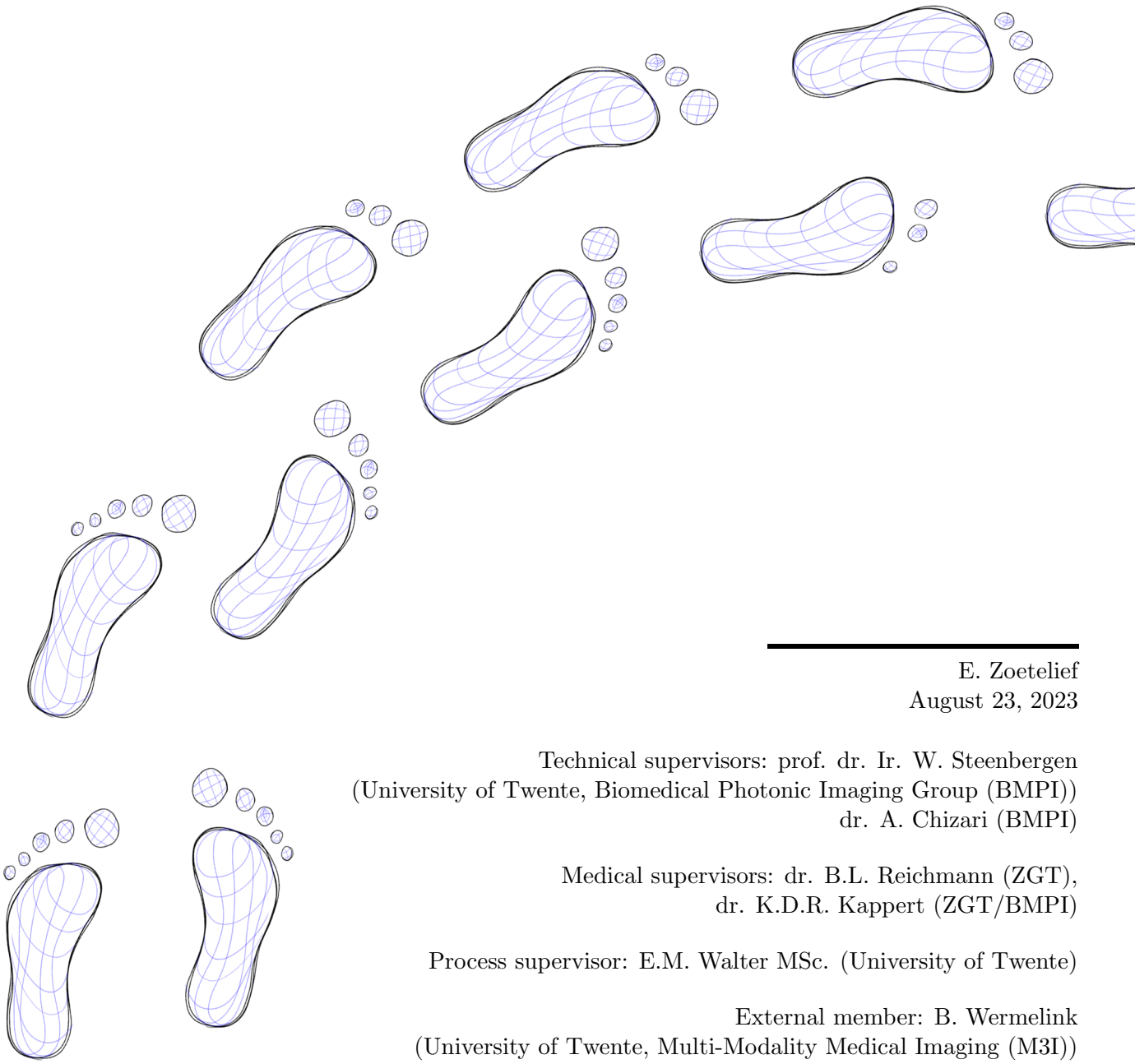
Explorative Study of Thermal Footprint Imaging as Method to Early Detect Diabetic Foot Ulcers in a Domestic Setting: the Bath Mat

Master Thesis Technical Medicine



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UNIVERSITY OF TWENTE. BMPI Biomedical Photonic Imaging zgt Topzorg voor uw levenskwaliteit

Abstract

Introduction Due to a combination of Diabetes Mellitus (DM) related complications, 19-34% of all DM patients develop a diabetic foot ulcer (DFU). The treatment of a DFU can take months, which could eventually result in a lower extremity amputation. Although 75% of all DFUs can be prevented with care, e.g. daily foot inspections, adherence is low in DM patients. In addition, monitoring is intensive and no low-threshold preventive tool is available to monitor high-risk patients. In recent years, several studies focused on measuring skin temperature on the plantar feet as low-threshold preventive tool, because increased local skin temperatures is believed to be an indication of inflammation. However, these studies primarily focused on the plantar foot side and used limited measuring locations, while only 50% of the DFUs occur at the plantar foot side. Therefore, the aim of this master's thesis is to investigate a new thermographic (Bath Mat) method, which measures the temperature in the whole feet.

Method This thesis researched a new method for measuring foot temperature in an explorative pilot study. The temperature distribution of the dorsal side was captured directly, while the temperature distribution of the plantar side was captured indirectly from thermal footprints present on a mat after the feet were removed. To test this method in a clinical environment, a non-WMO patient study was conducted. The data collected from this study was used to investigate four main topics: (1) similarities in temperature distribution between direct plantar images and thermal footprints, (2) visibility of DFUs on thermal footprints, (3) quantify DFUs in thermographic features and (4) reproducibility of thermal footprints between days.

Results For this study 20 subjects without a DFU and 30 subjects with a DFU were included. In subjects without a DFU, similarities in temperature distribution were visible between direct plantar images and thermal footprints. In subjects with a DFU, a change in temperature distribution was shown at the DFU location. This change is visible in both direct and indirect images. Most of the subjects with a DFU had a hotspot on the ulcer location, others had a coldspot. The two features examined in this thesis to quantify DFUs were: (1) left-right differences in mean plantar/dorsal temperature and (2) left-right differences in contralateral spots. Furthermore, between different days, the temperature distribution is similar in thermal footprints, yet the measured mean temperature varies. The extent of temperature deviation differs between days and foot areas among healthy subjects.

Discussion and Conclusion In this thesis, a new, non-invasive, method to detect DFUs was developed and tested in a clinical environment. With the Bath Mat device, we were able to obtain thermal images of the whole foot showing differences between feet with and without a DFU. Among the investigated features, left-right differences in mean foot temperature do not appear to be sufficient to quantify DFUs for all patients. Conversely, temperature differences in contralateral spots potentially can determine if a DFU is present. Although this new method still needs additional research, the thermal images collected with the use of this device have the potential to identify features beyond left-right differences.

Table of contents

1 Introduction

In 2021 approximately 537 million people worldwide were suffering from Diabetes Mellitus (DM).[1] DM is a chronic disease in which blood glucose levels are deregulated due to impaired insulin production caused by an autoimmune response (type 1) or insulin resistance (type 2). Long-term high blood glucose levels (hyperglycaemia) can cause various complications, which can be divided into two categories: macro- and microvascular complications.[2–4] The prevalence of microvascular complications (i.e. 12-15%) is higher than the prevalence of macrovascular complications (i.e. 1-10%).[2, 5] Macrovascular complications arise from inflammatory damage to the arterial wall, called atherosclerosis.[6, 7] This inflammation can cause plaques to accumulate on the inner layer of the artery wall (intima). As a result, blood supply is reduced and/or plaques may detach and cause occluded blood vessels elsewhere in the body.[8] This can lead to a diminished blood flow, for example to the extremities and/or heart, which in turn can lead to cardiovascular disease, stroke, and peripheral vascular disease (PAD). Microvascular complications arise from several metabolic injuries, causing changes in blood flow, endothelial permeability, extravascular protein deposition and coagulation.[9] This result in damage to smaller blood vessels and nerve cells, resulting in retinopathy (damage to retina), nephropathy (damages to the kidney), peripheral neuropathy (damages to the nerves in extremities), and limited joint mobility syndrome.[2–4, 10] Due to a combination of the above mentioned complications a DM patient can also develop a diabetic foot ulcer (DFU), which could eventually result in a lower extremity amputation. These amputations are ten times more common in DM patients compared to healthy individuals.[11] Additionally, DM complications account for around 60% of all lower extremity amputations.[11, 12] One possibility of reducing the amount of amputations could be the prevention of DFUs. Therefore, the aim of this master's thesis is to develop a method for early detection of DFU.

1.1 Anatomy of the foot

This thesis distinguishes between six different foot areas, which are shown in figure 1.

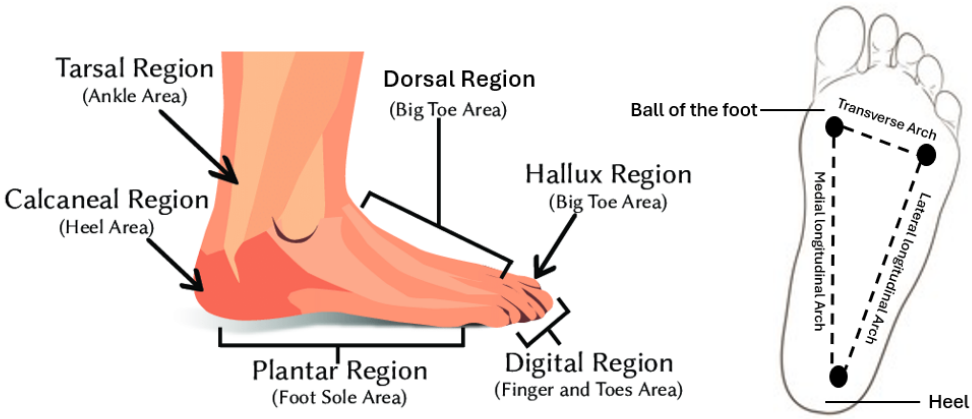

Figure 1: The anatomy of the foot.[13]

1.2 Diabetic foot ulcer

Around 19-34% of all DM patients develop a DFU at some point in their life, of which 77% heal within one year. However, 40% of patients with a healed DFU develop a new DFU within one year, rising to a recurrence rate of 65% in five years.[14]

The mechanism by which DFUs arise and persist can be divided in four main aspects: PAD, peripheral neuropathy, cell dysfunction and infection.[15] PAD causes a reduced blood supply, called ischemia.[6, 7] This prevents blood from reaching DFU, and can lead in severe circumstances to necrosis and gangrene.[15, 16] Peripheral neuropathy causes changes in sensory-, motor- and autonomic nervous systems, which causes loss of protective sensation, muscular atrophy of the leg and foot, motor paralysis, loss of muscle reflex, increased blood perfusion in the deep skin and decreased sweating.[14, 16, 17] This results in uneven foot pressure load and poor gait.[15] At foot areas with a higher load, a thicker skin (callus) is formed, further increasing the biomechanical loading, which in turn can cause subcutaneous haemorrhage and eventually skin ulceration/DFU.[18] The foot areas with highest risk for ulceration are visualised in figure 2.[18]

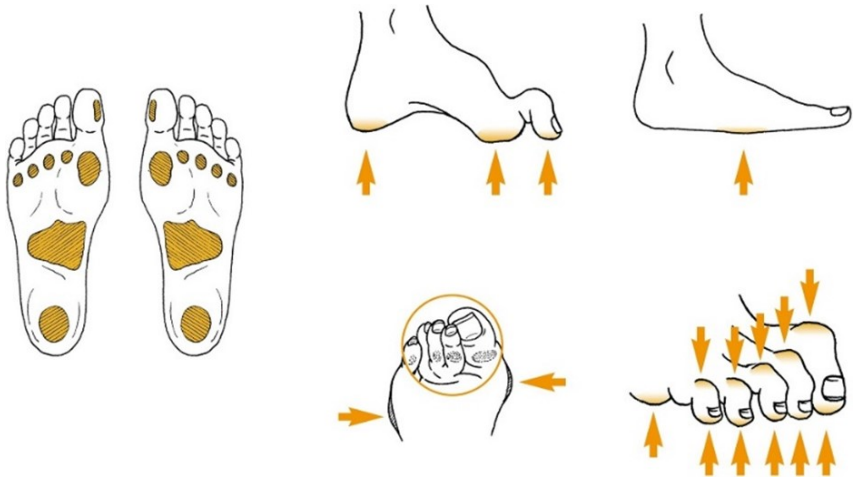

Figure 2: Areas of the foot at highest risk for ulceration.[18] This images shows different types of foot deformations: (top centre) claw foot, (top right) flatfoot or 'rocker-bottom', (bottom centre) overlapping toes, and (bottom right) hammer and/or claw toe.[19, 20]

The last two aspects, cell dysfunction and infection, are responsible for impaired wound healing. The function of different cells required at various stages of wound healing is disrupted by the high glucose environment. For example, DFUs maintain a chronic proinflammatory state, caused by an impaired macrophage function and phenotype transition. Another example, wound reepithelialisation is delayed by a disrupted keratinocyte function. Immune system cells also become dysfunctional, which is a reason that infections are common in diabetic patients. Furthermore, half of all DFUs get infected with a bacterium, microorganisms and/or fungal pathogens, hampering woundhealing.[14, 15]

As a result of the four aspects described, healing a DFU can take months.[14, 21] To classify DFUs in the outpatient clinic different classification systems can be used, such as the WIfI- or Texas classification.[22] In ZGT the Texas classification is used, table 1.[23]

Table 1: Texas classification[23]

		Grade			
		0	**1**	**2**	**3**
Stage	**A**	Pre-ulcerative	Superficial wound, not penetrating tendon, capsule, or bone	Wound penetrating tendon or capsule	Wound penetrating bone or joint
	B	Infection			
	C	Ischemia			
	D	Infection and ischemia			

1.3 Treatment possibilities for diabetic foot ulcers

Treatment possibilities to heal DFUs include surgical debridement, glycaemic control, and offloading wound pressure by wearing orthopaedic shoes or a cast.[14, 24] Also, DFUs should be closely monitored for infection and treated with antibiotics in case of an active infection. Furthermore, the vascular status can be mapped. This often starts by determining the toe pressures, the ankle-brachial index (ABI-index) and a duplex of the leg vessels.[25] If the blood supply is reduced, it could be helpful to improve the blood supply with a surgical procedure, such as percutaneous transluminal angioplasty (PTA) or thromboendarterectomy.[24] If the DFU does not heal, it may be necessary to amputate toes, (parts of) the foot or (parts of) the leg.[26] In conclusion, DFU care is intensive, complex, expensive and affects patients' quality of life.[27, 28]

1.4 Prevention of diabetic foot ulcers

To prevent DFUs, the IWGDF guideline recommends repeated foot inspections by a certified health professional every 1 to 12 months, depending on the patient's risk.[18] The patient's risk is determined in the guideline by a modified version of Simm's classification, which can be found in table 2.[18, 29]

Table 2: Modified Simm's classification[29]

Classification	**Risk level**	**Risk profile**
Sims 0	Low	No protective sensory loss No indications of PAD*
Sims 1	Slightly increased	Loss of protective sensory or indications of PAD* No signs of local increased pressure**
Sims 2	High	Presence of at least 2 of the following factors: - Loss of proactive sensory - Indication of PAD* - Signs of local increased pressure**
Sims 3	Strongly increased	DFU or amputation in medical history Inactive Charcot-foot End stage kidney failure or renal function replacement therapy (dialysis)

* Defined as presence of intermittent claudication and/or presence of rest pain and/or ankle brachial index <0.9 and/or toe brachial index <0.75 and/or tcpO2 <60mmHg

** Defined as excessive local callus formation (including corns) and/or local inflammatory signs and/or intra- or subcutaneous bleeding and/or blistering

In addition, patients are advised to perform a daily foot inspection, to check the entire surface of both feet and the inside of the shoes that will be worn.[18, 30, 31] However, two-third of all diabetic patient are not checking their feet, resulting in a low adherence.[32–35] In addition, self-inspections can be difficult in DM patients due to DM related complications (e.g. limited eyesight due to retinopathy or limited joint mobility).[36] Nonetheless, it is estimated that with high preventive care, 75% of all DFUs can be prevented.[37, 38]

1.4.1 Related works preventive tools diabetic foot ulcers

In recent years, several tools for early detection of DFUs have been investigated, in both hospital- and domestic setting.[28] Initial studies focused on measuring skin temperature on the plantar feet with a skin thermometer or heat sensors, because local skin temperatures would be increased due to inflammation (see section 1.2).[39] These studies showed that a temperature difference of >2.2°C between contralateral spots at the feet in consecutive days can be an early sign of ulcer development.[39–42] However, in recent randomized control trails with skin thermometers the incidence of ulcers is only 22% lower compared to usual care.[33] Moreover, the 2.2°C threshold should be corrected based on individual temperature differences at baseline.[43] Another study used thermal imaging to measure the plantar skin temperature, which suggests a cut-off value of >1.35 °C for the mean difference of the whole foot between left and right.[44] Additionally, studies investigated socks with built-in temperature sensors, to continuously measure the temperature in six spots at the plantar foot side.[33, 45–47] Furthermore, studies assessed (thermal) images through machine learning models.[48–51] A limitation of the aforementioned studies is that temperature is primarily investigated at plantar foot side, while only 50% of the DFUs occur at the plantar side.[49, 52] In addition, authors recommend follow-up research for a method where data of more than six to eight spots are collected.[43, 44]

1.5 Theory of thermal imaging

This project aims to measure foot temperature using a thermal camera. This camera detects infrared (IR) light, which is emitted by all objects with a temperature above 0 K (-273.15°C). When two objects have different temperatures heat transfer occurs, in which IR energy flows from a warmer object to a colder object by emitting and absorbing electromagnetic waves. The heat transfer occurs by radiation, which is non-contact and requires no medium. When radiation interacts with an object, three different types of interaction can occur: reflection, absorption and transmission, see figure 3.[53]

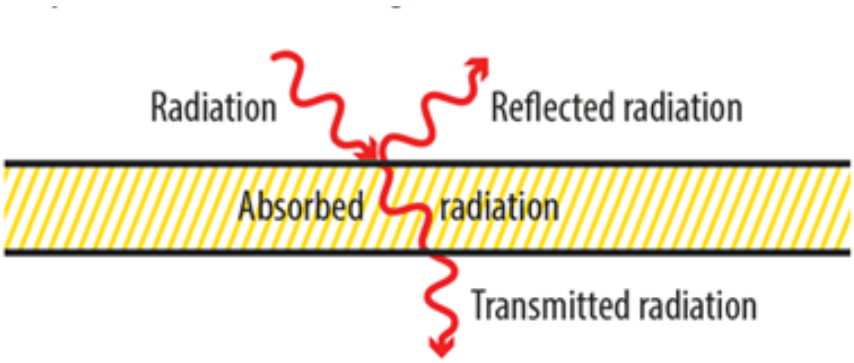

Figure 3: Total radiation object.[53]

The total power (P [W]) radiated from an IR source at a specific temperature can be estimated with the Stefan-Boltzmann Law[53]:

$$P = \varepsilon \sigma A T^4 \tag{1}$$

here σ is the Boltzmann constant, A the total surface of emitter [m2], T the absolute temperature [K], and ε is the emissivity. This emissivity is 1 for a perfect black body, which is defined as a physical entity that absorbs all electromagnetic radiation. The temperature in a black body affects the emissive power and peak wavelength, as described in Plank's Law. When the temperature of a black body increases, more emissive power will be produced and the peak wavelength becomes shorter, as illustrated in figure 4.[53]

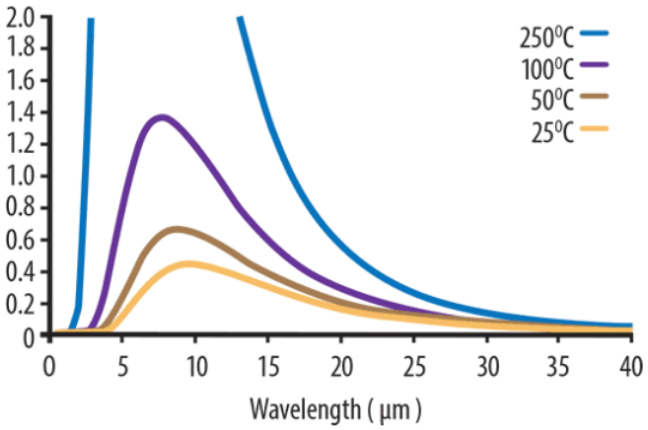

Figure 4: IR distribution for various emitter temperatures from 25°C to 250°C.[53]

The idea of the Bath Mat project is to identify trends in foot temperature to quantify ulcers. The foot temperature is assumed to be around 30°C. In figure 4, it can be estimated that the wavelength peak for this temperature is around 9µm.

1.6 The Bath Mat project

The aim of this project is to develop a new potential method for early detection of pre-stage of DFUs, which overcomes limitations described in section 1.4.1. This preventive method intends to provide temperature images of the entire feet with a thermal camera and a (thin) passive floor mat, see figure 5.[26]

The temperature distribution of the dorsal side will be captured directly, while the temperature distribution of the plantar side will be captured indirectly from thermal footprints present on the mat after the feet were removed. To explore the possibilities of this method, the BioMedical Photonic Imaging group (BMPI) of the University of Twente and ZGT Almelo collaborated in the Bath Mat project. The BMPI group developed a prototype and subjects will be recruited within ZGT to test the prototype. The study objective of this thesis is to validate and test the developed Bath Mat device on different groups of participants in an outpatient clinic.

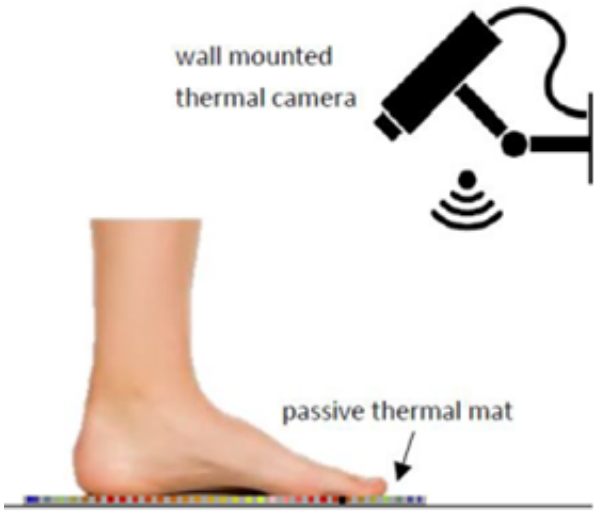

Figure 5: Schematic representation of the Bath Mat,[26]

1.7 Research questions

Associated with the study objective are the following research questions (and sub questions):

1. How do thermal footprints (indirect thermographic feet images) of individuals relate to direct thermographic feet images of the plantar foot side?
2. What features can be extracted from the obtained thermographic feet measurements from healthy individuals and DM patients?
   (a) Are we able to relate information and/or features obtained from the thermographic images to a wound or foot ulcer?
3. How reproducible are thermal footprints of healthy individuals over time and how do thermal footprints relate to each other?
4. How do diabetic patients experience the Bath Mat device?

To investigate the research questions, the Bath Mat device was optimised for measuring in a clinical setting. In chapter 2 the development of the device is discussed, with associated measurement protocol and post-processing steps. In chapter 3, the various clinical studies are discussed. Then in chapter 4, the implications of the clinical studies are discussed.

2 Bath Mat materials and development

This chapter discusses the materials used to collect patient data. To perform a patient-study, a non-WMO proposal was written, see Appendix A. This research protocol was approved by the local ethics committee of ZGT prior to the start of the study (study number ZGT23-06).

2.1 Device setup

The measuring part of the Bath Mat device for this study consists of an adjustable tripod, with an RGB- and a thermal camera mounted to it, see figure 6.

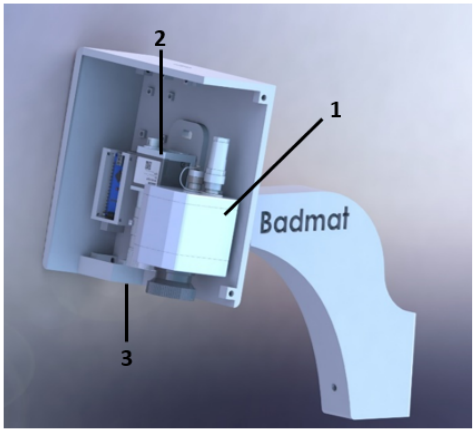

Figure 6: Computer aided design (CAD) model of the measuring part of Bath Mat device. The different components are (1) thermal camera, (2) RGB camera, and (3) white-light illumination.

The RGB camera is a Basler acA1920-25uc with a wide-angle lens (FUJINON HF6XA-5M).[54] The thermal camera is an Optris PI 450l, with a spectral range of 8-14 µm and thermal resolution of 0.04 K.[55] The distance between the mat and the lens of the cameras is 32 cm, with corresponding conversion factor of 1205 microns per pixel. During the clinical trial, the device was further developed. As a result, two different prototypes were used for clinical measurements. The first prototype had more movement freedom compared to the second prototype, resulting in different measurement angles.

The mat for the thermal footprint is 30×32×3cm and made of memory foam SG 50, made of polyurethane.[56] The mat sizes are based on a shoe size up to 45. The material was chosen by comparing different mats, which was done by M2-student J.A. Keurhorst.[26] Subsequently, the best thickness of memory foam for measurements was investigated, by M2-student F. Torrenga.[57] Furthermore, these students also determined several variables of the mat. For instance, it is stipulated that the minimum time to stand on the mat is 10 seconds, because then heat differences are most pronounced.[26] In order to use the same mat in several clinical trials it must be able to be sterilised between different subjects, so as not to transfer infections. Therefore, it was investigated whether the mat could be sterilised by using a cover. Six different covers were tested, but none proved usable due to appearance of artifacts in the thermal footprints, see figure 7.[57] Based on this study, it was decided to give each subject their own mat.

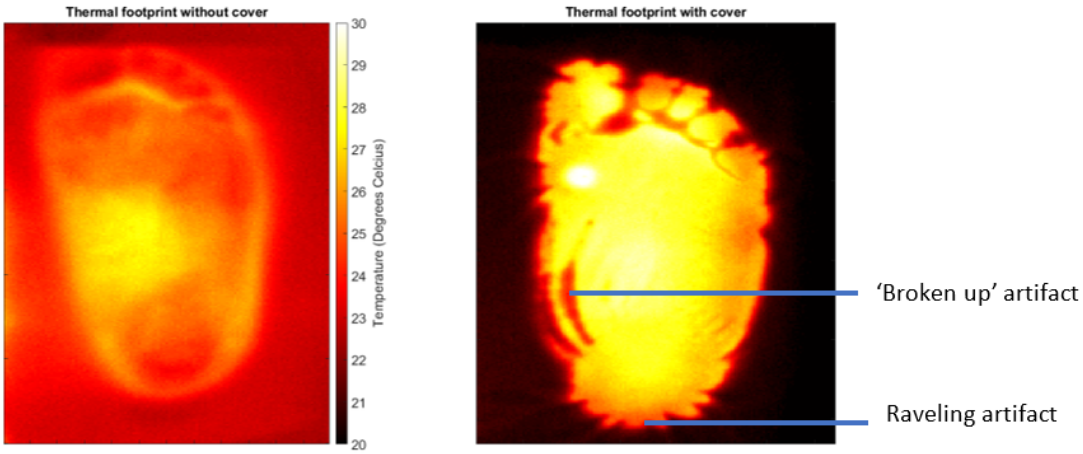

Figure 7: Two artifacts in thermal footprints by using covers for sterilization.[57] The left image is a thermal footprint without cover and the right image is a thermal footprint on 0.3mm silicone cover with anti-reflection coating. Both feet are from a healthy individual and have same temperature settings.

2.2 Measurement protocol

The protocol is the same for all measurements in this thesis, see figure 8. Each participant is asked to take off/remove shoes, socks, and bandages. Participants are then asked to sit down for 1-4 minutes, to normalise the temperature in the feet. After the rest period the participant places the legs horizontally on a treatment table, so a direct measurement of 10-20 seconds can be taken from the plantar side of the feet. Thereafter the participant is asked to stand on the Bath Mat for 10 seconds. After 10 seconds, the participant is asked to step off the mat. The footprint on the mat is measured for 40 seconds, to measure temperature change over time. Then the measurement on the mat is repeated one time, to ensure a successful measurement. All images are gathered using a MATLAB GUI (version R2022b), designed by dr. A. Chizari. The maximal frame rate is limited by the computer hardware and software capabilities.[58] A step-by-step protocol can be found in Appendix B.

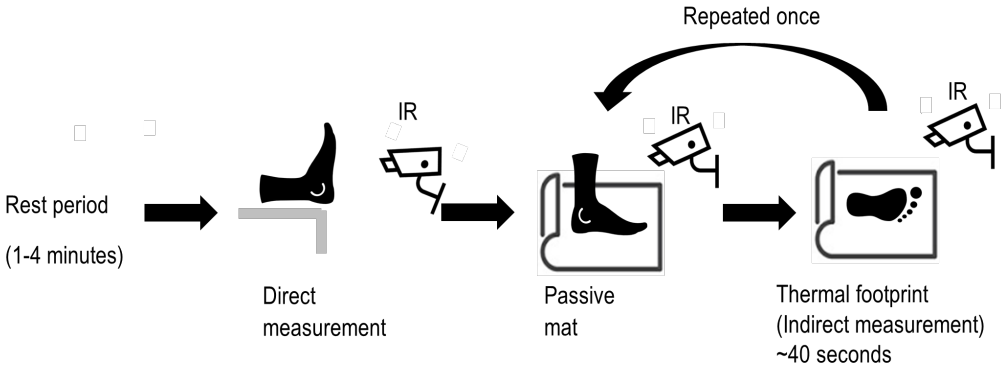

Figure 8: Schematic overview of the measurement protocol.

2.3 Postprocessing data

Different postprocessing steps are needed to collect the results. The different postprocessing steps are visualised in figure 9 and the MATLAB scripts can be found in Appendix C. In this thesis, three different types of images are distinguished: direct dorsal images, direct plantar images, and indirect plantar images (plantar footprints).
To compare feet at the same moment in time, individual frames are chosen for each subject according to a predetermined frame selection protocol. Each image type has a protocol for frame selection. For direct dorsal images, the image used is 10-20 frames before the first foot stepped off the mat. For direct plantar images, the 10th frame is used. For both direct images, if the feet were not in frame on the chosen frame according to this protocol, the author chose another frame that suited better. For plantar footprints, the first frame where the entire foot is off the mat was used, meaning it is a different frame for left and right foot.
Point registration was used to match different images, e.g., to match both feet. For point registration the MATLAB function *fitgeotform2d* with transformation type *affine* was used. This function matches different images based on four different landmarks present on each image. The four landmarks used are the edge of: hallux, heel, fifth toe and MTP1 joint. Deviation of these four landmarks by the author does not matter as there are just four landmarks needed.
Segmentation was done manually, using a pen tablet (One by WACOM[59]). These segmentations are used as masks in corresponding images, to obtain images and other results (e.g., mean foot temperature). Of each foot of each subject, one segmentation was obtained, due to time considerations. Furthermore, the same mask was used in all gathered images through matching.
To visually assess the same foot side, all thermal footprints are transformed to correspond to direct plantar feet images.

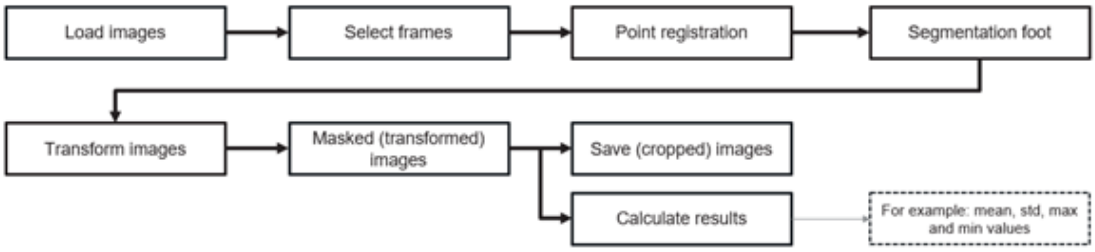

Figure 9: Flowchart of the postprocessing steps.

3 Clinical studies

3.1 Outline

To answer the research questions, the data is presented in different sections. Each section consists of a methodology, results, and discussion. An overview of the different sections with corresponding research questions:

- Section 3.2: Characteristics of the study population
- Section 3.3: Direct and indirect thermographic feet images
  - research questions 1 and 2a
- Section 3.4: Thermographic image features in different groups of subjects
  - research question 2
- Section 3.5: Reproducibility of thermographic images between days in healthy subjects
  - research question 3
- Section 3.6: Patient inputs about the Bath Mat device
  - research question 4

3.2 Charachteristics of the study population

3.2.1 Method

For this study 50 participants were recruited at the departments of internal medicine and vascular surgery in ZGT Almelo. All participants were older than 18 years and have given written informed consent. Participants were included in three different groups:

- Group 1 (n=15): Healthy subjects. A healthy subject is defined as a subject that is not suffering from DM and had no foot wound below the ankle.
- Group 2 (n=5): Subjects with DM and neuropathy, without a DFU in medical history.
- Group 3 (n=30): Subjects with DM and receiving treatment for a DFU.

General exclusion criteria include participants that (1) cannot stand independently, (2) have a wound larger than 3cm, (3) had an amputation in medical history of: hallux, forefoot, lower leg and/or upper leg, (4) strong suspicion of active Charcot foot. Furthermore, there is an additional exclusion criterium for group 3: wounds at both feet.

To compare groups, various medical data were collected from the electronic patient record in HiX by the author. General characteristics were collected from all groups, which include age, biological sex, BMI, and shoe size. Furthermore, for groups 2 and 3, diabetic type and vascular status were noted. Vascular status is mapped by three different variables: PTA in medical history, toe pressure and ankle-arm index (ABI-index). From group 3, the Texas score of the wound was noted. If there are multiple wounds at one foot, the highest Texas score was noted. All medical data mentioned were summarised in a table.

3.2.2 Results

Table 3 shows the characteristics of the different groups described in method. In the group diabetic patients with ulcer, it is noticeable that this group consists of more male subjects. In addition, figure 10 shows a schematic overview of all ulcer locations for each subject of group 3.

Table 3: Participant characteristics of different groups in study population

			Healthy subjects (n=15)	**Diabetic patients without ulcer (n=5)**	**Diabetic patients with ulcer (n=30)**
Biological sex	Men	Amount (%)	7 (46.7%)	1 (20%)	23 (76.7%)
	Women	Amount (%)	8 (53.3%)	4 (80%)	7 (23.3%)
Age		Mean in years (STD)	35.6 (10.5)	68.6 (8.0)	67.7 (8.9)
BMI		Mean (SD)	23.7 (3.8)	28.1 (4.9)	28.1(4.3)[1]
Shoe size		Mean (SD)	41.5 (2.6)	41.1 (1.6)	43.6 (2.4)[3]
Diabetic Type	Type 1	Amount (%)		3 (60%)	2 (6.7%)
	Type 2	Amount (%)		2 (40%)	28 (93.3%)
Texas score (wound)	UT1A	Amount			19[6]
	UT1B	Amount			2
	UT1C	Amount			2
	UT2A	Amount			2
	UT2B	Amount			1
	UT3A	Amount			2
	UT3B	Amount			2
PTA in medical	Yes	Amount			9[1]
	No	Amount			20
history **Toe pressure**	Left	Mean in mmHg (STD)		93.5 (13.4)[3]	98.5 (36.5)[2]
		Range		84-103	27–161
	Right	Mean in mmHg (STD)		112 (39.6)[3]	97.0 (41.5)
		Range		84-140	40–195
ABI-index	Left	Mean (STD)		1.25 (0)[2,4]	0.97 (0.28)[2,4]
		Range		-	0.43–1.32
	Right	Mean (STD)		1.25 (0.15)[2,4]	1.03 (0.42)[2,5]
		Range		1.14-1.35	0.55–2.23

[1]Data missing of one subject [2]Data missing of two subjects [3]Data missing of three subjects
[4]Not measurable for one subject [5]Not measurable for two subjects
[6]One subject had a spot for which there were doubts whether it was a wound or not (spot was treated as a wound), and eventually described as complete epithelium

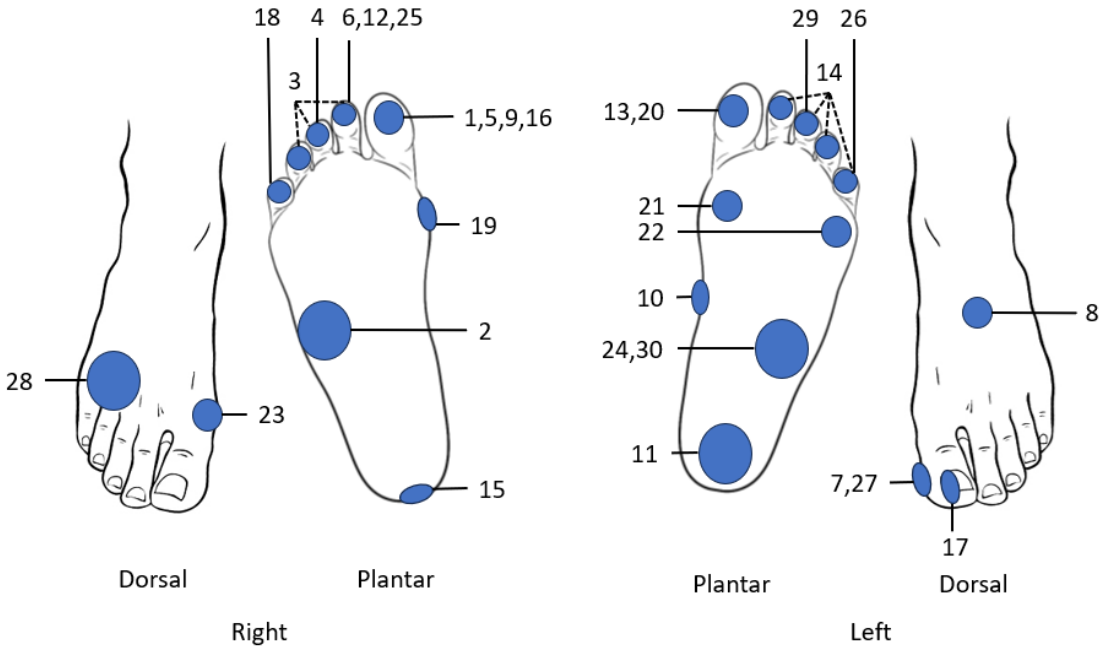

Figure 10: ulcer locations on plantar and dorsal foot of group 3. Each number represent a subject from group 3. On the two left images the right foot is shown and on two right images the left foot is shown.[60, 61]

3.2.3 Discussion

The results show characteristics of the different included groups. Between groups differences can be noted. For instance, mean age and BMI are lower in group 1 in comparison to groups 2 and 3. The shoe size is smaller in groups 1 and 2, which is probably due to the male/female ratio in group 3. Lastly, it should be noted that toe pressure and ABI index were only available for 2 subjects in group 2, because these measurements are not regular in the clinical workflow for this group of patients.

3.3 Direct- and indirect plantar thermographic feet images

3.3.1 Method

3.3.1.1 Study population

In this study data from all subjects in the study population was used, as described in section 3.2.

3.3.1.2 Data analysis

In this section, the direct and indirect plantar thermographic images were compared for three different groups of participants: (1) healthy subjects, (2) diabetic patients without foot ulcer, and (3) diabetic patients with ulcer. The thermographic images of all groups were visually examined by the author for similarities in temperature distribution in the feet. For the healthy subjects, four thermographic left foot images were randomly selected for visual examination. The amount of four images was chosen due to time considerations. The random selection was chosen due to time limitation and to reduce bias from the author. For the diabetic patients with an ulcer the author selected different ulcers at different locations of the plantar and dorsal foot side. From every selected ulcer, three different images are shown, namely the: (1) RGB image, (2) direct thermal image, and (3) thermal footprints. For the RGB image, the image with the best visible ulcer was selected by the author. Furthermore, manual segmentations of both direct and indirect feet images were made.[58] With the use of this segmentation, the mean plantar foot temperature was determined.

3.3.1.3 Statistical analysis

In this section possible differences in mean temperature of the plantar foot in the same foot between direct and indirect feet images were examined. To visualise the difference, a scatterplot for each group is created plotting direct and indirect mean plantar foot temperature. For the different groups, different distinctions were made. The distinction for the healthy- and DM without wound subjects were between left and right foot, while for the DM with wound the distinction was between feet with- and without a wound. Furthermore, it was investigated whether differences in mean plantar foot temperature between direct- and indirect measurements were significant by a paired t-test with a 95% confidence interval. This analysis was done using MATLAB and IBM SPSS Statistics version 28.0.1.0.

3.3.2 Results

3.3.2.1 Healthy subjects

Figures 11 shows four direct and indirect measurements of healthy subjects at the same day. It illustrates that the temperature distribution for direct and indirect measurements is similar, but the indirect temperature is lower. It is also noticeable that the medial side of the midfoot is warmer in all subjects, in comparison with surrounding area. Furthermore, in all patients the toes appear to be colder than other parts of the foot. Additional results can be found in Appendix D.

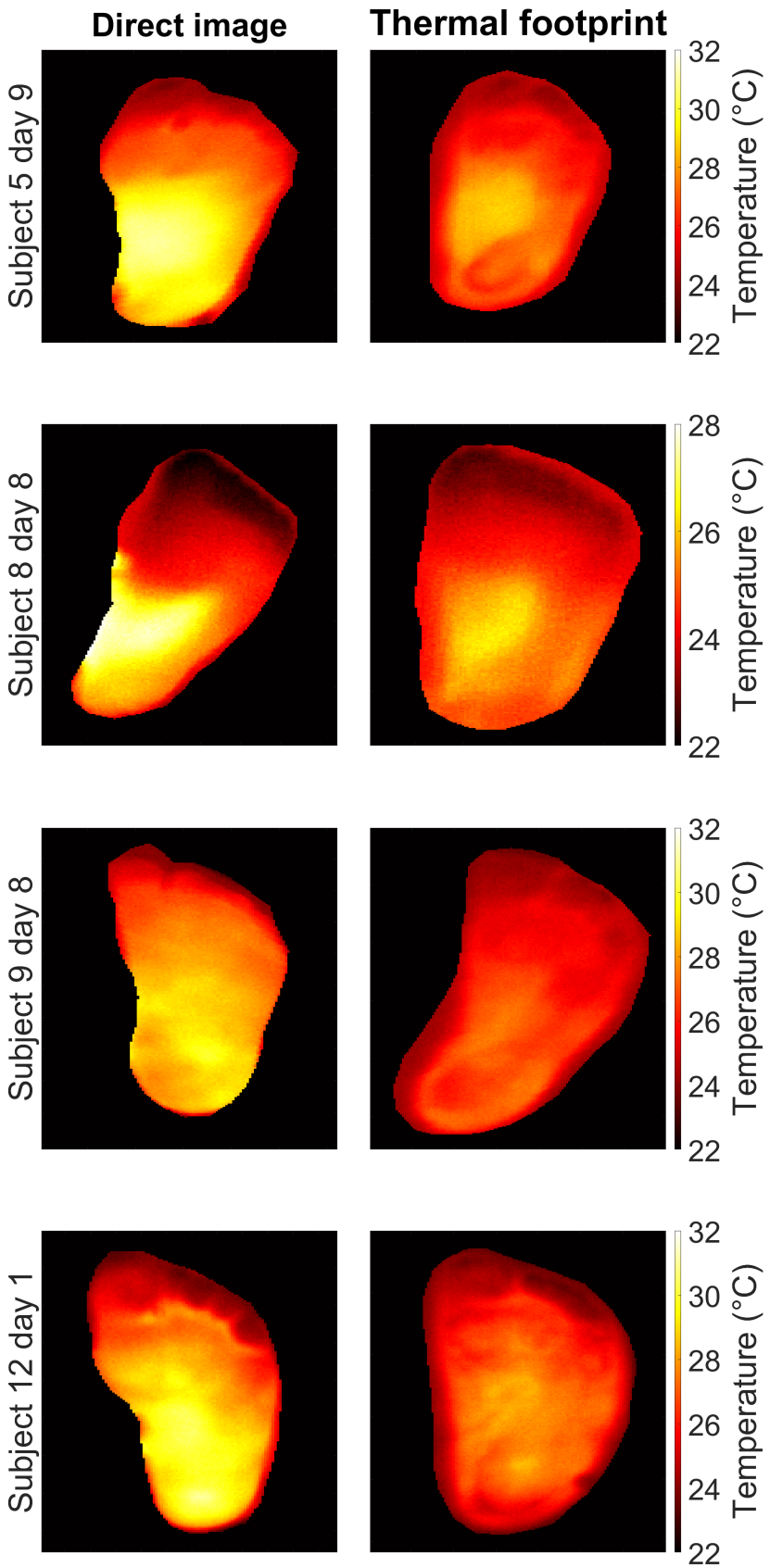

Figure 11: Four randomly selected thermal maps of the left foot of healthy subjects. The time between images is respectively: 96, 137, 81, and 120 seconds.

Figure 12 shows all 147 measurements of the healthy subjects of group 1. It is shown that most thermal footprints have a lowerr mean foot temperature than in direct plantar images. The ideal trendline (black line) shows the 1-to-1 comparison between direct plantar images and thermal footprints. The correlation coefficient of left foot is 0.812 and of the right foot is 0.761. The average difference between direct plantar images and thermal footprints is 1.64°C for the left foot and 1.65°C for the right foot. The paired-t test is $p < 0.01$ between direct images and thermal footprints for both feet.

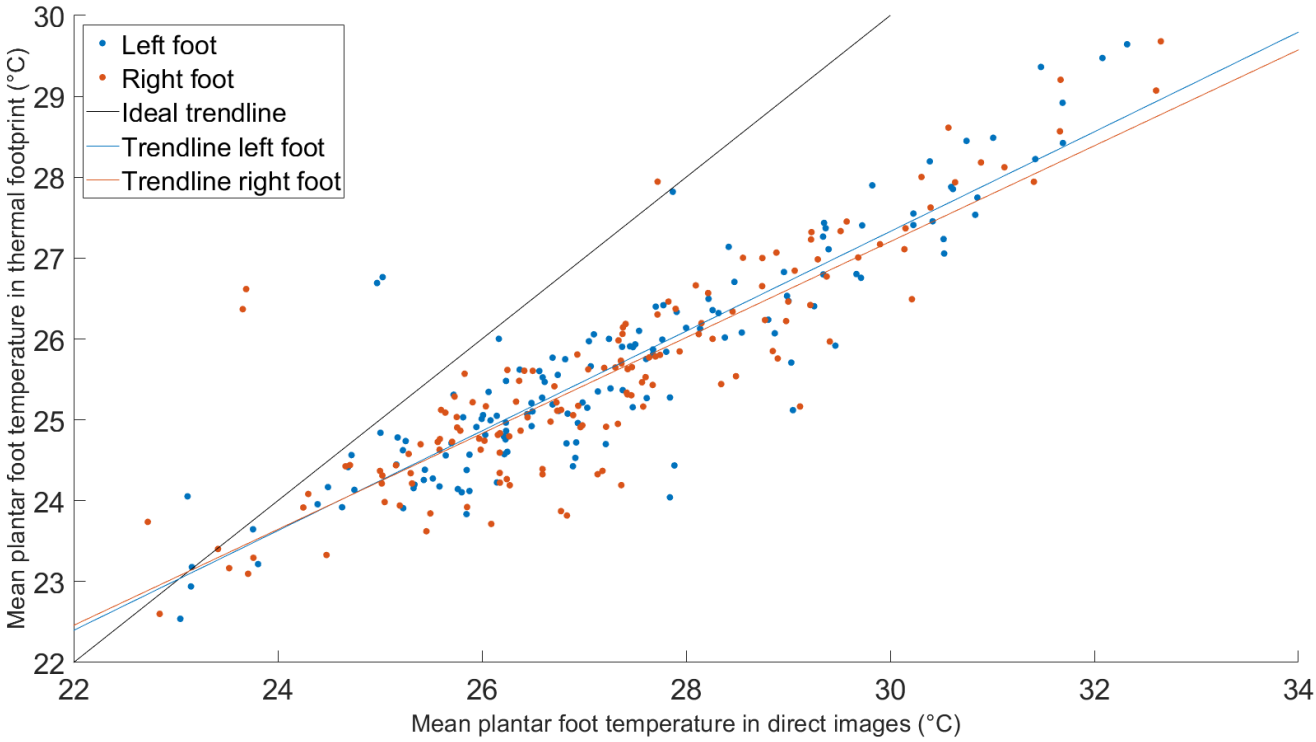

Figure 12: Scatterplot with overview of the mean plantar foot temperature between direct images (x-axis) and thermal footprints (y-axis) in healthy subjects (group 1). Blue points are left foot measurements and orange points are right foot measurements.

3.3.2.2 Diabetic patients without foot ulcer

Figure 13 shows five direct and indirect images in subjects with diabetes without a wound at the same day. The temperature distribution for direct plantar images and thermal footprints are similar, but the temperature is lower in thermal footprints. Furthermore, in patient 1, 3-5 the toes appear to be colder than other parts of the foot. The scatterplot with an overview between direct images and thermal footprints can be found in Appendix D.1.

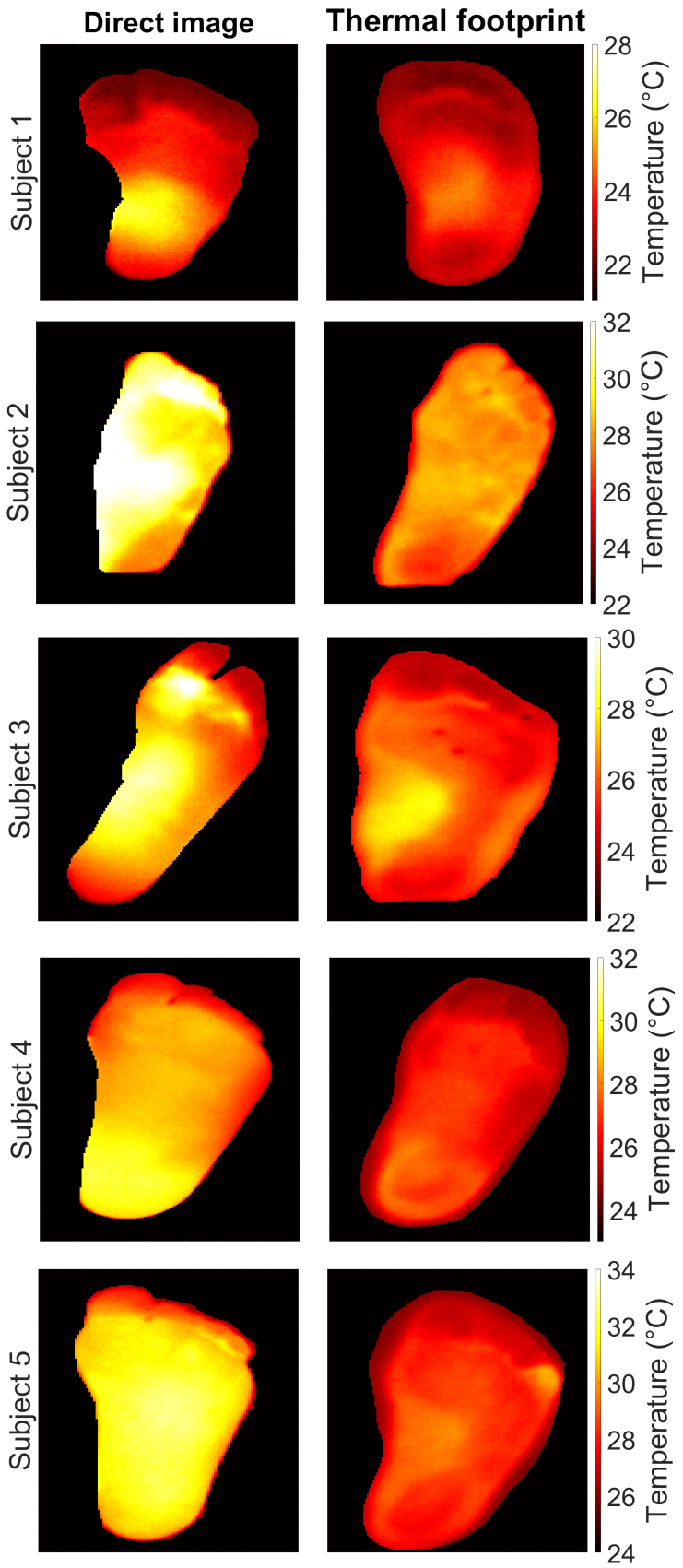

Figure 13: Five direct- and footprint images of the left plantar foot of diabetic subjects without a wound. The time between images is respectively: 96, 134, 152, 99 and 88 seconds.

3.3.2.3 Diabetic patients with foot ulcer

In figures 14 and 16 images of feet with and without diabetic foot ulcers are shown. The ulcers are in different areas of the foot. Most of the subjects have a hotspot on the ulcer side, while subjects 8 and 14 seem to have a coldspot. In figure 16, in patient 24 (d) a square is shown at the wound site, which is caused by a thin sterile gauze.

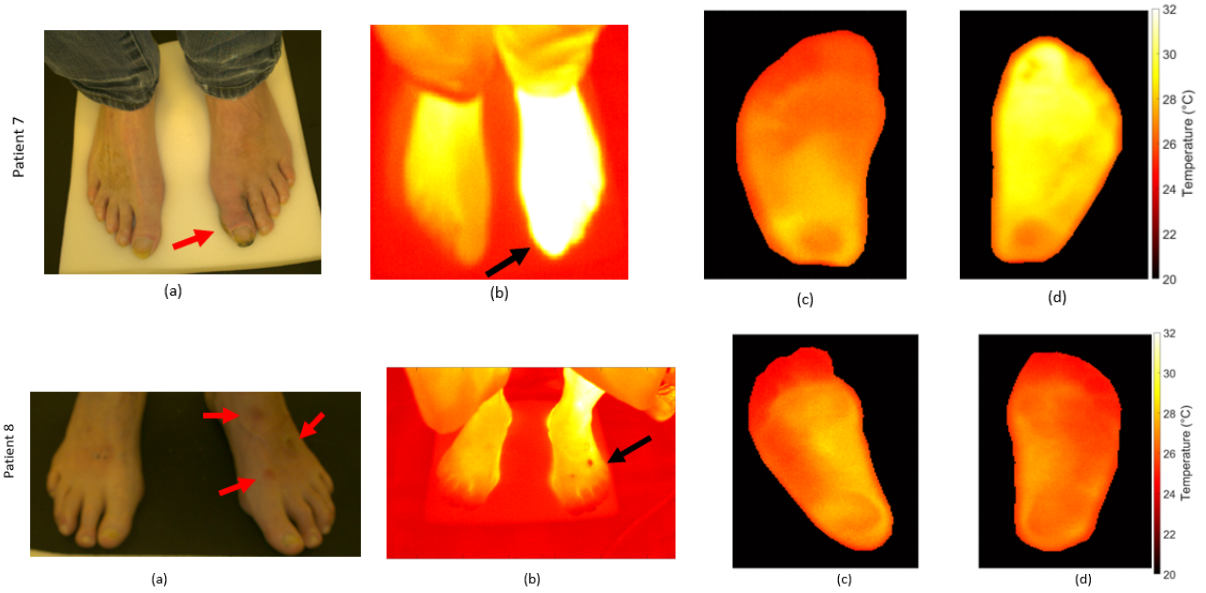

Figure 14: Diabetic foot ulcers at the dorsal foot side. For every patient four different images are available: (a) direct RGB images, (b) direct thermographic images, (c) thermal footprint of the right foot, and (d) thermal footprint of the left foot. The red/black arrows show the ulcer(s) on the images.

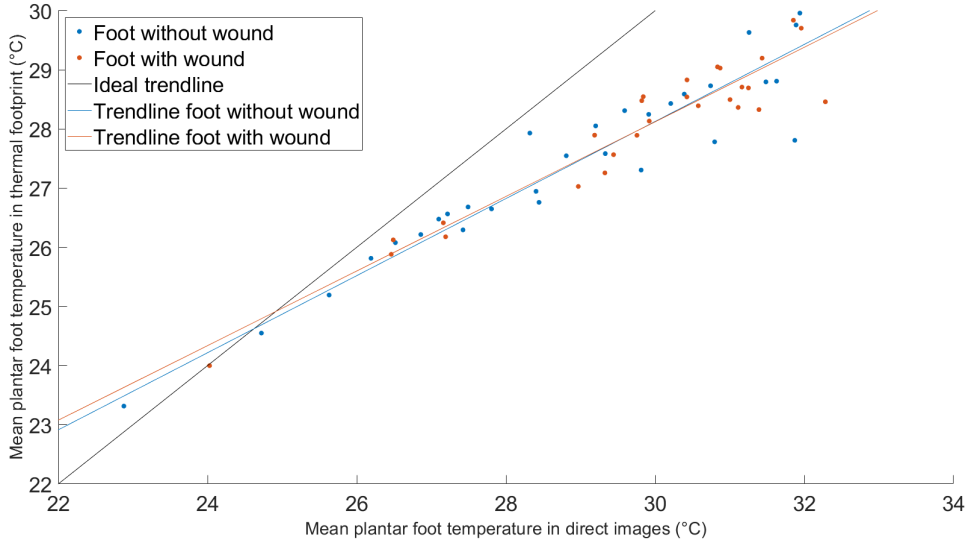

Figure 15: Scatterplot with overview of the mean plantar foot temperature between direct images (x-axis) and thermal footprints (y-axis) insubjects with diabetes and DFU (group 3). Blue points are foot without wound measurements and orange points are foot with wound measurements.

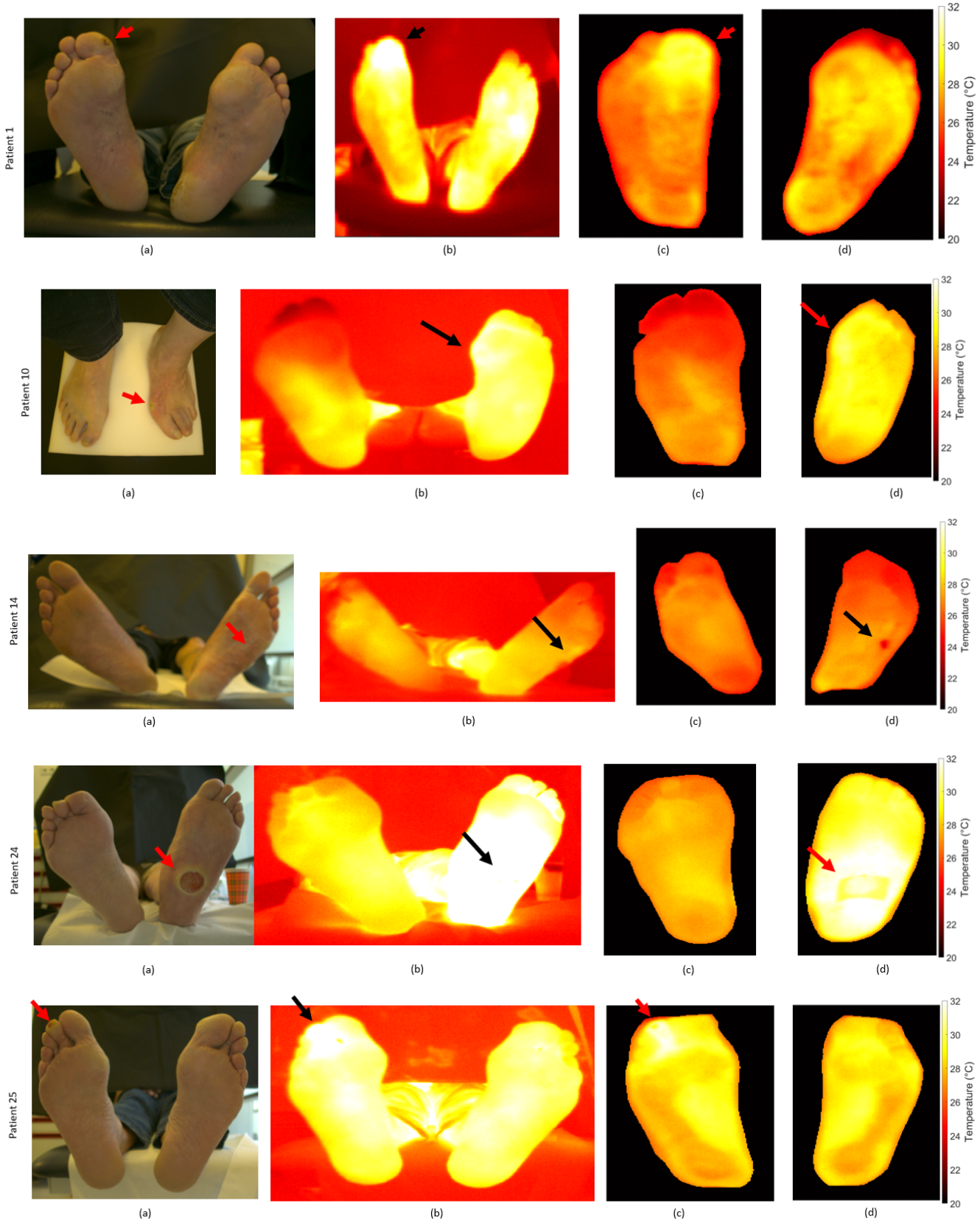

Figure 16: Diabetic foot ulcers at the plantar and medial foot side. For every patient four different images are available: (a) direct RGB images, (b) direct thermographic images, (c) thermal footprint of the right foot, and (d) thermal footprint of the left foot. The red/black arrows show the ulcer(s) on the images.

Figure 15 shows all measurements of group 3, distinguishing between feet with and without a wound. Most thermal footprints have a lower mean foot temperature than direct images. The ideal trendline (black line) shows the 1-to-1 comparison between direct plantar images and thermal footprints. The correlation coefficient of foot with wound is 0.926 and of the foot without wound is 0.903. The average difference between direct- and indirect measurements is 1.91°C for the foot with wound and 1.44°C for the foot without wound. The paired-t test is $p < 0.01$ between direct images and thermal footprints for both feet.

3.3.3 Discussion

In this section the relation between direct plantar image and thermal footprint was examined in different groups of subjects. For healthy subjects and diabetic subjects without a wound, similarities in temperature distribution are visible between direct plantar images and thermal footprints. Within the temperature distribution of healthy subjects, two foot areas are remarkable, namely the medial side of the midfoot and the toes. The medial side of the midfoot has a higher temperature compared to the rest of the foot, in other studies called the butterfly pattern.[50, 62] This is probably because the medial side of the midfoot has a thinner skin layer with less callus[63] compared to other foot areas, allowing more transmission of IR energy. Another possible explanation is that the medial side of the midfoot has a lower pressure load compared to other areas of the foot. The toes are often colder compared to other foot areas and background, which is consistent with findings in other articles.[64, 65] Furthermore, it is important to note that the measured temperature significantly differs between both images. In figure 12, thermal footprints are on average 1.65°C lower than direct plantar images. The temperature in thermal footprints is probably lower for the following reasons: the footprints have a bigger foot area compared to the direct images because medial and lateral foot side are also measured, and/or the stand time on the mat is too short to transfer the foot temperature to the mat.

In figure 13, the direct plantar measurement of subject 2 is remarkable. This subject was unable to hold the legs wider apart due to leg pain, making it difficult to distinguish left and right feet during manual segmentation. It is also notable that the butterfly pattern in images of diabetic patients is less visible compared with images of healthy subjects, due to the presence of neuropathy in the diabetic patients.[43, 66]

In figures 16 and 14, a change in temperature distribution is shown at the ulcer location. This change is visible at both direct and indirect images. Most of the subjects have a hotspot on the ulcer side, but patient 14 in figure 16 and patient 8 in figure 14 show a colder spot. This cold spot is probably caused by body fluids, such as wound fluid or blood, from the open wound. This fluid interferes with temperature transfer, causing less heat to transfer to the mat. Since the Bath Mat will be used as a prevention tool, it is expected that no open wounds will be detected, so no colder spots. In addition, several notable issues should be mentioned of figures 16 and 14. First, not all images are in focus, which is due to focus errors during measurement. The focus errors were caused by lens rotations during (dis-)mounting the system between measurements. Second, in figure 16 in images d of patient 24, a square can be observed around the wound. This is because the participating patient did not want to participate if his wound was not covered. Therefore, the choice was made to cover the ulcer with thin sterile gauze. This resulted in the observed square. Third, in figure 14 in image a of patient 8, it is visible that the

patient has not yet taken place on the mat. This patient was measured fully handheld because the system had broken down before the measurement.

In conclusion, this section shows that direct and indirect thermal foot images have a similar temperature distribution in different groups of subjects. However, the butterfly pattern is less visible in thermal feet images of diabetic patients. Furthermore, in diabetic subjects with an ulcer, the temperature distribution is disrupted. Lastly, the mean foot temperature in thermal footprints is lower than the mean foot temperature of direct images.

3.4 Thermographic image features in different groups of subjects

Based on the findings in the previous section, follow-up research was conducted to investigate whether features could be used to identity subjects with and without wounds. Due to time consideration, only images obtained using the Bath Mat method, e.g. direct dorsal images and thermal footprints, were used to investigate two features.

3.4.1 Method

3.4.1.1 Study population

In this study data from all subjects in the study population was used, as described in section 3.2.

3.4.1.2 Data analysis

The following features were investigated and compared for the three different groups of subjects:

1. *Left-right difference in mean foot temperature of plantar and dorsal side*
   The mean temperature of both dorsal- and plantar foot side were determined, as the Bath Mat method images both sides. Next, the difference in mean foot temperature between two feet was determined, see equation 2.

$$\Delta Temp = \overline{T_{right}} - \overline{T_{left}} \tag{2}$$

   In equation 2, the ($\Delta Temp$) is calculated using variables mean foot temperature right ($\overline{T_{right}}$) and left ($\overline{T_{left}}$) In addition, a normalised temperature difference in percentage (ΔT_{norm}) is calculated, see equation 3.

$$\Delta T_{norm} = 100\frac{\overline{T_{right}} - \overline{T_{left}}}{\overline{T_{left}}} \tag{3}$$

   In equation 3, the (ΔT_{norm}) is calculated using variables mean foot temperature right ($\overline{T_{right}}$) and left ($\overline{T_{left}}$). The differences in mean foot temperature will be displayed for each subject in a table. For the healthy subjects, the left-right difference is the mean difference in mean foot temperature off all measurements.

2. *Left-right difference in contralateral spots*
   To display contralateral left-right difference, left- and right foot were manually matched by point registration. This matching allows all contralateral differences at pixel level to be mapped. By doing so, we expect to better distinguish patients with- and without DFUs. For subjects without a wound, the left foot is used as reference. For subjects with a wound, the foot without wound is used as reference. To investigate differences in contralateral spots, different images could be displayed. All percentages per group were summarised in bar graphs. In addition, a cut-off value was determined for the percentage of suspected pixels with a value >2.2°C, by choosing the highest maxima of suspected pixels with a value >2.2°C from healthy subjects.

3.4.1.3 Statistical analysis

This study examined whether there are differences between groups of subjects for various features. To visualise differences in mean foot temperatures between groups, boxplots were made. In addition, it was investigated whether differences between group 1 and 3 were significant by an unpaired student t-test with 95% confidence interval. Group 2 is not included in the statistical analysis due to limited group size.

3.4.2 Results

3.4.2.1 Mean foot temperature plantar

Additional data obtained from the measurements can be found in Appendix E. Figure 17 visualises data from appendix E.1 by group. It shows that the median in temperature difference of the mean plantar temperature in group 1 is around 0°C for both image types. For group 3 the median in temperature difference of mean plantar foot temperature is above 1°C. Between groups 1 and 3 an unpaired t-test gives $p<0.001$ for thermal footprints. A negative number in this figure for the healthy subjects and diabetic subjects without wound means that the left foot is warmer than the right foot.

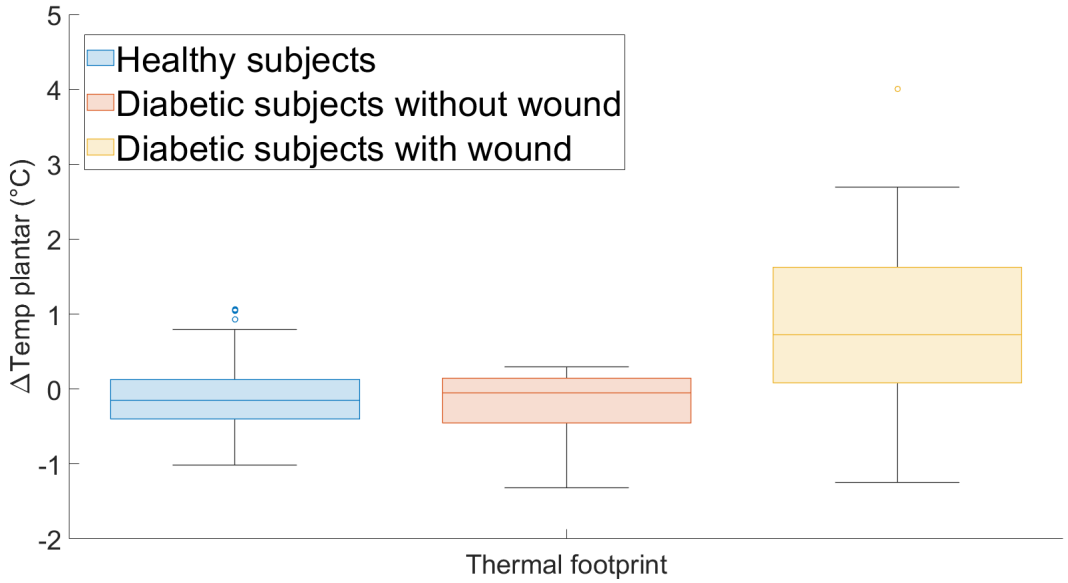

Figure 17: Boxplot showing difference in mean plantar foot temperature between groups of subjects.

3.4.2.2 Mean foot temperature dorsal

Figure 18 visualises data from appendix E.2 by group. It shows that the median in temperature difference of the mean dorsal temperature in group 1 is around 0°C for direct images. For group 3 the median in temperature difference of mean plantar foot temperature is around 1°C. Between group 1 and 3 an unpaired t-test gives $p<0.001$ for direct images.

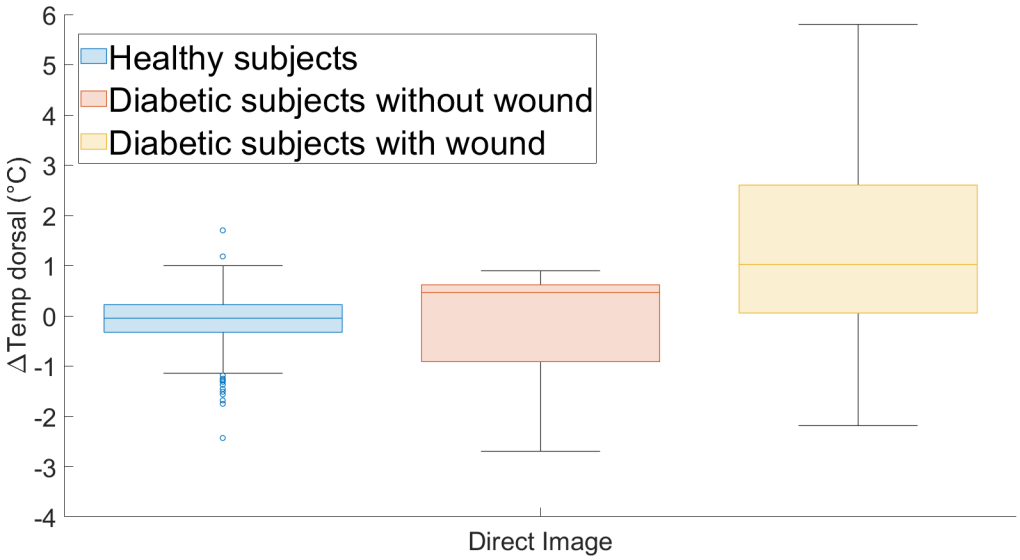

Figure 18: Boxplot showing difference in mean dorsal foot temperature between groups of subjects.

3.4.2.3 Temperature difference in contralateral spots

Figure 19 shows a visual representation of matched feet with deviated pixels, of a subject with diabetes and an ulcer. For all measurements, the percentage of the three different types of pixels are determined.

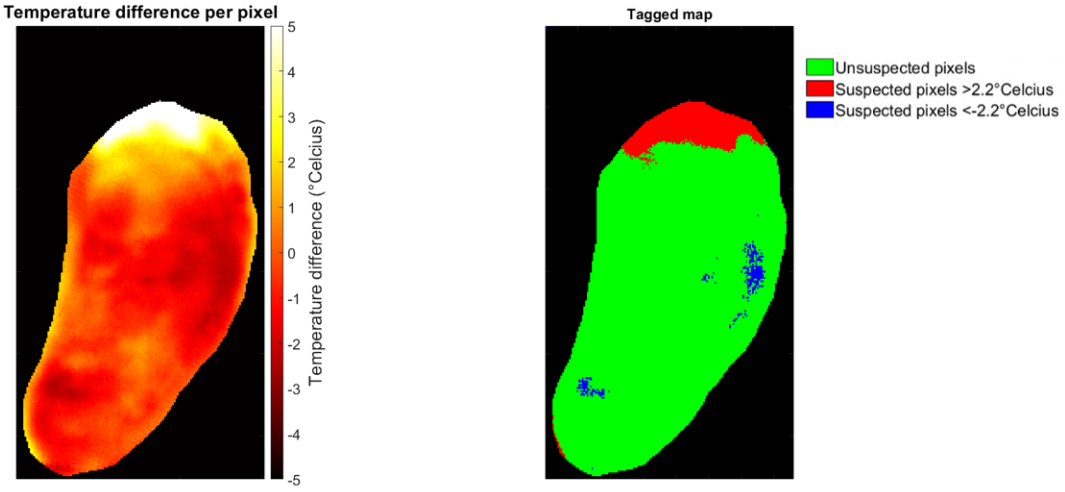

Figure 19: Visual example of how the deviated pixels are tagged. The left image shows the difference at pixel level in °C and the right image shows the tags assigned to each pixel.

Figure 20 shows bar graphs of all measurements of healthy subjects, sorted by subject. Eight measurements have a percentage >5% of suspected pixels above 2.2°C. These eight measurements are visually represented and discussed in appendix E.3.1. With the information in appendix E.3.1, the author has omitted the eight measurements for determining the cut-off value. The cut-off value chosen for the percentage of pixels >2.2°C is 3.3%. Furthermore, it is noticeable that subjects 1, 12 and 13 have a constant percentage of suspected pixels <-2.2°C per day. The bar graphs of the subjects with diabetes without an ulcer can be found in Appendix E.3.2.

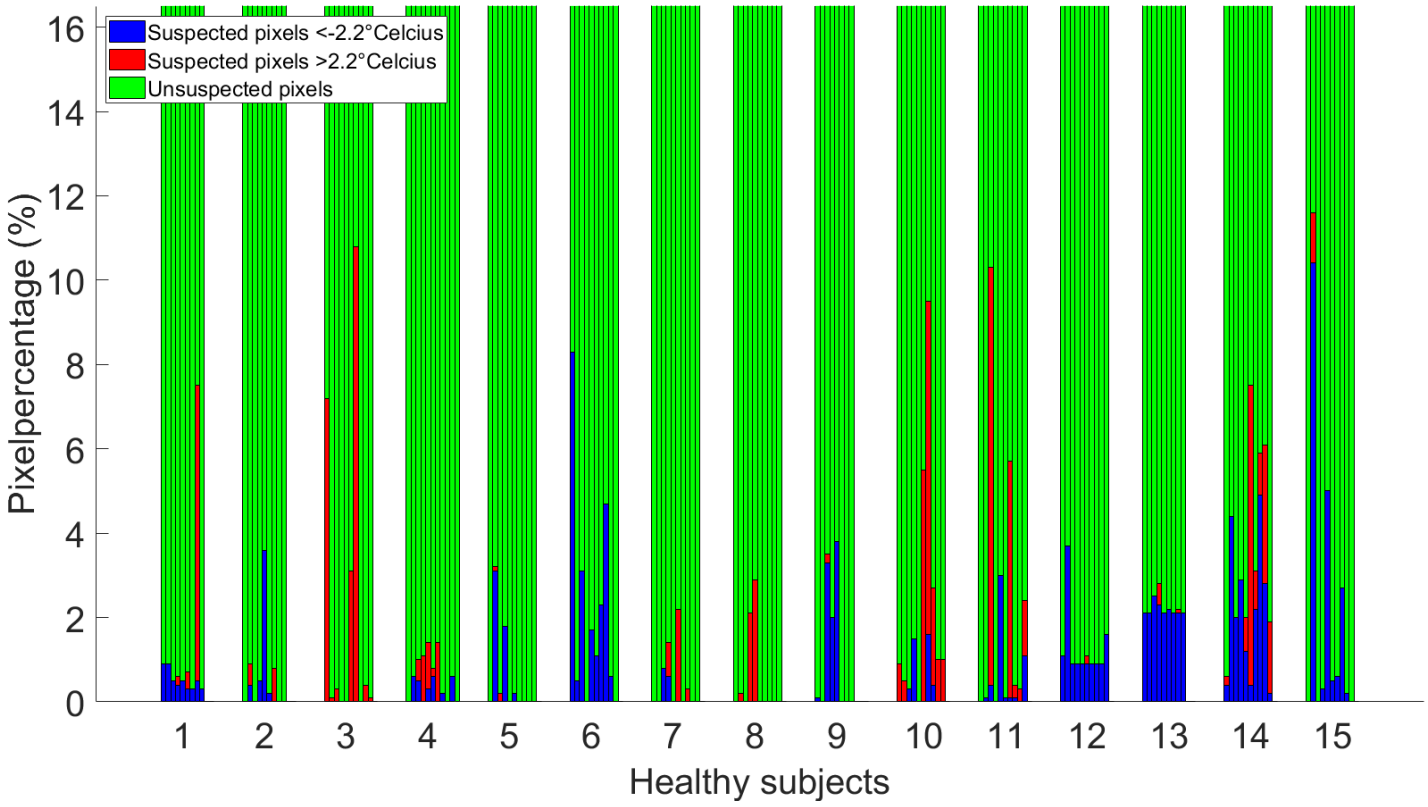

Figure 20: Bar graph with percentages unsuspected and suspected pixels of indirect measurements of plantar foot side in healthy subjects. Every bar represents a measurement. Note the adjusted y-axis. This figure was inspired by a MATLAB script of E. Bolling (2011).[67]

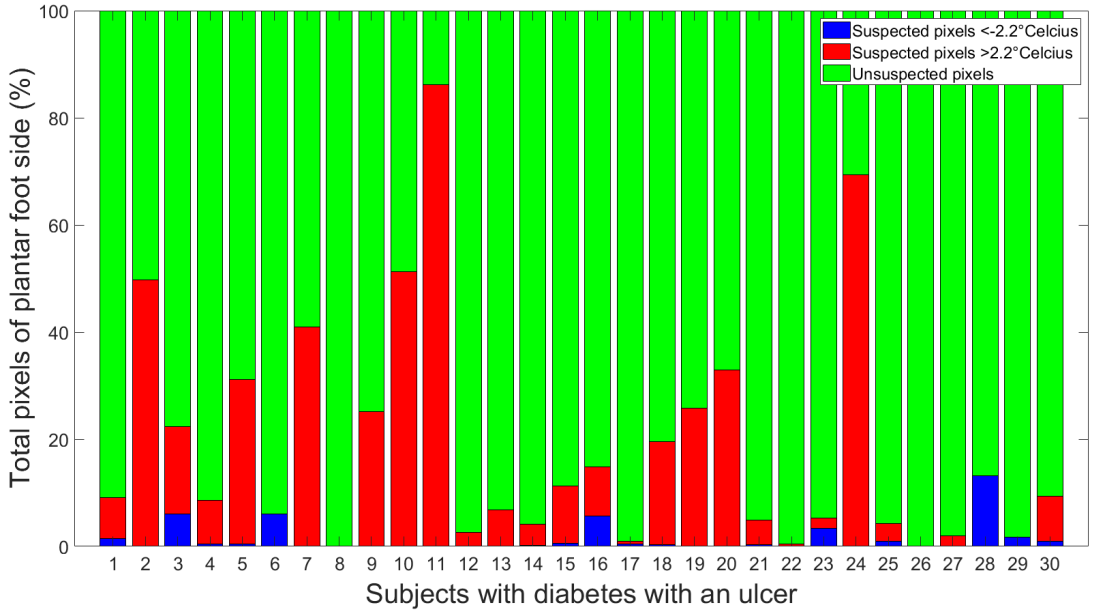

Figure 21: Bar graph with percentages unsuspected and suspected pixels of indirect measurements of plantar foot side in diabetic subjects with ulcer.

Figure 21 shows bar graphs of all measurements of subjects with diabetes and an ulcer. Of all these subjects, ten persons have a percentage below 3.3% for pixels >2.2°C. Figures of different subjects with diabetes and an ulcer are shown in Appendix E.3.3.

3.4.3 Discussion

In this section, several features were examined if they could be used to identify subjects with and without wounds. The use of mean foot temperatures between groups 1 and 3 has proved to be unable to make sufficient distinctions. A limitation of this feature is that small wounds do not stand out, as their temperature difference is not influencing the mean foot temperature enough. This is reflected in the results, as the boxplots between group 1 and 3 overlap.

Furthermore, this section investigated temperature differences at pixel level. Using the measurements of healthy subjects, the cut-off value of 3.3% of suspected pixels >2.2°C was determined. With this percentage, ten subjects with an ulcer were considered healthy. These subjects were: 6, 8, 12, 17, 22, 23, 26, 27, 28 and 29. These ten patients have been identified as 'healthy' for four different reasons. The first reason is that the ulcers of subjects 8, 17, 23 and 28 were located at the dorsal side, which were not visible at the plantar side. The second reason is that ulcers occur on ischemic foot sides in subjects 12, 26, 27 and 29. Due to ischaemia, less blood enters the foot, which disrupts wound healing and inflammation, causing less temperature change. The third reason is the ulcers of subjects 6 and 27 were covered by wet bandages just before the measurement. This fluid interferes with temperature transfer, causing less heat to transfer to the mat. The fourth reason is that the ulcer of subject 22 was measured during a check-up after an amputation. This ulcer was not caused over a longer period with pressure, but by trauma.

With all these side notes, it seems that temperature difference at contralateral spots on the plantar foot side could potentially be used as a predictor for the occurrence of ulcers. Currently the feature can only be used if it is known which foot has an ulcer. Also, the location of these pixels does not match the ulcer in all cases, see Appendix C.

3.5 Reproducibility of thermographic images between days in healthy subjects

3.5.1 Method

3.5.1.1 Study population

In this study data from healthy subjects (group 1) in the study population was used, as described in section 3.2.

3.5.1.2 Study protocol

For this group the general study protocol is repeated eight to eleven times on eight to eleven different calendar days within approximately four weeks. Subjects were measured at the beginning of a workday before they start working. Furthermore, subjects were asked to use the same transport to work and to indicate if they deviated from the normal pattern.

3.5.1.3 Data analysis

A mean foot temperature of the thermal footprints was determined for all subjects. From one healthy subject, all left foot segmentations are shown. In addition, a boxplot was made, to examine differences in mean temperature and temperature range between subjects. Furthermore, a standard deviation (SD) map (in °C) was determined for each subject in group 1. This map shows the SD per pixel, which is determined by comparing the segmentations of eight to eleven days. This map was used to investigate if different foot areas have equivalent SD.

3.5.1.4 Statistical analysis

This study examined if there were differences between days in mean foot temperature in thermal footprints of the same foot. It was investigated whether differences in mean foot temperature between left and right foot were significant by paired t-test with 95% confidence interval.

3.5.2 Results

Figure 22 shows a segmentation series of thermal footprints of the same foot at different days of a healthy subject. The amount of background in the image changes each day. Additional information from the measurements of healthy subjects can be found in Appendix F.

Figure 23 shows the range of mean plantar foot temperature in thermal footprints between days in healthy subjects. It shows that the range in which the mean temperature deviated corresponds between feet. The paired-test between left and right foot for subjects 1-14 were p-values between 0.10 and 0.98, while the p-value of subject 15 was 0.02. In addition, subject 15 shows the largest difference in mean plantar temperature between left and right foot. The temperature range and the extent of deviation differs between subjects.

Figure 24 shows the standard deviation maps of all left feet of healthy subjects. It is visible that STD varies in magnitude in different areas. For example, the STD is greater in the toes and lateral arch in comparison to the medial arch of the foot.

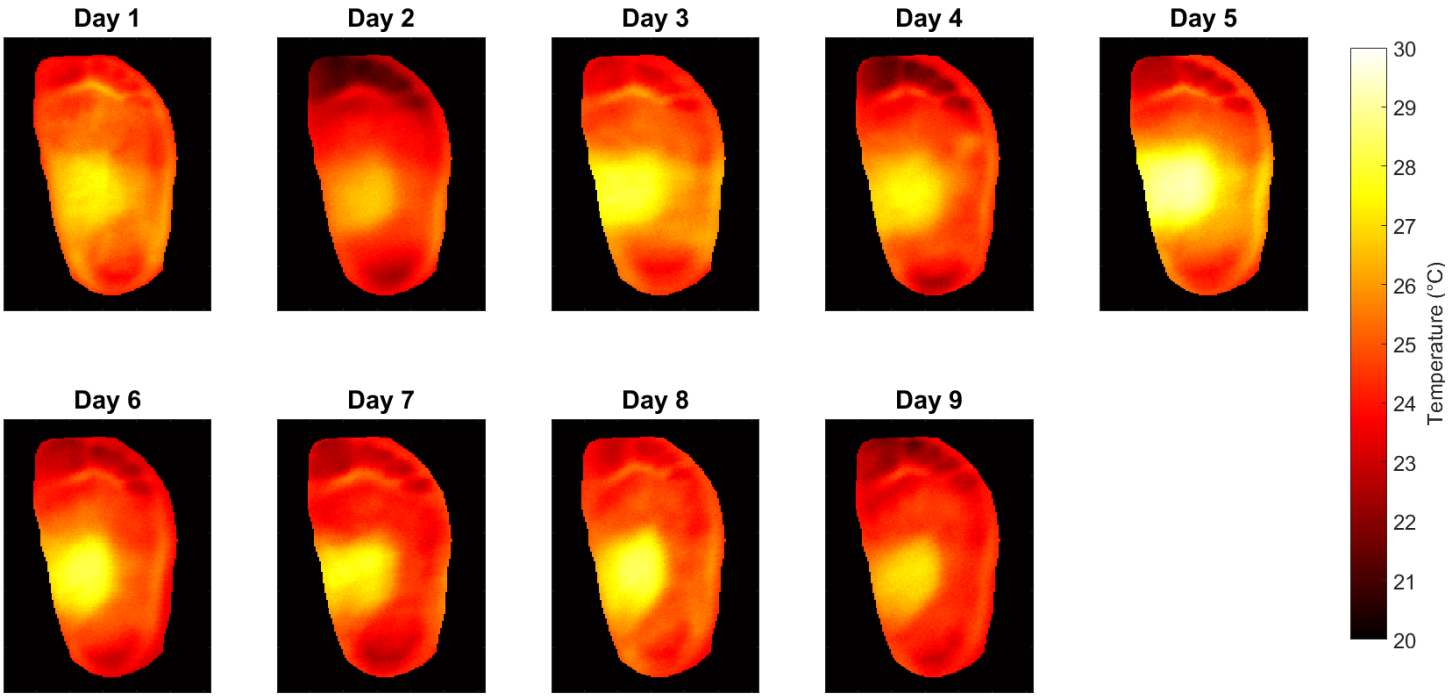

Figure 22: Series of thermal footprints of the same left foot from healthy subject number 2. All thermal footprints were made on a different work day

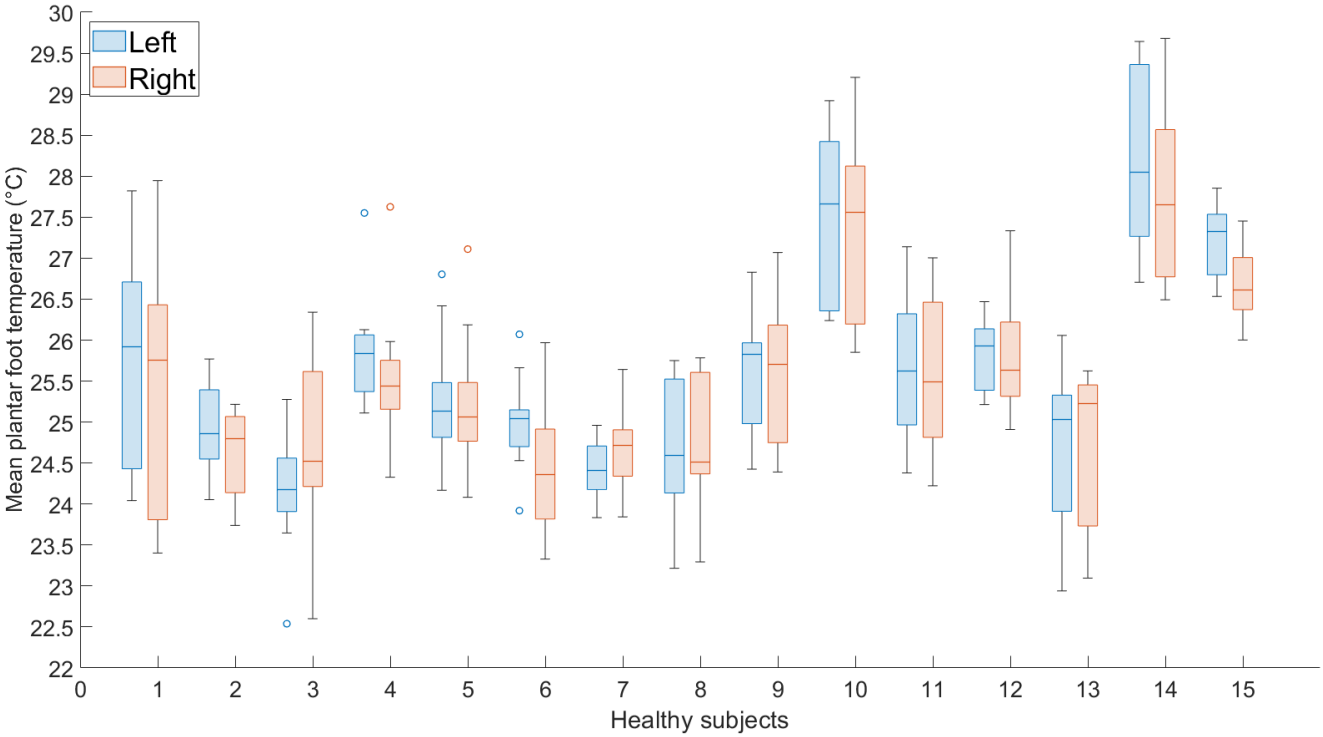

Figure 23: Mean plantar foot temperature in feet at thermal footprints of healthy subjects.

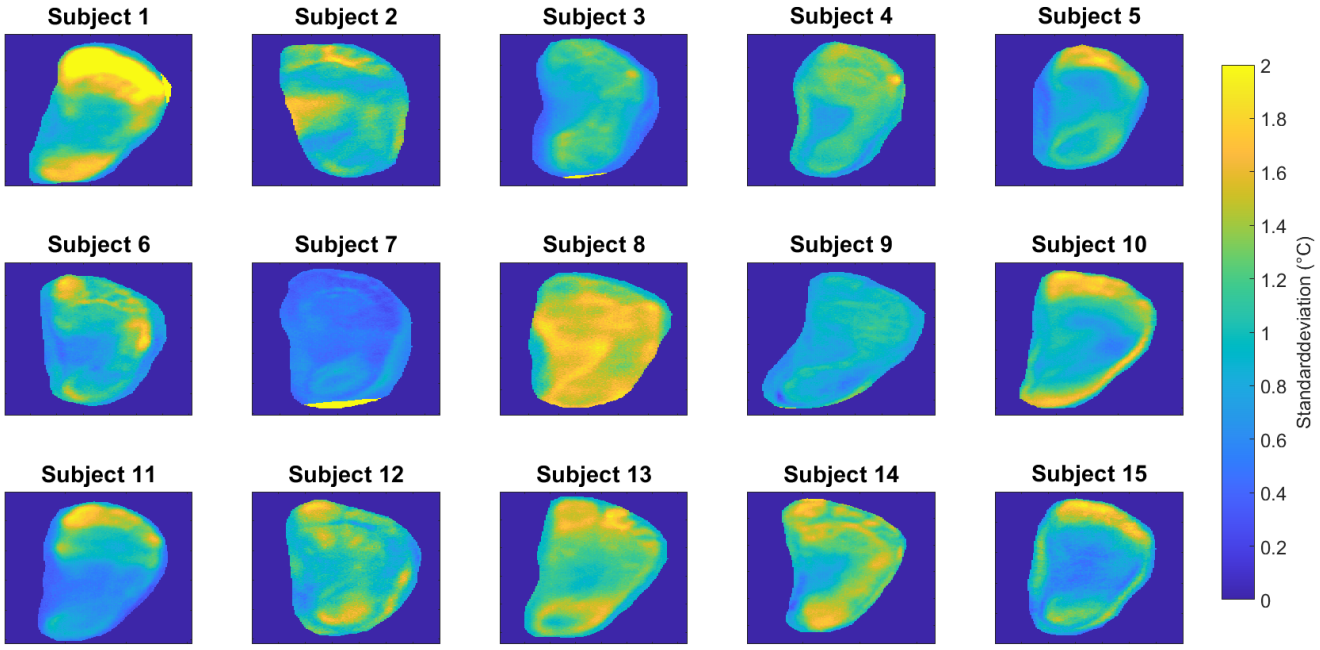

Figure 24: Standard deviation map of the left foot thermal footprints of each healthy subject. Each map is calculated based on 8-11 days, depending on the number of measurements.

3.5.3 Discussion

This section shows that for healthy subjects, different foot areas show different degrees of variation. For example, the toes and lateral arch have a larger standard deviation compared to the medial arch. This is probably because these areas have a higher pressure load in comparison to the medial arch.[63] In figure 23, all healthy subjects show a different temperature range for mean plantar foot temperature in thermal footprints. This indicates that one deviating mean temperature does not signify an ulcer is developing.[43] Follow-up studies should investigate how much temperature deviation is accepted to be 'healthy' and what temperature deviations are suspicious. In addition, the varying temperature range between subjects could indicate that the Bath Mat method needs a calibration period to determine 'normal' values for the user. Te temperature range in subject 15 is remarkable, for no particular reason. Subject 15 was the oldest individual in the group of healthy subjects.

3.6 Patient inputs about the Bath Mat device

After a measurement, a subject with diabetes was asked different questions, which can be found in Appendix G. This was a non-validated and structured questionnaire but gives insight into how participants of groups 2 and 3 thought about the method. The questionnaire was completed: fully seventeen times, partly thirteen times, and five times it was not filled in. The five not completed questionnaires were not included in the presented percentages. First remarkable finding was that approximately half of subjects initially indicated not walking barefoot anywhere at home, conform instruction/advice given to subject by specialists.[24] Asking again revealed that subjects mostly walk barefoot briefly before getting in and out of bed, in the bathroom and between both locations. The second finding was that around 80% of the participants indicated to stand stable on the mat. Simultaneously, 30% of the subjects indicated that standing stable only applied for the moment on the mat, while getting on and off proved difficulties. Due to neuropathy, patients with diabetes have problems with standing, for which aides are used, e.g. walker.[15] During developing the Bath Mat method, it should be taken into account whether the system can be used with aides or whether it is possible to measure while sitting down. Furthermore, 83.3% of the subjects indicated that they want to be notified if an abnormality is found in the images. The majority would be notified by phone or mail, and around 15% of the subjects had no preference. In addition, over 90% of the subjects were good with automatically notifying a health care provider when an abnormality is found.

4 General discussion

In this thesis, a new, non-invasive, method to detect DFUs was evaluated in a clinical environment. This signifies an initial step in the establishment of a novel approach for early detection of pre-stage of DFUs in a domestic setting. Nowadays, high-risk patients are advised to perform a daily foot inspection, which is only performed by one-third of all diabetic patients.[18, 30–35] Nonetheless, it is estimated that with high preventive care, 75% of all DFUs can be prevented.[37, 38] With the Bath Mat method developed in this thesis, we aim to simplify the daily advised foot inspection and hereby improve preventive DFU care. Within this thesis, the Bath Mat method has developed into a prototype, which was used in a clinical environment to gather images of different groups of subjects.

To assess the validity of the Bath Mat setup, we showed that thermal footprints are a valid substitute for direct plantar foot images, since the temperature distribution is similar between both images. Furthermore, DFUs can be visually identified in both direct images and thermal footprints. However, the mean plantar temperature of the thermal footprints is lower than in direct images in all groups of subjects. Although the foot temperature is affected by various environmental factors, e.g. ambient temperature[43], these factors affect both feet. Therefore, the obtained thermal images for this thesis can potentially be used to identify differences and pattern changes that can quantify DFUs. If these changes are identified, the Bath Mat could impact preventive DFU care. However, the Bath Mat method needs to be used by diabetic patients, which is a patient group showing low adherence in other studies.[32–35] The main insight from a questionnaire among diabetic subjets is that the device should be accessible with aides (e.g. walker), because standing can be a problem due to neuropathy.

In addition, the reproducibility of measuring the thermal footprints in healthy subjects between days was also researched. Between different days, the temperature distribution is similar, yet the measured temperature varies. The extent of the temperature range differs between healthy subjects. To correct for these deviations between individuals, the method can be personalized by adding a calibration period to determine accepted temperature range. Also different foot areas show a different extent of deviation. Potentially, different temperature ranges could be set for different foot areas.

However, after the research in this thesis, the fundamental question remains whether a DFU is accompanied with an increase in temperature. In this thesis, only known DFUs were measured, so nothing can be concluded about pre-stage ulcers. Different randomised controlled trials with the use of skin thermometers have been performed, giving mixed results.[33, 40, 43] Since the Bath Mat method can image the entire foot, an observational study could reveal whether all DFUs can be recognised using thermography. This could provide important insights into the pre-staging of DFUs.

Furthermore, results in this thesis show that the butterfly pattern is less visible in patients with diabetes and peripheral neuropathy compared to healthy subjects. It is known in literature that neuropathy can affect the skin temperature.[43, 66] Perhaps the Bath Mat method could be used to indicate the degree of peripheral neuropathy, by change of butterfly pattern in DM patients. For example, a patient could undergo a measurement at every appointment at the outpatient clinic after the patient is diagnosed.

4.1 Limitations

This study faced some limitations. In postprocessing, several steps were performed manually, e.g., matching and segmentation. All manual steps were performed by the same researcher, resulting in some subjectivity in the results. Moreover, all manual steps were challenged by the foot deformations present in the study population and background temperature from the lower legs. This made it complicated to distinguish between the foot and the background.
Another limitation in this study is the varying angle and distance between the cameras and the mat during measurements. For an indirect measurement, the distance between the cameras and the mat was predetermined and the set height was marked on the tripod. However, the distance between the cameras and the foot during a direct plantar measurement was not consistent, causing some images to be out of focus. The angle of the system on the tripod was not fixed or predetermined, which allowed for different imaging angles in measurements . Between measurements, the system was manually adjusted so that the mat was in view of both cameras. The different image angels made matching the same feet between days more challenging. Furthermore, the angle could have also impacted the measured temperature, due to a varying conversion factor.
The last limitation is associated with the used MATLAB GUI to gather data. The frame rate in this GUI is affected by hardware configuration and measurement times. This was investigated by M2-student S. Dasselaar, who showed unpredictable drop in frame rate during a longer measurement.[58] Due to this decrease in frame rate, frames were missing at key moments, e.g. stepping off the mat. This is not desirable in follow-up research. To overcome this problem, the GUI should be optimized into different tools for data collection and editing.

4.2 Future perspectives

The goal of the Bath Mat method is to be a daily used method in a domestic setting. Furthermore, the method ideally requires little to no effort for patients to use and will provide temperature of the entire feet. Several follow-up research directions are suggested to achieve this goal. A follow-up study could focus on finding new features which can identify DFUs. The features investigated in this thesis currently focus on left-right differences. However, in some cases DM-patients have no contralateral spots, due to a prior amputation. Therefore, further research can focus on pattern changes over time or discover features that do not use a left-right difference.
Another research could focus on improving the Bath Mat device, by writing software to improve image acquisition and automating postprocessing. In the acquisition software, images should be recorded at a fixed high frame rate, which does not decrease as the measuring time increases. The automatic postprocessing is recommended, because the manual segmentation and matching used in this thesis are not a viable option in the proposed domestic setting. Automatic postprocessing methods for automatic foot segmentation and matching are investigated by two technical medicine students.[57, 58] Automatic segmentation is attempted through thresholding, Otsu's method and an active shape algorithm. However, all these methods require rough manual feet selection, which now in done manual. A possible solution to this issue is to mark out landmarks and/or a consistent rectangle on the mat, which the user must then stand within. Subsequently, these landmarks can be automatically detected. Automatic matching is attempted through manual foot selection with iterative closet point (ICP). However, this method does not

seem to perform better than the manual point registration method. Further research can focus on improving the ICP matching method with scale space.[58]
Additionally, more research is needed to find a mat which can be cleaned with alcohol between measurements, to reduce waste. Furthermore, it is recommended to use a larger mat in further research, because the foot size in this study was found to be larger than pre-set hypothesis.
Another follow-up study can focus on expanding the clinical study performed in this thesis. This study should measure diabetic patients for a longer period, ideally in the domestic setting. Mainly high-risk patients should be included in this study, to increase the change of measuring a pre-stage ulcer. Within this study it can be investigated when an anomaly in the images is visible, how to respond to this image, and when to notify a deviating image to an expert. For example, how many days deviating values must occur before concluding a spot to be suspicious.

5 Conclusion

In this thesis, a new, non-invasive, method to detect DFUs in a domestic setting was developed and tested in a clinical environment. With the Bath Mat device, we were able to obtain thermal images of the whole foot showing visually differences between feet with and without a DFU. Furthermore, DFUs can be visually identified in both direct images and thermal footprints. In addition, we showed that the thermal footprints are a valid substitute for direct foot measurements, due to similarities in temperature distribution. Between different days, the temperature distribution is similar in thermal footprints, yet the measured mean temperature varies. The extent of the temperature range differs between healthy subjects and different foot areas. Among the investigated features, left-right differences in mean foot temperature do not appear to be sufficient to quantify wounds for all patients. Conversely, temperature differences in contralateral spots potentially can quantify wounds. Although this new Bath Mat device still needs additional research, the thermal images collected with this device have potential to look for features beyond left-right differences.

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A Appendix: NON-WMO study application

Onderzoeksprotocol Badmat versie 1.2

Onderzoeksprotocol voor een niet-WMO plichtige studie.

STUDIEGEGEVENS			
Titel onderzoek	Badmat: een automatisch systeem voor het vroegtijdig detecteren van diabetische voet wonden op de gehele voet		
Acroniem/ korte studie titel	Badmat		
Datum / Versie	3 mei 2023, versie 1.2		
Soort studie	Prospectief onderzoek		
Opdrachtgever / verrichter *De opdrachtgever/ verrichter is de instelling (ziekenhuis, bedrijf, etc) die opdracht heeft gegeven voor de organisatie en/of uitvoering van het onderzoek*	ZGT		
Leden onderzoeksteam *Indien noodzakelijk kunnen er natuurlijk regels worden toegevoegd of verwijderd*	Gegevens *Noteer hier de naam, functie, vakgroep/afdeling en instelling van elk lid van het onderzoeksteam*		Rol *Bijvoorbeeld lokale hoofdonderzoeker, coördinerend onderzoeker, onderzoeksverpleegkundige, supervisoropleiding,…*
	1	Eline Zoetelief	Onderzoeker
	2	Kilian Kappert	Hoofdonderzoeker
	3		
	4		
	5		
Indiener	Naam: Kilian Kappert Telefoonnummer: 0657915596 E-mailadres: k.kappert@zgt.nl		
(Lokale) hoofdonderzoeker ZGT	Naam: Kilian Kappert Telefoonnummer: 0657915596 E-mailadres: k.kappert@zgt.nl		

Het onderzoek wordt uitgevoerd in het kader van:	☒	Algemeen wetenschappelijk onderzoek (bijv. binnen onderzoekslijn binnen de instelling)
	☐	Promotieonderzoek
	☒	Wetenschappelijke stage/bachelor- of masterthesis. Naam opleidingsinstituut: University Twente
	☐	Anders, namelijk:

Inhoudsopgave

SAMENVATTING

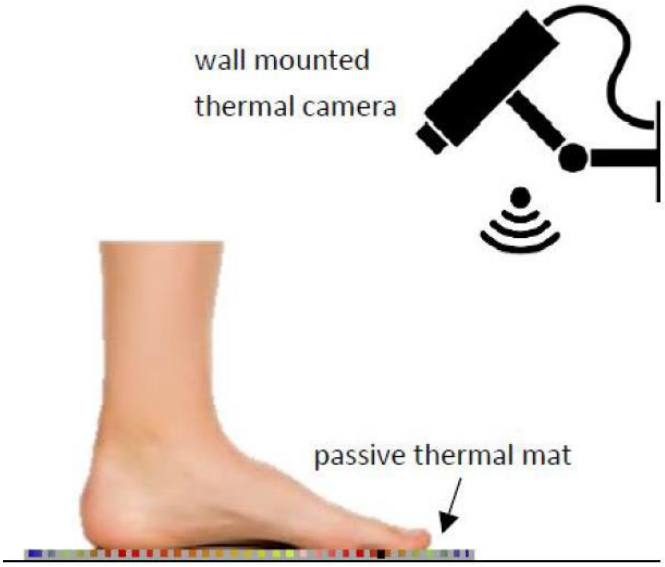
Tussen de 19-34% van alle diabetes mellitus (DM) patiënten ontwikkelen gedurende het leven een diabetische voetulcer (DFU). Echter, 65% van deze patiënten heeft een nieuwe DFU binnen 3 jaar.[1] Op dit moment bestaat er nog geen beeldvormende methode om DFU vroegtijdig te detecteren op een manier die weinig tijd kost in de thuissituatie voor de patiënt. Met dit prospectieve onderzoek wordt een methode onderzocht die wel non-invasief is en weinig tijd kost voor een patiënt. De methode wil met thermografische beelden van de gehele voet DFU vroegtijdig herkennen. De thermografische afbeeldingen worden gemaakt met de thermische camera Optris PI 400i/PI 450I[2] in een protype opstelling dat de thuissituatie moet nabootsen. De dorsale voetzijde wordt direct gemeten door de camera, terwijl de plantaire, mediale en laterale voetzijde indirect worden gemeten door een thermische voetafdruk op een memory-foam mat.

INTRODUCTIE

Tussen de 19-34% van alle diabetes mellitus (DM) patiënten ontwikkelen gedurende het leven een diabetische voetulcer (DFU), waarvan 77% geneest binnen 1 jaar. Echter, 65% van deze patiënten heeft een nieuw DFU binnen 3 jaar.[1] Als de voetulcer niet geneest kan het in een slecht geval nodig zijn om tenen, (delen van) de voet of (deel van) het been te amputeren. Op dit moment wordt in de praktijk patiënten geadviseerd om dagelijks de voeten te controleren op ulcera door middel van een spiegel.[3] Echter worden de voetulcera dan pas ontdekt op het moment dat er al een ulcer aanwezig is, terwijl je deze liever in een vroegtijdig stadium zou willen detecteren.

In de literatuur worden verschillende methoden beschreven die voetulcera vroegtijdig kunnen detecteren. Deze systemen zijn gebaseerd op het optreden van een temperatuurverschil van 2.2°C tussen de linker en rechter voet, wanneer een ulcer ontwikkeld op een van beide voeten.[4–6] De temperatuur wordt in deze onderzoeken met een huidthermometer gemeten op verschillende plekken op de plantaire zijde van de voet. Een tekortkoming van deze methoden is dat er alleen wordt gefocust op de plantaire zijde van de voet, terwijl 30% van de voetulcera op de dorsale zijde van de voet ontstaan.[7] Andere onderzoeken hebben sokken ontwikkeld met ingebouwde temperatuur sensoren, maar daarvan geven patiënten aan dat het dragen van de sokken intensief is.[8–10]

Op dit moment heeft de Biomedical Photonic Imaging vakgroep van de Universiteit Twente een methode ontwikkeld die in een korte tijdsperiode een gehele voet afbeelding maakt, die niet intensief is voor de patiënt. Bij deze methode (zie figuur 1) met een thermische camera (Optris PI 400i/PI 450I) thermische afbeeldingen van de gehele voet gemaakt. De dorsale voetzijde direct gemeten met een thermische camera. De plantaire, laterale en mediale voetzijde wordt indirect gemeten door een thermische voetafdruk op een memory-foam mat (traagschuim, schuimrubber SG 50). De mat kan tussen metingen worden gedesinfecteerd.



Figuur 1: Schematische opstelling methode

Om de bruikbaarheid van de methode te testen is het wenselijk thermische voetafbeeldingen van verschillende groepen proefpersonen te verzamelen. De thermische voetafbeeldingen worden prospectief verzameld van drie groepen. Groep 1: Gezonde proefpersonen, waaronder wordt verstaan personen niet betekend met diabetes mellitus. Groep 2: Proefpersonen bekend met diabetes mellitus en neuropathie, maar nog niet eerder een DFU hebben gehad. Groep 3: Proefpersonen die momenteel worden behandeld voor een DFU.

Door de afbeeldingen van verschillende groepen te verzamelen is het mogelijk om te onderzoeken welke informatie/features van thermische voetafbeeldingen kunnen worden gebruikt om de DFU te herkennen. Ook kan worden gekeken of de aanwezigheid van diabetes/neuropathie invloed heeft op de thermische afbeeldingen. Als laatste worden van groep 1 op meerdere momenten een thermische voetafbeelding gemaakt, om te onderzoeken of de thermische voetafbeeldingen op meerdere meetmomenten met elkaar te vergelijken zijn.

ONDERZOEKSVRAAG/ ONDERZOEKSDOEL

Het primaire doel van dit pilot-onderzoek is te onderzoeken of/welke verschillen kunnen worden gedetecteerd in thermische voetbeelden van proefpersonen die wel/geen DFU hebben.

Secundaire onderzoeksvragen:

- Welke informatie kan worden verkregen uit thermografische voetafbeeldingen van gezonde proefpersonen en DM patiënten?
  - Is het mogelijk om informatie of features vanuit de thermografische voetafbeeldingen te relateren aan beelden met een DFU?
- Zijn de thermografische voetafbeeldingen gemaakt op meerdere meetmomenten met elkaar te vergelijken? (Wat is de reproduceerbaarheid van de thermografische voetafbeeldingen?)

METHODEN

Mono- of multicenter studie

☒ Monocenter studie

☐ Multicenter studie

Deelnemende centra en lokale hoofdonderzoeker per centrum:
ZGT – Kilian Kappert

Studiedesign

Het onderzoek is een kwantitatief onderzoek, waarbij drie groepen worden gemeten.

Groep 1: Gezonde proefpersonen, waaronder wordt verstaan personen niet betekend met diabetes mellitus. Metingen van deze groep vinden plaats op 10 tijdsmomenten.
Groep 2: Proefpersonen bekend met diabetes mellitus en neuropathie, maar nog niet eerder een DFU hebben gehad. Metingen van deze groep gebeurt op één tijdsmoment
Groep 3: Proefpersonen die momenteel worden behandeld voor een DFU. Metingen voor deze groep gebeurt op één tijdsmoment.

Procedure en interventie (indien van toepassing)

Algemene procedure:
Proefpersonen zal eerst worden gevraagd of ze willen meedoen aan het onderzoek. Indien proefpersonen dit willen, wordt eerst het proefpersoneninformatieformulier (PIF, zie bijlage A) doorgenomen en een informed consent getekend (zie bijlage A).
Daarna wordt de proefpersoon gevraagd om schoenen, sokken en evt. verband uit/af te doen. Op teken van de onderzoeker wordt de proefpersoon gevraagd om 10 seconden op de mat te gaan staan. Na 10 seconden wordt de proefpersoon verzocht weer van de mat af te stappen. De voetafdruk op de mat wordt vervolgens nog 1 minuut gemeten. De proefpersoon neemt plaats op een werkbank, zodat er een RGB- en thermische afbeelding gemaakt kan worden van de plantaire zijde van de voeten. Na de meting wordt een korte vragenlijst (zie bijlage B) van maximaal 5 minuten afgenomen door de onderzoeker.

Toevoeging op algemene procedure voor groep 1:
De algemene procedure wordt op 10 verschillende dagen herhaald, aan het begin van een werkdag. De vragenlijst wordt alleen tijdens het eerste en tiende meetmoment afgenomen. Op het moment dat

Alle proefpersonen worden alleen gemeten indien deze al voor een andere afspraak in het ziekenhuis aanwezig zijn.

Apparatuur

Het apparaat in dit onderzoek (zie figuur 2) bestaat uit een vaststaand statief, met daaraan gemonteerd een RGB en thermische camera. De RGB camera is een Basler acA1920-150um met een breedhoeklens (FUJINON HF12XA5-M). De thermische camera is een Optris PI 400i/PI 450l. Deze is beschikbaar via de UT, maar momenteel loopt er ook een investeringsaanvraag (20220210) bij ZGT voor de aanschaf van deze camera. Beide camera's zijn CE gemarkeerd.[2,11]

Figuur 2: opstelling device, op statief links RGB camera en rechts thermische camera.

Duur van de studie

Maart 2023 tot en met juli 2023

Werving en selectie van proefpersonen

Screening/selectie

De proefpersonen worden gescreend en geworven door de (hoofd)onderzoeker. De screening is afhankelijk van de groep waarin de patiënten worden geïncludeerd.

Groep 1: De screening zal plaatsvinden door de(hoofd)onderzoeker door mogelijke proefpersonen (zorgmedewerkers) te benaderen en werven via interne kanalen ziekenhuis.
Groep 2: De screening van de tweede groep zal plaatsvinden door poli-afspraken bij de interne geneeskunde te bekijken. Bij potentiële inclusies kunnen deze worden gevraagd na de afspraak 10 minuten te blijven of ze worden van tevoren gebeld of ze willen meedoen aan het onderzoek.
Groep 3: De screening van de derde groep zal plaatsvinden door poli-afspraken bij de vaatchirurgie te bekijken. Proefpersonen worden tijdens een controle gevraagd of ze mee willen doen aan het onderzoek.

Studiepopulatie

De onderzoekspopulatie bestaat uit volwassen (>18 jaar).

Inclusiecriteria

Groep 1: leeftijd >18, geen DM
Groep 2: leeftijd >18, bekend met DM (type 1 of 2) en neuropathie
Groep 3: leeftijd >18, bekend met DM (type 1 of 2) en DFU

Exclusiecriteria

Alle groepen: proefpersoon kan niet zelfstandig (eventueel met hulpmiddel) staan. Proefpersoon heeft hallux-, voorvoet-, onderbeen- of bovenbeenamputatie gehad. Proefpersoon heeft wond groter dan 3 cm. Proefpersoon heeft een sterke verdenking op Charcot voet.

Groep 1: proefpersoon heeft wond aan voet onder de enkel, DM
Groep 2: proefpersoon heeft wond aan voet onder de enkel, geen neuropathie
Groep 3: voetenwonden aan beide voeten.

Aantal proefpersonen / steekproefgrootte

Groep 1: 15 personen
Groep 2: 30 personen
Groep 3: 30 personen

In eerder studies naar vergelijkbare onderwerpen zijn tussen de 40-600 proefpersonen geïncludeerd. Omdat dit een pilotstudie is, is gekozen voor kleinere aantal proefpersonen. Indien deze resultaten uitwijzen dat de methode, kan een amendement gedaan worden om het aantal proefpersonen uit te breiden en/of de duur van de studie te verlengen.

Dataverzameling: variabelen en meetmethoden

Primaire uitkomstmaat (afhankelijke variabele)

Een primaire uitkomst variabele van de studie is een lijst met features (o.a. temperatuurverschil, hotspot, temperatuurverloop, etc.) met een significante verschil tussen de groepen gezonde proefpersonen en met/zonder DFU.

Een ander primaire variabele is dat een waarneembaar verschil van >2.2°C tussen beide voeten niet meetbaar is voor alle groepen als gekeken wordt naar specifieke regio's of interest (ROIs) die gebruikt zijn in eerder literatuur onderzoek.

Overzicht variabelen en meetinstrumenten

Geef voor de primaire uitkomstmaat en de overige variabelen aan op welke manier deze worden gemeten (meetinstrument) en genoteerd (gecodeerd) in de database (uitkomstwaarden). Een aantal voorbeelden zijn hieronder weergegeven. Vergeet ook niet de missing values te definiëren.

Hiervoor kun je eventueel gebruik maken van onderstaande tabel. Mocht je de variabelen al in een tabel/document hebben genoteerd, dan mag je deze ook als bijlage aan dit protocol toevoegen.

Variabele	**Meetinstrument/ Bron van de data**	**Uitkomstwaarden**	**Meetmoment**
Basis karakteristieken (bijv. geslacht, leeftijd etc.)	Elektronisch Patiënten Dossier (EPD)	999 = missend	1
Percutane Transluminale Angioplastiek in voorgeschiedenis	EPD	0 = geen PTA in voorgeschiedenis / 1 = PTA aan linker been in voorgeschiedenis / 2= PTA aan rechter been / 4= PTA aan beide benen / 999 = missend	1
Teendrukken	EPD	Open vraag (getal in mmHg) / 888=niet afgenomen / 999 = missend	1
$TcpO_2$ meting (zuurstofspanning)	EPD	Open vraag (getal in mmHg) / 888=niet afgenomen / 999 = missend	1
Enkel-arm index (ABI)	EPD	Open vraag (getal tussen 0-1) / 888= niet afgenomen / 999 = missend	1
Diabetisch type	EPD	0 = type 1 / 1 = type 2 / 999 = missend	1
Voetulcera in voorgeschiedenis	EPD/vragenlijst	0 = ja / 1 = nee / 999 = missend	1
Wondinfectie	EPD	0 = ja / 1=ja, met antibiotica / 2=nee / 888 = niet van toepassing / missend	1

Diabetes onder controle	Vragenlijst	0 = ja / 1 = nee / 999 = missend	1
Momenteel een ulcer	EPD	0 = ja / 1= nee / 888 = niet van toepassing / 999 = missend	1
Locatie van het ulcer	EPD	Open vraag	1

Standaardisering

Proefpersonen van groep 1 worden gemeten aan het begin van de werkdag.
Proefpersonen van groep 2 worden gemeten na afloop van het consult.
Proefpersonen van groep 3 worden gemeten voordat ze behandeld worden door een wondconsulent.

Data-analyse

De inhoud van deze paragraaf is afhankelijk van het soort onderzoek en type onderzoeksvra(a)g(en).
Let op: De beschrijving van de data-analyse in een onderzoeksprotocol moet verder gaan dan het benoemen van de software die gebruikt zal worden voor de analyse en het soort analyse. Deze paragraaf moet een globaal overzicht geven van álle stappen die uitgevoerd worden met de verzamelde gegevens in het analyseproces.

Data-inspectie

Bij missende data wordt gekeken of deze data alsnog kan achterhaalt worden of wat de reden is van de missende data. Bij extreme waarden zal in overleg met de behandelaar worden gekeken wat de reden is. Bij onverwachte bevindingen zal de behandelaar ook worden ingelicht.

Analyses

<u>Beschrijvende statistiek</u>
De categorische variabelen worden genoteerd als frequentie en percentage per categorie (voorbeeld: N=11 (13%)). De continue variabelen met een normale verdeling worden genoteerd in termen van een gemiddelde en standaarddeviatie (voorbeeld: 45±12 jaar). Resultaten van niet-normaal verdeelde data worden meestal genoteerd in termen van een mediaan en interquartile range (IQR) (voorbeeld: Mediaan = 45 jaar, IQR = [32–57]).

<u>Statistische analyse</u>
Variabelen die normaal verdeeld zijn, kunnen worden geanalyseerd met parametrische toetsen: gepaarde t-test of linear mixed models.
Variabelen die niet normaal verdeeld zijn, kunnen met alternatieve, non-parametrische toetsen geanalyseerd worden: Wilcoxon signed rank, Friedman toets.
Categorische variabelen kunnen worden geanalyseerd met McNemar of Cochran's Q toets.

Interim analyse(s)
Er vind een interim analyse plaats op het moment dat de helft van de proefpersonen is geïncludeerd.

Kwalitatief onderzoek: Vanuit de thermografische beelden worden verschillende variabelen verkregen. Als eerste wordt de gemiddelde temperatuur van zowel de dorsale als plantaire zijde van de voet bepaald. Ook worden gemiddelde temperatuur van verschillende ROIs bepaald. De gemiddelde temperaturen worden per patiënt vergeleken voor de linker en rechter voet. Verder wordt door middel van data driven coding geprobeerd nieuwe variabelen voor de methode te definiëren.

Softwareprogramma

SPSS en Matlab

ETHISCHE OVERWEGINGEN

Niet WMO verklaring

Vanwege de lage, bijna verwaarloosbare, belasting van de patiënt wordt ervan uit gegaan dat dit onderzoek niet onder de WMO valt. Er is dus ook geen niet-WMO verklaring aangevraagd.

Belasting en vergoeding voor de proefpersoon

Groep 1: Proefpersonen dienen 10 keer 5 minuten beschikbaar te zijn voor metingen, welke worden uitgevoerd op momenten dat ze aanwezig moeten zijn in het ziekenhuis. Om deze reden wordt de meting uitgevoerd bij ziekenhuispersoneel.
Groep 2 & 3: Proefpersonen dienen één keer 5 minuten beschikbaar te zijn voor het maken van opnames, waarbij deze proefpersonen in het ziekenhuis aanwezig zijn voor een consult. Patiënten vullen een vragenlijst (zie bijlage B) in samen met de onderzoeker, wat maximaal 5 minuten in beslag neemt. Proefpersonen en patiënten ontvangen geen vergoeding.

Toestemming proefpersoon

Bij prospectief niet WMO plichtig onderzoek moet altijd toestemming worden gevraagd aan de proefpersoon. Bij retrospectief niet WMO plichtig onderzoek is dat afhankelijk van de manier van dataverzameling en de verwerking ervan.

Wordt toestemming aan de proefpersoon gevraagd?	☒ Ja (Vul optie A 'Informed Consent Procedure' in) ☐ Nee (Vul optie B 'Toestemming wordt niet gevraagd')
Optie A: Informed Consent procedure	
Benadering proefpersonen	Alle proefpersonen worden tijdens het bezoek aan het ziekenhuis door een van de onderzoekers benaderd of ze willen deelnemen aan het onderzoek.
Informeren proefpersonen	De proefpersonen worden op de hoogte gesteld van de inhoud van het onderzoek door een informatief gesprek door een van de onderzoekers,

	waarin eventuele directe vragen kunnen worden besproken. Daarnaast krijgen de proefpersonen een proefpersoneninformatieformulier (zie bijlage A) mee, daarop een telefoonnummer en emailadres van de hoofdonderzoeker voor eventuele vragen op een later moment.
Bedenktijd	Gezien de niet belastende aart van het onderzoek zal de patiënt maar enkele minuten bedenktijd hebben. De patiënt mag zich achteraf wel terugtrekken uit het onderzoek.
Tekenen toestemmings-verklaring	Het toestemmingformulier wordt getekend voordat de meting wordt uitgevoerd.

Optie B: Toestemming wordt niet gevraagd

Er zijn geen uitzonderingsregel(s) van toepassing

DATAMANAGEMENT & PRIVACY

Zie bijlage C

VALORISATIE EN PUBLICATIE

Valorisatie

De resultaten van de studie zouden de dagelijkse zorgpraktijk rondom voetulcera kunnen veranderen doordat de ulcers eerder kunnen worden gedetecteerd. Hierdoor kan eerder worden ingegrepen, waardoor voetwonden kunnen worden voorkomen. Met dit device kunnen patiënten worden gemonitord in de thuissituatie, waardoor patiënten eerder aangepaste behandelingen kunnen krijgen op basis van dagelijkse beeldvorming.

Publicatie

Er wordt verwacht dat deze studie kan leiden tot een publicatie van de eerste pilot data, wat kan bijdragen aan nieuwe wetenschappelijke inzichten.

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B Appendix: Measurement protocol

Dit is het protocol dat gebruikt is voor de metingen, opgedeeld in twee verschillende onderdelen: voor de meting en tijdens de meting.

B.1 Benodigde software

Voor een Badmat meting uitgevoerd kan worden, moeten verschillende programma's zijn geïnstalleerd op de computer:

- MATLAB versie R2022b of nieuwer
- Optrix PIX connect
- Pylon viewer

Als alle programma's geïnstalleerd zijn, kan de MATLAB GUI van het Badmat project gevonden worden op de BMPI schijf: \\ad.utwente.nl\TNWBMPI\Projects\LASCA AND LDPI CONNECTION\3. Standard and Realtime LSCI\clone_Bath Mat. Om de GUI op te starten moet Bath Mat_App geopend worden. Indien dit geopend is, wordt een apart scherm geopend, zie figure 25. In de statusbalk worden eventuele foutmeldingen in het programma weergegeven, bijv. welke camera niet verbonden kan worden met de software. Indien het programma niet functioneert of foutmeldingen geeft, in de beste manier om het weer werkend te krijgen MATLAB afsluiten en de GUI opnieuw op te starten.

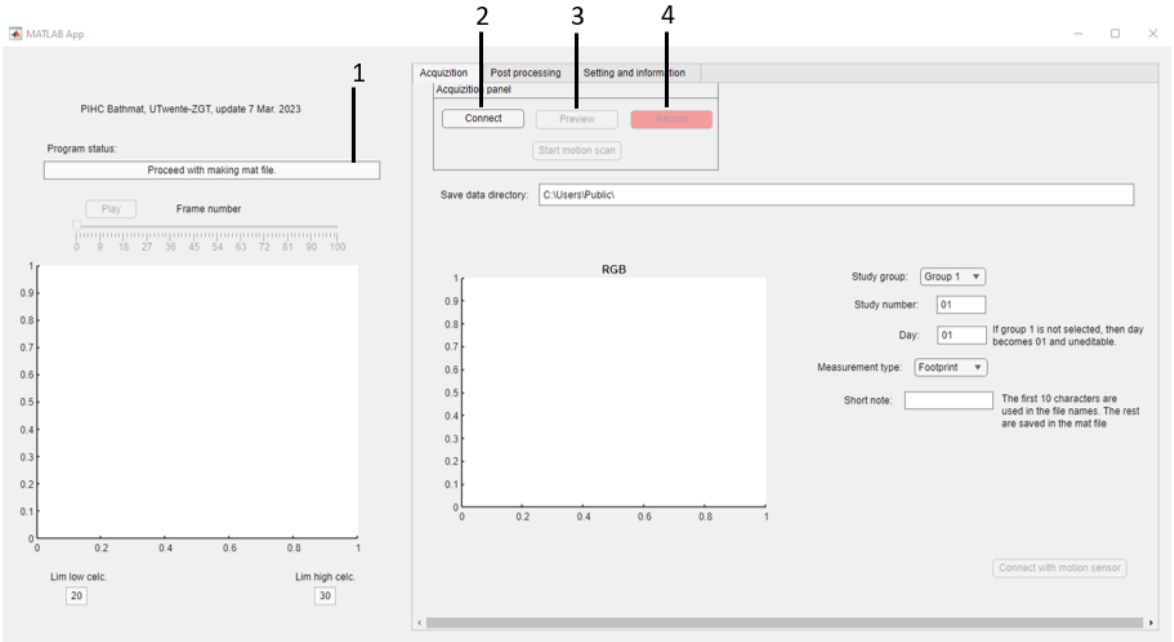

Figure 25: MATLAB GUI voor het badmat project. De vier genummerde onderdelen zijn: (1) statusbalk, (2) connect knop, (3) preview knop en (4) record knop.

B.2 Opzetten meetopstelling

- Monteer witte box op de het statief (indien het systeem uit de koffer komt, monteer ook het statief)
- Plug de grijze USB box in de computer (indien de snoeren van de camera niet vastzitten in de grijze USB box, zorg dat de RGB en IR camera in een blauwe poort zitten, en de Arduino in een zwarte poort)
- Laptop aansluiten aan netstroom
- MATLAB GUI opstarten
  - Verbind camera door op de knop connect te drukken.
  - Om te controleren of je de beelden goed kan maken kan je de knop 'Preview' drukken, waardoor je live beelden van te zien krijgt.

B.3 Tijdens de meting

B.3.1 Direct plantaire meting

- Zorg dat beide voeten goed zichtbaar zijn op beide camera (zowel RGB als IR camera).
- Zorg dat de voeten zoveel mogelijk in 90° op de beelden staan, liggend op een behandelbank of krukje. LET OP: dat de voeten niet rimpelen aan de onderkant, dit is te voorkomen door de onderbenen te los over de zijkant van de ondersteuning te leggen.
- Laat de proefpersoon het zwarte doek vasthouden om de rest van het lichaam zoveel mogelijk te bedekken.
- Probeer warme objecten (zoals kopjes warme drank of andere proefpersonen) te vermijden in de achtergrond.
- Stel de juiste waarde in de GUI in: study group, study number, day*, measurement type: Direct.
- Controleer of de voeten goed in het beeld staan, door op de knop preview te drukken.
- Start de meting.
  - Druk op de knop record om de meting te starten
  - Meet de plantaire voetzijde 10-15 seconde
- Na 10-15 seconden kan de meting gestopt worden door nogmaals op de knop record te drukken.

TIP: Mocht de camera niet vast gezet kunnen worden, dan kan je de draadloze muis gebruiken om de meting te starten en te stoppen (druk op record), terwijl je zelf de camera vasthoud. Noteren bij opmerking dat je een handmatige meting hebt gedaan. *Indien study group 2 of 3 wordt gekozen, zal de day automatisch op 01 blijven staan. Dit kan niet worden aangepast.

B.3.2 Thermische footprint

- Schuif het systeem (indien dat nog niet gebeurd is) in de zwarte mat en kantel de het systeem naar de vloer
- Zorg dat de mat goed zichtbaar is op beide camera's (Denk erom dat je de juiste mat voor de juiste proefpersoon gebruikt!)
- Stel de juiste waarde in de GUI in: study group, study number, day*, measurement type: Footprint
- Start de meting.
  - Druk op de knop record om de meting te starten
  - Zeg dat de proefpersoon op de witte mat mag staan
  - Nadat de proefpersoon 10 seconden met BEIDE voeten op de witte mat heeft gestaan, geef de proefpersoon aan dat deze van de witte mat mag afstappen
  - Meet na het afstappen van de laatste voet nog 40 seconden de witte mat (vaak tot ongeveer 55-60 seconden)
  - Stop de meting door nogmaals op de record knop te drukken, waarna de data zal worden opgeslagen (dit kan even duren)
- Draai de mat om en herhaal de meting nogmaals zoals hierboven beschreven
  - Denk erom dat de proefpersoon na de 2x afstappen al klaar is, dus deze kan zijn of haar schoenen alweer aantrekken.

TIP: Probeer de proefpersonen tussen de metingen zoveel mogelijk te laten zitten of liggen.
TIP: Probeer de proefpersonen tijdens de meting zoveel mogelijk op de zwarte en witte mat te laten staan.

B.4 Na de meting

- Controleer of de data goed in opgeslagen
- Vul overzichtsheet van gemeten dagen bij gemeten proefpersonen in.
- Opruimen:
  - Zwarte matten desinfecteren met alcohol.

B.5 Systeem instellingen

RGB camera:

- app.acq.cam_video_format="RGB8";
- app.acq.cam_color_space="rgb";
- app.acq.cam_adapter="gentl";
- app.acq.cam_dev_id=1;
- app.acq.white_light_exp_time_micro_sec=10e3;

Thermische camera: app.acq.IRInterface = EvoIRMatlabInterface;
Image height orig. (px) = 288 and Image width orig. (px) = 382

C Appendix: MATLAB scripts for postprocessing data

Function: Load images

```
function [thermal_data,images,foldernames] = loadim(n_images)
    thermal_data = cell(n_images,1);
    images = cell(n_images,1);
    foldernames = cell(n_images,1);
    for i = 1:n_images
        [file, foldername] = uigetfile({'*.mat'},'Select the
           data file');
        fullname = fullfile(foldername, file);
        data = load(fullname);
        thermal_data{i} = data;
        images{i} = data.temp_mat;
        foldernames{i} = foldername;
    end
end

% select data in datafolder: matlabfile named 'file analyzed.
   mat'
% n_images is amount of images
```

Frame selection

```
%% Select the frames
frames = zeros([1,n_images]);
for i = 1:n_images
    image = images{i};
    Frame_selection(image);
    frames_left(i) = frame;
end

% select correct frame,
% Als je 10 mappen selecteert, krijg je 20 beelden, neem aan
   voor links & rechts, maar wat moet er eerst? Links/recht?
```

Function: Point registration

```
function [feet_pr, tform] = pointregistration(feet)
    Im1 = feet{1};
    figure("Position", [2 50 958 946]);
    imagesc(Im1)
    daspect([1 1 1])
    hold on;
    [x1,y1] = getpts;
    plot(x1,y1,'o')
```

```
    feet_pr = cell(length(feet),1);
    feet_pr{1} = feet{1};
    for i=1:(length(feet)-1)
        n = i + 1;
        Im2 = feet{n};
        figure("Position", [962,50,958,946])
        imagesc(Im2)
        daspect([1 1 1])
        [x2(:,i),y2(:,i)] = getpts;
        tform(:,:,i) = fitgeotform2d([x2(:,i),y2(:,i)],[x1,y1
           ], "affine");
        Im3 = imwarp(Im2,tform(:,:,i),OutputView=imref2d(size
           (Im1)));
        feet_pr{n} = Im3;
    end
end
% IMPORTANT: click the same order of points! After you
   clicked all point on
% one image, you have to press enter
% tform is de transformatiematrix
```

Segmentation foot (with Notepad)

```
%% Segmentation notepad
sample_frames_l=feet_left{1};
sample_frames_r=feet_right{1};

figure(1),
imagesc(sample_frames_l)
colormap('hot'), colorbar

polygon_prop=drawpolygon('FaceAlpha',0);
polygon_prop.Color='White';
polygon_points=round(polygon_prop.Position);

poly_mask_left=poly2mask(polygon_points(:,1),polygon_points
   (:,2),size(sample_frames_l,1),size(sample_frames_l,2));
bw_l_feet{1}=poly_mask_left;
%func_draw_polygon

masked_l=sample_frames_l.*poly_mask_left;
```

D Appendix: Additional findings measurements

D.1 Scatterplot of diabetic subjects without an ulcer

Figure 26 shows all measurements of the subjects with diabetes without an ulcer. All thermal footprints have a lower mean foot temperature than direct images. The ideal trendline (black line) shows the 1-to-1 comparison between direct plantar images and thermal footprints.

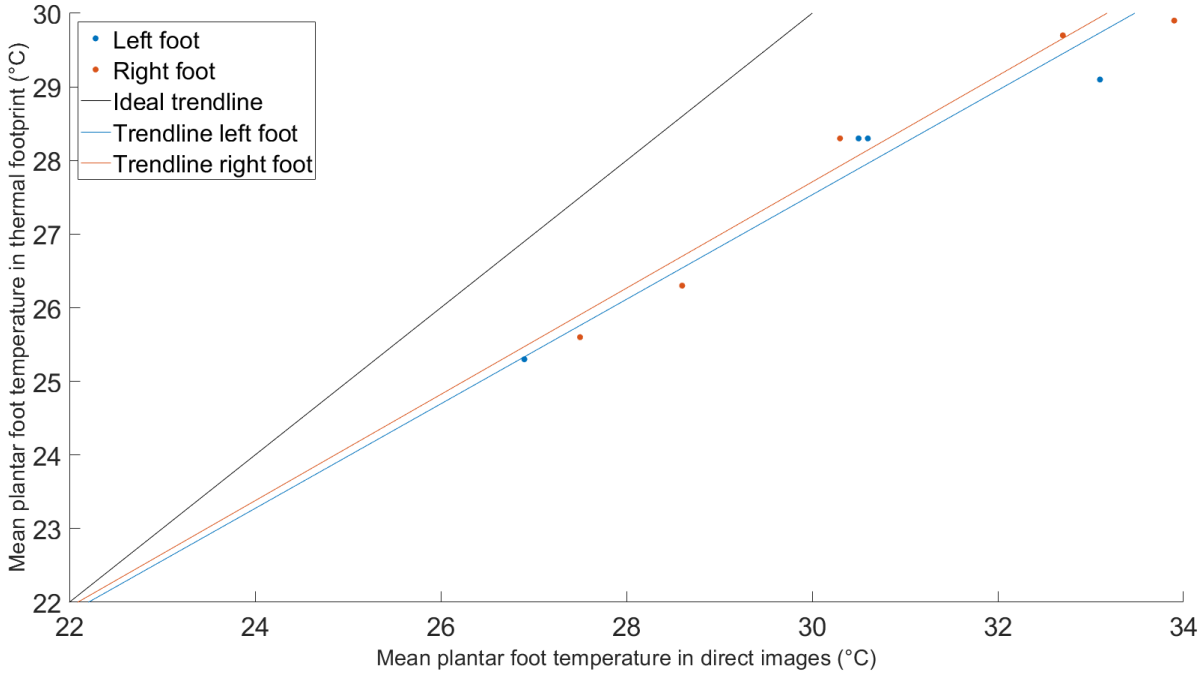

Figure 26: Scatterplot with overview of the mean plantar foot temperature between direct images (x-axis) and thermal footprints (y-axis) in diabetic subjects without ulcer (group 2). Blue points are left foot measurements and orange points are right foot measurements.

D.2 Feet stepping on and off the mat

Table 4: Which foot is dominant in stepping on and off the mat for healthy subjects

Subject	**Stepped on most with:**	**Amount**	**Stepped off most with:**	**Amount**
1	Right	9/10	Right	7/10
2	Left	6/10	Left	7/9
3	Left	7/10	Right	10/10
4	Right	8/11	Left	10/11
5	Right	9/10	Left	8/10
6	Right	7/10	Left	10/10
7	Left	9/10	Right	8/10
8	Right	7/10	Left	8/10
9	Left	8/8	Right	8/8
10	Right	10/10	Right	7/10
11	Right	7/10	Left	9/10
12	Right	7/10	Left/Right	5/10
13	Right	10/10	Left	8/9
14	Right	6/10	Left	8/10
15	Right	8/10	Right	6/10

Table 5: Which foot is dominant in stopping on and off the mat for groups 2 and 3

Wound	**Stepped on***	**Stepped off**	**Amount**	
			Group 2**	**Group 3**
Left	Left	Left	1	3
	Left	Right	1	6
	Right	Left	3	4
	Right	Right	-	1
Right	Left	Left		5
	Left	Right		1
	Right	Left		8
	Right	Right		-

*Two subjects stepped on with both foot at the same time

** This group did not have a wound

D.3 Footwear before measurement in patients with diabetes and an ulcer

Table 6: Footwear of diabetic subjects with an ulcer (group 3) before measurement

Subject	**Footwear**	Subject	**Footwear**
1	Extra-wide shoes with sole reinforcement, shock-absorbing, and settlement (NO orthopaedic shoes)	**16**	orthopaedic shoes
2	Bivalved Total Contact Cast (BTCC)	**17**	-
3	Removable cast	**18**	bandage shoes
4	orthopaedic shoes	**19**	convection shoes
5	orthopaedic shoes	**20**	orthopaedic shoes
6	- (shoe inspection adequate)	**21**	orthopaedic shoes
7	BTCC*	**22**	Left: bandage shoe Right: normal shoe
8	-	**23**	trainers
9	orthopaedic shoes	**24**	Left: Diabetic Walker Right: orthopaedic shoe
10	orthopaedic shoes	**25**	normal shoe (Nikes)
11	MABAL shoe (removable cast)	**26**	sandals with felt
12	- (shoe inspection adequate)	**27**	slippers with socks
13	rigid bandage shoe	**28**	orthopaedic shoes
14	bandages	**29**	sandals
15	Left: bandage shoe	**30**	sandals

E Appendix: Enhanced results on features

E.1 Mean foot temperature plantar

Table 7 shows left-right differences in mean foot temperature of plantar foot side for each subject per group. A negative number in this table for groups 1 and 2 means that the left foot is warmer than the right foot.

Table 7: Left-right differences in mean temperature of the plantar foot side

	Group 1		**Group 2**		**Group 3**	
	Δ *Temp (°C)*	ΔT_{norm} *(%)*	Δ *Temp (°C)*	ΔT_{norm} *(%)*	Δ *Temp (°C)*	ΔT_{norm} *(%)*
1	0.38	1.46	0.29	1.26	-0.28	-1.01
2	0.35	1.39	0.10	0.36	1.68	6.30
3	-0.51	-2.10	-0.16	-0.63	0.44	1.54
4	0.29	1.14	-1.32	-5.01	0.68	2.93
5	0.04	0.15	-0.05	-0.18	1.82	6.96
6	0.54	2.17			-0.18	-0.62
7	-0.28	-1.16			-1.68	-5.93
8	-0.06	-0.23			0.44	1.68
9	0.01	0.04			1.63	6.63
10	0.16	0.59			-2.33	-8.82
11	0.05	0.19			-4.00	-13.72
12	0.07	0.26			0.07	0.26
13	0.06	0.26			-0.97	-3.28
14	0.34	1.28			0.06	0.24
15	0.54	1.96			0.90	3.22
16					0.81	2.93
17					-0.25	-0.88
18					0.96	3.66
19					1.55	5.76
20					-1.95	-6.79
21					1.27	2.29
22					-0.31	0.81
23					-2.84	-1.02
24					12.76	8.90
25					-0.72	-0.39
26					-0.05	-0.56
27					1.45	3.18
28					6.91	4.31
29					-0.12	0.27
30					5.77	2.51

E.2 Mean foot temperature dorsal

Table 8 shows left-right difference in mean foot temperature of dorsal foot side for each subject per group. A negative number in this table for groups 1 and 2 means that the left foot is warmer than the right foot.

Table 8: Left-right differences in mean temperature of the dorsal foot side

	Group 1		**Group 2**		**Group 3**	
	Δ *Temp (°C)*	ΔT_{norm} *(%)*	Δ *Temp (°C)*	ΔT_{norm} *(%)*	Δ *Temp (°C)*	ΔT_{norm} *(%)*
1	1.05	3.71	-1.30	-5.29	-0.11	-0.36
2	0.11	0.38	-0.12	-0.37	-5.20	-18.76
3	-1.27	-4.99	-1.46	-5.30	-1.97	-6.53
4	0.16	0.57	1.34	4.82	-1.35	-5.64
5	0.01	0.03	-0.004	-0.01	-3.46	-12.65
6	0.35	1.27			-0.18	-0.60
7	0.01	0.05			4.87	14.81
8	0.31	1.20			0.26	0.94
9	0.38	1.38			-5.27	-20.44
10	-0.24	-0.81			4.59	14.66
11	-0.61	-2.17			7.35	22.31
12	-0.18	0.67			0.19	0.74
13	-0.04	-0.16			1.31	3.95
14	-0.06	-0.19			-0.77	-2.83
15	1.10	3.67			-2.03	-6.90
16					-0.72	-2.39
17					-0.002	-0.008
18					-2.98	-11.19
19					-3.69	-13.08
20					3.79	11.70
21					0.50	1.52
22					-0.24	-0.77
23					-2.11	-6.53
24					2.41	7.43
25					-1.56	-5.13
26					-0.56	-1.93
27					0.26	0.84
28					2.37	7.72
29					-0.61	-1.93
30					1.33	4.02

E.3 Temperature difference in contralateral spots

E.3.1 Outliers healthy subjects

The outliers of the healthy subjects can be divided into three different categories. The first category is that a part of the segmentation is lost due to transformation. This part get lost because it does not fit within a preset rectangle. This is illustrated in figure 27, as a white area appears at approximately the fifth toe.

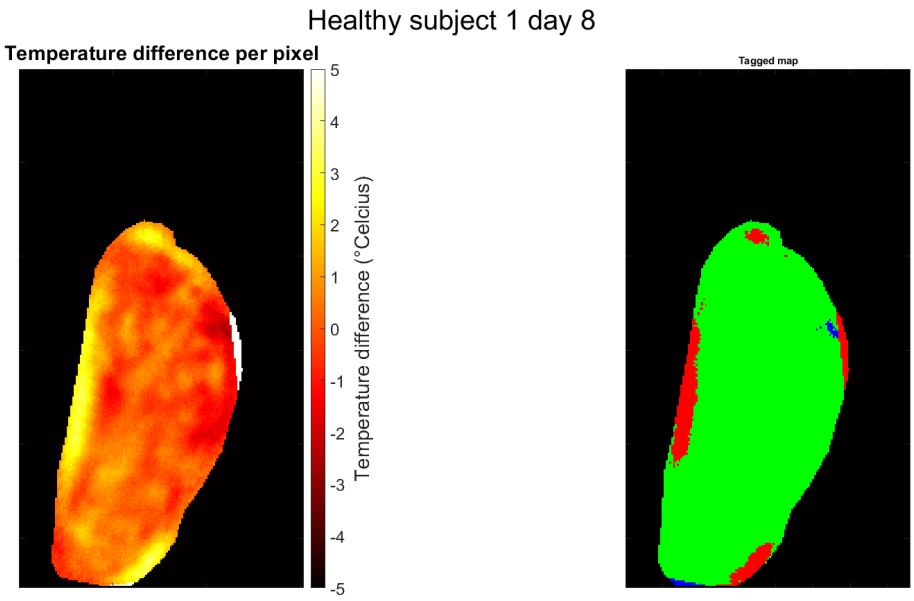

Figure 27: Day 8 of healthy subject 1. The left image shows the difference at pixel level in °C and the right image shows the tags assigned to each pixel. The green pixels are non-suspicious pixels, the red pixels are suspicious pixels >2.2°C and the blue pixels are suspicious pixels <-2.2°C.

The second category is where a healthy subject suffered a traumatic injury the night before the measurement. This is addressed in figure 28

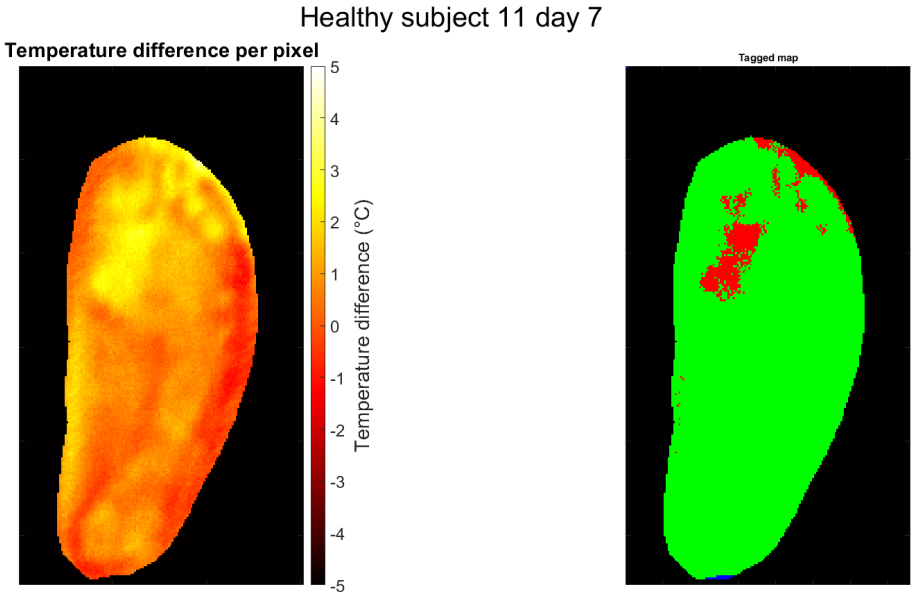

Figure 28: Day 11 of healthy subject 7. The left image shows the difference at pixel level in °C and the right image shows the tags assigned to each pixel. The green pixels are non-suspicious pixels, the red pixels are suspicious pixels >2.2°C and the blue pixels are suspicious pixels <-2.2°C.

The third category is that the matching between the left and right foot is not sufficient. This is reflected in two different abnormalities, namely on the lateral and medial sides (see figure 30) or on the toes (29. Because the matching does not go well, parts of the foot are compared with for example background or other areas, causing a temperature difference.

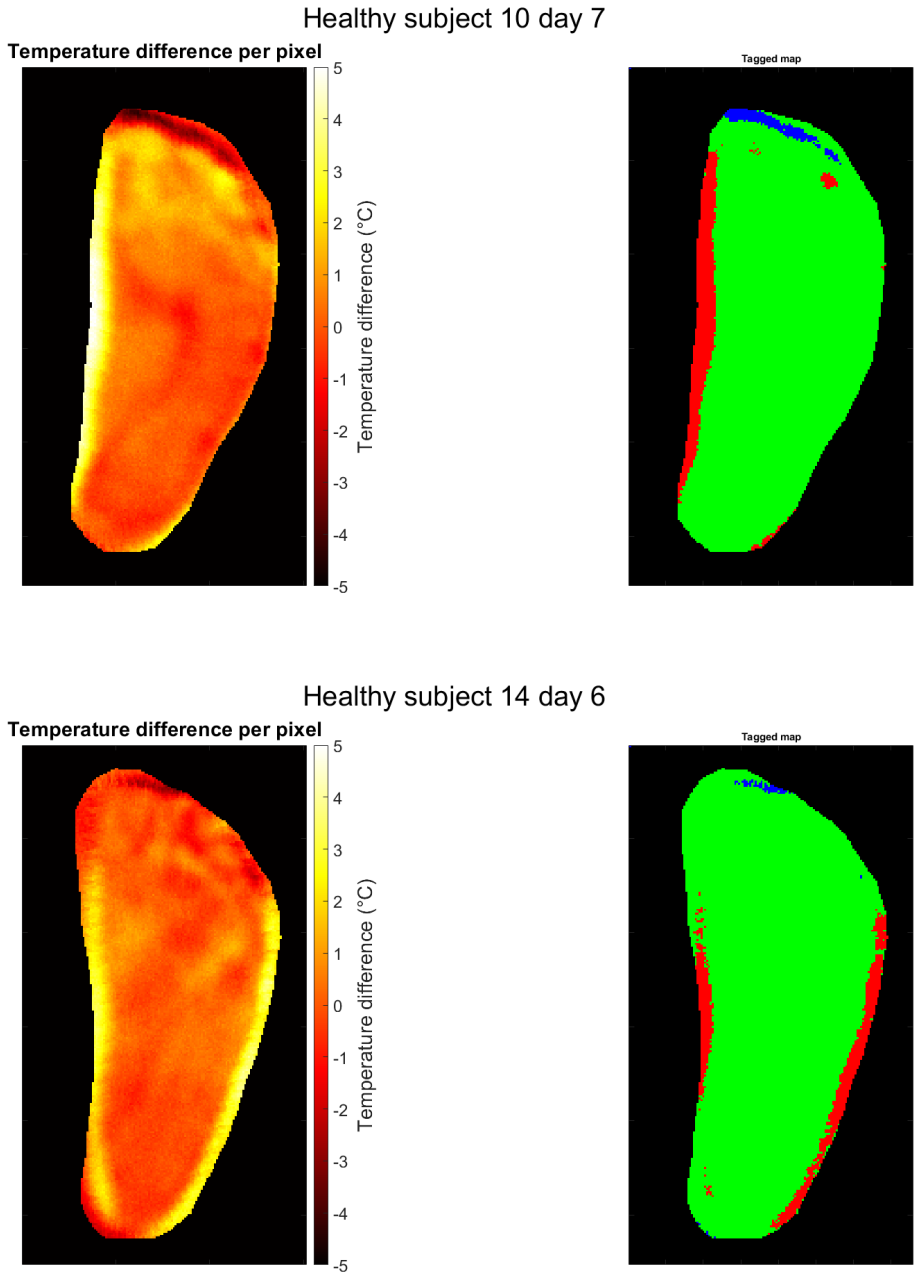

Figure 29: Days 7 and 6 of healthy subjects 10 and 14. The left image shows the difference at pixel level in °C and the right image shows the tags assigned to each pixel. The green pixels are non-suspicious pixels, the red pixels are suspicious pixels >2.2°C and the blue pixels are suspicious pixels <-2.2°C.

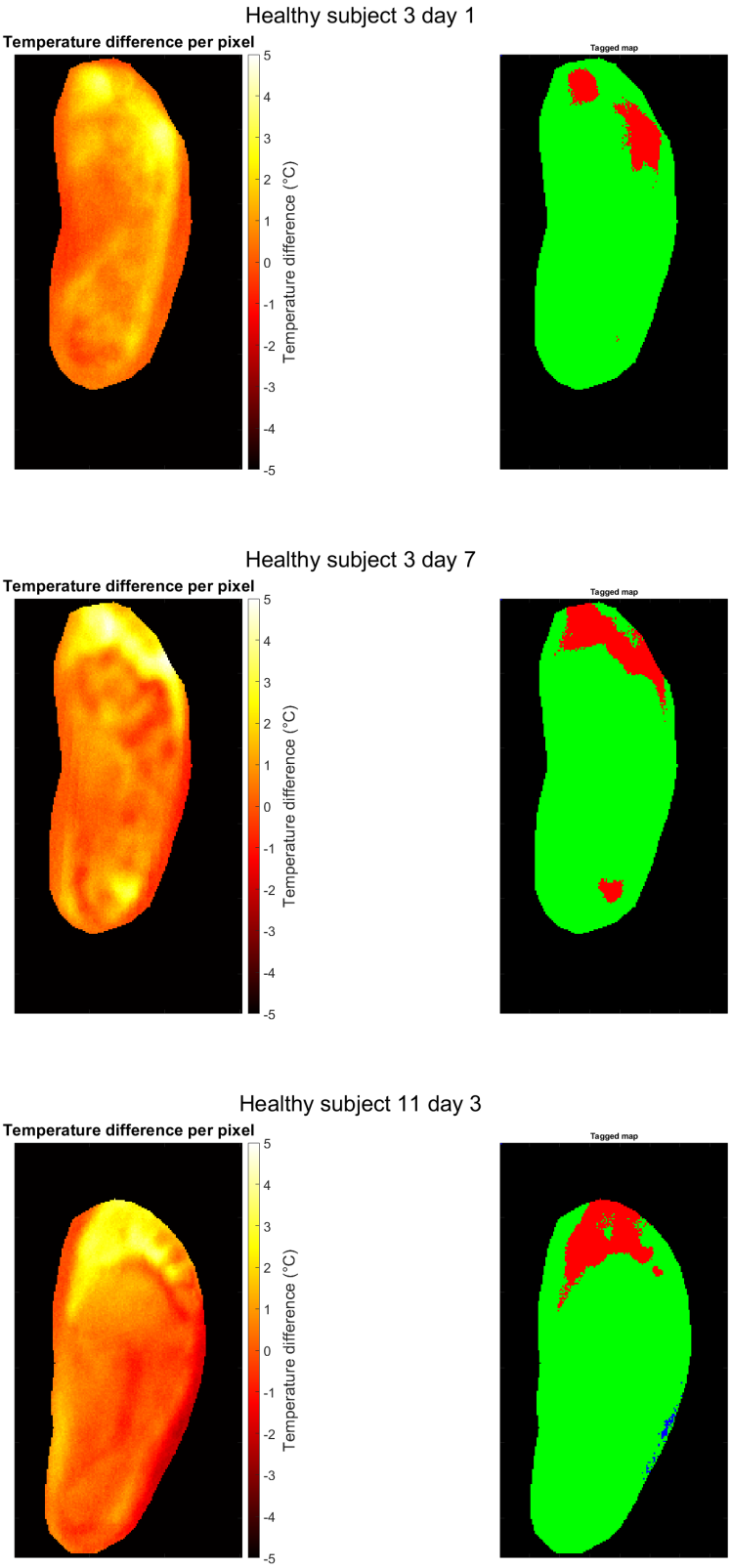

Figure 30: Day 1, 7 and 3 of healthy subjects 3 and 11. The left image shows the difference at pixel level in °C and the right image shows the tags assigned to each pixel. The green pixels are non-suspicious pixels, the red pixels are suspicious pixels >2.2°C and the blue pixels are suspicious pixels <-2.2°C.

E.3.2 Bar graph of unsuspected and suspected pixels of subjects with diabetes and without ulcer

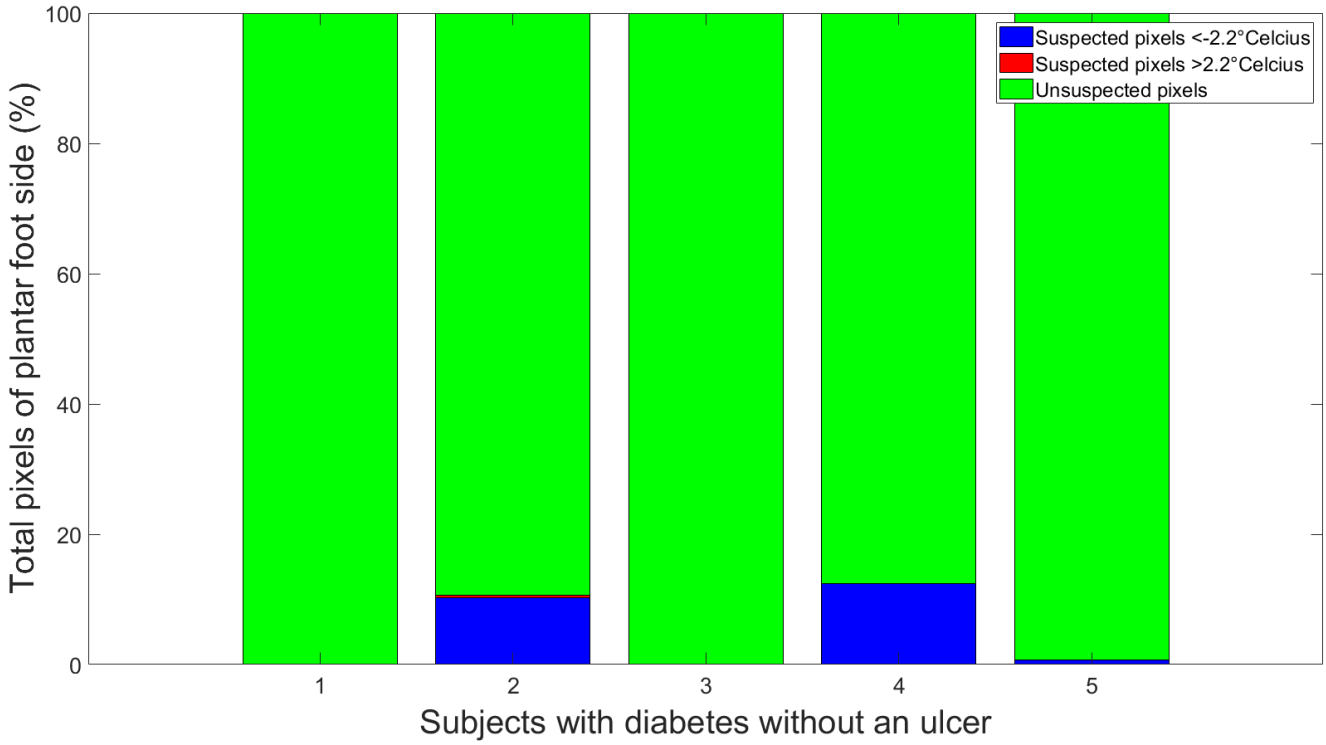

Figure 31: Bar graph with percentages unsuspected and suspected pixels of indirect measurements of plantar foot side in diabetic subjects without an ulcer.

E.3.3 Visualisation tagged maps of subjects with diabetes and an ulcer

Figure 32 shows two examples of subjects with a sufficient percentage of suspicious pixels with a temperature >2.2°C to be defined as 'suspected'. However, these suspicious pixels are not located on the ulcer location. In subject 13 the ulcer location can be identified visually on the hallux and in subject 30 on the midfoot.

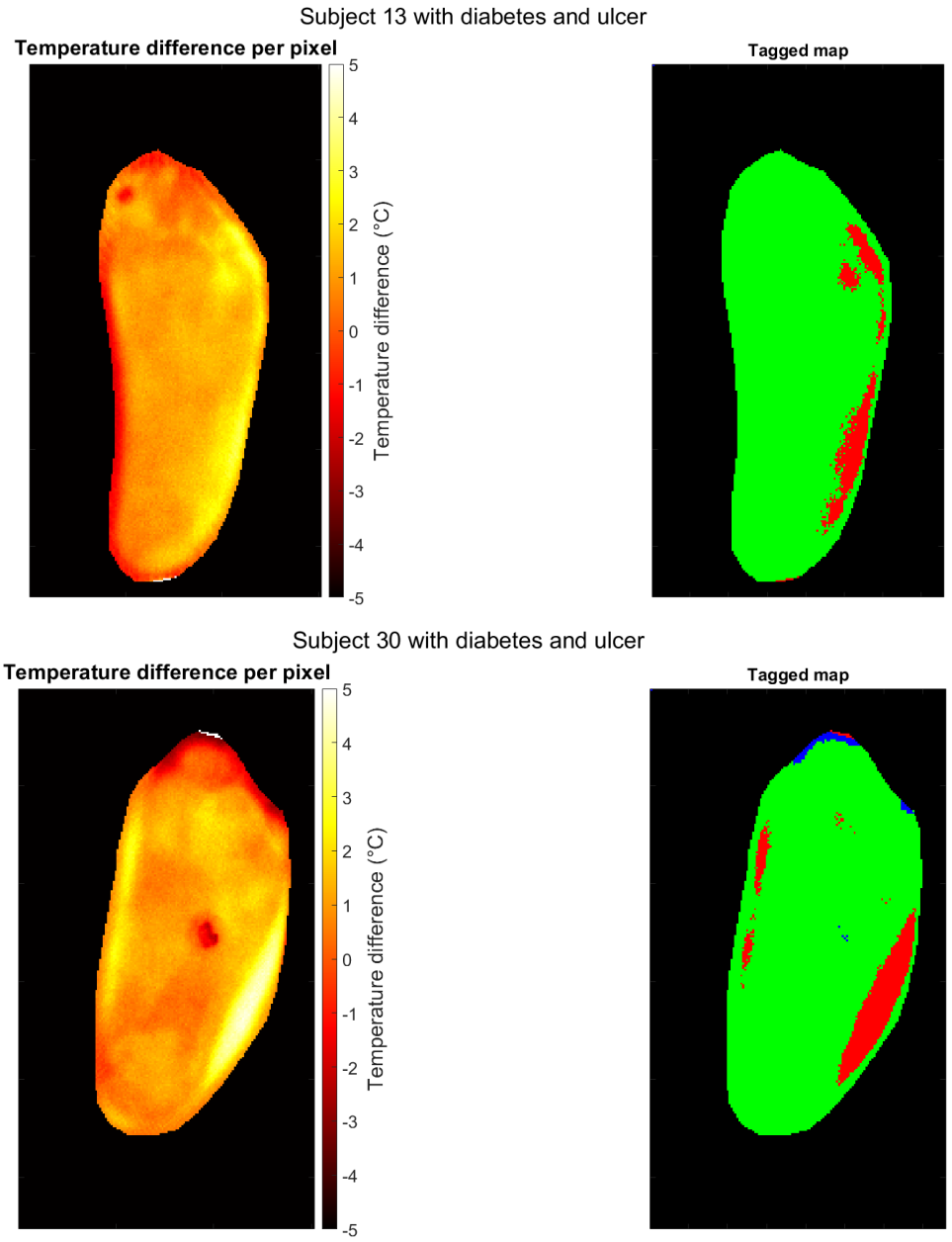

Figure 32: Diabetic subjects with an ulcer. The left image shows the difference at pixel level in °C and the right image shows the tags assigned to each pixel. The green pixels are non-suspicious pixels, the red pixels are suspicious pixels >2.2°C and the blue pixels are suspicious pixels <-2.2°C.

F Appendix: Additional information about measurements in healthy subjects

This appendix reports all deviations in measurements of healthy subjects. In table 9 the numbers are corresponds to the day measured, for example all measurements with 1 were measurement at the same day.

Table 9: Overview measurements dates of healthy subjects, with anomalous transport and deviations measurement protocol

Study number	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**	**Day 8**	**Day 9**	**Day 10**	**Day 11**
BM_G001	1	3	7	8	14 H	15 H	28 F	29	35 F	36	
BM_G002	1	2	7	8		14 H	15 H	21 N	22 N	24	
BM_G003	1 N	4	8	10	11	14 H	15 H	18	22	24	
BM_G004	1	3	4	8	10	11	15 H	18	22	24	29
BM_G005	3 A	4 A	7 F	9 A	14 AH	16 A	21 A	23 A	28 A	30 A	
BM_G006	3	4	7	9	14 H	16	21	23	28	30	
BM_G007	3	4	7	8	10	11 H	21 NM	22 N	23	28	
BM_G008	4	7 N	8	11	21	22	28	30 A	31 A	32 A	
BM_G009	8	10	11 H	28	29 H	35	36	43			
BM_G010	8	16	18	21	22	28	35	36 H	43	50	
BM_G011	9 H	11	14 H	16	18	21	23 T	28	30	32	
BM_G012	10	11 H	16	18 i	21	30	35	37 NH	42	46 H	
BM_G013	11 H	15	18 i	21	23	24	29	36 H	37 H		
BM_G014	18	21	22	23	24	30	32	37 H	43	45	
BM_G015	28	29	36	43	45 H	46 H	50	52	57	59	

Legend: A=car, F=bike, M=Motor bike, N=nail polish, H=handheld,
T=Trauma after football training, i=switched measurements

Subject-specific comments

- G001:
  - Day 1: 2nd measurement interrupted, measurement half foot.
  - Day 4: measurement after first patient
- G002:
  - Day 5: Not from this subject, but from subject 4 (day 6)
- G003:
  - Day 10: sunlight interrupt measurement
- G004:
  - Day 3: 2nd measurement started late
  - Day 4: first measurement stopped halfway (but started again after saving)
  - Day 11: Direct and first indirect measurement interrupted by sunlight (due to opening door)

- G005:
  - Day 1: More than 30/32cm between camera and math
- G006:
  - Day 1: More than 30/32cm between camera and math
  - Day 7: flare-up eczema
- G008:
  - Day 1: 2nd measurement > 10 seconds
  - Day 7: measured three times indirect, first measurement does not save due to software error
- G009:
  - Day 4: late measurement (8.30 AM)
- G011
  - Day 7: Trauma wound dorsal due to soccer training (after two weeks again soccer training)
- G013:
  - Day 4: trauma at 2nd toe left, due to tight shoe during jogging
  - Day 6: First indirect measurement not 10 seconds on the mat. Second indirect measurement good, but researcher forgot to stop measurement (measured ¿40 seconds after stepping off math)

G Appendix: Patient Questionnaire

Vragenlijst Badmat (versie 1, 18-1-2023)

Eerst: **standaard uitleg van badmat door onderzoeker: De badmat kan uw voeten meten zonder dat u hiervoor bewust iets voor hoeft te doen. U kunt de badmat plaatsen op een locatie waar u dagelijks met blote voeten staat.**

1. Heeft u in het verleden vaker voetwonden gehad?
    a. Oorzaken?
    b. Locaties?
2. Op welke locaties staat u met blote voeten? Welke locatie zou voor u het meest praktisch zijn.
    a. Is dit een locatie waar u het apparaat, in deze vorm, ook goed zou kunnen neerzetten?
    b. Welke momenten van de dag zijn dat?
    c. Komt u dan net van buiten, of het uit de douche?
    d. Voorziet u problemen voor deze locatie om langdurig op deze mat te staan?
3. Hoe ervaart u het gebruik van de mat? (1-5, 5-zeer prettig/1-zeer onprettig)
    a. Waarom?
    b. Heeft u het gevoel dat u stevig staat op de mat? / Kunt u evenwicht houden?

Deze mat maakt het mogelijk om uw voeten dagelijks automatisch te controleren.

4. Zou u de Badmat dagelijks kunnen en willen gebruiken? (Ja/Nee) zo niet, vertelt u de redenen.
5. Als u mag kiezen tussen 1cm en 3cm mat, welke heeft u voorkeur? (1cm, 3cm, geen voorkeur)
    a. Denkt u dat deze hoogte problemen zal opleveren?
    b. Heeft u moeite met de opstaande rand van de mat?
6. Zou u zelf willen kunnen zien of een meting wel of niet gelukt is?

Het apparaat kan zelfstandig bepalen over er verdachte plekken zijn op uw voet.

7. Zou u zelf direct willen weten over er een verdachte plek is gevonden? Zo ja, hoe zou u daarover geïnformeerd willen worden?
    a. Via mail
    b. Via App
    c. Via website
    d. Anders namelijk:
8. Vind u het goed dat uw zorgverlener een melding krijgt op het moment dat er een verdachte plek is gevonden?
9. Heeft u nog eventuele op-/aanmerking op de Badmat? (Ja/nee) zo ja, horen we het graag.