The roles of infrared thermography in pressure ulcer research with focus on skin microclimate induced by medical devices and prophylactic dressings

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Prevention of pressure ulcers (PUs) is becoming the focus of acute and chronic care facilities for a variety of reasons beyond human suffering. The literature demonstrates that pressure ulcer prevention (PUP) reduces hospital stays, leads to less aggressive medical procedures, yields substantial cost-benefit and lowers the risk for litigation. Infrared thermography (IRT) is a noninvasive quantitative method for mapping skin temperatures, which makes it effective and powerful in assessing the microclimate conditions associated with a risk for PUs. This article reviews current and potential future roles of IRT in mechanobiological and clinical research of PUP and pressure ulcer treatment (PUT), and presents relevant examples from studies by the authors' group that are currently under way with focus on measurements of skin microclimate conditions caused by medical devices associated with device-related PUs and assessment of polymeric membrane dressings and the microclimate conditions developing in their PUP application. The authors further discuss the potential for future use of IRT in PUP and PUT, and the strengths and limitations of IRT in these applications in view of present global PUP efforts.

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Prevention of pressure ulcers (PUs) is becoming the focus of acute and chronic care facilities for a variety of reasons beyond human suffering. The literature demonstrates that pressure ulcer prevention (PUP) strategies and actions reduce hospital stays, lead to less aggressive procedures, yield substantial cost-benefit outcomes and lower the risk for litigation and associated costs. Previous published work indicates that noninvasively monitoring of changes in peripheral microcirculation can reflect both local and systemic physiological changes (Ovadia-Blechman et al, 2015a; 2015b ; Ovadia-Blechman et al, 2017; Lustig et al, 2018). Infrared thermography (IRT) is a noninvasive quantitative method for mapping skin temperatures at a relatively low expenditure, which makes it powerful and effective in assessing the microclimate conditions and, in some cases, the tissue physiology changes associated with a risk for PUs (Linder-Ganz and Gefen, 2007; Judy et al, 2011; Cox et al, 2016).

All objects that are at a temperature above absolute zero emit infrared radiation as a result of the thermal motion of their molecules. Infrared thermography (IRT), the method and related technologies for measuring infrared radiation, is an imaging modality with applications in numerous fields — from preventative maintenance of motors and electrical distribution boards to medicine (Ring and Ammer, 2012; Gavish et al, 2018; Hoffer et al, 2018a; 2018b). Cameras for capturing IRT images convert the thermal radiation (within wavelengths from 900 to 14,000 nm) to a quantitative temperature map describing the temperature distribution at the examined surfaces of an object.

Since the human skin emits infrared radiation as well, IRT facilitates mapping of skin temperatures. Skin temperatures are different from the core temperature of the human body and vary considerably from this latter value in both magnitude and variability. Specifically, while core

body temperature maintains a stable day-night cycle that does not vary substantially, unless a disease or systematic dysfunctions are present, the localised skin temperatures are affected by local phenomena and interactions at the surface of the body, e.g. by warm or cold contacting objects and ambient conditions, as well as by local inflammatory processes and malignant tumours at superficial tissues (Hoffer et al 2018a; 2018b). As such, IRT offers effective and powerful means for research and, in the future, perhaps clinical applications concerning a variety of topics related to PUs and to PUP in particular. For example, there is a continuum of care between PUP and pressure ulcer treatment (PUT). Deep tissue injuries (DTIs) typically present themselves as changes in skin colour at a timeframe of approximately 48 hours from the initial insult, but the subsequent tissue breakdown up to a full-thickness wound may last 1 to 2 weeks (Cox et al, 2016).

The unaided eye will not reveal the tissue damage, which spreads under the skin until it is too late, however, early detection of a necrotic subdermal tissue mass may facilitate salvage of adjacent tissues through timely interventions. A necrotic mass of tissue would not be perfused and, hence, tissues around the necrotic mass may exhibit cooler temperatures measureable by IRT due to lack of blood flow as a heat convection mechanism. Likewise, skin inflammation due to sustained or repetitive friction and shear damage may increase the local skin temperature at the affected site and hence be detectable by IRT. Accordingly, IRT is generally useful for detecting localized changes in skin temperature (which may also reflect temperature changes in deeper tissues) as an adjunct to the unaided eye in detecting the risk for PUs.

The demand for imaging modalities that are inexpensive, accessible, and can be applied at the bedside without requiring expertise and expert training, and which can be applied at the basic healthcare level is constantly increasing as the costs of diagnostics escalate. For the nurses of the near future, IRT miniaturised to cellphones or tablet devices may become a tool used routinely for diagnostic and therapeutic decision-making in PUP and PUT; such technologies are already being assessed in clinical settings (Kanazawa et al, 2016a). For example, IRT facilitates measurements of the thermal conditions applied by medical devices in the context of research of medical device-related PUs (MDRPUs) and PUP. In addition, IRT allows characterisation of the microclimate conditions applied to skin by prophylactic and treatment dressings. As for any other method, however, IRT also has limitations that should be considered when it is applied for PUP and PUT. This article reviews the aforementioned applications of IRT at the laboratory of the first author, which are relevant to current global PUP efforts.

Measurements of the thermal conditions applied by medical devices

It has been reported that IRT images reflect the effect of local blood circulation on skin temperatures (Ring and Ammer, 2012). Hence, sites of locally reduced temperature may reflect an ischaemic burden on skin, which is caused by sustained deformations. In addition to impaired circulation causing less heat transfer in skin through convection and, hence, decreased local temperatures at the deformed tissue sites, the IRT measurements reflect the physiological response to the sustained deformations, such as vasodilation and tissue metabolism induced by the inflammatory response (Nishide et al, 2009; Nakagami et al, 2011; Kanazawa et al, 2016). Both vasodilatation and inflammation-related altered tissue metabolism can produce a thermal change at a distorted tissue site (Nishide et al, 2009; Nakagami et al, 2011; Kanazawa et al, 2016).

While IRT does not provide depth-specific temperature data, sites where tissue thickness are small (which by itself makes the tissue vulnerable to PUs) are effectively monitored by IRT since it can be assumed, with a high level of confidence, that the IRT measurements reflect the level of perfusion of skin, with little influence of systemic effects or deep tissue perfusion and metabolism. Good examples for that are the skin at the bridge of the nose, which is known to be fragile in geriatric patients during use of ventilation or continuous positive airway pressure (CPAP) masks, or the skin at the tip of the fingers, which is distorted by a pulse oximeter.

Nevertheless, in some cases, the device itself may emit or store heat or hinder clearance of heat away from the skin, which compromises skin integrity and tissue viability through increased metabolic demand of the heated tissues, as well as promotion of perspiration that is associated with skin maceration. The images provided in *Figure 1* demonstrate heating of the tip of the nose of a healthy individual after mounting a ventilation mask, which triggers perspiration in the mask that makes the skin-mask contact regions moist. The moisture, in turn, increases the coefficient of friction (COF) at the mask-skin contact sites and, hence, the static frictional forces, which distort tissues in shear and may, over time, cause deformation-

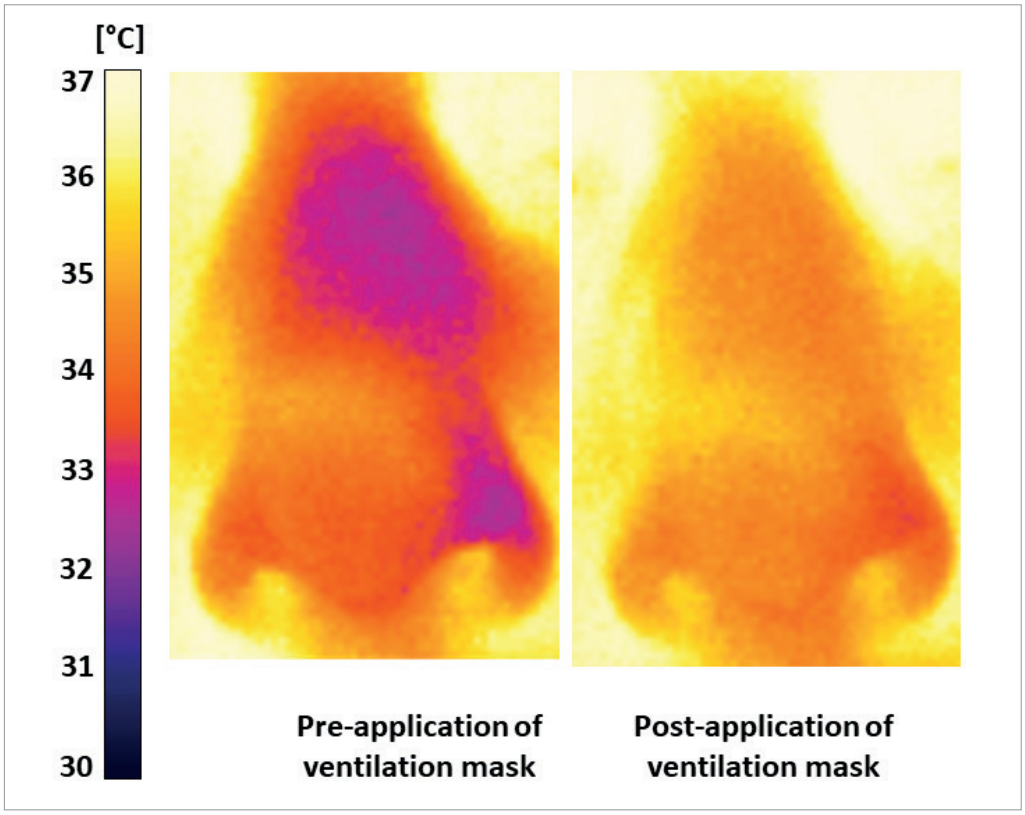

Figure 1. Heating of the nose within a ventilation mask as measured by our group using an infrared thermography (IRT) camera. The "post-application" IRT image is taken immediately after removal of the mask, which has been mounted for about 15 minutes. These measurements indicate that the tip of the nose is heated by ~2ºC which may increase the metabolic demand of skin (Stone et al. 2015) but is still within the acceptable (normative) facial skin temperature range (Kopp and Haraldson, 1983).

inflicted cell and tissue death (Gefen, 2018b). Friction in the context of PUs occurs between the body (skin) and the clothing or supporting surface, or between the body and any medical device in contact with the body. When the body and supporting surface move relative to each other, such as when a patient slides in bed or is being repositioned, they apply frictional force on one another in the direction opposite to the relative movement. This is the situation for dynamic friction (also known as kinetic friction). However, even if the body is at rest relative to the supporting surface or a contacting medical device, frictional forces are still involved. The physical meaning of these forces is that if one surface attempts to slide past the other, it needs to overcome a threshold force due to friction. This is the situation for static friction.

The power of IRT is in providing skin temperature measurements (possibly in real-time) that allow quantitative evaluation of the clearance of heat induced by a device or the heat generated, while a device is interacting with the body tissues. The aim in such analyses is to test whether tissue temperatures do not decrease or rise substantially, which interferes with tissue metabolism, physiology and susceptibility to injury. For example, 2–3ºC reductions in skeletal muscle tissue temperatures (which may be manifested by lower IRT measurements of skin temperature above the affected muscle) may be the result of poor circulation and lead to build-up of ischaemic stress and slowdown of biomolecule transport through free diffusion (Linder-Ganz and Gefen, 2007; Gefen et al, 2008; Ruschkewitz and Gefen, 2010; 2011).

Likewise, a considerable rise in skin temperatures may undesirably alter the microclimate leading to local perspiration, rise of the COF of skin with contacting objects and subsequently increase the device-skin shear forces resulting in deformation-induced damage (Gefen, 2011; Sopher and Gefen, 2011; Shaked and Gefen, 2013; Zeevi et al, 2018; Kottner et al, 2018). This is where the concept of thermal matching is important, meaning the thermal properties of the applied device, such as the heat production, thermal conductance of the components of the device or the convection of heat at the vicinity of the skin-device contacts. These parameters should be optimised to the skin and underlying tissues. Utilisation of IRT measurements in research and development of medical devices that contact the skin, as well as in device evaluations becomes increasingly important in this regard and is heavily employed by our group.

The tolerance of skin to heat and the physiological response of skin to elevated temperatures should be discussed in the context of MDRPUs. Temperatures of healthy skin range between 32–35ºC depending on the ambient temperature (Kopp and Haraldson, 1983). Pain

thresholds for touch are at around 42–44°C and vary across body sites (are highest in the foot and lowest in the chest; Defrin et al, 2006). Above these temperatures, accelerated cell death and irreparable protein damage may be initiated; the extent of cell death and structural damage would depend on the exposure time, according to the Arrhenius effect.

Nonetheless, it is known for many decades that when the skin temperature is around 44°C, the rate of an injurious change exceeds that of tissue repair by so little that it takes about 6 hours before irreversible damage is inflicted at the basal cell level (Moritz and Henriques, 1947). Now focusing on the temperature interval between healthy skin temperatures and pain thresholds, it has been shown that heating of the skin will affect skin elasticity parameters, and overall increase the stiffness of skin — allowing less dissipation of mechanical energy through skin deformation that promotes stress concentrations at and near skin-device contact areas (Patel et al, 1999; Held et al, 2018). The latter likely reflects physiological changes in the heated skin, including increased blood flow, metabolic demand of cells, interstitial and intracellular fluid contents, thermal contraction and expansion of collagen and elastic fibers, all of which are precursors of irreversible skin damage if the exposure is sustained beyond the said ~6 hours interval (Held et al, 2018).

Furthermore, the metabolic demand of skin is increased by ~10% per degree of warming (Stone et al, 2015). Taken together, the above literature suggests that warm skin is more susceptible to both direct deformation damage and ischaemic damage. This is highly relevant to medical devices that are in contact with the body for several hours, such as ventilation masks, tubing for respiration and feeding and ostomy patches. Adequate thermal matching between the device and skin would keep the temperature of skin in contact with the device and around the device as close as possible to the normal skin temperature. Based on the above literature and the current stage of research, temperatures sustained at the high end of the non-burn domain (near 40ºC) may increase the likelihood of skin breakdown (Held et al, 2018).

Accordingly, a practical bioengineering recommendation (given sometimes unavoidable heat trapping effects between devices and the skin) is to not exceed a skin temperature threshold of 37ºC (body core temperature) i.e. ~1ºC above the temperature domain of healthy skin. The studies under way by the authors' group, which are the first ever to use IRT in research of MDRPUs, are expected to shed additional light with regard to microclimate conditions caused by devices and desired relevant thermal conditions.

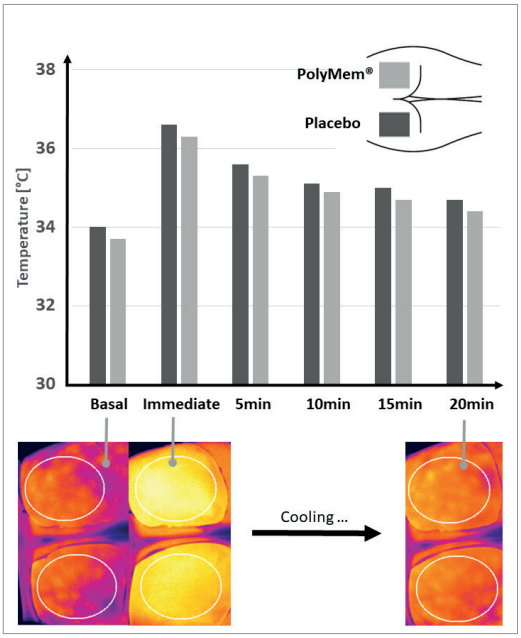

Figure 2. Infrared thermography (IRT) skin temperature measurements at the buttocks cheeks in a subject who has been lying in a Fowler position for an hour (no postural changes) with dressings tested for prophylactic use. The IRT data demonstrates that the microclimate is affected by the presence of the dressings, however the PolyMem® composition did not cause more heat trapping under the dressing than a placebo foam with identical thickness. Both the PolyMem and placebo dressings did not heat the skin of the buttocks of this studied subject more than when lying motionless in the Fowler position without the dressings (as per control measurements without dressings, which are not shown here). Hence, we found that PolyMem dressings exhibit good microclimate management which is important in both prevention and treatment of pressure ulcers. Immediate = the skin temperatures measured immediately after the lying session.

Microclimate conditions applied to skin by dressings

Much like in the case of medical devices, published information regarding heat trapping between dressings for PUP or PUT is poor. In fact, only one paper, by Call and colleagues (2013), addressed the issue of microclimate under prophylactic dressings empirically. They used a body phantom test fixture, rather than measurements in living humans and, hence, were not able to study the relevant physiology, such as skin heating due to vasodilatation and any inflammatory response. Preliminary human IRT data relevant to microclimate conditions of skin under prophylactic dressings used during cardiac ablation surgery were recently presented by the Cuddigan group at the 2018 National Pressure Ulcer Advisory Panel (NPUAP) Conference (Lier et al, 2018).

While the Lier et al (2018) work did demonstrate that IRT measurements are feasible in studies of microclimate conditions under prophylactic dressings (their IRT images were taken pre-application and immediately post-removal of dressings at the end of the ablation procedure), there are no journal publications relevant to this topic yet. The data presented in *Figure 2*, which are preliminary findings from our ongoing IRT work are, therefore, the first in the literature to describe human microclimate conditions and skin temperature changes under dressings used in a Fowler position.

The temperature data in *Figure 2* show the skin heating in the buttocks of a healthy young adult female, under two dressing types:

PolyMem® polymeric membrane dressing (Ferris Mfg. Corp., TX, USA) on one side of the buttocks versus placebo foam (lacking the inflammation modulating components of the PolyMem, but having the same thickness) on the other side.

Temperature data were acquired by IRT at the locations of the dressings immediately after removing both, following a session of motionless lying in a Fowler position for an hour, and every 5 minutes in a prone position thereafter, until 20 minutes post removal of the dressings. The basal temperatures of the buttocks cheeks were measured prior to the lying session. Subjects wore sports tights customised to the experimental protocol, where 'windows' were opened in the tights at the intended locations of application of the dressings (on the two buttocks cheeks). Those defined clear, consistent regions of interest for the thermal camera to focus on, in both basal and post-dressing use conditions. The data show the mild heating of skin under the dressings as heat accumulated between the body, dressing and (standard medical foam) support surface and then, the gradual return to basal temperatures when the subject was in a prone position.

Again, similarly to the case of medical devices, in a supine patient protected by a prophylactic sacral dressing, heat is potentially trapped between the prophylactic dressing and the skin (Call et al, 2013; Lier et al, 2018). The trapped heat causes increased metabolic stress on tissues, increased frictional forces due to the rise in COF associated with the accumulated moisture, and thus, elevated tissue distortions in shear (Gefen, 2011; Sopher and Gefen, 2011; Shaked and Gefen, 2013; Call et al, 2013; Stone et al, 2015).

Concurrently, the accumulated moisture results in maceration and softening of the hyaluronic acid intracellular bonds in skin, thereby increasing the potential for skin failure (Gefen, 2011; Call et al, 2013). As per the above discussion regarding IRT measurements in MDRPU research, some heat trapping at the skin is probably unavoidable. However, dressings should be evaluated for the skin microclimate conditions to ensure that the presence of the dressing does not cause heating of more than ~1ºC above the temperature domain of healthy skin without a dressing, in a supine or Fowler position (Call et al, 2013).

In other words, dressings used in prophylaxis should ideally not heat the sacral skin by more than ~1ºC with respect to the heating effect of an adequate support surface and reasonable clothing. The preliminary data in *Figure 2* demonstrate the heating of buttocks skin in a lying subject, as captured by high-resolution IRT, in a protocol that compares heat trapping under the PolyMem against a placebo foam of the same thickness, with the no-dressing case (data not shown) used as a control for both. The test protocol allows to determine whether the composition that is specific to PolyMem and its anti-inflammatory qualities (Gefen, 2018a) affects heat transfer properties of the dressing compared to a placebo foam.

The data in *Figure 2* show that the specific composition of PolyMem does not increase the heat capacity or thermal insulation of the dressing or overall allows less heat clearance from the dressing to the environment compared to foam. Moreover, the PolyMem dressing does not heat the skin more than in a condition of lying in a Fowler position with no dressing. In all our IRT data collected so far, the difference in skin temperatures for lying with a PolyMem dressing versus lying with no dressing did not exceed 1ºC. Hence, the IRT data show that the heat-trapping effect of the PolyMem dressing is low enough so that it should not negatively change skin physiology in prophylactic use.

Importantly, the experiment and data depicted in *Figure 2* demonstrate the utility and importance of IRT in evaluation of dressings for PUP and PUT purposes, and shows a way forward in objectively, standardly and quantitatively determining the microclimate conditions associated with use of dressings. Development of texture image analysis algorithms is under way in the authors' laboratories to also study extents of homogeneity of temperature distributions under dressings, as well as other medical devices.

Limitations of infrared thermography in pressure ulcer prevention and treatment

Inflammation of the skin and of deeper tissue layers, which is the response to cell and tissue damage in PUs is known to induce hyperthermia at or near the affected sites due to vasodilatation and increased skin perfusion causing convection of heat from the core of the body to the inflammation sites. An IRT camera visualises hyperthermia as hot spots and can quantify the locally elevated temperatures based on calibration. Theoretically, with the increasing spatial resolution of IRT cameras, that should make IRT the ultimate tool for early detection in PUP or for monitoring PUT, but published clinical work do not, overall, support use of IRT in clinical PUP and PUT work, the reasons of which are discussed below.

Temperature mapping by means of IRT provides images in which colours represent different temperatures. Considering that skin temperatures of contralateral regions of the body

should be nearly symmetrically distributed in a healthy person, thermal asymmetries in different areas that are prone to PUs can help in early-detecting tissue damage. Thermal asymmetry indices can be developed and used (analogue to pressure mapping asymmetry indices) to indicate asymmetry in skin temperature distributions over vulnerable and comparable areas. Examples for such potential comparisons are the two ischial tuberosities in the context of sitting-acquired PUs, the heels in supine patients or the two sides of the bridge of the nose in the context of MDRPUs caused by ventilation masks.

One thermal asymmetry index that varies linearly with the extent of the temperature asymmetry would be the ratio of the difference between the temperatures at the left and right sides of the body over the sum of these two temperatures. In such temperature asymmetry studies, an important question is — 'what is the absolute temperature difference between a suspected and a healthy site that may indicate a change in the tissue health status?'. The expected left-right temperature variance in facial skin is around 0.3–0.4˚C in healthy subjects (Kopp and Haraldson, 1983) and in about 90% of the performed measurements should be less than or equal to 1˚C (Johansson et al, 1985).

Consistently, small-to-medium group studies suggested that a 1.5–3˚C variance in skin temperatures (either cooler or warmer) between the comparable anatomical sites may point to a site-specific PU risk in patients who are generally at-risk, i.e. insensate or immobile or both (Judy et al, 2011; Farid et al, 2012; Mayrovitz et al, 2018). Nevertheless, such screening for temperature asymmetries would likely be efficient only if the focus is on skin health and integrity, as opposed to damage in deeper tissues. In other words, in the context of PUP, IRT becomes effective if a difference in temperatures between comparable sites subjected to sustained bodyweight forces relates to friction and shear causing skin inflammation, prior to formation of necrosis and ischaemia (Gefen, 2009).

Another potential application of IRT is in detecting undermining in existing PUs. Undermined PUs are difficult to heal; detection of the undermining is important for prognosis and timely interventions, e.g. skin incision and early debridement, which can prevent the deterioration of undermined PUs. It has been demonstrated that IRT focusing on lower temperature patterns at the wound edge may provide indication to reveal undermining or predict its development (Kanazawa et al, 2016a). The aforementioned work did not use an automated algorithm for detecting the potentially undermined (colder) regions, but rather, have classified IRT-visible low-temperature wound edges. Use of image processing, including, for example, texture analysis of the IRT images may improve the sensitivity of the approach and alert clinicians to this possible complication in PUT. However, lack of automatisation in image processing is not the only factor limiting clinical utility of the above approach.

Other work suggested that a greater temperature at the wound site when compared with periwound skin may imply the presence of critical colonisation. Therefore, there are contradicting factors, i.e. colder necrotic undermined tissues versus more superficial colonised tissues producing heat due to metabolism of the infecting pathogens (Nakagami et al, 2010).

Accordingly, IRT is not an ultimate indicator for potential cell death or tissue damage in PUs given that IRT captures the effective temperature distribution at the skin and subdermal tissues at which counteracting effects may occur. For example, a forming DTI may initially be cooler, but with the presence of an inflammatory response to the necrotic mass at the surroundings, which involves vasodilatation and increased blood flow, the effective result may be slight or non-detectable temperature changes at the skin surface. Clearly, the timing of the IRT measurements will also be important given that the inflammatory response has a time-course that is not synchronised with the development of the necrotic DTI mass (Gefen, 2009).

Computational modelling has shown that for a DTI, which is situated in muscle and fat layers, skin temperature changes are mild, due to shielding from the skin and the aforementioned interactions between ischaemic and inflammatory factors and effects. Skin temperature in the modeling increased between 0.25°C and 0.9°C during the inflammation phase but decreased between −0.2°C to −0.5°C as ischaemia developed (Bhargava et al, 2014).

Based on these theoretical data, a practicing clinician would be unable to detect consistent changes of the skin temperature above the DTI, at least at a certain period in the evolution of the injury as the effects of inflammation and ischaemia produce opposite temperature trends. This is an important limitation of IRT, which is seldom discussed. It should be highlighted that IRT measures temperatures at the surface or close to the surface of the body (similarly to interface pressure mapping, which is limited to skin pressure measurements), and hence, IRT is not suitable *per se* for early detection or risk assessments focusing on DTIs or which aim to minimise the occurrence of DTIs (Andersen and Karlsmark, 2008). Accordingly, as acquisition of infrared radiation data is limited to skin, IRT is inadequate as a direct means of early

detection in PUP and PUT since it cannot acquire thermal data that are specific to deeper tissues. This very likely explains the recent negative findings of Mayrovitz and colleagues (2018) who studied a hundred at-risk patients (the largest published IRT trial in PUP) and concluded that "although infrared thermal screening may provide visually impressive and potentially useful images in some cases, the use of temperature differentials to detect patients at particularly high risk for pressure injury owing to local blood flow is not supported by results of this study".

Similarly, a recent systematic review regarding the applicability of IRT in PUP concluded that thermography identifies skin temperature changes that may indicate early PU development but IRT data generally lacks specificity and sensitivity (Oliveira et al, 2017). Indeed, the group of professor Sanada in Japan have consistently proposed that IRT be combined with other imaging modalities, particularly ultrasound, for assessing the risk of or the healing progress of DTIs (Higashino et al, 2014). With that being said, IRT remains an excellent method in the bioengineering research of microclimate conditions, which is relevant to performance of medical devices in the context of preventing MDRPUs, as well as the use, evaluation and development of prophylactic dressings, as discussed in this paper.

Conclusions

There are good arguments for using IRT in PU research, particularly that IRT is non-invasive, non-ionising and non-contact examination, which eliminates risks for contamination and infection of skin and wounds, or for mechanically or otherwise damaging fragile tissues. Measuring skin temperatures using IRT is powerful in bioengineering research of microclimate conditions and, accordingly, is expected to support research on MDRPUs, including evaluation of equipment, consumables or device modifications to prevent MDRPUs.

Likewise, IRT is useful for microclimate characterisation in evaluations and development of prophylactic dressings. However, IRT does not appear to be effective, specific and sensitive enough for early detection of PUs or for monitoring PUT interventions, specifically since it cannot distinguish between opposite trends of effects on tissue temperature that originate from inflammation versus ischaemia. In evaluation of prophylactic dressings, IRT needs to be used methodologically in research to verify that there is no overheating of skin under a tested dressing. The experiments described here demonstrate that IRT is indeed suitable for characterising the skin microclimate under prophylactic and treatment dressings. Since warm skin is more susceptible to both direct deformation damage and ischaemic damage, IRT-based comparisons of skin temperature distributions across device options or prophylactic dressings and their protocols of application allow informed decision-making with regard to research and development, as well as selection and purchase of equipment and consumables.

The preliminary testing of PolyMem dressings, described here as an example, indicates that these dressings do not trap excessive heat as compared to placebo dressings or no usage of dressing. From a microclimate perspective, this makes the PolyMem dressings appropriate for prophylactic use, compatible with the '*Role of Dressings in Pressure Ulcer Prevention*' Consensus Document (2016). WINT

Disclosure

Professor Amit Gefen acts as a scientific advisor to multiple companies in the field of pressure ulcer prevention and treatment, including to Ferris Mfg. Corp. (USA) whose polymeric membrane dressing technology is referred to in this paper. This had no influence on the conclusions drawn from the analysis of literature and data, which is presented here.

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