Leveraging Smart Technologies to Improve the Management of Diabetic Foot Ulcers and Extend Ulcer-Free Days in Remission

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Short running title: Technologies to manage Diabetic Foot Ulcers

Abbreviations: (DFU) Diabetic Foot Ulcer; (DPN) Diabetic Peripheral Neuropathy ; (PTS) Plantar Tissue Stress; (AI) Artificial intelligent; (RFID) Radio-Frequency-Identification; (RF) Radio Frequency; (PTI) Pressure Time Integral

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Abstract:

The prevalent and long neglected diabetic foot ulcer (DFU) and its related complications rank among the most debilitating and costly sequelae of diabetes. Management of the DFU is multifaceted and requires constant monitoring from patients, caregivers, and healthcare providers. The alarmingly high rates of recurrence of ulcerations in the diabetic foot requires a change in our approach to care and to the vernacular in the medical literature. Our efforts should be directed not only on healing of open wounds, but also on maximizing ulcer-free days for the patient in diabetic foot remission. The increasing development and use of technology within every aspect of our lives represents an opportunity for creative solutions to prevent or better manage this devastating condition. In particular, recent advances in wearable and mobile health technologies appear to show promise in measuring and modulating dangerous foot pressure and inflammation to extend remission and improve the quality of life for these most complex patients. This review paper discusses how harnessing wearables and digital technologies may improve the management and optimize prevention of DFUs by identifying high-risk patients for triage and timely intervention, personalizing prescription of offloading, and improving adherence to protective footwear. While still in their infancy, we envisage a future network of skin-worn, jewelry-worn, and implantable sensors that, if allowed to effectively communicate with one another and the patient, could dramatically impact measuring, personalizing, and managing how we and the patients we serve move through our collective world.

Introduction:

It is estimated that up to one-third of people with diabetes will develop a diabetic foot ulcer (DFU) in their lifetime.[1] Failure to heal a DFU is a leading cause of hospitalization, amputation, disability and death among people with diabetes [1,2]. Globally, it is estimated that 20 million people currently have an active DFU; an additional 130 million have a history of DFU or the precursor risk factor diabetic peripheral neuropathy (DPN) and are expected to develop a DFU without intervention[1].

Diabetes foot care costs represent the single largest category of excess medical costs associated with diabetes. It is estimated that one-third of all diabetes related costs are spent on diabetic foot care in the United States, with two thirds of these costs incurred in the inpatient settings, constituting a substantial economic burden to society.[3,4] Unfortunately, even after the resolution of a DFU, recurrence is common and estimated to be 40% within 1 year, ~60% within 3 years, and 65% within 5 years [1].

In light of the impending diabetes epidemic and the high prevalence of DFU and its recurrence, the need for enhanced prevention of DFUs and/or keeping patients with ulcers in “remission”[1] is clear. DFU rates can be reduced, but effective management is multifaceted and requires constant monitoring from patients, caregivers, and healthcare providers[1]. Thanks to new “smart” sensors, which communicate with a handheld device or the cloud, and communication technologies such as smartphones and smart connected home infrastructure, new opportunities exist to improve management DFUs, as well as aim to prevent their initial occurrence [5]. With the help of artificial intelligent (AI), patients can be prompted to check their feet, glucose levels, or weight, and enter results into mobile patient portals. Even better: they can transmit the results to their physicians in real time. These fast-growing, low-cost, and widely available resources can help predict one's risk for foot ulcers, infections, peripheral arterial disease, frailty, and other diabetes-associated complications, ultimately saving limbs and lives[5].

In this manuscript some of the recent promising technology developments, which may assist not only in terms of improving the management of DFUs but also could assist in effective prevention of DFU are discussed. More specifically, recent developments in three specific areas have been discussed: 1) technologies to identify high-risk patients for triage and timely intervention, 2) technologies for effective and personalized prescription of offloading, and 3) technologies to improve adherence to protective footwear.

Technologies to identify high-risk patients for triage and timely intervention

Ideally, an at-risk diabetic foot should undergo regular podiatry evaluation. However, regular visits could easily overload an already overburdened healthcare system. Even in specialty diabetes centers with dedicated staff and top-shelf resources, the current model of regular visits is still associated with a very high ulcer recurrence rate [6]. Thus, an improved screening approach is required to facilitate timely referral of those who are at the edge of foot ulceration for timely intervention care. Recent advances in computer vision algorithms applied to images of diabetic feet have shown that diabetic foot ulcers can be detected automatically with high sensitivity and specificity by artificial intelligence technology[7-9]. This offers the potential for remote triage of patients and enhanced monitoring procedures.

Because inflammation is one of the earliest signs of foot ulceration, technologies that capture markers of inflammation may also assist in predicting DFU with sufficient lead time for effective intervention [6]. Inflammation has five symptoms: dolor (pain), calor (heat), rubor (redness), tumor (swelling), and functio laesa (loss of function). The most reliable measurement of inflammation, however, is based on thermography to measure heat, which has been shown to be promising for both prediction and prevention of DFU[6]. The rational for measuring plantar temperature is built on the notion that the skin heats up before it breaks down into ulcers. Isolated plantar regions displaying increased heat is mainly due to inflammation response of near damaged or damaged tissue and originally was suggested by Paul Brand and his team in 1975 as an effective method to predict DFU prior skin breakdown[10]. Almost two decades later in 1997, Armstrong, et al. [11] have proposed the use of a portable hand-held infrared skin temperature probe as an effective technique to predict foot injury as well as foot complications because of Charcot's arthropathy. Later on, in 2007, Lavery et al [12] suggested that using thermography as a self-assessment tool is effective to prevent recurrence of DFU.

Despite this evidence and the simplification of thermography using new devices such as the FLIR thermal camera (FLIR Systems, Inc. Wilsonville, Oregon, USA)[13] , daily plantar temperature monitoring is still not part of preventive care for managing the diabetic foot. This could be because of compliance issues such as adherence to daily use of thermography by the patient or his/her caregivers, the ease of use by non-tech savvy patients and caregivers (e.g., some may not be able to follow the instruction to accurately assess foot plantar temperature using either app or handheld thermography devices), or their ability to interpret the temperature difference (e.g., only the difference between two identical spots from left and right feet beyond of approximately 2 degrees C is clinically meaningful). To address this gap, Frykberg et al.[14] proposed a smart mat based on the telehealth concept, which could address the limitations of previous thermography tools. Specifically, they studied a novel in-home connected foot mat (Podimetrics Mat™, Somerville, MA, USA; **Figure 1**) to predict prospective incidents of DFU and better stratify those who need urgent foot care. This simple-to-use system was designed to require no configuration or setup by the users who simply needs to step on the mat with both feet for 20 seconds. Using an embedded cellular component the collected data are streamed to a cloud, thus there is no need to have WiFi or smartphones, which might not be available at the patient's home. Using an image processing tool, an integrated program compares the temperature profile between feet. In their study, they demonstrated that a threshold difference of ≥ 2.22 °C between corresponding sites on opposite feet correctly predicts 97% of DFU with an average lead time of 37 days. Adherence to the mat was high with 86% of participants using the mat at least 3 times per week, and an average use of 5 times per week. While this accuracy and lead time could be sufficient to better target those who need urgent care, the technology suffers from an important limitation: while the 2.22°C threshold provided 97% sensitivity in Frykberg's study, it yielded only 43% specificity. Increasing the threshold value increases specificity but decreases sensitivity. However, the observed high sensitivity and sufficient lead time (37 days) seem to be promising for effective triaging and coaching the individual and their caregiver to alter behavior to reduce DFU risk.

There are other wearables and digital health developments for improving daily monitoring of plantar temperature and potentially higher sensitivity and specificity to predict DFU and extend ulcer-free days in remission. Siren Care (Siren Diabetic Socks, Neurofabric, Siren Care Inc., San Francisco, CA; **Figure 2**)[15] is an example of such recent developments. It uses smart textiles which allow continuous monitoring of plantar temperature and thus may improve specificity for DFU prediction and engage patients to reduce risk. But the validity and acceptability of these technologies and their advantage compared to a daily single point assessment like that offered by the Podimetrics Mat remain to be studied. Similarly, new technologies enable temperature measurements between insole and shoe and simultaneous assessment of plantar pressure, temperature, and lower extremities joint angles [16]. These technologies may assist in improvement of triaging those at a high risk of DFU and eventually assist with personalized prevention strategies by indirect measurement of shear stress and sweating during daily physical activities. However, such developments are in their infancy and remain to be examined in prospective and clinical trials.

Technologies for Effective and Personalized Prescription of Offloading:

The most common pathway to develop a DFU is unchecked repetitive elevated plantar mechanical stress (shear or pressure) over time on insensate plantar foot tissue. Plantar tissue stress (PTS) is a concept introduced by Lazzarini et al [17] that attempts to integrate several well-known mechanical factors into one measure, including plantar pressure, shear stress, and daily weight-bearing activity time spent without protected footwear (adherence). If PTS remains elevated, then it results in sub-dermal inflammation and eventually a DFU. In a sensate foot, patients relieve (offload) the inflamed regions aided by feedback from their intact sensory pathways. Unfortunately, loss of plantar sensation, or “the gift of pain,” from DPN not only results in the inability to perceive elevated levels of PTS, but can also cause gait abnormalities and foot deformities that potentially exacerbate PTS [18].

Management of PTS is essential to mitigating DFU incidence and severity while prompting safe mobility in people with high DFU risk. Currently, providers frequently re-schedule patients for follow-up appointments and guide offloading treatments using their clinical intuition of the patient’s average build-up of their pre-ulcerative callus from activity and footwear. Over the last 20 years, these clinical judgements have been augmented by knowledge from objective laboratory measurements of PTS, demonstrating the capacity of various footwear and offloading devices to reduce PTS in controlled research settings. More recently, high-quality studies have gone further and demonstrated that objective measurements of plantar pressure can be used to successfully guide clinical treatment decisions and prolong ulcer-free days for the patient in diabetic foot remission [17]. This has led to international guidelines recommending that clinicians objectively measure plantar pressure to guide the prescription of their footwear-related offloading treatments [19-21].

Although measuring plantar pressure at one moment in time has proven clinically beneficial, it is not representative of a person’s entire PTS. A key limitation of the current PTS assessment modalities is that they only measure PTS over a short period of time which does not factor in daily weight bearing physical activities like walking, standing, and sitting while shifting weight to the feet. Currently, a major gap in managing

DFUs is a lack of understanding about the association between volume of weight-bearing activity and increased DFU risk. While incorporating a time dimension such as measuring pressure time integral (PTI) as a surrogate of cumulative plantar stress enables improved detection of those with history of DFU, such measurement still lacks specificity to predict DFU formation[18]. Even prediction of DFU location using plantar pressure assessment is uncertain. For example, Veves and colleagues[22] reported that only 38% of ulcer locations matched the peak pressure location. They also found that the peak pressure location actually changed in 59% of patients over the mean follow-up time of 30 months.

To improve the specificity of DFU prediction and personalize prescription of offloading, a person's weight-bearing activity should be considered when measuring PTS[17]. Early studies investigating weight-bearing activity in patients with DPN were dependent on participant's self-reporting this outcome. Such self-reporting suffers from both intentional (e.g., being afraid for potential consequence of carelessness) and unintentional (e.g., forgetting) errors. With advances in signal processing and multi-sensor devices, it is now possible to comprehensively monitor activity beyond counting steps. This includes measurements of total weight-bearing activity, bouts of weight-bearing activity, and activity intensity[23-25] . Najafi et al. [26]found that neuropathic patients spent approximately three fold as much time weight-bearing per day as walking, and that daily standing time may be predictive of worse DFU healing outcomes [27]. In a recent exploratory study[28], they revealed that walking more than 3000 steps per day lowers the rate of wound healing irrespective of type of offloading (i.e., removable and irremovable). These recent studies suggest the importance of understanding and managing the dosage of weight-bearing activity for both prevention and healing of DFU.

Thanks to advances in smart phones, mobile applications, and smart wearable sensors, the ability to continuously and simultaneously measure multiple mechanical factors comprising PTS has become more achievable. Smart flexible sensors implanted in insoles or socks combined with digital health apps have paved the way for monitoring PTS during activities of daily living. In 2017, Raviglione et al. [29] proposed the concept of daily monitoring of plantar pressure in people at risk of DFU using a smart textile (Sensoria socks, Sensoria Inc., Redmond, WA, USA; **Figure 3**). Their system contained a textile pressure sensor attached to a stretchable band, hardware that collects data and transmits them via Bluetooth to a smartphone, an app that gathers the data and stores them in the cloud, and a web dashboard that displays the data to the clinician. They concluded that this technology could determine optimal off-loading in the community setting and assist with DFU prevention. However, their study was limited to a proof-of-concept design and no clinical study was conducted to support the conclusion. Other digital health products available in the market exist to facilitate home monitoring of plantar pressure and gait. For example, FeetMe (FeetMe, Paris, France) uses a smartphone to monitor high plantar pressure. Surresense Rx® (Orpyx®, Calgary, Canada) uses smartwatch to monitor and notifies sustained plantar pressure (pressure above 30-50mmHg lasting for longer than 15 minutes) during activities of daily living. The same company designed Orpyx LogR™ that uses a smartphone to monitor and remotely visualize (via cloud) in-shoe plantar pressure with an autonomy lasting approximately 8-12 hours of active use. However, the clinical validation of these products and their ability to prevent DFU via daily plantar pressure screening are still unclear.

Technologies to improve adherence to protected footwear

Clinical care for management of DFUs and extend ulcer-free days in remission focuses on external offloading of the foot or shifting plantar pressure during gait from at risk area (e.g., the area with high plantar pressure or prior presence of wound) to a low risk area. However, clinical footwear trials are equivocal and approximately 40% of these patients still re-ulcerate within one year[1]. A lack of adequate adherence to prescribed footwear is the key factor often leading to the majority of these re-ulcerations. Specifically, despite taking over 50% of their steps at home, patients view their home as “safe zone” where they do not feel the need to wear their prescribed footwear[30]. As a result, high-risk patients wear their prescribed footwear only 15 - 28% of the time. Advances in technology now allows us to implement timely alerts, notifications, or auto-reminder programs to improve patient adherence.

Some technologies have been recently designed that enable objective monitoring of adherence to footwear. Orthotimer sensor (Rollerwerk, Balingen, Germany)[31] is an example of such technologies, which is using a microsensor and a unique individual ID number. The sensor could be integrated in shoes, insoles, orthotic devices, and offloading and enables wear time to be measured. Using a reading device the wear time could be wirelessly read and transferred to a software for wear time analysis. While such assessment could be beneficial for educational purpose and potentially improving adherence, it lacks an adherence reinforcement component to effectively engage patients and their caregivers on daily basis.

Thanks to advances in digital health, development of smart wearables capable of real-time notifying harmful plantar pressure throughout the day are now becoming a reality. Such development may also have the possibility to engage neuropathic patients to be part of their routine daily foot care and change their attitude toward using protected footwear and safe mobility. In 2017, Najafi et al.[32] tested effectiveness of a real-time alerting system (using smartwatch) to improve adherence to prescribed diabetic shoes over time. Participants were asked to wear on daily basis a pair of diabetic shoes equipment with a thin (< 0.5 mm) smart insole system, (the SurroSense Rx, Orpyx Medical Technologies Inc., Calgary, Canada; **Figure 4**) over a 3-month period. This device cues offloading by providing simple instructions via smartwatch (e.g., walk few steps after prolonged sitting or standing, check inside of shoes for a foreign object causing high pressure, check formation of callus, etc) to manage unprotected sustained plantar pressures in an effort to prevent foot ulceration; a successful response to an alert was defined as pressure offloading, which occurred within 20 minutes of the alert onset. Patient adherence, defined as daily hours of device wear, was determined using sensor data and patient questionnaires. They concluded that a real-time and comprehensive foot pressure alert method with a minimum number of alerts (one every two hours) are effective to allow optimal response to offloading cues from a smart insole system and for improving adherence to prescribed diabetic shoes over time. This could be explained by the fact that a real-time alert about comprehensive harmful weight-bearing physical activities (activities such as prolonged bout of standing that may occlude capillary bed perfusion in the soft tissues of the foot for significant period of time and potentially damage the tissue or leading to local ischemia [32]), may assist in improving perception of benefit of the technology, which in turn could improve the attitude toward using the protected footwear.

Some researchers have also proposed the use of smartwatches and smartphones to engage patients in wearing their offloading device. PAMTag (**Figure 5**) is one of these technologies introduced by Najafi et al.[33] to improve adherence to offloading. The platform includes a smartwatch and a smart tag named PAMTag, which is attached to an offloading device. The PAMTag includes an accelerometer to monitor activity, a Radio-Frequency-Identification (RFID) tag, and a radio-frequency (RF) component. The smartwatch is programmed to monitor weight bearing activities. In the case of any detected weight bearing activities (e.g., standing and walking) the smartwatch communicates with the PAMTag. If PAMTag is not in close proximity and/or does not confirm the offloading device was worn during those activities, a notification is provided to the patient via the smartwatch and text message is sent to a patient's caregiver to encourage use of the offloading device. In addition, the platform enables reporting daily adherence to offloading to care providers. The validity of this platform to improve adherence to offloading is however unclear.

Conclusion

In summary, lower extremity complications of diabetes remain all too common. Next-generation technologies should be geared to the long-term monitoring of people both with tissue loss and after healing in remission. This will likely consist of a multitude of epidermal, wearable, and implantable sensors. Creating unified methods of communicating and assessing these technologies that transcends the proprietary nature of individual devices will be critical to the long-term success in helping people remain active while optimizing DFU management and supporting DFU prevention strategies.

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Conflict of Interest: The authors have been involved in undertaking research studies using some of the products describing in this review paper. BN is one of the co-inventors of the product (PAMTag) indicated in this study. However, none of the authors claimed any financial conflict of interest.

Authors' Contribution Statement: BN has drafted the manuscript. NR and DA have critically reviewed and revised the manuscript. All authors significantly contributed to the discussion and included their expert opinions.

References

1. Armstrong DG, Boulton AJM, Bus SA. Diabetic Foot Ulcers and Their Recurrence. *N Engl J Med.* 2017;376(24):2367-2375.
2. Lazzarini PA, Pacella RE, Armstrong DG, Van Netten JJ. Diabetes-related lower-extremity complications are a leading cause of the global burden of disability. *Diabetic Medicine.* 2018;35:1297-1299.
3. Barshes NR, Sigireddi M, Wrobel JS, et al. The system of care for the diabetic foot: objectives, outcomes, and opportunities. *Diabet Foot Ankle.* 2013;4.
4. Skrepnek GH, Mills JL, Sr., Armstrong DG. A Diabetic Emergency One Million Feet Long: Disparities and Burdens of Illness among Diabetic Foot Ulcer Cases within Emergency Departments in the United States, 2006-2010. *PLoS One.* 2015;10(8):e0134914.
5. Basatneh R, Najafi B, Armstrong DG. Health Sensors, Smart Home Devices, and the Internet of Medical Things: An Opportunity for Dramatic Improvement in Care for the Lower Extremity Complications of Diabetes. *J Diabetes Sci Technol.* 2018;12(3):577-586.
6. Lavery LA, Armstrong DG. Temperature monitoring to assess, predict, and prevent diabetic foot complications. *Curr Diab Rep.* 2007;7(6):416-419.
7. Goyal M, Yap MH, Reeves ND, Rajbhandari S, Spragg J. Fully convolutional networks for diabetic foot ulcer segmentation. Paper presented at: 2017 IEEE International Conference on Systems, Man, and Cybernetics (SMC)2017.
8. Goyal M, Reeves ND, Davison AK, Rajbhandari S, Spragg J, Yap MH. Dfunet: Convolutional neural networks for diabetic foot ulcer classification. *IEEE Transactions on Emerging Topics in Computational Intelligence.* 2018.
9. Goyal M, Reeves N, Rajbhandari S, Yap MH. Robust methods for real-time diabetic foot ulcer detection and localization on mobile devices. *IEEE journal of biomedical and health informatics.* 2018.
10. Bergtholdt HT, Brand PW. Thermography: an aid in the management of insensitive feet and stumps. *Arch Phys Med Rehabil.* 1975;56(5):205-209.
11. Armstrong DG, Lavery LA, Liswood PJ, Todd WF, Tredwell JA. Infrared dermal thermometry for the high-risk diabetic foot. *Phys Ther.* 1997;77(2):169-175; discussion 176-167.
12. Lavery LA, Higgins KR, Lanctot DR, et al. Preventing diabetic foot ulcer recurrence in high-risk patients: use of temperature monitoring as a self-assessment tool. *Diabetes Care.* 2007;30(1):14-20.
13. van Doremalen RFM, van Netten JJ, van Baal JG, Vollenbroek-Hutten MMR, van der Heijden F. Validation of low-cost smartphone-based thermal camera for diabetic foot assessment. *Diabetes Res Clin Pract.* 2019;149:132-139.
14. Frykberg RG, Gordon IL, Reyzelman AM, et al. Feasibility and Efficacy of a Smart Mat Technology to Predict Development of Diabetic Plantar Ulcers. *Diabetes Care.* 2017;40(7):973-980.
15. Reyzelman AM, Koelewyn K, Murphy M, et al. Continuous Temperature-Monitoring Socks for Home Use in Patients With Diabetes: Observational Study. *J Med Internet Res.* 2018;20(12):e12460.
16. Najafi B, Mohseni H, Grewal GS, Talal TK, Menzies RA, Armstrong DG. An Optical-Fiber-Based Smart Textile (Smart Socks) to Manage Biomechanical Risk Factors Associated With Diabetic Foot Amputation. *J Diabetes Sci Technol.* 2017;11(4):668-677.

17. Lazzarini PA, Crews RT, van Netten JJ, et al. Measuring Plantar Tissue Stress in People With Diabetic Peripheral Neuropathy: A Critical Concept in Diabetic Foot Management. *J Diabetes Sci Technol.* 2019:1932296819849092.
18. Wrobel JS, Najafi B. Diabetic foot biomechanics and gait dysfunction. *J Diabetes Sci Technol.* 2010;4(4):833-845.
19. Bus SA, van Netten JJ, Lavery LA, et al. IWGDF guidance on the prevention of foot ulcers in at-risk patients with diabetes. *Diabetes/Metabolism Research and Reviews.* 2016;32:16-24.
20. Bus SA, Armstrong DG, van Deursen RW, et al. IWGDF guidance on footwear and offloading interventions to prevent and heal foot ulcers in patients with diabetes. *Diabetes/Metabolism Research and Reviews.* 2016;32:25-36.
21. van Netten JJ, Lazzarini PA, Armstrong DG, et al. Diabetic Foot Australia guideline on footwear for people with diabetes. *Journal of Foot and Ankle Research.* 2018;11(1):2.
22. Veves A, Murray HJ, Young MJ, Boulton AJ. The risk of foot ulceration in diabetic patients with high foot pressure: a prospective study. *Diabetologia.* 1992;35(7):660-663.
23. Crews RT, Yalla SV, Dhatt N, Burdi D, Hwang S. Monitoring Location-Specific Physical Activity via Integration of Accelerometry and Geotechnology Within Patients With or At Risk of Diabetic Foot Ulcers: A Technological Report. *J Diabetes Sci Technol.* 2017;11(5):899-903.
24. Lemaster JW, Reiber GE, Smith DG, Heagerty PJ, Wallace C. Daily weight-bearing activity does not increase the risk of diabetic foot ulcers. *Med Sci Sports Exerc.* 2003;35(7):1093-1099.
25. Sheahan H, Canning K, Refausse N, et al. Differences in the daily activity of patients with diabetic foot ulcers compared to controls in their free-living environments. *International Wound Journal.* 2017;14(6):1175-1182.
26. Najafi B, Crews RT, Wrobel JS. Importance of time spent standing for those at risk of diabetic foot ulceration. *Diabetes Care.* 2010;33(11):2448-2450.
27. Najafi B, Grewal GS, Bharara M, Menzies R, Talal TK, Armstrong DG. Can't Stand the Pressure: The Association Between Unprotected Standing, Walking, and Wound Healing in People With Diabetes. *J Diabetes Sci Technol.* 2017;11(4):657-667.
28. Najafi B, Armstrong DG. Gait Inefficiency Induced by Offloading – Critically Unintended Consequences For the Diabetic Foot in Remission. Paper presented at: 8th International Symposium on the Diabetic Foot2019; The Hague, The Netherlands.
29. Raviglione A, Reif R, Macagno M, Vigano D, Schram J, Armstrong D. Real-Time Smart Textile-Based System to Monitor Pressure Offloading of Diabetic Foot Ulcers. *J Diabetes Sci Technol.* 2017;11(5):894-898.
30. Armstrong DG, Lavery LA, Kimbriel HR, Nixon BP, Boulton AJ. Activity patterns of patients with diabetic foot ulceration: patients with active ulceration may not adhere to a standard pressure off-loading regimen. *Diabetes Care.* 2003;26(9):2595-2597.
31. Lutjeboer T, van Netten JJ, Postema K, Hijmans JM. Validity and feasibility of a temperature sensor for measuring use and non-use of orthopaedic footwear. *J Rehabil Med.* 2018;50(10):920-926.
32. Najafi B, Ron E, Enriquez A, Marin I, Razjouyan J, Armstrong DG. Smarter Sole Survival: Will Neuropathic Patients at High Risk for Ulceration Use a Smart Insole-Based Foot Protection System? *J Diabetes Sci Technol.* 2017;11(4):702-713.
33. Najafi B, Boloori A-R, Wrobel J. Intelligent device to monitor and remind patients with footwear, walking aids, braces, or orthotics. US Patent 8,753,275; 2014.

Figure legends

Figure 1: In a prospective cohort observational study of patients in foot ulcer remission, Frykberg et al. [14]demonstrated that 20 seconds of daily monitoring plantar temperature using a smart mat (Podimetrics LLC, MA, USA) and an asymmetry temperature of greater than 2.22 ^{o}C enables predicting incident of ulcer recurrence with 97% accuracy and an average lead time of 37±18 days (mean ± standard deviation). In this study, 129 eligible subjects were recruited and followed for up to 34 weeks leading to 53 incidents of DFU. Then using a machine learning model, an optimum threshold of 2.22 ^{o}C was identified to yield a tradeoff between longest lead time and detection with highest accuracy. This figure is built based results reported by Frykberg et al. study[14].

Figure 2: Siren Socks enables continuous home temperature monitoring, which may be used as an early warning system, to provide people with objective feedback so they can modify their activity and protect their foot before ulcers develop. This figure is built based on the images shared by Siren Care.

Figure 3: Sensoria Socks (Sensoria Fitness Inc., Redmond, WA, USA) monitor plantar pressure under three plantar regions of interest including heel, 1st metatarsal head, and 5th metatarsal head. They include an anklet that snap to socks' sensors for transmitting data. Via a mobile application, plantar pressure under regions of interest could be visualized in real-time. This figure is built based on the images shared by Sensoria Fitness Inc.

Figure 4: Recent advances in wearables enable providing timely and real-time feedback to patients to protect their feet against conditions that may increase risk of a

diabetic foot ulcer. The SurroSense Rx (Orpyx Medical Technologies Inc., Calgary, Canada) is an example of technologies that enable continuous screening plantar pressure through smart insoles and notify the patient via the smartwatch in form of visual, vibratory, and audio feedback in case of a sustained plantar pressure beyond a pre-defined threshold. This technology could be used to educate patients to avoid conditions leading to sustained plantar pressure (e.g., unbroken and prolonged standing), which in turn could assist with prevention of diabetic foot ulcers. A recent study by Najafi et al study [32] has also demonstrated the benefit of real-time feedback to improve adherence to footwear. This figure is built based on results reported by Najafi et al study [32]

Figure 5: PAMTag introduced by Najafi et al. and commercialized by Biosensics LLC to engage patients in wearing their offloading devices. This figure is built based on images shared by Najafi's research group.

Tables: None

Figures

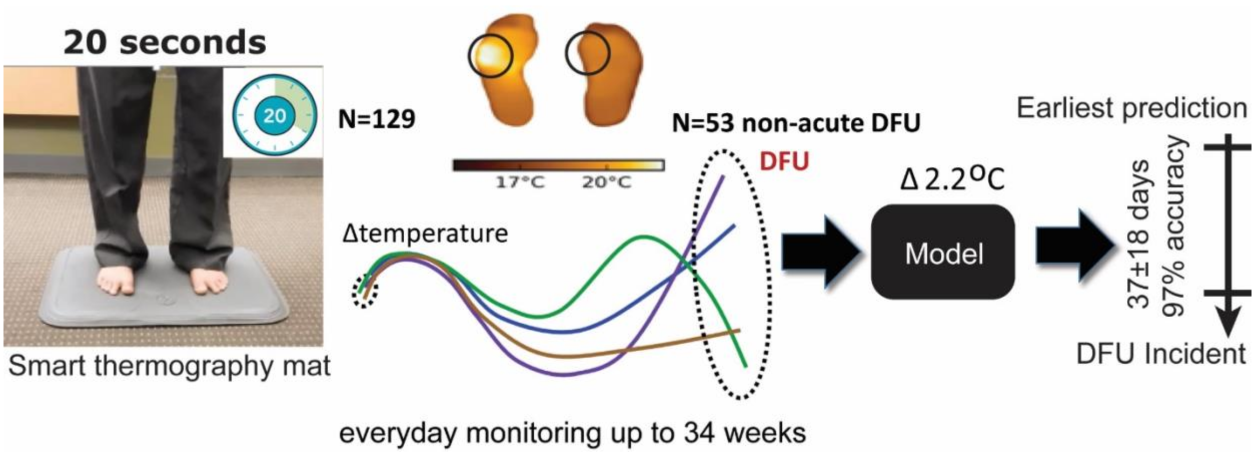

Figure 1

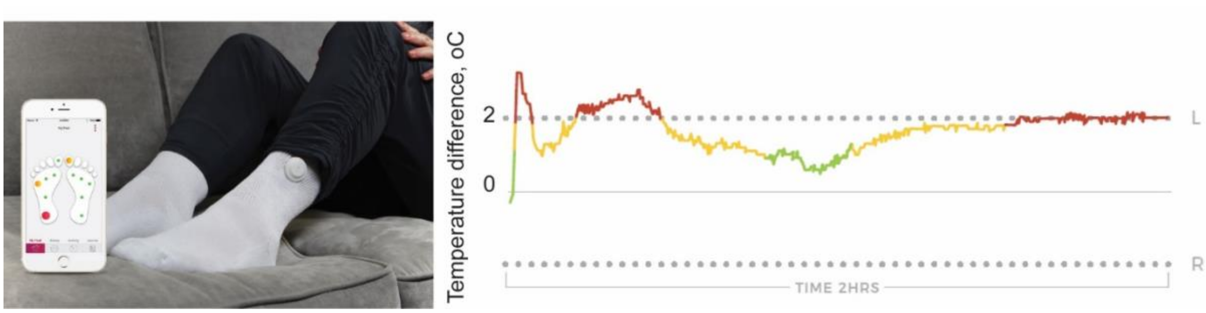

Figure 2


Sensoria sock+Sensoria App
Textile-based sensors to monitor plantar pressure
Inertial sensor, battery, and communication unit
Pressure visualization via a mobile application

Figure 3


Smart Insoles to screen sustained plantar pressure (15min or longer)
Smart watch to assist patients to avoid physical activities (e.g. prolong standing) leading to sustained plantar pressure
ORPYX
ORPYX
HIGH PRESSURE DETECTED
Dismiss
HELP
Menu

Figure 4


PAMTag
BioSensics
BioSensics
Please wear
offloading device.

Figure 5