Human Subjects Protocol

VA Puget Sound IRB

Do Rocker Bottom Shoes and Ankle-Foot Orthoses Reduce Pain and Improve Mobility for Ankle Osteoarthritis Patients?

MIRB # 01601

Funding Agency: Department of Veterans Affairs

Principal Investigator: Bruce Sangeorzan, MD

Version 10; 01/10/2022

Abstract

Background and Purpose: Ankle osteoarthritis (OA) is a painful, progressive condition that can severely limit physical activity and reduce quality of life. **Rocker bottom (RB)** shoes and **ankle-foot orthoses** (**AFO**; a type of ankle brace), are common non-surgical treatments to manage ankle OA, but their ability to reduce pain and increase mobility has not been fully evaluated. One way ankle OA pain can be managed is by reducing the ankle's **range of motion (ROM)**, the less the joint has to move during activities (like walking) the less load it has to carry/process. RB shoes have curved soles, front-to-back, that may alleviate joint pain by reducing the ankle's front-to-back ROM. RB shoes may allow the body's weight to rollover the curved sole of the shoe during activities (like walking) with less effort and movement needed from the ankle joint. Similarly, AFOs may reduce joint motion by securing the foot and ankle within the AFO structure.

The purpose of this study is to evaluate the ability of RB shoes and AFOs to improve mobility, by alleviating pain and reducing joint motion when compared to a standard shoe. This study has three specific aims (SA):

SA 1: Compare the daily step count, **self-selected walking speed (SSWS)**, and self-reported outcomes from a set of questionnaires assessing pain and mobility before and after wearing a control shoe, RB shoe and a AFO. Each footwear condition will be worn over a three-week period (one-week acclimation, two-week trial period). This will indicate how subjects respond to these treatment conditions – what their pain levels are compared to baseline, how they self-report functional change, and from their step count, a quantitative measure of their mobility in the treatment footwear.

SA 2: Evaluate the effect of a control shoe, a RB shoe and a AFO on the front-to-back ROM of the foot and ankle. This will determine how these devices shield the ankle from motion – potentially protecting it, and if they impose abnormal motion on adjacent foot joints – potentially exposing them to additional wear and increasing their risk for long term OA development.

SA 3: Compare the ankle OA clinical and biomechanical outcome measures for the control shoe, RB shoe, and AFO to a healthy control group wearing control shoes. This will determine the difference in clinical and biomechanical outcomes related to the presence of OA.

Methods: We will enroll 100 participants with ankle OA and 50 control participants without lower limb pain. Three study groups will participate in this project. Study group 1 is a single day study and have images taken using our biplane fluoroscopy system. Study group 2 is a three month take home, and Study group 3 is a three month take home and will have images taken using our biplane fluoroscopy system. At visit-1 all participants will do baseline measures (questionnaires and functional assessments, including **SSWS**) and have a CT scan. During the initial visit, group 1 will participate in a biplane assessment. Participants in Study group 2 & 3 will be assigned to a randomly selected order of footwear (RB shoe, control shoe or an AFO). Each footwear condition will be worn for a three-week trial period at-home/in-community (one-week acclimation, two-weeks continuous wear). Participants will complete brief weekly pain assessments and wear a step counter. At visit-2 participants will do a pain rating, repeat the questionnaires and SSWS test, and group 3 will have images taken using our biplane fluoroscopy system. Participants will continue wearing the step-counter during a one week washout period. For the next three weeks, participants will repeat the at-

home/in-community procedures (step counter, weekly pain rating) and come to the VA to repeat the visit-2 procedures. The same process will be repeated for the third footwear condition.

List of Abbreviations

Provide a list of all abbreviations used in the protocol and their associated meanings.

AE – adverse event

AFO – ankle-foot orthosis

CT – computed tomography

mSv - millisievert

OA – osteoarthritis

RB – rocker bottom

ROM – range of motion

ROP – report of other problem

SAE – serious adverse event

SSWS – self-selected walking speed

UW/HMC – University of Washington/Harborview Medical Center

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1.0 Key Study Personnel

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2.0 Introduction

Ankle osteoarthritis (OA) is a debilitating condition associated with severe pain, dysfunction, and reduced quality of life. In the end stage of the disease, many patients are unable to walk 100 meters or up a single flight of stairs[1], and the reduction in quality of life is similar to that of end-stage hip arthritis or congestive heart failure[1,2]. Ankle OA affects about 6% of the population[3] and is thus less common than hip or knee arthritis. However, ankle OA differs from hip or knee arthritis because most cases are post-traumatic[2] and consequently affect a younger demographic[4,5]. Data from the Health Care Utilization Project online indicate that hospital charges for the treatment of ankle arthritis exceed $370 million per year.

Ankle OA is an important health care concern for the Veterans Health Administration. Veterans are at greater risk of developing ankle OA than non-veterans due to the rigorous physical demands associated with training and combat during military service[6]. Traumatic OA from injury is also higher in the military population (up to seven times greater[7]). Data from the National Health Interview Survey of 1990 show a higher prevalence of foot and ankle OA among veterans of the pre- Gulf War era than corresponding non-veterans[8], and studies of Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) have shown both an increase in extremity injury and an increase in ankle OA compared to previous conflicts[9,10]. This increase in ankle OA has resulted in severe disability for many veterans. A recent study of 126 wounded warriors with OA as an unfitting condition that led to a medical separation from the military, found that those with ankle OA had higher disability ratings than those with knee or hip OA[11]. VA Medical Centers treat a significant number of veterans with ankle OA. A VHA Support Service Center (VSSC) database search for FY2014 of local (Seattle VA), VISN 20, and national outpatients yielded the following table of ankle OA populations, showing several thousand national cases in a single year.

End-stage ankle OA is defined as when all non-surgical treatment options (nonsteroidal anti-inflammatory drug therapy, other oral therapy, corticosteroid injections, bracing, etc.) for ankle OA have failed. The most common surgical treatments are talocrural arthrodesis and total joint arthroplasty. However, the long-term results are mixed, with most ankle arthrodesis patients developing arthritis of the subtalar or midfoot joints within 3-22 years of operation[12,13] and many ankle arthroplasty patients have a higher failure rate than the knee or hip[14]. These late effects suggest

that a longer delay in surgical treatment is desirable. Yet there are very few publications on efficacy of orthotic management.

The risks, the cost, and the time-limited outcomes are compelling reasons to explore non-surgical treatments options for ankle OA. Conservative interventions thought to limit joint range of motion (ROM) may delay or prevent the progression of arthritis, reduce pain, improve comfort and function, and thus improve quality of life. Two such treatment types are rocker bottom (RB) shoes and ankle-foot orthoses (AFOs). These devices are commonly prescribed to manage ankle OA; however, their ability to reduce joint motion and thus alleviate pain and increase mobility has not been scientifically evaluated. Towards that end, we aim to compare two conservative treatments (RB shoes and AFOs) in OA subjects by measuring mobility and pain during and after the completion of three-week trial periods. We will use biplane fluoroscopy to measure hindfoot and midfoot joint motion at the conclusion of each period. This study will provide evidence to support clinical decision making.

3.0 Specific Aims and Hypotheses

The purpose of this study is to evaluate the ability of RB shoes and AFOs to improve mobility, by alleviating pain and reducing joint motion when compared to a standard shoe. This study has three specific aims (SA):

SA 1: Compare the daily step count, **self-selected walking speed (SSWS)**, and self-reported outcomes from a set of questionnaires assessing pain and mobility before and after wearing a control shoe, RB shoe and a AFO. Each footwear condition will be worn over a three-week period (one-week acclimation, two-week trial period). This will indicate how subjects respond to these treatment conditions – what their pain levels are compared to baseline, how they self-report functional change, and from their step count, a quantitative measure of their mobility in the treatment footwear.

> **Hypothesis 1.1:** For ankle OA subjects, the RB shoe and AFO will exhibit increased step count, self-selected walking speed, improve physical function, and reduced pain when compared to a control shoe.
>
> **Hypothesis 1.2:** For ankle OA subjects, the AFO will increase step count, self-selected walking speed, improve physical function, and reduce pain more than the RB shoe or control shoe.

SA 2: Evaluate the effect of a control shoe, a RB shoe and a AFO on the front-to-back ROM of the foot and ankle. This will determine how these devices shield the ankle from motion – potentially protecting it, and if they impose abnormal motion on adjacent foot joints – potentially exposing them to additional wear and increasing their risk for long term OA development.

> **Hypothesis 2.1:** For ankle OA subjects, the sagittal ROM of the talocalcaneal, talocrural, talonavicular, naviculocuneiform, and first cuneometatarsal joints will be less when wearing the AFO than the RB shoe, which will be less than OA subjects wearing the control shoe.

SA 3: Compare the ankle OA clinical and biomechanical outcome measures for the control shoe, RB shoe, and AFO to a healthy control group wearing control shoes. This will determine the difference in clinical and biomechanical outcomes related to the presence of OA.

Hypothesis 3.1: For ankle OA subjects, daily step count, self-selected walking speed, PROMIS physical function, and FAOS will be less, while the PROMIS pain interference, AAOS-FAM, and numeric pain rating will be greater than the control subjects wearing the control shoes.

Hypothesis 3.2: For ankle OA subjects, the sagittal ROM of the talocalcaneal, talocrural, talonavicular, naviculocuneiform, and first cuneometatarsal joints when wearing RB shoes or AFOs will be less than the [sagittal] ROM of the control subjects wearing the control shoes.

4.0 Resources and Personnel

Data collection procedures for this study will be conducted at the VA Puget Sound in Seattle, WA. See Study Staff Sheet attachment for listing of personnel, ability to obtain consent, and access to PHI.

Under the supervision of the PI, designated study staff will be responsible for conducting recruitment, consent and scheduling study procedures. The PI, Investigators, and/or Research Engineers and assistants will conduct procedures with participants. The PI, Investigators, and the Biostatistician will be primarily responsible for data analysis and interpretation; Research Engineers and assistants may also assist with this. Under the supervision of the PI, the Program Coordinator is responsible for IRB related matters.

5.0 Study Procedures

5.1 Study Design

Participants in this research study will be men and women, age 18 and over, who can walk without difficulty for about an hour. People with and without ankle OA, will be enrolled. Targeted enrollment by ankle OA status is listed in the table below. Vulnerable populations will not be specifically targeted for enrollment. See inclusion/exclusion criteria below in section 5.4.

Study Groups	Total: 150
Controls, no ankle OA	50
People with Ankle OA	100

See section 5.5 below for data collection procedures and risk management.

5.2 Recruitment Methods and Initial Screening

Up to 3000 individuals may be approached during recruitment and enrollment procedures. Please note that all references in this section to in-person contact/initial-screening will follow the *Screening Script* attachment, all references to approach letters and postcards refer to the *Recruitment Letter* attachment.

Recruitment activities at the VA

Medical Record/Database: Letter/Phone/In-person (Seattle and American Lake)

Designated research staff will screen relevant clinic lists in CPRS to identify potential participants with a qualifying ankle OA diagnosis. After review, designated staff will go to the clinic or contact providers on the phone or on VA encrypted email to ask if a patient might be a good fit for the study. If the clinician agrees that the study may be a good fit for a patient, during an appointment the clinician will inform patients of the availability of the study and ask if they are interested in speaking with designated study staff; patients will be given a chance to opt out. For patients who are interested, designated study staff will speak to potential participants directly and/or use CPRS to obtain potential participants' contact information (i.e., name, address, telephone number). For potential participants who learned about the study in person and were introduced to us but may not have time to complete the eligibility screening, designated study staff may give them a flyer and/or business card, and make a follow-up approach phone call, arrange a time to meet later in-person, and/or send an approach letter to them. If potential participants are unable to meet with designated study staff in-person, then we will send an approach letter.

We may also search CPRS and the Corporate Data Warehouse (CDW) to identify individuals with a qualifying diagnosis and mail them the approach letter.

If potential participants have not spoken with us within 14 days of the first call and/or mailing the approach letter, designated study staff will contact them by phone up to two more times (three times total) about this study. The approach letter will also include an "opt out" postcard. The opt-out postcard will have a unique study recruitment identification code, e.g., "RBS-AFOd1", "RBS-AFOd2". If an individual returns the postcard to opt out they will not be approached about this study again.

Clinician Referral

Designated staff will inform providers working in relevant clinics about the study and inclusion/exclusion criteria, so they can refer potential participants to contact the study team. Flyers and business cards may be provided to clinicians (or their support staff) to give to patients that are interested in learning about the study. Clinicians may also provide us (via VA encrypted email/in-person/on the phone) with the names of patients that they are aware of who may be a good fit for the study and we will look up their contact information to send an approach letter. If a clinician informs patients about the study and the patient agrees to be contacted about it, the clinician may provide us with the patient's name (via encrypted email/in-person/on the phone). We will look up the patient's contact information in CPRS and make an approach call (in this instance – we will obtain printable documentation from the clinician, via encrypted email or a note in the medical record, that the patient agreed to be contacted on the phone).

Print/Text/Online/Flyers/Newsletter

Flyers may be posted in designated areas at the VA Puget Sound (Seattle and American Lake) on the CCTV system and in publicly accessible locations in the community (e.g., public libraries, community centers, coffee shops). The flyers may also be re-sized to be used in print publications or as a complete image in online ads. We may post classified ads in print and online publications. We may also post the classified ad text to our Center's webpage. We may also post recruitment information in our center newsletter.

VA Puget Sound Center Registry: Letter/Phone

Designated study staff may also identify potential participants using the VA Center for Limb Loss Prevention and Prosthetic Engineering Subject Registry (PI: Klute, #00433). The Registry contains contact information for participants who were screened for and/or participated in previous studies with our research group and consented to be contacted (via phone call and/or letter) for future studies. Designated study staff may make an approach phone call and/or send an approach letter to potential participants asking whether they are interested in the study. If potential participants have not spoken with us within 14 days of the first call and/or of the mailing the approach letter, designated study staff will contact them by phone up to two more times. The approach letter will also include an "opt out" postcard. The opt-out postcard will have a unique study recruitment identification code, e.g., RBS-AFOd1", "RBS-AFOd2. If an individual returns the postcard to opt out they will not be approached about this study again. Designated study staff may also speak with these potential participants in-person if they have an upcoming clinic visit.

Eligibility Screening
Interested individuals will be screened for eligibility in-person or over the phone.

Recruitment Activities at UW/Harborview
A confidentiality agreement will be obtained for this activity. The UW is engaged in all aspects of this study. Also, we spoke with Leah Miller at UW HSD and confirmed that Dr. Bruce Sangeorzan is not engaged as a UW agent for the purposes of this study or its recruitment activities.

Medical Record/Database: Letter/Phone/In-person (UW/Harborview)
Designated study staff will screen relevant UW/Harborview clinic lists, appointment calendars and patient medical records to identify potential participants with a qualifying ankle OA diagnosis. Study staff may also attend clinic at these facilities to identify and/or contact potential participants. Study staff will discuss with the clinician(s) (in-person or on the phone) any patients that might be appropriate candidates. If the clinician agrees that the study may be a good fit for a patient, the clinician will inform patients of the availability of the study and ask the patient if she/he is interested in speaking with study staff. For interested patients, study staff will speak to them directly to tell them more about the study, give them a study flyer, business card, and/or request their permission to screen them for initial eligibility (via the VA IRB approved screening script) and provide this information to the VA. If VA staff are not available in the clinic, the clinician or their support staff may provide the study flyer and/or VA research coordinator's business card.

If potential participants are screened in person, study staff will label the noted responses with an id code and no HIPAA identifiers or sensitive health information will be noted on the form. Study staff will transport the forms to the VA for storage. Study staff will use their VA remote access to add PHI to the screening log that is maintained on the VA server, or they will call other approved staff to provide the PHI, and the information will be added to the VA screening log.

For potential participants who learned about the study in person and were introduced to us but may not have time to complete the eligibility screening, staff may give them a flyer and/or business card, look up their contact information to make a follow-up approach phone call, arrange a time to meet later in-person, and/or send an approach letter to them. If potential participants are unable to meet

designated study staff in-person, then we will send an approach letter (the VA IRB approved letter with VA contact information would be sent per the process described above).

Staff may also search/access UW medical records to identify individuals with a qualifying ankle OA diagnosis, obtain their contact information (i.e., name, address, telephone number) and mail them the approach letter.

Clinician Referral
Designated staff will inform providers working in relevant clinics about the study and inclusion/exclusion criteria, so they can refer potential participants to contact the study team. Flyers and business cards may be provided to clinicians (or their support staff) to give to patients that are interested in learning about the study. Clinicians may also provide us (via in-person/on the phone) with the names of patients that they are aware of who may be a good fit for the study and we will look up their contact information to send an approach letter.

For potential participants who were initially contacted via letter and/or in-person but have not yet completed the initial screening, study staff may provide the potential participants' contact information and limited pre-screening criteria over the phone to other study staff at the VA who will enter it into the screening log for tracking and follow up. This information may also be added (via VA remote access) to the screening log maintained on the VA server. Study staff will follow up with potential participants based on the VA approved protocol.

5.3 Informed Consent Procedures

A waiver of informed consent and HIPAA authorization will be used for recruitment and screening purposes. A waiver of documentation of consent and HIPAA authorization will be used to in order to retain the preliminary eligibility screening responses *(see Screening Script)*. Informed consent will be obtained prior to enrollment in the study.

Designated study staff and/or the PI will conduct the informed consent process. All study personnel will complete the necessary human subjects' protections training per VA policy. For study group 4 (remote study) informed consent will be conducted remotely. The consent document will be mailed/ delivered to the participant. Designated study staff and/or the PI will conduct the informed consent process via phone. The participant will then mail (or researcher will pick up) the consent from and return back to the VA.

5.4 Inclusion/Exclusion Criteria

Our targeted range for the total number of study completions is up to 150.

Inclusion Criteria:

Participants with ankle OA:

1. radiographic evidence of tibiotalar OA
2. age 18 years or older
3. able to stand and walk for about an hour (with breaks) and at least 15m (about 50ft) at a time without difficulty
4. minimum pain 3+/ 10

Control participants without OA:

1. age 18 years or older
2. able to stand and walk for about an hour (with breaks) and at least 15m (about 50ft) at a time without difficultly

Exclusion Criteria: all participants

1. subtalar joint arthritis
2. prior ankle joint replacement or fusion on the foot of interest, or recent (<1 year) surgical, neurological, rheumatologic, or lower limb musculoskeletal problem (e.g., current foot ulcer, severe hip/knee OA, terminal illness, etc.) that impairs an individual's ability to do the walking tests
3. current user of AFO or rocker bottom shoe and has either been prescribed by doctor or is not willing to stop using the device for three months
4. plans to undergo surgical treatment for ankle OA within three months
5. inability to walk unassisted during short, repeated walking trials
6. rheumatoid arthritis
7. inadequate cognitive or language function to consent or to participate
8. no phone number or stable mailing address
9. currently incarcerated
10. currently pregnant
11. open wounds on the foot or ankle
12. below- knee surgery in the past 60 days

Additional Exclusion Criteria, Controls only:

1. Ankle pain or ankle OA in addition to the above exclusionary criteria

5.5 Study Visits, Data Collection, and Risk Management

Participants can be enrolled in one of three study groups for this project. The specific procedures for each item are outlined below.

Visits at the VA Puget Sound may last up to 4 hours each. Particpant schedules and the accessibility of facility resources may extend the study timeframe beyond these estimates. Study visits will be scheduled by contacting the participants on phone, or during in-person contacts. We may contact participants with appointment and/or at home activity reminders via email or phone.

Study group 1: One day visit

Participaton will be at the VA Puget Sound and last up to 4 hours wearing the participants own or study provided footwear during the activities. Activities may include a Screening, Functional assessments, CT scan with pregnancy test, Qualitative questions, Brief Pain Rating, and a Biplane assessment with one or more interventions including barefoot, their own footwear, a modified shoe (such as a rocker bottom shoe), an orthotic device (such as an AFO), or a control shoe provided by the researchers.

Study group 2: Take home portion only (~3 months)

Participants with ankle OA will conduct a initial visit that will include a Screening, Functional assessments, CT scan with pregnancy test, Questionnaires, Qualitative questions, and Brief Pain Rating followed by a 3 month intervention at home intervention, that will include three additional visits to the VA. Timeline and assessments during those visits is described below.

Study group 3: Take home portion with Biplane (~3 months)

This study group is simlar to Study group 2, however it does include three biplane assessments over the three additional visits.

Study group 4: Remote take home only (~ 3 months)

This study group is similar to Stuy group 2, however all procedurse ill be done remotley. Participants with ankle OA will conduct a initial assessemnt that will include a Screening, Functional assessments, Questionnaires, Qualitative questions, and Brief Pain Rating followed by a 3 month at home intervention, that will include three additional assessemnts. Timeline and assessments during those assessments is described below. In addition, we will ask you to wear a StepWatch Activity Monitor (a step counter) and to do brief weekly pain ratings, and daily pain rating and pain medication use over the course of the entire study.

Photos and video

We will take video and photos of participants during portions of this study for documentation and use in research publications. All videos and photos will be anonymized (to avoid facial or voice identification) and and tattoos and other distinguishing marks will be covered before images are captured or obscured during processing to protect the identity and privacy of our participants.

During study sessions, visitors and observers will not be allowed in the lab unless the participant agrees to their presence; the participant can change her/his mind at any time.

Study Footwear

Over the course of the study (one day or ~3 months participants will be asked to wear up to three different footwear conditions: control shoes (a typical walking shoe, such as the New Balance 928), RB shoes (walking shoes with a front-to-back curved sole, such as the New Balance 928 with a rocker sole), and an orthotic device (such as an AFO, an ankle brace, such as the Toeoff® AFO) with control shoes. Participants will wear each footwear condition, in a randomized order. For all footwear conditions a fitbit zip may be clipped or taped to the shoe. This will record steps taken in the footwear. The fitbit will be synced during the VA visits and will only record number of steps. A separate account for each fitbit will be created and the account number will be recorded on the participant crosswalk. There will be no additional methods to link the data to the participant. Additional assessements on the initial day may include barefoot and own shoe as footwear condtions.

Screening /Eligibility Verification

Participants will have been preliminarily screened during recruitment, then during the first visit, after informed consent, we will make a final elibility determination. This will include verifying that the information collected during recruitment is accurate and current.

If a participant cannot continue in the study, they will be compensated $50 for the visit.

Demographic Data collection

Participants' age, sex, race/ethnicity and Veteran status will be recorded.

Anthropometrics

Participants' weight, waist circumfrence, and height will be measured.

Pain/health screening

Short survery which will include questions regarding trauma history in the lower limbs, joint replacments, OA, and pain throughout the body.

Functional Assessments

Self-selected Walking Speed (SSWS)

Participants wear either their own footwear or resaercher provided footwear. Participants will be asked to walk 20 meters in a straight line, at their own pace, in the hallway while a researcher times how long each walk takes. This will be used to determine the participants' self-selected walking speed (SSWS). This assessment will be conducted up to three times and averaged.

Timed Up and Go (TUG)

Participants wear either their own footwear or resaercher provided footwear. Participants will start seated in a chair with arm rests, stand up, walk to a line 3 mters away, turn anround, walk back to the chair, then sit down. Time to complete this will be recorded. This assessment will be conducted up to three times and averaged.

10 m fast walking test (10 m walk)

Participants wear either their own footwear or resaercher provided footwear. Participants will be instructed to walk as fast as they are comfortable for 10 meters. Participants will start walking before the 10 meter line and continue past the finish line. Time to complete the 10 meter walk will be recorded. This assessment will be conducted up to three times and averaged.

Qualitative Assessment

Participants will be asked several questions and responses will be recorded.

1. Do you like the device? Why/ why not?
2. Would you continue to wear the device if you were not part of the study? Why/why not?
3. Do you have a preference to one of the treatments? Which one? Why?

Questionnaires

Participants will be asked to complete a series of questionnaires about their pain and physical function. This will include the Patient Reported Outcomes Measurement Information System (PROMIS) pain interference v1.1, PROMIS physical function v1.2, and the Foot Ankle Ability Measure (FAAM).

The PROMIS measures will be completed on a mobile tablet and the data is saved locally by the application. The participant will enter their responses or it may be conducted as an interview with staff entering responses. The PROMIS measures are computer adaptive tests – the responses to the items determine which question path the user is taken through. Only a study assigned ID code (e.g., RBAFO_OA_001) will be associated with the PROMIS data. The other measures will be administered on paper or as an interview and will also be labeled with the study ID code. See section 10 for additional Privacy and Information Security details.

Daily Pain Rating and Pain Medication Use

We may ask you to rate (on a scale of 1-10) what your pain level is now, what your average pain level was in the past 24 hours, and what your maximum pain level was in the past 24 hours. We may also ask you what if any pain medication you took.

Brief Pain Rating (BPR)

A brief three item pain rating (1) what is your pain level now (0-10)?, 2) what has been your average pain level this week (0-10)?, and 3) what was your maximum pain level this week (0-10)?).

StepWatch Activity Monitor

A StepWatch Activity Monitor and instruction sheet will be provided to the participants. The StepWatch Activity Monitor is a step-counter placed around the ankle and is to be worn at home and in the community.

Pregnancy test

At each visit that involves exposure to radiation female participants of child-bearing potential (under age 50) will undergo a pregnancy test (urine test) so we can verify that they are not pregnant. Designated study staff will escort female partipants to the bathroom and provide them with a specimen cup, pregnacy test strip, and a disposable container on which to place the used test strip. Staff will go over the test instructions, and verify the test result. Staff will not handle urine specimens, we will tell particpants how to handle and dispose of the materials. Pregnancy tests may also be conducted by the lab at the VA Puget Sound. If the test indicates that the participant is pregnant she will be not be able to participate in the study and we will advise her to see her regular clinical care provider.

CT Scan

CT scans will be done at the VA Puget Sound, however, if needed, CT scans may be collected by a third-party vendor on a fee for service basis as explained below. We hope to do the CT scan during the first visit, however the scan may be taken during any of the study visits depending on scheduling needs.

If participants have a VA or UW medical record(s) we will access them to collect information related to participants' foot/ankle diagnosis, related clinical treatment, and check to see if they have already had a CT scan that can be used for this study. If participants report that they have had a CT scan(s) at a different medical facility, we may request copies of them. If possible, we will use the previously collected images for our data set and analyses so that participants do not have to be exposed to additional radiation. We will search for CT scans that took place within the last 5 years. If participants' medical records are not at the VA they will be asked to sign a release form so that

we can obtain copies of these records. The CT scans and any other requested clinical notes from outside the VA will be delivered via the following methods:

- The images and other clinical treatment information may be burned to CD(s) or DVD by HMC or other facility and mailed to us via traceable shipping.
- A designated study staff member will pick up the CD(s) or DVD from HMC/UW or other facility and transport it to the VA.
- Information about lower extremity diagnoses and clinical treatment may be provided to designated study staff over the phone – the information will be labeled with the participants' study code and added to study records

(B) If scheduling a CT scan at the VA Puget Sound proves to be difficult, we may schedule the CT scan at a third-party vendor (i.e., a fee for service CT scanner). The vendor will use the Study Staff's name and a study ID code for scheduling purposes. We will provide participants with the address of the vendor. A study ID code (e.g., RBAFO_OA_01) will be entered in the name field of the CT scan file along with age in years (if 89 or younger). The vendor will not store subjects' PHI in their files and they will not have access to or create a study ID crosswalk. The vendor will make a copy of the CT scan with the study ID code and age. Study staff will pick up the CD and transport the scan to the VA and/or the vendor mail it to us via traceable shipping.

Additionally, a low lose CT scan of participants may be taken using our Center's LineUP system (http://www.curvebeam.com/products/lineup/) and/or using clinical resources at the VA Puget Sound. The scan will start at the mid-tibia (lower leg) and extend down to include the subject's feet. The CT scan will be used to generate a computational model of the participant's bony anatomy – a necessary step for generating results with the fluoroscopy system.

Paticipants will be instructed to perform up to 15 scans in various positions including: barefoot partial weight-bearing neutral position, barefoot partial weight-bearing maximum ankle dorsiflxion, barefoot partial weight-bearing maximum plantarflexion, full weight-bearing bearfoot in neurual position, and partial weight-bearing with 3 different footwear in a secured manner to sustain the posture while scaning. Repeated procedure may be necessary as the the scan requires the partipant to maintain the static position for less than one minute.

Biplane Fluoroscopy Laboratory

These procedures are utilized in study groups 1 and 3. Participants will be escorted to the Biplane Fluoroscopy Lab per our SOPs. While wearing shorts (their own or ones we provide) and the assigned footwear (barefoot, own shoe, rocker bottom (RB) shoes, control shoes, or an ankle-foot orthosis (AFO) with the control shoes) the participants will step onto an elevated walkway, which is flat, about 3 feet wide, level, and has handrails on both sides. Participants will walk freely up and down the walkway to get comfortable with the test environment.

While standing still on the platform, a force plate will capture ground reactions forces and two fluoroscopes will capture simultaneous X-ray images of the participant's foot of interest to record the standing position of the bones. These dual fluoroscopes allow for tracking of the bone motion in three dimensions while the participant is walking. Next, participants will walk along the platform

while simultaneous X-ray images of the foot of interest are taken; each X-ray exposure is expected to last about 0.5 seconds, and will image from about 3 inches above the ankle to below the bottom of the shoe or foot. Participants will do up to 26 walking trials with each footwear condition during which images of their foot are taken. For some participants, we may take images of both feet during the standing and walking X-ray procedures. Rest breaks will be provided as needed.

Over the course of the study, participants with ankle OA will repeat the biplane fluoroscopy session 3 times (once for each footwear condition). Participants in study group 1 will complete the biplane in one session while barefoot, or wearing their own shoes, the control shoes, RB shoes, and/or the AFO. Each participant will receive no more than 80 total biplane imaging trials as part of the study.

Participants enrolled in study group 3 will continue wearing the StepWatch. Those in study group 1 have completed their participation and will return the study footwear and StepWatch.

Take home study

Length of participation

For participants with ankle OA, study procedures will occur over ~3 months (11 weeks). Four study visits will be done at the VA Puget Sound where three at-home/in-community study footwear (control shoes, RB shoes, an AFO) condition periods will be conducted.

Visits at the VA Puget Sound may last up to 4 hours each. Particpant schedules and the accessibility of facility resources may extend the study timeframe beyond these estimates. Study visits will be scheduled by contacting the participants on phone, or during in-person contacts. We may contact participants with appointment and/or at home activity reminders via email or phone.

Assessment 1

During this initial assessment participants will complete the, Screening, Functional assessments, LineUP with pregnancy test (not Study group 4), Questionnaires, and Brief Pain Raiting. Participants will be given a StepWatch and the first footwear condition. At the first assessment, participants who elect to use Ilumivu will be assigned a randomized username for the ilumivu mobile application. The link between this unique ID and the Veteran's identity will not be stored in the mobile application, but rather, stored locally at the Seattle VA. Further information about data security can be found in the Data Security section of this application. Ilumivu, is an app downloaded onto your phone. This app and its developers do not have any information that can be linked back to the participant. Only the researchers will know the Ilumivu participant ID. The Ilumivu participant ID will be recorded on the participant crosswalk in the research folder on the R drive. There will be no additional methods to link the data to the participant.

In Home/Community – Footwear Condition 1: Acclimation and Continuous Wear Period (3 weeks)

On day-1 of the first at home period, participants will wear the study footwear for one hour, then for two hours on day-2, three hours on day-3, then continue adding one hour of wear per day until the seventh day is reached. For the next two weeks, participants will wear the study footwear thoroughout the day during their normal daily activities. Participants will wear the StepWatch throughout this 3-week period. Each day participants will receive two messages either via email or with Ilumivu from the study staff, one in the morning, reminding the participant to wear the selected

footwear for the suggested number of hours, and one in the evening, reminding the participant to record the number of hours he/she has worn the selected footwear.

Once per week we will call/email/ message through Ilumivi (which ever the participant prefers) participants to check in and complete the Brief Pain Rating and Qualitative assessment.

Participants will be instructed to contact us if they have questions or if the study footwear is painful/uncomfortable. We will address any issues on an as needed basis, which may require additional visits to the VA.

If a proper and comfortable fit cannot be achieved with a footwear condition, then participants may wear their own shoes for a one-week washout period (while contiuing other study procedures) and we will move them to the next footwear condition if they wish to continue their participation. If we determine that it is not in the participant's interest to continue in the study he/she will be withdrawn.

Assessment 2

After the 2-week continuous wear period, participants will come to the VA Puget Sound with the StepWatch and study footwear. The StepWatch data will be downloaded and participants will complete the Brief Pain Rating, Qualitative assessment, Questionnaires, and Functional assessments. For those enrolled in Study group 3, the Biplane assessment will be conducted during this visit using the current footwear condition.

Participants will be given instructions for the second footwear condition.

In Home/Community Footwear Condition 1 Washout Period (1 week)
For the next week, participants will be asked to wear their own self-selected footwear, continue wearing the StepWatch and complete the weekly pain rating over the phone.

In Home/Community – Footwear Condition 2: Acclimation & Continuous Wear Period (3 weeks)

Participants be asked to follow the same 1-week acclimation procedure, followed by 2-weeks of continuous wear that they did with Footwear Condition 1. Participants will be asked continue wearing the StepWatch and complete the weekly pain ratings.

Assessment 3

The procedures described in Assessment 2 will be repeated.

In Home/Community Footwear Condition 2 Washout Period (1 week)

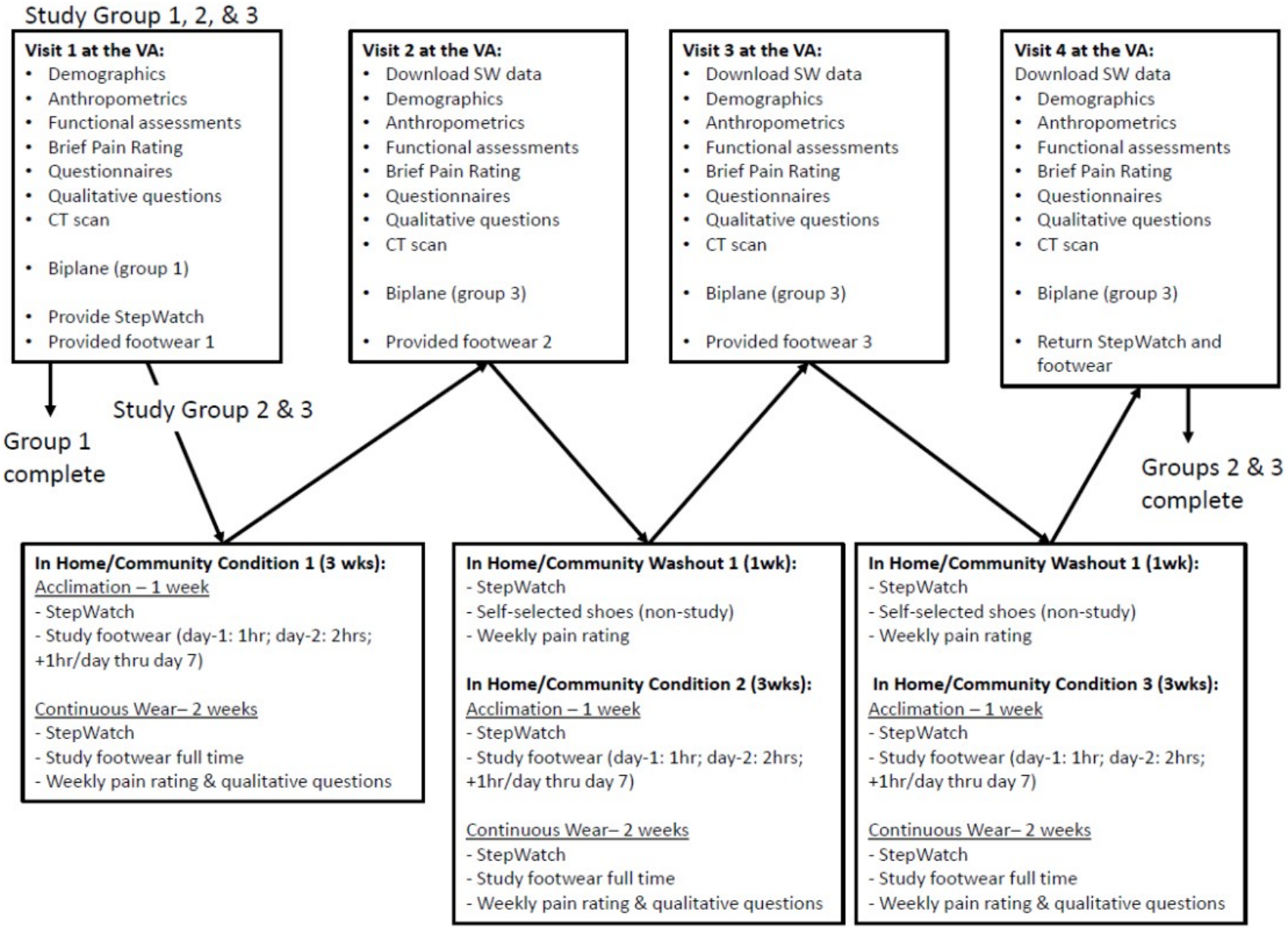
Participants will repeat the procedures described under In Home/Community Footwear Condition 1 Washout Period.

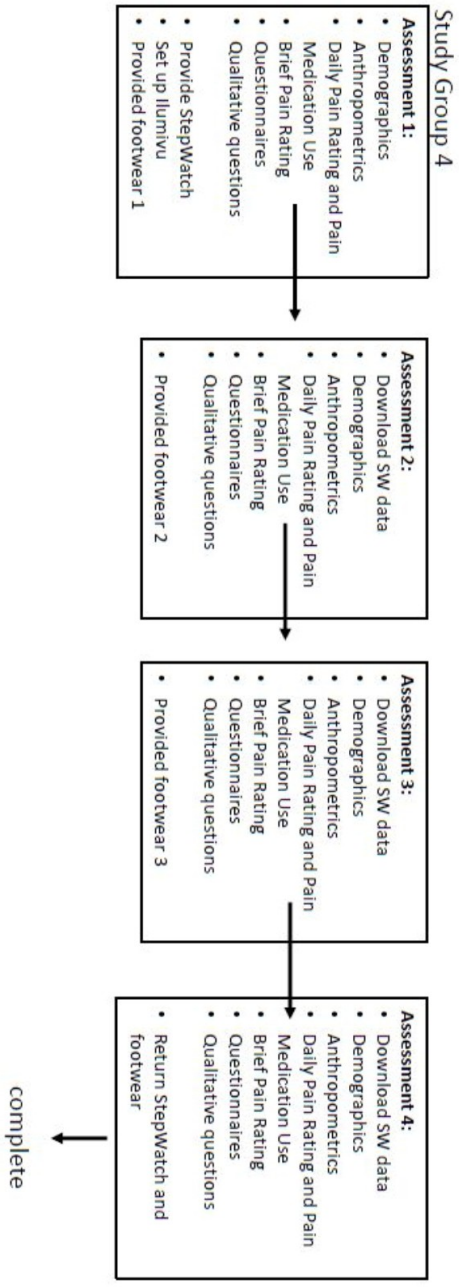
In Home/Community Footwear Condition 3: Acclimation & Continuous Wear Period (3 weeks)

Participants be asked to follow the same 1-week acclimation procedures, followed by 2 weeks of continuous wear that they did with Footwear Conditions 1 and 2. Participants will also continue wearing the StepWatch and completing weekly pain ratings.

Assessment 4

The procedures described under Assessment 2 will be repeated. Participants will return the study footwear and the StepWatch.


Study Group 1, 2, & 3
Visit 1 at the VA:
• Demographics
• Anthropometrics
• Functional assessments
• Brief Pain Rating
• Questionnaires
• Qualitative questions
• CT scan
• Biplane (group 1)
• Provide StepWatch
• Provided footwear 1
Visit 2 at the VA:
• Download SW data
• Demographics
• Anthropometrics
• Functional assessments
• Brief Pain Rating
• Questionnaires
• Qualitative questions
• CT scan
• Biplane (group 3)
• Provided footwear 2
Visit 3 at the VA:
• Download SW data
• Demographics
• Anthropometrics
• Functional assessments
• Brief Pain Rating
• Questionnaires
• Qualitative questions
• CT scan
• Biplane (group 3)
• Provided footwear 3
Visit 4 at the VA:
Download SW data
• Demographics
• Anthropometrics
• Functional assessments
• Brief Pain Rating
• Questionnaires
• Qualitative questions
• CT scan
• Biplane (group 3)
• Return StepWatch and footwear
Group 1 complete
Study Group 2 & 3
Groups 2 & 3 complete
In Home/Community Condition 1 (3 wks):
Acclimation – 1 week
- StepWatch
- Study footwear (day-1: 1hr; day-2: 2hrs; +1hr/day thru day 7)
Continuous Wear– 2 weeks
- StepWatch
- Study footwear full time
- Weekly pain rating & qualitative questions
In Home/Community Washout 1 (1wk):
- StepWatch
- Self-selected shoes (non-study)
- Weekly pain rating
In Home/Community Condition 2 (3wks):
Acclimation – 1 week
- StepWatch
- Study footwear (day-1: 1hr; day-2: 2hrs; +1hr/day thru day 7)
Continuous Wear– 2 weeks
- StepWatch
- Study footwear full time
- Weekly pain rating & qualitative questions
In Home/Community Washout 1 (1wk):
- StepWatch
- Self-selected shoes (non-study)
- Weekly pain rating
In Home/Community Condition 3 (3wks):
Acclimation – 1 week
- StepWatch
- Study footwear (day-1: 1hr; day-2: 2hrs; +1hr/day thru day 7)
Continuous Wear– 2 weeks
- StepWatch
- Study footwear full time
- Weekly pain rating & qualitative questions



Registry (optional)

Participants will be asked if they are interested in joining our Center's Subject Registry (MIRB# 00433). This registry is used to recruit for studies being conducted by our Center. If participants choose to join the registry they will sign a separate consent form. Data about their foot type that is collected under this study will be added to the Subject Registry; this will help us determine which studies may be a good fit for participants in the future.

Repository (optional)

Participants will be asked if they are interested in allowing their study data to be added to our de-identified data repository so that it may be used for additional research in the future. Participants who are interested will be asked to sign a separate consent form for the repository (MIRB# 00493). Once the consent form is signed, a copy of the data will be added to the repository on an ongoing basis throughout the course of the study.

Additional use of de-identified data

Throughout the course of the study we will place a copy of all de-identified data in publicly accessible online data repositories. Once posted, the de-identified data will publicly accessible to search, retrieve, and analyze for any purpose. Participants will be made aware of this use of de-identified data during the consent process and it will be described in the consent form. If participants do not wish to have a copy of their de-identified data placed in online repositories they can choose not to participate in the study.

Payment to Participants

Participants will be paid once at the end of the study. Participants in study group 1 will receive $30/hour after they complete all of the study procedures. Participants in study groups 2 and 3 will receive $400 and $500 respectively, participants in study group 4 will receive $300, after they complete all of the study procedures. If participants are withdrawn early they will be paid based on a daily prorated amount for the length of time they were expected to be in the study.

Checks will be mailed by the fiscal department about 6-8 weeks after each study visit or participants can pick up their check at the VA Puget Sound in approximately the same time frame. Participants that are screened out after consent will be compensated $50 for their good faith effort.

Risks and Risk Management

Procedures Involving Radiation Exposure

Biplane Fluoroscopy and CT scans: There is a very small increased risk of cancer due to the amount of radiation exposure involved in this study. Based on previous Radiation Safety Applications by our research group, and using conservative estimates, the estimated radiation exposure is from up to three sources the CT scans of subject anatomy (a) traditional CT, (b) LineUP CT and (3) three visits to the biplane fluoroscopy laboratory. For risk (a) the traditional CT imaging is conservatively estimated to expose participants to 0.20 mSv of ionizing radiation (b) the LineUP CT imaging is conservatively estimated to expose participants to 0.10 mSv of ionizing radiation and for the fluoroscopic exposure (c) an estimate (again conservative) of 0.21 mSv for 80 biplane trials. The total estimate of exposure for the whole study is 0.51 mSv. The upper limit of radiation exposure involved in this study is approximately ~16.5% of the estimated naturally occurring background radiation exposure (of 3.1 mSv) (http://hps.org/documents/) “Background Radiation Fact Sheet.” For additional comparison, the EPA (https://www.epa.gov/radiation/radiation-sources-and-doses) estimates of annual radiation exposure is 6.20 mSv (3.1 mSv from naturally occurring background radiation and 3.1 mSv man-made sources such as equipment used in medical procedures), this study will therefore expose participants to ~8.2% of the annual background radiation. Please note that this is the maximum anticipated exposure, in practice we find that participants normally complete their walking trials in well under 80 attempts (45 trials would be the minimum required), but we wish to be conservative with our

estimate. We will minimize the risk due to radiation by taking the minimum number of traditional CT scans, LineUP CT scans, and fluoroscope trials needed to obtain the necessary data. This means that some participants may only require 1 traditional CT scan, 8 LineUP CT scans (vs. up to 15), and 45 trials (vs. up to 80). It is anticipated that most participants, particularly controls, will be well under the maximum of 1 CT scan, 15 LineUP scans, and 80 exposures we have budgeted for in our radiation estimate.

Participants may be exposed to loud noises (like a heavy door slamming) when they are inside the building that houses the biplane fluoroscopy lab; this may startle some individuals. The building where lab is located also houses a blast machine. The blast machine is located in a separate lab, diagonally across the building from the biplane fluoroscopy lab. The blast machine can be quite loud when standing directly outside of the door of the lab where it is located, however when walking to or when inside the fluoroscopy lab the noise sounds like a muted bang/door slamming. We have a set of standard operating procedures that will be followed in order to minimize the risk that participants will be exposed to noises from the blast machine. The SOPs include escorting participants at all times and informing them of the potential noises prior to entering the building.

Biplane Trip and Fall: There is a risk of tripping and falling while walking on the Biplane imaging walkway. The the biplane imaging walkway is clear of obstacles and is level, dry, and rigid. Thus, walking on the biplane walkway is akin to walking on a well-maintained sidewalk. The biplane walkway also has support railings on both sides; these railings will be within easy reach of participants at all times. Participants will also have time to familiarize themselves with the shoes and the area in which they will be asked to walk.

Stress and Inflicted Insight: Participants may feel a mild level of emotional stress if they find it inconvenient to travel to the VA for study visits, or if they have difficulty sitting or standing still during the CT scan. It is possible that we could discover that female participants are pregnant. It is also possible that the imaging procedures (CT scans, and fluoroscopic images) could reveal that a participant has a serious health problem or anatomical abnormality (e.g., bone cancer). Potential participants will be screened during the telephone call, or in person screening, regarding their willingness to be made aware of the pregnancy test result and/or potential health problems discovered by the imaging procedures. Those who are not willing to be told about this information will be excluded from the study. Additionally, in the consent form, participants will again be made aware of this possibility and given the option to decline participation in the study if they choose. If a participant is determined to be pregnant and/or if we see an unexpected abnormality in a participant's radiological images we will advise them to follow up with their regular health care provider.

Wearing Study Assigned Footwear and the StepWatch

At Home Trip and Fall: There is a risk of tripping and falling while wearing the study assigned footwear at home and in the community, but this risk is not greater than that of daily life.

Increased Foot or Ankle Pain, Soft Tissue Irritation: There is a risk that the study assigned footwear could increase foot or ankle pain. There is a risk of minor discomfort, soft tissue irritation or skin break down (e.g. skin blister) in response to wearing the study assigned footwear and the SAM. Participants will be instructed to inform us if they feel discomfort or pain when wearing the control shoes, RB shoes, or AFO for the first time. Participants will have the opportunity to walk around to

confirm the shoe or orthosis fits them well and is comfortable before taking them home. Participants can change the size of the shoe or orthosis to achieve the best fit. The acclimation periods will give participants time to adjust and respond to the footwear which will minimize the risk of soft tissue irritation or discomfort. If proper fit and comfort cannot be achieved the participant will have the option to wear their own preferred footwear for a period of time or they can withdraw from the study. We may opt to move the participant to the next footwear condition after a washout period, if the participant wishes to continue in the study. Participants will be instructed to either drop out of the study or follow up with their regular clinician if they experience an increase in foot/ankle pain that concerns them (vs. their typical pain level) while wearing the study footwear. We will be regularly monitoring pain ratings throughout the study so participants will be aware of their pain and if it is changing significantly. If proper fit and comfort cannot be achieved the subject will have the option to wear their own preferred footwear for a period of time or they can withdraw from the study.

Quality Control

The PI will ensure the study procedures are being properly followed by keeping the research staff well informed of the current study procedures through regular/ongoing contact and meetings. The PI and/or designated research staff will verify visually that the data are sufficient and accurate as soon as possible after each data collection visit is complete.

Privacy and Confidentiality

See section 7.0 below for Information Security, Privacy and Confidentality related procedures.

5.6 Data Analysis

Means and SDs of daily step count, numeric pain rating, self-selected walking speed, PROMIS, AAOS-FAM, and FAOS survey scores will be calculated in MATLAB for each intervention (control shoe, RB shoe, AFO). Sagittal, frontal, and transverse plane ROM for the talocalcaneal, talocrural, talonavicular, naviculocuneiform, and the first cuneometatarsal joints will be defined as the difference between the maximum and minimum angular joint position in the sagittal, frontal, and transverse planes during the stance phase of gait. Means and SDs of ROMs will be calculated in MATLAB.

Anatomical Coordinate Systems for ROM Calculation:
In order to determine joint motion, we first must assign anatomical coordinate systems to the bones. To accomplish this in a repeatable manner, we employ a template-matching algorithm to embed anatomical landmarks onto each bone. This is done by “morphing” a standard foot geometry template onto a given subject’s bony anatomy. The selected template foot was verified to be free of bone deformities and image/object artifacts by a group consisting of engineers and an orthopedic surgeon. Using a custom graphical user interface (GUI), the landmarks were located and embedded with digital markers to determine the spatial positions. The template foot can then be registered to all of the feet in the study.

Example – Talocrural Coordinate Systems for ROM Calculation:
Three landmark points ($P1$, $P2$, and $P3$) are used in defining the coordinate systems for the tibia/fibula (the tibia and fibula are grouped together) and talus. The first directional unit vector $\vec{n}1$ is computed from the vector between $P1$ and $P2$. A dummy vector $\vec{n}d$ is calculated from $P2$ and the

last point $P3$. The cross product between $\vec{n}1$ and $\vec{n}d$ yields the second directional unit vector, $\vec{n}2$. Finally, the cross product between $\vec{n}2$ and $\vec{n}1$ yields the final directional unit vector $\vec{n}3$.

Talar landmarks: Landmark points for the talus were located at the lateral point of the talar head ($P1$), posterolateral (trigonal) process of the talus ($P2$), and medial point of talar head ($P3$). The direction unit vectors were calculated in the *y*, *z*, *x* order (Figure 8).

Tibia/Fibula Landmarks: Landmarks are placed on both bones to define their coordinate system. The landmarks are placed at the: lateral superior point of the Fibula ($P1$), lateral malleolus ($P2$), and medial malleolus ($P3$) while the order of
calculation of the direction unit vectors were *z*, *y*, *x* ($\vec{n}1, \vec{n}2, \vec{n}3$.) (Figure 8).

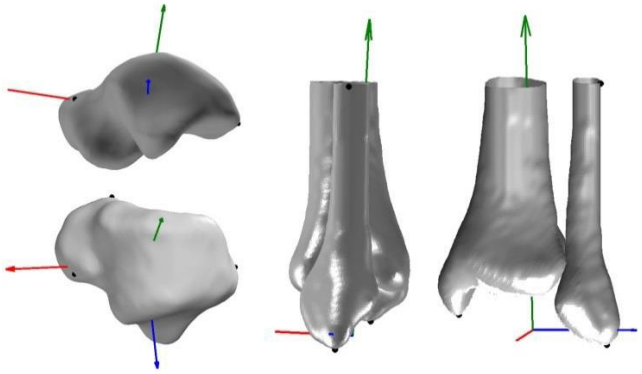


Figure 8: Template talus (left images, lateral view for top image, superior view for bottom image) and template tibia/fibula (right image pair, lateral view for left image, posterior view for right image). Landmark points are shown as black dots on the bone surface. Anatomical axes derived from landmark point locations are also shown (red, blue, green arrows).

Template Matching:
To register the template bones onto a study subject's bones, the template bone is first aligned to the subject bone by a rigid body registration and an affine transformation (i.e., uniform volumetric scaling to the template bone). The principal axes, obtained from a principal component analysis, and center of volume (COV) for both the template and subject bone are used to estimate the initial transformation parameters for the registration of the template bone to the subject bone. That is, the two bones are initially aligned along their principal axes, and isometrically scaled to have the same volume. At this point the template is roughly aligned and a similar size as the subject bone. To further match the template with the target, non-rigid B-spline registration was used to deform the template further onto the subject bone. This registration yields a deformation field of three-dimensional vectors defining the displacement of points on the template to the corresponding points on the subject bone.

Landmark Transformation:
The final step uses the registration results to perform a point mapping from the template to the subject bone. Using the affine transformation matrix (*T*) and the deformation field (*d*) points, points (*x*, *y*, *z*) on the template can be mapped directly to corresponding points (*x'*, *y'*, *z'*) on the subject. This formula is applied to the key anatomic landmark points on the template bone (i.e., points $P1$, $P2$, and $P3$ above), to determine their corresponding location on the subject bone. These transformed landmarks thus define the bone-embedded coordinate system

This process establishes a tibial anatomical coordinate system and a talar coordinate system for measuring talocrural joint ROM. These same methods will be used to measure talonavicular, naviculocuneiform, and the first cuneometatarsal kinematics. By performing this template matching algorithmically, we can ensure consistency in post processing of anatomical coordinate systems between subjects.

Statistical Methods:
For **Specific Aim 1**, linear mixed effects regression will be carried out to test for differences in mean step count, self-selected walking speed, physical function or pain (the dependent variables) by intervention, (control shoe vs. RB shoe vs. AFO, the independent fixed effect) with study subject as a random effect. If the omnibus test for the association between outcome variables and intervention is significant, pairwise comparisons will be carried out to assess differences in mean outcomes between the RB shoe or the AFO and the control shoe (Hypothesis 1.1) and between the RB shoe and the AFO (Hypothesis 1.2).

For **Specific Aim 2**, linear mixed effects regression will be used as above to examine differences in mean [sagittal plane] ROM (the dependent variable) by intervention (control shoe, RB shoe, AFO; the independent fixed effect) with subject and subject by intervention interaction as random effects. If the omnibus test for association between [sagittal plane] ROM and foot intervention is significant, pairwise comparisons will be carried out to assess differences in mean [sagittal plane] ROM between the RB shoe, the AFO, and the control shoe (Hypothesis 2.1). Secondary analyses will be carried out using methods similar to those described above to determine if the interventions affect frontal and transverse plane joint ROM.

For **Specific Aim 3**, hypotheses 3.1 and 3.2, the above model will be modified with the definition of the independent fixed effect, foot intervention, having an additional category representing the healthy control group. Post-hoc comparisons will focus on differences in mean step count, self-selected walking speed, physical function, pain or [sagittal plane] ROM between RB shoe or AFO and the healthy control subjects wearing the control shoes. Additional secondary analysis will be carried out using linear mixed effects regression to determine if pain (the dependent variable) correlates with [sagittal plane] ROM (the independent fixed effect, averaged over trial) and step count (the dependent variable) correlates with pain (the independent fixed effect) with study subject as a random effect in both sets of models. To determine if the mean differences in outcome by intervention (AFO vs. RB shoe) varies by OA severity, the regressions described above will be modified by adding two additional independent co-variates: OA severity and OA severity X intervention. The significance of the latter interaction term suggests that OA severity may influence outcome differences by intervention.

Power Analysis:
Ten thousand datasets were generated using mean [sagittal] ROM for the control foot of 15.3 degrees, between subject SD of 2.0 degrees, and within subject SD of 2.4 degrees.84 Power was estimated for sample sizes of 15 and 20 subjects and for a 1.5 degrees and 2.0 degrees difference in [sagittal] ROM between the control shoe and the RB shoe or AFO. Hypothesis testing for each bootstrapped sample for the reduction in ROM was carried out using a linear mixed effects regression of [sagittal] ROM (the dependent variable) on foot (ROM or AFO vs. control) with study subject and subject by intervention interaction as random effects. Power was estimated by determining the number of tests that were significant at the 0.05 level using the likelihood ratio test. The analysis indicated that if the footwear induces a 1.5 degrees change in ankle [sagittal] ROM then a sample size of 20 or 15 subjects results in 94% or 84% power, respectively. If the change in ROM is 2.0 degrees, then even with only 15 subjects the study has 98% power (Table 2). Note that we expect the change in [sagittal] ROM to be significantly more than 1.5 degrees but even for this small difference our study is adequately powered with 25 subjects. Based on these results, we plan to enroll 30 subjects into the

study and expect several to drop out leaving a sample size of at least 25 subjects and the study power greater than 94% (Table 2).

Simulated [sagittal] ROM difference between the control shoe and RB shoe or AFO	Number of subjects	Estimate power
1.5 degrees	15	84%
2.0 degrees	15	98%
1.5 degrees	20	94%

5.7 Withdrawal of Participants

This is not a treatment study; withdrawing or being terminated from this study will not have an impact on participant safety. A study clinician or the PI may withdraw a participant without their consent if he or she feels that it is not in a participant's best interest to continue in the. All data previously collected from participants who withdraw, or are withdrawn, or lost to follow-up will be kept and may be used in the study data analysis. If participants choose to withdraw, miss multiple visits or their participation is terminated, we will contact them to request that they return the study provided footwear; a mailer will be provided if needed. We will make up to three contact attempts to recover the study equipment. Participants may withdraw at any time by informing the Research Coordinator and/or the PI.

6.0 Reporting

All safety information on Adverse Events (AEs), Serious Adverse Events (SAEs), unanticipated events or problems, and protocol deviations will be collected. This information will be collected at study visits and whenever participants call to report a problem. It will be collected on VA IRB forms (Report of a SAE and/or Problem Form), or Report of Problems (ROP) Form. Safety data will be collected on an as-needed basis and will begin upon enrollment into the study. Any anticipated AEs will be recorded on a log sheet and reported annually with the CRQ. Although the risks identified in this study are relatively minimal, we will tabulate a list of any such reports that occur during the study and compare it with corresponding data available in the literature. Participant pain ratings will be collected weekly which will help us to monitor any significant changes. This will allow us to analyze how much of an increased risk was due to the administered protocol. Also please note, the anticipated maximum radiation dosage (0.40 mSv) is far below any dose that would have a measurable effect on participants. After each report of an AE, SAE or an unanticipated problem, we will evaluate study procedures for previously-assessed risks, and will determine whether any changes to the protocol are necessary to minimize risks. The study will be suspended until these changes have been fully implemented and approved by the IRB.

If we become aware of relevant findings or information that may affect participants' health or welfare we will contact participants by phone and/or a letter to notify them.

7.0 Information Security, Privacy and Confidentiality

As with most studies, it is possible that a loss of privacy or confidentiality could occur. Given the impresonal nature of the majority of the data that will be collected, the risk of harm is minimal. Electronic data with PHI/sensitive information will be stored on the secure server at the VA Puget

Sound. These data will only be accessed by authorized study personnel. Hardcopies of VA sensitive data and documents with PHI will be stored in a locked file cabinet in a locked office at the VA Puget Sound (Seattle). Study files/data with PHI or sensitive information will not be sent off-site. This is a locked facility to which only study investigators have access. Identifiable data will not be transmitted, transported, or stored on portable media or laptops outside of the VA, and the data will only be accessed by authorized VA study staff. We will notify the Information Security Officer of the location of the hardcopy data/files via the Data Inventory form. If study data is improperly used or disclosed we will notify the ISO and Privacy Officer within one hour of becoming aware of the issue.

Study data will be labeled with a study assinged code and de-identified data sets (data without any of the 18 HIPAA identifiers) will be created/used when data is made publically available and transmitted without restriction. The key to the code will be stored seperately from the study data and only designated study staff will have access to it. The key will be stored in a permissions restricted folder on the VA network. Study records with PHI/PII will be destroyed using VA approved procedures and in accordance with the records retention schedule after the study is completed; this will be a minimum of 6 years after the study has been completed. De-identified data with study assigned codes will be stored indefinitely. If participants choose to participate in the Subject Registry information about their foot type will be stored indefinitely in the Registry.

If the CT scan is obtained through a clinical service at the VA, it will contain the participant's name in the header, and it will be stored in the participant's medical record (CPRS). The CT data will be downloaded onto CD(s), and hand-transported by study staff to our data processing computers at the VA. Pre-existing CT scans released to the VA from the UW, or any other facility, via a Release of Information Form will be transported from the UW by study staff and/or mailed to the VA. Prior to any analysis of the CT data, all patient and institution identifiers will be removed from the headers of the radiograph files, and replaced with the study-unique code. When the de-identified copy of the CT data is properly created, it will then be uploaded from the CD(s) to our computer workstation for further analysis. The CDs/DVDs will be stored in a locked cabinet in a locked office when not being processed. We will take the CD containing PHI to our VA IT manager to be destroyed. At no time, will copies of any medical image data containing patient identifiers be placed on any computer. CT scans taken at a third-party vendor will be burned to CD and hand delivered by study staff, or sent via traceable mail, to the VA. The CT scan files will include a study ID code, age (if 89 or younger), but no PHI. The third-party vendor will not collect any PHI from subjects. CT scans obtained by our in-house LineUP system will be labeled only with the study assigned ID code.

Ilumivu: After participants complete mobile assessment, the data will be stored with the unique ID on ilumivu's main storage database in the USA. The ilumivu-based site may only be accessed after supplying a verified user ID and password. The core system implements a hierarchical, roles-based security model that determines access to information and system capabilities. Data are encrypted using TLS encryption 1.2 or greater before being transmitted to the database, while on the servers, and when being transmitted to the VA local site.

Electronic transmission of de-identified fluoroscopy images will occur between the Biplane Fluoroscopy Laboratory data collection computer and the data processing computers in a different room at the VA. The de-identified images/data will also be kept indefinitely.

De-identified, non-sensitive electronic data with the study assigned codes (described above) and all 18 HIPAA identifiers removed or converted to de-identified format, may be stored on non-networked equipment at the VA Puget Sound (computers/laptops/tablets/sd cards) and/or on the VA network and/or on non-VA owned computers. These devices are stored in locked areas. No mobile devices will be used to collect or house PHI/sensitive data. Mobile devices (tablets) will be used to collect de-identified data (PROMIS measures). No HIPAA identifiers will be entered into the PROMIS. The data will be labeled with study assigned ID codes and be stored by the PROMIS application on the tablet. A copy of the PROMIS data will be exported to an database file and emailed to the research team. StepWatch Activity Monitors will be used to collect step data during the study. The device itself will not contain any PHI, it will be associated with the study assigned ID code. StepWatch data will be downloaded to a computer during study visits at the VA. If needed, we will send a new StepWatch to participants using a trackable mail service and provide participants with a pre-paid/addressed/trackable envelope to return a StepWatch.

De-identified data files will be sent via email and/or other electronic media (CD/DVD, usb drive via hand delivery or trackable mail) to our biostatistician and off-site collaborators. De-identified electronic data will not be encrypted. These non-sensitive files may also be transported on usb drives or non-networked laptops by staff working at both the VA and UW. De-identified data may be transmitted by email between study investigators and collaborators and will not be secured. These data will be stored and used on electronic media outside of the VA.

De-identified data (as described above) will be stored and publicly accessible to search, retrieve, and analyze. Participants will be informed, via the consent form, about this additional use of data.

Any consented photography or video will protect participatnts' identity because they will be anonymized/edited during data collection or processing to remove or obscure any identifying features (such as scars and tattoos); and then the original file will be deleted. The video camera and the recording media (e.g., SD cards, optical disks) will be stored in a locked office at the VAPSHCS. Photos and videos that do not contain identifiable information may also be stored on password-protected computers/laptops for future use in scientific presentations and publications. These de-identified data will not be encrypted.

If participants choose to enroll in our data repository, a copy of their de-identified data will be placed in the repository and kept indefinitely.

8.0 Communication Plan

Students or staff at the University of Washington are participating as study staff at the VA. UW IRB approval has been obtained from the UW Human Subjects Division.

9.0 References

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