BIOMEDICAL APPLICATION OF THERMOCHROMIC LIQUID CRYSTALS AND LEUCO DYES FOR TEMPERATURE MONITORING IN THE EXTREMITIES

A dissertation submitted to the Kent State University College of Education, Health, and Human Services in partial fulfillment of the requirements for the degree of Doctor of Philosophy

By

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INTRODUCTION: The researcher developed a prototype of a novel thermochromic liquid crystal (TLC)-coated fabric with an extended temperature range and enhanced sensitivity. Employing both color and pattern recognition into the fabric, rapid determination of the underlying pedal temperature is facilitated. PURPOSE: The purpose of this study was to evaluate the accuracy of the fabric as a potential diagnostic aid for identifying complications in the high-risk foot. METHODS: The hands of one hundred subjects were used to compare the average maximum temperatures indicated by the fabric versus standard thermal camera images. Findings were statistically analyzed using a paired t-test with significance defined as $p<0.05$. RESULTS: With the exception of the tip of the thumb and regions in the palm, there were no significant differences between average maximum temperatures measured with the thermal camera and those detected with the TLC fabric. CONCLUSION: Using direct visual analysis, the researcher demonstrated that a novel TLC fabric was able to accurately map temperatures in the palmar surface of the hand. The findings support the continued development of a temperature-sensitive sock that can be used in home to monitor for temperature changes that may indicate the onset of high-risk foot complications.
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CHAPTER I
INTRODUCTION

Frostbite and cold weather injuries to the extremities are a common malady amongst many individuals who spend time in subarctic environments. Although little data or research exists to support the incidences of the cold weather injuries in the general population (Hutchinson, 2014), researchers have reported that cold injuries affect hundreds of service members each year (Connor, 2014). From 2013-2014, the number of armed forces members treated for cold injuries was higher than it has been in the past 5 years (Connor, 2014). There is currently no reliable measuring system to monitor or detect the temperature of the extremities while submerged in cold temperatures. As such, individuals exposed to such an environment are at increased risk of developing frostbite or other cold injuries.

Purpose of Study

The purposes of the current investigation were:

1. To determine the efficacy and reliability of the thermochromic leuco dye coated latex glove in detecting temperature changes within the glove by changing color at a specific temperature set point, thereby having the potential to serve as a tool for early prevention of frostbite;

2. To determine the reproducibility of the thermochromatic leuco dye coated latex glove by detecting temperature changes within the glove through color change at a specific temperature set point over multiple trials;
3. To evaluate the effects of decreasing environmental temperature on the following dependent variables: (a) water temperature inside the glove and (b) color changes observed on the thermochromic dye coated latex glove.

**Hypothesis**

Based on previous studies conducted on TLC coated material, the researcher hypothesized the following:

1. That the thermochromic leuco dye coated latex glove will change from white to magenta in direct accordance with temperature changes of water at 12°C and will remain magenta red once temperatures of 12°C or lower are attained.

2. Environmental temperature will have an effect on the thermochromic dye and will impact the water temperature at which color change is noted on the glove.
CHAPTER II

REVIEW OF LITERATURE

Thermochromic Liquid Crystals

Researchers have used thermochromic liquid crystals (TLCs) for decades for various quantitative and qualitative applications. TLCs are often used because they are a cost effective alternative to more expensive thermal imaging modalities. Liquid crystals are materials whose molecules exist in a state between the liquid and solid states. This liquid crystal state exhibits both fluidity and structure (Collings, 2002). TLCs are unique in that their optical properties are dependent on temperature and they react in a predictable and repeatable manner. Different chemical formulations of the TLCs allow for the selective reflectivity of light based on the temperature of the TLCs. This reflection of light occurs at a wavelength that is in the visible color spectrum (Smith et al., 2001). The TLCs can be modified to detect temperatures that vary from -30°C to 150°C (Bharara, Cobb, & Claremont, 2006). The TLCs exhibit red color at lower temperature ranges, and then pass through the yellow, green, and blue colors as temperature increases (Smith et al., 2001). TLCs need a black or dark background to absorb light and prevent the reflection of unwanted light.

Thermochromic Leuco Dyes

A leuco dye is a dye that can switch between two separate chemical forms. It changes between one form that is colorless, and one that exhibits color. Thermochromic leuco dyes change color with changes in temperature. They are reversible in nature, and can fluctuate with changes in temperature (Božič & Kokol, 2008). The colorless form is
referred to as the “leuco form.” Researchers have shown that a 3°C temperature change is required for the leuco dye to change color. Leuco dyes are available in a variety of temperature gradients, from low-refrigeration type temperatures to high-temperatures that exceed pain threshold. They are available in a wide variety of colors, temperatures, and forms, including powder, slurry, water- and solvent-based ink, epoxy, and master batch. The benefit to using leuco dyes is that they are both more robust and less expensive than liquid crystals (“Thermochromic Leuco Dyes,” 2016).

**Biomedical Application of Thermochromic Liquid Crystals and Thermochromic Leuco Dyes**

Research on the use of thermochromic liquid crystals in the biomedical realm is very new and extremely limited. With the recent spike in technology and advancement of information display, scholars are now conducting further TLC research in various biomedical applications, and are developing devices based on liquid crystal materials imaging, microscopy, spectroscopy, and optically probing biological systems. Biosensors are also being developed with TLC material to allow observations of biological marvels with the naked eye (Woltman, Jay, & Crawford, 2007).

The first reports of TLCs used for biomedical purposes appeared in the year 2000, with a product called “ThermoSpot.” ThermoSpot is a continuous temperature monitoring sticker designed originally for neonates. The sticker is designed to change color from green to black when applied to the skin of those suffering from hypothermia (core temperature of <35.5°C or peripheral temperature of <35.0°C). Researchers have conducted studies using ThermoSpots amongst children that suffered from severe acute malnutrition. Such investigators have concluded that ThermoSpots successfully detected
episodes of hypothermia in malnourished children and were acceptable to mothers (Mole et al., 2012).

“Thermochromic Temperature-Monitoring Clothing” (US Patent: US20090046760 A1) was published on February 19, 2009 by John Peter Matheson. The patent states that it is the “first apparel invention to provide early detection and prevention of cold exposure to skin surface via thermochromism.” Although this invention is previously patented, no product currently exists in the form of a glove for the prevention of frostbite through the use of thermochromism. The current investigator noted the potential health benefits of this technology and chose to bring John Peter Matheson’s invention to life. No previous researchers have conducted such research on the efficacy and reliability of the application of thermochromic leuco dyes on latex gloves for the purpose of prevention of frostbite by detection of skin temperature changes.

**Frostbite**

Frostbite is damage caused by the freezing of tissue due to exposure to extreme cold temperatures. In cold ambient environments, humans must maintain core temperature within a fairly narrow range, typically 36.5°C-37.5°C (Guyton & Hall, 1996). Body temperature is maintained by increasing metabolism through mechanisms such as shivering or peripheral vasoconstriction. Vasoconstriction of the peripherals will lower the convective heat loss and improve body insulation. The process begins by the mechanisms of norepinephrine, which binds to alpha-adrenergic receptors causing vasoconstriction (Guyton & Hall, 1996). Peripheral vasoconstriction results in the
decrease of blood flow to the extremities, thus decreasing the risk for hypothermia, but increasing the risk for frostbite if skin temperature decreases to ≤ 0°C (Wilson, Goldman, & Molnar, 1976). Researchers have shown that mild frostbite may occur in the fingers at an average skin temperature of 3.7°C. The damage manifested by frostbite is not always clinically relevant, and there may be a wide variation between the damage to the skin and the underlying damage to the internal anatomy. Treatment of frostbite involves the rewarming of tissue in order to stop permanent cell damage, active wound care to promote timely healing, and preventative methods to minimize progressive dermal ischemia (Muller, 2009). Frostbite can be broken down into four stages, described as degrees of frostbite. First-degree frostbite includes a superficial freezing of epidermis with minimal tissue necrosis. Second-degree frostbite includes hypothermia and edema, which results in partial systematic thickness injury. Third-degree frostbite includes the necrosis of the entire skin thickness and may extend varying depth into the subcutaneous tissue. Fourth-degree frostbite involves the full thickness of the skin and underlying tissue, even including bone (Khanday, 2013).

**Frostbite in the General Population**

Frostbite and cold weather injuries to the extremities are common in those who spend time in cold weather environments. Cold-sport athletes such skiers, snowboarders, mountain climbers, hunters, and ice skaters spend large amounts of time in cold environments and are at risk for developing frostbite as a result. Makinen et al. (2009) administered questionnaires to men and women in the general population, 25-74 years of age. The investigators found that 697 frostbites were reported, 425 of which had occurred
in the past year and 272 over a lifetime. The overall proportion of annually occurring mild frostbite was 12.9% (14.2% in men and 11.9% in women). The annual incidence of severe frostbite was 1.1% (1.6% in men and 0.6% in women). The cumulative lifetime incidence of severe frostbite was 10.6% (14.1% in men and 7.4% in women; Makinen et al., 2009). This study showed that frostbite is a serious problem amongst the general population.

Makinen et al. (2009) concluded that frostbite in the general population occurs more often in men than women, and decreases in frequency over the age of 65. Most frostbite incidents were reported amongst occupational groups such as skilled agricultural and fishery workers, crafts and related trades workers, plant and machine operators, assemblers and technicians, and associate professionals. Work-related risk factors included employment in certain industries, high physical strain, and weekly cold exposure at work; however, frostbite was also likely to occur during leisure time (Makinen et al., 2009). Individual risk factors that increase frostbite include diabetes, white fingers in the cold, cardiac insufficiency, angina pectoris, stroke, depressive feelings, and heavy alcohol consumption (Makinen et al., 2009).

**Frostbite in the Military**

Cold injuries are common in the military. Due to the assignments and duties of the military personnel in cold and wet environments, service members are susceptible to many cold injuries, including hypothermia and frostbite. Connor (2014) found that during the years of 2013-2014, a total of 719 active or reserve members of the military presented with a primary diagnosis of a cold injury. Cold injuries were most common in the Army...
compared to other branches of the military. Frostbite accounted for 50.9% of the cold injuries that season. Connor also noted that in the military, there was a predilection for females, younger than 20 years of age, and of black or non-Hispanic race/ethnicity.

Hall, Evans, and Pribyl (2010) conducted a retrospective analysis of military databases with a tabulation of all cases of cold-weather injuries in Operations Enduring Freedom and Iraqi Freedom. Casualties reviewed occurred between 2001 and 2009. Overall, the authors identified 19 cases of cold-weather injury in the Afghanistan conflict, including two cases of frostbite, with only one likely requiring surgical intervention. The authors did not identify any cases of such injuries in Iraq. These 19 cold-weather injuries represent a dramatic decrease from the 6300 cases of cold-weather injury reported in the last major cold-weather conflict, the Korean War. This decrease results from the shorter and weather-dependent engagements, cold-weather education, and improved equipment of United States and allied personnel (Hall et al., 2010). A big part of the decline in cold weather injuries in this analysis compared to the amount of cold-weather injuries during the Korean War is the warzone climate. The environment is much different in Afghanistan and Iraq than it was in Korea, and allows soldiers to avoid extreme cold temperatures.

The United States Army Medical Department (2016) stated that frostbite accounts for the largest number of cold-weather injuries each year and occurs when tissue temperature falls below ~28-30°F. The Department defined the causes of frostbite as exposure to below freezing temperatures (<32°F) causing freezing of the skin, fingers, toes, ears, and facial parts. Causes also may include exposure of skin to metal, super-cold
fuel, and POL (petroleum, oil, lubricants), wind chill, and tight clothing, particularly boots. Riding in open vehicles, exposure to propeller/rotor-generated wind, running or skiing, and altitude exposure where there is little tree cover can all contribute to greater wind-chill. The Department described the symptoms of frostbite as numbness in the affected area; tingling, blistered, swollen, or tender areas; pale, yellowish, waxy-looking skin (grayish in dark-skin), frozen tissue that feels wooden to the touch; and significant pain after rewarming. The Department then described several methods for prevention of frostbite: use of contact gloves to handle all equipment, use of gloves to handle all fuel and POL products, avoid cotton clothing, keep face and ears covered and dry, keep socks clean and dry, and avoid tight socks and boots. The Department stated that monitoring air temperature and wind speed, and using the wind-chill index is the only way to determine the relative risk of frostbite. (U. S. Army Medical Center, 2016)

**Skin Temperature**

Skin temperature is influenced by core body temperature due to the increase or decrease in the body’s metabolism to maintain thermal homeostasis. The skin sends slow and rapid sensory signals, via thin myelinated Aδ fibers, to the somatosensory area as a response to temperature (Levy, 2004). In times of extreme cold temperature, the most crucial sensory information comes from afferent fibers deriving from the cutaneous fingers.

The efferent response moves blood from the cutaneous vessels toward the deep veins and eventually the heart in order to increase stroke volume and cardiac output (Stocks et al., 2004). This thermoregulation varies among individuals and is influenced by factors
such as age, gender, body fat, and adaptation. With vasoconstriction, the skin loses finer elements of tactile sensation resulting in the first stages of numbness and pain (Khanday, 2013). Peripheral vasoconstriction will result in less blood flow to the extremities, which will help prevent hypothermia but may result in frostbite if skin temperature decreases ≤ 0°C (Wilson et al., 1976).

Khanday (2013) found that for every $\text{Ta} = (\text{-10°C})$. The skin surface dominates the body core temperature and reduces it up to 20°C, which is fatal for cell life. This results in immediate cold pain and eventually necrosis. Signs of frostbite include necrosis, leading to mummification, sloughing, and auto-amputation. The degree of injury correlates to temperature and duration of exposure (Lehmuskallio, Hassi, & Kettunen, 2000).

**Factors Affecting Thermoregulation**

Cold exposure in the laboratory can either be convective or conductive. Heat flow occurs 25 times faster in circulating water compared to air (Pandolf, Sawka, & Gonzalez, 1988). The hands must be kept covered in extreme cold or frostbite will rapidly occur (Wilson et al., 1976). Gloves are two to three times more efficient at preventing heat loss compared to skin alone under a variety of conditions (Sari, Gartner, Hoefl, & Candas, 2004); however, there considerable variability between fingers and different subjects in response to cold (Chen, Liu, & Holmer, 1996; Yoshimura & Iida, 1952). The dorsal side of the hand has been shown to have an active vasodilator (Johnson, Pergola, Liao, Kellogg, & Crandall, 1995). Researchers must therefore study multiple finger and palm sites. Chen et al. (1996) measured all the fingers of the right hand during convective
cooling. Conversely, Zander and Morrison (2008) have measured temperature at eight sites: right thumb, right index finger, back of right hand, right forearm, left index finger, back of left hand, chest, and head. Flouris et al. (2006) used skin thermistors on the chest, tricep, thigh, and calf, in addition to the pads of both ring fingers. Finally, Cheung et al. (2008) used the medial nail bed edge on all of the fingers in addition to the skin over the first dorsal interosseous muscle. Clearly, there are few consistent skin sites when measuring finger and hand cooling because all investigators have examined different dependent variables.

Physiological and psychological differences between males and females as well as effect of age on cold response have been documented. Yoshimura and Iida (1952) described physiological and psychological differences between subjects of various ages, genders, and ethnicities following immersion of the middle finger in ice water. Hormonal variations in females must be considered during cold research because they may impact thermoregulation (Gonzalez, Blanchard, & Allison, 1998). For this reason, males are typically examined. Gender influences physiological and psychological responses to cold pain/strain. Men are motivated to tolerate more pain than women (Lowery, Fillingim, & Wright, 2003) and women cope with cold-induced pain differently than men, likely due to a decreased pain threshold (Keogh, Bond, Hanmer, & Tilston, 2005). In addition, subjective cold pain intensity is predicted by sex (physiological) and gender (self-reported psychological gender roles), as well as the age-gender interaction (Myers et al., 2006).

Prepubescent boys (Smolander, Bar-Or, Korhonen, & Ilmarinen, 1992) and girls
(Klentrou et al., 2004) have a differential response to the cold compared to adults. Elderly males thermoregulate differently than younger males (Potkanowicz, Caine-Bish, Otterstetter, & Glickman, 2003) and are at risk to be inadequately clothed in the cold and also possess higher blood pressures (Goodwin, Taylor, Pearce, & Read, 2000). Age has a greater effect on cold response than aerobic fitness level, although the two tend to be highly correlated (Falk, Bar-Or, Smolander, & Frost, 1994).

Fitness and fatness also impact cold tolerance. Fit men maintain higher skin temperatures post exercise and shiver more effectively than unfit men during 3 weeks of heavy work in the cold (Keatinge, 1961). Bittel et al. (1988) showed that fit individuals had an increased shivering ability, a sooner onset of shivering, and more stable skin temperatures during two hours of cold air exposure. People with more subcutaneous fat can maintain core temperature more efficiently (same core temperature with less shivering) than leaner counterparts (Glickman-Weiss et al., 1993; Glickman-Weiss, Hearon, Nelson, & Kime, 1996; Keatinge, 1960).

**Thermal Conductivity and Water**

**Surface Area: Mass**

The amount of surface area exposed to a cold environment has been thought to play a role in the facilitation of heat loss (Toner, Sawka, Foley, & Pandolf, 1986). This has been proven controversial (Glickman-Weiss et al., 1993); however, the surface area to mass ratio (SA:MA) is a factor that may influence thermoregulation due to a greater surface area for heat to dissipate to the periphery. It has been shown that larger people (Glickman-Weiss et al., 1993) and people with more muscle mass (Veicsteinas, Ferretti,
& Rennie, 1982) tend to have more tolerance to cold, since they produce more body heat and have more mass for insulation. The influence of surface area to mass ratio of the hand on skin temperature has only been reported in one peer-review publication (Jay & Havenith, 2004) and utilized a small sample size of mixed genders (n=7 male, 7 female).

Craig and Dvorak (1966) evaluated 10 subjects during head-out water immersion in nine different water temperatures ranging from 24°C to 37°C. The period of immersion at each temperature was 1 hour, during which the researchers took time various measurements. The investigators found that in water temperatures less than 35.6°C there was a reduction in central body temperature despite the fact that vasomotor controls of heat loss were evident. Craig and Dvorak also found that increased heat production was noted in water temperatures 30°C or less. Exchange of heat at a conductive level in water, versus convective exchange in still air, allows rapid heat loss because of direct contact and increased interaction between particles (Craig & Dvorak, 1966).

Heat loss by conduction is due to the theory of Newtonian cooling, where conduction of heat from the subject is transferred to the cold surrounding water. This conductive loss reflects important factors of the individual, including the thickness of adipose at specific locations and the vasculature status and its resulting capability to maximally vasodilate and vasoconstrict. Vasodilation results in maximum conductivity while maximum vasoconstriction correlates to minimum conductivity between the body immersed in water. As a result, conductivity of the epidermis will decrease as the body is exposed to cold temperatures by means of vasoconstriction and shivering thermogenesis (Cannon & Keatinge, 1960).
Cannon and Keatinge (1960) examined eight healthy naval ratings between the ages of 17 and 21 years old. Each subject was repeatedly immersed over a period of one week in water at temperatures ranging from 38°C or below. The investigators designed this study to test fat and lean men in a steady state of heat exchange in water to confirm or refute evidence that stimulation of deep temperature receptors play a role in adjusting metabolic rates of fat and lean men to their different rates of heat loss during prolonged exposures to cold. The investigators found that metabolic rates of both fat and lean young men in heat balance in water rose when the bath temperature was lowered below 33°C, although the fat men did not achieve their maximal tissue insulation until the water temperature was much lower. Metabolic rate rose less in fat than in thin men when the bath temperature was lowered below 33°C; the stable rectal temperature of the leaner men was lower in cold than in warm water, while that of the fattest men was not. They concluded that the fat men’s small metabolic response to cold was due to reflexes from the skin, while in the less fat or leaner men, these were reinforced by a fall in deep temperature and stimulation of deep temperature receptors. The fat men achieved a higher maximal tissue insulation than thinner counterpart and could stabilize their body temperature in water down to 10-12°C in colder water heat loss from their fingers rose in a cyclical manner; their tissue insulation fell by about 50% and their rectal temperatures fell (Cannon & Keatinge, 1960).

Alterations in cutaneous temperature is the initial means of thermal homeostasis when in contact with external temperatures. Stephens, Argus, and Driller (2014) exposed participants to cold water immersion baths for 15 minutes. The subjects participated in
seated immersion in cold water (15°C) and the investigators recorded their skin thermal readings both immediately post-immersion and a final time at 30 minutes post-immersion. The scholars took readings at the following sites: chest, anterior forearm, anterior mid-thigh, and posterior calf. The authors calculated mean skin temperature (Tsk) using the following equation: 

\[ Tsk = 0.3 \times (T_{\text{chest}} + T_{\text{arm}}) + 0.2 \times (T_{\text{thigh}} + T_{\text{leg}}) \]

(Ramanathan, 1965). The scholars recorded an average baseline skin temperature of 34°C for the subjects. Results showed that immediate post immersion temperature dropped to 22°C with a 30-minute post immersion reading of 28°C. Cutaneous vasoconstriction showed an immediate drop of an average of 12°C instantaneously as a response to cold stress (Stephens et al., 2014).

Several researchers (Cannon & Keatinge, 1960; Craig & Dvorak, 1966; Stephens et al., 2014) have shown that a person immersed in water at a given temperature will exchange heat quicker than being exposed to an ambient temperature of still air. This is due to the thermal conductivity of water being 25 times that of still air (Pandolf et al., 1988). Cooper and Trezek (1971) showed that pure water has a thermal conductivity of 0.627 (W/mK), ice at 0°C has a thermal conductivity of 2.18 (W/mK), and human epidermis has a thermal conductivity of 0.209 (W/mK). Heat transfer occurs at higher rates across materials of high thermal conductivity than materials of lower conductivity. The authors proved that skin temperature, with a thermal conductivity of 0.209 (W/mK), although slightly lower has a thermal conductivity very similar to the thermal conductivity of pure water (0.627 W/mK; Cooper & Trezek, 1971).
In the reviewed studies, the investigators reduced the subjects’ cutaneous temperature to reflect similar temperatures to the cold water they were immersed in. Due to metabolic factors and thermoregulation, cutaneous temperatures remained slightly higher (about 10°C) than the cold water the subjects were placed in. This evidence provided a platform for the current investigator to substitute water with human subjects in the current study.
CHAPTER III

METHODOLOGY

Participants

The researcher invited employees and students from the Kent State University College of Podiatric Medicine (KSUCPM) who are between 18 and 40 years of age to participate in the study. The investigator chose to exclude individuals with type 1 or type 2 diabetes, inflammation and/or swelling of either hand, history of any underlying vasoactive disorder, underlying pathological condition (metabolic, endocrine, arthropathic, or vascular disorders), and medication history that include drugs that may directly affect peripheral circulation and/or temperature from the study. The Kent State University Institutional Review Board reviewed and approved the current study, and the researcher obtained written informed consent from each participant prior to performing any research-related activities.

Experimental Procedure

The TLC fabric used in this study consisted of a black knit fabric (Article #00865790, Jo-Ann Stores, LLC, Hudson, OH) coated with thermochromic liquid crystals (Product Code SPM100, Nematic LC Sprayable Coating, LCR Hallcrest LLC, Glenville, IL). The TLC fabric incorporated three TLC formulations in different patterns to obtain a total temperature range of 24 to 35 °C. The first formulation (ink lot number 130724-3), consisting of a temperature range from 24 to 27 °C, was applied to the fabric in a thin solid line. The second formulation (ink lot number 130724-1), ranging from 28 to 31 °C, was applied in rectangular patterns. Finally, the third formulation (ink lot
number 130724-2), ranging from 32-35 °C, was applied to the fabric in rhomboid patterns. Within each formulation, the color ranged from red to green to blue, with red indicating the lowest temperature and blue being the highest temperature. Three formulations were used to ensure that a wide range of temperatures can be detected, while three different patterns increased the sensitivity of the fabric and allowed the investigator to know which formulation (temperature range) was activated and exhibiting color.

For the purpose of this proof-of-concept study, the investigator recorded the temperatures on the palmer surface of the hand. This site was chosen because the hands are readily accessible, provide a range of temperatures based on location, and can be easily sanitized in order to keep the fabric clean in between subjects. The researcher aimed to enroll 100 subjects with data to be collected from both hands of each subject, resulting in a sample size of 200 hands. Once enrolled into the study, each subject removed any jewelry or other objects from the hands and sanitized his or her hands with an alcohol-based sanitizer (Purell®, GOJO Industries, Inc., Akron, OH). The subject sat at a desk for 10 minutes to allow his or her hands to acclimate to the conditions of the room and to recover any temperature decrease that may have occurred during sanitization of the hands. After 10 minutes, each hand, in turn, was positioned for data collection with the elbow placed on the desk and the forearm and hand positioned parallel to the desk with the palm facing up.

The TLC fabric, secured in a hoop 12 inches in diameter, was placed over the palmar surface of the subject’s hand and held in place. A thermal image was then taken
of the hand using an infrared thermal camera (FlexCam® TiR2, Fluke Corporation, Everett, WA) with 100% infrared light. Next, a digital image was taken of the TLC fabric on the palmar surface of the hands to capture the colors and patterns that represent the temperatures on the hands. This was repeated for the subject’s opposite hand. The room conditions, including temperature and humidity, were recorded for each subject.

The thermal and digital images were then used to determine the average maximum temperatures at the following regions: (a) tip of thumb, (b) tip of second digit, (c) tip of third digit, (d) tip of fourth digit, (e) tip of fifth digit, (f) first metacarpal head, (g) second and third metacarpal heads, (h) fourth and fifth metacarpal heads, and (i) hypothenar eminence. Maximum temperatures were obtained from the thermal images using image analysis software specific to the thermal camera (SmartView® 3.6, Fluke Corporation, Everett, WA). Maximum temperatures were obtained from the TLC fabric by assigning a temperature to the primary color (red, green or blue) and pattern (solid line, rectangle or rhomboid) combination indicated by the fabric, based on the thermal profiles for the specific thermochromic liquid crystals used (Figure 1). The difference in maximum temperature was then determined by subtracting the maximum temperature recorded by the fabric from that measured with the thermal camera, and the average difference in temperature for each region of the hand was calculated.

Statistical Analysis

For each region of the hand, the investigator compared the maximum temperatures recorded by the thermal camera to those detected with the TLC fabric using a paired t-test with significance defined as p<0.05. If the data was not normally
distributed (nonparametric), the researcher conducted statistical analysis using the Wilcoxon signed-rank test, with significance again defined as \( p < 0.05 \).
CHAPTER IV

MANUSCRIPT 1

A Novel Thermochromic Liquid Crystal Fabric Design for the Early Detection of High-Risk Foot Complications: A Proof-of-Concept Study

Abstract

Background: The researcher developed a prototype of a novel thermochromic liquid crystal (TLC)-coated fabric with an extended temperature range and enhanced sensitivity. Employing both color and pattern recognition into the fabric, rapid determination of the underlying pedal temperature is facilitated. The purpose of this study was to evaluate the accuracy of the fabric as a potential diagnostic aid for identifying complications in the high-risk foot. Methods: The researcher used the hands of 100 subjects to compare the average maximum temperatures indicated by the fabric versus standard thermal camera images. The researcher statistically analyzed the findings using a paired \( t \)-test with significance defined as \( p < 0.05 \). Results: With the exception of the tip of the thumb and regions in the palm, there were no significant differences between average maximum temperatures measured with the thermal camera and those detected with the TLC fabric. Minor differences were relatively consistent among all nine regions of the hand, and were not considered to be clinically significant. Conclusions: Using direct visual analysis, the researcher demonstrated that a novel TLC fabric was able to accurately map temperatures in the palmar surface of the hand. The findings support the continued development of a temperature-sensitive sock that can be used in home to monitor for temperature changes that may indicate the onset of high-risk foot complications.
Introduction

The term “high-risk foot” can generically be applied to those feet that are associated with underlying risk factors and are at increased risk for the development of major complications such as deformity, ulceration, infection, gangrene, and/or amputation. Whereas the presence of advanced underlying lower extremity peripheral vascular disease places the foot at increased risk of serious complication, the term “high-risk” is most often used in conjunction with the diabetic foot with significant underlying patient comorbidities/multi-morbidities. These commonly include peripheral sensory, motor, and autonomic neuropathy, peripheral vascular disease (both small and large vessel), and nephropathy. As the term multi-morbidity implies, these often occur in concert with one another, and can lead to significant foot complications that may necessitate a lower limb amputation. Moreover, once amputation occurs in the diabetic patient, the five-year mortality rate is greater than 40% (Armstrong, Wrobel, & Robbins, 2007). The early detection and management of impending diabetic foot complications can significantly alter such deleterious outcomes as advanced Charcot neuroarthropathy and amputation.

Researchers in the body of literature have supported the use of foot temperature measurement as a basis of early warning of impending foot/extremity problems in both high-risk vascular and diabetic foot complications. Papanas et al. (2009) demonstrated higher foot temperatures in type 2 diabetics with peripheral neuropathy as opposed to individuals without neuropathy. In a systematic review and meta-analysis, Houghton, Bower, and Chant (2013) concluded that temperature monitoring is an effective way to
predict and prevent diabetic foot ulcerations. Stess et al. (1986) reported on the use of contact thermography to identify temperature patterns associated with diabetic foot ulcers. Along these same lines, using liquid crystal contact thermography, Benbow et al. (1994) assessed whether the development of plantar foot ulcerations could be predicted from mean plantar foot temperature (Benbow et al., 1994). These results demonstrated that liquid crystal thermography was a viable noninvasive method of identifying neuropathic feet that are at an increased risk of ulceration. Higher temperatures were associated with an increased risk of foot ulceration, while the presence of a low mean foot temperature in the neuropathic foot was a marker of peripheral vascular disease indicating an individual at increased risk of ischemic foot disease (Benbow et al., 1994).

In addition to neuropathy and diabetic foot ulceration, researchers have utilized infrared thermography in the detection of osteomyelitis in patients with diabetes (Oe et al., 2013; Moura-Neto et al., 2012). Sinacore et al. (2008) demonstrated that Charcot neuroarthropathy may also be detected by increases in temperature that may exceed those of soft tissue complications. The authors reported an average increase of 6.7 °F compared to the uninvolved foot (Sinacore et al., 2008). Thermography has also been shown to be useful in revealing changes secondary to inflammation, detecting abnormalities of the peripheral circulation (including venous disease and arterial disease) and assessing amputation level in ischemic limbs (Bagavathiappan et al., 2009; Henderson et al., 1978; Ohsawa et al., 2001).

Currently, there are very few simple options by which high-risk diabetic and dysvascular patients can self-monitor for serious foot disorders. Liquid crystal plates
(SpectraSole Pro 100 thermal foot indicator, Linkoping, Sweden) and walking mats are limited in that they indicate only plantar foot temperatures, can be difficult for patients to evaluate, and/or are impractical for home use (Roback, Johansson, & Sarkhammar, 2009). The focus of the current research was to explore an improved application of liquid crystal thermography technology for the early detection of potential high-risk vascular and diabetic foot complications using self-administered home assessment. Given that the prevention of lower limb amputation is of utmost importance, the long-term goal of this project was to develop a simple, affordable sock coated with thermochromic liquid crystals that is both accurate and easy to interpret, thereby facilitating routine use by patients (for self-monitoring) and/or health care providers as an early warning system for impending foot complications. Areas of abnormally increased or decreased temperature, which can be detected by the sock, could correspondingly identify sites of inflammation (infection, trauma/Charcot) or vascular compromise. The purpose of this study was to evaluate the accuracy of an initial thermochromic liquid crystal (TLC) fabric prototype that has increased sensitivity and extended temperature range detection. Temperature ranges in the TLC fabric are indicated by both color and geometric pattern recognition. The specific aim was to determine if the temperature on the palmar surface of the hand recorded by a thermal camera is accurately reflected by that measured with the initial TLC fabric prototype. The hypothesis was that there would be no significant differences between the temperatures measured with a thermal camera and those measured with the TLC fabric.
Methods

The TLC fabric used in this study consisted of a black knit fabric (Article #00865790, Jo-Ann Stores, LLC, Hudson, OH) coated with thermochromic liquid crystals (Product Code SPM100, Nematic LC Sprayable Coating, LCR Hallcrest LLC, Glenville, IL). The TLC fabric incorporated three TLC formulations in different patterns to obtain a total temperature range of 24 to 35 ºC. The first formulation (ink lot number 130724-3), consisting of a temperature range from 24 to 27 ºC, was applied to the fabric in a thin solid line. The second formulation (ink lot number 130724-1), ranging from 28 to 31 ºC, was applied in rectangular patterns. Finally, the third formulation (ink lot number 130724-2), ranging from 32-35 ºC, was applied to the fabric in rhomboid patterns. Within each formulation, the color ranged from red to green to blue, with red indicating the lowest temperature and blue being the highest temperature. The researcher used three formulations to ensure that a wide range of temperatures could be detected, while three different patterns increased the sensitivity of the fabric and allowed the researcher to know which formulation (temperature range) was activated and exhibiting color.

Participants

The researcher invited employees and students from the Kent State University College of Podiatric Medicine (KSUCPM) who were between 18 and 40 years of age to participate in the study. The researcher excluded individuals with type 1 or type 2 diabetes, inflammation and/or swelling of either hand, history of any underlying vasoactive disorder, underlying pathological condition (metabolic, endocrine,
arthropathic, or vascular disorders), and medication history that included drugs that may directly affect peripheral circulation and/or temperature from the study. The Kent State University Institutional Review Board reviewed and approved the study, and the researcher obtained written informed consent from each participant prior to performing any research-related activities.

**Experimental Procedures**

For the purpose of this proof-of-concept study, the researcher recorded the temperatures on the palmar surface of the subject’s hand. This site was chosen because the hands are readily accessible, provide a range of temperatures based on location, and can be easily sanitized in order to keep the fabric clean in between subjects. The researcher aimed to enroll 100 subjects with data to be collected from both hands of each subject, resulting in a sample size of 200 hands. Once enrolled into the study, each subject removed any jewelry or other objects from the hands and sanitized his or her hands with an alcohol-based sanitizer (Purell®, GOJO Industries, Inc., Akron, OH). The subject sat at a desk for 10 minutes to allow the hands to acclimate to the conditions of the room and to recover any temperature decrease that may have occurred during sanitization of the hands. After 10 minutes, each hand, in turn, was positioned for data collection with the elbow placed on the desk and the forearm and hand positioned parallel to the desk with the palm facing up.

The TLC fabric, secured in a hoop 12 inches in diameter, was placed over the palmar surface of the subject’s hand and held in place. A thermal image was then taken of the hand using an infrared thermal camera (FlexCam® TiR2, Fluke Corporation,
Everett, WA) with 100% infrared light. Next, a digital image was taken of the TLC fabric on the palmar surface of the hands to capture the colors and patterns that represent the temperatures on the hands. This was repeated for the subject’s opposite hand. The room conditions, including temperature and humidity, were recorded for each subject.

The thermal and digital images were then used to determine the average maximum temperatures at the following regions: (a) tip of thumb, (b) tip of second digit, (c) tip of third digit, (d) tip of fourth digit, (e) tip of fifth digit, (f) first metacarpal head, (g) second and third metacarpal heads, (h) fourth and fifth metacarpal heads, and (i) hypothenar eminence. Maximum temperatures were obtained from the thermal images using image analysis software specific to the thermal camera (SmartView® 3.6, Fluke Corporation, Everett, WA). Maximum temperatures were obtained from the TLC fabric by assigning a temperature to the primary color (red, green or blue) and pattern (solid line, rectangle or rhomboid) combination indicated by the fabric, based on the thermal profiles for the specific thermochromic liquid crystals used (Figure 1). The difference in maximum temperature was then determined by subtracting the maximum temperature recorded by the fabric from that measured with the thermal camera, and the average difference in temperature for each region of the hand was calculated.

Data Analysis

For each region of the hand, the investigator compared the maximum temperatures recorded by the thermal camera to those detected with the TLC fabric using a paired $t$-test with significance defined as $p<0.05$. Comparisons in maximum temperature recorded were made between the TLC fabric and the temperatures recorded
by the thermal camera at the tip of the first digit, tip of the second digit, tip of the third digit, tip of the fourth digit, tip of the fifth digit, first metacarpal head region, second and third metacarpal head region, fourth and fifth metacarpal head region, and hypothenar eminence.

**Results**

A sample thermal image of a hand is shown in Figure 4 with its corresponding 1.3x (approximate) magnified TLC fabric image in Figure 5. The hot spots of the hand (bright red regions at the 1\textsuperscript{st} and 2\textsuperscript{nd} metacarpal heads and the hypothenar eminence) in Figure 4 are captured by the TLC fabric, as demonstrated by the activation of the 32-35 °C rhomboid pattern. This is clearly depicted in Figure 6 with an up-close digital enhancement (Photoshop, Adobe Systems Inc., San Jose, CA), illustrating the three patterns that have been activated by the temperature of the hand.

The results for the average maximum temperatures recorded with the thermal camera and with the TLC fabric at the nine different regions of the palmar surface of the hand are shown in Figure 7. With respect to the digits of the hand, the peak temperature measured with the thermal camera at the tip of the thumb ($n=196$) was significantly greater than that measured with the TLC fabric ($p<0.05$). There were no significant differences in maximum temperatures measured with the thermal camera and those measured with the TLC fabric at the tips of the second digit ($p=0.772$), third digit ($p=0.917$), fourth digit ($p=0.616$), and fifth digit ($p=0.326$). Regarding the palmar regions of the hand, the maximum temperatures measured by the thermal camera were significantly greater than those detected with the TLC fabric at the first metacarpal head,
second and third metacarpal heads, fourth and fifth metacarpal heads, and the hypothenar eminence \((p<0.05)\).

The average difference between maximum temperatures measured with the thermal camera and those detected with the TLC fabric at all regions of the hand ranged from -0.3 to 0.7 °C. The positive values for the average differences at the tip of the thumb \((0.2 \pm 1.4 \, ^\circ\text{C})\), first metacarpal head \((0.5 \pm 1.2 \, ^\circ\text{C})\), second and third metacarpal heads \((0.5 \pm 1.6 \, ^\circ\text{C})\), fourth and fifth metacarpal heads \((0.7 \pm 1.6 \, ^\circ\text{C})\), and the hypothenar eminence \((0.3 \pm 1.5 \, ^\circ\text{C})\) suggest that the temperature was slightly greater when recorded with the thermal camera compared to the TLC fabric. In contrast, the temperatures measured with the thermal camera were marginally less than those measured with the fabric at the tip of the third digit \((-0.1 \pm 1.5 \, ^\circ\text{C})\) and the tip of the fifth digit \((-0.3 \pm 1.8 \, ^\circ\text{C})\) as indicated by the negative average difference. The average differences between measurement techniques was zero at the tips of the second digit \((0.0 \pm 1.6 \, ^\circ\text{C})\) and fourth digit \((0.0 \pm 1.6 \, ^\circ\text{C})\).

On several occasions when assessing temperature in the digits with the TLC fabric, the temperatures were lower than the minimum that could be detected by the fabric \((24.8 \, ^\circ\text{C})\). In these instances, the fabric appeared black with no colors or patterns evident. The average maximum temperatures measured in the corresponding thermal images ranged from 24.3 °C at the tips of the fourth and fifth digits to 24.8 °C at the tips of the thumb and the second digit (Figure 8).

**Discussion**

A total of 125 subjects were enrolled into the study. Three of the subjects did not
return for data collection after signing the consent form, while two other subjects were ineligible to participate in the study based on the exclusion criteria. The data from 20 of the subjects was unsatisfactory; therefore, the researcher recruited an additional 20 subjects into the study to replace the insufficient data. As a result, 200 hands from 100 subjects were included in the analysis.

The temperature of the room where the study was conducted was reasonably consistent over the nine days of data collection. The temperature ranged from 21.8 to 23.8 °C, with an average of 22.7 ± 0.6 °C. The humidity of the room varied over the days of data collection, ranging from 26.0% to 49.0%, with an average of 39.2 ± 7.2%. The conditions of the room did not appear to meaningfully impact the temperatures of the hand.

Thermochromic liquid crystals (TLCs), or cholesteric liquid crystals, are materials that change reflected color in response to fluctuations in temperature. At lower temperatures, TLCs exist in a solid phase, while at higher temperatures they exist in a liquid phase (Collings, 2002). When in these phases, TLCs will appear transparent against a black, non-reflecting surface (Bharara et al., 2006). In between the solid and liquid phases, the material exists in the liquid crystal phase, which is a fluid phase with some degree of order (Collings, 2002). In this state, TLCs form layers that can slide over one another or twist around a fixed axis in response to temperature, thus changing the color of the reflected light. Different chemical formulations of TLCs allow for detection of various temperature ranges with a high sensitivity (Bharara et al., 2006). Within each formulation, the reflected color changes from red to green to blue as temperature
increases, and the response time is typically rapid.

The TLC fabric utilized in the current study is unique in that it has an extended temperature range with increased temperature sensitivity due to the addition of innate/inherent temperature-specific patterns. It also provides for whole field evaluation as opposed to being restricted to smaller areas. The results of this proof-of-concept study suggest good correlation between the thermal camera and the TLC fabric, with the average differences ranging from -0.3 °C at the tip of the fifth digit to 0.7 °C at the fourth and fifth metacarpal heads. These differences were not considered to be clinically relevant. The purpose of the desired end product, a sock, is to display changes in temperature that may occur in one or both feet as a result of the early onset of high-risk foot complications. The actual temperature values are not as important as the change in temperature.

The variability in maximum temperature values between subjects was greater at the tips of the digits than at the regions in the palm of the hand, as indicated by the larger standard deviations for the digit temperatures. In several instances, the temperatures in the digits could not be detected by the fabric because they were below the minimum of the temperature range that the fabric can detect, but the temperatures in the regions of the palm were easily detected by the fabric. The researcher postulated that this is most likely due to, separately or in combination, (a) decrease in circulation at the tips of the digit, (b) some degree of distal digital vasoconstriction, (c) increased vascularization due to the muscle mass in the palm of the hand, or remotely (d) air gap/loss of fabric contact compared to the palm of the hand.
The investigator found that maximum temperatures recorded by the thermal camera for the regions of the palm were significantly greater than those detected by the TLC fabric. The power of these analyses ranged from 0.917 to 0.999. The differences between temperatures measured with the two techniques at all nine regions of the hand were less than 1 °C. The investigator noted that the accuracy of the thermal camera is ±2 °C or ±2 %, whichever is greater, while the accuracy of the thermochromic liquid crystals are ±1 °C. Thus, while the differences in temperatures between the thermal camera and TLC fabric were consistent, the values fall within the range of the accuracies of the camera and the liquid crystals.

**Limitations**

One limitation of this study was that, while the thermal camera displays the equivalent of a temperature continuum, the temperatures indicated by the TLC fabric fall into nine possible temperatures based on a combination of color (blue, green or red) and pattern (solid line, rectangle or rhomboid). For this preliminary study, no intermediary colors were considered when assigning temperature to the observed color. It should be noted, however, in the practical detection of extremity complications, the observed change in color is more important than the exact temperature.

Another potential limitation pertains to the fabric employed—that is, the initial prototype evaluated in this study allowed for fabric stretch in only one direction, thus raising the possibility that there may have been loss of contact between the skin and the fabric. With loss of contact, one would surmise that the temperature measured by the fabric would be less than the actual temperature of the skin due to dissipation of heat.
through the gap. The current researcher was able to visually confirm that contact was made between the fabric and the skin at all nine regions of the hands that were evaluated and therefore concluded that this was not a limitation to the study.

Still another area of concern occurred when the TLC fabric was placed against the hand, there appeared to be a “bleeding” of color away from the point of contact between the skin and the fabric. This suggests the possibility that the fabric was not accurately measuring the temperature at the desired locations. This effect can be clearly seen around the fingers in Figures 3 and 4, as the dark blue color fades into green and then red. After close examination, the researcher determined that this was not a limitation to the study, for in actuality the color is not bleeding from the point of contact. Rather, the fabric is recording the heat that is dissipating from the hand.

Finally, one other potential limitation to the study is that the time between the first and last days of data collection was 77 days, raising the concern that the TLCs on the fabric may have degraded over the course of the study. To this end, the researcher conducted a statistical analysis to determine if there was a correlation between the differences in temperatures recorded with the thermal camera and the fabric and the number of days from the start of data collection. Using a Spearman Rank Order Correlation test with significance defined as $p<0.05$, the analysis determined that there are no significant relationships between the difference in temperature and the day that the data was collected. This suggests that degradation of the TLCs did not occur to an extent that it would affect the data collected from the TLC fabric.
Conclusion

In conclusion, as the data suggests, with direct visual analysis, the researcher determined that the TLC fabric is able to accurately map temperatures for specific regions of the hand, thereby validating the concept of an extended range temperature-sensitive fabric. This supports the continued development of the temperature-sensitive sock. The next step is to refine components toward the production of a sock (or glove) that can monitor for temperature changes in the foot (or hand). The material used in this current proof-of-concept study allowed for stretch in only one direction, and did not focus on maximizing TLC color saturations. Optimal fabrics that will enhance the colors displayed by the TLCs while ensuring the appropriate elasticity to allow for complete contact of the sock with the foot are to be determined. In addition, the patterns in which the various TLC formulations are arranged will be optimized so that individuals can easily discern and recognize which temperature formulations are activated.
CHAPTER V
MANUSCRIPT 2

A Novel Thermochromic Leuco Dye Coated Latex Glove for the Prevention of Frostbite in Cold Environments: A Proof-of-Concept Study

Abstract

Background: The researcher developed a prototype of a thermochromic leuco dye coated latex glove designed for the early prevention of frostbite in cold environments. Thermochromic leuco dye was calibrated to detect contact temperature and change color accordingly at temperatures of 8°C and below. PURPOSE: The purpose of this study was to evaluate the reliability and efficacy of the glove as a potential tool for the early detection of frostbite. Methods: The researcher conducted two trials in a constant environmental temperature set at 24°C and 6°C using an environmental chamber. Using a water bath, water was cooled to temperatures between 5°C and 15°C in 1°C increments and was placed into the same thermochromic dye coated latex glove five times at each temperature set point, in each trial. The researcher recorded visual findings and analyzed all data using paired samples t-tests. Results: Color change was noted in 20/100 individual trials at all internal contact temperatures of 8°C and below. Mean internal contact temperature measurements were 8.54 (±) 0.05 °C in Trial 1 (24°C ambient) and 8.48 (±) 0.04°C in Trial 2 (6°C ambient). The researcher concluded that there is no significant difference (p=0.208) between threshold mean internal water temperature between the two trials at the targeted color change of red. Conclusion: The glove demonstrated a consistent color change at a threshold of 8°C and below, with all of the
100 individual trials, at 2 different external environmental temperature set points proving that ambient temperature has minimal influence on contact temperature required to elicit a color change. This demonstrates that the thermochromic dye coated latex glove can be used as a visual, real-time diagnostic tool for the prevention of cutaneous frostbite. Future work may therefore focus on developing this material for the military or outdoorsman for the early detection of cold injury in the field.
Introduction

Frostbite and cold weather injuries to the extremities are a common malady amongst many individuals who work in cold environments. Although little data or research exists to support the incidences of the cold weather injuries in the general population (Hutchinson, 2014), the data suggests that cold injuries affect hundreds of service members each year (Connor, 2014). From 2013-2014, the number of armed forces members treated for cold injuries was higher than it has been in the past 5 years (Connor, 2014). There is currently no reliable measuring system to easily monitor or detect the temperature of the extremities while immersed in cold temperatures. As such, individuals exposed to such an environment are at increased risk of developing frostbite or other cold injuries.

Purpose of Study

The lack of monitoring capabilities for skin temperature necessitates further investigation of technologies which may be able to reduce the risk of, or even prevent, frostbite or other cold injuries. Thermochromic liquid crystals (TLCs) and thermochromic leuco dyes, when coated on fabrics or other wearable materials, can be used to detect changes in skin temperature. TLCs and thermochromic dyes can be formulated to reflect specific colors that correlate with specific temperature ranges. A previous study conducted at Kent State University evaluated a fabric coated with three different formulations of TLCs that could identify temperatures in three distinct ranges: 24-27°C, 28-31°C, and 32-35°C. Each formulation was applied to the fabric in a unique pattern (solid lines, rectangles and rhomboids) to allow for recognition of changes in skin
temperature. Prior to this investigation, a study has never been conducted with thermochromic technology specifically formulated to detect cold temperatures for the prevention of frostbite. Collaborators at Kent State University’s College of Podiatric Medicine, Exercise Physiology Program and Liquid Crystal Institute have demonstrated the ability to apply thermochromic technology to a disposable latex glove. The goal of this research is to determine the efficacy and reliability of the thermochromic dye coated latex glove in detecting temperature changes within the glove, by changing color at a specific temperature set point, thereby having the potential to serve as a tool for early prevention of frostbite. If efficacy and reliability is proven, the thermochromic dye coated latex glove will aid in the early prevention of frostbite, thus reducing the occurrence of frostbite and its concomitant morbidities.

In order to control for undesirable external variables and provide the most accurate assessment of the efficacy and reliability of the thermochromic dye coated latex glove, the investigator did not use any subjects for this investigation but, instead, placed water at different temperatures inside the glove. This research protocol aimed to find a correlation between the water temperature inside the glove and the color change observed on the thermochromic dye coated latex glove. Further, the investigator also evaluated the effects of decreasing environmental temperature on the following dependent variables: water temperature inside the glove and color changes observed on the thermochromic dye coated latex glove.
**Methods**

In this focused research study, the investigator at Kent State University’s College of Podiatric Medicine and Exercise Physiology Program collaborated with the university’s Liquid Crystal Institute to develop a thermochromic dye coated latex glove. The investigator created a glove using white disposable latex gloves (Curad latex disposable gloves, one size fits most, powder free) coated with thermochromic dye (Chromazone, Product Code: NA, Product: Water based slurry, Colour: Magenta, Temperature: 12°C, Batch Code: A9-08069-4, LCR Hallcrest LLC, Glenville, IL) to detect skin temperatures below 12°C. The investigator hypothesized that the thermochromic dye coated latex glove would change colors at a water temperature set point of exactly 12°C, and would remain magenta red once temperatures of exactly 12°C or below were attained. This technology aimed to serve as an early warning system for cutaneous frostbite in those exposed to cold temperatures.

**Experimental Procedure**

One thermochromic dye coated latex glove was used during each of two experimental trials. In order to avoid risks to research participants that may occur from exposure to an extreme cold environment for a sufficient period of time to induce the onset of frostbite, a water bath was used to cool water and simulate skin temperatures inside the glove.

Measurements were taken during two separate experimental trials. One thermistor was suspended inside the glove 6-cm from the distal tip of the third digit in the palmar region to determine the actual temperature of the water once it was placed into the glove.
The researcher recorded the thermistor measurements at each 1°C temperature decrease, from 15°C to 5°C.

This experiment followed a repeated measures, within subjects design. Each specific temperature served as its own control, which allowed the investigator to test for potential color change in the glove at each temperature point. This allowed the investigator to test for potential activation and color change of the thermochromic leuco dye coated latex glove, and prove the reliability and efficacy of the glove in providing users with a diagnostic warning sign for decreased cutaneous temperature.

All of the trials took place in a temperature controlled environmental chamber (Cincinnati Sub Zero, Cincinnati, OH) in the Exercise Physiology laboratory at Kent State. Pilot data from the researcher’s laboratory showed that air temperature was maintained within a range from -10°C to 40°C. Within the chamber, one long table was established for the researchers to permit accurate data collection.

Water temperature was cooled to exact temperatures using a water bath (Fisher Scientific, Isotemp) which was placed inside the environmental chamber to allow for minimal transition time of the water from the bath to the gloves (Figure 1). The temperature was measured after it was transferred inside the gloves via a thermistor (ER400-12, Respiratory Diagnostic Products, Irvine, CA and Model 409B, Yellow Springs Instruments, Yellow Springs, Ohio). The thermistor was suspended into the glove by the investigator (CV). Water temperature data was interfaced to a computer (iNet-100HC, Omega Engineered, Stamford, Connecticut).
The researcher measured and transferred 350 mL of water from the water bath to the gloves in a 2-L measuring cup in order to allow for the same amount of water to be poured into each glove, during each trial. During experimentation, 1 chemistry ring stand (American Education 7-G87-A Stamped Steel Support Ring Stand with 4”x6” base and 3” ring) was present on the table in the environmental chamber, allowing the investigator to tape (Hytape, Brooklyn, New York) the glove to the ring stand and keep the base of the glove open (Figure 2).

**Experimental Trials**

On the day of data collection, the investigator arrived at the Applied Physiology Laboratory at 010:00 to prepare for data collection for Experimental Trial 1. In order to control for ambient temperature, the investigator set the temperature in the environmental chamber to a standard room temperature of 24°C. This was done the night prior. The thermochromic dye coated latex glove was suspended by the base of the glove to a chemistry ring stand.

The investigator began by heating two liters of water to 15°C in the water bath. Once the water reached 15°C and remained constant at that temperature for two minutes, the water was extracted from the water bath, using 350-mL of water in a 2-L measuring cup, and poured into the thermochromic leuco dye coated latex glove. The base of the glove was taped to a ring stand (Hytape, Brooklyn, New York), allowing the gloves to remain open and aiding in the avoidance of contact between the investigator and the thermochromic dye coated latex gloves. After a 10 second acclimation period, the thermistor measurement was taken from the glove, to get a reliable temperature reading.
of the water once it was inside the glove. Digital images were taken of the gloves from both an anterior and posterior view using a digital camera (Nikon D5200 DSLR Camera w/18-55mm VR II Lens (Black)), in order to allow the investigator to make subjective readings of the color of the glove at each temperature set point. Thermistor readings and digital images were recorded at the same time exactly 10 seconds after the water filled up the glove (Table 1). Five separate trials were conducted at 15°C, using the same glove. The same experimental design was repeated with water temperature decreased in 1°C increments down to a final temperature of 5°C for the rest of Experimental Trial 1. The same procedure was repeated in Experimental Trial 2, with the water temperature decreased in 1°C increments from 15°C down to a final temperature of 5°C; however, the temperature in the environmental chamber was decreased to 6°C.

Keeping the environmental temperature consistent at 24°C during the first experimental trial allowed the investigator to control for any external ambient temperature. If the thermochromic dye changed to magenta red in accordance with a specific temperature point in all five trials using the same glove, the investigator could prove the reliability and reproducibility of the glove. The second experimental trial demonstrated the impact external environmental temperature played on the thermochromic dye coated latex glove. The results of this study will facilitate the development of a functional prototype for use in cold climates.

**Data Analysis**

The researcher utilized SPSS version 17.0 to conduct the statistical analysis. The experiment was a within subjects repeated measures design. The researcher conducted
two paired sample $t$-tests to analyze the data. The first $t$-test compared the internal environmental temperatures of water inside the gloves between Trial 1 (24 °C of external environmental temperature) and Trial 2 (6 °C of external environmental temperature) at the water temperature point where the gloves turned magenta red. The second $t$-test compared the temperature of the water prior to pouring it into the gloves between Trial 1 (24 °C of external environmental temperature) and Trial 2 (6 °C of external environmental temperature) at the water temperature point where the gloves turned magenta red. Data were presented as mean ± SD and the level of significance was set a priori at $p \leq 0.05$.

**Results**

Two trials were conducted, with external environmental temperature set to 24 °C during Trial 1 and external environmental temperature set to 6 °C during Trial 2. During each trial, water was set to 10 different set points ranging from 5 °C to 15 °C and poured into a single thermochromic leuco dye coated latex glove 5 times. Internal water temperature and color change (yes or no) was recorded at each run and no data was thrown out for any reason.

Results showed that during Trial 1 (24 °C of external environmental temperature), the leuco dye coated latex glove changed color from white to magenta red at all internal water temperature points of 8 °C and below (Figure 3). At 9 °C and above of internal water temperature, the glove remained white (Figure 4). During Trial 2 (6 °C of external environmental temperature), the leuco dye coated latex glove changed color from white to magenta red at all internal water temperatures of 8 °C and below (Figure 5). Results
showed that during Trial 2, the leuco dye coated latex glove stayed white and had no color change at 9 °C and above (Figure 6). A paired sample t-test comparing the internal water temperature between Trial 1 and Trial 2 showed that the leuco dye coated latex glove changed color from white to magenta red at a mean temperature of 8.54 ± 0.05 °C in Trial 1 and 8.48 ± 0.04 °C in Trial 2. The paired sample t-test showed that there was no significant difference (p=0.208) between mean internal water temperatures at which the leuco dye coated latex glove changed color from white to magenta red.

For both of these trials, water temperature was measured at the point of extraction from the cooling bath and again once inside of the glove by using thermistors. Temperature values changed slightly during this time due to the influence of heat conduction from the glove and external environmental temperature. At the point of color change from white to magenta red, mean temperature readings at the time of water extraction from the water bath was 7.8 ± 0.2 °C for Trial 1 and 9.0 ± 0.0 °C for Trial 2. The paired sample t-test showed that there was a significant difference (p=0.004) between mean water temperatures at the point of extraction from the cooling bath at the point in which the glove changed color from white to magenta red.

Discussion

The purpose of this study was to find a correlation between the water temperature inside the glove and the color change observed on the thermochromic dye coated latex glove. Further, the researcher evaluated the effects of decreasing environmental temperature on the water temperature inside the glove, and color changes observed on the
thermochromic leuco dye coated latex glove. The investigator hypothesized that the thermochromic dye coated latex glove would change color from white to magenta red in direct accordance with temperature changes of water at 12°C, and would remain magenta red once temperatures of 12°C or lower were obtained. The investigator also hypothesized that environmental temperature would have an effect on the thermochromic dye and would have an impact on the water temperature at which color change was noted on the glove.

The researcher was unable to support the hypothesis that the thermochromic dye coated latex glove would change color from white to magenta red at all temperatures of 12°C and below. The results showed that in both Trials 1 and 2, the thermochromic dye coated latex glove actually changed color from white to magenta at all temperatures of 8°C and below. Although it was not in agreement with this hypothesis, this result supports the concept that this glove can be used to prevent cutaneous frost bite in the extremities. By changing color at a lower temperature than the researcher originally anticipated, this glove becomes a more valuable diagnostic tool for its user by providing a visual, real-time warning sign that cutaneous temperature has crossed a significant threshold and is approaching a range at which one should be aware of the risk of frost bite.

It remains clear that these TLCs do render further investigation to discern their actual temperature range, as the researcher actually suspected. This was the primary reason that the investigator decided to explore this hypothesis. The investigator was certain that the temperature ranges were too broadly defined as “hot” or “cold” and
needed to better define them in this study. This study therefore, builds upon and extends the results of the first study and clarifies the data and the need to study TLC’s.

The data from this investigation did not support the second hypothesis that environmental temperature would have an effect on the thermochromic dye coated on the latex glove; therefore, having an effect on the threshold temperature at which the glove would change color from white to magenta red. The results of Trial 2 demonstrated that even though the water did cool down from the time that it was extracted from the water bath to the time it was measured inside the glove, due to heat convection from the external environment, the glove did not actually change color until the water temperature inside the glove was 8°C or below. This finding proves that the external environmental temperature of 6°C, although less than the threshold for color change of 8°C, had minimal effect on thermochromic dye coated on the gloves, leading to the conclusion that color change to the glove is produced primarily through physical contact at 8°C or below inside the glove. The researcher observed that the thermochromic dye coated gloves actually showed an even more vibrant and bright magenta red during Trial 2, which would be an advantage to the wearer of the glove who would be donning them in cold environments.

The results of the second t-test, comparing the temperatures, at color change, of the water at the time when it was extracted from the cooling bath, showed significant differences ($p=0.004$) between Trials 1 and 2. This demonstrated that the external environmental temperature had an effect on the water itself during the 10 second acclimation period that the researcher allowed, increasing the water temperature during
Trial 1 and decreasing it during Trial 2, prior to placing it into the glove. This finding allowed the researcher to recommend that the user allow for a 10 second acclimation period after placing their hands inside the glove prior to reading and diagnostically evaluating the color change.

One limitation of this study was that only one glove was tested over 100 individual trials. Although the researcher does not believe that this effected the results of the study in any way, one may suggest that the glove may have been stretched out over time and the thermochromic dye may have worn out with repetitive trials, making it less effective. Researchers performing future trials should utilize several different gloves to increase the argument for reproducibility. Although the use of multiple gloves does then impart a risk, as the TLC’s may not be equally distributed throughout the glove. Clearly, further research is rendered in this area of inquiry.

During the experimental trials, the glove was suspended from a chemistry ring stand in order to decrease the chance of contact from the investigator. This experimental design was desirable for the present study; however, future investigators should evaluate the gloves applicability during trials at colder temperatures.

During the investigation, the researcher evaluated 100 individual trials at two temperature set points, with 6°C being the lowest environmental temperature evaluated. The researcher recommends that future investigators evaluate colder temperatures and their effects on the thermochromic dye and the glove.

The purpose of this thermochromic leuco dye coated latex glove is to be worn by individuals in cold environments as a visual, real-time diagnostic tool for the prevention
of frostbite. One of the limitations to the study is that no human test subjects were evaluated. The methodology and experimental design was the first step to thereby simulate the human test subjects and the results of this “modeling” or proof-of-concept study to discern the efficacy of this new glove. As the researcher now has a better understanding of the temperature ranges of the thermochromic dye coated latex glove and its ability to evaluate temperatures at $8^\circ C$ and below without the influence of external environmental temperatures, a final prototype can be produced with human subjects. Therefore, the next experiment may evaluate lower ambient temperature ranges.

The results of the present study have validated the use of a thermochromic leuco dye coated latex glove for the detection of contact temperatures below $8^\circ C$. The researcher believes that this glove can be manufactured and produced on a large scale for use by the general population and military personnel for the prevention of frostbite. The researcher believes that this glove also has the potential to impact the healthcare industry, with benefits to patients with vascular and systemic diseases that have an effect on the extremities, such as Raynaud’s disease. Future researchers should explore human test subjects with vascular diseases to validate the efficacy of the glove for this patient population.

**Conclusion**

The results of this investigation demonstrated a consistent color change in the glove at a threshold of $8^\circ C$ and below, over 100 individual trials, at two different external environmental temperature points. The results of this investigation also demonstrated that environmental temperature did not have an effect on the thermochromic leuco dye coated
on the latex gloves. Based on the data presented from this present investigation, the researcher discerned that regardless of external environmental temperature, the thermochromic dye coated latex glove changes color in direct accordance with contact within the glove, with temperatures of 8°C and below. These findings validate the purpose of the study, and prove that the thermochromic dye coated latex glove can be used as a visual, real-time diagnostic tool for the prevention of cutaneous frostbite. Further research is needed on this glove using human test subjects and a broader range of cutaneous and environmental temperature set points.
CHAPTER VI

SUMMARY

In the present studies, the researcher used thermochromic liquid crystal and leuco dye technology in the creation of two novel prototypes for temperature detection in the extremities. To present knowledge, this technology has not been previously investigated for this purpose. The investigator conducted two proof-of-concept studies with the purpose of exploring the efficacy of these prototypes and validating them as effective diagnostic tools for real-time visual analysis of temperature in the extremities.

In the first study, the investigator demonstrated that the novel TLC fabric was able to accurately map temperatures for specific regions of the hand, thereby validating the concept of an extended range temperature-sensitive fabric. This supports the continued development of the temperature-sensitive sock that can be used by diabetics and vasculopathies as a self-diagnostic tool for the detection of temperature changes in their extremities.

In the second study, the investigator demonstrated more clearly that the novel thermochromic leuco dye coated latex glove accurately detects cutaneous temperature changes in the hands at all temperatures below 8°C. This study validated the concept of a glove used to prevent frostbite by changing color from white to magenta red at a threshold temperature of 8°C and below. Future researchers should focus on examining the applicability and validity of the TLC glove in individuals exposed to cold ambients prior to subsequent development. The researcher believes that this glove may be a valuable tool for outdoor athletes, military personnel, and may even be useful amongst
adults and children who dwell in cold environments.

The biomedical application of thermochromic liquid crystal and leuco dye technology is an exciting and unexplored realm. The utilization of this technology can provide researchers with real-time analysis of temperature profiles on the skin. Further research and development in this area is indicated, with endless potential for its use.
Figure 1. Thermal profiles of the thermochromic liquid crystals used on the fabric, indicating the temperatures that correspond to the start of each of the three primary colors. (a) Formulation 1 (24-27 °C; solid line).

Figure 2. Thermal profiles of the thermochromic liquid crystals used on the fabric, indicating the temperatures that correspond to the start of each of the three primary colors. (b) Formulation 2 (28-31 °C; rectangle).
Figure 3. Thermal profiles of the thermochromic liquid crystals used on the fabric, indicating the temperatures that correspond to the start of each of the three primary colors. (c) Formulation 3 (32-35 ºC; rhomboid).
Figure 4. Sample thermal image of the hand.
Figure 5. Corresponding digital image of the TLC fabric from the same hand. Warmer temperatures are represented by reds in the thermal image and blues in the TLC fabric. For the TLC fabric, the solid line indicates a temperature range of 24 to 27 ºC, rectangle.
Figure 6. Enlarged and digitally enhanced image of Figure 2b, demonstrating the three patterns of the TLCs. The yellow arrow indicates the solid line (24-27 °C), while the red arrow shows the rectangle pattern (28-31 °C) and the green arrow points to the rhomboid pattern (32-35 °C).
Figure 7. Average maximum temperatures for nine different regions of the palmar surface of the hand.

Figure 8. Average maximum temperatures recorded by the thermal camera when the TLC fabric indicated temperatures below 24.8 °C.
Figure 9. The water bath used to cool the water to the exact temperature was placed into the environmental chamber.
Figure 10. Ring stands were used to suspend the thermochromic leuco dye coated latex glove from the base using Hytape.
Figure 11. During Trial 1, at 24 °C of environmental temperature, the thermochromic leuco dye coated latex glove turned magenta red at 8 °C of internal water temperature.
Figure 12. During Trial 1, at 24 °C of environmental temperature, the thermochromic leuco dye coated latex glove stayed white at all temperatures above 9 °C of internal water temperature.
Figure 13. During Trial 2, at 6°C of environmental temperature, the thermochromic leuco dye coated latex glove turned magenta red at 8 °C of internal water temperature.
Figure 14. During Trial 2, at 6 °C of environmental temperature, the thermochromic leuco dye coated latex glove stayed white at all temperatures above 9 °C of internal water temperature.
Table 1

Data Collection Table showing Trial 1 with 24 °C and Trial 2 with 6 °C of Environmental Temperature Along with 5 Individual Trials Conducted with the Water Cooled to Each Temperature from 5 °C to 15 °C during Both Trials

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APPENDIX A

LETTER OF CONSENT
Appendix A

Letter of Consent

STUDY 1

Informed Consent to Participate in a Research Study

Study Title: Evaluation of a Thermochronic Liquid Crystal Fabric for the Detection of Human Extremity Temperature Profiles: A Proof-of-Concept Study

Principal Investigator: Jill Kawalet, PhD

Co-Investigators:
Larry Osher, DPM
Vincent Hetherington, DPM
Jonathan LeSar, DPM
Nilin Rao
Nicholas Williams

Jeffrey Pantano
Melissa Ricci
Lauren Sciarappa
Scott Bastian

You are being invited to participate in a research study. This consent form will provide you with information on the research project, what you will need to do, and the associated risks and benefits of the research. Your participation is voluntary. Please read this form carefully. It is important that you ask questions and fully understand the research in order to make an informed decision. You will receive a copy of this document to take with you.

Purpose:
Changes in skin temperature often occur early in various disease processes, many of which are associated with diabetic foot disorders. Such disease processes include foot ulcers, diabetic neuropathy (loss of sensation in the feet) and peripheral artery disease, or PAD (reduced blood flow to the feet). Various methods of measuring temperature in the extremities (arms/hands and legs/feet) range from simple skin thermometers to high-resolution thermal cameras. The problems with many of these devices are that they are impractical for use by the patient at home and they can only measure temperature change in small areas. The investigators have worked with a team at the Kent State University Liquid Crystal Institute to develop a fabric into which thermographic liquid crystals have been incorporated for the purpose of measuring temperature. The fabric will change colors and patterns based on the temperatures in the extremity. The purpose of this study is to evaluate whether this newly developed LC fabric can accurately measure temperatures and temperature gradients in the extremities. For this study, the hands will be used for data collection.

Procedures
Your participation in this study will take approximately 15-20 minutes. In order to determine if you are eligible for the study, the investigators will ask you questions relating to your health information, specifically your relevant past medical history and current medication.

After it has been determined that you are eligible to participate, you will cleanse your hands with Purell hand sanitizer and then sit in the biomechanics laboratory on the 2nd floor of the Kent State University College of Engineering.
Podiatric Medicine (KSUCPM) for 10 minutes to allow your hands to adjust to the temperature of the room. After 10 minutes, a series of 4 images will be taken of the palm surface of each hand using an infrared thermal camera and a digital camera:

- **Image #1** – thermal image of the palmar surface of the hand, using 100% infrared light
  - This image will allow the investigators to measure the temperature at different locations of the hand

- **Image #2** – thermal image of the palmar surface of the hand pressed against the LC fabric, using 100% infrared light
  - This image will allow the investigators to measure the temperature at different locations of the hand with the fabric in place

- **Image #3** – thermal image of the palmar surface of the hand pressed against the LC fabric, using combined infrared and visible light at a 1:1 ratio
  - This image will allow us to show the temperature profiles of the hand, as measured by thermal imaging and as measured by the LC fabric, on one picture.

- **Image #4** – digital image of the palmar surface of the hand pressed against the LC fabric
  - This image will allow the investigators to measure the temperature at different locations of the hand, as indicated by the colors and patterns reflected in the fabric

Once the 4 images are captured for both hands, you will cleanse your hands once again with Purell hand sanitizer and then your participation in the study is complete.

For each hand, images #1, #2 and #4 will be used to determine the maximum temperatures at the following regions: 1) tip of the thumb, 2) tip of 2nd digit, 3) tip of 3rd digit, 4) tip of 4th digit, 5) tip of 5th digit, 6) 1st metacarpal head, 7) 2nd/3rd metacarpal head region, 8) 4th/5th metacarpal head region, and 9) heel of the palm. These results will be used to evaluate two different outcomes: 1) differences in temperature of the hand without the fabric in place (image #1) and with the fabric in place (image #2), and 2) differences in temperature with the LC fabric in place as recorded by the thermal camera (image #2) and as recorded by the LC fabric (image #4). Image #3 will be used to capture the overlaying thermal image/LC fabric pattern/color for direct comparison of temperature gradients.

**Audio and Video Recording and Photography**

Thermal images and digital photographs will be taken of the palmar surface of both of your hands. You will be asked to remove any jewelry and/or other items from your hands that may identify you. The images may be used in publications resulting from this study, but any information that may identify you will be removed from the images prior to use. If you would like to, you may see the photographs and thermal images prior to use.
Benefits
This research will not benefit you directly. However, your participation in this study will help us to determine if a new thermochromic LC fabric may be a useful tool in preventing diabetic foot complications.

Risks and Discomforts
There are no anticipated risks beyond those encountered in everyday life.

Privacy and Confidentiality
Your study related information will be kept confidential within the limits of the law. If you agree to participate in this research project, health information that may identify you will be collected. We will collect your birth date, medical history and any medications that you are currently taking. This information will only be used to determine if you are eligible to participate in the study.

All data collected for this study, including images, will be coded with your initials and a unique subject number. Signed consent forms and completed data collection forms will be stored in a locked cabinet in Dr. Kawalec’s office. Data and images will also be stored electronically on a computer that is password protected.

Research participants will not be identified in any publication or presentation of research results; only aggregate data will be used.

Your research information may, in certain circumstances, be disclosed to the Institutional Review Board (IRB), which oversees research at KSUCPM, or to certain federal agencies. Confidentiality may not be maintained if you indicate that you may do harm to yourself or others.

Compensation
You will not be compensated for your participation in this study.

Voluntary Participation
Taking part in this research study is entirely up to you. You may choose not to participate or you may discontinue your participation at any time without penalty or loss of benefits to which you are otherwise entitled. You will be informed of any new, relevant information that may affect your health, welfare, or willingness to continue your study participation.

Contact Information
If you have any questions or concerns about this research, you may contact Dr. Jill Kawalec at 216-916-7549. This project has been approved by the KSUCPM IRB. If you have any questions about your rights as a research participant or complaints about the research, you may call the IRB at 216-916-7549.
Consent Statement and Signature
I have read this consent form and have had the opportunity to have my questions answered to my satisfaction. I voluntarily agree to participate in this study. I understand that a copy of this consent will be provided to me for future reference.

Participant Signature

Date

I have witnessed the consent process and believe that the participants listed above have been fully informed, understand the project and what they will have to do, and have voluntarily agreed to participate.

Witness Signature

Date

Evaluation of a Thermochromic Liquid Crystal Fabric for the Detection of Human Extremity Temperature Profiles: A Proof-of-Concept Study
Page 4 of 4
APPENDIX B

DATA COLLECTION FORMS
Appendix B

Data Collection Forms

STUDY 1
DATA COLLECTION FORM

Evaluation of a Thermochromic Liquid Crystal Fabric for the Detection of Human Extremity Temperature Profiles: A Proof-of-Concept Study
Subject Initials: __________ Subject Number: __________ Date: __________

Informed Consent Information:
(Informed Consent must be obtained prior to enrollment)
1. Did the subject sign the Informed Consent form? ☐Yes ☐No
2. Did the subject receive a copy of the signed Informed Consent form? ☐Yes ☐No

Screening Questions:
Inclusion Criteria: (The answer to inclusion question must be “Yes” for the subject to be eligible for the study)
1. Is the subject between the ages of 18 and 40 years? ☐Yes ☐No

Exclusion Criteria: (All answers to exclusion questions must be “No” for the subject to be eligible for the study)
1. Does the subject have Type I or Type II diabetes? ☐Yes ☐No
2. Does the subject have inflammation and/or swelling of the hands? ☐Yes ☐No
3. Does the subject have a history of any underlying vasoactive disorder? ☐Yes ☐No
4. Does the subject have a medication history that includes any drug that may directly or indirectly affect peripheral circulation and/or temperature? ☐Yes ☐No
5. Does the subject have any underlying metabolic, endocrine, arthropathic, vascular, or other pathological condition that can affect the temperature of the hand? ☐Yes ☐No

List of medications currently taken by the subject:
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

Is subject eligible for the study? ☐Yes ☐No

Demographic Data:
Subject’s Date of Birth: __________ Subject’s Gender: ☐Male ☐Female

Room Conditions:
Temperature of Room: __________ of Humidity of Room: __________ %

Left Hand:

Image #1 (thermal image, no fabric) taken? ☐ Yes ☐ No   If “No”, why not?

Image #2 (thermal image, fabric) taken? ☐ Yes ☐ No   If “No”, why not?

Image #3 (thermal image with combined IR/visible light, fabric) taken? ☐ Yes ☐ No If “No”, why not?

Image #4 (digital image, fabric) taken? ☐ Yes ☐ No   If “No”, why not?

Maximum temperatures recorded (oF):

<table>
<thead>
<tr>
<th>Location</th>
<th>Image #1</th>
<th>Image #2</th>
<th>Image #4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tip of thumb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tip of 2nd digit</td>
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</tr>
<tr>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tip of 5th digit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st metacarpal head</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd/3rd metacarpal head region</td>
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<tr>
<td>4th/5th metacarpal head region</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Heel of the palm</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Right Hand:

Image #1 (thermal image, no fabric) taken? ☐ Yes ☐ No   If “No”, why not?

Image #2 (thermal image, fabric) taken? ☐ Yes ☐ No   If “No”, why not?

Image #3 (thermal image with combined IR/visible light, fabric) taken? ☐ Yes ☐ No If “No”, why not?

Image #4 (digital image, fabric) taken? ☐ Yes ☐ No   If “No”, why not?

Maximum temperatures recorded (oF):
<table>
<thead>
<tr>
<th>Location</th>
<th>Image #1</th>
<th>Image #2</th>
<th>Image #4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tip of thumb</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Tip of 2\textsuperscript{nd} digit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tip of 3\textsuperscript{rd} digit</td>
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<td></td>
</tr>
<tr>
<td>Tip of 4\textsuperscript{th} digit</td>
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<tr>
<td>Tip of 5\textsuperscript{th} digit</td>
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<tr>
<td>1\textsuperscript{st} metacarpal head</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2\textsuperscript{nd} / 3\textsuperscript{rd} metacarpal head region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4\textsuperscript{th} / 5\textsuperscript{th} metacarpal head region</td>
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</tr>
<tr>
<td>Heel of the palm</td>
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**STUDY 2**

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<th></th>
<th>5°C</th>
<th>6°C</th>
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<th>8°C</th>
<th>9°C</th>
<th>10°C</th>
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<tr>
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<td>W r</td>
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</tr>
<tr>
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Trial 1

Gl 1

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</table>

Trials:
1.

1. Glove 1
2. Glove 2
REFERENCES
REFERENCES


