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TITLE: Mechanisms Underlying Stress Fracture and the Influence of Sex and Race/Ethnicity

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14. ABSTRACT

This cross-sectional clinical study aims to examine potential mechanisms contributing to stress fracture risk. In Aim 1 we will perform advanced skeletal imaging along with gait-assessments in subjects with history of a single vs multiple vs no prior stress fractures. In Aim 2 we will perform advanced skeletal imaging to delineate variation in skeletal features according to sex and race/ethnic-origin that may contribute to or protect from stress fracture. To date, we have achieved the enrollment goal for Study 1 of 45 subjects, 42 of whom have completed all study visits. Data collection and cleaning are ongoing, and preliminary analysis has been performed for biomechanical and bone microarchitecture data. For Aim 2, 146 subjects (81% of targeted enrollment) have been enrolled and have completed testing. Data collection and cleaning are ongoing.

15. SUBJECT TERMS

Stress fracture, bone stress injury, gait analysis, bone microarchitecture, race/ethnic origin, sex-related differences, bone biomechanics, skeletal alignment

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Introduction

Lower extremity stress fractures are one of the most common musculoskeletal injuries plaguing military recruits, causing lost-duty days and delays in completion of military training more so than any other training-related injury. Furthermore, stress fracture recurrence poses a particular problem, as 10.6% of recruits with a history of stress fracture will sustain a new stress fracture within one year of the initial injury. Disparities in stress fracture incidence are also known to exist based on both sex and race/ethnicity, but the origins of these discrepancies are incompletely understood.

Our first aim (*Study 1*) is a cross-sectional study designed to determine differences in bone structure, bone quality, skeletal alignment and gait mechanics in female athletes with recurrent stress fractures (n=15), a history of one stress fracture (n=15), or no history of stress fracture (n=15). The discrepancies in these parameters between groups will help to explain underlying differences in women who experience stress fracture recurrence.

Our second aim (*Study 2*) is a cross-sectional study designed to assess the race/ethnicity- and sex-based differences in bone structure, bone quality, and skeletal alignment in Asian, Black, and Caucasian men and women (n=30 for each group; n=180 total). This will serve to identify factors that contribute to the differences in stress fracture incidence due to race/ethnicity and sex.

Keywords: stress fracture, bone stress injury, gait analysis, bone microarchitecture, race/ethnic origin, sex-related differences, bone biomechanics, skeletal alignment

Accomplishments

Major Goals

The objectives, timeline, and status for the project are shown below in Table 1. Major goals for year 2 included continuing to recruit and enroll participants in Study 1, acquiring and analyzing HR-pQCT images, performing standard whole bone finite element analysis, performing EOS and DXA scans and reference point indentation, performing biomechanical analysis, and beginning data cleaning and statistical analysis.

	Objective	Timeline	Site	Status
Study 1	1) Obtain Institutional Review Board (IRB) approval	Quarter 2	MGH	*Complete*
	2) Obtain Human Research Protections Office (HRPO) approval	Quarter 2	MGH	*Complete*
	3) Recruit and enroll 45 subjects [15 women athletes with multiple stress fractures, 15 women athletes with one stress fracture, 15 women athlete healthy controls; 15 in year 1-3]	Quarters 2-12	MGH	*42/45 complete*
	4) Acquire and analyze high-resolution peripheral quantitative computed tomography (HR-pQCT) images for 45 subjects	Quarters 2-12	MGH	*42/45 complete*
	5) Perform standard whole bone finite element analysis	Quarters 3-14	MGH	*42/45 complete*
	6) Perform EOS and DXA scans and reference point indentation (RPI) for 45 subjects	Quarters 2-12	MGH	*42/45 complete*
	7) Perform biomechanical analysis for 45 subjects	Quarters 2-12	SNRC	*42/45 complete*
	8) Perform data cleaning and statistical analyses	Quarters 3-14	MGH, SNRC	*Ongoing*
	9) Renew IRB approval	Quarters 4, 8, 12	MGH, SNRC	*Will renew in Feb. 2020*
Study 2	1) Obtain Institutional Review Board (IRB) approval	Quarter 2	MGH	*Complete*
	2) Obtain Human Research Protections Office (HRPO) approval	Quarter 2	USARIEM	*Complete*
	3) Recruit and enroll 180 subjects [30 per group: Asian women, Black women, Caucasian women, Asian men, Black men, Caucasian men; equal enrollment years 2, 3, and 4]	Quarters 2-12	MGH	*146/180 complete*
	4) Acquire and analyze high-resolution peripheral quantitative computed tomography (HR-pQCT) images for 180 subjects	Quarters 4-12	MGH	*146/180 complete*
	5) Perform standard whole bone finite element analysis	Quarters 5-14	MGH	*146/180 complete*
	6) Perform EOS and DXA scans and reference point indentation (RPI) for 180 subjects	Quarters 4-12	MGH	*146/180 complete*
	7) Perform data cleaning and statistical analysis	Quarters 5-14	MGH	*Ongoing*
	8) Develop race-, sex-, and age-specific databases of bone microarchitecture, reference point indentation, and skeletal alignment	Quarters 5-14	MGH	*Ongoing*
	9) Renew IRB approval	Quarters 4, 8, 12	MGH	*Will renew in Feb. 2020*

Table 1. Status of objectives and goals as listed in Statement of Work (SOW)

Accomplishments

Initial approvals from the Institutional Review Board (IRB) at Massachusetts General Hospital (MGH) and from Human Research Protections Office (HRPO) were received on February 24, 2017 and on March 10, 2017, respectively. These items were completed according to schedule. We renewed our IRB protocol in February 2018, February 2019, and will renew it again in February 2020.

We recruited subjects for Study 1 via letters sent to patients with a stress fracture diagnosis as identified by their physician or the Partners Research Patient Data Registry, advertisements on the Partners Clinical Trials website, recruitment flyers posted in the greater Boston area, and recruitment emails sent to local running clubs and college coaches. Through these avenues, we enrolled a total of 48 female athletes for Study 1: 17 with multiple stress fractures, 15 with a single stress fracture, and 16 without a history of stress fracture. Of these, 47 subjects who were enrolled in the study successfully completed the treadmill run and biomechanical gait analysis at the Spaulding National Running Center (SNRC) (Study 1, Objective 3). One multiple stress fracture subject was unable to complete the treadmill run and gait analysis at SNRC and was thus withdrawn from the study.

To date, 42 subjects have completed all requirements for the study. One multiple stress fracture subject sustained an injury to her ACL and underwent surgery prior to her MGH study visit; since she no longer met the inclusion criteria for physical activity, she was withdrawn from the study. An additional two subjects with multiple stress fractures, one subject with a single stress fracture, and one subject with no history of stress fracture did not complete their MGH study visit and were lost to follow up. Recruitment outcomes and enrollment for Study 1 are shown in Figure 1 below.

Image acquisition via high-resolution peripheral quantitative computed tomography (HR-pQCT) has been completed for 42 subjects to date, and analysis of these images is ongoing (Study 1, Objective 4). Standard whole bone finite element analysis of these images is also in progress (Study 1, Objective 5). Assessment of skeletal alignment via whole body X-ray imaging (EOS) and bone mineral density by dual X-ray absorptiometry (DXA) has also been completed for 42 subjects (Study 1, Objective 6). Analysis of biomechanical gait for the 47 subjects who completed their SNRC visit has been ongoing during this reporting period, and is expected to continue through Quarter 12 (Study 1, Objective 7). A preliminary analysis was conducted of biomechanical gait data in September 2018; the results were presented as an abstract for poster presentation at the American College of Sports Medicine Annual Meeting in May 2019.

We recruited subjects for Study 2 via advertisements on the Partners Clinical Trials website, recruitment flyers posted in the greater Boston area, and recruitment emails sent to local student groups. Through these avenues, to date we have enrolled 146 subjects for Study 2: 30 Asian females, 22 Black females, 29 Caucasian females, 20 Asian males, 18 Black males, and 27 Caucasian males. All 146 enrolled subjects have successfully completed all requirements for the study. Recruitment outcomes and enrollment for Study 2 are shown in Figure 2 below.

Image acquisition via high-resolution peripheral quantitative computed tomography (HR-pQCT) has been completed for 146 subjects to date, and preliminary analysis of these images is shown below in Table 1 (Study 2, Objective 4). Standard whole bone finite element analysis of these images is also in progress (Study 2, Objective 5). Assessment of skeletal alignment via whole body X-ray imaging (EOS) and bone mineral density by dual X-ray absorptiometry (DXA) has also been completed for 146 subjects (Study 2, Objective 6).

Other activities during this period included weekly study staff meetings, facilitated by the principal investigator. Data entry and cleaning for Study 1 (Objective 8) and Study 2 (Objective 7) are ongoing.

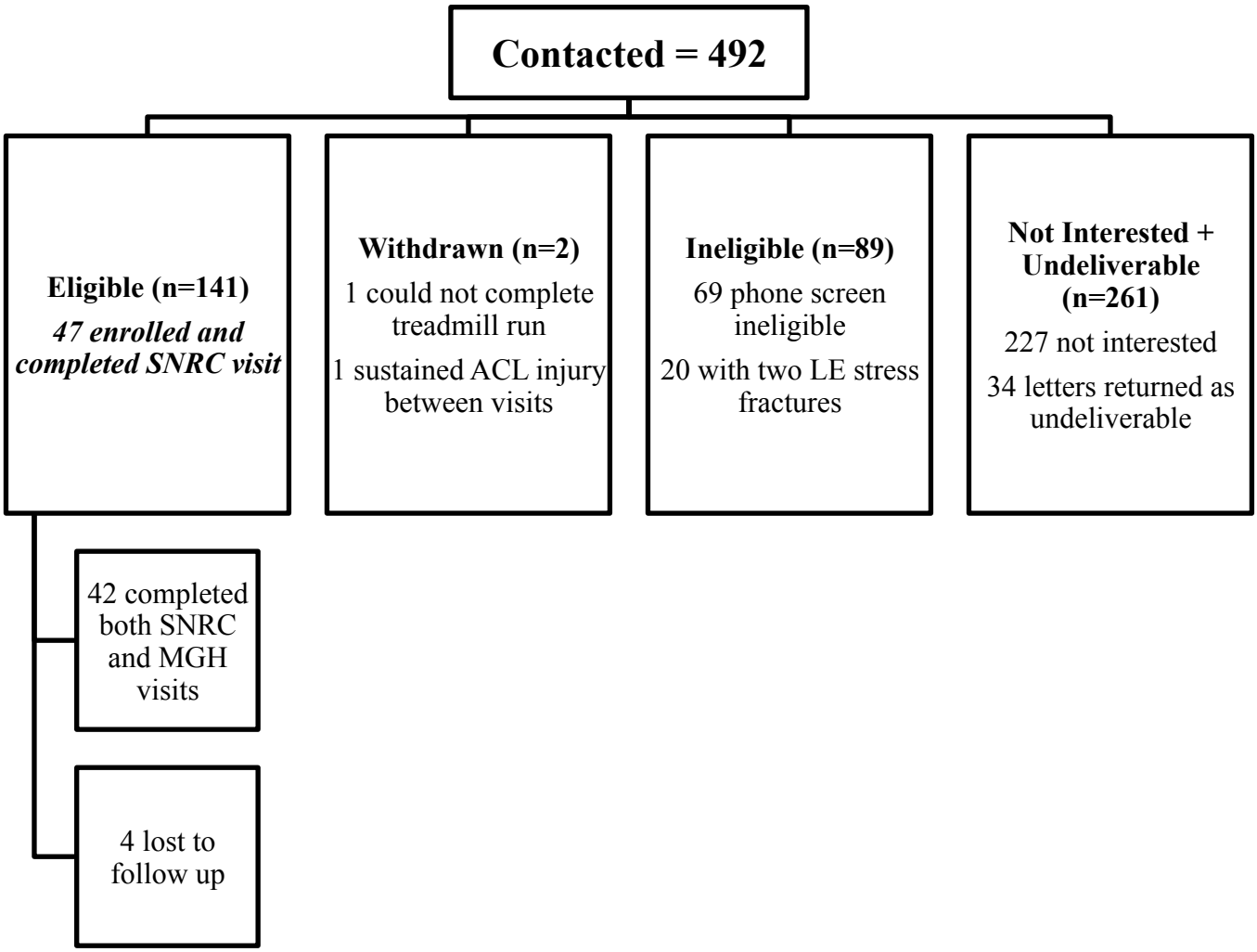

Figure 1. Recruiting efforts and enrollment for Study 1.

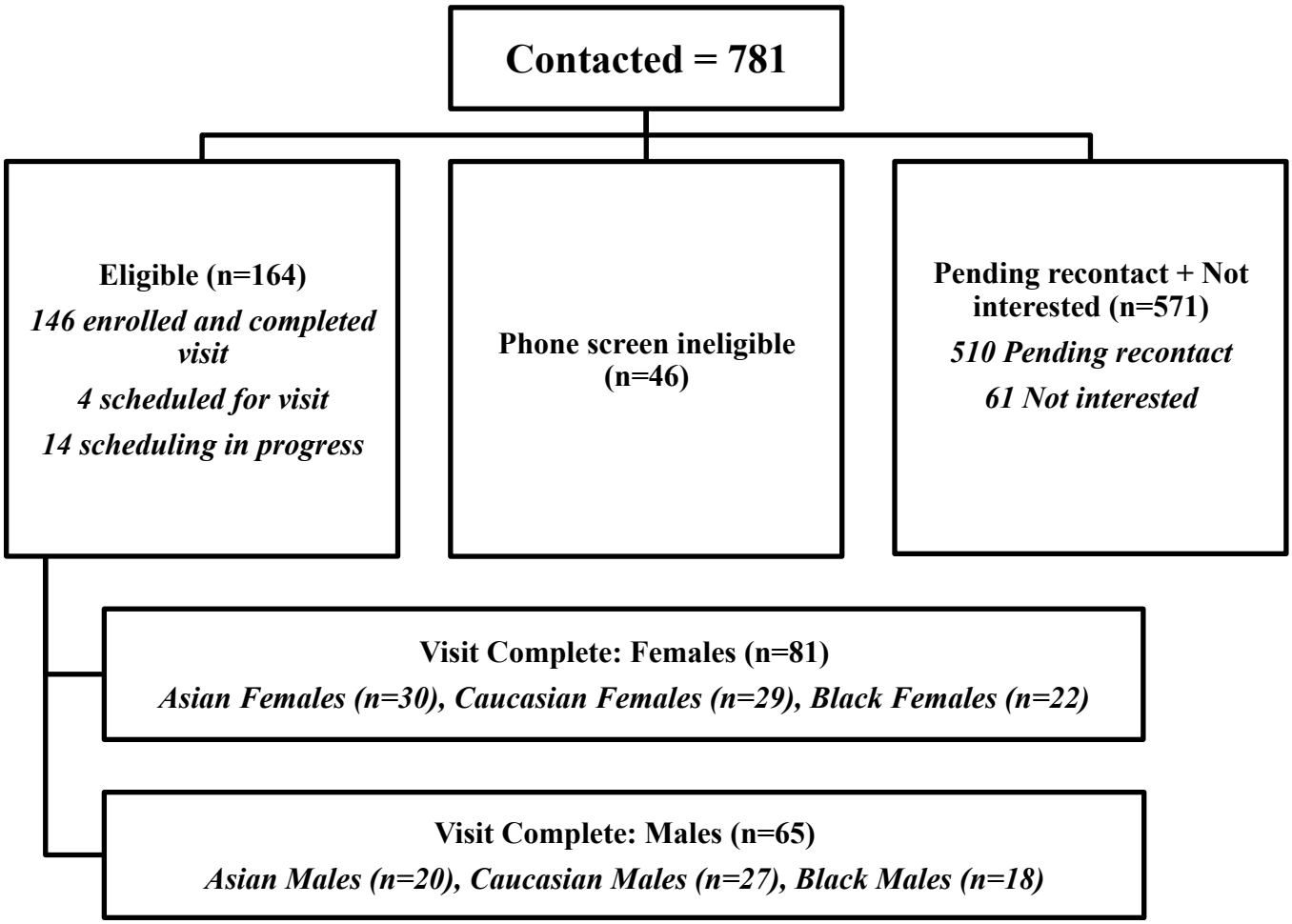

Figure 2. Recruiting efforts and enrollment for Study 2.

Preliminary Findings for Study 1:
Impact Mechanics in Female Runners with Single and Multiple Stress Fractures Following Fatigue (Presented by Dr. Outerleys at Annual Meeting of American College of Sports Medicine, 2019)
BACKGROUND: Stress fractures are common injuries in runners and military recruits, with females being at greater risk than their male counterparts. Impact variables, including peak axial tibial shock and vertical average load rate during running have been shown to be higher in females with a history of tibial stress fractures and increase with fatigue. However, the relationship between mechanics and injury in those with multiple lower extremity stress fractures has not been examined.
PURPOSE: To investigate whether impacts increase with fatigue in runners with no history of stress fractures (CON), one (1SFX), and 3 or more (3SFX) stress fractures.

METHODS: Impact variables were calculated for 43 females (14 CON, 14 1SFX, and 15 3SFX) at a speed of 2.67 m/s before and after a fatigue run. Variables included peak axial and resultant tibial shock (VTA, RTA) and vertical average and instantaneous loading rates (VALR, VILR). The fatigue run was performed at a 5 km predicted pace and concluded when the subject's rating of perceived exertion reached ≥ 18/20. Group comparisons were made using one-way ANOVAs, with follow-up post-hoc tests.
RESULTS: 3SFX had larger changes after fatigue than CON or 1SFX for all variables, although only VALR was statistically higher ($p<0.05$) with VILR ($p=0.06$), VTA ($p=0.2$) and RTA ($p=0.07$) not reaching significance. Additionally, those subjects with the largest changes in these variables exhibited a change in their foot strike towards a more posterior strike pattern.
CONCLUSION: Women with recurrent stress fractures showed larger increases in loading rates after fatigue compared to those with history of single stress fractures. Change in foot strike pattern can greatly influence impact mechanics before and after fatigue.

Bone Indentation as an In Vivo Measurement of Bone Quality if Female Athletes with a History of Bone Stress Injuries (Presented by Dr. Popp at American College of Sport Medicine Annual Meeting, 2019)
BACKGROUND: Bone mass, bone architecture and material properties of bone determine bone fragility. Bone stress injuries (BSI), a common injury among athletes, have been reported in up to 20% of female runners, with many athletes sustaining recurrent stress BSIs. While it has been previously reported that women with a history of BSI have smaller bones, with thinner cortices and worse bone microarchitecture, the role of impaired bone material properties remains to be characterized.
PURPOSE: To identify features of bone structure and bone quality that identify women with a history of multiple BSIs
METHODS: We enrolled 40 women, ages 18-30, with a history of 1 lower extremity BSI, ≥ 3 lower extremity BSIs or no BSI (HC), for this cross-sectional study. We collected high-resolution peripheral quantitative computed tomography (HR-pqCT) scans of the ultradistal tibia (4% of tibia length), areal bone mineral density (aBMD) by dual-energy x-ray absorptiometry, bone material strength index (BMSi) using microindentation (Osteoprobe), background and lifestyle questionnaires, and a physical activity assessment.
RESULTS: There were no differences between groups in age, height, weight, BMI, physical activity, or aBMD. Those with multiple lower extremity BSIs had smaller total tibial bone area with greater trabecular volumetric BMD compared to healthy controls ($p<0.05$). Those with a single BSI had higher BMSi compared to HC and those with multiple BSIs ($p=0.04$, Fig 1), and a trend for lower cortical porosity compared to HC ($p=0.07$). Among the cohort, BSMi was significantly associated with BMI ($p=0.02$) and cortical porosity ($p=0.04$), but not with age, cortical volumetric BMD, cortical tissue mineral density, or aBMD.
CONCLUSION: Bone microarchitecture and BMSi parameters suggest differences between those with a history of BSI compared to HC. Those with multiple BSI appear to have smaller but denser bones compared to HC. However our findings of higher BMSi among the single BSI group compared to the multiple BSI group are unexpected. BMSi is significantly correlated with cortical porosity.

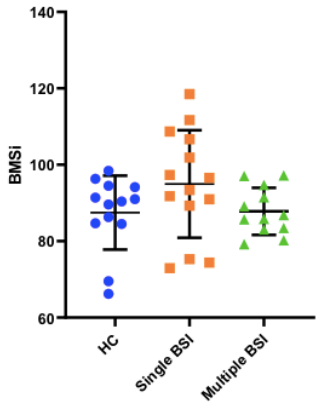

Figure 3: Bone material strength index (BMSi) by microindentation in women with a no history of bone stress injuries (BSI), women with a history of 1 lower-extremity BSI, and women with a history of multiple BSIs.

Preliminary Findings for Study 2:

Demographic characteristics, bone mineral density and bone microarchitecture results for subjects enrolled in Study 2 are shown below. Consistent with our prior studies, Black women and men have higher bone mineral density, assessed by dual-energy x-ray absorptiometry, than their White and Asian counterparts (Table 2 and Table 3). In addition, Black subjects tend to have move favorable bone microstructure, particularly in the cortical compartment (Tables 4 and 5). We anticipate that more of the differences will become statistically significant as additional subjects are enrolled and we complete the data cleaning.

Table 1. Demographic characteristics of subjects enrolled to date in Study 2. Values are Mean (SD) or n (%)

	White Women n=28	Black Women n=22	Asian Women n=29	White Men n=26	Black Men n=18	Asian Men n=18
Age (yrs)	25.0 (3.3)	21.8 (2.2)	23.9 (3.2)	24.2 (2.6)	21.4 (1.4)	23.2 (2.7)
Height (cm)	65.3 (2.5)	65.6 (3.3)	63.3 (2.1)	71.2 (2.5)	71.4 (2.6)	68.5 (3.4)
Weight (kg)	141 (20)	160 (27)	130 (21)	175 (20)	180 (21)	155 (21)
BMI (kg/m$^{2)}$	23.2 (2.7)	26.1 (3.9)	22.8 (3.5)	24.3 (2.7)	24.9 (2.9)	23.1 (2.3)
Prior fracture (yes)	7(25%)	3 (14%)	4 (14%)	11 (42%)	4 (22%)	4 (22%)
Smoker (yes)	0 (0%)	2 (9%)	0 (0%)	2 (8%)	0 (0%)	0 (0%)

Table 2. Bone mineral density from dual-energy X-ray absorptiometry of the femoral neck, total hip and lumbar spine (mean ± SD) in women from Study 2

	White Women n=28	Black Women n=22	Asian Women n=28
Femoral Neck aBMD (g/cm^2)	0.88 (0.02)[c]	0.90(0.02)[a,b]	0.84 (0.02)
Total Hip aBMD (g/cm^2)	0.99 (0.02)	0.99 (0.02)	0.94 (0.02)
Spine aBMD (g/cm^2)	1.04(0.02)	1.07 (0.03)	1.05 (0.03)

* Adjusted for height, weight, and age

a=Black women > White women $p<0.05$; b= Black women > Asian women $p<0.05$; c= White women > Asian women $p<0.05$

Table 3. Bone mineral density from dual-energy X-ray absorptiometry of the femoral neck, total hip and lumbar spine (mean ± SD) in men from Study 2

	White Men n=26	Black Men n=18	Asian Men n=18
Femoral Neck aBMD (g/cm^2)	0.95 (0.04)	1.12 (0.05) [a, b]	0.97(0.05)
Total Hip aBMD (g/cm^2)	1.04 (0.03)	1.18 (0.04)[a, b]	1.05 (0.04)
Spine aBMD (g/cm^2)	1.04(0.03)	1.12 (0.03)	1.05 (0.03)

* Adjusted for height, weight, age, and physical activity

a= Black men > White men $p<0.05$; b= Black men > Asian men $p<0.05$; c= Asian men > White men $p<0.05$

Table 4. Preliminary results from high-resolution peripheral computed tomography (HRpQCT) scans at the radius and tibia in women. Values are Mean (SE)

	White Women n=29	Black Women n=22	Asian Women n=29
Ultradistal Radius			
Size/morphology			
Tt.Ar (mm^2)	254.5 (13.3)	246.7 (16.3)	263.3 (13.4)
Ct.Ar (mm^2)	56.9 (1.8)	56.6 (2.2)	57.9 (1.8)
Microarchitecture			
Ct.Th (mm)	0.97 (0.03)	0.98 (0.04)	1.02 (0.03)
Ct.Po (%)	3.36 (0.04)	3.15 (0.05)	3.05 (0.04)
Tb.Th (mm)	0.219 (0.003)	0.227(0.004)	0.224 (0.003)
Tb.Sp (mm)	0.623 (0.021)	0.620(0.026)	0.677 (0.021)
Tb.N (1/mm)	1.51 (0.04)	1.50 (0.05)	1.42 (0.04)
Density			
Tt.vBMD ($mgHA/cm^3$)	315.5 (10.7)	326.8 (12.9)	315.9 (10.4)
Tb.vBMD($mgHA/cm^3$)	157.7 (7.3)	167.2 (8.8)	150.8 (7.2)
Ct.vBMD ($mmHA/cm^3$)	914.9 (7.2)	916.8 (8.7)	920.3 (7.1)
Distal Tibia			
Size/morphology			
Tt.Ar (mm^2)	557.7 (45.5)	508.6 (55.9)	616.6 (45.9)
Ct.Ar (mm^2)	120.3 (3.4)	133.8 (4.2)[a]	123.4 (3.2)
Microarchitecture			
Ct.Th (mm)	1.41 (0.05)	1.63 (0.06)[a,b]	1.46 (0.04)
Ct.Po (%)	1.14 (0.14)	0.96 (0.17)	1.43 (0.13)[c]
Tb.Th (mm)	0.248 (0.006)	0.261 (0.007)	0.254 (0.005)
Tb.Sp (mm)	0.672 (0.028)	0.743 (0.034)	0.741 (0.026)
Tb.N(1/mm)	1.41 (0.04)	1.28 (0.05)	1.31 (0.04)
Density			
Tt.vBMD ($mgHA/cm^3$)	320.5 (9.1)	350.4 (11.3)	322.2 (8.5)
Tb.vBMD($mgHA/cm^3$)	178.4 (7.5)	177.1 (9.3)	175.9 (7.0)
Ct.vBMD ($mmHA/cm^3$)	955.6 (6.2)	989.0 (7.7)[a, b]	950.6 (5.8)

***** Adjusted for height, weight, and age

[a] = Black women > White women $p<0.05$

[b]= Black women > Asian women $p<0.05$

[c]= Asian women > Black women $p<0.05$

Table 5. Preliminary results from high-resolution peripheral computed tomography (HRpQCT) scans at the radius and tibia in men. Values are Mean (SE)

	White Men n=26	Black Men n=18	Asian Men n=17
Ultradistal Radius			
Size/morphology			
Tt.Ar (mm^2)	322.6 (14.3)	344.2 (17.8)	334.9 (18.4)
Ct.Ar (mm^2)	72.22 (2.78)	80.07 (3.37)	73.25 (3.48)
Microarchitecture			
Ct.Th (mm)	1.11 (0.05)	1.22 (0.06)	1.13 (0.06)
Ct.Po (%)	5.39 (0.59)	5.16 (0.70)	4.48 (0.73)
Tb.Th (mm)	0.240 (0.004)	0.252 (0.005)	0.239 (0.005)
Tb.Sp (mm)	0.588(0.020)	0.573 (0.024)	0.619 (0.025)
Tb.N(1/mm)	1.56 (0.04)	1.60 (0.05)	1.50 (0.06)
Density			
Tt.vBMD ($mgHA/cm^3$)	340.2 (11.9)	371.4 (14.4)	333.2 (14.9)
Tb.vBMD($mgHA/cm^3$)	189.6 (7.7)	205.3 (9.3)[a]	176.1 (9.6)
Ct.vBMD ($mmHA/cm^3$)	876.8 (6.4)	895.3(7.8)	893.8 (8.1)
Distal Tibia			
Size/morphology			
Tt.Ar (mm^2)	729.4 (38.8)	730.2 (48.3)	759.8 (49.9)
Ct.Ar (mm^2)	162.7 (5.8)	178.6 (7.2)	155.9 (7.5)
Microarchitecture			
Ct.Th (mm)	1.79 (0.07)	1.97 (0.02)[a]	1.68 (0.09)
Ct.Po (%)	1.98 (0.02)	2.01 (0.03)	1.70 (0.03)
Tb.Th (mm)	0.275 (0.005)	0.278 (0.006)	0.281 (0.006)
Tb.Sp (mm)	0.684 (0.026)	0.721 (0.032)	0.740 (0.033)
Tb.N(1/mm)	1.41 (0.05)	1.37 (0.06)	1.29 (0.06)
Density			
Tt.vBMD ($mgHA/cm^3$)	354.9 (9.8)	380.0 (12.2)	344.1 (12.6)
Tb.vBMD($mgHA/cm^3$)	202.3 (8.3)	204.8 (10.3)	198.6 (10.6)
Ct.vBMD ($mmHA/cm^3$)	925.1 (7.8)	944.4 (9.7)	936.4 (10.0)

* Adjusted for height, weight, and age

[a] = Black men > Asian men $p<0.05$

Opportunities for Training and Professional Development

Nothing to report

Dissemination of Results

2018

We reported preliminary findings at the In Progress Review meeting for the Injury Prevention & Reduction Research Program managed by the MOMRP in June 2018.

2019

Outerleys J, Popp K, Rudolph SE, Caksa S, Ackerman K, Bouxsein ML, Davis IS. *Impact Mechanics in Female Runners with Single and Multiple Stress Fractures Following Fatigue*. American College of Sports Medicine Annual Meeting, Orlando, FL. Abstract #2309.

Goals for Year 4

We will continue to conduct MGH visits for our remaining Study 1 subjects, and we anticipate that all will complete the study in the next reporting period (Study 1, Objective 3). We also plan to complete acquisition and analysis of HR-pQCT images, standard whole bone finite element analysis, whole body X-ray imaging via EOS, and bone mineral density assessment via DXA (Study 1, Objectives 4-6). Biomechanical analysis of Study 1 subjects is ongoing, and we anticipate this to complete in the next reporting period (Study 1, Objective 7). We began statistical analysis in Year 3 (Study 1, Objective 8) and will continue to perform statistical analyses of the full dataset during Year 4. Lastly, we will renew Partners IRB approval of the study protocol in February 2020 (Studies 1 and 2, Objective 9).

We will continue to conduct MGH visits for our remaining Study 2 subjects, and we anticipate that all will complete the study in the next reporting period (Study 2, Objective 3). We also plan to complete acquisition and analysis of HR-pQCT images, standard whole bone finite element analysis, whole X-ray imaging via EOS, and bone mineral density assessment via DXA (Study 2, Objectives 4-6). Data cleaning and statistical analysis for Study 2 is ongoing and expected to be complete in the next reporting period. Development of race-, sex-, and age-specific databases of bone microarchitecture, impact microindentation, skeletal alignment, and gait mechanics (Study 2, Objective 8) is ongoing.

Impact

Nothing to report.

Changes/Problems

In our progress report at the end of Year 1, we indicated a delay in beginning recruitment for Study 2, as we were awaiting arrival of the 2nd generation HR-pQCT. The machine has since arrived and been installed, and we have completed ~80% of recruitment for Study 2.

Technical Issue to Note: We have ceased use of the investigational device (Osteoprobe, Active Life Scientific) that we were employing in these studies to assess cortical bone quality. On October 4, 2019 we were officially informed by Maureen Dreyer, Acting Assistant Director, Policy & Operations Team

of the Office of Product Evaluation and Quality, Food and Drug Administration (FDA) that FDA has conducted a risk determination for studies of this device and generally found that they would be considered significant risk. This means that investigational use of the Osteoprobe device would require an investigational device exemption (IDE) approval from FDA. As this IDE approval has not been acquired by the manufacturer of the device (ActiveLife Scientific), we removed the Osteoprobe from all study protocols. We will not re-introduce the Osteoprobe into study protocols until an IDE is approved by the FDA. We have reported this change in our study protocol to the Partners Investigational Review Board, and also to HRPO. We have performed measurements in 162 subjects as part of these ongoing studies, with no adverse events. We have several outcome assessments, and do not anticipate that this change in protocol will impact the scientific validation of our studies.

Products

Nothing to report.

Participants and Other Collaborating Organizations

Personnel

Name:	Mary Bouxsein, PhD
Project Role:	Principal Investigator
Research Identifier:	N/A
Nearest Person-Month Worked:	0.84
Contribution to Project:	Dr. Bouxsein performed work in the areas of data and safety monitoring, study sponsor correspondence, study data and procedure review, and budget review.

Name:	Irene Davis, PhD
Project Role:	Site-Responsible Investigator
Research Identifier:	N/A
Nearest Person-Month Worked:	0.96
Contribution to Project:	Dr. Davis performed work in the areas of data and safety monitoring as well as study data and procedures review.

Name:	Kathryn Ackerman, MD
Project Role:	Co-Investigator
Research Identifier:	N/A
Nearest Person-Month Worked:	0.60
Contribution to Project:	Dr. Ackerman helped to identify potential subjects and assisted with data and safety monitoring, and data and procedures review.

Name:	Kristy Popp, PhD
Project Role:	Collaborator (ORISE fellow via USARIEM)
Research Identifier:	N/A

Nearest Person-Month Worked:	0.00
Contribution to Project:	Dr. Popp continues her work with the study by assisting with data analysis and interpretation.

Name:	Jereme Outerleys
Project Role:	Research Technician
Research Identifier:	N/A
Nearest Person-Month Worked:	6.00
Contribution to Project:	Mr. Outerleys performed biomechanical analyses for Study 1 subjects, as well as work in the areas of data and safety monitoring and review of data and procedures.

Name:	Elizabeth Loranger
Project Role:	Research Coordinator
Research Identifier:	N/A
Nearest Person-Month Worked:	6.36
Contribution to Project:	Ms. Loranger performed work in identifying, recruiting, and screening potential subjects, obtaining informed consent, data entry, data and safety monitoring, maintenance of IRB documents, and review of study data and procedures for Study 1 & Study 2.

Name:	Sarah Gehman
Project Role:	Research Coordinator
Research Identifier:	N/A
Nearest Person-Month Worked:	0.96
Contribution to Project:	Ms. Gehman performed work in identifying, recruiting, and screening potential subjects, obtaining informed consent, data entry, data and safety monitoring, maintenance of IRB documents, and review of study data and procedures for Study 1 & Study 2.

Name:	Sara Rudolph
Project Role:	Research Coordinator
Research Identifier:	N/A
Nearest Person-Month Worked:	2.40
Contribution to Project:	Ms. Rudolph performed work in identifying, recruiting, and screening potential subjects, obtaining informed consent, data entry, data and safety monitoring, maintenance of IRB documents, and review of study data and procedures for Study 1 & Study 2.

Name:	Sara Stewart
Project Role:	Summer Intern

Research Identifier:	N/A
Nearest Person-Month Worked:	1.92
Contribution to Project:	Ms. Stewart performed work in identifying, recruiting, and screening potential subjects, obtaining informed consent, data entry, data and safety monitoring, and review of study data and procedures for Study 2.

Name:	Sabina Yosif
Project Role:	Summer Intern
Research Identifier:	N/A
Nearest Person-Month Worked:	1.92
Contribution to Project:	Ms. Yosif performed work in identifying, recruiting, and screening potential subjects, obtaining informed consent, data entry, data and safety monitoring, and review of study data and procedures for Study 2.

Post-doctoral fellow Kristin Popp joined USARIEM as an ORISE fellow in 2018, though she continues to assist with the data analysis and interpretation of study results for the current study. The study coordinator at MGH, Sara Rudolph, left to attend medical school. We have two new study coordinators, Elizabeth Loranger and Sarah Gehman. There are no other significant changes to study personnel.

Partner Organizations

- **Organization Name:** Spaulding National Running Center
- **Location of Organization:** Cambridge, MA
- **Partner's contribution to the project:** facilities and collaboration; data collection for gait mechanics was performed at the Spaulding National Running Center. SNRC staff assist with study visits, data collection, and biomechanical data analysis.