STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

Official title: Pressure Alternating Shoes (PAS) for Prevention of Diabetic Foot Ulcers

NCT number: NCT06026813

IRB Approved date: 11-10-24

Form A

IRB #	STU-2022-1038 Pressure Alternating Shoes (PAS) for Prevention of Diabetic Foot Ulcers

PROTOCOL FORM / RESEARCH DESCRIPTION

If an item does not apply to your research project, indicate that the question is "**not applicable**" – do not leave sections blank

Click once on the highlighted entry in each box to provide your response. Click the item number/letter or word, if hyperlinked, for detailed instructions for that question. If your response requires inserting a table, picture, etc, you may need to first delete the box that surrounds the answer and then insert your table or other special document.

1. Purpose and objectives. *List the purpose and objectives:*

In this study, we will develop pressure-alternating shoes (PAS) that will provide selective rest to the plantar aspect of the foot to prevent diabetic ulcers. The ultimate aim of this footwear will be to limit:

- Repetition of plantar stresses, particularly at peak stress sites, and provide the tissue an opportunity to recover
- Ischemic conditions in the plantar tissue, particularly in diabetic patients who stand for prolonged times

2. Background.

- Describe past experimental and/or clinical findings leading to the formulation of your study.
- For research involving investigational drugs, describe the previously conducted animal and human studies.
- For research that involves FDA approved drugs or devices, describe the FDA approved uses of this drug/device in relation to your protocol.
- Attach a copy of the approved labeling as a product package insert or from the Physician's Desk Reference.

You may reference sponsor's full protocol or grant application (section number and/or title) or if none, ensure background includes references.

Please respond to all components of this item, or clearly indicate which components are not applicable.

a. Background

Various diabetic footwear has been created to help prevent foot ulceration by reducing peak pressures, which are typically passive. Many patients who are prescribed pressure-reducing insoles/footwear still develop foot ulcers most likely due to the complicated pathology of ulcers. Diabetic foot ulcers have a multifactorial etiology that involves elevated pressure, shear, and/or prolonged or repetitive mechanical loading on the same area of the plantar surface. This is particularly apparent in patients suffering from peripheral neuropathy who fail to adjust their stance or gait to relieve stress upon sensitive areas because of their lack of sensation.

In order to effectively prevent foot ulceration, one needs to address as many causative factors as possible in a therapeutic device. We propose a preventive footwear that will address at least four causative factors; (i) elevated peak pressures, (ii) elevated shear stresses, (iii) repetitive loading of certain plantar regions and (iv) prolonged ischemia at certain locations of the foot. The first two factors will be addressed by maximizing the plantar surface area. By increasing available surface area that bears forces, we will reduce stress magnitudes. We will also incorporate a gel material that will help achieve this goal, as well as act as a shock absorber.

The primary novelty of our proposed design will be addressing repetitive application of mechanical stresses on the plantar surface. We believe it would be beneficial to develop an automated insole system capable of cyclically shifting the mechanical loading experienced by the foot to different areas of the plantar surface at a prescribed frequency while walking/standing. Additionally, this insole could provide continuous load relief to sensitive areas as needed; for instance, inside a Total Contact Cast (TCC) where ulcers already exist. Ulcer areas can be gradually loaded in a TCC using the insole, making tissue adapt to mechanical stresses.

If future research demonstrates that ulcers develop at peak shear stress sites and/or locations that experience abnormal temperatures, PAS shoes can be used to off-load such locations to prevent a predicted ulcer. PAS may also be used in the future to minimize incidence of metatarsal stress fractures.

The team is made up of engineers, biomechanists, and clinicians, all selected for their ability to bring the prototype device to form and conduct the validation study effectively. The team members have been involved in several complex R&D projects where multiple areas of related technology were required. The principal investigator (PI) is Dr. Lawrence Lavery, DPM, MPH, who is an internationally recognized expert in diabetic foot ulcers and prevention strategies. He has about 300 peer-reviewed journal articles on diabetic foot, numerous research projects funded by the NIH, American Diabetes Association, Qatar Foundation, other non-profit organizations as well as private sector. Dr. Muthu Wijesundara at UTARI, has extensive experience related to development of the PAS. In his current work, funded by the CDMRP, air cell-based pressure modulating interfaces

are being implemented in prosthetic interfacing for improved fit and in a preventive seat cushion for wheelchair users. Dr Lavery will work with Dr. Wijesundara to conduct human subjects research and provide clinical input during the project. Dr Subhash Aryal of the Biostatistics Department at UNTHSC will serve as the biostatistician. The team is exceptionally well-qualified as demonstrated by publications in high-impact journals like the Lancet and Diabetes Care and numerous national research awards like Pecoraro (LL)) Award from the American Diabetes Association.

We have conducted a pilot study to examine gait variability during prolonged walking at the Yavuz Lab. We obtained triaxial loading patterns of two subjects, who walked for 30 mins on a treadmill, at 10-min intervals. The results indicated that one subject started changing her loading pattern within 10 minutes of walking. We observed a different shear stress pattern at each interval. However, the loading pattern observed at the end of 30 mins was similar to the baseline pattern (Fig 2). In the other subject, the change occurred within minutes 20-30. Although limited, these findings indicate that healthy subjects alter their loading patterns (and thus exhibit variation in pressure/shear loading) due to prolonged walking.

Pressure mapping and modulation using active actuators have been demonstrated previously by the Wijesundara group. The group successfully designed, fabricated, and characterized active actuator arrays made of silicone rubber in different sizes and shapes for use in a dynamic prosthetic liner and in a novel wheelchair cushion [30-31].

We have recently developed a preliminary prototype of PAS (Figure 3D) consisting of 14 active regions. We have collected in-shoe pressure data with this prototype. A healthy male subject (25 yrs, 185lbs, 5’10”) wore the PAS shoe on one foot and a matching control shoe on the other foot and walked for approximately 10 minutes on a treadmill at self-selected speeds while a number of regions were deflated one at a time. We also collected static pressure measurements. Figure 3E provides a depiction of the offloading effect in one of the regions (#12) during one of these static trials. Once a region was offloaded, other areas of the foot experienced the differential stress. However, we have not observed abnormal pressures at other foot regions or at the gaps in between the cells. This is also demonstrated in Figure 4, which depicts pressures during bipedal standing. The favorable results may be attributed to the excellent conforming and compressibility characteristics of air. We anticipate seeing even more uniform pressure redistribution once we incorporate the shock absorbing cushion layer. [Work is under way to quantify and compare in-shoe pressures in dynamic conditions. Initial findings indicated good pressure distribution, peak pressure values around or below 200 kPa. We believe addition of the top layer as well as optimizing the actuator pressure (internal cell pressure), which will provide good conforming characteristics while not causing any balance problems, will further improve pressure distribution.]

The proposed project also aligns well with the new NIH initiative on care and prevention of ulcerative wounds (PA-16-231). Ultimately, such a study has the potential to significantly impact the long-term care of diabetics with a high prevalence of foot ulceration and improve their quality of life.

References:

1. Bloomgarden, Z.T., The diabetic foot. Diabetes Care, 2008. 31(2): p. 372-6.

2. Rogers, L.C., L.A. Lavery, and D.G. Armstrong, The right to bear legs--an amendment to healthcare: how preventing amputations can save billions for the US Health-care System. J Am Podiatr Med Assoc, 2008. 98(2): p. 166-8.

3. Armstrong, D.G., J. Wrobel, and J.M. Robbins, Guest Editorial: are diabetes-related wounds and amputations worse than cancer? Int Wound J, 2007. 4(4): p. 286-7.

4. Cavanagh, P.R., J.S. Ulbrecht, and G.M. Caputo, New developments in the biomechanics of the diabetic foot. Diabetes Metab Res Rev, 2000. 16 Suppl 1: p. S6-S10.

5. Boulton, A.J., et al., Dynamic foot pressure and other studies as diagnostic and management aids in diabetic neuropathy. Diabetes Care, 1983. 6(1): p. 26-33.

6. Ctercteko, G.C., et al., Vertical forces acting on the feet of diabetic patients with neuropathic ulceration. Br J Surg, 1981. 68(9): p. 608-14.

7. Stess, R.M., S.R. Jensen, and R. Mirmiran, The role of dynamic plantar pressures in diabetic foot ulcers. Diabetes Care, 1997. 20(5): p. 855-8.

8. Stokes, I.A., I.B. Faris, and W.C. Hutton, The neuropathic ulcer and loads on the foot in diabetic patients. Acta Orthop Scand, 1975. 46(5): p. 839-47.

9. Lavery, L.A., et al., Predictive value of foot pressure assessment as part of a population-based diabetes disease management program. Diabetes Care, 2003. 26(4): p. 1069-73.

10. Hsi, W.L., et al., Plantar pressure threshold for ulceration risk using the EMEDSF platform. Diabetes Care, 1993. 42(S1).

11. Ledoux, W.R., et al., Diabetic foot ulcer incidence in relation to plantar pressure magnitude and measurement location. J Diabetes Complications, 2013. 27(6): p. 621-6.

12. Murray, H.J., et al., The association between callus formation, high pressures and neuropathy in diabetic foot ulceration. Diabet Med, 1996. 13(11): p. 979-82.

13. Veves, A., et al., The risk of foot ulceration in diabetic patients with high foot pressure: a prospective study. Diabetologia, 1992. 35(7): p. 660-3.

14. Yavuz, M., American Society of Biomechanics Clinical Biomechanics Award 2012: plantar shear stress distributions in diabetic patients with and without neuropathy. Clin Biomech (Bristol, Avon), 2014. 29(2): p. 223-9.

15. Yavuz, M., et al., Temperature as a predictive tool for plantar triaxial loading. J Biomech, 2014. 47(15): p. 3767-70.

16. Yavuz, M., et al., Association Between Plantar Temperatures and Triaxial Stresses in Individuals With Diabetes. Diabetes Care, 2015. 38(11): p. e178-9.

17. Yavuz, M., et al., Peak plantar pressure and shear locations: relevance to diabetic patients. Diabetes Care, 2007. 30(10): p. 2643-5.

18. Yavuz, M., et al., Peak Plantar Shear and Pressure and Foot Ulcer Locations: A Call to Revisit Ulceration Pathomechanics. Diabetes Care, 2015. 38(11): p. e184-5.

19. Yavuz, M., et al., Temporal characteristics of plantar shear distribution: relevance to diabetic patients. J Biomech, 2008. 41(3): p. 556-9.

20. Yavuz, M., et al., Temperature as a Causative Factor in Diabetic Foot Ulceration: A Call to Revisit Ulcer Pathomechanics JAPMA, 2018. in press.

21. Edmonds, M.E., et al., Improved survival of the diabetic foot: the role of a specialized foot clinic. Q J Med, 1986. 60(232): p. 763-71.

22. Dargis, V., et al., Benefits of a multidisciplinary approach in the management of recurrent diabetic foot ulceration in Lithuania: a prospective study. Diabetes Care, 1999. 22(9): p. 1428-31.

23. Uccioli, L., et al., Manufactured shoes in the prevention of diabetic foot ulcers. Diabetes Care, 1995. 18(10): p. 1376-8.

24. Chantelau, E., T. Kushner, and M. Spraul, How effective is cushioned therapeutic footwear in protecting diabetic feet? A clinical study. Diabet Med, 1990. 7(4): p. 355-9.

25. Reiber, G.E., et al., Effect of therapeutic footwear on foot reulceration in patients with diabetes: a randomized controlled trial. JAMA, 2002. 287(19): p. 2552-8.

26. Bus, S.A., et al., The effectiveness of footwear and offloading interventions to prevent and heal foot ulcers and reduce plantar pressure in diabetes: a systematic review. Diabetes Metab Res Rev, 2008. 24 Suppl 1: p. S162-80.

27. Brand, P.W., Tenderizing the foot. Foot Ankle Int, 2003. 24(6): p. 457-61.

28. Yavuz, M., et al., Plantar shear stress distribution in patients with rheumatoid arthritis: relevance to foot pain. J Am Podiatr Med Assoc, 2010. 100(4): p. 265-9.

29. Najafi, B., R.T. Crews, and J.S. Wrobel, Importance of time spent standing for those at risk of diabetic foot ulceration. Diabetes Care, 2010. 33(11): p. 2448-50.

30. Carrigan, W., et al. A Pressure Modulating Sensorized Soft Actuator Array for Pressure Ulcer Prevention. in International Design Engineering Technical Conferences & Computers and Information in Engineering Conference IDETC2017. 2017. Cleveland, Ohio.

31. Carrigan, W., et al., Pneumatic actuator inserts for interface pressure mapping and fit improvement in lower extremity prosthetics, in 2016 6th IEEE International Conference on Biomedical Robotics and Biomechatronics (BioRob). 2016: Singapore. p. 574-579.

32. Bus, S.A., et al., Effect of custom-made footwear on foot ulcer recurrence in diabetes: a multicenter randomized controlled trial. Diabetes Care, 2013. 36(12): p. 4109-16.

33. Paton, J., et al., Getting the right balance: insole design alters the static balance of people with diabetes and neuropathy. J Foot Ankle Res, 2016. 9: p. 40.

34. Van Geffen, J.A., et al., Effect of flat insoles with different Shore A values on posture stability in diabetic neuropathy. Prosthet Orthot Int, 2007. 31(3): p. 228-35.

35. Connelly, L.M., Pilot studies. Medsurg Nurs, 2008. 17(6): p. 411-2.

b. Current practice

To our knowledge, no such device exists in the market or has been discussed in the literature. This low-risk/high-reward method has the potential to revolutionize the preventive care provided to diabetic patients.

3. Study Design.
Describe the study design (e.g., single/double blind, parallel, crossover, etc.) Consider inserting a scheme to visually present the study design.

The overall purpose of this clinical trial is to develop and test Pressure Alternating Shoes (PAS), which will periodically off-load certain regions of the foot in order to prevent foot ulcers. We will utilize an automated dual layer insole comprised of an active pressurized actuator array in combination with a passive compliant layer on top of each actuator to modulate and distribute the plantar surface pressure as desired. This device will allow us to simultaneously load and offload select areas of the foot using the active layer by inflating and deflating individual actuators using pressurized air. After offloading, the remaining load will be distributed to other areas with inflated actuators. Automatic modulation will be provided through programmable control hardware which will cyclically relieve mechanical loading based on a prescribed duration and frequency.

We will report the mechanical and physical characteristics of our dual layer insole structure and evaluate its safety, usability, and comfort with healthy and diabetic subjects. To our knowledge, this will be the first study on the effect of a device actively modulating mechanical loading at the plantar surface for foot ulcer prevention. This system will allow for a systematic study of cyclical offloading in ulcer prevention.

4. Research Plan / Description of the Research Methods:

4.a. Provide a **comprehensive narrative** describing the **research methods**.

1) Provide the **order in which tests/procedures will be performed**,
2) Provide the **setting** for these events and a description of the **methods used to protect privacy** during the study.
3) Provide the **plan for data analysis** (include as applicable the **sample size calculation)**

Please respond to all components of this item, or clearly indicate which components are not applicable.

A two-tier human subjects study will be conducted to assess the biomechanical characteristics of PAS. All subjects will be assigned a study number. Data will be collected on paper forms and kept in subject binders in a locked research office. Forms will be scanned to a password-protected drive. In the first tier we will test PAS in healthy subjects. Exclusion criteria will be diabetes and foot complications. On the right foot, subject will wear diabetic footwear equipped with PAS device, and on the left foot, subjects will wear diabetic footwear equipped with PAS sealed at ambient pressure. Pressure sensing insoles (Pedar, NovelUSA, MN) will be placed between the foot and the insole and subjects will be asked to walk on a treadmill at self-selected speeds for 5 minutes. During minutes 0:30-4:30, each of the active cells of PAS will be offloaded consecutively for 30 seconds. Five mid-gait steps from each offloading period will be evaluated for each subject. Pressure values in the selected 5 steps will be averaged and a mean pressure profile will be obtained. Subjects will then be asked to walk with their daily shoes on the treadmill for 5 minutes at self-selected speeds. This additional session will provide control data for comparison. The order of the sessions will be randomized.

We will assess insole plantar pressures using a Tekscan pressure mapping (Tekscan, Inc., Norwood, MA) and XSENSOR (XSENSOR Technology Corporation, Calgary, Canada).Body-worn sensors (BalanSens, BioSensics, Watertown, MA, USA) will be used to measure static (postural sway) conditions. Postural sway and estimated Center of Mass (COM) will be quantified with the body-worn sensors with (i) eyes-open, firm surface in normal gait pattern on a straight path. . .

We will also explore tissue perfusion values at offloaded regions in all healthy subjects and in select diabetic patients (individuals who can walk longer). After a 30-minute wash-out period, baseline oxyhemoglobin (Oxy) values of both feet will be captured with a portable hyperspectral camera (SnapShot NIR, Kent Imaging, Calgary, Canada). Subjects will then walk with PAS for 5 minutes at self-selected speeds while a region is offloaded for the entire time. We may repeat this a few times in healthy individuals in order to study different regions. After each walking session, subjects' shoes and socks will be removed within 30 seconds of gait termination and Oxy levels under both feet will be recorded. We will mask each hyperspectral image of the foot, based on the cell mapping of the PAS insole. We will calculate Deoxy values in this manner; DeOxy (region i) = post-walking Oxy (region i) – baseline Oxy (region i). We will then compare DeOxy values between contralateral foot sites. The results will indicate whether PAS insoles can promote tissue perfusion in offloaded regions. This method will help us determine required offloading periods to promote tissue perfusion under the foot. [We plan to study tissue perfusion data in diabetic patients in detail in the next study. We will also monitor temperature of the sole of the foot for potential hot spots using a commercial infrared thermal camera (FLIR Systems, OR)..] The infrared thermal camera is a non-contact optical based camera that does not add any additional risk.

Further, 1 healthy subject will undergo either 1.5T or 3T magnetic resonance imaging (MRI) of the foot and ankle. This subject will have to meet the inclusion/exclusion criteria and must be a willing participant to undergo imaging. MRI imaging will enable us to

create a 3D model of a foot without any distortion. Only 1 subject would be required for the MRI for analysis. This model will be used in computational analysis (FEA- Finite Element Analysis) to investigate the loading effect on plantar tissues as well as insole-foot interactions.

After testing with healthy subjects we may revisit the design parameters and improve the technology. We anticipate the study procedures in tier 2 will be the same as in tier 1. Design improvements will be done to the devices themselves. In tier 2, we will test PAS in diabetic neuropathic subjects.

Data Analysis: All subjects will be assigned a study number. Data will be collected on paper forms and kept in subject binders in a locked research office. Forms will be scanned to a password-protected drive. For analysis purposes, de-identified data will shared with the University of Texas Health Science Center at San Antonio. As all data will be deidentified, subjects will not need to be reconstented. A study by Bus et al [32] compared a group of subjects in custom-made footwear versus standard therapeutic footwear. Results indicated 221±51kPa pressure in custom shoes vs 274±66kPa in standard shoes ($p<.001$) in a total of 171 subjects. To detect a similar difference, at 85% power and type I error rate of 1.7%, a sample size of 18 is sufficient for a within subjects analysis (paired t-tests). Alpha was adjusted using a Bonferroni correction since there are three primary variables of interest; peak pressure, RMSE and velocity of COP. Due to limitations in tissue perfusion measurement which cannot be acquired in real time (inside the shoe), the Oxy variable will not be a primary variable of interest. For balance variables, our study will have a power of 80% to detect an effect size of 0.8 if we increase the sample size to 20. Two previous studies revealed a comparable effect size when authors compared balance between the use of various diabetic insoles and control insoles [33,34]. Therefore we will recruit 20 healthy subjects in the first tier and 10 diabetic neuropathic subjects in the second tier (total N=30). Investigation of diabetic neuropathic subjects will further increase the statistical power and hence we will not account for a potential drop-out which may reduce the sample size by approximately 10%. Moreover, for pilot/proof of concept studies, it has been suggested in the literature that a minimum of 10% of subjects of the larger parent clinical trial should be studied [35]. A future clinical trial with PAS will be very similar to the study by Bus et al [32]. Hence even after a 10% dropout, we will still meet this 10% rule for a pilot study. In case the data does not follow normal distribution, we will use the non-parametric Signed Rank test to compare the differences. Our expectation is that we will observe only non-significant differences in comparing pressure and balance between PAS and control shoes as we do not expect PAS to impair gait of subjects.

[Sex as a biological variable: We anticipate to recruit approximately 15 female subjects (50%). To the best of our knowledge, there is no report in the literature that suggests that foot biomechanics in female diabetic patients is different than that of males. Therefore, we do not anticipate to change design/testing criteria between sexes. If we notice a difference between sexes we will make necessary modifications.]

4.b. List of the study intervention(s) being tested or evaluated under this protocol

☐ **N/A -** this study does not test or evaluate an intervention. Skip to item 4.d.

#	Study intervention(s) being tested or evaluated under the protocol *Add or delete rows as needed*	Affiliate Place a check next to institution(s) where the intervention will be performed	Local Standard Practice? Indicate whether the intervention is considered acceptable practice locally for applicable institutions
1	Treadmill walk for 5 minutes at self-determined speed with Control footwear which is comprised of extra-extra depth diabetic shoes for men and women and commonly used multilayer off-the-shelf diabetic orthotics. The shoes will be the same make and model that will accommodate the PAS. Pressure sensing insoles (Pedar, NovelUSA, MN) will be placed between the foot and the insole	☐ UTSW	☐ Yes
		☐ PHHS	☐ Yes
		☐CMC	☐ Yes
		☐THR	☐ Yes
		☐TSRH	☐ Yes
		☒ Other: SHP	☐ Yes
2	Treadmill walk for 5 minutesat self-determined speed with their daily shoes	☐ UTSW	☐ Yes
		☐ PHHS	☐ Yes
		☐CMC	☐ Yes
		☐THR	☐ Yes
		☐TSRH	☐ Yes
		☒ Other: SHP	☐ Yes
3	Pressure mapping using a TekScan (TekScan, Inc., Norwood, MA) and body worn sensors (BalanSens, BioSensics, Watertown, MA, USA) in kinetic (postural sway) condition. This will be done twice, once in PAS and once using daily shoes.	☐ UTSW	☐ Yes
		☐ PHHS	☐ Yes
		☐CMC	☐ Yes
		☐THR	☐ Yes
		☐TSRH	☐ Yes
		☒ Other: SHP	☐ Yes
4	Baseline oxyhemoglobin (Oxy) values of both feet will be captured with a portable hyperspectral camera and again after 5 minute treadmill walk (SnapShot NIR, Kent Imaging, Calgary, Canada).	☐ UTSW	☐ Yes
		☐ PHHS	☐ Yes
		☐CMC	☐ Yes
		☐THR	☐ Yes
		☐TSRH	☐ Yes
		☒ Other: SHP	☐ Yes
5	Temperature of the sole of the feet will be measured using a commercial infrared thermal camera after treadmill walk (FLIR Systems, OR).	☐ UTSW	☐ Yes
		☐ PHHS	☐ Yes
		☐CMC	☐ Yes
		☐THR	☐ Yes
		☐TSRH	☐ Yes
		☒ Other: SHP	☐ Yes

6	Magnetic resonance imaging will be performed of the foot and ankle	☐ UTSW	☐ Yes
		☐ PHHS	☐ Yes
		☐CMC	☐ Yes
		☐THR	☐ Yes
		☐TSRH	☐ Yes
		☒ Other: SHP	☐ Yes

4.c. Risk:Benefit Analysis of study interventions being tested or evaluated under this protocol

For each study intervention identified in section 6b above, complete a risk:benefit analysis table.

(Two tables are provided, copy & paste additional tables as needed or delete both tables if this study does not test an intervention)

4.c.
Study Intervention #1
Treadmill walk in PAS

List each group exposed to this intervention on a separate line. (e.g., experimental, control, Arm A, Arm B, etc) **Or** state All Groups/Subjects	For each group, list the **benefits** of this intervention. (Benefits can be directly from the intervention or from a monitoring procedure likely to contribute to the subject's well being). If there are no benefits, state "none".
All Subjects	None

If you are requesting a Waiver of Informed Consent, complete the table below.

If you have a consent form, **list the reasonably foreseeable risks in the consent form (and do not complete this section).**

List the risks according to the probability (likely, less likely or rare) and magnitude (serious or not serious).
(include: 1) expected adverse events; 2) rare and serious adverse events; 3) all other psychological, social, legal harms)
Do not delete frequency. Frequency must be estimated because it will assist you with determining which adverse events will require prompt reporting.

	Not serious	**Serious**
Likely These risks are expected to occur in more than **20** out of **100** subjects.	•	•
	Not serious	**Serious**
Less likely These risks are expected to occur in **5-20** subjects or less out of **100** subjects.	•	•
		Serious
Rare These risks are expected to occur in less than **5** subjects out of **100**		•

IRB #	STU-2022-1038 Pressure Alternating Shoes (PAS) for Prevention of Diabetic Foot Ulcers

4.c.
Study Intervention #2
Treadmill walk in daily shoes

List each group exposed to this intervention on a separate line. (e.g., experimental, control, Arm A, Arm B, etc) **Or** state All Groups/Subjects	For each group, list the **benefits** of this intervention. (Benefits can be directly from the intervention or from a monitoring procedure likely to contribute to the subject's well being). If there are no benefits, state "none".
All Groups	None

If you are requesting a Waiver of Informed Consent, complete the table below.

If you have a consent form, **list the reasonably foreseeable risks in the consent form (and do not complete this section).**

List the risks according to the probability (likely, less likely or rare) and magnitude (serious or not serious).
(include: 1) expected adverse events; 2) rare and serious adverse events; 3) all other psychological, social, legal harms)
Do not delete frequency. Frequency must be estimated because it will assist you with determining which adverse events will require prompt reporting.

	Not serious	**Serious**
Likely These risks are expected to occur in more than **20** out of **100** subjects.	•	•
	Not serious	**Serious**
Less likely These risks are expected to occur in **5-20** subjects or less out of **100** subjects.	•	•
		Serious
Rare These risks are expected to occur in less than **5** subjects out of **100**		•

IRB #	STU-2022-1038 Pressure Alternating Shoes (PAS) for Prevention of Diabetic Foot Ulcers

4.c.
Study Intervention #3
Pressure mapping and Balance testing

List each group exposed to this intervention on a separate line. (e.g., experimental, control, Arm A, Arm B, etc) **Or** state All Groups/Subjects	For each group, list the **benefits** of this intervention. (Benefits can be directly from the intervention or from a monitoring procedure likely to contribute to the subject's well being). If there are no benefits, state "none".
All Groups	None

If you are requesting a Waiver of Informed Consent, complete the table below.

If you have a consent form, **list the reasonably foreseeable risks in the consent form (and do not complete this section).**

List the risks according to the probability (likely, less likely or rare) and magnitude (serious or not serious).
(include: 1) expected adverse events; 2) rare and serious adverse events; 3) all other psychological, social, legal harms)
Do not delete frequency. Frequency must be estimated because it will assist you with determining which adverse events will require prompt reporting.

	Not serious	**Serious**
Likely These risks are expected to occur in more than **20** out of **100** subjects.	•	•
	Not serious	**Serious**
Less likely These risks are expected to occur in **5-20** subjects or less out of **100** subjects.	•	•
		Serious
Rare These risks are expected to occur in less than **5** subjects out of **100**		•

IRB #	STU-2022-1038 Pressure Alternating Shoes (PAS) for Prevention of Diabetic Foot Ulcers

4.c.
Study Intervention #4
Measurement of oxyhemoglobin (Oxy) values of both feet

List each group exposed to this intervention on a separate line. (e.g., experimental, control, Arm A, Arm B, etc) **Or** state All Groups/Subjects	For each group, list the **benefits** of this intervention. (Benefits can be directly from the intervention or from a monitoring procedure likely to contribute to the subject's well being). If there are no benefits, state "none".
All Groups	None

If you are requesting a Waiver of Informed Consent, complete the table below.

If you have a consent form, **list the reasonably foreseeable risks in the consent form (and do not complete this section).**

List the risks according to the probability (likely, less likely or rare) and magnitude (serious or not serious).
(include: 1) expected adverse events; 2) rare and serious adverse events; 3) all other psychological, social, legal harms)
Do not delete frequency. Frequency must be estimated because it will assist you with determining which adverse events will require prompt reporting.

	Not serious	**Serious**
Likely These risks are expected to occur in more than **20** out of **100** subjects.	•	•
	Not serious	**Serious**
Less likely These risks are expected to occur in **5-20** subjects or less out of **100** subjects.	•	•
		Serious
Rare These risks are expected to occur in less than **5** subjects out of **100**		•

IRB #	STU-2022-1038 Pressure Alternating Shoes (PAS) for Prevention of Diabetic Foot Ulcers

4.c.
Study Intervention #5
Temperature Measurements

List each group exposed to this intervention on a separate line. (e.g., experimental, control, Arm A, Arm B, etc) **Or** state All Groups/Subjects	For each group, list the **benefits** of this intervention. (Benefits can be directly from the intervention or from a monitoring procedure likely to contribute to the subject's well being). If there are no benefits, state "none".
All Subjects	None

If you are requesting a Waiver of Informed Consent, complete the table below.

If you have a consent form, **list the reasonably foreseeable risks in the consent form (and do not complete this section).**

List the risks according to the probability (likely, less likely or rare) and magnitude (serious or not serious).
(include: 1) expected adverse events; 2) rare and serious adverse events; 3) all other psychological, social, legal harms)
Do not delete frequency. Frequency must be estimated because it will assist you with determining which adverse events will require prompt reporting.

	Not serious	**Serious**
Likely These risks are expected to occur in more than **20** out of **100** subjects.	•	•
	Not serious	**Serious**
Less likely These risks are expected to occur in **5-20** subjects or less out of **100** subjects.	•	•
		Serious
Rare These risks are expected to occur in less than **5** subjects out of **100**		•

IRB #	STU-2022-1038 Pressure Alternating Shoes (PAS) for Prevention of Diabetic Foot Ulcers

4.c.
Study Intervention #6
Foot and Ankle MRI

List each group exposed to this intervention on a separate line. (e.g., experimental, control, Arm A, Arm B, etc) **Or** state All Groups/Subjects	For each group, list the **benefits** of this intervention. (Benefits can be directly from the intervention or from a monitoring procedure likely to contribute to the subject's well being). If there are no benefits, state "none".
Healthy Subjects	None

If you are requesting a Waiver of Informed Consent, complete the table below.

If you have a consent form, **list the reasonably foreseeable risks in the consent form (and do not complete this section).**

List the risks according to the probability (likely, less likely or rare) and magnitude (serious or not serious).
(include: 1) expected adverse events; 2) rare and serious adverse events; 3) all other psychological, social, legal harms)
Do not delete frequency. Frequency must be estimated because it will assist you with determining which adverse events will require prompt reporting.

	Not serious	**Serious**
Likely These risks are expected to occur in more than **20** out of **100** subjects.	•	•
	Not serious	**Serious**
Less likely These risks are expected to occur in **5-20** subjects or less out of **100** subjects.	•	•
		Serious
Rare These risks are expected to occur in less than **5** subjects out of **100**		•

4.d. List ALL other research procedures or components not listed in table 4.b.
The combination of Tables 4b and 4d should account for all of the research procedures that will take place during this study.

Consider grouping similar procedures under a single component (e.g., blood work, CT = safety assessments)

#	Research component • **individual procedures** *example:* **Eligibility Assessments** • History and physical • Questionnaire • Laboratory tests *Add or delete rows as needed*	**Column A** **Local Standard Practice** Indicate the number of times each procedure will be performed as stipulated in the research plan **that would be performed if the participant were not participating in the study.**	**Column B** **Research Only** Indicate the number of times each procedure will be performed solely for research purposes *(meaning that the participant would not undergo the same number of procedures or would not undergo the procedure(s) at the same frequency if they were not participating in the study)*	**Column D** **Risks** **If you are requesting a Waiver of Informed Consent, complete the table below.** List the reasonably expected risks for each procedure or group of procedures under the following categories as appropriate: • Serious and likely; • Serious and less likely; • Serious and rare; • Not serious and likely; • Not serious and less likely
1	**Eligibility Assessments**			Loss of confidentiality, feelings of discomfort.
	Medical History	0	1	Not serious and less likely
	Inspection of Feet	0	1	Not serious and less likely
	Neuropathy assessment	0	1	Not serious and less likely

5. Safety Precautions. *(Describe safeguards to address the serious risks listed above.)*

a. Describe the procedures for protecting against or minimizing any potential risks for each of the more than minimal risk research procedures listed above.

N/A

b. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse events, or unanticipated problems involving subjects.

If needed, subjects will be provided first aid treatment (at no cost) from a team member who is a certified Physical Therapist or Doctor of Podiatry and who will be at all tests. If there is a serious concern, we would recommend the subject visit the ED or we would call the campus emergency number; researchers will not pay for this care.

c. Will the safeguards be different between/among groups?

☐ Yes ☑ No

N/A