women with a history of low bone density at the spine and foot were more likely to sustain stress fractures (Bennell et al. 1996). Interestingly, these researchers report that BMD in runners who sustained a stress fracture were significantly lower than their active counterparts but greater than inactive counterparts. This suggests that current BMD guidelines would not identify these runners as osteopenic and indicates that individuals undergoing large strains during exercise may require greater than normal bone mass to resist applied loads.

More recent evidence confirms that lower whole body BMD is associated with increased risk for stress fracture in young female cross country runners. In a study of 127 runners, girls had a 170% increase risk of stress fracture per standard deviation decrease in BMD (293.2g) (Kelsey et al., 2007). Furthermore, long distance runners (55.6±15.8
miles/week) with a history of one or more stress fractures (n = 50) had lower BMD of the lumbar spine, total hip and femoral neck than those who had never experienced a stress fracture (n = 59), independent of the number of years in training and weekly running distance (Hind et al., 2006). Recently presented data obtained from a large sample of high school athletes shows that 32% of female runners had low (Rauh, 2009) bone mass, and those with low bone mass were 6 times more likely to sustain injury and 4.6 time more likely to experience a shin injury. Thus while studies of military and track and field populations do not suggest BMD differences between persons with and without a stress fracture, research in long distance runners suggests otherwise. It is probable that the underlying mechanism of stress fracture differs in these populations. Long distance running on consecutive days may represent an upper limit to the benefit of loading for optimization of bone health. It is possible that with excessive loading either excessive remodeling is taking place or mechanosensitivity of the bone is dampened. Either case would result in the accumulation of microdamage.

A well established relationship of low bone density, eating disorders, and amenorrhea in female runners exists and is called the female athlete triad. This relationship, which can result in osteoporosis, will not be elaborated upon in this dissertation. However, it is important to note that a recent theory attempts to explain stress fracture risk in long distance runners relative to energy expenditure. Briefly, increased running distances result in greater energy expenditure; if a caloric deficit is present, bone may be negatively affected (Ihle & Loucks, 2004). However, this theory alone does take into account the effects of training patterns and applied load which likely interact with bone characteristics to result in stress fracture. Due to methodological barriers, studies examining the interaction of bone health,
gait mechanics and training patterns simultaneously are lacking. Because of the nature of biomechanical research, past work has been limited to laboratory settings and has tended to have relatively small sample sizes. Key biomechanical variables need to be identified and efficient field measures must be developed for large scale studies. Furthermore, the study of training patterns has predominantly been limited to self report. Given the recent advances in physical activity monitoring and the current lack of knowledge of the upper limit of beneficial bone loading patterns, more research on physical activity patterns and injury is necessary.

**Bone geometry.** While bone mass has not been clearly identified as a risk factor across all running populations, bone geometry offers promising insight to fracture resistance by resisting bending and torsional loads. Bone geometry includes measures such as cross sectional area (CSA) and area moment of inertia (Im). For compression, tensile and bending loads, the strength of bone is proportional to the CSA (Siu *et al.*, 2003). For bending loads, not only CSA but the distribution of bone about the neutral axis is important. The Im is the index that accounts for these two factors. A larger Im indicates that the bone tissue is distributed further from the neutral axis, the axis where stresses and strains are zero. Bones with larger Im are more effective in resisting bending strains. Therefore, a larger bone is more resistant to bending as it distributes forces over a larger area resulting in lower stresses. CSA and Im both have the potential to influence an individual’s risk for stress fracture. In fact, in a matched case control study of 46 male running athletes, tibial stress fracture runners had 8.4% smaller CSA than non stress fracture runners (Crossley *et al.*, 1999). Additionally, aerobically active persons with MTSS and stress fracture (n=34) have smaller tibial CSA and smaller Im dimensions than a control group of uninjured counterparts (n=34) (Franklyn *et al.*, 2003).
Similar findings exist in the military literature; a prospective study among military recruits showed that military recruits with low Im of the tibia at the mediolateral and anterioposterior axes sustained a greater incidence of stress fracture in not only the tibia, but also the femur and feet (Milgrom et al., 1989). In this study, the Im about the anterioposterior axes, a measure of resistance to bending of the tibia in the frontal plane, was the most significant risk factor associated with stress fracture as determined from logistic regression. In 1996, it was determined that CSA of the diaphyses and not the joints was associated with stress fracture (Beck et al., 1996). This finding is important as it is the diaphyses that are more influenced by applied loads. Both Milgrom et al. (1988) and Ghiladi et al. (1987a) have also found significant differences in tibial width between recruits with a history of stress fractures and those without. In both studies, recruits with narrower mediolateral tibia were more likely to sustain stress fracture. Recruits and athletes with smaller, weaker bones who are subjected to intense and unaccustomed physical activity may experience higher rates of microdamage with little time for recovery and remodeling.

Unfortunately, the ability to screen for bone size prior to training is clinically limited. Subsequently, there is a need to develop alternative clinical indicators of stress risk. However, the fact that size and shape of bone relate consistently to stress fracture risk is promising as in the future, training programs to optimize bone can be developed and implemented prior to the start of an aggressive training program in order to increase bone’s tolerance to loading.

*Training factors.* While impacts have been reported as crucial to positive bone adaptation, repetitive impacts nearing microdamage thresholds are related to the development of stress fracture. Tibial strains during running do not typically exceed this value. However,
repetitive strains with inadequate recovery time lead to accelerated remodeling and if loading continues, stress fracture may result. In this way training factors of magnitude, frequency and duration of loading and rest periods between bouts of impact may impact potential for stress fracture. In fact, large epidemiological studies have related training errors with stress fracture (Nativ, 2000; Taunton et al., 2002). However, the contribution of type, volume, intensity, frequency, and rate of change had not been elucidated. In running populations, work on training volume has been done in the area of stress fracture. Several studies have demonstrated the risk of injury as a function of increased mileage (Brunet et al., 1990; Koplan et al., 1982; Macera et al., 1989; Walter et al., 1989). In general, odds of stress fracture more than double in civilian populations when running more than 30 miles per week. In fact, a general increasing trend of injury risk with increased mileage suggests a dose-response relationship exists. Moreover, reducing weekly mileage from 55 miles to 33 miles in military populations decreased incidence of stress fracture (Friedl et al., 2008). This line of research suggests an upper limit to running activity at which point continued loading may not beneficial for building bone health. However, this upper limit may very well differ among individuals.

Physical activity patterns. Predominately, research has focused on comparison between physically active and sedentary populations prior to initiating a training program. In a study of 505 males entering an intensive military school, those who ran 25 miles per week or more in the year prior to admission sustained fewer (3%) tibial stress fractures than those running less than 4 miles per week (Montgomery et al., 1989). Gardner et al (1988) also found that military recruits self reported as very active, although not clearly defined, were less likely to sustain stress fracture compared to all other recruits (Odds ratio = 2.6). In
females, historical running patterns of less than 4.5 km per session are associated with injury (Winfield et al., 1997). Of importance to note is that persons with a history of ball sports are less likely to sustain stress fractures in military training (Milgrom et al., 2000). This is likely to lend credence to the importance of fitness and the types of activity that are essential to the building of strong bone. As a whole, these studies suggest that persons who are more active or fit prior to onset of a new training regimen are less at risk for injury. It is important to note that persons in the more active and fit groups of these studies were not immune to stress fracture. Rather their risk was less.

Skeletal alignment. Given the repetitive nature of running, even small increases in loading may be magnified over thousands of consecutive foot strikes. Gait mechanics have been associated with stress fracture and are closely related to impact attenuation. Included in the category of gait mechanics are skeletal alignment, foot type, and altered gait patterns or kinematics. Lower extremity alignment has the potential to predispose an individual to injury by creating areas of stress concentration in bone or by promoting muscular fatigue. Knee, tibia, subtalar, and forefoot static alignments are often associated with overuse injury (Matheson et al., 1987) and have the potential to increase the bending moments associated with vertical loading. A Q-angle greater than 15 degrees has been associated with greater odds of stress fracture development in high school cross country runners and military recruits (Cowan et al., 1996; Rauh et al., 2006; Shaffer, 2006) and is perhaps the most strongly associated static measure of skeletal alignment. Additionally, several researchers have found a correlation between leg length and stress fracture odds (Bennell et al., 1996; Brunet et al., 1990).
While studies are contradictory, arch height has been associated with stress fracture risk. Low arch height has been found to be protective of overall stress fracture in a prospective study of military recruits (Giladi et al., 1985). However in another prospective study of 295 recruits, low arch height was associated with metatarsal stress fractures and high arch height was associated with femoral and tibial stress fracture (Simkin et al., 1989).

Additionally, Army personnel with varus alignment of the forefoot were 8.3 times at risk of metatarsal stress fracture (Hughes, 1985). Studies of the relationship between foot type and stress fracture in civilian populations are also contradictory. In a prospective study of track and field athletes, no relationship between foot type and stress fracture risk was found (Bennell et al., 1996). But, in a study of 320 athletes, a pronated foot type was associated with tibial and tarsal stress fractures and a high arched foot type was associated with metatarsal and femoral stress fractures (Matheson et al., 1987).

**Kinematics.** While static measures may predispose an individual to stress injury, some researchers argue that dynamic alignment contributes more to injury. Magnitude of rearfoot eversion has been associated with overuse injury (Messier & Pittala, 1988; Myburgh et al., 1988; Willems et al., 2006), but is not well documented in the stress fracture literature. Hreljac (2000) documented increased rate of pronation and touchdown supination angle in runners with a history of overuse injury. In a recent prospective study of the subtalar kinematics in 405 recruits, no differences in maximal pronation angles or ranges of motion existed between persons who sustained or did not sustain a stress fracture during 14 weeks of basic training. However in this study, increased time to maximum pronation as a percent of the total stance time was protective for tibial and femoral stress fracture (Hetsroni et al., 2006).
In a retrospective study using logistic regression, peak rearfoot eversion was a key predictor of stress fracture in female runners (Pohl et al., 2008).

Beyond the foot, the alignment of the lower extremity has the potential to impact the likelihood of injury. If the knee falls medial to the foot during the stance phase, a greater offset between the longitudinal axis of the tibia is created and increased bending forces are likely to occur. Retrospective research on female recreational runners with a history of stress fracture reveals increased odds of greater peak hip adduction, knee internal rotation, and knee abduction angles in the gait cycle in women with a history of stress fracture (Milner et al., 2005). Furthermore, these variables remained key predictors of stress fracture when combined with kinetic measures in a recent article using logistic regression analysis in a retrospective analysis and were significant predictors of injury in a prospective study of stress fracture (Pohl et al., 2007). Consequently, while faulty kinematics are not direct causes of elevated bone strain to the point of stress fracture, the gait mechanics presented above may result in detrimental loading environment and contribute to the development of stress fracture.

**Kinetics.** As mentioned at the beginning of this section, kinematic gait characteristics are closely related to impact and attenuation. The fatigue limit of bone is dependent on the magnitude and rate of the load per impact or cycle and the number of cycles over which this load is performed. Ekenman et al. (1998) report that the tibia is exposed to a combination of bending, shearing, and torsion simultaneously during impact related physical activities, including running; and ultimately, it is the deformation or bone strain due to these combined loads that leads to fracture (Taylor, 2003). Direct measurement of bone strain is often not feasible or practical due to methodological constraints and ethical issues in most countries.
Thus, surrogate kinetic measures from force platform data and accelerometry have been studied in relationship to stress fracture. This area of research has been insightful as recent evidence suggests the occurrence of stress fracture is associated with greater external loads (Milner et al., 2006a; Milner et al., 2006b; Milner et al., 2007; Pohl et al., 2007; Pohl et al., 2008).

In running, ground reaction forces (GRF), as measured by a force platform embedded in the floor, are typically 2.5-8 x body weight in the vertical direction. The GRF provides a measure of the magnitude and rate of external loads acting on the center of mass during physical activity and an indirect estimate on lower extremity loading. While not consistent in all literature, increased impact peak of the vertical ground reaction force has been associated with stress fracture (Milner et al., 2006b). In a cross sectional study of runners with a history of injury, Hreljac (2000) found greater peak impacts in runners with a history of injury. Grimston and colleagues (1998) found also significant differences in GRF (vertical, impact, max anterior/posterior, max medial) between runners with and without a history of injury. And, in a study of female runners with stress fractures compared to controls, females with a history of stress fracture had greater impact peaks and active ground reaction force peaks vertically (Milner et al., 2006b). On the contrary, Crossley et al. (1999) reported no significant differences in male runners with and without a history of fracture.

Evidence exists that some stress fractures of the lower extremity are spiral fractures (Spector et al., 1983). This suggests that, in addition to vertical forces, torques may be involved in the development of a stress fracture. The free moment, a moment about a vertical axis, is the amount of torque occurring due to friction between the foot and the ground.
(Holden & Cavanagh, 1991). It is easily measured using a force platform and is calculated by the following equation:

\[ FMv = Mv + (Fml \times COPap) - (Fap \times COPml) \]

The vertical free moment is \( FMv \); the vertical moment is \( Mv \); the medio-lateral (ml) GRF is \( Fml \); the antero-posterior (ap) GRF is \( Fap \); the center of pressure position along the ap platform axis is \( COPap \) and along the ml plate axis is \( COPml \). Studies of tibial stress fractures have used the free moment as an indicator of torsional load acting on the tibia as a higher free moment would likely contribute to a higher torque to the tibia (Milner et al., 2006a). Peak adduction, braking peak and absolute peak free moment were compared in female runners with and without a history of stress fracture. Average values across groups were greater in the stress fracture group. Using logistic regression, runners with a history of stress fracture were 1.365x (95% confidence interval 1.099–1.695, \( p = 0.005 \)) more likely to have greater absolute peak free moment values. Furthermore, absolute peak free moment accurately predicted group membership 66% of the time. Prospectively, both adduction free moment and impulse were greater in the stress fracture group of a cohort of female runners (Pohl et al., 2007). Greater peak adduction free moment implies that there is more resistance to toe out (due to increased friction between the foot and the ground as the foot attempts to rotate outward in the stance phase) in runners who went had a history of stress fracture/reaction. This association between the free moment and odds of stress fracture has also been confirmed prospectively in female runners who went on to sustain stress fracture. Thus, greater torsional loads may occur at the tibia due to this torsional moment, elevating risk for injury in an individual with this characteristic gait pattern. Given the anisotropic quality of bone, bone is stronger in compression than tension and in tension more than in
shear/torsion. Thus, it is not surprising that this surrogate measure of torsion, the free moment, has been strongly associated with stress fracture. Interestingly, the same association has not been confirmed in male military populations (Creaby & Dixon, 2008). Future work needs to elucidate the potential gender or population differences in the role of the free moment in stress injury.

**Loading rates.** While activities with greater rates of loading are beneficial for bone health, elevated rates of loading seem to play a role in stress injury development. Higher vertical loading rates are documented in both runners with overuse injury and stress fracture (Hreljac *et al.*, 2000; Milner *et al.*, 2006b; Pohl *et al.*, 2007; Pohl *et al.*, 2008). Peak positive tibial acceleration (PPA), closely related to vertical ground reaction force loading rates (Laughton *et al.*, 2003) may represent elevated rates of loading resulting increased strains due to the viscoelastic properties of bone. Retrospective cross sectional studies have positively associated PPA with stress fracture (Milner *et al.*, 2006b; Milner *et al.*, 2007; Pohl *et al.*, 2008). In one study of female runners, the magnitude of PPA predicted group membership successfully in 70% of the cases (Milner *et al.*, 2007). In a prospective study of stress fracture, the only vertical loading variable that was significantly different between cases and controls was PPA (15% greater) (Pohl *et al.*, 2007).

**Cumulative mechanics.** The above research highlights that many loading factors have been associated with stress injuries to bone. Most likely, it is the cumulative effect of these factors that results in stress fracture. Overall, specific kinetic loading parameters most commonly associated with stress fracture in prospective and retrospective studies include: peak positive tibial acceleration, vertical instantaneous load rate (VILR), and the free moment. In both prospective and retrospective studies of female runners, elevated levels of
all three variables are strongly associated with stress fracture (Milner *et al.*, 2006a; Milner *et al.*, 2006b; Milner *et al.*, 2007; Pohl *et al.*, 2007; Pohl *et al.*, 2008). Recently, knee stiffness during the initial impact phase of running was also significantly related to stress fracture group (Milner *et al.*, 2007). Sagittal plane knee stiffness was calculated by a dividing a change in joint moment by the change in joint angle over a specified time period; thus, it is a combination of both kinematics and kinetics. The authors found a large effect size (0.79) for increased stiffness in persons with a history of stress fracture and that in this group knee stiffness was positively associated with peak positive acceleration if the tibia. The same research group has evaluated the cumulative effect of kinetics and kinematics on stress fracture (Pohl *et al.*, 2008). Using hierarchical modeling and after assessing for collinearity, VILR, free moment, hip adduction, knee internal rotation and rearfoot eversion were variables included in a gold standard model. In the final model, hip adduction, free moment and rearfoot eversion accounted for 50% of the variance and correctly classified 83% of runners (OR=2.08). Individually, odds ratios for each variable were 1.29, 1.37, 1.18, respectively, indicating that increased measures of hip adduction, free moment, and rearfoot eversion were associated with stress fracture. This research underscores the importance of the cumulative effect kinetics and kinematics has on musculoskeletal loading. Importantly, it appears that vertical loading, torsional moments and kinematics in combination may serve to increase the load on the lower extremity and lead to stress injury. However outside of small studies of bone strain during physical activity, studies examining internal load differences between persons with and without a history of stress fracture are lacking.

Previous research has assessed collinearity of loading rate variables from both force platform data and accelerometry. However, it is possible that kinematics and kinetics are
closely related as well. In fact, research from our lab suggests that a combination of knee abduction, knee flexion, knee internal rotation and hip rotation account for 62% of the variance in the free moment (Meardon et al., 2007). In fact, knee abduction alone accounted for 46% of the variance in the free moment. Thus in choosing which factors to study, consideration needs to be made regarding the relationship between movement kinematics and kinetic outcomes. It is possible that a greater magnitude of vertical load in combination with altered gait mechanics, which create bending or torsional moments, results in greater physiologic loads that near the microdamage threshold. In an animal study evaluating fatigue life of bone under combined axial and torsional load, bone fractures seven times sooner when these loads occurred at the same time, or in phase (George & Vashishth, 2005). Additionally, an increased effective load and smaller distribution of load was experienced. The same authors report that this combined loading does occur in human activity, specifically walking and running uphill (Muller et al., 2004). However, combined loading differences have not been examined in stress fracture populations. Pilot work from our lab indicates, using the free moment and the vertical ground reaction force as surrogate measures of torsion and axial loading, that females tend to be more in phase during the impact and midstance phases of running. In-phase loading was measured by the magnitude of the average phase angle during the impact and active phases of the gait cycle. Future work needs to be done to uncover the relationship of combined loading on lower extremity bone stresses.

**Fatigue.** Muscular factors related to impact and attenuation include: fatigue, muscle strength and endurance/fitness. *In vivo*, contraction of muscles influence stress magnitude and distribution. Research indicates that intact soft tissue and muscle contraction substantially increases structural capacity (*i.e.* bending moment, energy absorption, bending...
stiffness and deflection) of tibiae in an animal model (Nordsletten & Ekeland, 1993; Nordsletten et al., 1994). Additionally, it is well established that muscle force production diminishes with prolonged running (Gleeson et al., 1998; Greig, 2008; Millet & Lepers, 2004; Ross et al., 2007). Yoshikawa et al. (1994) found increased canine bone strains on compressive surfaces (10-12%) and on tensile surfaces (26-35%) after a 20 minute exercise protocol. Scott and Winter (1990) calculated large bending moments at the tibia as a result of the ground reaction forces. In their model, bending moment was counteracted by the calf muscles. Extrapolating from this, if lower extremity musculature is unable to provide adequate eccentric force to resist bending moments, then excessive strain and ultimately injury may result. Several authors report increases in strain rates and magnitudes and altered strain locations with fatigue (Burr, 1997; Grimston & Zernicke, 1993). Additionally, human modeling studies suggest that muscle acts to add structural support to bone by decreasing the bending moments. Reductions in gluteus medius forces during running resulted in a 1.8% increase in stress on the superior femoral neck for every 10% reduction in abductor force (Hageman et al., 2009). Thus, muscles may serve to attenuate the loads applied to bone.

Further support for this viewpoint can be found in accelerometer based work. Shock waves traveling up bone result in accelerations at the shank during running. This shock wave, as measured by segmental acceleration, is attenuated by muscles, bones, and joints so that by the time it reaches the head, a significant portion is reduced. As mentioned later in this document, elevated tibial accelerations are associated with both prospective and retrospective stress injury. This is relevant because increased tibial acceleration after marching has been reported in military groups (Milgrom, 1989). Similarly, ten runners who fatigued over a 30 minute run experienced increased tibial acceleration from 6g at the beginning of the run to
approximately 10g at the end of the run (Verbitsky et al., 1998). Others have confirmed this relationship of increased impact accelerations measured at the tibia increase with fatigue (Derrick et al., 2002; Mizrahi et al., 2000; Voloshin et al., 1998).

**Fitness.** Interestingly, while obviously not a measure of strength, decreased calf girth in women is one key predictor of femoral and tibial stress fracture in male and female runners (Bennell et al., 1996); and similarly less lean muscle circumference was associated with femoral and tibial stress fractures in recruits (Milgrom, 1989). While measurements of calf girth may be anecdotal support at best, the strongest evidence for the role of fitness, and thus the ability to resist fatigue, has been reported prospectively in military recruits where individuals are exposed to large training volumes and intensities in a short time period. Decreased performance on leg press and increased run times have been positively associated with stress fracture (Hoffman et al., 1999; Shaffer, 1999, 2006). Recruits with 2.4 km run times of greater than 12 minutes were more likely to sustain stress fractures (Shaffer, 1999) and the females in the two slowest quartiles of run times were 3.5x more likely to sustain a stress fracture during training than females in the fastest quartile. This research suggests unaccustomed impacts in combination with decreased ability to attenuate the impacts may result in excessive bone strain leading to stress fracture.

**Flexibility.** Muscle flexibility and joint range of motion may influence stress injury by altering forces applied to the bone. Giladi et al. (1987b) and Milgrom (1994b) found that increased hip external rotation greater than 63-65 degrees was associated with stress fracture in military recruits. The authors’ discussion of how this increase in hip joint motion would alter bone forces was limited, but one possibility suggested was that excessive mobility and lack of stability at the pelvis and trunk may translate into greater torsional or bending loads to
the lower extremity. Restricted ankle dorsiflexion was also associated with stress fracture odds; recruits with decreased range of motion on ankle dorsiflexion, a commons measure of gastrocnemius length, were 4.6x more likely to sustain a metatarsal stress fracture (Hughes, 1985). Restricted ankle range of motion could theoretically result in an early heel rise during the gait cycle equating to increased time spent on the toes and increased bending moments applied to the metatarsals. Other studies have examined the role of muscle flexibility (hamstrings, quadriceps, calf, hip adductors, and hip flexors) and joint range of motion (rearfoot inversion/eversion, knee flexion/extension, and hip flexion/extension) with conflicting outcomes reported (Bennell et al., 1996; Ekenman et al., 1996; Giladi et al., 1987b; Hughes, 1985; Milgrom et al., 1994b; Montgomery et al., 1989; Winfield et al., 1997). This conflicting evidence or lack of evidence is most likely due to study design, imprecise methods of measurements and subject heterogeneity. Subsequently, the exact role of muscle flexibility and joint range of motion remains unclear. While clinically it makes senses that altered length of tissue away from optimal could influence loading and ultimately injury risk, current group analyses only support the role of hip rotation and ankle dorsiflexion in stress fracture causation. However, the influence of tissue length on an individual basis is not known and is an area for future research.

*Surface.* Long considered a contributor to injury development, especially stress fracture development, training surfaces can alter kinematics and ground reaction forces. Specifically, detrimental skeletal alignment and kinematics can be accentuated by cambered or uneven surfaces. For example when running on the right side of a cambered road, functionally the left leg would need to shorten by increasing hip and knee flexion and the right leg would need to lengthen, by increased hip and knee extension. Furthermore, the
slope of the road would result in the need for the left foot undergo greater rearfoot eversion to get the foot to the ground. Ground reaction forces may be increased on less compliant surfaces in the absence of kinematic adjustment (Bates & Stergiou, 1998; Ferris & Farley, 1997; McMahon & Greene, 1979); or, on the contrary, softer surfaces may lead to more muscle fatigue as the stabilizing costs of locomotion are greater. Despite these reasonable arguments, large epidemiological studies have failed to show an effect of training surfaces when weekly mileage is controlled (Marti et al., 1988; Walter et al., 1989). However, these studies of self report may bias results to the null as individual mechanics are not taken into consideration.

Research in the areas of footwear and landing suggest that persons may adjust their leg alignment or stiffness depending in response to the surface on which they are landing. In a footwear study using a single subject analysis design, nearly half of the subjects asked to run in shoes of varying midsole hardness did experience significant increases in ground reaction force parameters when midsole harness increased, while the other half did not. Consequently, when group analysis was performed, no significant differences existed in ground reaction force parameters between midsole hardness conditions (Bates & Stergiou, 1998). One mechanism that may account for this effect is the ability for individuals to adapt to their environment. Those who change characteristics of their landing technique, i.e. kinematics, to maintain optimal loading conditions can be classified as having a neuromuscular response (Caster & Bates, 1995). No studies have examined why some individuals respond to their environment and why some do not. Furthermore, it is not known whether persons who sustain stress fracture respond adequately to their environment. Although there is no clear consensus on the role of training surface on stress injuries, it is
possible that some persons may not adequately respond to their environment by adjusting
kinematics and landing forces. Runners who do not respond to their environment may well
be the ones who need to optimize surface and footwear for injury prevention.

Footwear. Related to training surface is footwear and orthotics. Running shoes and
orthotics aim to attenuate shock sustained by contact between the foot and ground during
landing and to control motion of the foot and ankle. Footwear changes and orthotic
prescription are common interventions for stress injuries to bone. In studies of footwear,
Gardner et al. (1988) found greater incidence of stress fracture in recruits wearing older or
worn out running shoes. Authors hypothesized this finding was related to the fact that older
shoes may have experienced a loss of shock absorbing qualities and mechanical support. In
support of this theory, changing footwear in military recruits from military boots with a hard
surface to basketball shoes with increased cushioning properties resulted in a decrease of
overuse injuries to the foot, but not necessarily overall lower extremity stress fracture rates
(Finestone et al., 1992). The authors suggest that this finding may have resulted from
cushioning properties minimizing injuries resulting from vertical impact forces but not
minimizing injuries resulting from bending forces.

While it seems logical to create an interface between the foot and the ground that
attenuates impact forces, increasing the amount of cushioning in a shoe is not always
positive. Shoes with a less stiff outersole have been found to result in an increase in second
metatarsal bone strain at the end of a walking protocol (Arndt, 2003). Additionally, in a study
of shoes with a deep heel cup to control rearfoot pronation and an extended proximal support
of the sole to the metatarsal heads (both designed to minimize bending forces) decreased
axial strains and strain rates in the tibia during walking, but not running (Milgrom et al.,
1998). As a group, this research suggests that a balance between support and cushioning properties of footwear is necessary. If persons fail to make adjustments to potentially detrimental surface conditions, they will benefit from enough stability in their footwear to minimize detrimental bending moments and enough cushion to aid in shock attenuation. Unfortunately, large scale studies of footwear are limited by the existence of individual responses to footwear changes.

Orthotics. By providing external support to the metatarsals and thus potentially minimizing the bending moment that occurs during the stance phase of gait and the bending and torsional forces that get translated up the leg, foot orthotics have the potential to minimize stress injury to the lower extremity. In general, observational studies support the use of orthotics in military populations. Milgrom and colleagues report decreased tibial, metatarsal and femoral stress fractures with the use of a non-custom semi-rigid orthotics (Milgrom et al., 1985). Furthermore, some individuals may benefit more than others from the use of orthotics. Another military based study found lower femoral stress fractures in persons with a high arch and lower metatarsal stress fractures in persons with a low arch with the use of semi-rigid orthotics (Simkin et al., 1989). In addition, stress fracture incidence decreased 50% when custom foot orthotics were worn in military boots (Finestone et al., 1999).

However, a later study on semi-rigid foot orthotics reported that use of these devices resulted in decreased bone strains and strain rates in the tibia during walking, but increased compression and tension strain rates during running (Ekenman et al., 2002). However it is important to note that due to the invasive nature of the methodology employed in this study, sample size was small. For the most part the above cited works suggests that on a large scale orthotics are beneficial at minimizing stress fracture odds in military populations. However, a
certain degree of support or stiffness to the device is necessary. Use of viscoelastic and neoprene inserts, both less rigid and shock absorbing, had minimal effect on decreasing stress injuries (Gardner et al., 1988; Milgrom et al., 1990; Schwellnus et al., 1990).

Discussion

Obviously, as highlighted above, a number of factors influence response of bone to loading. Bone loading is the result of interactions between bone properties, training patterns and gait mechanics. Clinically, it is important to obtain a detailed health and training history to identify factors within the individual that contribute to stress injury. Despite lack of evidence on a large scale for some potential risk factors in the development of stress fracture, researchers and clinicians must acknowledge the way in which multiple risk factors can interact within an individual in his/her environment to result in stress injury. Specifically, it is important to identify:

- underlying bone health
- training patterns
- fitness level
- strength and flexibility of the lower extremity
- static alignment
- dynamic movement patterns
- applied loads
- need for footwear intervention

In the absence of adequate measures of bone health, historical bone loading questionnaire (Dolan et al., 2006), nutritional assessment and pointed menstrual history questions may assist in understanding one’s potential for injury.

The number of young runners with low bone mineral density is alarming. Identifying the upper limit of loading to maximize osteogenic potential is essential and should take into
consideration the multiple factors that interact to result in injury. Given the state of current research, training patterns and gait mechanics, as influenced by fitness, strength and flexibility, are perhaps the most modifiable risk factors associated with stress injury to bone. Future efforts need to be made to identify global variables to predict stress fracture so that guidelines and recommendations can be made for the promotion of optimal bone health and to enable large scale screening and prevention efforts.

References


CHAPTER 3. EFFECTS OF CUSTOM AND SEMI-CUSTOM FOOT ORTHOTICS ON 2ND METATARSAL BONE STRAIN DURING DYNAMIC GAiT SIMULATION

Modified from a paper published in Foot & Ankle International

Stacey A. Meardon, W. Brent Edwards & Timothy R. Derrick

Abstract

Background: Stress fractures of the lower extremity are common in military and running populations. Research on the effectiveness of orthotics in modifying bone strain is limited. Hypothesis: Custom and semi-custom foot orthotics would equally decrease bone strain of the second metatarsal (2nd met). Methods: Eight cadaver specimens were cast for two types of orthotics, a custom and semi-custom device, using neutral plaster casts. Cadaver specimens, mounted to a dynamic gait simulator, walked over a force platform while force and bone strain data were collected. Peak bone strains, strain rates and tendon forces during the stance phase for each condition were analyzed using repeated measures analysis of variance and effect sizes. Results: Condition effects were present for tension strain, shear strain, compression rate and shear rate. Specifically, custom orthotics significantly decreased the aforementioned bone strains and strain rates ($p \leq 0.01$ for all) and the semi-custom orthotic decreased tension strains and shear strain rates ($p=0.05$ and 0.03, respectively). The effect of custom and semi-custom devices only differed significantly for compression and shear strain ($p=0.04$ and 0.02) with custom orthotics having a greater effect. Conclusion: Both custom and semi-custom orthotics modified the 2nd met bone strain and strain rate. The use of custom orthotics during simulated walking decreased 2nd met bone strains and strain rates more effectively than semi-custom orthotics. Orthotics minimize the strain magnitudes and rates of
the 2\textsuperscript{nd} met in walking and therefore may be feasible treatment option for the treatment and prevention of stress injury to the 2\textsuperscript{nd} met.

**Introduction**

Stress fractures occur in 5.1\% to 24\% of recruits during basic training (Milgrom \textit{et al}., 1994a; Shaffer, 2006) and in 8\% to 37\% of athletes (Brunet \textit{et al}., 1990; Nattiv \textit{et al}., 1997; Taunton \textit{et al}., 2002) Metatarsal stress fractures account for 19\% to 22\% of stress fractures in the lower extremity, (Orava, 1978; Shaffer, 2006) of which 35\% to 55\% of metatarsal stress fractures occur in the second metatarsal (2\textsuperscript{nd} met). Stress fractures of the 2\textsuperscript{nd} met are also common in patients with diminished function of the first metatarsal phalangeal joint, neuropathy, metabolic disorders, and hindfoot malalignments.

Whereas exact causes of metatarsal stress fractures are multifactorial, repetitive bone strain of high magnitude and rate results in micro-fracture and can ultimately lead to a stress fracture (Burr \textit{et al}., 1990; Li \textit{et al}., 1985). Thus, minimizing bone strain and strain rate would seem a logical goal in preventing metatarsal stress fracture. Peak bone strain on the dorsal surface of the 2\textsuperscript{nd} met occurs during the push off phase of gait when Achilles tendon force and axial loading are at a maximum (Donahue & Sharkey, 1999). This strain is likely due to combined bending and compression occurring in the 2\textsuperscript{nd} met. Materials of sufficient stiffness crossing the plantar surface of the foot would plausibly minimize this bone strain.

In a prospective study of infantry recruits, stress fracture incidence decreased 50\% when custom foot orthotics were worn in military boots (Finestone \textit{et al}., 1999) and decreases in tibial, metatarsal, and femoral stress fractures occurred with the use of a non-custom semi-rigid orthotics (Milgrom \textit{et al}., 1985). Little research has examined the role of
foot orthotics in decreasing metatarsal bone strain. However, shoes with a lesser amount of outer sole stiffness were found to minimize fatigue effects on 2nd met bone strain at the end of a walking protocol and are associated with a greater incidence of stress fractures to the 2nd met in recruits (Arndt, 2003).

One reason for the limited research on in vivo bone strain is the methodological and ethical considerations associated with this type of research. Human subject review boards in the United States are wary of approving invasive procedures needed for in vivo bone strain attachment to human bone due to potential for pain, injury and infection. Cadaver studies are a feasible alternative for measuring local bone deformation. Strain gages can be easily applied to the surface of the bone without risk. Additionally, dynamic gait simulation studies using cadaveric specimens report similar kinematics, ground reaction forces, muscle forces, and bone strains when compared to in vivo results (Sharkey, 1998; Sharkey et al., 1995; Ward et al., 2003).

The specific device used to capture gait activity in this study has been used in previous publications of kinematics, tissue forces, bone stresses and joint contact pressures (Edwards et al., 2007; Edwards et al., 2008b; Nester et al., 2007; Ward et al., 2003). The simulation starts at heel strike and stops just prior to toe off lasting an estimated 1.5 seconds; however, since there is no built in feedback mechanism this is a purely mechanical model. Previous work has compared kinematics of this model with other cadaver and in vivo studies. The values obtained using this model were in the range of previously reported literature (Nester et al., 2007). The fast walking speed enables greater analysis of the dynamics of gait. However, the trade off for speed obtained using open loop control is a compromised ability to generate force. Nester and colleagues (2007) report less of a match with vertical ground
reaction forces but near normal center of pressure trajectories. However, the focus of this work was foot kinematics and the criterion for successful trials was a good match with *in vivo* kinematics, not *in vivo* kinetics.

The purpose of this application was to measure the effect of two types of orthotics, semi-custom and custom foot orthotics, on 2\textsuperscript{nd} met bone strain using a dynamic gait simulation. We hypothesized that custom fit orthotics would lessen bone strain and bone strain rates occurring in the 2\textsuperscript{nd} met. The second hypothesis was that no significant difference would exist between the custom and the semi-custom orthotics.

**Methods**

**Specimens**

Institutional Review Board approval for this study was obtained. Eight fresh cadaver specimens (45 ± 5 years) severed 20cm above the malleoli were obtained for this study. All anatomical specimens were tested for disease and bloodborne pathogens and stored frozen at -5 degrees C until the time of testing. Specimens were thawed at room temperature and evaluated for injury and/or deformity by an experienced podiatrist. Five male and three female specimens free from lower extremity deformity were cast in plaster while in a nonweight bearing subtalar neutral position and fitted with a Bite running sandal that accommodates foot orthotics (Table 1).

Plaster casts were sent to a single orthotic laboratory where a custom and semi-custom foot orthotic was fabricated for each foot (KLM Orthotic Labs, Valencia, CA). Semi-flexible graphite with vinyl covers were used for both devices. In both devices, all forefoot
deformities were balanced to neutral intrinsically. The semi-custom device used in this study combined three major contours (medial arch, lateral arch, and heel) of the foot and four discrete measurements (heel width, medial arch height, lateral arch height and foot length from 1st metatarsal bisection to the most posterior point on the heel along the 1st metatarsal). Technical standards established by The Board for Accreditation of Prescription Foot Orthotic Laboratories were followed in the fabrication of both devices. All orthotics were labeled with a number corresponding to a respective specimen. One of the orthotics for each specimen was labeled with a star to enable balancing of conditions, otherwise the orthotics were identical in appearance. In this manner, the investigators were unaware of orthotic type until after conclusion of the study.

**Protocol**

In order to expose individual extrinsic muscles of the foot for later attachment to electric actuators, skin and subcutaneous tissue were removed from the superior shank to 5 cm proximal to the tibial plafond. All tissues below this point (*i.e.* plantar skin, fat pad, retinacula, and intrinsic muscles) were left intact.

### Table 1. Individual characteristics of specimens.

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>43</td>
<td>50</td>
<td>42</td>
<td>51</td>
<td>45</td>
<td>37</td>
<td>50</td>
<td>49</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
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<td>female</td>
<td>male</td>
<td>male</td>
<td>female</td>
<td>male</td>
<td>male</td>
<td>male</td>
</tr>
<tr>
<td><strong>Mass (kg)</strong></td>
<td>54.30</td>
<td>58.82</td>
<td>58.37</td>
<td>101.81</td>
<td>63.35</td>
<td>58.37</td>
<td>81.45</td>
<td>108.60</td>
</tr>
<tr>
<td><strong>Cross Sectional Area (mm$^2$)</strong></td>
<td>39.0</td>
<td>21.7</td>
<td>58.9</td>
<td>64.6</td>
<td>48.6</td>
<td>42.8</td>
<td>42.0</td>
<td>34.6</td>
</tr>
<tr>
<td><strong>Iml (mm$^4$)</strong></td>
<td>207.0</td>
<td>40.2</td>
<td>399.4</td>
<td>456.2</td>
<td>274.7</td>
<td>247.8</td>
<td>231.3</td>
<td>90.0</td>
</tr>
</tbody>
</table>
A stacked rectangular rosette strain gage (Model # SK-06-060WR-350, Vishay Micro-Measurements, Raleigh, NC) was mounted to the dorsal surface of the 2nd met diaphysis. Strain gages were applied in accordance with manufacturer specifications. Previous research and common location sites of stress fracture guided choice of strain gage placement (Donahue & Sharkey, 1999; Ekenman et al., 2002). Strain gage voltage was amplified (Model 2120B, Vishay Micro-Measurements Group, Raleigh, NC) and data were collected using Peak Motus (with synchronized force platform and muscle forces collected at 1200 Hz).

An intra-medullary rod connected the tibia to a Dynamic Gait Replicator (Figure 1). This Dynamic Gait Replicator (DGR) is capable of simulating the stance phase of walking in approximately 1.5 sec and can replicate human ground reaction force profiles (Nester et al., 2007; Ward et al., 2003). Eight extrinsic muscle tendons crossing the ankle joint (Achille’s, tibialis anterior, extensor digitorum/hallucis longus, flexor digitorum longus, flexor hallucis longus, peroneus brevis, peroneal longus, and the tibialis posterior) were connected to load cells in series with electric actuators to simulate muscle activity. Braided lines that can withstand 667.5 N of force were pre-tensioned and used to connect the muscle tendons to the load cells. Tendon forces, produced by electric actuators, were applied dynamically using a trapezoidal waveform. Tendon onset and offset times corresponded to previously published EMG data (Perry, 1992). Magnitude of tendon forces was determined by motor size and pre-tensioning. Because the motors are equipped with open loop controllers, DGR is a feed-forward simulator without the ability to make online adjustments. Ground reaction forces and tension forces were examined after each trial to ensure consistency, but were not held at constant force levels.
Each cadaver foot was walked across a force platform (AMTI, Watertown, MA) in three conditions: no orthotic, custom orthotic and semi-custom orthotic. A Bite running sandal, which accommodates orthotics, was used in all conditions (Figure 2). During the control condition, the manufacturer insert that came with the sandals was used for all specimens. All specimens had their own sandals. In the orthotic conditions, Velcro was used to secure the orthotic to the sandal. Eight successful trials were captured. Order of orthotic condition was balanced across specimens.

Following data collection, a thin cross section of the 2nd met at the strain gage mounting site was extracted. A digital photo of the cross section was taken and the image file was read into MATLAB. Cross sectional area (CSA) and area moment of inertia about the medial lateral axis ($I_{ML}$) of the 2nd met were calculated from the scaled thresholded image as follows:

\[
CSA = \sum_{i=1}^{N} a_i
\]

\[
I_{ml} = \sum_{i=1}^{N} a_i r_i^2
\]

where $a_i$ is the $i^{th}$ bone pixel area (mm$^2$) and $r_i$ is the $i^{th}$ perpendicular distance to the medial lateral axis.

**Analysis**

All raw force and strain data were imported and analyzed in (MathWorks, Natick, MA). Ground reaction forces and strains were filtered using a 4th order Butterworth filter with low-pass cutoff frequencies of 6 Hz and 30 Hz, respectively. Rosette strain information was used to calculate maximum and minimum principal strains and maximum shear strains and the
Figure 1. The Dynamic Gait Replicator is composed of a platform on a rail, with a variable motor and cable attached to the platform capable of pulling the platform linearly. Nine motors with open loop controllers and gear reducers are attached to the platform, with an encased cable attached to each gear reducer. Each of these cables extends from the platform and is attached to a strain gauge. A pneumatic cylinder capable of applying 1,112.5 N of force is also attached to the platform. A manufactured functional knee joint is attached to the cylinder ram.

The first central difference method was used to calculate strain rates from heel strike to maximal metatarsal joint dorsiflexion. Peak ground reaction forces, tendon forces, strains and strain rates were identified using a search algorithm for local minima or maxima. These peak values were exported to SAS for statistical analysis. Condition averages of the aforementioned peak variables, calculated from five successful trials, were used for analyses. Tests for normality revealed that the muscle forces, ground reaction forces and bone strain data were not normally distributed; thus non-parametric statistics were used in statistical
analyses (Thomas et al., 1999). Data were ranked and standard parametric tests were done on the ranked data. An L-statistic was calculated as the significance test and compared to a chi square table. Consequently, repeated measures analysis of variance (ANOVA) assessed condition effects for ground reaction forces, tendon forces, bone strains and strain rates. Multiple t-test comparisons were used for post hoc analysis with Scheffe adjustment for multiple comparisons. Alpha level of 0.05 was set to minimize the likelihood of Type I error. Effect sizes on unranked data were calculated as a standardized mean difference, the difference between the means divided by the average standard deviation for the two groups being compared.
Results

Individual specimen characteristics are reported in Table 1. Average trial to trial reliability (intraclass correlation coefficient) for bone strains was 0.92. An exemplary example of ground reaction force, muscle force, and bone strain are shown in Figure 3.

Maximal principal strains were positive (tension) and minimal principal strains were negative (compression) and will be referred to as tension and compression for the remainder of the paper. Peak vertical ground reaction forces did not differ significantly between conditions \( (p > 0.05) \). While average peak vertical ground reaction force was low \( (452.7 \pm 56.9 \text{ N}) \), the shape of the curve was typical of \textit{in vivo} data compared to walking. Achilles tendon, flexor hallucis longus and flexor digitorum longus tendon forces were not significantly different across conditions \( (p > 0.05) \); however, within specimen differences in Achilles tendon forces existed between conditions. For some subjects, because of the high forces, the braided line attached to the Achilles tendon slipped or broke. Given this, the slack length of the lines could have changed and therefore affected the Achilles tendon forces necessitating the adjustment for Achilles tendon force. However, due to the lack of neuromuscular adaptability of this mechanical model, the Achilles tendon forces were not expected to differ between conditions within each foot. Furthermore, given the attachment site of the Achilles tendon, differences in Achilles tendon forces due to passive tension changes from the orthotic spanning the arch was not expected. As bone deformation under applied force is affected by Achilles tendon forces, (Edwards \textit{et al.}, 2007; Sharkey \textit{et al.}, 1995) individual peak strain results were adjusted for respective Achilles tendon forces. Adjusted condition averages for bone strains and strain rates, reflecting similar Achilles
Figure 3. An exemplary example of forces and strains over 0 to 100% stance is shown. Stance initiation was considered the time at which the vertical ground reaction force exceeded 30N (heel strike). End of stance was 1.5 seconds from the onset of heel strike. Full toe off was not obtained with this study methodology.

tendon forces across conditions, are reported in Table 2. Significant condition effects were present for tension and shear strains ($p<0.01$) and compression and shear strain rates ($p<0.01$). As evidenced in the Table 2 with effect sizes, the custom orthotic generally had a larger effect on bone strain and strain rate minimization when compared to the semi-custom orthotic and the custom orthotic had significant effects on compression, tension and shear strains ($p=0.04$, $p<0.01$, $p<0.01$) and compression ($p=0.01$) and shear rates ($p<0.01$). The semi-custom orthotic had a statistically significant effect on tension strain ($p=0.05$) and shear strain rate ($p=0.03$). However, the custom and semi-custom devices only performed differently for compression and shear strains ($p=0.04$ and $p=0.02$, respectively).

In evaluation of individual specimen response to orthotics, 6 of the 8 specimens responded positively to both custom and semi-custom orthotics across nearly all variables of
interest. Assessment of 2\textsuperscript{nd} met $CSA$ and $I_{ML}$, revealed that these 6 specimens had, on average, lower values than non responders ($p=0.05$) (Table 1). Moreover, no significant difference in age or mass existed between responders and non-responders ($p>0.05$).

### Discussion

Qualitative research supports the use of orthotics; however, quantitative evidence presents varied outcomes with orthotic intervention (Bates, 1979; Bennett \textit{et al.}, 1996;
Brown et al., 1995; Ferber et al., 2005; Johanson et al., 1994; Nawoczenski et al., 1995; Nawoczenski et al., 1998). The purpose of this study was to measure the effect of two types of orthotics, semi-custom and custom foot orthotics, on 2nd met bone strain using dynamic gait simulation. Our results suggest that decreases in compression, tension and shear strain and compression and shear strain rate occur with custom orthotics. Similarly, semi-custom orthotics decreased tension bone strain and shear strain rate.

Previous research on walking reports peak Achilles tendon forces of 1320±500N at slow speeds (Finni et al., 1998). As a result of our lower magnitude external loads, average axial strains (750µε) were slightly less than those reported for in vivo walking (934µε) (Milgrom et al., 2002). The means and confidence intervals for the variables of interest in this study are lower than previously reported. Although our vertical ground reaction force profile resembled those of a normal human walking, the magnitudes were approximately half the values reported in the literature (Chao et al., 1983). The relatively low Achilles tendon force (670N) may account for this difference.

The area moment of inertia is a measure of a bone’s resistance to bending. Specimens with large area moments of inertia would undergo less deformation under applied loads and would not benefit as much from the use of an orthotic as compared to a bone with small area moment of inertia. A similar relationship exists for cross sectional area of bone. Thus, a larger effect of orthotics on bone strain values would be expected in bones with small area moment of inertia and smaller cross sectional areas. The specimens used in this study had $I_{ML}$ values ranging from 40.2 to 456.2mm$^4$ and $CSA$ ranging from 21.7 to 64.6mm$^2$, a wide range of values that may have distorted the effect of the orthotics on bone strain variables. As such, specimens in this study with smaller $I_{ML}$ and $CSA$ responded more positively to the orthotic
conditions in comparison to specimens with larger $I_{ML}$ and $CSA$. Further strengthening this position was the finding of a negative relationship between individual effect sizes and bone characteristics; lower $I_{ML}$ and $CSA$ were associated with greater compression and shear strain and strain rates found ($I_{ML}$ : -0.74, -0.85, -0.10, and -0.44 respectively; $CSA$ : -0.81, -0.89, -0.18, and -0.40 respectively). However, weaker relationships were found for strain rate; this is not surprising since strain rates are more dependent on the viscoelastic properties of bone. Previous work on orthotics has also demonstrated effectiveness when individual characteristics are considered (Simkin et al., 1989).

Custom orthotics significantly decreased five of the six bone strain characteristics measured and had moderate to large effect sizes for compression and shear strain rates; semi-custom orthotics significantly decreased two characteristics with a moderate to large effect size for shear strain rate. Custom orthotics may have performed better than semi-custom orthotics due to the lack of “custom fit” of the medial, lateral and longitudinal arches in the semi-custom device. The small sample size and variability in $I_{ML}$ and $CSA$ of the specimens may also have been contributory.

During locomotion, the anterior shift of the center of gravity over the metatarsal heads during stance phase results in 2.7x greater load when compared to the center of gravity over the midfoot (Salathe, 2002). As the second and third metatarsals are relatively fixed proximally and the metatarsal phalangeal joint is hinged distally, this load is associated with a bending moment occurring about the medial lateral axis of the bone (Donahue & Sharkey, 1999; Gross, 1989; Salathe, 2002; Sharkey et al., 1995). Bending moments have been calculated in the metatarsals in human subjects using ground reaction forces and radiographs during the heel-lift as well as in other cadaveric gait simulations (Donahue & Sharkey, 1999;
Sharkey et al., 1995; Stokes et al., 1979). All studies reported that plantar flexor activity, specifically the flexor hallucis longus and flexor digitorum longus,(Donahue & Sharkey, 1999; Sharkey et al., 1995) minimized the bending moments occurring at the 2\textsuperscript{nd} met. Orthotics likely minimize 2\textsuperscript{nd} met bone strain, resulting from a combination of bending and compression, and strain rates by providing external support to the plantar surface of the metatarsals. However, this study cannot confirm the direct effect of orthotics on bending moments as characteristics need to calculate bending moments were not measured.

Foot orthotic devices are designed to support foot structures and limit abnormal and potentially harmful motions that may lead to lower extremity pain and dysfunction. The effects of orthotics on bone strain parameters measured \textit{in vivo} are presented in this study and have not previously been reported. This is important because excessive bone strain and strain rates are associated with microdamage and stress fracture of bone (Burr et al., 1990; Li et al., 1985). The results of this study suggest orthotics decrease 2\textsuperscript{nd} met bone strain rate during walking. Hence, orthotics may be an effective prevention and treatment strategy for strain injuries to the 2nd met.

While cadaver research is not without its limitations, it does allow for research to be performed that otherwise could not be done due to methodological complexity and ethical concerns. Limitations of this study include lower bone strain and strain rates than previously reported and a small sample size. However despite these limitations, this study does provide a conservative estimate of the effects of orthotics on 2\textsuperscript{nd} met bone strain parameters. Further work needs to be done evaluating the effectiveness of orthotics in minimizing 2\textsuperscript{nd} met bone strains and strain rates in running and other strenuous activities. Moreover, the exact
mechanism underlying the effectiveness of orthotics needs to be explored to optimize orthotic prescription.

References


CHAPTER 4. EFFECT OF STEP WIDTH VARIATIONS ON TIBIAL STRESSES DURING RUNNING

A paper to be submitted to

*Applied Biomechanics*

Stacey A. Meardon, Samuel Campbell & Timothy R. Derrick

Abstract

*Background:* A crossover running pattern has previously been associated with gait mechanics commonly reported in persons with a history of tibial stress fracture. *Methods:* Fifteen experienced runners ran at their preferred 5k race pace during three conditions: preferred step width, wide step width (+5% of leg length), and narrow step width (-5% of leg length). Synchronized force platform and kinematic data were collected and a combination of experimental and musculoskeletal modeling techniques were used to determine joint contact forces acting on the knee. Centroid moments and forces were calculated at the distal tibia (25%). Peripheral stresses were estimated at 4 locations of the tibia (anterior, lateral, medial, and posterior) by modeling the tibia as hollow cylinder. *Results:* Significant condition effects were found for normal stress at all locations except the anterior aspect of the tibia. Additionally, a significant linear trend indicated greater normal stresses with decreasing step width. No significant step width effects were found for shear stresses. Normal stress rates differed only at the medial tibia with greater stress rates in the normal condition. Shear stress rates were different across conditions at the anterior, posterior and medial locations with greater shear rates at these locations. *Conclusion:* This research suggests that the stress environment of the tibia is influenced by gait mechanics. In general, narrow step width conditions were associated with greater stresses and stress rates; and while not always
significant, stresses and stress rates linearly declined with wider step width conditions. These findings have implications for rehabilitation of bone stress injury and technique training for runners. However, consideration of the overall coordination and mechanics of the system should be made prior to suggesting a change to an individual runners’ step width.

Introduction

Gait mechanics have long been implicated in the development of stress fracture in runners as have underlying bone characteristics (Crossley et al., 1999; James et al., 1978; Milner et al., 2006a; Milner et al., 2006b; Pohl et al., 2008). However, the effect of gait mechanics on the stress environment of the bone independent of bone characteristics is unclear. While many studies have assessed the effect of stride length manipulations on lower extremity kinematics and kinetics, relatively few published studies have examined the effect of step width on gait mechanics. Foot placement is considered normal when the medial border of the foot is in line with the line of progression (McClay, 1995). A crossover pattern arises when the foot crosses medial to this line of progression. Williams and Ziff (1991) strategically manipulated step width during running and found that a 2 cm crossover pattern results in approximately a 15% increase in rear foot pronation and a 25% increase in pronation velocity. Similar findings are reported in a study by Pohl et al. (2006) who found that tibial excursion increases with a cross over pattern (18%) as well as peak rearfoot eversion (Pohl et al., 2006; Williams & Ziff, 1991). Marked increased step width has also been found to increase peak knee flexion, extension, abduction and internal rotation values (Chappell et al., 2002) but decrease peak rearfoot eversion and excursion values (Pohl et al., 2006; Williams & Ziff, 1991) during running.
Foot placement has been shown to not only alter kinematics, but also mediolateral forces (McClay, 1995). In a study of systematic variation of foot placement, researchers found that a crossover gait pattern resulted in increased lateral ground reaction forces throughout the midstance phase of gait when compared to a neutral pattern (McClay, 1995). Similarly, a wider step width resulted in greater medial reaction forces throughout midstance compared to normal width. Depending on the angle of the force vector relative to the longitudinal axis of the tibia, increase in both lateral forces and medial forces creates a larger bending moment about the anterior-posterior axis of the tibia. The aforementioned gait mechanics may contribute to the development of stress fracture. In support of this, Creaby and Dixon (2008) report a greater medial directed ground reaction force vector during the time of peak active ground reaction force in military personnel with a history of stress fracture.

It is also possible that a greater magnitude of vertical load in combination with increased bending or torsional moments results in greater physiologic loads. In an animal study evaluating fatigue life of bone under combined axial and torsional load, bone fractured seven times sooner when these loads occurred simultaneously, or in-phase (George & Vashishth, 2005). Additionally, an increased effective load and smaller distribution of load was experienced. To the authors’ knowledge, in-phase loading has not been studied in running.

Traditionally, ground reaction forces and kinematics have been used to estimate the musculoskeletal load during running. However, these measures only capture a portion of the loading environment since contribution from the musculature is not considered. Ankle muscles contribute 3 to 7 bodyweights of force during slow jogging and running respectively
Furthermore, total joint contact forces at the ankle, knee and hip approach 9.0 BW, 15.9 BW, and 11 BW, respectively (Edwards et al., 2008; Sasimontonkul et al., 2007). A recent study of runners incorporates muscle forces into a musculoskeletal model of running and indicates that the greatest femoral stresses are at common stress fracture sites (Edwards et al., 2008). Applying similar techniques at the tibia would enable researchers to estimate tibial stresses during the stance phase of running and gain insight into the mechanisms of injury. Furthermore, knowledge of factors that increase or decrease tibial stresses can be gained by strategically altering step width in a repeated measures design using a standard model focusing on gait differences. Therefore, the purpose of this study was to evaluate the effect of step width manipulation on estimated tibial stresses at the periphery of bone in the distal tibia. A secondary goal was to determine the amount of in-phase loading that occurs in the tibia during running. It was hypothesized that the greater tibial stresses would occur with decreasing step widths.

Methods

Subjects

Prior to the study, all subjects gave written informed consent and Institutional Review Board approval was obtained for this study. Area runners were recruited by word of mouth, email lists and flyers. Fifteen experienced runners volunteered for this study (8 males and 7 females, 23.7±5.4 years, 70.3±9.2 kg, 1.7±.08 m). All runners were free from injury at the time of data collection and were running on average more than 10 miles/week. A priori sample size was calculated based on values from a previous study of distal tibia contact forces (Sasimontonkul et al., 2007). A 15% difference was used in calculation as this has
been considered clinically relevant (Butler et al., 2007; Milner et al., 2007) with an alpha level of 0.05 and 80% power. Given a true difference in the condition means of 15%, a minimum of 8 control subjects were needed to be able to reject the null hypothesis that the condition means are equal with probability 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05 (Dupont & Plummer Jr, 1990).

Protocol

Anthropometric data of height, weight, thigh length, leg length, malleolar height, foot length, thigh circumference, calf circumference, malleolar width and foot breadth were collected for later use in a musculoskeletal model. Twenty-nine retro-reflective markers were placed on the lower extremity and pelvis. A static trial with the runner in an anatomical neutral alignment was collected.

Subjects ran at their preferred 5k running speed over a force platform (AMTI, Watertown, MA) until ten trials of each condition were successfully completed on the right limb. The mean step width over the 10 trials in the preferred step width condition was calculated as the mediolateral distance between the right and left heel markers when each heel marker was at its minimum during consecutive steps (Figure 1). The mean step width value obtained in the preferred running style condition was then used to calculate minimum target values for the narrow and wide conditions. Minimal acceptable narrow step width was calculated as normal step width minus 5% of leg length. Minimal acceptable wide step width was calculated as normal step width plus 5% of leg length. Adjusting the step width by a percentage of leg length insured that step width adjustments were scaled to individuals and minimized the potential for biased influence of step width on frontal plane joint moments.
The normal step width condition was performed first and trials were considered successful if they were within 5% of their preferred speed with no visible aiming for the force platform. Order of narrow and wide conditions was balanced to minimize fatigue effects. Trials were considered successful if they were within 5% of their preferred speed and step width was at least 5% of leg length more (wide condition) or less (narrow condition) than the preferred step width with no targeting of the force platform observed. Feedback was provided after each trial regarding speed and step width. Feedback on running speed and step width was provided. Running speed was monitored with motion capture using the horizontal component of the sacral marker; step width was monitored using the right and left heel markers. Motion capture data were collected with an 8 camera 3D motion capture system (Vicon Nexus, Centennial, CO) at a sampling rate of 160 Hz. Force platform data were collected simultaneously at a sampling rate of 1600 Hz (AMTI, Watertown, MA). Motion capture data and force platform data were exported to (The Mathworks, Natick, MA) for signal processing and analysis.

Figure 1. Measurement of step width was done by measuring the mediolateral distance between the heel markers of consecutive steps.
Analysis

Motion capture data and force platform data were processed as per Edwards et al. (2008, 2009). Briefly, motion capture data were interpolated to 1600 Hz using a cubic spline technique. Motion capture and force data were filtered using a 4th low-pass Butterworth filter with a cutoff frequency corresponding to the 95th percentile frequency of the vertical ground reaction force. Motion data and kinematic data were smoothed at this same frequency which corresponded to the cumulative sum of the integrated power spectral density curve. Static trials were used to estimate joint center locations of the ankle, knee, and hip. Three-dimensional Cardan segment and joint angles were calculated with a flexion/extension, abduction/adduction, internal/external rotation order of rotations.

Anthropometric measurements were used to calculate segment masses, center of mass location, and moments of inertia (Vaughan et al., 1992) and used to calculate joint moments and reaction forces at the hip, knee, ankle and subtalar joints with inverse dynamics. Joint angles were imported into a scaled SIMM model (Musculo-Graphics Inc., Santa Rosa, CA) to estimate the maximal muscle forces, muscle moment arms, and muscle orientations for 43 lower extremity muscles during the stance phase of running. Muscle forces were optimized using a static optimization program with a cost function minimizing the sum of squared muscle stresses (Glitsch & Baumann, 1997). Resulting hip (all 3 planes), knee (sagittal plane), ankle (sagittal plane), and subtalar moments were constrained to equal those obtained from the inverse dynamics procedure. Next, 3D joint tibio-femoral contact forces were calculated by vectorially summing the knee reaction force and muscle forces crossing the knee joint:
\[
F_{\text{knee\_contact}} = F_{\text{knee\_reaction}} + \sum F_{\text{knee\_muscles}}
\]

Three dimensional internal forces and moments of the tibia were calculated in the manner of Duda et al. (1998) at a centroid located 75% of the distance from the proximal end of the tibia. This cross-sectional level has the narrowest tibial width and is the general area commonly reported stress fracture (Milgrom et al., 1989). Muscles crossing this centroid that influenced the loading environment were: soleus, tibialis anterior and posterior, flexor digitorum and flexor hallucis, peroneal brevis, longus, and tertius, and extensor digitorum and hallucis. The following general equations were used:

\[
F_{\text{centroid}} = F_{\text{knee\_reaction}} + \sum F_{\text{centroid\_muscles}}
\]

\[
M_{\text{centroid}} = M_{\text{knee\_reaction}} + \sum M_{\text{centroid\_muscles}}
\]

Normal (longitudinal) and shear stresses at four areas of the peripheral surface of the tibia (anterior, lateral, posterior, and medial) were estimated by assuming a hollow cylinder cross-section with inner and outer diameters 15 mm and 25 mm, respectively (Milgrom et al., 1989). Normal stresses were calculated from the stresses due to the longitudinal centroid forces and the corresponding centroid bending moment. Shear stresses were calculated from the corresponding centroid shear forces and the centroid torsional moment using the following general equations.

\[
\sigma_{\text{normal}} = \sigma_{\text{longitudinal\_force}} + \sigma_{\text{bending}}
\]

\[
\sigma_{\text{shear}} = \sigma_{\text{shear\_force}} + \sigma_{\text{torsion}}
\]

Phase lags between peak normal stress and peak shear stress were calculated using a cross correlation technique and reported as percent lag in stance time. Peak values were
correlated. Heel strike index was calculated as the location of the center of pressure during heel strike relative to the length of the foot.

Statistics

Subject condition averages for peak normal stress and stress rates, peak shear stress and stress rates, and phase lag at four sites of the periphery of the tibia were exported for statistical analysis. Data were analyzed using a one way (condition [3 levels]) repeated measures ANOVA. Prior to repeated measures testing, data were assessed for normality using the Kolmogorov-Smirnov test for normality (α = 0.05). Non-normal data were log transformed. Sphericity of repeated measures was assumed if the Huynh-Feldt test result was > 0.75; the test of significance with a Huynh-Feldt adjustment of the degrees of freedom was used if sphericity was not met. Comparisons of main effects were adjusted for multiple comparisons using Sidak adjusted p-values. Polynomial contrasts were done to further identify the magnitude of and trends in the relationship between step width and tibial stress and stress rates.

Results

Table 1 indicates that subjects were able to manipulate their step widths during running while maintaining a consistent running velocity. Two subjects were forefoot strikers, but overall heel strike index did not differ between conditions. Ensemble averages across the stance phase for ground reaction forces and the free moment are illustrated in Figure 2. Large differences between conditions were present in the medio-lateral ground reaction forces and the free moment. Peak longitudinal forces acting on the tibial centroid were -15.15± 1.92 BW during normal running and were predominately compressive. Forces perpendicular to the
longitudinal axis were much smaller and averaged 1.02 ± 0.14BW anteriorly and 1.72 ± 0.35 BW medially. Bending moments were greater around the mediolateral (ML) axis (0.274 ± 0.078 BWm) when compared to the anterio-posterior (AP) axis (0.182 ± 0.046 BWm); the torsional moment about the longitudinal axis (-0.014 ± 0.006 BWm) was the smallest in magnitude of all the moments.

Peak bone normal stresses were predominately tensile on the anterior and medial locations of the tibia. On the posterior and lateral surfaces, normal stresses were compressive (Figure 3). Means and confidence intervals for estimated stresses and stress rates for the normal condition are reported in Table 2. Additionally, results of the polynomial contrasts are provided in Table 2. Step width influenced normal stress on the lateral, posterior, and medial aspects of the tibia, $F(2) = 15.71, p < 0.01; F(2) = 6.77, p < 0.01, F(1.08) = 3.94, p <0.01$. Specifically, the narrow and the preferred step width conditions resulted in greater tibial stresses in the lateral and posterior regions of the tibia than the wide condition. At these two regions, the narrow and preferred conditions were not significantly different. In the medial tibia, significant differences in normal stress were found in all step width comparisons. Moreover, in the lateral, posterior and medial tibia, significant linear and quadratic trends were found. This suggests that an overall increase in normal stress occurred at these sites as participants decreased their step widths (within the range assessed in this

<table>
<thead>
<tr>
<th></th>
<th>Velocity (m/s)</th>
<th>Step Width (m)</th>
<th>Heel Strike Index(%)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>CI</td>
<td>Mean</td>
</tr>
<tr>
<td>Normal step width</td>
<td>4.04 [3.68, 4.33]</td>
<td>0.02 [0.00, 0.05]</td>
<td>31.19 [19.3, 43.2]</td>
</tr>
<tr>
<td>Narrow step width</td>
<td>4.04 [3.69, 4.32]</td>
<td>-0.06 [-0.09, -0.04]</td>
<td>26.74 [17.3, 37.5]</td>
</tr>
<tr>
<td>Wide step width</td>
<td>4.03 [3.68, 4.32]</td>
<td>0.10 [0.08, 0.12]</td>
<td>26.92 [17.7, 37.9]</td>
</tr>
</tbody>
</table>

Table 1. Mean condition variables reported with 95% confidence intervals.
Figure 2. Ensemble averages for anterio-posterior (AP), vertical, and medio-lateral (ML) ground reaction forces, and the free moment.

study). Even though no significant differences between conditions were found for shear stress, a significant linear trend existed in the anterior tibia indicating an increase in normal stress as participants decreased their step width.

Log of normal stress rates were examined (Figure 5) and only the log of normal stress rate on the medial aspect of the tibia differed significantly with step width, $F(2) = 4.38, p = 0.02$. The narrow condition differed from the wide condition ($p = 0.02$). A significant quadratic trend for step width indicates an overall increase in the normal stress rates medially as participants changed step width from wide to narrow; additionally, it indicates a
curvilinear trend existed. Log of the shear stress rates demonstrated differences with step widths at the anterior, posterior and medial aspect of the tibia, $F(2) = 5.22, \ p = 0.01$; $F(2) = 3.70, \ p = 0.04$; and $F(2) = 4.31, \ p = 0.02$. Again, only the narrow step width differed from the wide step width at these locations ($p > 0.05$). Significant linear and quadratic trends for shear stress rates in the lateral site indicate an overall curvilinear increase in stress rate in the narrow condition relative to the wide condition.

![Graphs showing normal stresses](image)

Figure 3. Normal stresses illustrated across the stance phase. Ensemble means for each condition are presented with overall standard deviation (SD). Positive values indicate axial tension, anterior shear and lateral shear.
Normal stress:shear stress phase lags in the normal condition ranged from 5 to 15% on average. Average phase lags in the normal condition per location on the tibia are as follows: anterior 9.5%, lateral 6.53%, posterior 4.53%, and medial 15.2% indicating relative in-phase loading in all regions. Step width significantly altered the phase lag at the anterior and lateral location of the tibia, $F(2) = 3.52, p = 0.04$ and $F(2) = 3.88, p = 0.03$, for in-phase loading. At both sites, greater in-phase motion was evident during the narrower step widths. Post hoc analyses indicated that significant differences between the narrow (9.47 ± 3.40%)
and preferred step widths (9.60 ± 3.14%) and the wide step width (10.60 ± 3.44%) existed for the anterior tibia ($p = 0.01$, $p=0.04$ respectively); significant differences between the phase lags in the narrow (4.90 ± 2.48%) and the wide step width (7.53 ± 3.31%) at the lateral tibia were also found ($p = 0.02$).

Figure 4. Percent change from normal is illustrated for stresses of the tibia. Four locations of estimation (anterior, lateral, posterior, and medial aspects of the tibia) are presented. Individual subject condition means were converted to a percent of the group mean for the normal condition. Error bars represent standard deviation of standardized subject values within a condition. Standard deviation is expressed as a percent of the condition mean. Significant step width effects are labeled with asterisks.
Figure 5. Percent change from normal is illustrated for stress rates of the tibia. Four locations of estimation (anterior, lateral, posterior, and medial aspects of the tibia) are presented. Individual subject condition means were converted to a percent of the group mean for the normal condition. Error bars represent standard deviation of standardized subject values within a condition. Standard deviation is expressed as a percent of the condition mean. Significant step width effects are labeled with asterisks.

Discussion

The purpose of this study was to evaluate the effect of step width manipulation on estimated tibial stresses at the periphery of bone in the distal tibia. A secondary goal was to examine in-phase loading of the tibia during running. We hypothesized that the tibial stresses increase would increase with decreasing step widths.
The peak normal stresses calculated in this study are along the material axes of the tibia. Strains on the tibia during over ground running collected in vivo (N = 3) range from 998 to 1163 µε and -1446 to -2446 µε (Milgrom et al., 2003). Using Hooke’s Law and a Young’s modulus of 17 GPA (Reilly & Burstein, 1975) the estimated strains observed in this study (N=15) range from 44 to 1125 µε and -675 to -2398 µε, within the ranges previously reported.

The results of this study generally suggest an increase in tibial bone stresses and stress rates with decreased step width. Stresses were calculated from a standardized bone model rather than a model based on subject specific bone characteristics. This neglects the influence of bone geometry on the stress environment but illustrates that the stresses are influenced by gait mechanics. On the medial aspect of the tibia, 14 out of 15 subjects exhibited an increase in normal stresses from the wide step width to the narrow step width conditions. Thus, changes in underlying bone characteristics was the same for all individuals. Closer evaluation of the stresses and stress rates reveal marked inter-individual differences due to the standardized bone model and individual gait characteristics. Bone stress calculations are sensitive to the location of stress measurement relative to the neutral axis of bending and the principal axes; stress calculations done close to the neutral axis will be low and stresses along the principal axes will be high. Likewise, normal and shear stresses vary continuously as the orientation of the axis changes throughout the stance phase; thus these between subject variations are not surprising.

Overall, we found that axial forces acting at the centroid contribute up to 44% of the stress environment. Post hoc descriptive analysis of the components of stress analysis revealed larger centroid moments about the medial-lateral axis of the tibia and about the
anterior-posterior axis in the narrow conditions. Consequently, the anterior and posterior stresses and the medial and lateral stresses, respectively, will be increased with narrow step widths. Stepping further back, large differences were also found in the direction of the mediolateral ground reaction forces. In the narrow condition, peak mediolateral forces were \(~100\) N, in the normal condition \(~0\) N, and in the wide condition \(~-100\) N. This change of direction of the ML ground reaction forces is consistent with work by McClay (1995) and directs the ankle contact force vector closer to the longitudinal axis of the tibia in the wide condition. This effect proportionally decreased the bending moment about the AP axis at the centroid moment proportionally reducing the normal stress on the medial and lateral surfaces of the tibia (Figures 1 and 2).

Differences in centroid moments were found about the ML axis, even though there were no observable differences in AP ground reaction forces. Evaluation of the muscle forces indicated greater lateral and anterior forces in the narrow condition. The larger muscle forces resulted in an overall increase in the subtalar joint moments and ultimately the ankle joint contact forces and moments. By creating a larger moment about the ML axis of the ankle joint, the moment at the centroid increased normal stress anteriorly and posteriorly on the tibia correspondingly. Normal stress was only significantly different between conditions for the posterior location but showed a trend for significance in the anterior location, \(F(1.11) = 3.63, p = 0.07\).

Finally, evaluation of the free moment illustrates that the free moment also varies between conditions. Larger absolute free moments and positive free moments (acting to resist toe out) were observed in the narrow condition. Interestingly, we also found the peak positive free moment to be positively correlated with peak normal stresses on the medial aspect of the
tibia \((r = 0.57)\). Similarly, the absolute peak free moment was positively correlated with peak shear stresses at the medial tibia \((r = 0.60)\).

In phase axial and torsional loading of the tibia has been studied in vivo. Downhill walking results in a more in-phase pattern than uphill or level walking (Muller et al., 2004). Our study is the first to evaluate in-phase motion during running and the results illustrated that in-phase loading occurred at all four areas of the tibia (anterior, lateral, posterior, and medial) during running. The consequences of such loading have been documented by George and Vashish (2005) and include decreased fatigue life and a more narrow range of force distribution. This could partially explain why the tibia is the most commonly fractured bone of the lower extremity in active populations (Kelsey et al., 2007; Shaffer et al., 2006).

Interestingly, the factors we identified post hoc related to the stress changes observed in this study have been implicated in the cause of tibial stress fracture. Female runners both prospectively and retrospectively are reported to have greater absolute free moments and positive free moments (Milner et al., 2006a; Pohl et al., 2007; Pohl et al., 2008). However, in a group of military recruits, no differences in free moments were found, rather differences in the frontal plane force vector in mid to late stance were more discriminate (Creaby & Dixon, 2008). It is possible that both factors lead to increase tibial stresses, but population and subject specific characteristics dictate which factor dominates the stress environment. Future work should attempt to identify individual factors that lead to increases in bone stress.

Moreover, prior to prescribing step width changes to modulate these factors, consideration must be made on the overall coordination and mechanics of the system. At least in walking, narrow step width is associated with an 8% increase in metabolic costs when compared to preferred; wider step widths are associated with 54 and 45% increases in
mechanical and metabolic costs, respectively. In a study of sprinting, wider step widths are reported early in the sprint, but are decreased greater than 50% once full stride length is obtained. These results suggest that wider step width may be suitable for the force development needed for acceleration and that the narrow step width may be preferred during fast velocity conditions. Another factor to consider is the role of step width in gait dynamics (Ito et al., 2005). In walking, balance control is related to step widths and wider step widths may be more stable (Gabell & Nayak, 1984) and step width is indicative of falls in older persons who walk at or greater than normal speeds (Brach et al., 2005). Step width and step width variability roles in balance control in running has not been studied extensively; however, given the dynamic nature of running and single leg loading, location of the foot under the center of mass may create a more stable stance phase with less muscular stabilization required. Thus, wider step widths may result in lower tibial stress, but there may be an energy cost associated with it. Full mechanisms of optimal step width in long distance running need further clarification. Loading at the knee joint and the effects on the hip musculature need to be assessed at wider step widths before recommendations for optimal step width can be made. Additionally, if suggestions are made to alter gait characteristics for the minimization of injury potential or the rehabilitation of injury, training parameters will need to be modified to allow for tissue adaptation.

In conclusion, this research suggests that the stress environment of the tibia is influenced by gait mechanics independent of bone geometry. In general, narrow step width conditions were associated with greater stresses and stress rates; and while not always significant, stresses and stress rates generally increased with the decreasing step width conditions of this study. These findings in combination with findings from previous studies
of injury may suggest that future gait retraining efforts and studies consider step width characteristics, especially if persons demonstrate a crossover pattern. However, studies are needed to ascertain the relationship between step width and injury, bone forces, moments, and stresses with injury, and to identify optimal step characteristics for minimization of tissue loads during running prior to implementation into prevention and rehabilitation protocols.

References


CHAPTER 5. INTERNAL BONE FORCES AND MOMENTS IN RUNNERS WITH A HISTORY OF STRESS FRACTURES

A paper to be submitted to
British Journal of Sports Medicine

Stacey A. Meardon, W.B. Edwards & Timothy R. Derrick

Abstract

Background: Given the multitude of studies reporting faulty gait kinematics and increased external forces, runners with stress fracture likely demonstrate increased tibial bone forces and moments, key components of bone stresses. The purpose of this exploratory study is to evaluate internal bone forces and moments in runners with a history of stress fracture. Additionally, timing differences of combined loading between runners with history of stress fracture and those without were assessed. It was hypothesized that persons with a history of stress fracture would demonstrate more in-phase patterns of axial and torsional loads and greater internal bone forces and moments in the distal tibia. Methods: Thirty-three experienced runners, 11 cases and 22 controls, ran across a force platform maintaining a self-selected 5K race pace, ± 5% during each trial. A model of human running based gait mechanics was used to calculate tibial bone forces and moments along three points of the tibia (25%, 50%, and 75% of the distance from the proximal tibia). Phase lag using cross correlation of axial forces and torsional moments were calculated to characterize the degree of in phase loading. Results: Anterioposterior (AP) centroid forces differed between groups at the proximal, mid and distal tibia (ES = 0.75, CI95% = 0.01, 1.49; ES = 0.83, CI95% = 0.08, 1.58; ES = 0.82, CI95% = 0.07, 1.57). The stress fracture group experienced 8-12% greater shear forces than the control group. Moments about the AP axes, axial and mediolateral (ML)
axes were greater in the stress fracture group in the distal tibia (ES = 0.98, CI95% = 0.22, 1.74; ES = 3.46, CI95% = 2.35, 4.56; ES = 0.09, CI95% = 0.09, 1.59). The stress fracture group underwent more medial surface tension (33%), internal rotation torsion (263%), and anterior surface tension (26%). In phase loads did not appear to be different between groups.

Conclusions: In this group of subjects, moderate increases in forces and moments were observed in the stress fracture group; torsional moment values and change were small compared to other moments reported. It was suggested that, in addition to bone geometry, internal bone forces and moments may play a role in stress fracture in this population.

Introduction

Running is the exercise of choice for more than 70% of active persons (Hootman et al., 2002). In fact, over 35 million Americans participated in running as a form of exercise in 2007 (National Sporting Goods Association, 2007). Unfortunately, the risk for overuse injury is well documented in the literature with annual rates as high as 52% (Macera et al., 1989). Stress fractures, comprising 6-25% of all injuries to runners (Clement, 1974; James et al., 1978; McBryde, 1985; Snyder et al., 2006), are a serious injury that results in significant health care costs, lost training time, and interference with job performance, competition, and exercise abilities. The most common site for stress fracture of the lower extremity in both military and running populations is the tibia (Barrow & Saha, 1988; Beck et al., 1996; Shaffer et al., 2006). As the merits of exercise for health and wellness have gained public acceptance, it is critical to understand the mechanical factors contributing to running injury. Ultimately, this understanding will lead to interventions and preventative strategies for running injuries which, in turn, will minimize barriers to exercise and promote overall health.
Previous research has focused on biomechanical factors of skeletal alignment, ground reaction forces, impact accelerations and free moments as contributory factors for stress fractures in runners (Bennell, 1999; Milner et al., 2005, 2006a; Milner et al., 2006b; Milner et al., 2007; Pohl et al., 2007; Pohl et al., 2008). Retrospective research on female recreational runners with a history of stress fracture reveal increased odds of peak hip adduction, knee internal rotation, and knee abduction angles occurring in the gait cycle in runners with a history of stress fracture (Milner et al., 2005). Furthermore, these variables remain key predictors of stress fracture when assessed with kinetic measures using logistic regression analysis (Pohl et al., 2008) and were significant variables in prospective studies of stress fracture (Pohl et al., 2007). By creating a larger offset of the compressive load from the longitudinal axis of the tibia, the abovementioned gait mechanics may increase the bending moment of the tibia and ultimately contribute to the development of stress fracture.

While not consistent in all literature, increased magnitudes of the impact peak of the vertical ground reaction force and the peak ground reaction force have also been associated with stress fracture (Milner et al., 2006b; Milner et al., 2007; Pohl et al., 2008). Furthermore, the free moment (FM), a moment about a vertical axis due to friction between the foot and the ground (Holden & Cavanagh, 1991), has also been associated with stress fracture (Milner et al., 2006a; Pohl et al., 2007; Pohl et al., 2008). These studies in combination suggest that, in recreational runners, a vertical load component combined with a torsional component is associated with stress fracture.

Greater physiologic loads, that near the microdamage threshold, occur when axial and torsional loading occur simultaneously (George & Vashishth, 2005). Furthermore, the authors report a seven fold decrease in the fatigue life of bone and a more concentrated load
distribution during in-phase loading. Results of *in vivo* studies indicate in-phase loading of the tibia occurs in human physical activity, but running was not studied (Muller *et al*., 2004). Preliminary work from our laboratory indicated less than a 15% lag between peak normal and peak shear stresses of the tibia (Meardon & Derrick, unpublished). To the authors’ knowledge, in-phase loading has not been studied in runners with a history of stress fracture.

External loads can influence the loading environment, but it is bone’s ability to resist stress that ultimately dictates bone’s response to loading. Bone cross sectional parameters such as narrow tibial bone width, small cross sectional area, low moment of inertia, and small section modulus are associated with stress fracture (Giladi *et al*., 1987a; Milgrom, 1989; Milgrom *et al*., 1988; Milgrom *et al*., 1989). These parameters are also related to fracture thresholds. Greater values are associated with greater resistance to skeletal loads. However, much of the research in this area has been done on military populations. Findings in civilian runners are less conclusive (Bennell *et al*., 2004; Crossley *et al*., 1999, 2008; Milner *et al*., 2006b). More recently, Franklyn *et al*. (2008), reports that a small cross sectional area and small section modulus were predictive of tibial injury in male athletes (n=43); a small section modulus and a narrow tibial width is predictive in female athletes (n=45). This research highlights the important role that bone geometry may play in athletes.

Most likely, it is the cumulative effect of kinetic and kinematic factors with underlying bone characteristics that result in increased bone stress. The first step in evaluating this cumulative effect is to assess site specific bone forces and moments throughout the stance phase of running. In this way, internal bone loading can be assessed independent of bone characteristics. The purpose of this exploratory study was to assess the internal bone forces and moments acting on the tibia in runners with a history of stress
fracture. Additionally, timing of combined loads, specifically the axial internal bone force and the torsional moment of the centroid, throughout the stance phase of running were assessed. Runners with a history of stress fracture to bone were compared to runners with no history of stress fracture. It was hypothesized that runners with a history of stress fracture would demonstrate larger tibial forces and moments and greater in phase loading.

Methods

Subjects

Prior to the study, all subjects gave written informed consent and Institutional Review Board approval was obtained for this study. Area runners were recruited by word of mouth, email lists and flyers and thus cases and controls were chosen from same population (Rothman et al., 2008). Cases were considered persons with a history of stress fracture to the tibia that diagnosed by a physician and/or diagnosed by a positive imaging technique (mean time from injury = 3.2 ± 3.0 years). As the exposure of interest, internal bone forces and in-phase loading, was unknown at the time of recruitment, controls were selected independent of their exposure status (Rothman et al., 2008). Because gender influences lower extremity mechanics in running (Butler et al., 2007; Milner et al., 2007), groups were matched on gender. Thirty-three experienced runners, 11 cases and 22 controls, volunteered for this study. All runners were free from injury at the time of data collection and were running on average more than 20 miles/week.
Protocol

Health history questionnaires were completed by all subjects. Anthropometric data for later use in a musculoskeletal model was collected. Kinematic and kinetic data were collected as subjects ran at their preferred running speed (based on their 5k time) over a force platform (AMTI, Watertown, MA). A twenty-nine retro-reflective marker set was used such that bilateral foot, leg and thigh segments consisted of five markers and the pelvis consisted of three. Neutral alignment was determined by capturing a neutral stance trial prior to the start of the running protocol. Medial markers were removed for the running trials. Subjects ran repeatedly down a 30m runway through the viewing area of the cameras until 10 successful trials were completed on each limb. Pace was monitored continuously using the sacral marker. Successful trials were within 5% of preferred speed with no obvious targeting of the force platform.

Motion capture data were collected with an 8 camera 3D motion capture system (Vicon Nexus, Centennial, CO) at a sampling rate of 160 Hz and synchronized with the force platform (1600 Hz). Signal processing and analysis of exported data was done in (The Mathworks, Natick, MA).

Analysis

Motion capture data and force platform data were processed as per Edwards et al. (Edwards et al., 2009, 2008). In brief, three dimensional joint moments and reaction forces were calculated at the hip, knee and ankle using individual anthropometrics to calculate segment masses, center of mass location, and moments of inertia (Vaughan et al., 1992). A rigid body model with pelvis, thigh, leg, and foot segments was created. Ensemble joint
angles were exported into a SIMM model (Musculo-Graphics Inc., Santa Rosa, CA) and scaled to individual anthropometrics to estimate the maximal muscle forces, muscle moment arms, and muscle orientations for 43 lower extremity muscles during the stance phase of running.

Using muscle optimization previously described by Edwards et al. (2008), 3D joint tibio-femoral contact forces were calculated by the vector summation of the muscle forces crossing the knee joint and the knee reaction force:

\[ F_{\text{knee\_contact}} = F_{\text{knee\_reaction}} + \sum F_{\text{knee\_muscles}} \]

Three dimensional internal forces and moments of the tibia were calculated in the manner of Duda et al. (Duda et al., 1998) at a centroid located 25, 50 and 75% of the distance from the proximal end of the tibia. The cross-sectional level corresponding to 75% of the distance from the proximal end of the tibia (25% from the distal end) has the narrowest tibial width and is the general area commonly reported stress fracture (Milgrom et al., 1989); therefore, it was an area of particular interest. The, soleus, tibialis anterior and posterior, flexor digitorum and flexor hallucis, peroneal brevis, longus, and tertius, and extensor digitorum and hallucis muscles crossed the centroid and thus were included in the force calculations. The following summary equations were used to calculate internal forces and moments at the three centroid locations:

\[ F_{\text{centroid}} = F_{\text{knee\_reaction}} + \sum F_{\text{centroid\_muscles}} \]

\[ M_{\text{centroid}} = M_{\text{knee\_reaction}} + \sum M_{\text{centroid\_muscles}} \]

Positive antero-posterior forces (AP Force) indicated anterior shear; positive axial force (Axial Force) indicated axial tension; and, positive medio-lateral forces (ML Force)
indicated lateral shear. Positive internal moments about the AP axis (AP Moment) corresponded to lateral-surface compression; about the vertical axis (Torsion) corresponded to internal-rotation torsion; and, about the medio-lateral axis (ML Moment) corresponded to posterior-surface compression.

Cross correlation of the peak axial force and the peak torsional moment was used to determine the timing of combined loading. Results are reported as percent lag in stance time. Heel strike index was calculated as the location of the center of pressure during heel strike relative to the length of the foot to ensure equal distribution between groups.

Statistical Analysis

Univariate analyses of cases and controls were performed using Chi-square table analysis with categorical demographic and health history data. All analyses modeled the history of stress fracture. Odd ratios (OR) were considered significant if 1.00 was not included in the 95% confidence interval. Continuous health history and demographic data were assessed with one way analysis of variance (\(\alpha = 0.05\)).

The injured limb of the stress fracture group was selected for analysis. The corresponding limb was used for analysis in the control group. However, the control group consisted of two persons for each case in the stress fracture group. Thus, for every left limb analyzed in the stress fracture group, two left limbs were analyzed in the control group. Similarly, two right limbs were analyzed in the control group for every right limb in the stress fracture group. Peak internal bone forces, moments, and phase lags were calculated at three levels for each subject and exported for statistical analysis.

Effect sizes and 95% confidence intervals of the effect size were calculated to assess group differences in continuous demographic, health history, and biomechanical variables.
Effect sizes (ES) were calculated to express differences relative to the control standard deviation. The control group standard deviation was chosen as the denominator because injury has previously been demonstrated to influence kinetic variability (James et al., 2000). Furthermore, differences in standard deviations between the injured group and control group were evident in the majority of outcome variables explored in this study. Cohen (1988) proposed that effect size values of 0.2 represent small differences; 0.5, moderate differences; and greater than 0.80, large differences; however confidence intervals of the effect size were also calculated to aid in interpreting the meaningfulness of the results. A critical value of $t$ at $p = 0.05$ with two tails was used for the calculation of the confidence intervals. Confidence intervals of the effect size that did not include zero were considered to exemplify meaningful results.

Results

Key subject characteristics are reported in Table 1. No significant differences were present in non-categorical variables. The control group had two forefoot strikers and the injured group had one forefoot striker; thus the groups were balanced on this factor. History of caloric restriction and menstrual dysfunction was more prevalent in the injured group. Univariate analysis revealed increased odds of stress fracture associated with both caloric restriction and menstrual disturbances, $OR = 5.0$ ($CI_{95} = 0.75-33.21$) and $OR = 7.88$ ($CI_{95} = 0.71-87.17$) respectively.

Figure 1 illustrates the centroid forces and moments at the three sites of the tibia. Overall, the loading environment of the tibia was dominated by internally compressive forces and medio-lateral (ML) moments. The proximal tibia (25% of the length of the tibia) was
subjected to the greater anterior shear forces and bending about the ML axis. Greatest axial forces, medial shear forces and anterior-posterior (AP) moments occurred distally (75% of the length). The torsional moment appeared more equally distributed throughout the tibia with a trend for high values in the proximal tibia.

Means, standard deviations, and effects sizes for all biomechanical variables are reported in Table 2. Effects favoring the stress fracture group for higher values were found for peak AP internal bone force at all three sites of the tibia ($E_{S_{Proximal}} = 0.75$, $E_{S_{Mid}} = 0.83$, $E_{S_{Distal}} = 0.82$). The stress fracture group experienced 8-12% greater anterior shear forces than the control group throughout the tibia. Additionally, the stress fracture group exhibited

| Table 1. Subject characteristics reported. Standard deviations are reported in parentheses for continuous data. |
|-------------------------------------------------|-------------------------------------------------|
| Stress Fracture | Non-Stress Fracture |
| Age (yrs.) | 26.3 (10.4) | 26.5 (9.4) |
| Mass (kg) | 62.6 (10.4) | 64.8 (9.2) |
| Height (cm) | 168.4 (9.5) | 167.8 (6.7) |
| Study Pace (m/s) | 4.3 (1.0) | 4.2 (0.7) |
| Miles run per week | 37.8 (20.9) | 40.3 (22.8) |
| 1 Mile Time (min.) | 6.0 (2.0) | 6.2 (1.3) |
| Years Running | 12.4 (8.3) | 8.6 (4.9) |
| Years since Stress Fracture | 3.2 (3.0) | --- |
| Number of Stress fracture episodes | 1.6 (0.5) | --- |
| Number of participants with a history of caloric restriction | 3 | 1 |
| Number of participants with a history menstrual dysfunction | 6 | 6 |

Note: Stress fracture group was comprised of 3 men and 8 women; 6 men and 16 women comprised the non-stress fracture group (N=33).
larger peak internal AP, torsional and ML moments ($ES = 0.98, 3.46, 0.84$ respectively). In the stress fracture group the distal tibia demonstrated $33\%$ more lateral surface compression, and therefore medial surface tension, and $26\%$ more posterior surface compression/anterior surface tension. The torsional values at the distal tibia were three times greater in the stress fracture group; however the values and differences are small in comparison to other moments reported in this study.

Figure 1. Three dimensional centroid forces and moments during the stance phase of running at the three sites of the tibia: proximal (25\% of tibial length from the proximal tibia), middle (50\% of tibial length from the proximal tibia), and distal (75\% of tibial length from the proximal tibia). Positive forces indicate anterior shear, axial tension, and lateral shear. Positive internal moments correspond to lateral-surface compression, internal-rotation torsion, and posterior-surface compression.
Table 2. Group means (SDs) of all variables at three locations of the tibia. The proximal, middle, and distal tibia correspond to centroid locations at 25, 50, and 75% of the distance from the proximal tibia. Positive forces indicate anterior shear, axial tension, and lateral shear. Positive internal moments correspond to lateral-surface compression, internal-rotation torsion, and posterior-surface compression. Glass’s Δ effect size (ES) with 95% confidence intervals are provided (CI).

<table>
<thead>
<tr>
<th></th>
<th>Stress Fracture</th>
<th>Non-Stress Fracture</th>
<th>ES (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak Values</td>
<td></td>
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<tr>
<td>Phase lag (%)</td>
<td></td>
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<tr>
<td>proximal tibia</td>
<td>6.82 (2.09)</td>
<td>7.41 (1.64)</td>
<td>0.22 (-0.51, 0.94)</td>
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<tr>
<td>mid tibia</td>
<td>9.55 (2.02)</td>
<td>10.45 (3.60)</td>
<td>0.25 (-0.48, 0.97)</td>
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<td>distal tibia</td>
<td>10.18 (10.95)</td>
<td>7.18 (9.63)</td>
<td>0.30 (-0.42, 1.03)</td>
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<tr>
<td>AP Force (BW)</td>
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<tr>
<td>proximal tibia</td>
<td>1.52 (0.31)</td>
<td>1.40 (0.15)</td>
<td>0.75 (0.01, 1.49) *</td>
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<tr>
<td>mid tibia</td>
<td>0.99 (0.25)</td>
<td>0.86 (0.14)</td>
<td>0.83 (0.08, 1.58) *</td>
</tr>
<tr>
<td>distal tibia</td>
<td>1.11 (0.26)</td>
<td>0.99 (0.14)</td>
<td>0.82 (0.07, 1.57) *</td>
</tr>
<tr>
<td>Axial Force (BW)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>proximal tibia</td>
<td>-7.07 (1.26)</td>
<td>-7.15 (0.94)</td>
<td>0.09 (-0.64, 0.81)</td>
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<tr>
<td>mid tibia</td>
<td>-13.43 (2.54)</td>
<td>-13.28 (1.40)</td>
<td>0.10 (-0.62, 0.83)</td>
</tr>
<tr>
<td>distal tibia</td>
<td>-15.10 (2.91)</td>
<td>-14.93 (1.75)</td>
<td>0.10 (-0.63, 0.82)</td>
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<td>ML Force (BW)</td>
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<td>proximal tibia</td>
<td>-0.06 (0.04)</td>
<td>-0.09 (0.08)</td>
<td>0.40 (-0.33, 1.13)</td>
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<tr>
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<td>-0.15 (0.14)</td>
<td>0.20 (-0.53, 0.92)</td>
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<tr>
<td>distal tibia</td>
<td>-1.65 (0.46)</td>
<td>-1.66 (0.45)</td>
<td>0.02 (-0.71, 0.74)</td>
</tr>
<tr>
<td>AP Moment (BWm)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>proximal tibia</td>
<td>0.101 (0.035)</td>
<td>0.085 (0.022)</td>
<td>0.71 (-0.05, 1.44)</td>
</tr>
<tr>
<td>mid tibia</td>
<td>0.159 (0.070)</td>
<td>0.129 (0.038)</td>
<td>0.76 (0.01, 1.50) *</td>
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<tr>
<td>distal tibia</td>
<td>0.219 (0.154)</td>
<td>0.164 (0.054)</td>
<td>0.98 (0.22, 1.74) *</td>
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<tr>
<td>Torsional Moment (BWm)</td>
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<tr>
<td>proximal tibia</td>
<td>0.027 (0.014)</td>
<td>0.024 (0.005)</td>
<td>0.59 (-0.15, 1.33)</td>
</tr>
<tr>
<td>mid tibia</td>
<td>0.021 (0.010)</td>
<td>0.018 (0.005)</td>
<td>0.51 (-0.23, 1.24)</td>
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<tr>
<td>distal tibia</td>
<td>0.023 (0.050)</td>
<td>0.006 (0.005)</td>
<td>3.46 (2.35, 4.56) *</td>
</tr>
<tr>
<td>ML Moment (BWm)</td>
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<td></td>
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</tr>
<tr>
<td>proximal tibia</td>
<td>0.365 (0.124)</td>
<td>0.321 (0.069)</td>
<td>0.62 (-0.12, 1.36)</td>
</tr>
<tr>
<td>mid tibia</td>
<td>0.320 (0.114)</td>
<td>0.276 (0.069)</td>
<td>0.62 (-0.12, 1.35)</td>
</tr>
<tr>
<td>distal tibia</td>
<td>0.286 (0.130)</td>
<td>0.228 (0.068)</td>
<td>0.84 (0.09, 1.59) *</td>
</tr>
</tbody>
</table>

*indicates confidence intervals excluding zero
Phase lags illustrated that the peak axial forces and the peak torsional moments were predominately in phase, less than $8.60 \pm 1.64\%$ on average across all locations (Table 2). While slight, the proximal tibia appears to undergo more in-phase loading when compared to the mid and distal tibia. Differences between groups for this measure of combined loading were minimal ($ES_{Proximal} = 0.22$, $ES_{Mid} = 0.25$, $ES_{Distal} = 0.30$) with confidence intervals indicating the standardized difference of the mean effect size could be as much as $\sim 0.50$ favoring the stress fracture group for being more out of phase or as much as $\sim 1.00$ favoring the control group for being more out of phase.

**Discussion**

The purpose of this exploratory study was to assess the differences in internal bone forces and moments acting on the tibia between runners with a history of stress fracture and those without. Additionally, the timing of the peak axial bone force and the torsional moment was assessed as a measure of in-phase loading. We hypothesized greater internal bone forces and moments, as well as more in-phase loading, would be found in runners with a history of stress fracture.

The internal bone force magnitudes reported by Scott & Winter (1990) range from 10.3 -14.1 body weights axially at slower speeds of running. The forces reported at the distal tibia in this study are slightly above this range (14.9 -15.1 BW). Additionally, the shear forces were similar to those reported by Sasimontonkal *et al.*, (2007). Interestingly the greatest forces and moments tended to occur in the distal tibia. This is a site that does tend to have a low cross-sectional area and is a common site for stress fracture (Bennell, 1999; Kelsey *et al.*, 2007; Shaffer *et al.*, 2006). The results of this study suggest that differences
between internal bone forces and moments of the distal tibia between runners with a history of stress fracture may exist. Anterior shear forces were greater in the stress fracture group at all sites of the tibia that were studied. Additionally, three dimensional moments acting at the distal tibia, a common area for tibial stress fracture, were greater in the stress fracture group. Thus the stress fracture group experienced greater bending and torsional moments when compared to the non-stress fracture group. However, since this is a retrospective study, causation cannot be determined. While the confidence intervals of the effect size associated with these variables does not include zero, they do tend to be wide. Likely, this is due to the small sample size, the variability inherent to the data, and the critical t-value choice (Rosnow & Rosenthal, 2009). Nonetheless, this suggests that the magnitude of applied loading in this group of subjects may be related to the injury status. However, the exact translation to tissue strain cannot be stated since bone stress or strains were not calculated. Given relationship between bending moments and normal stress of bone ($\sigma_{normal}$)

$$\sigma_{normal} = \frac{(M_{bending} \cdot y)}{I}$$

where $M_{bending}$ is the bending moment, $y$ = distance from the neutral axis, and $I$ is the area moment of inertia, it is likely that stress increases with increasing bending moments.

Although bone scan data were not available for the current study, we did explore the impact the applied load differences in this study using reported cross sectional information for persons with a history of stress fracture and active controls. Data from Franklyn et al. (2008) were used to estimate the effects of altered cross sectional size on the resulting stresses on the peripheral aspect of the medial tibia modeling the tibia as a hollow cylinder. In this study, bone parameters for persons with a history of stress fracture and active controls
are reported and cross sectional area is lower in the stress fracture group. Group specific cross sectional area parameters were calculated using the average inner and outer diameters reported for the stress fracture group and active control group in Franklyn et al (2008). Using beam theory, ensemble forces and moments of all subjects, and group specific cross sectional areas, tibial stress were up to 9% greater in the stress fracture group. This signifies the effect of bone characteristics on the loading environment of the tibia. The increase is due to the smaller cross sectional area in the stress fracture group. However, using group specific forces and moments, which were moderately higher in the stress fracture group, in combination with the smaller cross sectional areas resulted in up to 17% greater tibial stress in the stress fracture group. In effect, bone characteristics influenced tibial stresses but they may interact with internal forces and moments to result in greater tibial stresses. Further work with subject specific models will need to verify these findings.

Despite the potentially detrimental consequences of in-phase loading between internal axial forces and torsional moments, no differences were seen between groups as hypothesized. This study did however confirm previous findings that the tibia is undergoing a significant amount of in-phase motion during running. This is evidenced by the small lag times between peak axial forces and torsional moments in both the injured and non injured tibia.

The questionnaire results of this study also indicate that in this group of subjects, other characteristics differentiated between our groups. Of our stress fracture subjects 3 out of 11 had a history of disordered eating as compared to 1 out of 22 in the control group, \( OR = 7.88 \) (CI\(_{95}\) = 0.71-87.17). Moreover, 75% of the females in the stress fracture group had a history of abnormal menses versus 38% in the control group \( OR = 5.0 \) (CI\(_{95}\) = 0.75-33.21).
The strong association between bone health, disordered eating and menstrual disturbances is well documented (Nichols et al., 2006; Otis et al., 1997). However, the interaction between these characteristics, underlying bone health, physical activity patterns and gait mechanics remains unclear.

In conclusion, this research suggests that internal bone forces and moments of the tibias may be greater in runners with a history of stress fracture. It is important to note that only forces and moments were calculated. Rates were not taken into consideration; given the role of loading rates in stress fracture, they will need to be incorporated into future efforts. Elevated loading rates and peak positive acceleration (PPA), closely related to vertical ground reaction force loading rates (Laughton et al., 2003), are documented in runners with a history of stress fracture (Milner et al., 2006b; Milner et al., 2007; Pohl et al., 2007; Pohl et al., 2008). Future studies should seek to ascertain the integrated relationship of underlying bone health, gait mechanics, and health history.

References


Abstract

Locomotor variability is inherent to movement and, in healthy systems, contains a predictable structure. Here, detrended fluctuation analysis (DFA), a modified root mean square analysis of fluctuations, is used to quantify the structure of variability in locomotion. Using DFA, long range correlations ($\alpha$) are calculated in over ground running and the influence of injury and fatigue on $\alpha$ is examined. An accelerometer was mounted to the tibia of 18 runners (9 with a history of injury) to quantify stride time. Participants ran at their preferred 5K pace ± 5% on an indoor track to volitional fatigue. Mean, standard deviation (SD), coefficient of variation (CV) and $\alpha$ of stride times were calculated for three intervals of the run. Averages for all variables were calculated per group for statistical analysis. No significant interval, group or interval x group effects were found for mean, SD or CV of stride time. A significant linear trend in $\alpha$ for interval occurred with a reduction in $\alpha$ over the course of the run ($p = 0.01$) indicating that over the run, runners were more unpredictable in their stride time, likely due to movement errors associated with fatigue necessitating frequent corrections. The injury group exhibited lower $\alpha$ ($M = 0.79$, $CI_{95} = 0.70, 0.88$) than the no injury group ($p = 0.01$) ($M = 0.96$, $CI_{95} = 0.88, 1.05$); a reduction hypothesized to be
associated with altered complexity. Overall, these findings suggest injury and fatigue influence neuromuscular output, as measured by \( \alpha \), during running.

**Introduction**

Running is a complex task involving the coordination of the trunk and extremities. The coordination arises from the interaction of the nervous system and the musculoskeletal system of the runner with the environment. Previous research has shown that the time it takes to complete one gait cycle during both walking and treadmill running of healthy persons is stable with little variation (coefficient of variation (CV), ~4% and 1.3% respectively). However, the structure of this cycle to cycle variability is not random; rather patterned fluctuations are present that exhibit long range correlations (Hausdorff, 1995; Hausdorff et al., 1999; Jordan et al., 2006).

Variability in human movement is no longer considered random noise in the system. Rather across a variety of tasks, variability seems to have a functional purpose with a window of optimal variability that is dependent on the task. Variability has been postulated to be important for exploration, distribution of tissues stress, and flexibility to adapt to an ever changing environment (Glass & Mackey, 1988). While magnitudes of distributional measures of variability (standard deviation (SD) and CV) offer insight into system organization, one cannot assess patterns in the variability with these measures alone. Identification of patterns within the fluctuations of movement dynamics strengthens the postulate that variability is in fact functional and not random.

Detrended fluctuation analysis (DFA) has been used to study long range correlations in running and walking stride times (Hausdorff, 1995; Jordan et al., 2006), and is a modified
root mean square analysis of a random walk that produces a self-similarity parameter, $\alpha$. White noise, $\alpha$ equaling 0.50, corresponds with a random walk where one data point in time is uncorrelated with previous data points. An $\alpha$ value between 0.50 and 1.0 is indicative of the presence of persistent long-range correlations (a pattern of stride times that continues over many strides and results in a predictable pattern). Less than 0.50 is considered evidence of long term anti-correlations (a short stride time followed by a long stride time and vice versa, an error corrective strategy). Values greater than 1.0 indicate the existence of long term correlations, but they no longer decay according to the power law (Goldberger et al., 2000; Peng et al., 1993).

In healthy persons, variability and the structure of the variability are speed dependent. Variability and $\alpha$ of stride time both increase with gait speeds faster and slower than preferred speeds (Hausdorff et al., 1996; Jordan, 2007; Jordan et al., 2007). Jordan et al. (2006) suggests that running speeds away from preferred is a biological stressor that results in a more predictable structure of stride time variation and a subsequent loss of system adaptability. Thus, the system’s response to a greater control problem is to effectively reduce the dynamical degrees of freedom using a “control strategy” resulting in a more patterned structure of stride time fluctuations.

However with neurologic disease and elderly fallers, stride time variability increases, but $\alpha$ of stride time during walking decreases (Hausdorff et al., 1997; Hausdorff et al., 2001b; Herman et al., 2005). This indicates that cycle to cycle variation of stride time becomes more random and less predictable, lacking the recurrent pattern of healthy individuals. One proposed explanation for a reduction of $\alpha$ is a change in central processing associated with neurologic pathology and aging (Gates & Dingwell, 2007; Hausdorff et al.,
2001a; Herman et al., 2005). This change within central processing, among other factors, may lead to altered complexity, a less predictable output and an “error correcting strategy”. This research, in combination with evidence from healthy young adults, suggests variability and $\alpha$ are characteristics of a healthy locomotor system and an optimal window of functional variability exists for locomotion and is illustrated in Figure 1 (Goldberger et al., 2000).

Little is known about the effect of fatigue on motor control strategies in gait. In a study of upper extremity target tracking, fatigue increases movement variability (Selen et al., 2007). Temporal long term correlations have been examined in standing posture and a seated repetitive push/pull task. Corbeil et al. (2003) studied the effect of ankle plantar flexion fatigue and report center of pressure trajectories are less correlated with fatigue. Similarly, in a study of a seated goal-directed repetitive task, $\alpha$ for movement speed decreases (Gates & Dingwell, 2008). Both groups of authors suggest this decrease is due to the increase in corrective strategies (postural sway in one direction is followed by sway in the opposite direction and a short movement time is followed by a long movement time and vice versa). Corbeil et al. (2003) proposes that this reduction is due to a stiffening strategy associated with antagonist muscle recruitment and/or the central or peripheral effects of fatigue on force development. While limited in number, these studies suggest increased variability and reduction of $\alpha$, or an “error correcting” strategy occur with fatigue but is yet unstudied in gait.

During a prolonged run, runners must organize physiologic and neuromuscular responses to the environment as well as fatigue, a state in which many injuries are thought to occur (Gerlach et al., 2005; Orchard et al., 1996). In order to make the most reliable, effective and safe response, persons need to adequately explore the immediate environment,
one of the proposed roles of variability (Riccio, 1993). Therefore, it seems reasonable that runners with a history of injury may lack the functional variability needed to make the best available response to an ever changing environment. This is supported in the literature, as measures of kinematic variability are lower in injured runners (Hamill et al., 1999; Heiderscheit et al., 2002; Miller et al., 2008). However, $\alpha$ has not been examined in runners with a history of injury. Given that Jordan and Newell (2006) suggest that the increased long ranges correlations are an indicator of decreased dynamical degrees of freedom, injured runners could be expected to demonstrate greater $\alpha$ (i.e. less adaptability).

To further our understanding of the role of $\alpha$ in running and the effects of exertion and injury history, the purpose of this study was to evaluate stride time variability and $\alpha$
during a prolonged run in runners with and without a history of injury. It was hypothesized that overall variability, as measured by SD and CV, would increase over the course of the run as muscles fatigue and recruitment strategies change. However, as dynamical degrees of freedom diminish throughout the run, $\alpha$ was expected to decrease as more errors would necessitate greater corrective actions. Persons with a history of injury were hypothesized to be less adaptable, as demonstrated by higher $\alpha$ levels.

Methods

Subjects

Prior to the study, all subjects gave written informed consent and Institutional Review Board approval was obtained for this study. Participants were obtained from a population of area runners recruited by word of mouth, email lists and flyers. Persons with a history of at least one running related injury of the lower extremity that was severe enough to prohibit running for more than one week were included in the injured group. Injury severity classification scales indicate that interruption in normal training for 0 days is defined as slight; 1-3 days is minimal; 4-7 days is mild; 8-28 days is moderate and $>$28 days is severe (Fuller et al., 2006). Twenty experienced runners, 10 with a history of injury and 10 without, volunteered for this study. The injury and no injury groups were matched on gender. All runners were free from injury at the time of data collection.

Based on a priori sample size analysis using values from Jordan et al. (2006), 5 subjects were needed for paired comparisons and 8 subjects in each group were needed for group comparisons. A difference of 15% was considered clinically relevant (Butler et al., 2007; Milner et al., 2007) with an alpha level of 0.05 and 80% power. PS Power and Sample
Size Calculation was used to calculate sample size for this study (Dupont & Plummer Jr, 1990).

Protocol

A uni-axial low mass (1.7 g) accelerometer (Analog Devices, ADXL250) capable of measuring impacts up to 50 g’s was secured to the distal anteromedial tibia of each runner to quantify impacts. In runners with a history of injury, data were collected on the injured limb and data were collected on matched limbs in runners without a history of injury. The accelerometer was mounted to a 1.5 cm x 2 cm piece of thermoplastic and wrapped in soft rubber. Double sided adhesive tape was used to secure the accelerometer to the tibia with the long axis of the accelerometer in line with the longitudinal axis of the tibia. A circumferentially wrapped elastic strap and Coban (Johnson & Johnson, Arlington, TX) were used to stabilize the accelerometer against the tibia to prevent excessive movement due to the weight of the accelerometer. A waist worn data logger (BioRecorder BM4 Biomedical Monitoring Ltd., Glasgow, Scotland) recorded leg impacts with a sampling frequency of 1000 Hz.

After a 600 m warm up, participants ran at their preferred 5 K race pace ± 5% on a 300 m indoor track while data were continuously recorded. In order to ensure that subjects maintained a consistent speed, subjects were fitted with a PolarRS200SD running computer and footpod (Polar Electro Inc., Kempele, Finland). Using the pace setting, an audible alarm alerted the runner that he or she was out of predetermined acceptable speed ranges ± 5%. To ensure accurate speed calculations, the running computer was calibrated per manufacturer instructions for each runner during the warm up run. Additionally, subjects were given
feedback every lap on pace and were instructed to speed up or slow down if needed. Lap time for each lap was recorded using a digital stopwatch. Heart rate data were recorded using the auto lap function on PolarRS200SD (Polar Electro Inc., Kempele, Finland). Accelerometer, the running computer, and stopwatch were manually synchronized at the start of the run (i.e. turned on at the same time). All subjects were instructed to run until they felt they could no longer continue. Rate of perceived exertion (RPE) was recorded every 5 laps and at the end of the run.

Analysis

Custom written software was used to process the impact and lap. Accelerometer data were filtered with a 4th order Butterworth filter with a high pass cut off of 0.9 Hz and a low pass cut off of 50 Hz. Local maximum peaks above a threshold value (2 g) were identified as peak tibial accelerations and the time between peak accelerations was calculated as stride time. Only laps with acceptable velocity ranges were used for data analysis and the first lap was excluded from analysis. End of individual prolonged runs, for analysis purposes, was considered the point at which subjects were no longer able to maintain their self-reported 5k race pace (±5%). Length of run was normalized from 0% exertion to 100% exertion and segmented into three equal intervals. Stride time data were processed separately for the three intervals to examine the effect of a prolonged run. Three intervals were chosen to ensure the number of strides available for the DFA analysis within each interval were consistent with previous reports (Hausdorff, 1995; Jordan et al., 2006). The mean, standard deviation (SD), coefficient of variation (CV) and α were calculated for each interval. Heart rate data per lap were downloaded per manufacturer instructions.
Long range correlations were calculated using DFA (Goldberger *et al.*, 2000). Steps of DFA, described by Peng (1993) in the evaluation of heart rate variability, are as follows: 1) integration of a time series creating a cumulative sum 2) division of the integrated time series into equal box lengths 3) calculation of a local trend within each box by applying a least squares fit line 4) subtraction of the local trend from the integrated time series 5) calculation of the fluctuation for a given box size using root mean square analysis 6) plot the log of the fluctuation for a given box length by the log of the box length and 7) the slope of the log-log plot represents the self-similarity, or $\alpha$.

Means, SD, CV and $\alpha$ were calculated within subject for each interval. Group averages were calculated per group from subject values for the variables of interest. Data were analyzed using a two way (interval [3 levels] by group [2 levels]) repeated measures ANOVA. Prior to repeated measures testing, data were assessed for normality using the Kolmogorov-Smirnov test for normality. Non-normal data were log transformed (SD and CV). Sphericity of repeated measured was assumed if the Huynh-Feldt test result was >0.75; the test of significance with a Huynh-Feldt adjustment of the degrees of freedom was used if sphericity was not met. Comparisons of main effects were assessed using Sidak adjusted p-values. Heart rate data and RPE data were analyzed descriptively.

**Results**

Subject characteristics are reported in Table 1. Average months since injury for the injury group was 10.67 (SD 7.05). All subjects except one were able to complete the run. One female subject did not complete an adequate number of laps for the calculation of long range correlations and her data were removed from analysis. A second female subject had
extremely low tibial accelerations prohibiting accurate auto-identification of peak tibial acceleration excluding her from analysis. The average running speed for the group with a history of overuse injury and the group without a history of overuse injury were not significantly different ($p > 0.05$). The average number of strides per interval across all subjects was 661 ($CI_{95} = 590, 731$) and was not significantly different between groups. Percentage of age predicted heart rate max on the last lap obtained was also not different between groups and averaged 97% ($CI_{95} = 0.93, 0.99$).

Raw stride times during the three intervals of the run of a typical subject are illustrated in Figure 2. No interaction of interval by group existed for mean stride time, SD, CV, or $\alpha$. Mean stride time, SD and CV did not change over the course of the run $F(2) < 1, p > 0.05$. In contrast, $\alpha$ demonstrated a main effect of time, $F(2) = 6.97, p < 0.01$ with significant linear ($p = 0.02$) and quadratic trends ($p = 0.01$) ($M =1.05; 0.77; 0.81; CI_{95} = 0.89,1.21; 0.67,0.86; 0.73, 0.89$). Post hoc tests for $\alpha$ revealed that the first interval was significantly different from the second ($p = 0.01$) but the second interval was not significantly different from the last interval ($p > 0.05$) (Figure 3).

Group effects were present only for $\alpha$, $F(1) = 8.470, p = 0.01$; the injury group exhibited lower $\alpha$ ($M = 0.79, CI_{95} = 0.70, 0.88$) than the NOI group ($M = 0.96, CI_{95} = 0.88$,

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Mass (kg)</th>
<th>Height (cm)</th>
<th>Training volume (km/week)</th>
<th>Speed (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Injury</td>
<td>26.9 (11.0)</td>
<td>62.6 (8.3)</td>
<td>170.2 (10.9)</td>
<td>30.3 (9.7)</td>
</tr>
<tr>
<td>Injury</td>
<td>28.5 (10.3)</td>
<td>66.3 (7.8)</td>
<td>170.6 (9.3)</td>
<td>33.3 (12.3)</td>
</tr>
</tbody>
</table>

Table 1. Mean descriptive characteristics of groups are presented with standard deviation in parentheses. Speed reported here is their study pace determined by their preferred 5k race pace. Means are reported with standard deviations in parentheses.
Figure 1. Raw stride times of a typical subject. Visual observation reveals a reduction in the pattern of oscillations over the course of the run.
Figure 2. Long range correlations calculated from the stride time data averaged over participants. Error bars indicate 95% confidence intervals.

1.05). Statistically, mean stride time, SD and CV of stride time were not significantly different between groups, $F(1) < 4.0, p > 0.05$. Means and confidence intervals for group stride time variables are reported in Table 2.
Discussion

The purpose of this study was to evaluate the effects of a prolonged run on stride time variability and $\alpha$. Additionally, differences between runners with a history of overuse injury and runners without a history of overuse injury were examined. It was hypothesized that stride time variability would increase over the course of the run and $\alpha$ would decrease;
additionally, the injury group was expected to exhibit greater $\alpha$. No group differences in response to fatiguing conditions were expected.

Variability and $\alpha$ of stride time have previously been reported for treadmill running. The magnitude of variability in this study was higher than those reported in preferred running speeds by Jordan et al. (2006, 2007); however this could be attributed differences of running on a treadmill versus running over ground on a track. Research in both walking and running suggest variability during over ground locomotion is greater than treadmill locomotion (Dingwell et al., 2001). Lower $\alpha$ values in previous published running studies may be due to the constant motorized treadmill speed since long range correlations have been shown to break down with metronomic walking (Jordan et al., 2006). In addition, while long range correlations using DFA have been found in treadmill running, turns associated with running on a track may have imposed a pattern on the stride time and resulted in greater correlations in this study when compared to previous reports.

However, it is important to note that the subject characteristics and techniques to determine preferred speed in this study also differed from previous published reports. Previous studies of running included only females and determined preferred running speed by calibrating the treadmill speed to subjects preferred pace. In contrast, this study included males and females and asked participants to run at preferred 5k race pace, which is likely faster than their preferred speed on a treadmill. Comparison of the overall $\alpha$ level reported in this study to those reported at 120% preferred speed in Jordan et al. (2007) are more similar (0.88 vs. 0.85). However, because of the aforementioned factors, the relationship between over ground running and treadmill running on $\alpha$ remains unclear.
The α in this study across all subjects and conditions was 0.88 (CI 95 = 0.80, 0.95) and falls on the high end of the ranges previously reported for both over ground and treadmill locomotion in healthy populations (Barrett et al., 2008; Hausdorff, 2009; Jordan et al., 2007). However, in a study of treadmill walking and running, greater α occurs in running when compared to walking (Jordan & Newell, 2008). Thus, it is possible that the task of running is biologically more stressful with a greater need than walking for a control strategy.

In agreement with our hypothesis, a significant interval effect was observed for α. Runners initially demonstrated high α, likely due to the search for correct running velocity and optimal stride characteristics acting as constraints in the initial stages of the run. Consistent with previous reports of fatigue, the significant linear tread suggests an overall decrease of long range correlations over the course of the run (Corbeil et al., 2003; Gates & Dingwell, 2008; Jordan & Newell, 2008). One possible explanation provided for this reduction is an increased need for correction of movement errors. This explanation is plausible given loss of motor unit firing and force production and the more variable motor unit firing that occurs with fatigue (Contessa et al., 2009; Higham & Biewener, 2009; Selen et al., 2007). Interestingly, no significant differences existed between the middle and end portions of the run. The quadratic nature of the response to fatigue can be explained in part by loss of fast fatigable and decline of fatigue-resistant motor unit firing that occurs within the first portion of the run (Kandel et al., 2000).

As mentioned earlier, α has been shown to be influenced by neuromuscular health and speed. This is the first study to examine stride time α based on lower extremity musculoskeletal injury history in otherwise young healthy adults. In the present study, marked differences in α emerged when runners were differentiated by injury status. Runners
without a history of injury exhibited much higher $\alpha$ than the injury group. Contrary to our hypothesis, the injury group had much lower overall $\alpha$ than the no injury group. Consequently, runners with a history of appeared to use an error correcting strategy rather than a control strategy. Interestingly, looking closer at Figure 3, the range of $\alpha$ displayed by the injury group was less than the no injury group (0.24 vs. 0.35) and while not significant, magnitude of variability was also moderately lower in the injured group. Thus, the injury group was more unpredictable in their stride time and tended to operate within a more narrow range throughout the run.

An altered level of complexity may underlie the more unpredictable nature of long range correlations found in the injury group (Lipsitz & Goldberger, 1992). Complexity of the system is suggested to be influenced by impairment or loss of components (i.e. strength, cardiovascular status, balance, peripheral sensation, reflexes, proprioception) or altered interaction of components (Lipsitz & Goldberger, 1992). By all means, previous studies of injury have acknowledged altered strength, motor recruitment, lower extremity joint couplings, and balance in the role of injury. Unfortunately, measures of these components were not included in this study so a direct relationship in this population cannot be established. Assuming normal central processing in the otherwise healthy injury group, the results of this study suggest that factors other than central processing are altered in injury states.

Stride time is considered an output variable of a “multi-dimensional neuromuscular control system” (Hausdorf, 2007) and is typically associated with lower magnitudes of variability and higher $\alpha$ levels in healthy locomotor systems. Consistent with previous running research, magnitude of variability when assessed with SD and CV of stride time
were not sensitive to group differences in this study (Barrett et al., 2008). On the contrary, runners with a history of injury demonstrate decreased variability in local measures of lower extremity kinematics and coordination (Hamill et al., 1999; Heiderscheit et al., 2002; Miller et al., 2008). Stride time SD and CV, as measured in this study, are comprehensive measures of system output rather than a specific measure local function, and thus may not have been sensitive to group differences (Barrett et al., 2008; Van Emmerik et al., 1999).

Readers must exercise caution in interpreting causation of injury due to the retrospective nature of this study; at best compensatory strategies can be suggested. However, given the high likelihood of injury recurrence in running, close examination of post-injury strategies and their contribution to injury is warranted. This study does suggest that group differences can be identified with long range correlations of stride time more so than magnitude of stride time variability. Future work needs to prospectively determine the sensitivity of stride time long range correlations for injury prediction. Additionally, further studies are needed to delineate the factors that influence these long range correlations in runners to better determine the clinical implications of this study.

The role of functional variability and adaptability in gait is becoming clearer across the lifespan, across speed variations and in the presence neurologic impairment. The results of this study add to this ever growing body of knowledge of gait dynamics and suggest that both fatigue and injury status play a role in the neuromuscular control system output during running. Specifically, this research suggests that long range correlations of stride time during gait, as measured by DFA, are reduced with fatigue and injury. Thus, for the task of running a certain degree of consistency as demonstrated by higher $\alpha$ levels may be optimal.
References


CHAPTER 7. GENERAL CONCLUSIONS

General Discussion

The overall purpose of this dissertation was to explore factors that can influence the loading environment of the lower extremity with a specific goal to provide insight into injury mechanisms and potential treatment strategies.

The first study reported in this dissertation measured the effect of orthotics, a common intervention for stress fracture, on bone strain in the second metatarsal. Research on the effectiveness of orthotics in modifying bone strain is limited. Cadaveric gait simulation was used to test the effect of custom and semi-custom orthotics on second metatarsal bone strain during walking. It was hypothesized that custom and semi-custom foot orthotics would equally decrease bone strain of the second metatarsal (2\textsuperscript{nd} met). The major finding of this study was that both custom and semi-custom orthotics modified the 2\textsuperscript{nd} met bone strain and strain rate. The use of custom orthotics during simulated walking decreased 2\textsuperscript{nd} met bone strains and strain rates more effectively than semi-custom orthotics. Thus, orthotics minimize the load magnitudes and rates of the 2\textsuperscript{nd} met in walking and therefore are a feasible treatment option for the treatment and prevention of stress injury to the 2\textsuperscript{nd} met.

Bone strain measurement \textit{in vivo} is limited to cadaver tissue in most countries. Thus, alternative measures of bone strain are needed. Ground reaction forces have been used to examine skeletal loading in human locomotion, as have joint moments. However, these measures are only surrogates. Ground reaction forces reflect the acceleration of the total body, not just the support limb. Joint moments quantify patterns of force produced by muscles, ligaments and bones and produce a net effect of all the internal forces and moments.
acting across the joint. However, joint moments do not reflect forces and moments in specific anatomical structures. Ground reaction forces and joint moments make up only a portion of the total loading environment. Rather, a musculoskeletal model of running incorporating individual muscle forces can be used to estimate local bone stresses based on gait mechanics if bone geometry is known. The use of such a model allows the effect of running patterns on bone stress to be studied without invasive procedures.

Stress fractures have been associated with faulty gait mechanics, but conflicting evidence exists. The effect of stride length manipulations on lower extremity kinematics and kinetics is well studied. Conversely, few published studies have examined the effect of stride width on gait mechanics. Additionally, the relative contribution of gait mechanics to bone geometry in the stress environment is unclear. The purpose of the second study of this dissertation was to evaluate the effect step width during running on tibial bone stress using a standardized tibia model. It was hypothesized that tibial stresses would be greater in the narrow step width condition when compared to normal and wide step widths.

In general, narrow step width was associated with greater stresses and stress rates; and while not always significant, stresses and stress rates linearly declined with wider step width conditions. The findings from this study indicate that the stress environment of bone can be influenced by gait mechanics. These results have implications for rehabilitation of bone stress injury and technique training for runners. However, consideration of the overall coordination and mechanics of the system should be made prior to suggesting a change to an individual runners step width.

Given the retrospective and prospective evidence reporting faulty gait mechanics and increased ground reaction force data, it seems likely that these factors would result in greater
increased bone forces and moments, key components of bone stresses. Furthermore, evidence suggests that the timing of the application of axial and torsional loads alters fatigue life of bone. The purpose of this study was to assess differences in internal bone forces and moments and to evaluate timing differences of combined loading in persons with and without a history of tibial stress fracture. It was hypothesized that persons with a history of stress fracture would exhibit greater internal bone forces and moments in the distal tibia and would demonstrate more in-phase patterns of axial and torsional loads.

The tibia was found to be predominantly under in-phase loading of axial forces and torsional moments, but no group differences were found. No differences in internal bone forces and moments were found; although small to moderate increases in forces and moments were seen in runners with a history of stress fracture. This indicates that bone geometry may play a large role in stress fracture in this group of runners. Future models need to incorporate subject-specific bone geometry to verify these findings. While no group differences were found in the forces and moments, it is possible that small increases in bone forces and moments are magnified within the context of the smaller bone geometry and elevated levels of physical activity. Future prospective or well designed case control studies will need to incorporate measures of bone geometry and physical activity patterns to establish causation and/or predict risk. The overall degree of in-phase loading found in this study provides an explanation for the frequency of injury to the tibia.

Assessment of only one component does not adequately assess the multi-dimensional nature of gait and injury. A global measure of gait functioning is needed to facilitate future large scale studies to ascertain the interaction of the many facets of stress fracture in a prospective study design. Stride time and stride time variability is considered a global output
from a multi-dimensional system. They have been shown to be sensitive to a myriad of changes including but not limited to age, speed, and neurologic disease. Additionally, they are predictive of falls in elderly. Healthy gait is characterized by a certain degree of consistency in the pattern of stride times, as demonstrated by long range correlations. However, an optimal window of long range correlations exists: 1) too high and flexibility to adapt to the environment may be limited 2) too low and a less predictable output emerges.

The purpose of the final study of this dissertation was to evaluate the effect of a prolonged run on stride time variability and long range correlations in persons with and without a history of injury. Over an exhaustive run, it was hypothesized that variability would decrease and the structure of that variability, as measured with long range correlations, would become less patterned (i.e. lower long range correlations). Secondly, persons with a history of lower extremity injury were hypothesized to have less variability and be more patterned (i.e. higher long range correlations).

Over the course of the run, runners were more unpredictable in their stride time and exhibited lower long range correlations. This is likely due to movement errors associated with fatigue necessitating frequent corrections. Contrary to our hypothesis, the injury group exhibited lower long range correlations. The lower long range correlations in the injured group may be attributed to altered complexity of the system. Complexity of a system is influenced by the loss of components or the loss of coupling between components (i.e. strength, coordination, range of motion, etc.). These findings suggest injury and fatigue influence neuromuscular output, as measured by long range correlations, during running and that long range correlations are sensitive to injury status. Future work needs to prospectively
determine the sensitivity of stride time long range correlations for injury prediction. Additionally, factors that alter these long range correlations need to be identified.

**Significance of Research**

The outcomes of this dissertation provide an overview of skeletal loading and methods used to measure musculoskeletal loads. Clinical implications exist for both the etiology of and the potential intervention for stress injury to bone. The work presented contributes to the general body of knowledge and offer a deeper understanding of the following: 1) bone loads can modified by gait mechanics and orthotics 2) when assessed apart from effect modifiers, the internal loading environment of the tibia is not associated with stress fracture in recreational runners, and 3) gait dynamics of running are influenced by fatigue and injury status.

**Recommendations for Future Research**

The methodology and study designs used in this dissertation are not without limitations. First, in humans, gait characteristics may change depending on the internal and external environment. It is well reported not all individuals respond similarly to interventions. Thus, future work needs to examine individual response to footwear changes. Subject specific characteristics may determine response to interventions such as orthotics and footwear changes, but are not clearly defined currently. This will likely require the application of a single subject design nested within a group design study.

Future work needs to examine the role of step width in injury as this remains unclear. Group comparisons of injured runners need to include subject specific characteristics, such as
underlying bone geometry, to fully capture the stress environment of the tibia. Once accomplished, data can be incorporated with probabilistic models for subject specific stress fracture prediction models. Additionally, the bone stresses obtained could be used in conjunction with other health history and physical activity patterns to determine the key factors associated with the odds of injury. However, the utility of these models on a large scale for injury prediction is limited. Rather a simple measure that is predictive of injury status would be easier to incorporate into epidemiological studies. The results of the final study in this dissertation are promising, as the pattern of stride time variability was sensitive to injury status.

In summary, from a clinical and research perspective, the interaction of the multiple factors that can lead to stress fracture remains unclear and difficult to study. In order to incorporate dynamic movement into the study design, a global output variable is needed. Only then will we be able to create accurate prediction models for stress fracture. This line of research is important because the ability to identify optimal patterns of bone loading throughout the lifespan is crucial for identification of exercise patterns to promote bone health yet minimize injury.
COMPLETE REFERENCE LIST


