

Human Subjects Protocol

VA Puget Sound IRB

Novel Custom Foot Orthotics to Improve Foot Health

MIRB #01777

Funding Agency: Department of Defense and Department of Veteran Affairs

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Abstract

Background:

The effects of diabetes and other forms of vascular disease frequently result in impaired blood flow to the individual's feet as well as nerve damage that may negatively affect sensation. Combined, these conditions place the individual at risk of developing foot wounds of which they may be unaware, and which may be substantially slower to heal than for a healthy individual. For the individual with elevated risk, an otherwise minor foot wound may lead to ulceration, infection, and eventual amputation. The leading cause of lower-extremity amputation in the US is this disease progression in individuals with diabetes. The current standard for prevention of plantar foot ulcers for at-risk individuals is specialty diabetic shoes and custom foot orthotics (CFOs). The purpose of the CFOs is to cushion the plantar surface of the feet, evenly distribute plantar pressures, and to selectively offload areas of increased pressure. The current standard conventional CFO (C-CFO) is made from several layers of sheet foam of varying durometer, which are laminated together and heat-molded to a model of the patient's foot. Under normal usage conditions, C-CFOs last about four months, after which time the foam under the highest-pressure areas becomes too compressed and compacted to provide necessary cushioning. At this point, in order to maintain the benefits, the C-CFOs must be replaced with a new pair. Inherent shortcomings based on material properties limit the utility of C-CFOs, resulting in relatively short lifespan and limited capacity to offload high-pressure areas.

The results of this study will be used to determine efficacy of novel custom foot orthotic (N-CFO) for VA patients with elevated risk for development of foot ulcers. The study outcomes are expected to fill the current knowledge gap and greatly improve care of Veterans beyond giving them a device, but by investing into their overall rehabilitative care.

Purpose:

The purpose of this study is to determine efficacy of N-CFOs for VA patients that are at an elevated risk for foot ulcers. It is our hope that this innovative project will advance the state of rehabilitation and take us one step closer to reducing amputations for individuals with diabetes and other vascular disease.

Methodology:

There are two study groups in laboratory and take home. Participants will be assigned to a group based on the needs of our study. Study group 1: In laboratory - All research procedures will be conducted at the VA Puget Sound in Seattle in session(s) lasting up to 4 hours. You will not take home any study devices, but may be asked to visit the laboratory up to 12 times. Activities may include the following items.

- Demographic information
- Health history
- Clinical lower extremity/foot evaluation
- Foot scan
- Outcome measures

Study group 2: Take Home - All data collection procedures will be conducted at the VA Puget Sound in Seattle in session(s) lasting up to 4 hours, however you will be asked to take home and wear the study devices, and may be asked to visit the laboratory up to 12 times in 24 months. Activities may include the following items.

- Demographic information
- Health history
- Clinical lower extremity/foot evaluation
- Foot scan
- Outcome measures
- At home monitoring

List of Abbreviations

CFO	Custom foot orthotic
CMS	Centers for Medicare and Medicaid Services
CPG	Clinical Practice Guideline
CPO	Certified Prosthetist/Orthotist
CPRS	Computerized Patient Record System
Fig	figure
H	hypothesis
IRB	Institutional Review Board
K	thousand
N	number of participants
O&P	orthotic & prosthetic
PBRN	Practice-based Research Network
PI	principal investigator
PRAF	project revision/amendment form
RCS	Rehabilitation Care Services
ROM	Range of motion
RR&D	Rehabilitation research and development
VA	Veterans Affairs
VAPSHCS	VA Puget Sound Health Care System
VAPORHCS	VA Portland Health Care System
WA	Washington
Yr	year
3D	Three dimensional

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Protocol Title: Novel Custom Foot Orthotics to Improve Foot Health

1.0 Key Study Personnel

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2.0 Introduction

In 2017 over 30 million individuals in the US had diabetes, representing almost 10% of the total population [1]. Veterans are more likely to be affected by diabetes, with a prevalence close to 25% among VA patients [2]. Several conditions affecting the lower extremities are associated with diabetes, including peripheral vascular disease, neuropathy, and foot deformity. For individuals with diabetes and one or more of these secondary conditions, a common disease progression involves development of a foot ulcer leading to infection and amputation. Individuals with diabetes represent the largest group to experience lower extremity amputations [3]–[5]. Footwear, involving specialty diabetic shoes and custom foot orthotics (CFOs) have been shown to decrease the incidence of trauma to the feet, thereby staving off the first events in a chain reaction that often ends in amputation.

To create a conventional CFO (C-CFO), an impression of the foot must first be obtained. This can be accomplished through several different techniques, including plaster casting, stepping the foot into a box filled with light crushable foam, or scanning the foot with a digital scanner. The foot impression is used to create a positive model of the foot, generally formed from a hard material such as plaster or wood composite. In order to optimize C-CFO performance, the shape of the positive model can be modified according to clinical judgment. The hard positive model is then used as a form over which several layers of sheet-form closed-cell foam or other elastic and dampening materials, such as sheet cork, are heated, vacuum-formed, and glued together. Sheets are layered such that the most compliant layer sits adjacent to the plantar surface of the foot, and the layers get progressively firmer toward the bottom of the C-CFO. The resulting CFO has a soft top surface contoured to match the plantar surface of the foot, and a firm bottom surface that matches the interior shape of the shoe. Ideally, the thickness of the C-CFO provides ample cushioning but also allows for adequate space for the foot within the shoe. Specialty diabetic shoes tend to be deeper than conventional footwear for the purpose of accommodating thick CFOs without crowding the foot.

While C-CFOs provide valuable protection to the plantar foot, they have several shortcomings related to the nature of the materials from which they are crafted. The first shortcoming is one of durability: the soft sheet foam which provides cushioning to the foot fairly quickly becomes over compressed, and within about 4 months no longer provides cushioning to the most high-pressure areas. Due to this constraint, patients are advised to replace the C-CFOs in their shoes every 4 months. The second shortcoming relates to a limited capacity to evenly distribute plantar pressures and to selectively

offload areas of high pressure: because C-CFOs are made from a series of full-length layers of compliant materials, the potential to selectively alter the durometer (hardness) of specific areas of the C-CFO is highly limited. Selective offloading of specific areas is typically accomplished by grinding away some of the firmer under-layers in the area of concern. The durometer of the resulting “soft spot” is not well quantified, nor is its location readily duplicable in subsequent C-CFOs.

Little has changed in the manner in which C-CFOs have been fabricated since they were first introduced several decades ago. Novel CFOs (N-CFOs) have been proposed, using fabrication techniques and/or materials not used in the fabrication of C-CFOs, such as 3D printing. It is currently unknown if N-CFOs are capable of meeting or exceeding the durability or the pressure distributing characteristics of C-CFOs. This proposed study aims to determine if novel CFOs (N-CFOs) can meet or exceed the performance of C-CFOs in the areas of durability, pressure distribution, selective off-loading, facilitating overall foot health, mobility, and community locomotion. To determine the comparative effectiveness of N-CFOs, participants will be provided with either C-CFOs or N-CFOs. At a series of regular intervals, participants will come to the VA lab for foot evaluation, review of activity, and to measure plantar pressures while wearing the CFOs (C- or N-). This project will advance the state of rehabilitation practice and potentially help all stakeholders in the mission to improve mobility and prevent amputations among many high-risk Veterans.

Significance: The target population of the proposed research is Veterans with diabetes and other vascular disease resulting in elevated risk for foot ulcers and subsequent infection and amputation. CFOs represent first-line prevention of foot trauma that frequently results in catastrophic health problems for this high-risk population. However, CFO technology has not appreciably changed or improved for many years, and shortcomings with the current standard limit the efficacy of the device. Emerging materials and fabrication technologies provide the possibility for greatly increased performance of this critical orthotic device. The outcomes of this study are expected to greatly improve the care of Veterans beyond giving them a device, but by investing into their overall rehabilitative care and quality of life. N-CFOs will be substantially more customizable to the individual, representing a key advancement in personalized healthcare for this patient population. Furthermore, the information gained from this project will inform subsequent VA Merit Award proposals to better optimize this rehabilitation care across the VA and impact the Clinical Practice Guidelines. The ultimate aim of this and future projects is to maximize the quality of life and long-term rehabilitation outcomes in Veteran CFO users.

3.0 Specific Aims and Hypotheses

Our proposed research has six specific aims:

- 1. To compare the short-term and long-term effects of novel custom foot orthotics (N-CFOs) and conventional custom foot orthotics (C-CFOs) on foot health.**
- 2. To determine the short-term and long-term capacity to evenly distribute plantar foot pressures of novel custom foot orthotics (N-CFOs) as compared to conventional custom foot orthotics (C-CFOs).**
- 3. To compare the durability of novel custom foot orthotics (N-CFOs) with conventional custom foot orthotics (C-CFOs).**
- 4. To compare the short-term and long-term effects of novel custom foot orthotics (N-CFOs) and conventional custom foot orthotics (C-CFOs) on community mobility.**
- 5. To compare the short-term and long-term effects of novel custom foot orthotics (N-CFOs) and conventional custom foot orthotics (C-CFOs) on laboratory locomotion.**
- 6. To compare various methods of N-CFO fabrication on the proposed outcome measures.**

H1.1: Short-term foot health outcomes will not be significantly different between N-CFOs and C-CFOs.

H1.2: Long-term foot health outcomes will be significantly different between N-CFOs and C-CFOs.

H2.1: Short-term even distribution of plantar pressure will be significantly improved for N-CFOs as compared to C-CFOs.

H2.2: Long-term even distribution of plantar pressure will be significantly improved for N-CFOs as compared to C-CFOs.

H3: N-CFOs will be significantly more durable than C-CFOs.

H4: Community mobility will be greater with the N-CFOs as compared to C-CFOs.

H5: Laboratory locomotion will be improved with the N-CFOs as compared to C-CFOs.

H6: No specific hypotheses

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

We propose to employ both between and within-subject study design. We will compare the effects of C-CFOs and N-CFOs on the proposed outcome measures. Specifically, participants will be men and women age 18+ years old some of whom may have diabetes or have been prescribed or currently use CFOs. Targeted enrollment for this study is 290 participants. Vulnerable populations will not be specifically targeted. See recruitment criteria for specifics of the study populations.

In addition to recruiting through the corporate data warehouse (CDW) we will be extracting de-identified participant information on timelines of disease progression, treatments/ surgeries related to foot health and dates of treatments/ surgeries related to foot health.

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

5.2 Recruitment Methods and Initial Screening

Up to 800 individuals may be approached during recruitment and enrollment procedures for the device arm. Up to 50 clinicians and 50 patient users may be approached during

recruitment and enrollment procedures for the focus groups. 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. Patient users for the focus groups and participants for the device will be recruited using similar procedures. We may contact people who have previously participated in the device arm to inquire if they're interested in the focus group sessions and vis-versa. Additionally if the opportunity presents itself, we may enroll someone into the device arm and the user focus group simultaneously. Potential subjects will be informed of the different options for study participation (i.e., free choice) if they qualify. In the case they prefer one over the other, we will let them choose their preferred participation (device arm and/or focus group).

Medical Record/Database: Letter/Phone/In-person

Designated research staff will screen relevant clinic lists in the VA (podiatry, orthotics and prosthetics, diabetes clinic) to identify potential participants.

After review of relevant clinic lists in CPRS/ the VA medical record system, designated staff will go to the clinic or contact providers on the phone or via encrypted VA email to ask if a patient might be a good fit for the study. If the clinician agrees that a patient may be an appropriate study participant, during an appointment the clinician will ask the patient if she/he is 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 after a clinic visit and/or use CPRS/ the VA medical record system to obtain potential participants' contact information (i.e., name, address, telephone number). For potential participants who learned about the study in person but may not have time to complete the eligibility screening with us, designated study staff may give them a flyer and/or business card and make a follow-up approach phone call and/or send an approach letter. 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/ the VA medical record system and the Corporate Data Warehouse (CDW) to identify individuals with qualifying health conditions and potential risk for plantar foot ulcers 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. 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 to give to patients that are interested in the study. 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/ the VA medical record system 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).

Flyers/Text

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). Flyers and study staff business cards will also be posted and distributed to potential participants at clinics in the community (*copies of the letters of support will be submitted to the IRB as miscellaneous submissions, as they are obtained*); clinicians and support staff will direct interested individuals to contact us to learn more about the study. 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.

VA Puget Sound Center Registry: Letter/Phone

At the VA Puget Sound, 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 agreed 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. If an individual returns the postcard to opt out they will not be approached about this study again. Interested individuals will be screened for eligibility. 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; see attached screening script.

Clinicians for the focus groups

Clinicians for the focus groups will be recruited through flyers in local clinics in addition to asking local orthotists and podiatrists for references of individuals who may be interested (i.e. word of mouth).

Recruitment Activities at UW/Harborview

Designated VA study staff may screen relevant UW/Harborview clinic lists, appointment calendars and patient medical records to identify potential participants. Study staff may also attend clinic at these facilities to identify and/or contact potential participants. Before or after clinic, study staff will discuss with the clinician 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 ask the patient if she/he is interested in speaking with study staff. For patients who are interested, study staff will speak to potential participants directly during/after a clinic visit to tell them about the study, give them a study flyer, 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 potential participants are screened for initial eligibility in person, study staff will label the noted responses with a recruitment 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. If patients are interested in learning about the study and/or in doing the initial screening but are unable to meet in person with study staff, we will look up the patients' contact information in

their medical record and contact them on the phone and/or send them the VA recruitment letter (the VA IRB approved letter with VA contact information would be sent per the process described above).

Staff may also search/access UW/Harborview medical records to identify potential participants, obtain their contact information (i.e., name, address, telephone number) and mail them the approach letter.

Clinician Referral

Designated VA 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 to give to patients that are interested in 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.

Also, 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 retain the preliminary eligibility screening responses (*see Screening Script*). Informed consent will be obtained prior to enrollment in the study.

The Research Coordinator, the PI, and/or other designated staff, as indicated on the study staff form, will conduct the informed consent process. All study personnel will complete the necessary human-subjects protections training per VA policy.

5.4 Inclusion/Exclusion Criteria

We aim to have 6 participant groups for a total of 290 participants.

1) Healthy controls (N=100)

Inclusion criteria:

- 1) Age 18+ years

2) Individuals with diabetes (N=50)

Inclusion criteria:

- 1) Age 18+ years
- 2) Diagnosis of diabetes

3) Individuals with Current diabetic CFO prescription (N=50)

Inclusion criteria:

- 1) Age 18+ years
- 2) Valid prescription for diabetic custom foot orthotics or current diabetic CFO user

4) Individuals with Current diabetic CFO prescription (N=50)

Inclusion criteria:

- 1) Age 18+ years
- 2) Valid prescription for diabetic custom foot orthotics or current diabetic CFO user

- 3) Plantar pressure greater than or equal to 250 KPa (assessed at first study visit)
- 5) Focus group Clinicians: (N=20)
 - a. Clinicians both VA and non-VA employees that are involved in the care of diabetic feet.
- 6) Focus Group Users: (N=20)
 - a. Individuals that use current diabetic CFOs.

Exclusion criteria for all participants:

1. Healed or non-healed foot ulcer within the last month
2. Prior amputation of more than 1 digit
3. Requirement for boots, custom shoes, or other specialty footwear for daily activities
4. Non-ambulatory status
5. Terminal illness that would make two-year survival unlikely
6. Pregnant (determined by self-report)
7. Inadequate cognitive function or language proficiency to consent to participate

5.5 Study Visits, Data Collection, and Risk Management

There are two study groups in laboratory and take home. You will be assigned to a group based on the needs of our study. It will be made clear to the participant which study group they are enrolled in through check boxes on the consent forms. The specific procedures for each item are outlined below.

All consent and data collection procedures will be done at the VA Puget Sound in Seattle. Participants will be asked to do between 1 and 12 visits lasting up to four hours each that may span up 24 months. The exact number of visits will depend on the development timeline. This is a progressive study where as we design and develop the materials and fabrication techniques. Once we have developed the insole and ensure its functionality, we will be more interested in the long-term benefits of the devices. Thus, initially 1-2 visits may be enough, while in a few years participants may be wearing the devices for 24 months and multiple visits may be necessary. If we find that data are missing or corrupt, participants may be asked to do another study visit. All procedures are for research purposes and provide no clinical treatment. Participants will be provided rest breaks throughout the procedures and may request one at any time. We may call and/or email participants to remind them about upcoming study visits. Upon completion of the study future contact may be made for publications, media, and outreach.

Progression through the study is as follows:

- Healthy controls or those with diabetes can enroll in the in laboratory study at any time
- Healthy controls or those with diabetes can enroll in the take home after either;
 - o That individual has completed the in laboratory sessions and the Research Prosthetist (on study staff) determines that the subject is safe to wear the device as part of an at home study.
 - OR
 - o Ten healthy control participants or those with diabetes have completed the in laboratory sessions and Research Prosthetist (on study staff) determines that the subject is safe to wear the device as part of an at home study.
- At risk populations can enroll in the in laboratory study at any time

- At risk populations can enroll in the take home after either;
 - o That individual has completed the in laboratory sessions Research Prosthetist (on study staff) determines that the subject is safe to wear the device as part of an at home study.
 - OR
 - o Ten at risk participants have completed the in laboratory sessions and the Research Prosthetist (on study staff) determines that the subject is safe to wear the device as part of an at home study.
- I. Practicing clinicians and research staff (Research Prosthetist on study staff) will evaluate foot health and plantar pressure (explained in the procedures section of the protocol) to determine safety of the device based on their knowledge of best practices and current clinical standard for care to ensure that the N-CFO is not worse than the C-CFO.
- II. The device may also be visually and/or mechanically examined for degradation and strut failure.

Study group 1: In laboratory

All research procedures will be conducted at the VA Puget Sound in Seattle. Participants will not take home any study devices, but may be asked to visit the laboratory between 1 and 12 times.

- Demographic information
- Health history
- Clinical lower extremity/foot evaluation
- Foot scan
- Outcome measures

Study group 2: Take home

This portion of the study will not start until preliminary in lab results indicate satisfactory progress, such as durability/longevity of the insole. All data collection procedures will be done at the VA Puget Sound in Seattle, however participants will take home and wear the study devices. Participants may be asked to visit the laboratory between 1 and 12 times in up to two years.

- Demographic information
- Health history
- Clinical lower extremity/foot evaluation
- Foot scan
- Outcome measures
- At Home Monitoring

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

Protocol

Once participants have passed the screening and have been provided informed consent, we will collect the following required demographic information with a questionnaire: sex, race, ethnicity, and Veteran status.

Data collection

Each visit we may ask the participant to conduct any of the following items. These will be made clear to the participant through check boxes on the consent forms.

Study Footwear

- In either study group (in laboratory or take home), participants may be asked to wear either our control shoes (such as the New Balance 928, Dr. Comfort extra depth or similar) or their own shoes. Demographic information: age, body weight, and height.
- Health history: Diabetes: none, Type 1, or Type 2, years since diabetes diagnosis, previously used CFOs, and body mass index (BMI).
- Clinical lower extremity/foot evaluation: including checking for localized lower extremity edema, peripheral pulses, sensation as measured with a 5.07 Semmes-Weinstein monofilament, and foot deformity.
- Foot scan: During the first visit, a foot impression will be taken using one or more of the following methods:
 1. Foam crush box: the subject, in either a sitting or supported standing position, will be asked to place each of their feet into a box containing lightweight crushable foam. The study orthotist may push on the top of the subject's foot to help compress the foam. The subject will then lift their foot out of the box, leaving an impression in the foam. Foam box impressions take about 30 seconds per foot.
 2. Direct digital scanning: the subject, in either a sitting or supported standing position, will lift each of their feet into space and hold it steady while the study orthotist captures a 3-dimensional impression using a handheld scanner. Scanning takes about 30 seconds per foot.
 3. Flatbed scanner: The participant will stand on the scanner, similar to a paper scanner, and the sole of the foot will be scanned and a 3D image rendered. Scanning takes less than one minute.
 4. Plantar pressure scanner: In-shoe pressure measurement system may be used. Participants' shoes may be fitted with insoles that record in-shoe pressures under the foot. The insoles will be attached with wires to a data acquisition unit; the wires are routed so they are not a trip hazard. Care will be taken to ensure that the insoles fit comfortably.
 5. EMED: Subjects will be asked to remove their shoes and then walk barefoot in a straight line for about 20 feet over an instrumented platform in our Motion Analysis Laboratory. This platform is flush with the surface of the floor. This platform measures the distribution of pressure beneath the surface of the foot, providing additional baseline data about how the subject's body weight is distributed during walking. This procedure will be repeated several times.
 6. In-shoe embedded ultrasonography: subjects will walk in a pair of our instrumented footwear that includes an ultrasound probe mounted on force transducers embedded in the sole of the shoe, positioned under the second metatarsal head. They should not feel the probe. This equipment provides a means of visualizing the dynamic compression of the plantar tissues during gait and allows soft tissue strain and stress to be determined.
 7. 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 the participant is a women of child-bearing potential a pregnancy test will be conducted prior to the scan. If she is pregnant she will not be eligible for this method of scan.

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 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 participants' 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.

8. LineUP: a low dose 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. If the participant is a women of child-bearing potential a pregnancy test will be conducted prior to the scan. If she is pregnant she will not be eligible for this method of scan.
9. Existing scan: If participants have a VA 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
- CFO fabrication
Once a foot impression has been obtained, C-CFOs and/or N-CFOs will be fabricated for each subject. Fitting of C-CFOs and/or N-CFOs will take place within six weeks of the first visit. Participants will be contacted to schedule the second visit for fitting of the CFOs. C-CFOs and/or N-CFOs may require modification in order to ensure proper fit within the subject's shoes. Any necessary modifications will take place during the second visit during fitting or any visit thereafter.

At each visit, participants may undergo any of the following outcome measures in C-CFOs, N-CFOs, and/or in no CFOs:

- Outcome measures
 - *Lower extremity/foot neuromusculoskeletal and skin evaluation:*
 - Checking for localized lower extremity edema
 - Checking peripheral pulses
 - Assessing sensation on the lower extremities as measured with a 5.07 Semmes-Weinstein monofilament
 - Assessing for foot deformity
 - Assessing for presence of wound or ulcer

- Assessing skin health using skin-health measurement tools
- *Pressure Mapping*: In-shoe pressure measurement system may be used. Participants' shoes may be fitted with insoles that record in-shoe pressures under the foot. The insoles will be attached with wires to a data acquisition unit; the wires are routed so they are not a trip hazard. Care will be taken to ensure that the insoles fit comfortably.
- *Survey*: We will survey participants in order to determine amount of time spent in bed, out of bed, wearing socks, slippers, other footwear or diabetic shoes, which will help determine footwear compliance. This may be done over the phone, on Ilumivu, or in lab with pencil and paper.
- *User Experience Questions*: We will ask participants open-ended questions about their experience using C-CFOs and/or N-CFOs. For example, we may ask what they like and do not like about the CFOs, about how and when they use the CFOs, about the comfort, or similar questions. We may note participants' answers for our study records.
- *Gait Lab Testing*: Participants will be asked to change into a tight fitting shirt and shorts that we provide; a private changing area will be provided. We will record a series of standard body measurements such as height, weight, and leg length. We will use double-sided tape to attach up to 100 small reflective markers to specific locations on the participants' hands, arms, head, trunk, legs, and feet. Once instrumented, participants will be asked to do a series of walking tests while we record their movements with an infrared camera system. The infrared cameras only record the location of the markers; they do not record a picture of the body. Data will also be collected by force plates embedded in the floor of the lab and while walking on the instrumented treadmill.
- *Walking Tests*: Participants will be asked to perform several walking tasks during each study visit. The total duration of all walking tests will be no more than 90 minutes per visit. During the laboratory walking tests, the motion analysis camera system will record the position of the retroreflective markers worn by participants. The electromyographic sensors, metabolic cost device, and insoles will record data during the walking procedures. Participants will be asked to perform up to three different walking tasks during study visits:
 - Walking at their self-selected speed about 65 feet down a straight hallway. They will be asked to do this three times so we can determine their average self-selected walking speed.
 - Walking on a level instrumented treadmill at 1.5 m/s (just over 3 miles per hour) or less. Walking will be performed in bouts no longer than 30 minutes at a time, with the opportunity to rest at any time and between each bout. Participants may be asked to walk at different speeds (not faster than 1.5 m/s), but will only walk at speeds at which they are comfortable.
 - Walking across the lab (<30 feet) while stepping on force plates embedded flush with the floor at a speed of 1.5 m/s or less. The subject will have the opportunity to rest after each walk as needed. Participants may be asked to walk at different speeds (not faster than 1.5 m/s), but will only walk at speeds at which they are comfortable.

During the walking tasks we may ask participants to rate their perceived exertion by asking them a standardized question: "How hard is the activity?, 0 – Not at all, 0.5 – Just noticeable, 1 – Very light, 2 – Light, 3 – Moderate, 4 – Somewhat heavy, 5 – Heavy, 7 – Very heavy, 10 – Very, very heavy"

- At Home Monitoring

Finally, at home monitoring may be conducted to record physical activity with and without the study devices.

- Physical activity: will be measured using an activity monitor (stepwatch and/ or Fitbit) that is worn when participants are away from the VA lab.
- Check-ins: Once per week we may call/email/message through Ilumivi (which ever the participant prefers) participants to check in and complete the check-in qualitative assessment. Ilumivu, is a non-VA app downloaded onto your phone. Data will be captured by this non-VA entity. This app and its developers do not have any information that can be linked back to you. Only the researchers at the VA will know your Ilumivu participant ID. As Ilumivu is not sponsored by the VA, we recommend that you read their privacy policy and ensure you feel comfortable for data being collected by this app and stored on their servers. The data collected will be accessed only by the study research staff and stored on the VA network.

Focus groups

Clinician (N=20) and patient user (N=20) feedback will be solicited through focus group meetings (~5-10 individuals at a time) comprised of patients who currently have a prescription of custom diabetic insoles and practicing orthotists and podiatrists. Recruitment methods will mirror recruitment methods utilized for the device arm of the study, reference section 5.2 above.

Focus groups will last up to 1.5 hours. Participants may attend up to two focus groups sessions. The first session will concentrate on the pros and cons of existing insole design and our existing designs with requests for suggestions for improvements. The second session will be a show-and-tell of the prototype insoles, where participants can give their clinical feedback and preferences before we conduct the larger study. Focus group sessions will be audio recorded and responses transcribed following the meeting.

Following established human-centered design processes we will 1) empathetically engage with the clinicians and consumers to understand their needs regarding custom insoles, and 2) brainstorm to identify design opportunities that address stakeholder needs, and 3) implement the design and iterate on the process.

The responses for each question will be grouped into themes in the style of constant comparison analysis. These themes will emerge from the collected data and not be generated a priori by the researchers. We will use this process to address user requirements and direct modifications to the device. Applying the user and clinical focus group feedback will increase the likelihood of translating the 3DP insoles into the clinic. Informal user requirements have already been applied to determine the preliminary design. However, based on feedback from the initial meeting, any additional specifications will be incorporated into the design. At the second session, participants will have the opportunity to indicate which insole design they would like to see used for the larger study. Further, thought out the data collections feedback from participants will be solicited to inform us on comfort and likelihood of use at home. Feedback solicited from the clinicians and users is invaluable as it will aid in our practical understanding of the needs and applications of the 3DP insoles. This in conjunction with the scientific pressure analysis will increase likelihood of clinical application.

Photos and Video

We may take video and photos of participants during portions of this study for documentation and use in research publications. To protect the identity and privacy of our participants, all videos and photos will be edited later to de-identify the images (e.g., blurring of faces, tattoos, and other distinguishing marks).

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.

Additional use of de-identified/coded data

Throughout the course of the study we will place a copy of all de-identified/coded data in publicly accessible online data repositories. Once posted, the data will publicly accessible to search, retrieve, and analyze for any purpose. Participants will be made aware of this use of 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 data placed in online repositories they can choose not to participate in the study. Further, data will be shared with the PI's research team at the University of Washington as described in section 5.6.

Payment to Participants

Study Group 1, will receive \$30/hour for all visits to the lab.

Study Group 2, will receive \$30/hour for all visits to the lab and an additional \$30/month for participating in the at home portion.

Users will be paid \$20 for each focus group session they attend.

Clinicians will not be compensated for participating.

Risks and Risk Management

Risks associated with use of study provided orthoses and laboratory procedures:

Please note, the increase in physical risks associated with participation in this study only represent a small increase from those encountered in daily life of the participant population.

It is possible that participants may experience an injury such as a blister arising from rubbing inside the shoe. There is potential for development for plantar foot ulcer using C-CFO or N-CFO, however risk for ulcer development is very similar to what is encountered during daily life for study participants. There is also the possibility that participants could experience a fall while participating in study activities, however fall risk is considered no greater than during daily activities.

It is also possible that participants may experience stress or inconvenience by coming to the VA for multiple visits.

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. The study orthotist will assess and ensure proper shoe and CFO fit prior to sending participants home and prior to performing laboratory tests. Although an injurious fall or a device failure related to

this protocol is highly unlikely, we will tabulate a list of any such reports that occur during the study and compare it with corresponding data available in the literature. This will allow us to analyze how much of an increased risk was due to the administered protocol. 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.

Privacy and Confidentiality

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

5.6 Data Analysis

Coded pressure and ultrasound data may be transferred to UW team members to design the insoles and conduct analyses.

Means and SDs of all outcome variables will be calculated in MATLAB for each intervention (C-CFO and N-CFO).

Qualitative reports will be recorded and analyzed for themes to determine comfort and device durability.

Statistical Power Analysis

Much of this study is exploratory as we determine the best methods for design and development on the N-CFO. Thus no power analysis has been conducted.

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 study or the person is unable to complete the study procedures. All data previously collected from participants who withdraw or are withdrawn will be kept and may be used in the study data analysis. Participants may withdraw at any time by informing the Research Coordinator and/or the PI. If a participant wants to withdraw or we choose to withdraw a participant, while she/he are using study equipment (i.e., study-fabricated C-CFO or N-CFO) we will arrange for the device to be returned to the VA study team.

Participants could be withdrawn if they do not meet plantar pressure requirements or if the research team/Research Prosthetist indicates that it is unsafe to continue participation.

6.0 Reporting

All safety information on AEs, 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. The information will be collected on VA IRB forms (Report of a SAE and/or Problem Form, or Report of Problems (ROP) Form) and in AE log forms as needed. Safety data will be collected on an as-needed basis and will begin upon enrollment into the study. All safety reporting requirements will be followed. Any anticipated AEs will be recorded on a log sheet and reported annually with the CRQ.

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 any study, it is possible, although unlikely given the impersonal nature of the data collected, that participants may experience a loss or invasion of privacy or confidentiality because of participation in this study. The risk of harm is minimal and the protections described here will be followed.

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 staff will only have access to the minimum necessary identifiable information needed to perform their role. Study staff that depart the VA or are removed from the research team will be promptly removed from the research application and will no longer have access to sensitive study data.

Study data will be labeled with a study assigned code and de-identified data sets will be created/used when data is made publicly available and transmitted without restriction. A copy of de-identified/coded data will also be made available to public search, retrieval, and analysis per the limitations the Data Management Access Plan (DMAP). The key to the code will be stored separately from the study data, and only designated VA study staff will have access to it.

Illumivu: After participants complete mobile assessment, the data will be stored with the unique ID on illumivu's main storage database in the USA. The illumivu-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.

De-identified, non-sensitive electronic data labeled with the study assigned codes, and all 18 HIPAA identifiers removed or converted to de-identified format, may be stored on password-protected equipment (computers/laptops/SD cards) but will not be encrypted. De-identified/coded data files may be sent off-site via email, file transfer software, and/or other electronic media (CD/DVD, usb drive) to our biostatistician, off-site collaborators, between study investigators, and to the public.

Any consented photography or video will protect participants' identity (e.g., by obscuring the subject's face and any identifying marks like tattoos). The videos and photos may include the participant's entire body, but they will be anonymized during data processing; the participant's face will be blurred, any identifying marks will be covered or blurred, and then the original file will be deleted. If a participant's voice is accidentally recorded, that section of video would be altered prior to any use outside of the VA study team. The video camera and the recording media (e.g., SD cards, optical disks) will be stored in a locked office at the VA Puget Sound. Photos and videos that do not contain identifiable information may also be stored on password-protected computers for future use in scientific presentations and publications.

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. Hard copy data with identifiable and/or sensitive information will be shredded per VA approved policies. Electronic data containing identifiable information will be wiped using VA approved software. De-identified/coded data will be stored indefinitely.

8.0 Communication Plan

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

9.0 References

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