

Exploratory Thermal Imaging Assessments of the Feet in Patients with Lower Limb Peripheral Arterial Disease

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Abstract Peripheral arterial disease (PAD) is an atherosclerotic condition that can result in reduced lower limb tissue perfusion. It is associated with significant comorbidity including coronary artery disease (CAD) and cerebrovascular disease. One of the most currently utilised diagnostic tools is the ankle brachial pressure index, which is time consuming, requires significant user training and is unreliable in diabetics due to vessel calcification leading to falsely elevated results. The aim of this pilot study was to explore the potential use of thermal imaging in identifying PAD. In 44 patients (24 male; mean (SD) age 67 [12] years) thermal images of three regions of interest (ROI's) on the feet were collected within a normothermic measurement room. The ROI's for each foot included the first toe (T), proximal foot (PF) and whole foot (WF). The ankle brachial pressure index (ABPI) reference test was collected to make a diagnosis of PAD (ABPI < 0.9). Parametric statistics were employed and a p value <0.05 considered statistically significant. Twenty-three patients had significant PAD in at least one leg (Mean ABPI 0.64; Range 0.32–0.86) while 26 patients had a normal ABPI (non-PAD) in at least one leg (Mean ABPI 1.14; Range 0.9–1.46). There were no significant ROI differences between PAD (Mean WF temperature 30.3 °C; SD 0.8) and non-PAD feet (Mean WF temperature 31.0 °C; SD 0.7) for their mean or SD values. The temperature gradient (toe-proximal foot) was close to -1 °C but this was not significantly different between the groups. Furthermore, right minus left whole foot temperature

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differences were not significant. Absolute, gradient, spatial and bilateral skin temperature differences of the feet have been quantified in PAD and non-PAD legs and have found no significant differences overall. This pilot study indicates that thermal imaging from resting measurements is unlikely to be of diagnostic value in detecting significant PAD. Furthermore, the study also raises questions about the apparent misconception that in PAD the foot temperatures are usually significantly reduced.

Keywords Thermal imaging · Peripheral Arterial Disease (PAD) · Vascular disease · ABPI · Cardiovascular disease · Skin temperature

1 Introduction and Research Context

1.1 *Peripheral Arterial Disease (PAD): The Overlooked Cardiovascular Disease with Great Implications*

Peripheral arterial disease (PAD), which is an atherosclerotic process effecting nearly 20% of all people aged over 70 years old worldwide, causes reduced lower limb tissue perfusion [1]. Atherosclerosis results from atheroma (fatty deposits) and can progress to thrombosis and vessel occlusion [2]. This can result in ischaemia, pain, tissue necrosis and potentially even limb loss or death [3].

Atherosclerosis can occur in any vessel within the arterial system leading to not only PAD but ischaemic heart disease (IHD) and cerebrovascular disease, which can result in myocardial infarction (MI) and stroke, respectively [4] (Fig. 1). These conditions are commonly grouped as cardiovascular diseases (CVD) and they have overlap in pathoetiology, diagnosis, prognosis and treatment [5]. The risk factors

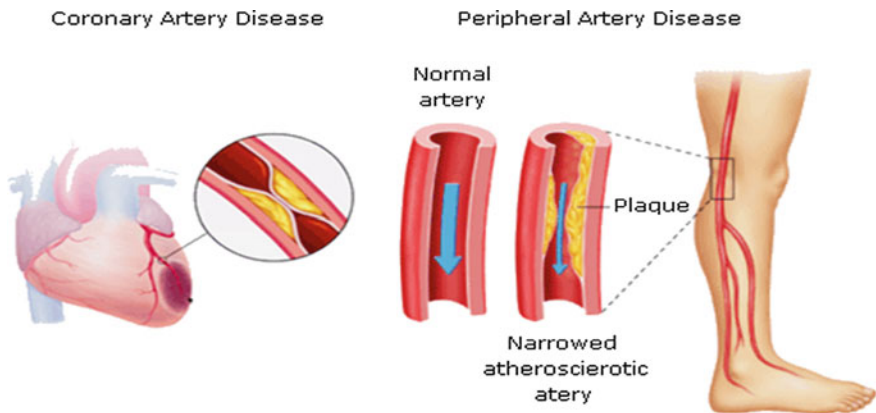


Fig. 1 Atherosclerosis affecting the periphery leading to PAD and the heart leading to CAD and MI. Source <http://www.angioslide.com/USA/Patients/peripheral-artery-disease>

for all CVD's include smoking, high blood pressure, diabetes, high cholesterol, obesity, renal disease and family history of vascular disease [3]. Therefore, diagnosis of PAD should alert to the patient's concurrent risk of MI and stroke. It was found that 65% of PAD patients also have coronary or cerebral artery disease [6]. Thus, improved diagnosis of PAD may have the added benefit of leading to earlier diagnosis of other CVD's and the improved outcomes secondary to earlier identification and management.

The most common symptom of PAD is intermittent claudication, defined as the repeatable, predictable onset of pain in the lower limbs (typically in the calf) that occurs on exertion as a result of impaired blood delivery and reduced oxygen supply to the muscles. The pain is characteristically worse uphill, and as disease progression occurs the distance a patient is able to walk before they have to stop due to pain will shorten. Pain resolves with rest and predictably re-occurs again on exertion. There are a number of classification systems of PAD which consider claudication distance such as the Fontaine and Rutherford classification systems [3]. As disease progresses, patients may suffer with rest pain and eventually develop arterial ulcers and gangrene, known as critical limb ischaemia (CLI), which once established leaves the patient with only a 50–60% five-year survival [7].

However, patients do not always give a clear history of their symptoms and especially in the early stages of the disease it can be difficult for the physician to confidently identify PAD. Other conditions that may produce similar pain include lumbar spinal stenosis (neurogenic claudication), osteoarthritis, chronic venous insufficiency and degenerative disc disease, which need to be excluded. On examination, the PAD patient's feet and legs may feel cold, hairless and a pulse may not be palpable. In severe disease, arterial ulcers and tissue necrosis/gangrene may be observed.

Investigations include screening for risk factors such as performing blood tests (total cholesterol, LDL cholesterol, triglycerides, blood glucose, HBA1c, C-reactive protein, urea and electrolytes) and electrocardiography (ECG). More specific investigations within a primary care setting include performing the ankle brachial pressure index (ABPI), which involves measuring the blood pressure from the upper and lower limbs of a patient in the supine position after they have rested for 10 min and calculated performing the following calculation:

$$\text{ABPI} = \frac{\text{*Leg systolic BP}}{\text{Highest arm systolic BP}}$$

* Performed on each leg to calculate an ABPI for both legs, usually using the highest of dorsalis pedis (DP) and posterior tibial (PT) arterial pressure measurements.

The value calculated can then be cross-referenced to the table below

ABPABPI score	Diagnosis
0.9–1.3	Normal
0.5–0.89	Mild/moderate PAD
<0.5	Severe PAD

Typically, values greater than 0.9 are considered normal, however, arterial calcification can lead to an ABPI result of greater than 1.3 due to reduced vessel compressibility. This can result in the arterial calcification masking arterial stenosis leading to a falsely reassuring ABPI. In addition, arterial calcification is common in diabetics who are also twice as likely to have PAD [8]. Therefore, the ABPI is potentially missing patients who have one of the highest risk factors for PAD, which is another limitation of the test. Furthermore, the ABPI requires the patient to lie in a supine position for 10 min before performing a measurement, which places a significant time commitment on a busy GP service. In order to perform the ABPI correctly also requires an element of formal training and expertise.

Once a patient is suspected to have PAD, they are referred to secondary care for definitive imaging via ultrasound Doppler of the lower limb arteries, often followed by either magnetic resonance angiography (MRA) or computed tomography angiography (CTA), which is able to identify the severity and level of an arterial stenosis/occlusion. First-line management is through modification of lifestyle factors followed by endovascular procedures such as angioplasty and stenting. Only in severe PAD, when a patient's quality of life is significantly impaired, surgery is considered an option. This would include bypass operations or amputation.

However, further objective, reliable screening tests for PAD that could be used in primary care are required due to the limitations of ABPI outlined above [9]. This is where the potential use of thermal imaging in identifying PAD arose. It is widely thought that a patient who has PAD would have reduced limb perfusion, leading to a reduction in skin temperature at the feet. We propose in this work that if a reduced skin temperature in PAD patients exists, then it would be identified using an infrared thermal imaging camera.

1.2 Thermal Imaging: The Fast, Non-contact Solution to Improved Diagnosis of PAD in Primary Care?

For thousands of years a raised body temperature, in the form of a fever, has been recognised as an indication of illness. Around 400 BC Hippocrates wrote “Whatever part of the body excess of heat or cold is felt, the disease is there to be discovered” [10]. A fever is the generalised, symptomatic manifestation of the presence of inflammation, infection or malignancy within the body. In addition,

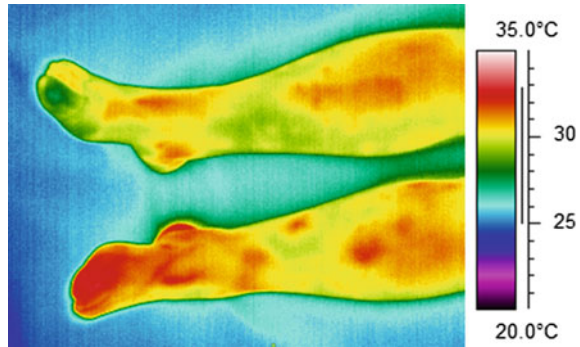
increased localised skin temperature has also long been recognised as an indicator of local pathology, perhaps the most well known being the red, hot great toe which occurs in gout and or the hot, swollen joints of the hand in rheumatoid arthritis. Whether generalised or localised, the change in skin temperature is recognised as the presence of illness or pathology. This is because injury, infection, inflammation or malignancy is associated with localised vasodilation leading to tissue hyper-perfusion to the affected area and increased metabolic processes, all which lead to a higher emitted temperature [11]. The detection of increased body temperature in illness was purely subjective until the invention of the thermometer in the seventeenth century when objective measurements could then be made [12]. Traditional glass thermometers worked through detecting temperature changes via conduction but heat also leaves the body via radiation, evaporation and convection. It remained difficult to objectively measure the temperature of specific areas of the body until the invention of the first electronic sensor of infrared radiation in 1934 and the developments in infrared sensors since then [12].

Infrared thermal imaging involves the identification and quantification of naturally emitted infrared radiation from skin which is then represented as an infrared thermogram [13]. The different areas of skin temperature are represented as different colours on the thermogram making the image easily interpretable. It also has the advantages of being noninvasive, non-contact, quick and sensitive. The technology has progressed considerably since the first published paper which presented the use of infrared thermal imaging in preclinical diagnosis of breast cancer in 1956 [14]. Thermal imaging cameras are now able to detect differences in skin temperature at much smaller scales and with increased spatial accuracy. This has led to its increased use as a medical imaging tool with a vast number of potential applications including diabetes, Raynaud's Disease, the detection of breast cancer and the identification of flap viability in reconstructive surgeries [14].

However, despite the increasing research interest and potential clinical applications of thermography, often the clinical interpretation of the results remains challenging. This is because the relationship between skin temperature and skin perfusion is complex. It depends on many factors including site (central vs. peripheral), skin thickness, perspiration, core body temperature and ambient room temperature [9]. In addition, ingestion of caffeine or alcohol and certain drugs can affect skin temperature. Pertinently, the change in skin temperature in relation to blood flow may depend on whether the change in blood flow has occurred for physiological adaptation, for example due to a change in ambient temperature, or in response to pathology (Fig. 2).

Nonetheless, it is often taught to medical students learning to examine a patient for peripheral arterial disease to feel for skin temperature, as a limb with arterial disease may be cooler than a limb without blockage [1]. This is because it is thought, possibly incorrectly, that reduced blood flow to the limb may result in reduced cutaneous limb temperature that may provide the physician with a further clinical sign to help make a diagnosis. There have been a number of studies which have correlated skin temperature with PAD, however most studies have evaluated subjective assessments of skin temperature. A large scale cross-sectional study

Fig. 2 Thermal imaging of a PAD patient. A PAD patient with a cool right foot (ABPI 0.53; whole foot temperature 30.4 °C) and a warmer left foot (ABPI 0.86; whole foot temperature 31.3 °C). There is only a physiologically small difference in skin temperature between the feet despite having clearly asymmetric PAD



performed in the Netherlands in 1997 which evaluated the diagnostic value of signs and symptoms of PAD in primary care found a relatively high specificity of palpating skin temperature and a diagnosis of PAD. Interestingly, in the same study, there was no diagnostic value in the patients reporting of cold feet [15].

The use of thermal imaging to detect peripheral vascular disorders including venous insufficiency, Raynaud's phenomenon and diabetes, has been studied previously, with some interesting observations. Bagavathiappan et al. [16] published a case series of four patients in which thermal imaging was concluded to reliably detect vascular diseases including chronic venous insufficiency and arterial obstruction. Distal tissues were found to be cooler than more proximal, surrounding tissue which was hypothesised to be due to arterial obstruction, whereas areas of venous compromise were warmer than surrounding skin, due to tissue inflammation [16]. In Clark et al. [17], the comparison of laser Doppler and thermal imaging in the detection of digital blood flow in Raynaud's was poorly correlated, however, in Schlager et al. [18] good correlation between thermal imaging and skin perfusion (determined using laser Doppler perfusion imager) was demonstrated in patients with Primary Raynaud's Phenomenon. In Cheng et al. [19] thermal imaging was demonstrated to be able to identify poor blood supply surrounding diabetic ulcers and Sivanandam et al. [20] demonstrated reduced peripheral foot temperature in type 2 diabetes mellitus, which correlated with HbA_{1c} level. Ring [21] concluded in a review paper that thermal imaging is useful in the assessment of peripheral circulation in diabetes mellitus. In diabetic neuropathy, the thermoregulatory mechanisms are no longer functioning correctly leading to impaired neurovascular function and abnormal skin temperature [21].

However, there is limited evidence in the literature of the use of thermal imaging in detecting PAD. A study by Huang et al. [22] demonstrated that resting skin temperatures between PAD and control subjects were non-significant. However after a 6-min exercise test, the feet of PAD patients was either the same as or cooler than at rest but in the control group the feet were warmer or the same as at rest [22].

Therefore, the aim of this pilot study was to explore the potential of thermal imaging in identifying PAD. In this chapter, we describe the results of 44 patients who had thermal images taken of their feet, looking specifically at three regions of interest

(ROI) and the correlation of peripheral skin temperature with evidence of peripheral arterial disease, as diagnosed by ABPI. The results of this study may inform as to whether there is potential use of thermal imaging in the diagnosis of PAD.

2 Methods

Vascular measurements comprised ABPI and TI (thermal imaging). Thermal imaging was performed in a temperature-controlled microvascular imaging facility, based in the Medical Physics Department at Freeman Hospital, Newcastle upon Tyne. The room has a normothermic control which allowed all experiments to be performed at 25 °C.

Vascular patients were recruited from the Northern Vascular Centre (NVC) wards or NVC outpatient clinics. Healthy controls were recruited from hospital staff and local retired engineering groups. After consent was gained for the study, participants were asked to remove their shoes and socks, ensuring they were bare from the mid-shin down before lying supine on a standard medical examination couch. Participants were acclimatised at rest for at least 10 min in the measurement facility to allow for thermal equilibration before imaging took place.

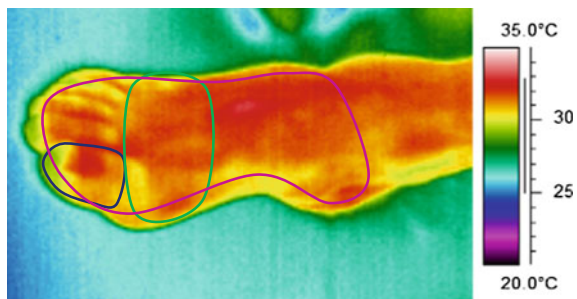
Thermal imaging was performed using a FLIR SC300 (FLIR Systems) with standard view lens. The thermal camera was placed on an imaging stand that was placed approximately 1 m above a patient's legs so that both feet were captured in the same image. All images were taken by 1 thermal imaging operator (JA).

Ankle brachial pressure index (ABPI) measurements were performed shortly after the thermography using standard methods. An ABPI value of <0.9 was considered as diagnostic for significant PAD.

Thermal images of three regions of interest (ROI's) on the feet were collected from each patient. The ROI's for each foot included the first toe (T), proximal foot (PF) and whole foot (WF) (Fig. 3). The thermal imaging analysis was performed by a single operator (DK).

Thermal images were visualised and analysis was performed using FLIR ThermoCAM Researcher Pro 2.10 software. Temperature was colour-coded using a rainbow palette across a range of 18–36 °C.

Fig. 3 Regions of interest (ROI). (1) First toe (T) (*blue outline*), (2) Proximal foot (PF) (*green outline*), (3) Whole foot (WF) (*purple outline*)



Three ROI's were measured, as described above. The mean temperature of each respective ROI was calculated and results were exported to a Microsoft Excel spreadsheet for analysis. Parametric statistics were employed using Minitab Statistical Software (Version 17) and a p value <0.05 considered statistically significant. Data were mainly displayed graphically using nonparametric statistical measures. Numerical summaries for the data were provided using parametric measures and with standard parametric statistical tests used throughout.

3 Results

A total of 44 patients were studied (24 male; 20 female) with a mean age of 67 ± 12 years (range 44–91 years old). The mean height was 168 cm [(Range 152–181 cm); mean PAD group 167.2 cm; non-PAD 168.2 cm]. Mean weight was 78 kg [(Range 51–111 kg) mean PAD group 80 kg; mean non-PAD 76 kg] Mean BMI 27.8 [(Range 20.8–38.4) mean PAD group 28.6; mean non-PAD 26.9]. There were a total of eight patients with diabetes in the study, seven in the PAD group (five non-insulin dependent diabetic (NIDDM); two insulin dependent) and one in the non-PAD group (1 NIDDM).

Twenty-three had significant PAD in at least one leg [mean ABPI: 0.64 (SD 0.15)]. Five patients were found to have PAD in only one leg, which provided interesting individual comparison. There were no significant ROI differences between PAD and non-PAD legs for their mean or SD values (Figs. 4 and 5). However, the mean temperature of PAD feet at each ROI was close to 0.6 °C cooler

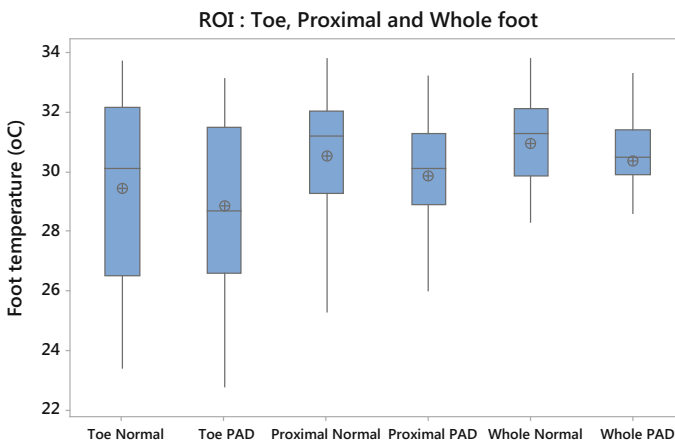


Fig. 4 ROI average temperature for PAD versus non-PAD. Figure shows the mean (as cross within circle), the median (as line within boxplot), interquartile range (either ends of the main box) (IQR (25–75%)), lower and upper quartile ranges with outliers removed (either end of the lines). There was no significant difference in ROI average between PAD and non-PAD legs ($p \geq 0.05$)

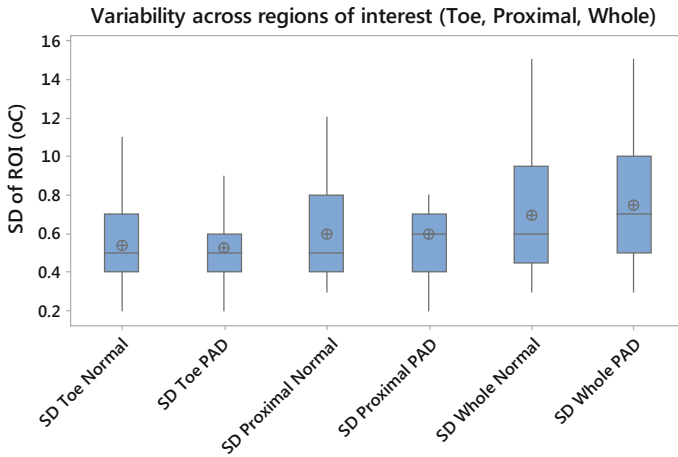


Fig. 5 Variation across each ROI (using SD values) for PAD versus non-PAD. Figure shows the mean (as cross within circle), the median (as line within boxplot), interquartile range (either ends of the main box) (IQR (25–75%)), lower and upper quartile ranges with outliers removed (either end of the lines). There was no significant difference in ROI SD between PAD and non-PAD legs ($p \geq 0.05$)

Table 1 Temperature gradients for each ROI expressed using mean and SD values for PAD and non-PAD groups

	Toe (°C) (SD)	Proximal (°C) (SD)	Whole foot (°C) (SD)
PAD	28.9 (0.53)	29.9 (0.60)	30.4 (0.75)
Non-PAD	29.4 (0.54)	30.6 (0.60)	31.0 (0.70)

The foot is progressively warmer as you move proximally, but there is no significant difference in temperature gradients between groups

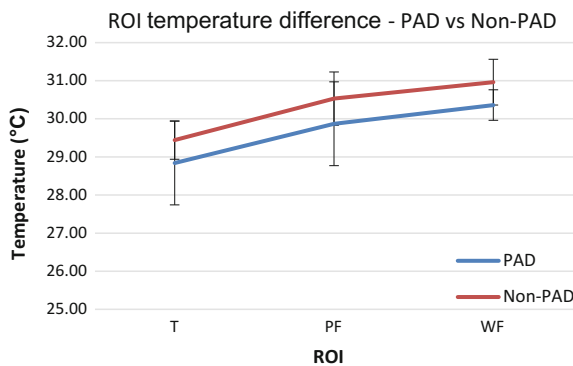


Fig. 6 ROI temperature difference between PAD and non-PAD patients. PAD feet are approximately 0.5 °C cooler than non-PAD feet across each ROI, which was non-significant. In addition, the temperature gradient from toe to proximal foot was close to -1 °C but this was also non-significant. (T First Toe; PF Proximal foot; WF Whole foot). ROI Region of interest

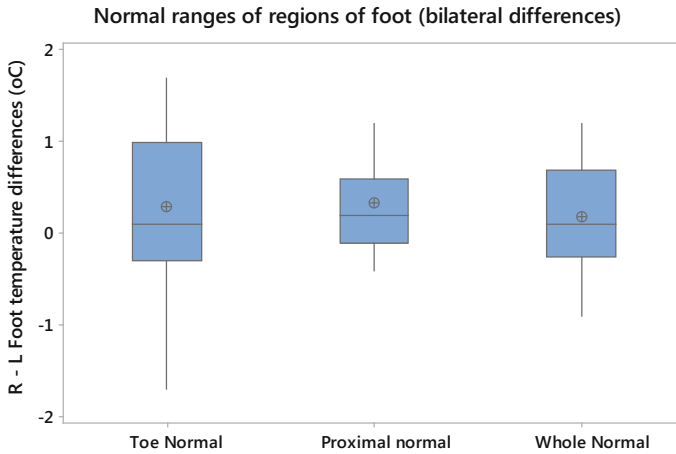


Fig. 7 The Bilateral differences in non-PAD patients. Figure shows the mean (as *cross within circle*), the median (as *line within boxplot*), interquartile range (*either ends of the main box*) (IQR (25–75%)), lower and upper quartile ranges with outliers removed (*either end of the lines*). There were no significant right minus left ($R - L$) differences in non-PAD patients. The 95% CI of the differences for the whole foot would be -0.9 to $+1.2$ °C

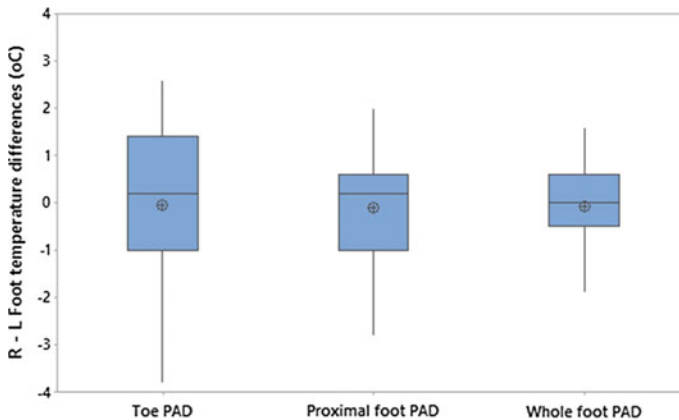


Fig. 8 The Bilateral differences in PAD patients i.e. with PAD in at least 1 leg. Figure shows the mean (as *cross within circle*), the median (as *line within boxplot*), interquartile range (*either ends of the main box*) (IQR (25–75%)), lower and upper quartile ranges with outliers removed (*either end of the lines*). Overall, there were no significant $R - L$ differences in PAD patients. However, there was significantly wider variance seen in PAD group ($p < 0.05$: for whole foot and proximal foot)

than non-PAD feet, which was statistically non-significant. The temperature gradient (toe-proximal foot) was close to -1 °C but this was not significantly different between groups (Table 1; Fig. 6). Right–left whole foot temperature differences were also not significant (Figs. 7 and 8).

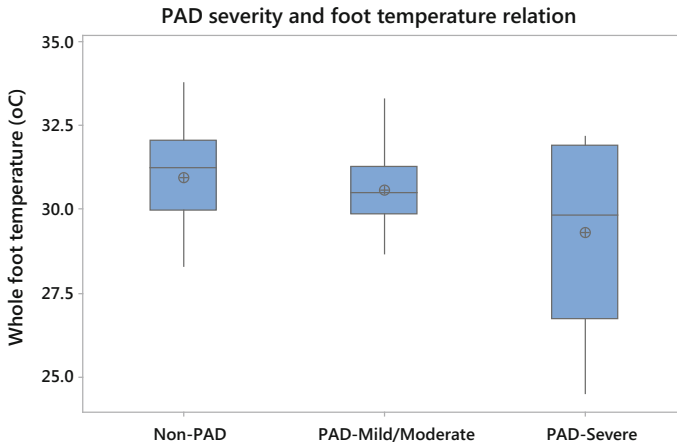


Fig. 9 The whole foot temperature is no different between healthy subjects and patients with mild/moderate PAD. Figure shows the mean (as cross within circle), the median (as line within boxplot), interquartile range (either ends of the main box) (IQR (25–75%)), lower and upper quartile ranges with outliers removed (either end of the lines). In the higher grade PAD (ABPI < 0.5) the foot temperature appears reduced only in a fraction of the patients

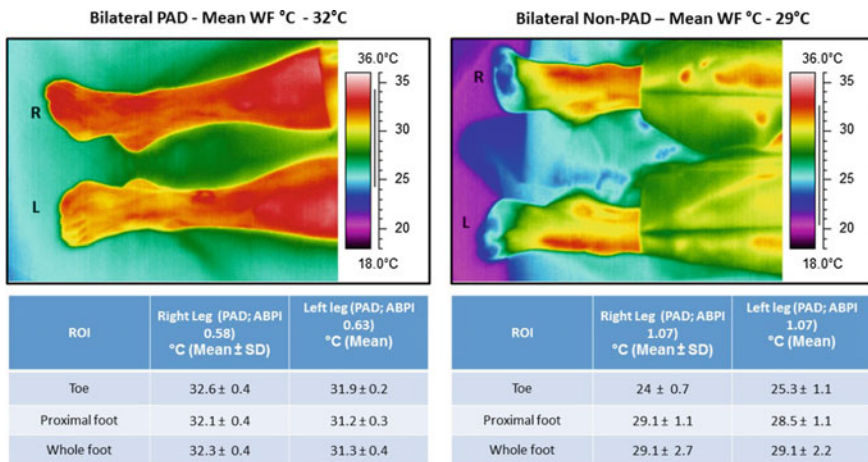


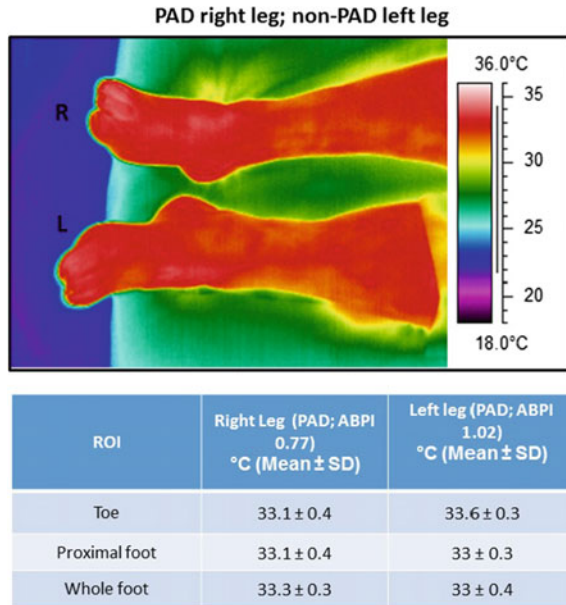
Fig. 10 Example thermograms highlighting the range of normal for toe temperatures since healthy subjects can have very cold toes without arterial pathology. In the cases shown the PAD patient has bilateral disease (*left panel*) with feet at 32 °C and the healthy subject has cooler feet at 29 °C

There was no significant difference between foot temperature in non-PAD subjects compared to PAD patients with mild/moderate disease, but appeared to be reduced in some of the severe PAD subjects but was not significant overall (Fig. 9). Individual patient examples of this point are given in Figs. 10, 11 and 12.

Some examples of patients who had one PAD (ABPI < 0.9) foot and one non-PAD (ABPI ≥ 0.9) foot

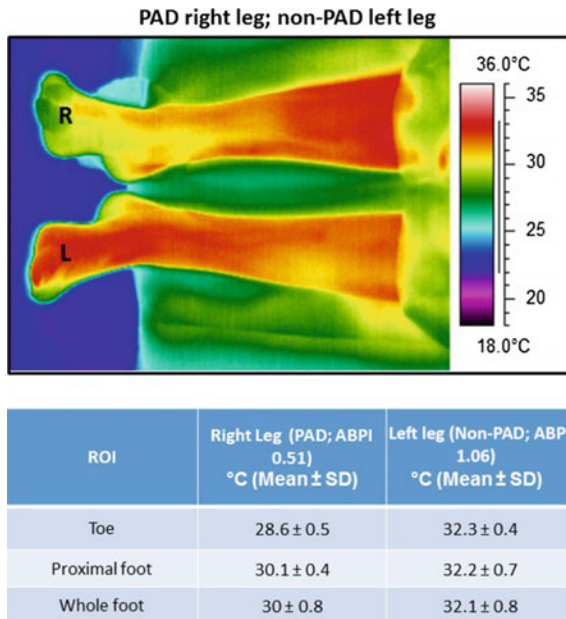
Example 1

Fig. 11 No significant temperature differences between the right PAD leg (ABPI 0.77) and the left non-PAD leg (ABPI 1.02)



Example 2

Fig. 12 The *right* PAD first toe (ABPI 0.51) is close to 4 °C cooler than the *left* non-PAD first toe (ABPI 1.06). In addition, the right foot is approximately 2 °C cooler for the proximal and whole foot ROI's



4 Discussion and Summary

In this pilot study, we have quantified absolute, gradient, spatial and bilateral skin temperature differences in PAD and non-PAD legs and have found no significant differences between groups. However, a trend towards cooler feet in PAD patients of close to 0.6 °C was observed, but this was non-significant overall. Good perfusion of superficial tissues was maintained despite PAD. This pilot study indicates that thermal imaging is unlikely to be of diagnostic value in detecting significant PAD. The BMI of patients in the PAD group was approximately 2 kg/m² greater than the non-PAD group and patients in the PAD group were also more likely to be diabetic (PAD group 8; non-PAD 1). This is consistent with the expected co-morbidities of a PAD patient, as it well known that being overweight and diabetes are significant risk factors for the development of PAD.

There are a number of reasons as to why there were no significant differences observed between the temperature of PAD and non-PAD feet. First, it is possible that the sample size in this pilot study was insufficient to reach statistical power and with increasing patient numbers, significance may become apparent. However, temperature differences would still be small and detection through skin palpation as part of a clinical examination would be unlikely to sense a significant difference in individual patients.

The microcirculation of the peripheral tissues is partly controlled via the autonomic nervous system and thermoregulation mechanisms. Therefore, despite reduced gross tissue perfusion to the distal tissues in PAD, the superficial tissues are compensated via the autonomic response of the microcirculation, which results in maintained cutaneous temperatures. In addition, thermal imaging techniques are highly sensitive to detecting differences from so-called normal values. However, thermal imaging is not able to inform us as to why such a deviation exists. This is why care is always required when interpreting thermal images in the clinical context. For example, in PAD, as a consequence of impaired tissue perfusion, tissue necrosis may occur. Tissue necrosis may result in increased metabolic response of the tissue, leading to the accumulation of catabolic waste products which are known to be vasodilatory. As a consequence, tissue inflammation may be increased as part of the immune response towards necrosis, leading to increased heat production despite reduced gross perfusion to the tissues. Therefore, despite reduced perfusion to the feet due to PAD, thermal imaging is unable to detect the changes as cutaneous temperature is maintained and often even elevated, due to inflammation.

Furthermore, we have indicated that it is only at the extremes of PAD (e.g. ABPI < 0.5) that a reduced temperature begins to become apparent. Perhaps once such severe disease is established compensatory microcirculatory autonomic mechanisms that were maintaining skin perfusion and hence normal skin temperature are overwhelmed and the foot then becomes palpably cold. It is also possible that if the study was performed at a cooler room temperature, the effects of reduced tissue perfusion due to PAD would become more apparent. There is scope for

further work and future studies should consider disease severity across the spectrum of PAD in relationship to measurement room ambient temperature and thermal imaging diagnostic test accuracy in PAD.

Nevertheless, this study has revealed some interesting findings. Not least whether it is still valid to teach medical students, as part of a clinical examination of the vascular system, to palpate for skin temperature, as an indication of potential peripheral arterial disease. Perhaps, assessing skin temperature as part of a peripheral vascular examination has been a long held misconception that holds limited diagnostic weight.

However, it is apparent that further PAD detection tests are still required which may be informed from the observed findings in this pilot study. Other infrared-based technologies such as photoplethysmography (PPG) have been shown to possess diagnostic value although this is based on near infrared rather than far infrared technology [9, 23]. In PAD, the PPG waveform becomes damped and delayed, even for lower grade disease. The nature of PPG signals however is not well understood. We believe that a future cross-comparison of thermal imaging and PPG in PAD could help in the understanding of such technologies and the development of reliable tests.

In summary, we found no significant differences in the overall absolute, gradient, spatial or bilateral skin temperature differences between PAD and non-PAD legs. This pilot study indicates that thermal imaging from resting measurements is unlikely to be of diagnostic value in detecting significant PAD. Furthermore, it also raises questions about the apparent misconception that the foot temperatures are always significantly reduced in a patient with PAD. Finally, reliable fast, non-invasive devices for the detection of PAD are still required to aid the diagnosis of this under-diagnosed but significant cardiovascular disease.

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