Title: Improving DFU Outcomes: Early Detection of Foot Ulcers Using Novel Technology

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Improving DFU outcomes: early detection of foot ulcers using novel technology

(AIM III: Technology innovations)

Protocol Number:

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IRB NUMBER: 2023-14915
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STATEMENT OF COMPLIANCE

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. In addition, all changes to the consent form will be IRB-approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title: Adherence to novel foot mat technology for early detection of DFU.

Study Description:

Innovations toward the prevention of DFU are needed. Early detection of changes in the foot that predict the development of DFU could allow timely intervention to prevent the limb damage that occurs with advanced DFU.

Studies have demonstrated that increased temperature in the foot presage the development of DFU. Temperature changes can accurately be detected by home monitoring devices and predict impending ulceration. Here we will test the uptake of novel foot temperature monitoring technology for a future intervention study to determine if a home monitoring device could prevent the occurrence of severe DFU for our patients at MMC.

We will conduct a longitudinal study to determine the adherence to an FDA cleared device, Podimetrics, which has been tested in other populations and shown to 1) decrease the risk of severe DFU, and 2) decrease the utilization of health care resources in high risk patients with a history of DFU. For this study, we will identify and enroll patients who are high risk for DFU. They will be identified from the EMR. After informed consent, study subjects will receive the foot mat and obtain training remotely from Podimetrics, which provides a standardized training program. Study subjects briefly stand on the mat daily, and the temperature data automatically is sent for analysis to Podimetrics to interpret the information. The study subjects will be evaluated over a six-month period to measure their daily use of the technology. Secondary outcomes of this study include the occurrence of DFU and use of health care resources. Study subjects will be contacted every month by the study team to assess foot health. Study subjects will be instructed to contact the study team during the study period to inquire if they develop any changes in the foot such as the diagnosis of DFU or require a foot cast for offloading or have any concerns about their feet.

If patients have an increase in temperature, the study team will be contacted by Podimetrics. After a review of symptoms, a standard care protocol will be executed: offloading (decrease in weight bearing) will be recommended. In one study 68% of cases

resolved via offloading alone without an outpatient visit. Should the inflammation persist (increased temperature), despite off loading, an examination would be necessary to identify and resolve its cause. In this case the patient will be instructed to follow up with their physician.

Objectives:

Primary Objective:

1. Determine the adherence to the foot monitoring device over six months.

Secondary Objectives:

1. Determine the prevalence of ulcers as detected by the device.
2. Determine the use of the health care system.

Endpoints:	Adherence to daily monitoring, development of ulcers
Study Population:	*The study cohort are derived from patients who are at highest risk to develop a DFU. They are patients who had a prior DFU within 24 months. Other criteria include: 1. have no active ulcer at the time of enrollment, 2. Presence of neuropathy, 3. ambulatory, and 4. provide informed consent.*
Description of Sites/Facilities Enrolling Participants:	*The study will be conducted at one site Albert Einstein College of Medicine (AECOM) and its affiliated Montefiore Medical Center.*
Description of Study:	*Subjects will undergo observation for 6 months*
Study Duration:	*12 months*
Participant Duration:	*6 months*

1.2 SCHEMA

A. Overall study design

1. *Subjects will be identified from the EMR: Adults that were treated for DFU within past 24 months, who presently have no active DFU at the time of study consent.*
2. *Consent and enrollment: we will approach patients via email if available, and/or phone call/phone text to learn about the study. Subjects can also be enrolled during routine clinic visit by study member.*
3. *Interested patients will be seen in the CTSA study clinic or enrolled in their care clinic (primary care, vascular, podiatry etc), if they fulfill criteria we will obtain informed consent.*
4. *For consented patients: baseline demographic data will be extracted from the EMR and case report filled out.*
5. *All study subjects receive the intervention and training from Podimetrics.*
6. *Study subjects will be instructed how to set up the mat and directed to step on the mat daily*
7. *If they do not step on the mat, they will be contacted by Podimetrics to reinforce use*

IRB NUMBER: 2023-14915
IRB APPROVAL DATE: 12/20/2024

8. *Increase in foot temperature (increase in 2.2°C over two consecutive uses between and of six contralaterally sites), a marker for early ulcer, will trigger a call to the study team to the study subject and the PI for management (SOP of elevated temperature management below).*
9. *All study subjects will be called each month to determine if any ulcer development or health care utilization.*

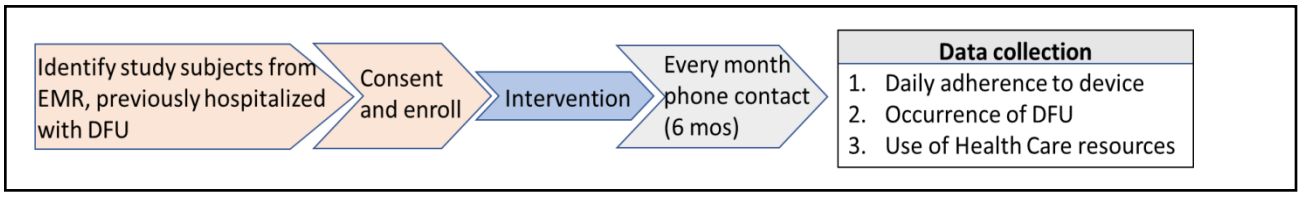
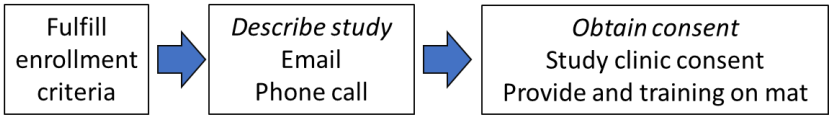


Figure 1. Overall study protocol

B. Enrollment

1. *Potential study subjects will be contacted by email, if no response will follow up with phone call. If by email they are interested to hear more about the study we will then follow up with description of study. Patients will also be recruited from outpatient clinics (podiatry, primary care, vascular, endocrine) by study team members.*
2. *For patients who are interested in the study we will obtain consent in a study clinic visit (they will get reimbursed for travel to study clinic).*



3. Study clinic: obtain informed consent ,obtain history, examine feet, review enrollment criteria,

Figure 2. Enrollment protocol

C. Intervention

1. *After informed consent at study clinic, we will provide the mat and standardized training (45 minutes by phone preferably within one week of receiving mat-this is the Activation or on boarding). Subjects step on mat daily and Podimetrics will receive and interpret daily data generated by the mat. A prescription for the Mat will be faxed to Podimetrics.*

IRB NUMBER: 2023-14915
IRB APPROVAL DATE: 12/20/2024

2. *Podimetrics will provide reinforcement in the case of four days of monitoring is missed. The nurse will remind the participant of the importance of daily use of the study device to identify foot inflammation that can lead to diabetic foot complications; to continue completing daily foot self-exams (this is standard of care); to always use diabetic shoes or other prescribed footwear, even indoors; and to immediately notify the clinic if they notice any concerning changes to their feet.*
3. *Participants will be instructed to discontinue use of the mat in certain circumstances, including incidence of new DFU, new infection, Charcot arthropathy flare, or when using an offloading device, such as a total contact cast or removable cast walker, that would prevent the participant from using the study device.*
4. *At end of study the mat is mailed back to Podimetrics (the box has a shipping label).*

D. *Management of foot temperature elevation/risk management plan*

1. *Podimetrics will contact patient, determine if patient notes any skin changes, pain, fever.*
2. *If clinically well, advise patient to decrease mobility by 50% (a "routine" temp elevation). If clinical symptoms (pain fever, discharge)(an "emergent" elevation) : see provider*
3. *Continued monitoring of temperature daily, call patient daily to review symptoms and Podimetric data. If persistent patient the study team will recommend that they present to their foot care provider.*
4. *Podimetrics will also contact the PI if there is a temperature elevation and discuss plan. The PI will also record this increase in temperature and follow up with Podimetrics for resolution or need for physician visit. Thus both Podimetrics and the PI are aware of the temperature change and will follow till resolution.*

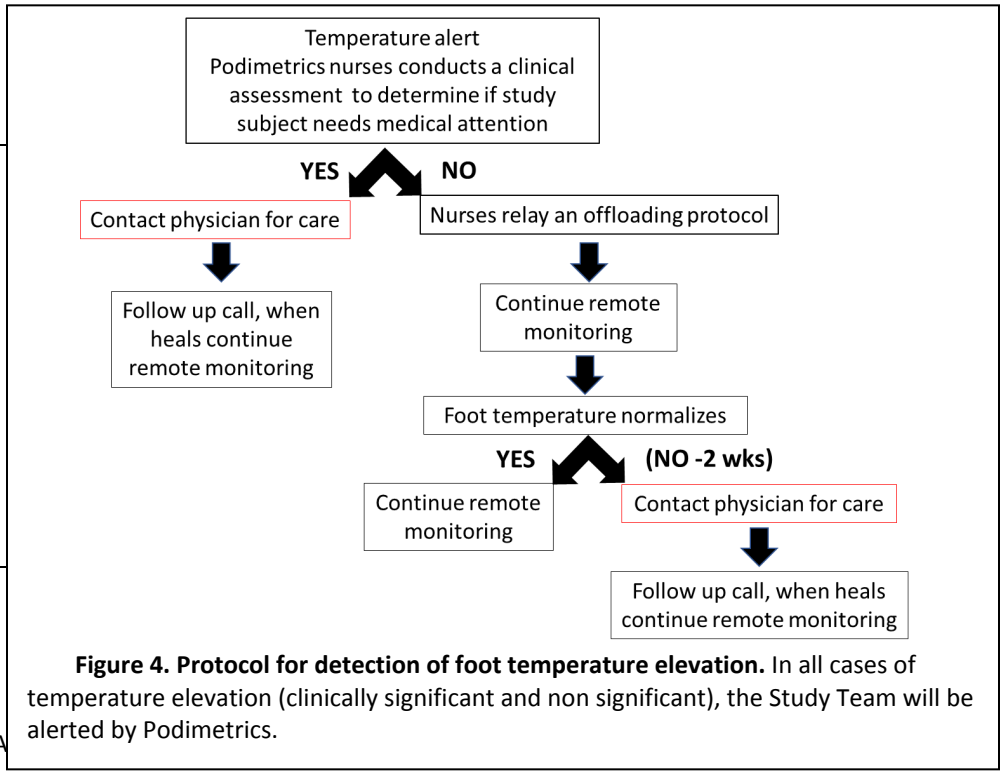


Figure 4. Protocol for detection of foot temperature elevation. In all cases of temperature elevation (clinically significant and non significant), the Study Team will be alerted by Podimetrics.

IRB NUMBER: 2023-14915
IRB APPROVAL DATE: 12/20/2024

1.3 SCHEDULE OF ACTIVITIES (SOA)

2 INTRODUCTION

2.1 STUDY RATIONALE

Early detection of foot ulcers in diabetics can allow timely intervention to prevent severe disease and amputation. New technology to allow home monitoring of foot temperature has been developed and demonstrated to be effective to detect early foot changes. Knowledge of uptake and adherence of this device is needed to determine if this technology could be effectively deployed to our patient population to improve outcomes.

2.2 BACKGROUND

A.1 Diabetic Foot Ulcers represent a major public health crisis, resulting in large morbidity for individuals and extracts large resources from health care systems.

Diabetic foot ulcers (DFU) remain a prevalent and highly morbid complication of diabetes. The effects of DFU and amputation on the individual are substantial with declines in well-being, economic instability, and depression. The impact of DFU's on U.S. health care costs is large and have been estimated to be 9-13 billion dollars annually. Furthermore, the prevalence of DFU differs by race and ethnicity. Non-Hispanic Black (NHB) or Hispanic/Latino (H/L) persons have a higher prevalence of diabetes, and amputations than persons who are non-Hispanic white (NHW). This crisis of DFU is seen every day on the inpatient service at Montefiore Medical Center (MMC), which offers health care to one of the most diverse and poorest communities in the U.S.

A.2 Need for technologic innovations for foot monitoring that is feasible, sustainable, and robust

The mechanism of the development of neuropathic foot ulcerations involves repetitive trauma at pressure point on the sole of the foot over several days. Due to the neuropathy, patients do not detect subtle inflammatory changes in the foot such as pain, erythema, swelling which are harbingers of ulceration. It has been shown that an increase in foot temperature as defined as increase by 2.2◦C or 4◦F, can detect early inflammatory changes, and if offloading is instituted, healing can occur to prevent ulceration. We will test the feasibility of a home foot temperature monitoring system in our MMC patients with Type 1 or Type 2 diabetes. Study subjects will stand on the mat daily, the temperatures are transmitted and if there are significant changes, the provider is alerted. There is a growing literature that demonstrating that these devices allow prompt detection and treatment to prevent severe DFU and need for a lower extremity amputation (LEA). Using FDA approved technology from Podimetrics (Somerville, Massachusetts), study subjects can use a telemedicine foot temperature monitoring mat to monitor the bottoms of their feet daily. This requires them to step on the mat, and the data will be automatically transmitted to Podimetrics for analysis. The mat embeds cellular technology for the transmission to occur. The use of this device has shown to (1) reduce the rate of hospitalization (RRR 0.52), (2) lower extremity amputation (RRR 0.71), (3) reduce the number of outpatient visits and (4) reduce the development of severe wounds (RRR 0.91). Podimetrics is an FDA 510 (k) cleared medical device for evaluation of the temperature over the soles of the feet for signs of inflammation.

Podimetrics provides the mat, wireless transmission of data, patient/subject training in the use of the mat, and reinforcement in the case of non-adherence. The Podimetrics team monitors the data and when there is an increase in 2.2◦C over two consecutive uses between and of six contralaterally matched locations, the study team is contacted. Accuracy of this approach predicts 97% of plantar DFU in patient in diabetic foot remission.

3 STUDY DESIGN

3.1 OVERALL DESIGN

This is a longitudinal cohort study. We will test the uptake and adherence of a novel foot monitoring device and collect data regarding the occurrence and severity of DFU and use of health care resources to inform future larger clinical trials.

4 STUDY POPULATION

4.1 INCLUSION CRITERIA

1. Type 1 or Type 2 diabetes mellitus
2. Prior treatment of DFU within 24 months
3. Subject had at least one outpatient follow up with a provider after treatment for DFU
4. No active ulcer at time of enrollment
5. Male or female, aged <18-75 yrs>
6. Presence of neuropathy
7. Ambulatory
8. Provision of signed and dated informed consent form
9. Stated willingness to adhere with all study procedures and availability to participate for the duration of the study

4.2 EXCLUSION CRITERIA

1. Active DFU
2. Unable to comply with study requirements.
3. Prior AKA or BKA

4.3 A STUDY SUBJECT DEVELOPS A DFU REQUIRING HOSPITALIZATION

1. Data is censored from the date of hospital admission.

4.4 STRATEGIES FOR RECRUITMENT AND RETENTION

- *We will enroll up to 8 participants per month depending on the time within the study.*
- *Study team will call participants monthly to maintain contact and obtain interim history regarding development of new DFU.*

5 INFORMED CONSENT PROCESS

• The study team will obtain informed consent in the study clinic (CTSA)

- There will be no waiver to obtaining signed informed consent
- This study is limited to adults
- Costs of transport from study clinic will be $60 (enrollment only)

• during clinic visit, the study will be explained, history (see Case Report Form) taken, and an examination of both feet will be recorded. No other tests will be performed
- There are no costs incurred by the study subject.

- Participant Recruitment is as described, patients with a history of DFU, will be recruited: inclusion and exclusion criteria are noted in section 4.0
- Risk/Benefit: Study subjects may or may not receive personal, direct benefit from taking part in this study. The possible benefits of taking part in this study include identification of early signs of diabetic foot ulcer that we can manage to prevent ulcers.
- Data quality control and database management: all data will be maintained in a password protected database: MONTEBOX. Only IRB approved study team members will have access.

6 STATISTICAL CONSIDERATIONS

This study is primary to assess adherence to the monitoring device. It is not powered to assess clinical outcomes or use of health care resources.

- We will plan for 20 subjects to complete the study, and plan to enroll up to 40 patients to account for drop out or exclusion.
- Measurement of adherence (primary outcome)
  - Adherence is defined as > 3 days/week during the six month period
  - We will record the number of re-engagement calls per participant over the 6 month study period
  - We will record the number lost to follow up, unable to comply, or are hospitalized (4.2, 4.3)
- Measurement of secondary outcomes
  - Number of subjects who develop a DFU over the course of the study
  - Utilization of health care resource use (total number of: ER visits, outpatient visits) over the course of the study

7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY

Participant discontinuation would occur if the participant were unable or unwilling to continue in the study.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL OR LOSS TO FOLLOW UP

Participants are free to withdraw from participation in the study at any time upon request.
An investigator may discontinue or withdraw a participant from the study for the following reasons:

- Significant non-compliance
- If any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant.

- If the participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation
- Loss to follow up will be if he or she cannot be reached by the study staff.

The reason for participant discontinuation or withdrawal from the study will be recorded on the Case Report Form (CRF). In the event a participant withdraws from the study or is lost to follow up, we will enroll an additional participant.

Figure 5. Image of foot monitoring device

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