Thermography and Thermometry in the Assessment of Diabetic Neuropathic Foot: A Case for Furthering the Role of Thermal Techniques

M. Bharara, MSc, J. E. Cobb, PhD, CEng, and D. J. Claremont, MSc, DPhil, FIPEM
Academic Biomedical Engineering Research Group, Bournemouth University, Bournemouth, UK

There are currently 3 established techniques employed routinely to determine the risk of foot ulceration in the patient with diabetes mellitus. These are the assessment of circulation, neuropathy, and foot pressure. These assessments are widely used clinically as well as in the research domain with an aim to prevent the onset of foot ulceration. Routine neuropathic evaluation includes the assessment of sensory loss in the plantar skin of the foot using both the Semmes Weinstein monofilament and the biothesiometer. Thermological measurements of the foot to assess responses to thermal stimuli and cutaneous thermal discrimination threshold are relatively uncommon. Indeed, there remains uncertainty regarding the importance of thermal changes in the development of foot ulcers. Applications of thermography and thermometry in lower extremity wounds, vascular complications, and neuropathic complications have progressed as a result of improved imaging software and transducer technology. However, the uncertainty associated with the specific thermal modality, the costs, and processing times render its adaptation to the clinic. Therefore, wider adoption of thermological measurements has been limited. This article reviews thermal measurement techniques specific to diabetic foot such as electrical contact thermometry, cutaneous thermal discrimination thresholds, infrared thermography, and liquid crystal thermography.

Key words: *diabetic foot, neuropathy, thermological measurements, liquid crystal thermography*

Previous reviews[1-3] on thermological techniques have described the requirements, available transducers, and applications without focusing on any special technique/sensor for assessment of the diabetic foot. The aim of this article is to summarize the performance of such thermal measurement techniques as thermal perception thresholds, electrical contact thermometry, infrared thermography, and liquid crystal thermography (LCT) specifically for diabetic foot assessment.

The study of thermal patterns under the foot is potentially useful in the clinical management of the diabetic foot.[4,5] Progressive degeneration of sensory nerve pathways is thought to affect both thermoreceptors and mechanoreceptors.[6,7] High temperatures under the foot coupled with reduced or complete loss of sensation can predispose the patient to foot ulceration.[5,8] An approach combing routine measurements and thermal techniques may improve the quality of research in diabetes and facilitate detection/control of diabetic foot problems. This aim is keeping with the guidelines of the St. Vincent's Declaration that targets a 50% reduction of lower limb amputations due to diabetic foot complications.

THE DIABETIC FOOT

Diabetes mellitus is a disease with multisystem complications. Currently, there are 1.8 million people suffering from diabetes in the United Kingdom.[9] Recent statistics by the American Diabetic Association suggest that the prevalence of diabetes in the United

Correspondence should be sent to: M. Bharara, P238, Poole House, Bournemouth University, Bournemouth, BH12 5BB United Kingdom, e-mail: mbharara@bournemouth.ac.uk.

Conflict of interest: None

DOI: 10.1177/1534734606293481

States is 18 million and the onset of type 2 diabetes mellitus preceded its diagnosis by a mean 7 years.[10] The diabetic foot is a major long-term complication of type 2 diabetes mellitus.[11-14]

Primary etiologic factors of diabetic foot disease include peripheral neuropathy and peripheral vascular disease (PVD).[8,15] The risk of hospital admission for PVD, neuropathy, and ulceration is greater for patients with diabetes.[16] Fifty percent of patients with diabetes have some degree of neuropathy, resulting in at least 1 foot ulcer during the lifetime in 15% of the cases.[17] Clinical guidelines suggest foot ulcers occur in 5% of diabetic patients in the United Kingdom.[18] Foot ulcers are the main cause of lower extremity amputation in patients with diabetes,[12,19,20] resulting in a huge economic burden for health services.

Ulcers invariably occur as a consequence of interaction between environmental hazards and specific changes in the lower limbs of certain patients.[15,21] Such factors as microangiopathy and autonomic neuropathy, together with loss of sensation, high foot pressures, local deformity, trauma, and susceptibility to infection,[16] lead to a propensity for foot ulcers. The insensate foot is prone to ulceration, especially at sites of abnormal pressure such as the prominent metatarsal heads.[8] Classic neuropathic ulcers occur frequently on the plantar surface but may occur on medial and lateral surfaces.[8]

Several studies have identified neuropathy as important in the impairment of blood flow in the diabetic foot.[22,23] Flynn and Tooke[24] suggested that patients with long-standing neuropathy may have poor regulatory mechanisms and hence altered blood flow. Microcirculatory dysfunction is considered to be associated with foot ulceration.[25] Cutaneous microvascular blood flow in diabetic patients is abnormal.[22-24] This is linked to existing neuropathic complications that alter the regulatory mechanisms controlling blood flow. Laser Doppler studies of diabetic foot[26-28] confirm these findings.

Foot ulcers can be classified as neuropathic, neuroischemic, and ischemic. It is suggested that on average, the rate of occurrence for neuropathic ulcers is 40%, whereas the rate of occurrence for ischemic ulcers is just 10%.[15,29] One of the longer studies in the United Kingdom, involving 6336 diabetic patients, showed a 58% and 16% rate of occurrence for neuropathic and ischemic ulcers, respectively, in type 2 diabetic patients.[30] The study population was limited to tertiary referrals. It is important to discriminate between the neuropathic and neuroischemic foot; the clinical presentation of these conditions is different, and so are subsequent therapeutic strategies.[31] Three parameters that may be used for identification of neuropathy or neuroischemia in the diabetic foot are skin temperature, pain, and the Ankle Brachial Pressure Index (ABPI).[8] Of these, both temperature and ABPI are objective measurements, with the latter being widely available. It is important to point out that ABPI in the diabetic foot may be subject to errors (falsely high) on account of stiffening of the intimal layer of the arteries that is known to occur.

ASSESSMENT OF DIABETIC NEUROPATHY

The clinical criteria for diagnosing complications of diabetic foot is known. It is common in clinical practice to assess the presence and extent of peripheral neuropathy to identify risk for foot ulceration. Diabetic neuropathy accounts for almost 60% to 80% of foot ulcers,[11,12,19,29] especially on the plantar surface of the foot at areas subjected to high pressure during walking. Traditionally, the Semmes-Weinstein monofilament (SW) is used though biothesiometry may also be used for the assessment of neuropathy.[7,32] According to the National Institute of Health and Clinical Excellence (NICE) guidelines, neuropathy may be detected by using a 10-g SW nylon monofilament that buckles at a reproducible stress and measures cutaneous pressure perception threshold. A vibration perception threshold of greater than 25 V is also considered to be consistent with the presence of neuropathy. However, these methods are subjective, and to the authors' knowledge, objective data in support of specific sites to be tested and minimum number of insensate sites required for prediction of foot ulceration have not been published.[32]

IMPORTANCE OF THERMAL MEASUREMENTS IN DIABETIC FOOT

Presently, clinicians assess circulatory function, neuropathic complications, and pressure distribution under the foot on its plantar skin (where the technique is available) to identify the risk of foot ulceration.[33] This combined approach is accepted in diabetic clinics and research centers as a means of preventing the onset of foot ulceration. NICE guidelines suggest considering the risk category of patients and the relative contribution of all contributory factors and incorporating the respective management strategies for the treatment of diabetic foot disease.

Pathways leading to ulceration and the underlying pathophysiology have been well described, although there is a lack of unanimity among workers. A reliable

diagnosis based on clinical presentation and appropriate tests may help to reduce the risk of foot ulcers.[12] The diagnostic criteria for diabetic foot is well documented in literature.[33]

Modern medical imaging techniques such as magnetic resonance imaging, scintigraphy, radiography, and ultrasonography are now routinely used to test the bone and vascular supply to the peripheries and the foot. Thermography and scintigraphy (to detect infection in the bone) are also used. Although imaging is used for a broad range of clinical conditions, its application in diabetic foot is recent.[14,34-37] Traditionally, clinicians use careful visual inspection of the superficial skin surface followed by histopathology of the biopsy samples. The authors' research group is involved in a collaborative research initiative, using thermal imaging to determine the association between thermal changes in plantar foot and sensory loss in diabetic foot disease.

Thermal changes under the plantar foot may be the result of vascular insufficiency, diabetic neuropathy, skeletal changes, infection, or a combination of these factors. The reactive hyperemia that follows a period of loading of healthy skin in an upright individual is impaired in the foot of a patient with neuropathy.[22,26] Systemic thermal stimulation increases skin blood flux (as assessed using a laser Doppler flowmeter) through reduced sympathetic neural action on arteriovenous (AV) shunts, whereas local heating affects capillary perfusion irrespective of sympathetic neural activity.[38-40] A laser Doppler study[23] demonstrated impaired hyperemic response to thermal injury in type 1 diabetic patients on the skin over the dorsum of the foot.

It has been suggested that diabetes disturbs unmyelinated nerve fiber function prior to and more severely than large fiber function.[6,41] The neuropathic foot exhibits increased skin temperature and heightened coloration under rest, indicative of increased blood flow.[24] There is supporting evidence from other studies.[4,5] These findings lend support to the hypothesis of the capillary steal theory, which incorporates AV shunting.[42] There are 2 main types of capillaries involved in skin perfusion: nutritive and thermoregulatory. Thermoregulatory capillaries facilitate in primary heat exchange mechanism to maintain body temperature. The flow in these vessels is controlled by the hypothalamus in response to thermoreceptor signals. Heightened metabolic activity produces vasoactive substances,[43] which trigger the vasodilatory response in skin. This is an autoregulatory mechanism. It leads to a hyperemic response resulting from either a short-term occlusion of the blood vessels or thermal stress. At rest, a minimal part of perfusion supplies nutritional needs, whereas a larger part serves a thermoregulatory function.[44] According to the capillary steal theory, the arterial blood supply bypasses nutritional capillaries through the dermal thermoregulatory capillaries, leading to tissue hypoxia due to maldistribution of skin microvascular blood flow. Mork et al[45] offer a hypothesis similar to the popular capillary steal theory for AV shunting as the pathogenetic factor in erythromelalgia (condition of red, warm, and burning, painful extremities). Mork et al suggested that disease etiology may be of neural or local vasoactive origin. Erythromelalgia is a rare disorder of unknown etiology[45] producing similar symptoms (AV shunting and denervated sympathetic pathways) as in diabetic neuropathy.[46,47] There is another hypothesis (the hemodynamic hypothesis[48]) that argues that microangiopathy leads to rheological changes in blood vessels, a consequence of which is impaired hyperemic response. This involves only nutritive capillaries.

At present, there is not a comprehensive understanding of the significance of small local temperature variation in the lower extremities, especially in patients with diabetic neuropathy. Thermoreceptors are structurally simple and are located near the skin surface, unlike mechanoreceptors. Mechanoreceptors, on the other hand, are of 3 types: slowly adapting, which are sensitive to the intensity of pressure; rapidly adapting; and very rapidly adapting. Both types of rapidly adapting receptors respond to dynamic changes in plantar pressure.[26] Skin temperature changes activate both specific thermoreceptors and tactile receptors. Sensory receptors have a punctuate distribution on the skin surface; that is, specific points are sensitive to specific modalities. Cold receptors are located at a depth of 0.16 mm at the endings of thin myelinated Aδ fibers and increase their firing rate with a decreasing temperature.[49] Warm receptors are located at a depth of 0.45 mm at the endings of slower unmyelinated C fibers and increase their firing rate with increasing temperature.[49] Cold receptors outnumber warm receptors by a factor of 3 to 10 in most areas of the body.[43]

The use of thermal techniques to evaluate diabetic foot has largely remained a research topic. The authors believe that thermal techniques can be significantly useful in diabetic foot assessment, with the intent of determining risk of foot ulceration.

THERMAL MEASUREMENT PARAMETERS FOR DIABETIC FOOT

Measurement of plantar pressure and determination of extent of sensory neuropathy help to determine respective dysfunctions but are of less use in understanding causative factors. Thermological techniques may be used to supplement measurements by providing both qualitative and quantitative data. Skin temperature is a product of influences arising from both internal structures and external conditions. In early stages of diabetic neuropathy, the affected areas on the plantar foot appear as hot spots but later on appear cold because of significant vascular impairment.

There is increased blood flow in the diabetic foot, which is also warm and therefore dissipates heat due to an increased metabolic rate.[4,5,50,51] Dynamic measurements may be sensitive for detection of perfusion abnormalities because of neuropathy in diabetic subjects. The change in temperature when warming or cooling the foot is described by the change in color, heat exchange between surrounding tissue by conduction, heat exchange due to perfusion, and heat production by metabolism. It is therefore appropriate to consider the effect of neuropathy on regulation of blood flow in the foot. Neurogenic modulations result from neuroregulatory processes, which involve feedback from peripheral and visceral thermosensors.[52]

Boyko et al[53] reexamined the association of skin temperature with diabetic neuropathic foot in their study of diabetic subjects. The results showed that diabetic patients with sensory or autonomic neuropathy do not have higher foot skin temperature. These results are contradictory to those published in other studies that report that diabetic neuropathy results in elevated microcirculation in the foot and hence raised foot temperature.[4,5] First, the 2 studies used different thermal modalities, and hence there is no direct correlation between the results. Second, there were no measurements of the healthy controls to assess the range of variation in foot temperatures in the study by Boyko et al.[53] There remains uncertainty with the protocol as to location of the patient feet (exposed to air or on a thermally conductive sheet) and lack of baseline temperature measurements prior to walking.

It is clear that thermological measurements provide data related to influence of total blood flow (ie, both thermoregulatory and nutritional) in the tissue. Results from infrared studies show that the rate of warming, maximum recovery temperature, degree of temperature variation at the anatomical site, and lag time (time interval between onset of thermal stress to onset of cooling/warming) are useful when assessing the response to thermal cycling.[54] The results need to be interpreted carefully before inferring any likely physiological significance.

TECHNIQUES FOR THERMAL MEASUREMENTS OF DIABETIC FOOT

The diagnostic criteria for diabetic neuropathy varies across clinical centers. This variability combined with subclinical (symptomatic with absent clinical or neurophysiological signs) neuropathy in certain diabetic patient groups adds to the problem of identifying patients with increased risk of foot ulceration. It has been discussed that the assessment of small-fiber function can further clinicians' understanding of the extent of neuropathic damage. This can be extremely useful in patients with subclinical neuropathy.[55] Quantitative assessment of small-fiber degeneration offers the possibility of monitoring effects of drugs and metabolic status in lower extremities due to altered glycemic levels in diabetes.

Different methods used clinically to assess small-fiber function can be classified as electrical contact thermometry, cutaneous temperature discrimination thresholds, infrared thermography, and LCT. Each technique is independently discussed in the following sections with a brief background, data-processing requirements, medical applications, and suitability for diabetic foot assessment.

ELECTRICAL CONTACT THERMOMETRY

Electrical contact thermometry in general means use of appropriate transducers (individual or arrays) to measure surface temperature of the body in contact. Thermistors or semiconductor resistors are used for local measurements of skin temperature. Thermocouples are an application of the Seebeck effect, in which 2 different metals under a temperature differential produce a contact voltage or thermal electromotive force (depending on contact site).

Kelechi et al[56] proposed a limit of agreement of ±1.5°C between infrared and thermistor thermometers. This limit of agreement is acceptable as a reference standard for infrared (IR) thermometers to measure localized skin temperature in clinical settings. However, these are suitable only for localized skin temperatures and do not have whole-field capability. Arrays of the size of a human foot or smaller local arrays can be built to measure foot temperatures under the plantar surface of the foot.[57] Fundamental considerations associated with electrical contact

thermometry are response time, calibration, temperature dependence of measured variable, and effects of thermistor/electronic thermometer on the test object. Response time may be expected to depend on measurement conditions, sensor (or probe) size, and its heat capacity. It takes a certain amount of time for the thermistor, depending on the heat capacity, and a certain amount of time to produce an associated change in resistance. Calibration for skin surface measurements is difficult (unlike for fluid calibration). Special thermal phantoms may be developed for comparative measurements, calibrated using electrical surface thermometers. Excessive pressure from the sensor (or probe) could alter the blood supply and hence surface temperature. However, there are issues relating to patient isolation, variable response times for different thermocouple units, compensation electrical circuits for thermocouple units, and real-time data-logging instrumentation.

CUTANEOUS TEMPERATURE DISCRIMINATION THRESHOLDS

Temperature discrimination threshold is a measure of small-fiber function and is clinically relevant as temperature sensation is affected early on in patients with diabetes.[6,41,55] Loss of small-fiber function due to diabetic neuropathy is a major cause of morbidity in diabetic patients.[58] Viswanathan et al[7] investigated cutaneous temperature discrimination using a TipTherm (Axon GmBh, Dusseldorf, Germany) device (based on different conductivity of materials) for the diagnosis of distal symmetrical polyneuropathy. The TipTherm is a penlike device with 2 flat sides (one made of metallic material and the other of synthetic material), independent of external power sources, easy to handle, and lightweight. Its validity and accuracy were evaluated against established methods of assessing neuropathy. It was found that the TipTherm had sensitivities and specificities of 97.3% and 98.3% and 100% and 92.1% compared to biothesiometry the SW monofilament, respectively. A total of 910 consecutive patients (628 men and 282 women) were selected. The mean age (SD) of the patients was 53.7 (10.4) years, and the mean (SD) duration of diabetes was 9.7 (8.0) years.

Bertelsmann et al[55] used 2 alternative forced-choice procedures that employed a thermostimulator (based on the Peltier principle) to assess cutaneous thermal perception at the foot dorsum and hand dorsum. Both warmth and cold receptors were tested using the thermal stimulator. The 2 most important findings of this research study were the age-related differences in thermal discrimination and length-dependent nature of diabetic neuropathy. Thirty-six healthy subjects and 20 diabetic subjects with neuropathy were selected for this study. This study has limitations. First, subjects in this study were not age and sex matched. The age range of the study group was also limited. Thirty-six nondiabetic subjects (25 women and 11 men, aged 24-91 years) and 20 diabetic subjects (11 women and 9 men, aged 22-69 years) were investigated. Operator bias, intrasubject variability, and the overall subjective nature of the technique discount its use as a routine assessment tool for thermal measurements in diabetic patients. Operator bias is specific to this technique because the readings recorded depend on the attention of the subject and therefore on the handling skills of the operator. The size of the Peltier stimulator (3 cm $\times$ 4 cm) permits only measurement local to small areas every single time. This technique is based on the patient's subjective assessment and considers the response of either cold receptors or warmth receptors because of 2 reasons: (1) specific points are sensitive to either warmth/cold stimuli, and (2) cold receptors outnumber warmth receptors by a factor of 3 to 10 in most areas of the body.[43] The latter is a limitation as it is not possible to acquire a whole field image of the foot using Peltier's device.

Liniger et al[58] assessed thermal sensitivity in diabetic neuropaths using a specially developed Thermocross (Medical School, Geneva, Switzerland) tool (based on thermoresistances). They reported that the deficit in thermal sensation detected by Thermocross paralleled the decline of nerve conduction.

INFRARED THERMOGRAPHY

IR thermography is a real-time temperature measurement technique used to produce a colored visualization of thermal energy emitted by the measured site at a temperature above absolute zero. Jones and Plassmann[59] have provided an excellent review on IR technology along with related image-processing considerations. Traditionally, a 2-dimensional image representing 3-dimensional thermal distribution is acquired using standard image acquisition hardware. Each pixel in the image depicts the radiance falling on the focal plane array/microbolometer–type detector used in an IR camera.

Technological advances in IR cameras in speed and spatial resolution now make it possible to quantitatively assess thermal patterns. It is recommended that IR imaging equipment must be regularly calibrated, and characteristic parameters be determined using simple tests such as spatial resolution, stability of

temperature measurement, and linearity of field. The imaging protocol and quantitative techniques in medical thermography have been well described.[60] Jones et al[61] identified a common need to establish a reference database of normal thermograms from all major areas of the human body, from which the abnormal findings can be reliably assessed. The reference database is a multicenter effort to standardize IR imaging for reproducible and clinically relevant thermal measurements.

IR thermography has applications in medicine that include breast thermography, vascular disease,[62] skin disease,[63] studies of inflammatory response,[64] Raynaud phenomenon,[54] sleep research,[65] and pain-related thermal dysfunction. IR thermography is a noninvasive and high-resolution technique used to measure physiological changes complementing standard radiographic investigations.[59] Wang et al[62] used IR thermography in a small patient group with vascular or neurological complications and emphasized the need for establishing normal variations of skin temperature before attempting to quantify abnormal criteria. The technique has been used to assess both anatomical and functional changes.

Langer and other researchers used IR thermography to study vascular complications and foot ulceration in patients with diabetes mellitus.[66-70] Ideally, using thermographic measurements to prevent foot ulceration by studying and documenting thermal findings in lower extremities in well-designed clinical studies[13,71] would be a very useful extension of the use of the technique.

Blood vessels close to the skin surface can be easily traced from IR images[59] that are sensitive to the heat from blood vessels. Merla et al[54] used IR thermography to assess vasoconstrictive responses to cold stress for patients with Raynaud phenomenon in a pilot study. One of the significant findings of this study was that it permitted the effect of treatment to be followed up.

High-sensitivity IR cameras are available, although at an increased cost. IR thermography has poor specificity: thermographic images cannot identify the increased cutaneous perfusion. The presence of inflammatory effects in both deep and superficial vessels can be misleading when using the IR technique as indeed would the presence of nonvascular pathology such as Baker cyst of the knee joint.

IR measurements can complement other modalities. Dynamic area telethermometry is a useful biomedical technique based on IR imaging and can be used to assess diabetes mellitus.[52] It employs assessment of hemodynamic and neurogenic variations in the tissue and offers an objective and quantitative diagnostic figure of merit.

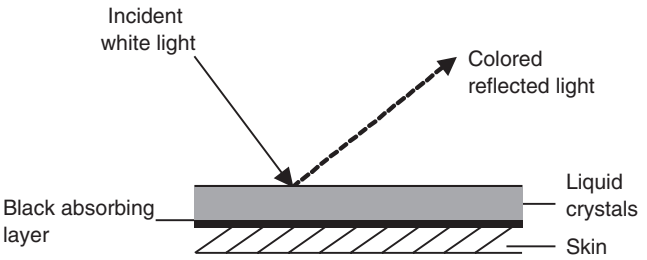

Fig. 1 Principle of the measurement of skin surface temperature with liquid crystals.

LCT

LCT provides a color response proportional to the temperature of a heated surface in contact with the thermochromic liquid crystals (TLCs). Figure 1 shows the principle of measurement of skin surface temperature with liquid crystals. The black absorbing layer acts as a barrier between the skin and liquid crystals; it prevents reflection by skin surface.

The temperature range over which the TLC material actively reflects visible light and can be distinguished by the imaging equipment is termed the *color bandwidth* or *color play interval*.[72,73] The operating range of TLCs varies from –30°C to 150°C. Liquid crystals with color bandwidth less than 5°C are narrow band, and those with a bandwidth greater than 5°C are wide-band liquid crystals.

The sequence of color most commonly observed is red followed by yellow, green, blue, and violet.[74] However, some liquid crystals produce only selective transitions, that is, red-green-red or green-red, during warming. The chemical formulation of liquid crystal material determines its color versus temperature characteristics at the manufacturing stage.[74] Details related to the physics and characteristics of TLCs are widely published.[72,73,75-77]

Figure 2 shows the reflected wavelength versus temperature response of a temperature-sensitive thermochromic liquid crystal mixture. The clearing point is the temperature at which the TLC becomes transparent as a consequence of the crystals' achieving a nonreflecting isotropic state. When the TLC is cooled, they change back to the anisotropic semicrystalline state is principally dependent on the rate of cooling, which leads to a shift in the hue versus temperature profile. This change is reversible provided that the

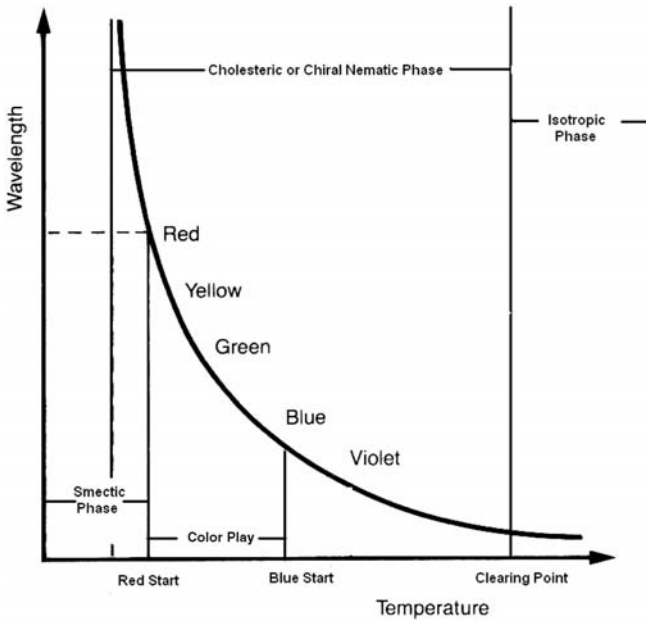

Fig. 2 Typical reflected wavelength versus temperature response of a temperature-sensitive thermochromic liquid crystal mixture.

TLC is allowed to cool to a formulation-dependent temperature termed the *event temperature*.

Pure TLC material is difficult to work with because of its oily form, risk of chemical contamination, and exposure to ultraviolet light. These difficulties can be avoided through polymer microencapsulation of the TLC.[74,78] Various production techniques are used to enable TLC to be offered in the form of an emulsion, polymer sheet, or latex support.

Hue-temperature calibration is the most common technique used for almost all applications of LCT.[75,76,79,80] However, modern approaches to LCT calibration employ red-green-blue imaging sensors[81] and artificial intelligence techniques such as neural networks.[82] Recently, the authors' research group has developed a novel approach using neural networks for calibration of TLC to minimize the dependence on variations in background illumination.[83] It offers significant advantages over the hue-temperature calibration that may be useful in certain research or industrial applications, for example, determination of temperature distribution in complex geometries, in which illumination can have a significant effect on the hue of the color response.

The earliest applications of liquid crystals were qualitative and limited in scope because of a lack of efficient imaging equipment. LCT is primarily used in thermal mapping, nondestructive testing, fluid flow visualization, aerospace engineering, and studies of electronic cooling and boiling heat transfer.[76] There are numerous applications in medicine, namely, andrology, rheumatology, sports medicine, dermatology, dolorology, vasculopathies,[84] podiatry,[85] pulmonological diagnostics,[86] and consumer thermometry.[74] Portnoy[87] and Ashforth et al[79] have reviewed the specialized use of liquid crystals in quantitative thermal imaging for biomedical applications. LCT was used in evaluation low-back pain for study groups including patients with degenerative discogenic lesions, acquired lesions, congenital and developmental lesions, and back pain resulting from unknown causes.[88] LCT was also used in determination of baseline data for thermal patterns in the face of healthy individuals.[89] The detector plate contained microencapsulated liquid crystals in a latex membrane. Such data sets are important for objective assessment in cases of nerve injuries and monitoring recovery. A positive relationship exists between temperature changes and nerve injuries in lower and upper limbs.[90,91] Dribbon[85] suggested the use of LCT in assessing neurovascular complications by studying characteristic patterns of hypoemissivity, taking the contralateral foot as a control. Meyers et al (cited in the work of Stess et al[4]) suggested that normal thermographic patterns in humans are characterized by remarkable symmetry of temperature in homologous body parts as confirmed in their study of controls. This fact is useful in bilateral studies of various pathologies, in which thermographic patterns in the contralateral part are compared to the affected part. Diabetic neuropathy is generally symmetric; that is, both feet should represent similar thermal patterns in our study. Diaz[92] used LCT to evaluate sympathetic blocks. In the study under consideration,[92] emulsion-based liquid crystals were used on a single patient for qualitative analysis. However, using emulsion-based liquid crystals carries the risk of cross-contamination when used in medical applications. However, wiping with an alcohol swab will be satisfactory in most cases.

In cases of tissue trauma, liquid crystals can be used to differentiate between regions of normal and impaired vascularity.[87] Stess[4] and Benbow[5] have used LCT for diabetic foot assessment. Two major problems with these studies were low image resolution and pressure sensitivity of TLCs. This is the reason that LCT has not been widely adopted for diabetic foot assessment. In addition, both the studies under consideration had supine measurements for feet, which do not replicate the normal loading condition to which the feet are subjected most of the time. Both studies used TLC on latex support to

evaluate plantar thermal emission patterns. According to the TLC characterization study within the authors' research group, TLC on latex support has been found to be pressure sensitive.[93] It suffers from nonhomogenities resulting in high uncertainties in measured hue values and limited temperature resolution due to its manufacturing and material properties.

Tables 1 and 2 list the results from the 2 LCT studies for their respective patient groups. Both the tables present temperature readings for the study groups. Stess et al[4] have reported significantly increased plantar foot temperature and mottled thermographic patterns for patients with active foot ulceration. Three patient groups were studied: diabetic patients with a history of foot ulceration but without any active foot ulceration, diabetic patients with active foot ulceration, and nondiabetic healthy controls.

The study by Benbow et al[5] found increased mean foot temperature (MFT) in diabetic neuropathic patients leading to foot ulceration, measured using temperature-sensitive liquid crystals. The study was composed of 3 groups: neuropathic patients with PVD, neuropathic patients without PVD, and nondiabetic healthy controls.

Elevated temperatures at weight-bearing sites (ie, metatarsal heads and heel) may indicate pressure trauma or increased AV shunting.[94] Benbow et al[5] proposed that a normal or low MFT in the neuropathic foot may be a marker of PVD, which confers an increased risk of ischemic foot disease. This was a hypothesis based on the prospective study of 50 subjects with diabetic neuropathy. Benbow's suggestion must be considered preliminary but one with potential for the future.

Table 1. Foot Temperature (°C) for 3 Study Groups as Determined by Liquid Crystal Thermography in the Research Study by Stess et al[4]

	$\bar{x}$	SD
Group 1 (nondiabetic controls	27	0.3
Group 2 (diabetic without ulcers)	26	0.3
Group 3 (diabetic with active ulcer)	28	0.3

Table 2. Foot Temperature (°C) for 3 Study Groups as Determined by Liquid Crystal Thermography in the Research Study by Benbow et al[5]

	$\bar{x}$	SD
Group 1 (nondiabetic controls)	25.7	2.1
Group 2 (diabetic with neuropathy, without peripheral vascular disease ulcers)	28.2	2.9
Group 3 (diabetic with neuropathy, with peripheral vascular disease ulcers)	25.6	1.9

DISCUSSION

The aim of this article was to examine the means of measuring thermal changes in the skin of patients. Vascular changes due to abnormal neuronal control involve changes that can be identified and monitored through their effects on the dynamics of thermal behavior on human skin.[95] Previous studies of diabetic neuropathy have used several instruments to detect the lack of protective sensation in the foot. However, there has not been any instrument designed specifically for the evaluation of thermal patterns under the foot and other temporal parameters such as rate of change of vascularity and thermal hyperemia. Ideally, there should be an instrument to evaluate neuropathy independently and objectively that is easy to use, readily available, reproducible, sensitive, and specific. It would appear that limitations exist resulting from the techniques themselves discussed and their applications.

Increased temperatures in lower extremities may cause differences in thermal drive (skin temperature inputs) for diabetic neuropaths. This justifies employing thermal measurements for lower extremities to evaluate physiological differences between diabetic neuropaths and healthy subjects. While evaluating these differences, the age- and sex-related differences in thermoregulatory mechanisms must also be determined. Diabetic foot ulcers occur because of irregularities in the underlying microangiopathy and neuropathy. Therefore, either measurements should be made at several discrete locations or a whole-field technique such as LCT or IR thermography should be used. LCT is a factor of magnitude cheaper than the IR thermography system.[93,95] Spin-off techniques using IR imaging, such as dynamic area telethermometry, study thermal behavior in time domain and are therefore less sensitive to reflection artifacts.[52] The technique may be suitable for specialty diagnostic centers. In the past, LCT was limited by poor thermal resolution (±0.5°C), poor spatial resolution (±5 mm), slow response time (>60 seconds), and subjective assessment.[95] Recent advances in liquid crystal technology now offer the potential for better thermal mapping and

accuracy, faster response time,[73] and better temperature resolution using digital image processing.[72,73,83,96] In addition, neurogenic modulation of perfusion is exhibited at lower frequencies.[52] Therefore, using LCT over IR thermography to assess diabetic neuropathic foot may yield useful diagnostic information at a lesser cost of thermal accuracy.[97] There is clearly a need for rigorously controlled studies.

The results from the 2 studies[4,5] discussed in Tables 1 and 2 cannot be directly compared as they are different in many ways. Ideally, the LCT technique should be developed to identify preulcerous changes in the diabetic patient who is at increased risk of foot ulceration.

Currently, there are no guidelines for thermal assessment of the diabetic foot. A low-cost thermal technique such as LCT offers the potential to measure static and dynamic parameters on plantar foot skin. Electrical contact thermometry or cutaneous thermal perception need more time to make point measurements over the same surface area.

CONCLUSION

Past research and clinical studies related to diabetic foot have particularly focused on the nutritive blood supply, AV shunts, and systemic or local control mechanisms without any detailed assessment of the thermal patterns in diabetic foot. In this article, thermal measurement of diabetic foot has been shown to be a useful technique in clinical management of the diabetic foot. Various parameters of interest and measurement techniques have been identified to study the pathophysiology of the vascular system and neuronal control in diabetic foot disease.

The authors' research group is developing and applying engineering techniques to further the current understanding of pathogenetic mechanisms of plantar ulceration in diabetic patients. An LCT system is currently under development for both static and dynamic assessment of diabetic foot. Three physical forms of TLC materials have been assessed for use in the system[93] as reported in this article. It does appear reasonable to conclude that at present, a great deal of ground needs to be covered to develop the potential offered by thermal techniques to improve the potential to diagnose diabetes and other disorders.

ACKNOWLEDGMENTS

The authors are grateful to the Engineering and Physical Sciences Research Council (GR/S0732201) and to the European Foundation for Study on Diabetes for the Albert Renold Travel fellowship for providing funding to carry out this work. The authors also acknowledge Professor Ann Anderson at Union College (Schenectady, New York) for providing access to the LCT laboratory and technical support.

REFERENCES

1. Childs P, Greenwood J, Long C. Review of temperature measurement. Rev Sci Instrum 2000:71:2959-78.

2. Tatsuo T. Body temperature measurement. Clinical Physiology and Physiological Measurements 1985:6:83-108.

3. Yang W, Yang P. Literature survey on biomedical applications of thermography. Biomed Mater Engineer 1992;2:7-18.

4. Stess RM, Sisney PC, Moss KM, Graf PM, Louie KS, Gooding GA, et al. Use of liquid crystal thermography in the evaluation of the diabetic foot. Diabetes Care 1986;9:267-72.

5. Benbow S, Chan A, Bowsher D, Williams G, Macfarlane I. The prediction of diabetic neuropathic plantar foot ulceration by liquid-crystal contact thermography. Diabetes Care 1994;17:835-9.

6. Ziegler D, Mayer P, Wiefels K. Assessment of small and large fibre function in long term type 1 (insulin dependent) diabetic patients with and without painful neuropathy. Pain 1988;34:1-10.

7. Viswanathan V, Snehalatha C, Seena R, Ramachandran A. Early recognition of diabetic neuropathy: evaluation of a simple outpatient procedure using thermal perception. Postgrad Med J 2002;78:541-2.

8. Pendsey S. Diabetic foot: a clinical atlas. New Delhi (India): Jaypee Brothers Medical Publishers; 2003.

9. World Health Organization. The diabetes programme. Geneva, Switzerland: World Health Organization; 2004.

10. O'Brien J, Patrick A, Caro J. Estimates of direct medical costs for microvascular and macrovascular complications resulting from type 2 diabetes mellitus in the United States in 2000. Clin Ther 2003;25:1017-38.

11. Viswanathan V, Madhavan S, Rajasekar S, Chamukttan S, Ambady R. Urban-rural differences in the prevalence of foot complications in South Indian diabetic patients. Diabetes Care 2006; 29:701-3.

12. Viswanathan V, Madhavan S, Rajashekar S, Chamukuttan S, Ramachandran A. Amputation prevention initiative in South India. Diabetes Care 2005;28:1019-21.

13. Armstrong D, Lavery L, Wunderlich R, Boulton A. Skin temperatures as a one-time screening tool do not predict future diabetic foot complications. J Am Podiatr Med Assoc 2003;93:443-7.

14. Armstrong D, Sangalang M, Jolley D, Maben F, Kimbriel H, Nixon B, et al. Cooling the foot to prevent diabetic foot wounds. J Am Podiatr Med Assoc 2005;95:103-7.

15. Boulton A, Connor H, Cavanagh PR, editors. The foot in diabetes. New York: John Wiley & Sons; 1998.

16. Currie C, Morgan C, Peters J. The epidemiology and cost of inpatient care for peripheral vascular disease, infection, neuropathy and ulceration in diabetes. Diabetes Care 1998;21:42-8.

17. Palubo P, Melton L. Peripheral vascular disease and diabetes. In: Hamman R, editor. Diabetes in America. Washington, DC: Government Printing Office; 1985. p. 1-21.

18. Hutchinson A, McIntosh A, Feder G. Clinical guidelines and evidence review for type 2 diabetes: prevention and management of foot problems. London: Royal College of General Practitioners; 2000.

19. Morbach S, Lutale J, Viswanathan V, Mollenberg J, Ochs H, Rajashekar S, et al. Regional differences in risk factors and clinical presentation of diabetic foot lesions. Diabet Med 2004;21:91-5.

20. Viswanathan V, Snehalatha C, Sivagami M, Seena R, Ramachandran A. Association of limited joint mobility and high plantar pressure in diabetic foot ulceration in Asian Indians. Diabetes Res Clin Pract 2003;60:57-61.

21. Perkins B, Bril V. Diagnosis and management of diabetic neuropathy. Curr Diabetes Rep 2002;2:495-500.

22. Flynn M, Edmonds M, Tooke J, Watkins P. Direct measurement of capillary blood flow in the diabetic neuropathic foot. Diabetologia 1988;31:652-6.

23. Rayman G, Williams S, Spencer P, Smaje L, Wise P, Tooke J. Impaired microvascular hyperaemic response to minor skin trauma in type 1 diabetes. Br Med J 1986;292:1295-8.

24. Flynn M, Tooke J. Diabetic neuropathy and the microcirculation. Diabet Med 1995;12:298-301.

25. Cobb J, Claremont D. Noninvasive measurement techniques for monitoring of microvascular function in the diabetic foot. Int J Low Extrem Wounds 2002;1:161-9.

26. Cobb JE. An in-shoe laser Doppler sensor for assessing plantar blood flow in the diabetic foot [dissertation] in DEC. Bournemouth (UK): Department of Design, Engineering, and Computing, Bournemouth University; 2000.

27. Belcaro G, Vasdekis S, Rulo A, Nicolaides AN. Evaluation of skin blood flow and venoarteriolar response in patients with diabetes and peripheral vascular disease by laser Doppler flowmetry. Angiology 1989;40:953-7.

28. Bornmyr S, Svensson H, Lilja B, Sundkvist G. Skin temperature changes and changes in skin blood flow monitored with laser Doppler flowmetry and imaging: a methodological study in normal humans. Clin Physiol Funct Imaging 1997;17:71-82.

29. Grunfield C. Diabetic foot ulcers: etiology, treatment and prevention. Adv Intern Med 1992;37:103-32.

30. Nabarro J. Diabetes in the United Kingdom: a personal series. Diabet Med 1991;8:59-68.

31. Tanenberg R, Schumer M, Greene D, Pfeifer M. Neuropathic problems of the lower extremities in diabetic patients. In: Pfeifer M, editor. The diabetic foot. St. Louis (MO): Mosby; 2001.

32. Miranda-Palma B, Sosenko J, Bowker J, Mizel M, Boulton A. A comparison of the monofilament with other testing modalities for foot ulcer susceptibility. Diabetes Res Clin Pract 2005;70:8-12.

33. National Health Service. Type 2 diabetes: prevention and management of foot problems. London: National Institutes of Health and Clinical Excellence; 2004.

34. Fisher A, Gilula L, McEnery K. Imaging of the diabetic foot. In: Bowker J, Pfeifer M, editors. The diabetic foot. St. Louis (MO): Mosby; 2001. p. 333-54.

35. Minamishima C, Kuwaki K, Shirota E, Matsuzaki M, Yamashita K, Kamatani M, et al. Thermal imaging properties of toes after walking stress test in diabetic patients. Rinsho Byori 2005;53:118-22.

36. Aspres N, Egerton I, Lim A, Shumack S. Imaging the skin. Aust J Dermatol 2003;44:19-27.

37. Brash P, Foster J, Vennart W, Anthony P, Tooke J. Magnetic resonance imaging techniques demonstrate soft tissue damage in the diabetic foot. Diabet Med 1999;16:55-62.

38. Hales J. Thermoregulatory requirements for circulatory adjustments to promote heat loss in animals. J Therm Biol 1983;8:219-24.

39. Hales J, Jessen C, Fawcett A, King R. Skin AVA and capillary dilation and constriction induced by local skin heating. Pflugers Arch 1985;404:301-7.

40. Hales J, Iriki M, Tsuchiya K, Kozawa E. Thermally induced cutaneous sympathetic activity related to blood flow through capillaries and arteriovenous anastomoses. Pflugers Arch 1978;375:1724.

41. Guy R, Clark C, Malcolm P, Watkins P. Evaluation of thermal and vibration sensation in diabetic neuropathy. Diabetologia 1985;28:131-7.

42. Uccioli L, Mancini L, Giordano A, Solini A, Magnani P, Manto A, et al. Lower limb arteriovenous shunts, autonomic neuropathy and diabetic foot. Diabetes Res Clin Pract 1992;162:123-30.

43. Guyton A, Hall J. Human physiology and mechanisms of the disease. 5th ed. Philadelphia: W. B. Saunders; 1992.

44. Fagrell B. Microcirculation of the skin. In: Fagrell B, editor. The physiology and pharmacology of the microcirculation. London: Academic Press; 1984. p. 133-80.

45. Mork C, Asker C, Saleurd E, Kvernebo K. Microvascular arteriovenous shunting is a probable pathogenetic mechanism in erythromelalgia. J Invest Dermatol 2000;114:643-6.

46. Vendrell J, Nubioda A, Goday A, Bosch X, Gomis R, Esmatjes E, et al. Erythromelalgia associated with acute diabetic neuropathy: an unusual condition. Diabetes Res 1988;7:149-51.

47. Staub D, Munger B, Uno H, Dent C, Davis J. Erythromelalgia as a form of neuropathy. Arch Dermatol 1992;128:1654-5.

48. Netten P, Wollersheim T, Lutterman J. Skin microcirculation of the foot in diabetic neuropathy. Clin Sci 1996;91:559-65.

49. Van Someren EJW, Raymann RJEM, Scherder EJA, Daanen HAM, Swaab DF. Circadian and age-related modulation of thermoreception and temperature regulation: mechanisms and functional implications. Ageing Res Rev 2002;1:721-78.

50. Clark R, Goff M, Hughes J, Klenerman L. Thermography and pedobarography in the assessment of tissue damage in neuropathic and atherosclerotic feet. Thermology 1988;3:15-20.

51. Archer AG, Roberts VC, Watkins PJ. Blood flow patterns in painful diabetic neuropathy. Diabetologia 1984;27:563-7.

52. Anbar M, Milescu L. Prerequisites of dynamic area telethermometry (DAT). Proceedings of the 20th Annual International Conference of the IEEE Engineering in Medicine and Biology Society; 1998 29 Oct–Nov 1; Hong Kong.

53. Boyko EJ, Ahroni JH, Stensel VL. Skin temperature in the neuropathic diabetic foot. J Diabetes Complicat 2001;15:260-4.

54. Merla A, Di Donato L, Di Luzio S, Farina G, Pisarri S, Proietti M, et al. Infrared functional imaging applied to Raynaud phenomenon. IEEE Eng Med Biol Mag 2002;21(6):73-9.

55. Bertelsmann FW, Heismann JJ, Weber EJ, van der Veen EA, Schouten JA. Thermal discrimination thresholds in normal subjects and in patients with diabetic neuropathy. J Neurol Neurosurg Psychiatr 1985;48:686-90.

56. Kelechi T, Michel Y, Wiseman J. Are infrared and thermistor thermometers interchangeable for measuring localized skin temperature? J Nurs Meas 2006;14(1):19-30.

57. Anderson K. End of the year NSF scholarship student report. Golden: Colorado School of Mines; 2001.

58. Liniger C, Albeanu A, Moody J, Richez J, Bloise D, Assal JP. The Thermocross: a simple tool for rapid assessment of thermal sensation thresholds. Diabetes Res Clin Pract 1991;12:25-34.

59. Jones B, Plassmann P. Digital infrared thermal imaging of human skin. IEEE Eng Med Biol Mag 2002;21:41-8.

60. Ring E, Ammer K. The technique of infrared imaging in medicine. Thermology International 2000;10:7-14.

61. Jones C, Ring E, Plassmann P, Ammer K, Wiecek B. Standardisation of infrared imaging: a reference atlas for clinical thermography—initial results. Thermology International 2005; 15:157-8.

62. Wang H, Wade D, Kam J. IR imaging of blood circulation of patients with vascular disease. Proceedings of Thermosense XXVI; 2004 Apr 13-15; Bellingham, WA.

63. Otsuka K, Okada S, Hassan M, Togawa T. Imaging of skin thermal properties with estimation of ambient radiation temperature. IEEE Eng Med Biol Mag 2002;21:49-55.

64. Cook RJ, Thakore S, Nichol NM. Thermal imaging—a hotspot for the future? A case report. Injury Extra 2005;36:395-7.

65. Heuvel C, Ferguson S, Dawson D, Gilbert S. Comparison of digital infrared thermal imaging (DITI) with contact thermometry: pilot data from a sleep research laboratory. Physiol Meas 2003:24:717.

66. Reardon J, Curwen I, Jarman P, Dewar M, Chodera J. Thermography and leg ulceration. Acta Thermographica 1982; 17:17-20.

67. Langer L, Fagerberg S, Johnsen C. Peripheral circulation in diabetes mellitus—a study with infrared thermography. Acta Med Scand 1972;191:17-20.

68. Armstrong D, Lavery L. Monitoring healing of acute Charcot's arthropathy with infrared dermal thermometry. J Rehab Res Dev 1997;34:317-21.

69. Armstrong D, Lavery L, Liswood P, Todd W, Tredwell J. Infrared dermal thermometry for the high-risk diabetic foot. Phys Ther 1997;77:169-75.

70. Harding J, Wertheim D, Williams R, Melhuish J, Banerjee D, Harding K. Infrared imaging in diabetic foot ulceration. Proceedings of the Annual International Conference of the IEEE, Engineering in Medicine and Biology Society; 1998; Hong Kong.

71. Lavery L, Higgins K, Lactot D, Constantinitides G, Zamorano R, Armstrong D, et al. Home monitoring of foot skin temperatures to prrevent ulceration. Diabetes Care 2004;27:2642-7.

72. Anderson M. Thermochromic liquid crystal thermography: hysteresis, illumination and imaging system effects, image processing and applications [dissertation]. Davis: Department of Mechanical and Aeronautical Engineering, University of California; 1999.

73. Bakrania S, Anderson A. A transient technique for calibrating thermochromic liquid crystals: the effects of surface preparation, lighting and overheat. Proceedings of the ASME International Mechanical Engineering Congress and Exposition; 2002 Nov 17-22; New Orleans, LA.

74. Hallcrest. Handbook of thermochromic liquid crystals. Glenview (IL): Hallcrest; 1991.

75. Hay JL, Hollingsworth DK. Calibration of micro-encapsulated liquid crystals using hue angle and a dimensionless temperature. Experimental Thermal and Fluid Science 1998;18:251-7.

76. Hay JL, Hollingsworth DK. A comparison of trichromic systems for use in the calibration of polymer-dispersed thermochromic liquid crystals. Experimental Thermal and Fluid Science 1996;12:1-12.

77. Behle M, Schulz K, Leiner M, Fiebig M. Color based image processing to measure local temperature distributions by wide band liquid crystal thermography. App Sci Res 1996;56:113-43.

78. Massi N. Technological aspects of IPS plates with microencapsulated liquid crystals. Milan (Italy): International Products and Services; 2004.

79. Jambunathan K, Hartle S, Asforth-Frost S, Fontama V. Evaluating convective heat transfer coefficients using neural networks. International Journal of Heat Mass Transfer 1996;39:2329-32.

80. Chan TL, Ashforth-Frost S, Jambunathan K. Calibrating for viewing angle effect during heat transfer measurements on a curved surface. International Journal of Heat and Mass Transfer 2001;44:2209-23.

81. Matsuda H, Ikeda K, Nakata Y, Otomo F, Suga T, Fukuyama Y. A new thermochromic liquid crystal temperature identification technique using colour space interpolations and its applications to film cooling effectiveness measurements. Journal of Flow Visualisation and Image Processing 2000;7:103-21.

82. Kimura I, Uchide K, Ozawa M. Temperature measurement using liquid crystals based on colour image processing (improvement of color to temperature calibration line by neural networks). In: Proceedings of the Japanese Visualisation Association 1992;12(1):7-10.

83. Grewal G, Bharara M, Cobb J, Dubey V, Claremont D. A novel approach to thermochromic liquid crystal calibration using neural networks. Meas Sci Technol 2006;17:1918-24.

84. Leinidou A. Contact thermography [CD-ROM]. Milan (Italy): International Products and Services; 2003.

85. Dribbon B. Application and value of liquid crystal thermography. J Am Podiatr Assoc 1983;73:400-4.

86. Klosowicz S, Jung A, Zuber J. Liquid crystal thermography and thermovision in medical applications: Pulmonological diagnostics. Proceedings of SPIE: optical sensing for public safety, health and security; 2000 Oct 25; Warsaw, Poland.

87. Portnoy WM. Tutorial: liquid crystal thermography. J Assoc Adv Med Instrum 1970;4:176-80.

88. Rubal B, Traycoff R, Ewing K. Liquid crystal thermography: a new tool for evaluating low back pain. Phys Ther 1982;62:1593-6.

89. Ariyaratnam S, Rood J. Measurement of facial skin temperature. J Dent 1990;18:250-3.

90. Nakano K. Liquid crystal contact thermography (LCT) in the evaluation of patients with upper limb entrapment neuropathies. Neurol Orthop J Med Surg 1984;5:97-102.

91. Uematsu S. Thermographic imaging of cutaneous sensory segments in patients with peripheral nerve injury: skin temperature stability between sides of the body. J Neurosurg 1985;62:716-20.

92. Diaz P. Use of liquid crystal thermography to evaluate sympathetic blocks. Anaesthesiology 1976;44:443-5.

93. Bharara M, Cobb J, Claremont D, Anderson A. Liquid crystal thermography: application in neuropathic assessment of diabetic foot. Thermology International 2005;15:154-5.

94. Chan A, MacFarlane I, Bowsher D. Contact thermography of painful diabetic neuropathic foot. Diabetes Care 1991;14:918-22.

95. Anbar M. Clinical thermal imaging today. IEEE Eng Med Biol Mag 1998;17:25-33.

96. Roth T, Anderson A. Light transmission characteristics of thermochromic liquid crystals. Proceedings of the International Mechanical Engineering Conference and Exposition; 2005 Nov 5-11; Orlando, FL.

97. Cavanagh P, Ulbrecht J, Caputo G. The biomechanics of the foot in diabetes mellitus. In: Pfeifer M, editor. The diabetic foot. St. Louis (MO): Mosby; 2001. p. 125-96.