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In vivo strains at the middle and distal thirds of the tibia during exertional activities

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ABSTRACT

There is a known variance in the incidence and anatomical site of tibial stress fractures among infantry recruits and athletes who train according to established uniform training programs. To better understand the biomechanical basis for this variance, we conducted *in vivo* axial strain measurements using instrumented bone staples affixed in the medial cortex, aligned along the long axis of the tibia at the level of the mid and distal third of the bone in four male subjects. Strain measurements were made during treadmill walking, treadmill running, drop jumps from a 45 cm height onto a force plate and serial vertical jumps on a force plate. Significance levels for the main effects of location, type of activity and their interaction were determined by quasi-parametric methodologies. Compared to walking, running and vertical jumping peak axial tensile strain (με) was 1.94 ($p = 0.009$) and 3.92 times ($p < 0.001$) higher, respectively. Peak axial compression strain (με) values were found to be greater at the distal third than at the mid tibia for walking, running and vertical jumping ($PR = 1.95$, p-value<0.001). Peak axial compression and tension strains varied significantly between the subjects (all with $p < 0.001$), after controlling for strain gauge location and activity type.

The study findings help explain the variance in the anatomical location of tibial stress fractures among participants doing the same uniform training and offers evidence of individual biomechanical susceptibility to tibial stress fracture. The study data can provide guidance when developing a generalized finite element model for mechanical tibial loading. For subject specific decisions, individualized musculoskeletal finite element models may be necessary.

1. Introduction

Stress fracture is considered to be initiated by repetitive loading, of a magnitude exceeding or in a direction different from the usual bone stress environment. Accordingly, anatomical sites within a bone that experience the highest strains should be the most prone to develop stress fracture. The tibia is a common site of stress fracture in runners and infantry recruits (Fredericson et al., 2006; Matheson et al., 1987; Waterman et al., 2016). A survey of the anatomical locations of tibial stress fractures among athletes found that they occurred along the entire length of the tibia, with the most frequent site being at the level of the junction of the middle and distal thirds (Orava, 1980). In a prospective military study among infantry recruits, most tibial stress fractures were found to occur in the middle third of the tibia (Milgrom et al., 1985). Most occur in the posteromedial cortex (Milgrom et al., 2015).

The variance in the incidence and anatomical level of tibial stress fractures among athletes is readily explainable by the wide variety of training and sport activities they perform. The reason for such variances among military recruits who train according to an established uniform protocol is less clear because all are subjected to similar bone loading (Milgrom and Finestone, 2017). Based on prospective clinical studies and epidemiological data, individual risk factors for stress fracture have

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been identified (Cosman et al., 2013; Giladi et al., 1991; Jepsen et al., 2013; Nunns et al., 2016). While multiple risk factors have been found, the maximum variance explained by these factors has been reported to be low (Cosman et al., 2013).

To understand the strain environment in the tibia during exertional activities, *in vivo* strain gauge measurements at the level of the mid-shaft have been performed during activities that mimic those of military recruits and athletes (Burr et al., 1996; Lanyon et al., 1975; Milgrom et al., 2000). Simultaneous *in vivo* strain measurements from the anterior mid-diaphysis and posteromedial distal tibia have been reported in a single subject (Ekenman et al., 1998). The goals of the present study were to better understand the inter-subject variance of medial tibial strains during exertional activities and to see how this might reflect susceptibility to medial tibial stress fracture and the predilection of most to occur either in the middle third or at the junction of the middle and distal thirds of the diaphysis. The study hypothesis was that the peak axial compression and tension strains during exertional lower extremity activities would be higher at the distal third than at the middle third of the tibia. We report the simultaneous *in vivo* tibial axial strain measurements at the middle and the distal thirds of the tibia in a group of subject volunteers while they performed standardized lower extremity exertional activities.

2. Materials and methods

2.1. Participants

Permission to perform *in vivo* tibial strain measurements in four adult subjects using instrumented bone staples was received by the Helsinki Committee of the Hadassah Medial Organization (Ref: device-457-HMO). Subject recruitment was limited to males between the ages of 21 to 40, with physically active life styles and no history of orthopaedic knee, or leg problems. Subjects received no financial or other benefits and signed informed consent.

2.2. Instrumented bone staples

Instrumented bone staples made from16 × 15 mm bone staples (CONMED, Utica, New York, USA) with a MicroMeasurements EA-06-031DE-350 strain gauge (Measurements Group Inc., Raleigh, North Carolina, USA) bonded to the undersurface of the staple, were used to measure *in vivo* axial tibial strains in four adult male subjects (Rolf et al., 1997; Milgrom et al., 2000). Two strain gauged staples were implanted percutaneously under local anesthesia, aligned along the long axis of the bone in the flat medial aspect of the left tibia, closer to the posterior than anterior border. The proximal gauge was centered at a point corresponding to the mid diaphysis. The distal gauge was centered at the point corresponding to the distal third of tibia (Fig. 1).

The surgical technique for applying the strain gauged staples has previously been described (Rolf et al., 1997; Milgrom et al., 2000). The surgical wounds were left open and were dressed with a gauze dressing. Exiting wires from the strain gauges were connected by a cable to a strain gauge conditioner (Model 2120A, Measurement Group, Inc.).

2.3. Data collection

Data were sampled at 1000 Hz and recorded using a digital data collection software (BioWare, Kistler, Switzerland). Data were imported into MATLAB (The MathWorks Inc., Natick, MA) for analysis. A Fast Fourier Transform function was utilized to remove high frequency noise. A cutoff frequency of 30 HZ was chosen as the fundamental frequency at which all *in vivo* activities were included and hence all frequencies above this range were considered to be noise. Ground reaction forces were recorded by means of a floor-mounted piezoelectric force plate and analysis done using a biomechanical software analysis system (BioWare, Kistler Instrumente AG, Winterthur, Switzerland). Ground reaction forces were used to determine the sequence of activities. Simultaneous *in vivo* axial tibial strain measurements were made for subjects at the mid diaphysis (proximal strain gauge) and distal third of the diaphysis (distal strain gauge) while wearing Nike running shoes during the following activities: treadmill walking at a speed of 5 km/h; treadmill running at a speed of 13 km/h, drop jumps from a 45 cm height onto a force plate; serial jumps on a force plate. An instructor demonstrated to the subjects how the drop jumps and serial jumps should be performed prior to the recordings, but no practice trials were done. Activities were not filmed. At the beginning of each activity recording the left leg was lifted from the ground so as to establish the no strain baseline. At the conclusion of the experiment the strain gauged staples were removed under local anesthesia, prophylactic antibiotics given and the wounds sutured.

2.4. Statistical analysis

Absolute values of peak axial compression strain (με) were used in the analysis. No other transformations were applied to these values, as well as to tension measurements.

Normality of peak axial tension and compression strain (με) parameters was assessed using Shapiro-Wilk test, which indicated a statistically significant departure from this distribution. Likewise the logarithmic transformation of peak axial tension and compression strain (με) did not normalize the values sufficiently to meet normal distribution assumptions. Homogeneity of variance across the subgroups used for comparison, *i.e.* distal *vs.* proximal, and mode of activity, *i.e.* running, jumping and walking, was estimated by Levene's test. Based on this test, heterogeneity of variances was observed in the majority of comparisons.

Fig. 1. Instrument staples at the level of the middle and distal third of the tibia along the flat medial border.

As the distribution of peak axial tension and compression strains (με) did not follow the assumption of the Normal distribution, the nonparametric test (Wilcoxon) was chosen for comparing these values within each subject. Furthermore, for analyzing peak axial compression and tension strains we used quasi-parametric methodologies. Specifically, we used generalized estimating equations (GEE) coefficient approach to account for clustering effect of repeated observations belonging to the same subject. We used Poisson distribution as the basis for modeling, where Pearson scaling was performed to correct for over-dispersion. Likewise, we chose a conservative sandwich estimator approach for estimating standard errors while comparing between locations and activities. These models provided the significance levels for the main effects of location, type of activity and their possible interaction. The magnitude of a difference between the subgroups was presented by prevalence ratio (PR), calculated as an exponent of the regression coefficient, which reflects the multiplicative effect of one subgroup over another, *e.g.* of jumping as compared to walking, *etc*.

The analysis was performed using SAS 9.4 (SAS Institute, Cary NC).

3. Results

3.1. Subject details

Technically successful recordings were made from both strain gauged staples for all activities in three out of the four study subjects, with the exception of Subject 1 who only performed one drop jump. Subject 1 was a 38 year-old male, height 187 cm and weight 80 kg. Subject 2 was a 40 year-old male, height 178 cm and weight 82 kg. Subject 3 was a 29 year-old male, height 181 cm and weight 83 kg. None of the subjects experienced tibial pain during the experimental recordings.

Two of the four subjects developed mild discomfort at the site of the distal staple three weeks post-experiment. The discomfort resolved in one subject after three months and after six months in the other. There were no signs of infection.

3.2. Examples of strain output for each activity performed

Fig. 2 illustrates the proximal and distal strain gauge outputs for Subject 1 while performing treadmill walking and running.

Fig. 3 illustrates the inter subject differences in proximal and distal strain gauge outputs while performing serial vertical jumps on a force plate.

Fig. 4 illustrates the proximal and distal strain gauge outputs for Subject 2 while performing a vertical drop on a force plate.

3.3. Strain comparison by location and activity

Table 1 compares the mean peak axial compression and tension strains for each activity performed for the three subjects. Compared to walking, running and jumping activity peak axial tension was 1.94 ($p = 0.009$) times and 3.92 ($p < 0.001$) times higher, respectively. Peak axial compression strain (με) values were found to be greater at the distal third than at the mid tibia for walking, running and vertical jumping (PR = 1.95, p-value$<$0.001). The peak axial compression and tension measures varied significantly between the subjects (all with $p < 0.001$), after controlling for location and activity type.

4. Discussion

This study made simultaneous *in vivo* measurements of axial tibial strains at two anatomical levels. Both were along the medial tibial border closer to the posterior than the anterior aspect, with one at the level of the midshaft and the other at the level of the distal third of the tibia, sites where there are high incidences of stress fracture (Orava, 1980; Milgrom et al., 1985). Because successful data collection was limited to three subjects, statistical analysis was done using quasi-parametric methodologies. The peak axial compression and tension strains varied significantly between the subjects (all with $p < 0.001$), after controlling for location and activity type. This finding indicates that there may be individual trainees within a uniform training cohort

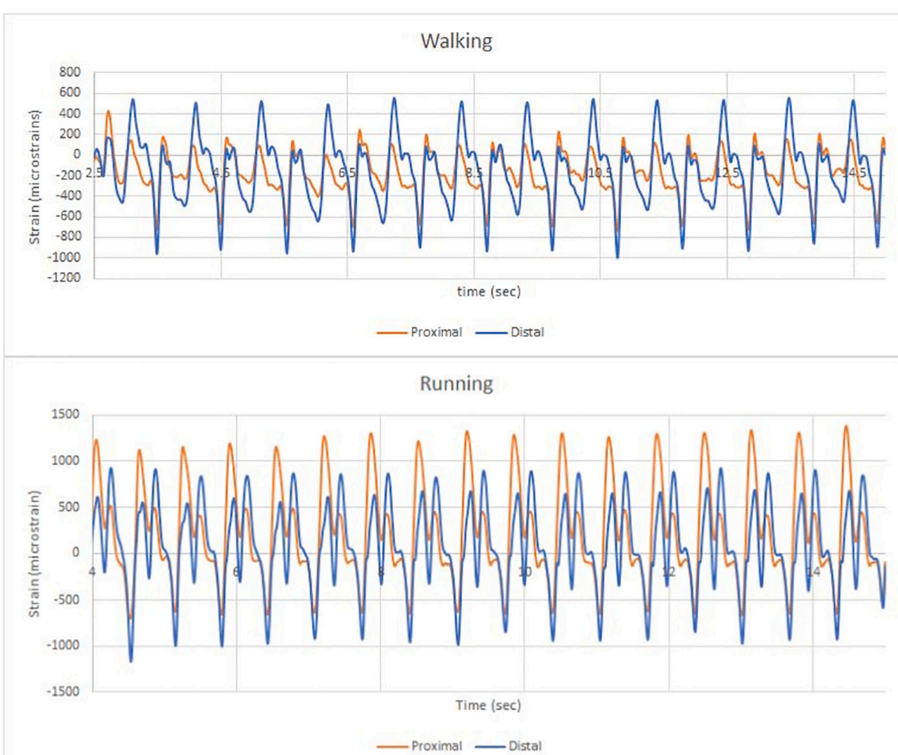

Fig. 2. Proximal and distal tibial strains during treadmill walking and running for Subject 1. The interval between two vertical lines represented 2 s of time.

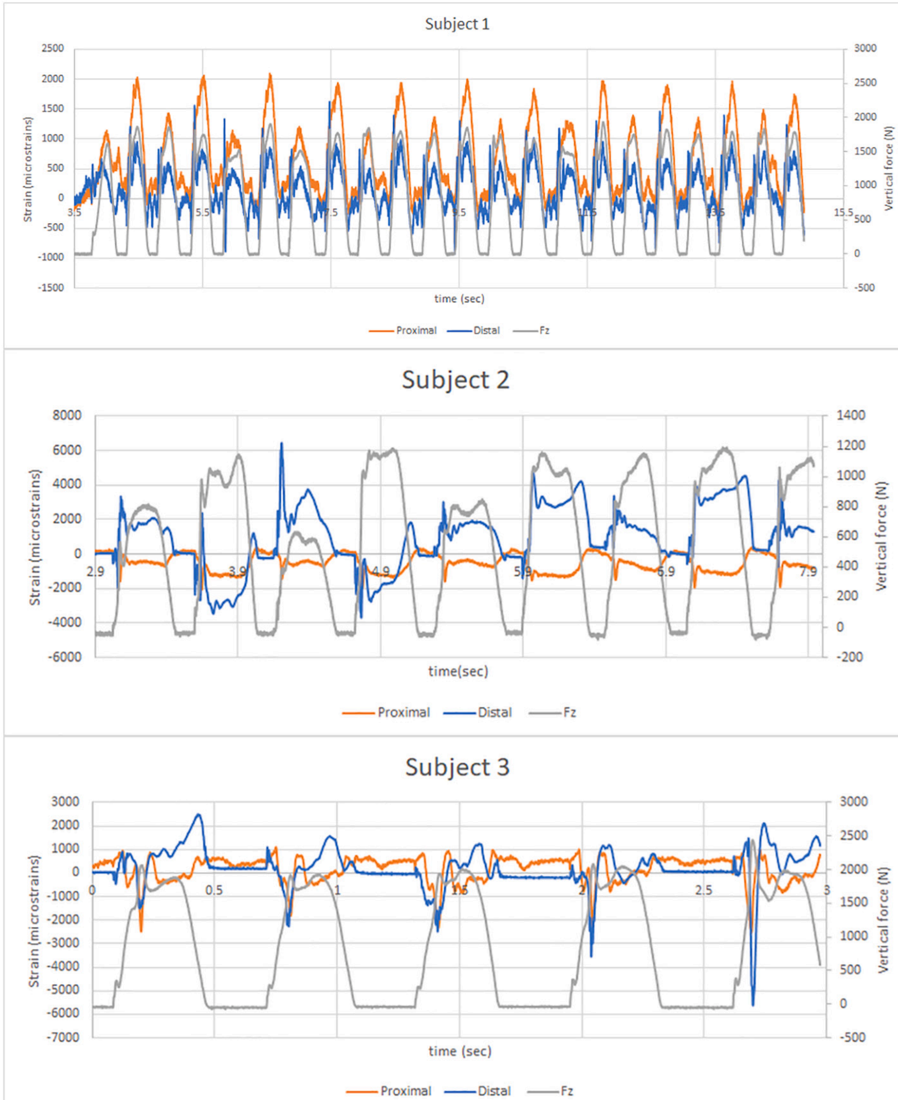

Fig. 3. Inter subject differences in proximal and distal tibial strains while performing serial vertical jumps on a force plate for three subjects. The interval between two vertical lines represents 0.5 s of time. Strain output from the proximal gauge is presented in green, from the distal gauge in blue and from the force plate in grey.

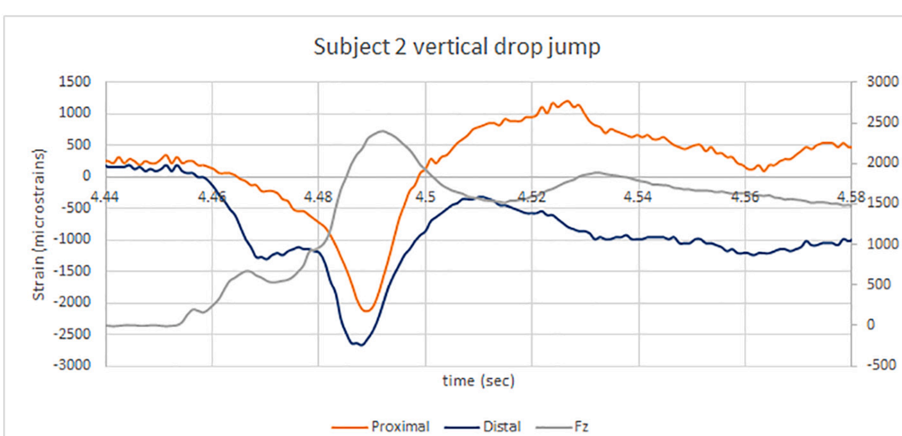

Fig. 4. The differences in proximal and distal tibial strains while Subject 2 performed a vertical drop jump on a force plate. The interval between two vertical lines represents 1 s of time. Strain output from the proximal gauge is presented in green, from the distal gauge in blue and from the force plate in grey.

Table 1
Summary of the peak axial tibial strains from the middle of the tibia (proximal gauge) and the distal third of the tibia (distal gauge). Statistical analysis is for treadmill walking, treadmill running and vertical jumps. Drop jumps are not included in the analysis because of the low number of repetitions.

Activity	Cycles	Mean peak axial compression Mean ± SD Median				Mean peak axial tension Mean ± SD Median			
		Proximal gauge	Distal gauge	p value (Wilcoxon test)	p value for comparison between activities, based on GEE model[a]	Proximal gauge	Distal gauge	p value (Wilcoxon test)	p value for comparison between activities, based on GEE model[a]
Treadmill walking					Reference				Reference
Subject 1	11	−696.6 ± 22.9 −691.2	−936.5 ± 28.9 −932.4	0.002		187.0 ± 37.2 194.3	532.5 ± 19.0 533.8	<0.001	
Subject 2	10	−135.4 ± 29.6 −129.2	−927.5 ± 19.9	0.001		439.8 ± 39.4 455.1	351.6 ± 18.3 352.7	0.001	
Subject 3	14	−493.0 ± 25.3 −503.2	−459.6 ± 78.5 −465.2	0.070		90.9 ± 27.4 86.9	865.9 ± 27.6 858.9	<0.001	
Treadmill running					0.106[b] (PR = 0.95)				<0.009[b] (PR = 1.94)
Subject 1	18	−631.2 ± 48.0 −643.6	−933.4 ± 114.2 −940.7	<0.001		1256.0 ± 77.9 1281.6	878.6 ± 31.1 875.3	<0.001	
Subject 2	16	−101.6 ± 115.1 82.7	−1364.7 ± 183.1 −1400.3	<0.001		791.8 ± 47.7 787.2	778.6 ± 23.1 778.0	0.534	
Subject 3	18	−268.5 ± 31.7 −259.5	−1950.9 ± 932.3 −1437.7	<0.001		286.5 ± 39.4 286.5	703.2 ± 296.8 858.7	0.002	
Vertical jumps					0.479[c] (PR = 0.93)				<0.001[c] (PR = 3.92)
Subject 1	21	−242.0 ± 237.8 −222.3	−491.5 ± 230.2 −476.4	0.003		1651.0 ± 342.8 1143.3	1117.6 ± 290.3 1175.1	<0.001	
Subject 2	9	−1722.0 ± 242.8 −1587.9	−1231.6 ± 1303.5 −698.7	0.145		305.7 ± 58.7 317.6	3874.5 ± 1470.5 3350.5	0.002	
Subject 3	5	−2280.2 ± 287.0 −2318.3	−3074.2 ± 1598.4 −2477.1	0.674		*1003.6 ± 65.9 984.5	1740.0 ± 563.4 1587.9	0.012	
p value for comparison of distal to proximal location, based on GEE model		0.001 (PR = 1.95)		0.002 for interaction between distal location and running; 0.251 for interaction between distal location and jumping		0.347 (PR = 1.37)		0.028 for interaction between both locations and running 0.693 for interaction between both locations and jumping	
Drop jumps									
Subject 1	1	−158.8	−1270	n/a		1588	2670	n/a	
Subject 2	3	−2370 ± 3676	−2085 ± 122	n/a		519.0 ± 720.0	603.0 ± 3240	n/a	
Subject 3	3	−1757 ± 363	−6440 ± 946	n/a		688.0 ± 79.2	254.0 ± 51.9	n/a	

[a] Significance levels represent the findings based on Poisson models, where compression and tension parameters were regressed over activity type, location and their interaction. P values < 0.05 are considered to be statistically significant.
[b] Compares running activity to walking (the reference activity). PR (prevalence ratio) represents a multiplicative effect of running as compared to walking.
[c] Compares vertical jumps to walking (the reference activity). PR (prevalence ratio) represents a multiplicative effect of jumping as compared to walking.

who experience different peak axial tibial compression strains than those of their fellow trainees. If these strains are higher, then they would be more likely to sustain tibial stress fracture (Yerby and Carter, 2000).

Peak axial compression strain was found to be higher at the distal third of the tibia than at the mid-diaphysis (PR = 1.95, $p < 0.001$), but no similar relationship was found for tension. This may help to explain the observed increased predilection for tibial stress fracture to occur at the junction of the middle and distal tibia in runners (Orava, 1980). Peak axial compression strain was not found to be higher during running than during walking in this study, both of which were performed on a treadmill. Compression strains during free running may be expected to be considerably different. In a comparison study, peak axial compression strains at the mid-tibial diaphysis were found to be 2.9 times higher during free running compared to treadmill running (Milgrom et al., 2003). The effect of increased muscle force used to perform activities is reflected by the tension being 1.94 times higher during running and 3.92 times higher during vertical jumping compared to walking.

Human *in vivo* long bone surface strain gauge measurements are difficult to perform. Only a few *in vivo* human long bone surface strain experiments have been reported (Lanyon et al., 1975; Burr et al., 1996; Aamodt et al., 1997). Application of surface strain gauges requires invasive surgery and there can be a high degree of technical failure including gauge de-bonding (Burr et al., 1996). Surface strain gauge bonding to bone has been achieved either by using cyanoacrylate adhesive or polymethyl methacrylate (Hoshaw et al., 1997). Accurately duplicating the gauge application between specimens is also difficult because gauges are placed freehand. This leads to differences in alignment. To overcome these problems, the technique of instrumented bone staples was developed (Rolf et al., 1997). The advantage of this instrument is that it is applied percutaneous and its fixation is robust. This also makes subject recruitment easier (Milgrom et al., 2000). Because of these advantages, this study used instrumented bone staples to measure strain. Two of the study subjects developed mild but bothersome discomfort at the distal strain gauge site three weeks after bone staple removal. The symptoms fully resolved subsequently, but its occurrence shows that even the percutaneous instrumented bone staple technique is not always completely benign.

No test-retest reliability studies of *in vivo* bone surface strain gauge measurements or instrumented bone staple measurements have been reported. A comparison study of surface strain gauges with instrumented bone staples has been reported using cadaver specimens tested in a dynamic gait simulator (Milgrom et al., 2004). The axial output of both gauge types demonstrated a strong linear relationship for the tibia ($r^2 =$ 0.78–0.94). The coefficients between the gauges were found to vary between measurements made in the tibia and metatarsal. Davies (2009) reported an *ex vivo* calibration and validation of *in vivo* equine bone strain measurements done in the third metacarpal of thoroughbred racehorses using surface strain gauges. After completing *in vivo* trials, animals were euthanized and the strain gauged third metacarpals harvested. An additional strain gauge was bonded just proximal to the existing strain gauge. In subsequent *ex vivo* mechanical testing, 11/14 of the gauges used for *in vivo* testing had output within 80–115% of that of the newly bonded proximal gauges and three showed markedly reduced function.

The problem of developing a general musculoskeletal finite element model for tibial mechanical loading is evidenced by the study finding that peak axial compression and tension strains varied significantly between the subjects, after controlling for location and activity type. Hadid et al. (2018) reported a finite element model for tibial stress fracture. There was no clinical correlation with the site they reported as having the highest strains, the anterior cortex, with the usual location of tibial stress fracture in soldiers and runners. These occur predominantly in the posteromedial cortex. The strain magnitudes found in their model are also much lower than those found in this study and in other *in vivo* recordings (Milgrom et al., 2007). Xu et al. (2020) reported the importance of individualized musculoskeletal finite element models in assessing mechanical loading in different individuals.

The present study is limited in that the strain recordings are only from three male subjects (O'Leary et al., 2021) in a non-fatigued state (Milgrom et al., 2007) and that only axial strains were measured. We had initially planned to apply for a continuation of the study after completing the four subjects allowed in our IRB approval. Because of the prolonged discomfort experienced by two of the subjects at the site of the distal strain gauged staple beginning several weeks after it was removed, we thought it not proper to continue implanting gauges at this site. Additionally, tibial CT scans were not performed in this study. Without such scans we were not able to assess the effect of tibial morphology on strain magnitudes and patterns. Repetitive high strains or strains with an unusual pattern are considered to initiate stress fracture. In a prospective study using standardized AP and lateral radiographs, a correlation was found between tibial mediolateral diaphyseal width and stress fractures incidence among infantry recruits. Those with narrower tibias had a higher incidence of both tibial and femoral stress fractures (Giladi et al., 1987). The present study however is unique in that it is the first to compare strains simultaneously from two sites in the same bone in multiple subjects.

5. Conclusions

This study found larger peak axial compression stains at the distal gauge than at the proximal gauge. The proximal gauge was located at the middle and distal gauge at the junction of the middle and distal thirds, along the posteromedial aspect of the tibia. Repetitive loading at an anatomical location where high strains occur increases the location's risk for stress fracture. This helps explain the higher predilection of runners to develop stress fractures at the junction of the middle and distal tibia. The study also offers evidence of individual biomechanical susceptibility to tibial stress fracture based on a variance in compression and tension strains between subjects, after controlling for activity and strain measurement location. The study is unique in that it measured simultaneously strains from two anatomical sites in the tibia, in multiple subjects, during exertional activities. The study data can provide guidance when developing a finite element model of tibial loading. Such a model can potentially help in the design of effective athletic and military training programs to decrease tibial stress fracture risk. For subject specific decisions, individualized musculoskeletal finite element models may be necessary.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CRediT authorship contribution statement

Charles Milgrom: Conceptualization, Methodology, Writing – original draft, Writing – review & editing. **Arkady Voloshin:** Formal analysis. **Lena Novack:** Formal analysis, Writing – review & editing. **Yael Milgrom:** Project administration, Funding acquisition. **Ingrid Ekenman:** Investigation, Supervision. **Aharon S. Finestone:** Methodology, Investigation, Writing – review & editing.

Declaration of competing interest

None of the authors has a conflict of interest.

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