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ROOPE LASANEN

Infrared thermography in the evaluation of skin temperature

Applications in musculoskeletal conditions

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ABSTRACT

All objects with a temperature above absolute zero emit infrared radiation as a result of the thermal motion of their molecules. Infrared thermography (IRT) is an imaging modality that can be used to detect this radiation which is also called thermal radiation. Human skin emits infrared radiation almost like a perfect black body and thus IRT is well suited for the measurement of skin temperature. However, although the human core temperature may be indicative of several bodily dysfunctions, there is still a lack of scientific evidence about which musculoskeletal diseases or conditions can be diagnosed by evaluating skin surface temperature with IRT. Nonetheless, since it is a non-invasive and straightforward technique, IRT may represent a cost-effective alternative to the more traditional imaging modalities.

This thesis investigated the skin temperature related to various musculoskeletal conditions. Computer work ergonomics was evaluated by means of IRT, surface electromyography (sEMG) combined with a subjective assessment conducted by a neck disability index (NDI) (Study I). Furthermore, the capability of IRT to detect inflammation in the knee and ankle joints was evaluated in children (Study II). In study III, the effect on the skin temperature of the menthol content in a topical cold gel and its subjective cooling sensations were investigated by using IRT and visual analog scale (VAS).

It was found that IRT demonstrated potential in evaluating work ergonomics and that spatial variation of upper back skin temperature was a promising measure in ergonomic assessments (Study I). In study II, skin surface temperatures were significantly (p_{max} = 0.044, p_{mean} < 0.001) elevated in inflamed ankle joints, but not in inflamed knee joints. Thus, IRT may have the potential for detecting joint inflammation in ankle joints but further research will be required to determine whether this property of IRT can be extended to the knee joints. In study III, changes in the menthol concentration did not seem to exert any significant effect on skin cooling. Furthermore, it was noted

that cold gels did not have a significant effect on the skin temperature in surrounding skin areas adjacent to the gel application site.

To conclude, IRT was found to be able to evaluate changes in skin temperature related to various conditions affecting tissues underneath the skin. Even though the skin temperature does vary due to different subcutaneous and superficial conditions, IRT imaging of skin surface possessed diagnostic potential. However, in order to optimize the potential of this diagnostic technique, the relationship between skin temperature and pathological conditions deeper in body will need to be clarified.

As the healthcare costs are continuously spiraling, there is a clear demand for new diagnostic imaging modalities at the level of basic healthcare. This could ease the workload in specialized healthcare, make diagnostics more accessible and help to reduce the overall costs. Based on the present results, one may speculate that in the future, IRT may become a complementary tool to be used in a patient's clinical assessment and to help in therapeutic decision making.

National Library of Medicine Classification: QT 36, WB 270, WE 100, WN 205

Medical Subject Headings: Diagnostic Imaging; Thermography; Infrared Rays; Skin Temperature; Musculoskeletal System; Human Engineering; Workplace; Posture; Back Muscles; Electromyography; Neck; Joint Diseases; Knee Joint; Ankle Joint; Inflammation; Arthritis, Rheumatoid; Menthol; Gels

Yleinen suomalainen asiasanasto: kuvantaminen; lämpökuvaus; infrapunasäteily; lämpötila; iho; ergonomia; työasennot; tuki- ja liikuntaelimet; lihakset; niska; nivelet; nivelsairaudet; niveltulehdus; geelit

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This study was carried out during the years 2011-2015 in the Department of Applied Physics in the University of Eastern Finland and in Departments of Clinical Neurophysiology and Physical Medicine and Rehabilitation in the Kuopio University Hospital.

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Roope Lasanen
Kuopio, September 2015

LIST OF ABBREVIATIONS

ACR	American College of Rheumatology
BCE	Before the Common Era
BMI	Body mass index
CV	Coefficient of variation
CV (%)	Short-term precision error
EULAR	European League Against Rheumatism
FOV	Field of view
HDI	Heat distribution index
IFOV	Instantaneous field of view
ILAR	International League of Associations for Rheumatology
IR	Infrared
IRT	Infrared thermography
ISO	International Organization for Standardization
JIA	Juvenile idiopathic arthritis
LSD	Least significant difference
MAD	Median absolute deviation
MRI	Magnetic resonance imaging
NDI	Neck disability index
RA	Rheumatoid arthritis
RF	Rheumatoid factor
ROI	Region of interest
SD	Standard deviation
sEMG	Surface electromyography
SLE	Systemic lupus erythematosus
TI	Thermographic index
US	Ultrasound
VAS	Visual analog scale
VDU	Visual display unit

LIST OF SYMBOLS

A	Total area of the ROI
a	Area occupied by the isotherm
c	Speed of light
Δt	Temperature difference between the measured isothermal temperature and a constant
ε	Emissivity
E	Energy
f	Frequency
h	Planck's constant
λ	Wavelength
σ	Stefan Boltzmann's constant
T	Temperature
T_{max}	Maximum temperature
T_{mean}	Mean temperature
T_{med}	Median temperature
T_{SD}	Temperature standard deviation

LIST OF PUBLICATIONS

This thesis is based on data presented in the following articles, referred to by the Roman numerals.

I Lasanen R, Airaksinen O, Karhu J, Töyräs J and Julkunen P. Effect of working posture on back muscle activity and skin temperature in office workers. (Submitted 2015)

II Lasanen R, Piippo-Savolainen E, Remes-Pakarinen T, Kröger L, Heikkilä A, Julkunen P, Karhu J and Töyräs J. Thermal imaging in screening of joint inflammation and rheumatoid arthritis in children. *Physiological Measurement* **36**, 273-282 (2015).

III Lasanen R, Julkunen P, Airaksinen O and Töyräs J. Menthol concentration in topical cold gel does not have significant effect on skin cooling. *Skin Research and Technology.* In press.

AUTHOR’S CONTRIBUTION

The publications in this thesis are original research papers on measuring skin temperature by using infrared thermography (IRT). The author has contributed to the design of the studies and carried out all measurements and analyses. The author has been the main writer of each paper. The contributions of the co-authors have been significant in all of the studies.

Contents

1 Introduction

Everyone is familiar with the measurement of skin temperature to. A thermometer can probably be found in most households as it is commonly used to self-diagnose fever, typically from armpit skin. The significance of measuring skin temperature was first observed by Hippocrates (460-377 BCE) who used a clay soaked cloth to detect the elevated temperatures caused by a tumorous swelling [1]. Warm areas dried faster than surrounding skin areas and revealed the abnormalities under the skin. A giant leap was needed to reach to the next level in temperature measurement as it took almost two thousand years until the first thermoscope was developed by Galileo in 1592 [2]. The first clinical thermometer was introduced in 1868 by Dr. Carl Wunderlich [3]. Dr. Wunderlich conducted groundbreaking research on the body temperature and discovered that due to the homoeothermic nature of human body, changes in body temperature could be used as indicators of bodily dysfunctions. Meantime in 1800, an amateur astronomer William Herschel discovered infrared (IR) radiation beyond the visible spectrum [4]. He discovered that IR could be reflected and refracted like light and that it could be detected by thermometry beyond the red end of the visible spectrum. In the early 1940s, the first electronic sensors for the detection of IR radiation were built and they were quickly adapted by the military to be used as night vision systems [5]. Since that time, the military industry has been one of the main developers of IR technology.

The time after the Cold War has been especially fruitful for IR imaging technology and for its medical applications. Before this time, acquiring a thermal image was very time consuming and the image quality was poor [6]. However, today the technology has become much more user-friendly. Uncooled bolometer cameras, originally developed in the 1970s and released to public use from military restrictions in the early 1990s [7], are virtually maintenance free and have advanced IR imaging significantly. Furthermore, as the cameras are becoming more common for many applications, the cost of the cameras has decreased to such an extent that this technology can become available to non-military consumers. A huge milestone was reached when the very first commercial IR camera for smartphones was released by FLIR (FLIR Systems Inc., USA) in 2014, for just 250 British pounds. This technology which can fit into the palm of your hand offers numerous medical opportunities. However, research and development are needed to identify the applications where this technology can be optimally applied.

The emissivity of human skin is 0.96-0.98 for IR wavelengths in the range of 2-14 μm [8, 9], whereas emissivity for a perfect blackbody is 1. Hence, the thermal radiation emitted from skin represents closely the actual skin temperature. Thus, IR thermography (IRT) is very well suited for measuring skin surface temperature. The most common factors known to affect skin temperature and indicate abnormalities are inflammation in the subcutaneous/underlying tissues and increased or decreased blood flow [10]. However, standardization of the imaging technique has been problematic as the normal skin surface temperature varies between individuals. Smart image processing with automatic or user-assisted recognition of regions of interest (ROI) may offer a solution to this issue.

The increasing healthcare costs are good incentive for this development; imaging costs in the primary health care have increased in Finland in the past ten years[1] (years 2002-2012) by 10.3 % and in private sector health care[2] by 70.4 % [11]. Furthermore, a high rise in healthcare costs can be expected when the so-called baby boomers are aging and will need increased amounts of care. This will require that expensive, high-technology healthcare must be replaced, at least to some

[1] Excluding occupational, student and oral health care

[2] Reimbursed under National Health Insurance

extent, with low cost techniques better suited for basic healthcare. Modern IRT equipment with smart image processing represents an exciting and economical alternative for various diagnostic purposes.

It is known that the human core temperature is indicative of several pathological conditions. However, it is still unknown which musculoskeletal diseases or conditions could be diagnosed by evaluating skin surface temperature with IRT. The aim of this thesis was to investigate the potential of IRT in measuring skin temperature in various musculoskeletal conditions. First, it was decided to evaluate whether IRT could detect muscle activity related to work ergonomics. Next, the capability of IRT to detect joint inflammation in juvenile knee and ankle joints was studied. Finally, IRT was used to evaluate the effect on skin temperature of the menthol concentration in a cold gel, a commonly used remedy for the treatment of muscle injuries.

2 Medical thermography

2.1 PHYSICS OF IR-RADIATION

Electromagnetic radiation consists of oscillating electric and magnetic fields that propagate at the speed of light. The radiation has wave properties and thus it does not require a medium for propagation. Furthermore, sinusoidal electromagnetic waves are functions of time and position and they possess a definite frequency and wavelength. These waves form the electromagnetic spectrum *i.e.* radio and TV radiation, microwaves, visible light, IR and ultraviolet radiation, X-rays and gamma rays. As the frequency of the radiation increases, the wavelength shortens and photon energy (E) increases:

$$E = hf = \frac{hc}{\lambda}, \qquad (2.1)$$

This is the equation of photon energy, where h is Planck's constant ($h = 6.626 \times 10^{-34}$ Js), f is the frequency of the radiation, c is the speed of light (3×10^{8} m/s) and λ is the wavelength of the radiation.

In this thesis, the region of IR (the word infrared means "below red") radiation is the most important part of the light spectrum. IR radiation has a lower energy than visible red light. The IR spectrum ranges from 0.77 μm to 1000 μm. Furthermore, IR radiation is emitted by all objects which have a temperature above absolute zero as a result of the thermal motion of their molecules [12]. The relationship between the radiated energy and temperature is described by the Stefan-Boltzmann law:

$$E = \sigma T^{4}, \qquad (2.2)$$

where E is the total emissive power (W/m^2), σ is the Stefan Boltzmann's constant ($\sigma = 5.67 \times 10^{-8}$ W/m^2 K^4) and T is the absolute temperature (K). This equation applies only for perfect black bodies that absorb all incident electromagnetic radiation (emissivity ε = 1). For real surfaces (ε < 1), the equation can be expressed as:

$$E = \varepsilon \sigma T^4, \tag{2.3}$$

where ε is the emissivity of the emitting surface at a fixed wavelength. Emissivity depends on the material and surface properties. Thus, it is crucial to use the correct emissivity value which is optimized for the wavelength range in use and surface being investigated [13]. A perfect blackbody does not reflect or transmit any incident radiation but absorbs all of it [14]. Moreover, emissivity depends on the viewing angle. It remains constant until ~50° but at greater angles, the emissivity decreases because real surfaces, unlike a perfect blackbody, do not emit IR radiation similarly in all directions.

2.2 IRT TECHNOLOGY

IR detectors can be divided into two general classes of detectors: photon and thermal detectors [15]. In photon detectors, the absorbed photon energy is detected by a direct interaction of the radiation with the atomic lattice of the material. This changes resistance, inductance, voltage or currents in the photon detector. In thermal detectors, the absorbed photon energy changes the temperature of the detector and causes (or induces) a change in some measurable parameter, typically resistance, which can be detected.

Photon detectors can be further divided into photoconductive and photovoltaic detectors. In photoconductive detectors, bound electrons are excited to a mobile state where they can move freely through the material. While radiation increases the number of conductive electrons, more current flows through a bias circuit. In photovoltaic detectors, the photoexcited carriers are collected in a diode junction. [16]

In thermal detectors, the changed temperature in the detector is typically sensed by a bolometer. In a bolometer element, the resistance changes in parallel with the temperature. Furthermore, a bias circuit across the bolometer converts the changing current into a signal output [16]. The technological improvements in bolometers occurring in the past decade have enabled manufacturing of uncooled microbolometers that can be fabricated on top of silicon-integrated circuitry (Figure 2.1). With this method, the change in resistance in each pixel in the array can be detected [16]. Furthermore, the use of uncooled microbolometers has led to reductions in both the size and the price of these types of camera.

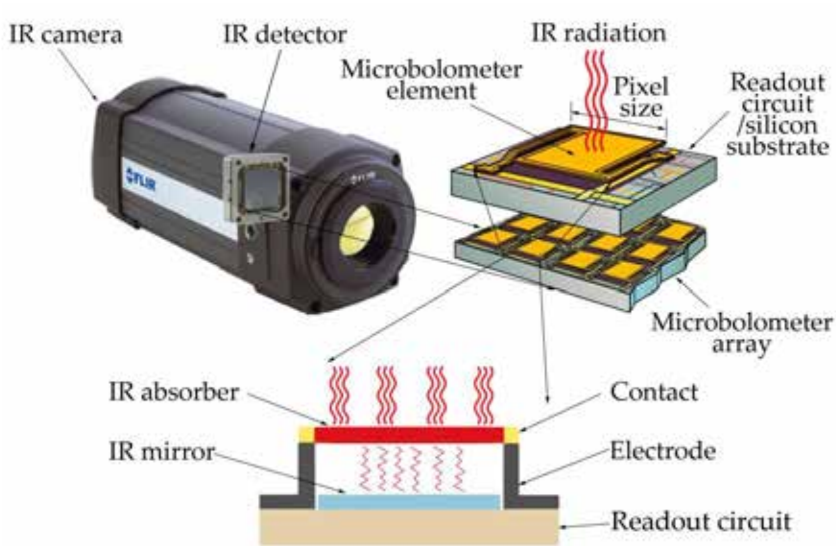

Figure 2.1. *Schematic illustration of an IR-camera construction and its uncooled microbolometer detector.*

2.3 HUMAN THERMOREGULATION

The human skin has a major role in temperature regulation (thermoregulation). Skin is the largest organ in human body with an area of 1.5 – 2 m^2 [17] and over 30 % of the body's temperature receptive cells are located within the skin [18]. In addition to its role in thermoregulation, skin protects other organs against various injuries (mechanical stresses, electromagnetic radiation, chemicals, etc.) [19]. Skin consists of the epidermis and the dermis (Figure 2.2). The epidermis is an epithelial layer of the skin with no vascularity [19] (Figure 2.2). The thickness of epidermis varies in different parts of the body from 0.03 to 0.64 mm [20, 21] and it has a high capacity for regeneration after damage [19]. The dermis is a dense bed of vascular connective tissue (Figure 2.2) which is tough, flexible and highly elastic [19]. Dermis contains various nervous endings and sensory receptors which help to detect pain, pressure and temperature. Furthermore, the dermis houses the sweat glands that are responsible for generating sweat and sebum [19, 22]. The thickness of the dermis ranges from 0.5 mm to 4.0 mm [23, 24].

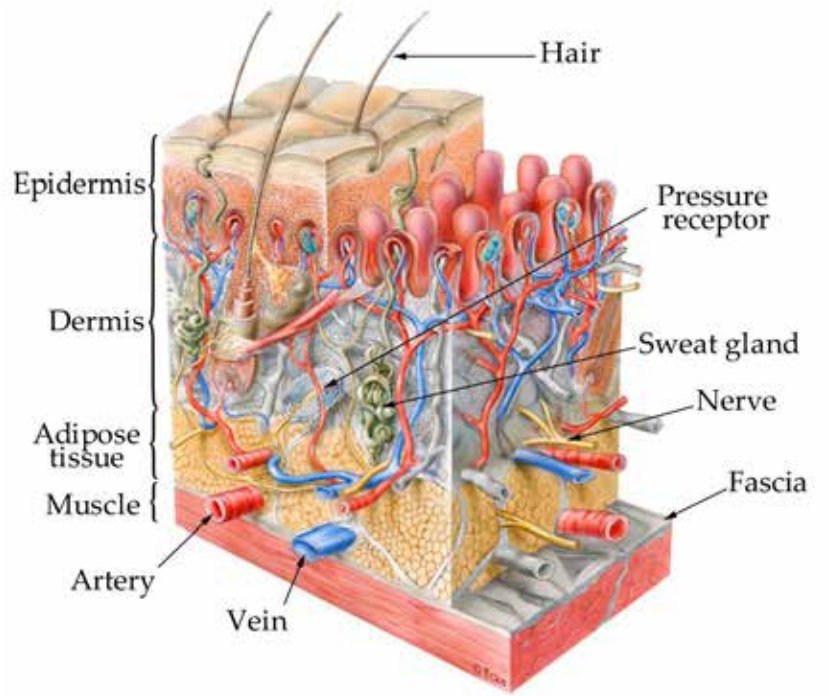

Figure 2.2. *Human skin structure. Image modified and reproduced with kind permission of Skin Care Forum, www.skin-care-forum.basf.com, Copyright: Julius Ecke, München, Germany.*

Although the human core temperature of a healthy individual is almost constant (within ± 0.6 °C) (Figure 2.3), skin temperature can alter greatly depending on the need and extent of thermoregulation [17]. There are two main temperature generators in human body: digestion together with metabolism and muscle activity. The parts of the body where these mechanisms are not located, are heated by the transport of warm blood in the circulatory system. Under normal conditions, heat is transferred from the body through IR radiation (60 %), thermal conduction (18 %), evaporation and perspiration (22 %) (Figure 2.3) [17]. Heat is conducted into the air and may be carried away by the convection air currents.

The body temperature is controlled by nervous feedback mechanisms situated in the hypothalamus, where specialized thermoreceptor neurons monitor the blood temperature [9]. If there is a need for loss of heat, the body starts to decrease heat production, vasodilation occurs in the skin blood vessels and perspiration is triggered. In contrast, if the body needs to increase temperature, there is an increase in thermogenesis accompanied by piloerection and vasoconstriction of blood vessels in the skin [17]. Vasodilation and vasoconstriction of skin blood vessels are very effective methods for temperature regulation because skin can act both as an effective heat radiator and as an insulator, depending on the amount of blood flowing through the organ [25]. The nutritive blood flow needed by skin is only 0.2 mL/min [26], whereas the maximum blood flow rate can be as high as 24 mL/min during heat stress [27].

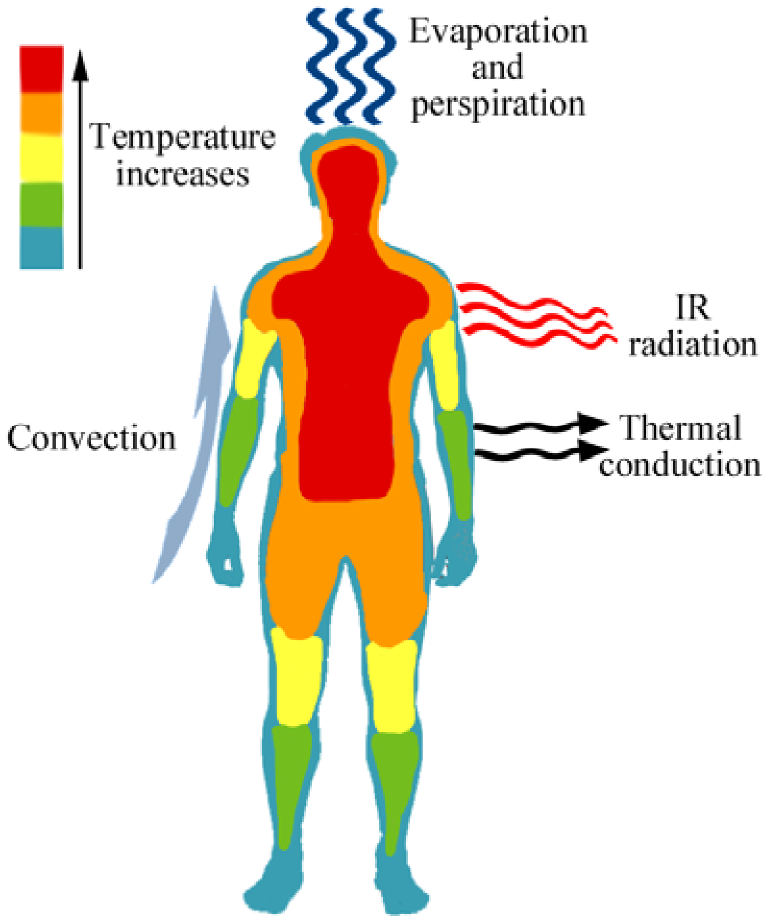

Figure 2.3. *Heat transfer mechanisms from human body and a rough illustration of temperature distribution in different parts of the body.*

2.4 IRT APPLICATIONS IN MEDICINE

IRT with a modern high resolution camera enables accurate thermal mapping of human skin. Thus, abnormal thermal patterns can be detected with this technique. IRT possesses many advantages; it is a non-invasive, non-contact and mobile imaging modality which can be used in real time measurements and monitoring. Furthermore, with modern cameras, quantitative imaging is possible because these devices can combine accurate thermal measurements with modern image processing methods. These methods enable image processing in a way not possible with earlier thermal imaging systems. For this reason, the non-specific results obtained with older, lower resolution cameras greatly hindered the development of this method [28]. Nonetheless, IRT has found acceptance in the medical community due to these breakthrough technological advances. Several recent studies [10, 29] have concluded that IRT has more potential in many applications than previously considered.

Skin temperature can be influenced by many abnormalities such as the presence of tumors, inflammation, infection or changes in nervous system function [9]. The skin surface temperature is always the sum of all thermal processes taking place under the skin and an awareness of the underlying physiology must be considered when making clinical decisions [16].

The use of IRT to detect breast cancer has been one of the most extensively studied, and probably the most severely criticized, areas since this technology was introduced into medical use. Tumors typically enhance the local blood circulation and they have an increased metabolic rate which elevates local temperature [30]. Unfortunately, because of unsuccessful studies in this research area, IRT lost its credibility for a long time [28]. The poor reputation can be partially blamed not only on the use of the old technology with its limited thermal sensitivity (± 2 °C) but also that the IRT imaging was performed by inexperienced individuals [28, 31]. However, the more recent studies have reported that IRT has some complimentary value in detecting breast cancer when used together with mammography [32, 33]. While used alone, IRT had a sensitivity of 83 % (mammography alone 66 %) but when both techniques were combined then sensitivity was increased to 95 %. Furthermore, Rassiwala et al. reported that IRT showed 97.6 % sensitivity, 99.17 % specificity, 83.67 % positive predictive value and 99.89 % negative predictive value in screening of breast cancer [34]. Moreover, Tepper et al. reported that IRT could be used for monitoring tumor state and aggressiveness either in a single image or with continuous assessment of multiple images [35]. In contrast to the other breast cancer imaging modalities, such as mammography, MRI, CT and ultrasound (US), IRT is cost effective and an easily portable imaging modality which could be especially suitable for breast cancer screening in the developing countries.

Diabetes is another application where IRT has been reported to have potential. In particular, the monitoring of the feet of diabetics has been claimed to be a potential application for IRT [36-40]. Vascular disorders and neuropathy are some of the complications associated with diabetes, especially in the extremities such as the foot which makes IRT suitable for examining this symptom [29]. Even though these types of complications are very common in diabetics [41, 42], there are very few reliable clinical markers for assessing their severity [37]. However, before IRT can be integrated into the clinical routine, quantitative tools will need to be developed for this assessment [37]. For this purpose, a Dutch research group has been developing an automated system which could act as a pioneering approach in this area [43, 44].

Rapid mass screening techniques are required for the prevention of pandemic infectious diseases [45]. Since fever is a common indicator of such diseases, IRT is a potential tool for this task. IRT was used during the influenza A pandemic (H1N1) in 2009 [46-50] and it appeared to enable early detection of febrile individuals [48, 51-53]. Furthermore, Nguyen et al. reported that IRT was an effective tool for non-contact mass screening of fever and it was better at predicting fever than self-reports [45]. However, the standardization of the imaging is crucial to avoid the uncertainty inherent in the accuracy, much of which is attributable to the equipment being used [10, 54]. Thus, guidelines for equipment and imaging protocol, such as the ISO recommendation (ISO/TR 13154:2009), should always be considered when applying this technique for mass screening.

2.4.1 Evaluation of computer work ergonomics

It is not uncommon that individuals doing computer work suffer from musculoskeletal symptoms [55-58]. Sillanpää et al. [57] reported that the symptom prevalences of visual display unit (VDU) workers were 63 % for neck, 24 % for shoulders, 18 % for elbows, 35 % for elbows and 16 % for wrists and fingers. Other investigators have also reported that upper body symptoms are common [55, 56, 59, 60]. It is generally believed that regular movement and changing the posture during the working day can reduce these symptoms [61]. An upright posture has been proposed to be well suited for computer work [62]. In the upright posture, the lower back retains lordosis The suggested advantages of upright posture are that it reduces the risk of damage to the intervertebral discs due to the pressure associated with a traditional seating position and that it may reduce the muscle tension in neck-shoulder area.

Surface electromyography (sEMG) is the gold standard with which to evaluate the work related muscle load and fatigue, [63-67]. However, sEMG has its limitations such as a poor correlation with subjective measures [68, 69]. IRT has been shown to be capable of detecting heat generation produced by muscle activation near to skin level [70-76] and it has been proposed that this technique would be applicable in ergonomics [77-79]. Despite some promising results in this field, there are rather few published studies. One disadvantage of this imaging method is that clothing must be removed from imaging area and, thus, real work time imaging can be difficult. However, IRT can be used to evaluate different working postures in test arrangements and to evaluate the related risks of injury.

2.4.2 Diagnosis of RA related joint inflammation

RA is an autoimmune disease which has a prevalence between 0.5-1 % in European [80-87] and North American populations [88, 89]. The severity of RA can vary from a mild illness to the aggressive, drug resistant disease which can cause joint destruction and deformity [90] (Figure 2.4). RA causes chronic inflammation and is characterized by pain, joint swelling, joint tenderness and destruction of the synovial joints [91-95] because inflammation of the synovium is typically present in the rheumatic joint [96] (Figure 2.4). RA is diagnosed by the confirmed presence of synovitis in at least one joint, by exclusion of other possible diseases, and a total score of 6 or greater (0 to 10 scaling) from the 2010 ACR/EULAR classification criteria. The scoring is done in four domains: joint involvement, serology, acute-phase reactants and duration of symptoms [90].

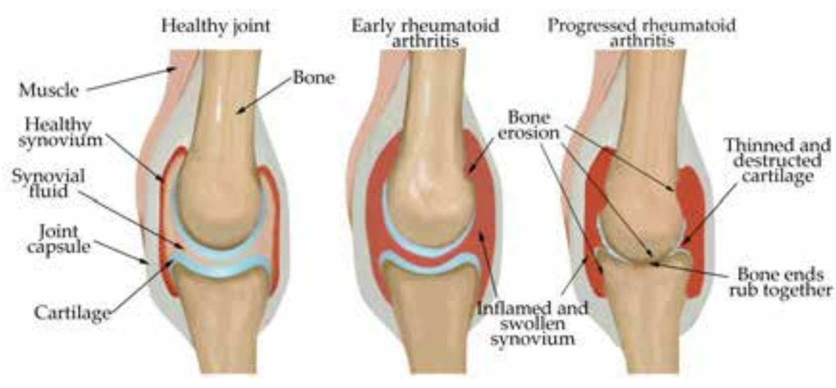

Figure 2.4. *Comparison between healthy joint, early RA joint and a joint displaying progressed RA. RA causes joint destruction as the disease progresses.*

In children, juvenile idiopathic arthritis (JIA) is a term that encompasses all forms of arthritis that begin before the age of 16 years, persisting for more than 6 weeks [97]. It is the most common chronic rheumatic disease in children with a prevalence that varies from 7 to 400 per 100 000 children [98-100]. JIA is a very heterogenetic disease and, thus the drug treatment varies in the different subtypes of JIA. The most widely used classification for these subtypes was issued by the International League of Associations for Rheumatology (ILAR) [101]. The classification consists of evaluating the number of arthritic joints, the duration of arthritis, accompanied symptoms (such as rash, lymphadenopathy, hepatomegaly or splenomegaly, serositis, dactylitis, nail pitting, onycholysis, psoriasis, sacroiliac joint tenderness, inflammatory lumbosacral pain, uveitis, etc.) and the presence or not of rheumatoid factor (RF) in blood.

Warmth of the affected joint is a typical feature of articular inflammation [5, 17] because it causes activation and proliferation of the synovial membrane [102]. IRT has been proposed as representing a supplementary method for detecting arthritis [103, 103-110, 110-114]. Ring et al. reported that several immune diseases *e.g.* rheumatoid arthritis, juvenile arthritis, osteoarthritis, gout etc. increase the skin temperature over the joints [115, 116]. Collins et al. developed a thermographic index (TI) which could be used to detect joint inflammation [117]. Furthermore, Salisbury et al. discovered that joints with synovitis display a different thermal pattern than normal healthy joints and these workers developed a heat distribution index (HDI). HDI was discovered to correlate better with the clinical assessment than TI [118] and to reduce the environmental influences on skin temperature [104]. Despite the improvements to various analytical procedures, researchers have not been able to develop the specificity and sensitivity of IRT to a sufficient level that the technique could be applied in the diagnosis of RA. However, due to the many advantages of IRT mentioned above, this technique is still under research and development and it may well become a valuable tool in the diagnostics of RA in the future.

2.4.3 Evaluating topical ointments affecting skin temperature

Cryotherapy is a widely used method for treating acute soft tissue injuries. It has been shown to have a positive effect on pain relief and recovery [119]. Furthermore, cold decreases metabolism, inflammation and muscle spasm and increases tissue stiffness [120, 121]. Tissue cooling can be achieved by various methods, such as application of ice packs or other cold materials. Topical cold gels and ointments are used to treat various painful conditions as an alternative to the more traditional cold treatments. Menthol-based cooling gels evoke a cooling effect through the activation of TRPM8 channels [122-124] which leads to pain relief [125-128]. Furthermore, it has been reported that menthol reduces vascular conductance [129-133]. Despite the wide use these so-called menthol-based "cold gels", very little is known about how the menthol concentration affects the skin temperature. For this purpose, modern IRT imaging with high spatial and temperature resolution is a potential tool [134].

2.5 IRT PROTOCOL FOR HUMAN STUDIES

As the human skin is strongly influenced by the environment, it is important that a standardized protocol is used when acquiring IRT images. The environment for imaging should be relatively neutral such that it does not cause shivering (too cold) or perspiration (too hot) in the subject [135]. In the literature, room temperatures of 20 to 24 °C have been used [108-111, 113, 136, 137]. Although the skin has a high emissivity ($\varepsilon \approx 0.98$ [8, 9]), it is also important that there are no radiative sources near to the skin so that IR radiation from them will not reflect from the skin [138]. Clothing from the imaging area should always be taken off for a long enough time before image acquisition in order to remove all effects caused by the clothing or ambient temperature [139]. The acclimation time has varied in the literature. Rather different acclimation times have been used *e.g.* 5 minutes [43, 44, 140], 10 minutes [109, 141, 142], 15 minutes [113, 143-149], 20 minutes [79, 150, 151] and 30 minutes [152]. Furthermore, subjects should not use any topical cosmetics or ointments [153], smoke cigarettes [154-157] or drink alcohol [158] prior to imaging. Contact with heavy meals, consumption of coffee and tea are also recommended to be avoided before imaging although there are no conclusive reports on their effect on the skin temperature [159-162]. Moreover, intensive exercise, massage and other physiotherapies should be avoided before thermography as they can influence the skin temperature [163]. In addition, the subjects should not be exposed to IR sources or to draughts [135]. Finally, other skin affecting conditions, such as sunburns [164], can exert a significant effect on skin temperature and they must be considered when interpreting IRT results.

The standardization of the ROIs and the setting of diagnostic limits for abnormal temperatures are two important issues. At present, there is no consensus on either standardized ROIs or the parameters best suited for measuring temperature. A "reference atlas for clinical thermography" was published in 2008 [165], where 24 body positions and 90 ROIs were defined. However, this atlas has not achieved much popularity. Furthermore, absolute temperature limits are difficult to define because the temperature variation between subjects has been noted to be large [166-169] and thus it is very problematic to make any decisions based on a single image. However, it has been proposed that asymmetry between the disease-affected and the contralateral sides of the body could be a feasible way of detecting abnormalities [170-173]. Unfortunately this type of comparison is not always possible *e.g.* due to a missing limb or to conditions that affect both sides of the body. Thus, it would be beneficial to adopt more sophisticated analyzing techniques, for example detecting certain temperature distributions, such as proposed by Salisbury et al. [118].

The camera needs to possess sufficient thermal and spatial resolution capabilities. There are very few studies that have compared the effect of resolution in determining the variation in temperature. However, Vainionpää et al. compared three IRT cameras with 80 × 80, 180 × 180 and 320 × 240 pixel resolutions and concluded that the camera with the lowest resolution exhibited lower repeatability between thermographers in comparison to cameras with higher resolution [174]. Image resolution and size are compared in Figure 2.5. In this image set, image resolution was downsampled from 320 × 240 IR image. Images taken with cameras with different resolution may differ from these images.

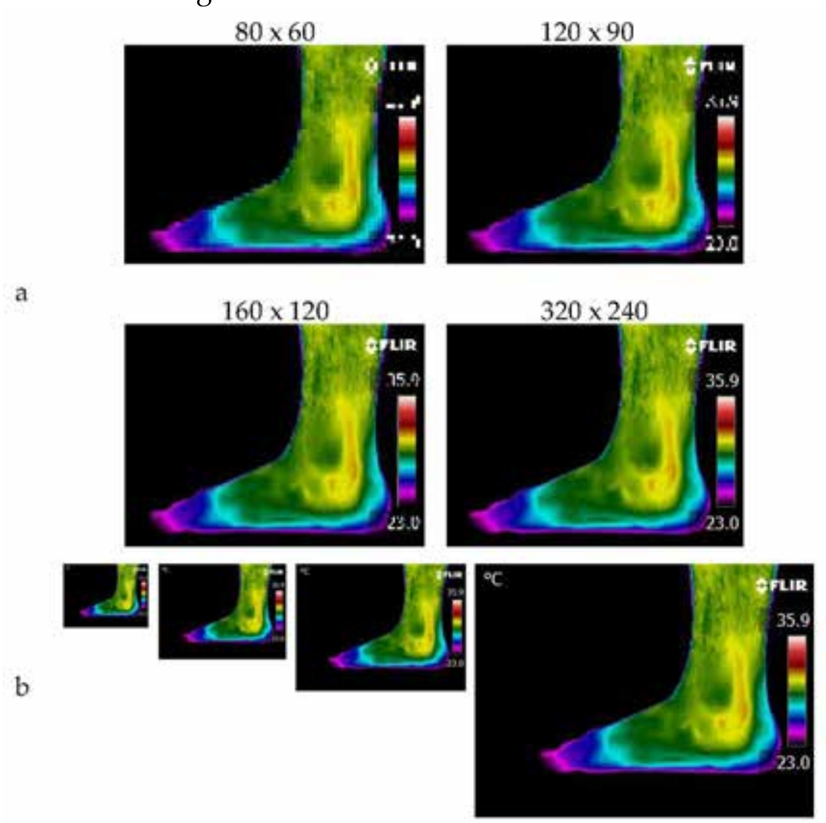

Figure 2.5. *Resolution (downsampled images) (a) and image size (b) comparison for 80 × 60, 120 × 90, 160 × 120 and 320 × 240 pixels sized IR images.*

Furthermore, the camera should be calibrated either by the manufacturer or by the user. Although absolute temperature values may not be required for many medical applications, it is important to use calibrated cameras, especially if more than one camera systems are being used and the images acquired with different cameras need to be compared [175].

3 Aims of the study

Due to recent technical developments, IRT is a promising imaging method for diagnostics of various conditions affecting body surface temperature. However, its potential use in the diagnostics of musculoskeletal conditions is still unclear. It was hypothesized that IRT could be used for detecting different musculoskeletal conditions.

To test this hypothesis, the specific aims of this thesis were:

- To investigate the potential of IRT for evaluation of computer work ergonomics.
- To evaluate whether IRT is capable of detecting inflammation in knee and ankle joints in children.
- To examine the effect on the skin temperature of the menthol content in a topical cold gel by using IRT.

4 Materials and methods

This thesis consists of three studies investigating the use of IRT in several musculoskeletal conditions. The potential of IRT for evaluation of computer work ergonomics was evaluated in Study I. In Study II, the pros and cons of IRT in the evaluation of joint inflammation were investigated. Study III examined whether IRT could be useful in revealing the effect of menthol concentration in topical cold gel on skin cooling. The methods applied in studies I-III are summarized in this section (Table 3.1).

Table 4.1: *Summary of the materials and methods utilized in studies I-III*

Study	Subjects	Location of measurement	Anatomic region	Methods
I	14	Workplace measurements	Neck, shoulder, upper back	IRT, sEMG, NDI
II	58	Outpatient clinic	Knees, ankles	IRT, Clinical examination
III	10	Laboratory setup	Lateral thigh	IRT, VAS

4.1 SUBJECTS

Research Ethics Committee of Kuopio University Hospital had a favorable opinion on the studies included in this thesis (Study I: 70/2011, Study II: 28/2012, Study III: 86/2013). All subjects and/or their parents provided written informed consent.

In Study I, sixteen healthy female volunteers were recruited through an e-mail invitation sent to the secretarial staff of Kuopio University Hospital. The invitation included a link to a web questionnaire where they were asked about their daily computer use, working station set up and neck pain severity (NDI-questionnaire). A group of fourteen volunteers completed the entire experiment (age: 50.9 ± 8.8 years, height: 160.4 ± 5.7 cm, weight 68.6 ± 15.5 kg). To qualify to be a participant in the work ergonomic study, a volunteer should have exhibited a mild disability score in the NDI-questionnaire and she could not be using a saddle chair before the measurements.

In study II, fifty-eight volunteer pediatric outpatient clinic patients were recruited (age 1.5-17.0 years, height 140.8 ± 22.5 cm, weight 39.2 ± 16.5 kg, BMI 18.7 ± 3.8). All patients willing to participate were accepted into the study. Forty-four out of fifty-eight patients had diagnosed with JIA or systemic lupus erythematosus (SLE)

In study III, ten healthy male volunteers were recruited from the staff of the University of Eastern Finland (age: 25-30 years). The only inclusion criterion was that participants had no lower leg injuries.

4.2 EQUIPMENT

All IRT recordings in this thesis, were acquired with a digital IR camera FLIR A325 (FLIR Systems Inc., USA) with 320 × 240 pixel spatial and 0.05 °C thermal resolution. This camera model detects IR radiation in the 7.5–13.0 μm wavelength range and has a 25° × 19° field of view (FOV). Furthermore, the instantaneous field of view (IFOV) value is 1.36 mrad, which means that at a distance of 1 m from the skin surface, each pixel has a size of 1.36 mm in the viewing object. The manufacturer recommends that at least a 3 × 3 pixel area should be averaged in the analyses, which means that the smallest area of ROI from a 1 m distance is 4.08 × 4.08 mm^2. The camera was calibrated by the manufacturer and it applies a predefined emissivity value of 0.98 for skin. No reference source was used in the present studies because the manufacturer of the camera stated that this was not needed. The camera was stored indoors and thus only a short stabilization time was required. This was achieved by having the camera powered on for five minutes before imaging. Camera stability during warm-up was confirmed by performing measurements during a one hour test period (images taken 5, 10, 15, 20, 30, 45 and 60 minutes after the camera power was turned on). In this procedure, a test object was immersed in a water filled tank with the surface level above the water level. The water temperature was set to 30 °C and its temperature was constantly measured with a thermocouple. The surface temperature of the test object was measured with the thermal camera. Temperatures measured with the thermal camera varied by 0.2 °C, whereas thermocouple readings from the water varied by 0.1 °C, indicating that after 5 minutes of warming, thermal readings made by the thermal camera were stable and within the accuracy rating of the camera (± 2 % of the reading).

In studies I and II, thermal images were acquired with software specially designed for anatomical and medical imaging (Thermidas Ltd, Rovaniemi, Finland). In study III, images were acquired with FLIR ResearchIR MAX (FLIR Systems, Inc., Wilsonwille, OR, USA) software.

4.3 METHODS

Study I compared the effect of using traditional and upright computer working station to neck and upper back muscle activity. In this evaluation, IRT and surface electromyography (sEMG) measurements were performed using a portable 8-channel EMG amplifier (ME6000, Mega Electronics Ltd., Kuopio, Finland). Furthermore, a questionnaire related to subjects' daily routines and neck pain (neck disability index (NDI)-questionnaire) was filled in by the subjects before the first and after the last measurement. IRT images were acquired before and after each measurement day and sEMG recordings were performed for a full working day. The first measurement was conducted in the subjects' traditional work stations which consisted of an office chair with back rest and a regular office table with or without height adjustability. After this, subjects were given a saddle chair (Easydoing Ltd., Rautalampi, Finland) and a height-adjustable office table if their working station was not equipped with one before. All subjects were instructed on how to adjust the chair and table to an appropriate height. Before the second measurement, subjects had one month to adapt to the new working station. The second measurement was performed in same fashion as the first one.

In Study II, subjects were first examined by a clinician and diagnosed based on clinical findings, ultrasound findings, puncture or combination of all the information gathered with these methods. Next, IRT imaging was performed in a separate examination room. From knee and ankle joints, anterior, medial and lateral aspects were imaged from a 1 m distance perpendicularly to skin surface.

In Study III, the effect of varying the menthol concentration in topical gel on skin temperature was evaluated by means of IRT and visual analog scoring (VAS). VAS can be used to measure the intensity of the symptoms (*i.e.* pain), and in this thesis it was used to measure the intensity of the cooling sensation [176]. Three gels with different menthol concentrations (0.5 %, 4.6 % and 10.0 %) were tested under laboratory conditions. The gels were custom-prepared and coded at Fysioline Ltd. (Tampere, Finland) for this study. First, subjects were directed to take a comfortable position in an office chair with their feet lifted to the horizontal level. Next, the corners of a 10 × 5 cm measurement area in left lateral thigh were marked with 1 × 1 cm pieces of 3M 425 aluminum tape (3M Corporation, Minneapolis, MN, USA) to mark the measurement area in the IRT images. After this, the IRT recording was commenced. After 15 minutes of acclimation, 1.5 grams of gel at room temperature were manually applied to the measurement area. Five minutes after application, subjects evaluated the cooling effect by marking a line between the two extremes of the VAS (a 100 mm long straight line where 0 means no cooling sensation and 100 represents the greatest imaginable cooling sensation). IRT recording was continued for 90 minutes after the application of the gel. Gels were tested on separate days with at least one day between the measurements. The study was executed in a double-blinded fashion and the coding of the different gel versions was revealed only after all analyses were performed.

4.4 ANALYSES

In study I, IRT analyses were performed with a custom-made application in Matlab (Mathworks Inc, MA, USA). Two methods were used for each image. First, mean temperature was recorded from a circular area with a radius of five pixels from the locations where sEMG-electrodes were placed (Figure 4.2). Second, median temperature (T_{med}) and median absolute deviation (MAD) were calculated from a polygonal ROI located on the upper back area (Figure 1). T_{med} and MAD were used instead of mean temperature and standard deviation, because temperatures within the ROI were not normally distributed, as indicated by Kolmogorov-Smirnov test [177]. sEMG data was root-mean-square averaged with a 60 minute time interval by using Megawin Software (Mega Electronics Ltd., Kuopio, Finland).

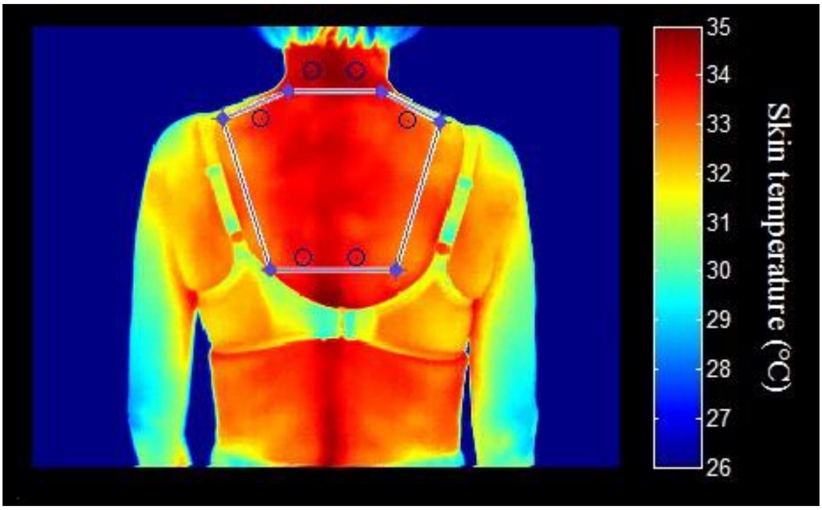

Figure 4.2. *ROIs used in Study I. The circular ROIs are placed to the locations where sEMG-electrodes were located. The polygonal ROI is located to fit into the upper back area.*

In study II, all analyses were conducted in a double-blinded fashion. Medial and lateral aspects of knee and ankle were used for analyses (Figure 4.3). The operator-defined ROIs were maximized to fit within the joints as described by Ammer [165] and were placed on the same standardized locations in all patients (Figure 4.3). From these ROIs, mean and maximum temperature, standard deviation (SD) of temperatures and the heat distribution index (HDI) were determined. HDI was calculated as described by Salisbury et al. [118] by multiplying by two the SD value within the ROIs. Mean temperature was calculated as a mean value of the pixel values inside the ROI. In the estimation of the maximum temperature, the image was first filtered with a median filter (3 × 3 pixels). Furthermore, repeatability of placing the ROIs was investigated by calculating the coefficient of variation (CV) and short-term precision error (CV (%)) [178]. Four repeated measurements were performed for a subject group of 14 individuals. Furthermore, CV was calculated by dividing the SD of the four repeated measurements by the subject mean. CV (%) was calculated as the root mean square average of the CV values determined for the individuals.

In this thesis, further analyses related to Study II were performed to evaluate whether the thermographic index (TI) would be a sensitive method for detecting knee joint inflammation. It was decided to evaluate TI from an anterior aspect and it is defined as follows [117]:

$$TI = \frac{\sum(\Delta t \times a)}{A}, \quad (4.1)$$

where Δt is the difference between the measured isothermal temperature and a constant, 26 °C, a is the area occupied by the isotherm (pixels) and A is the total area of the ROI (pixels) placed on the knee joint. In the analyses, a rectangular ROI was placed on top of the knee joint with the patella approximately in the middle (Figure 4.4).

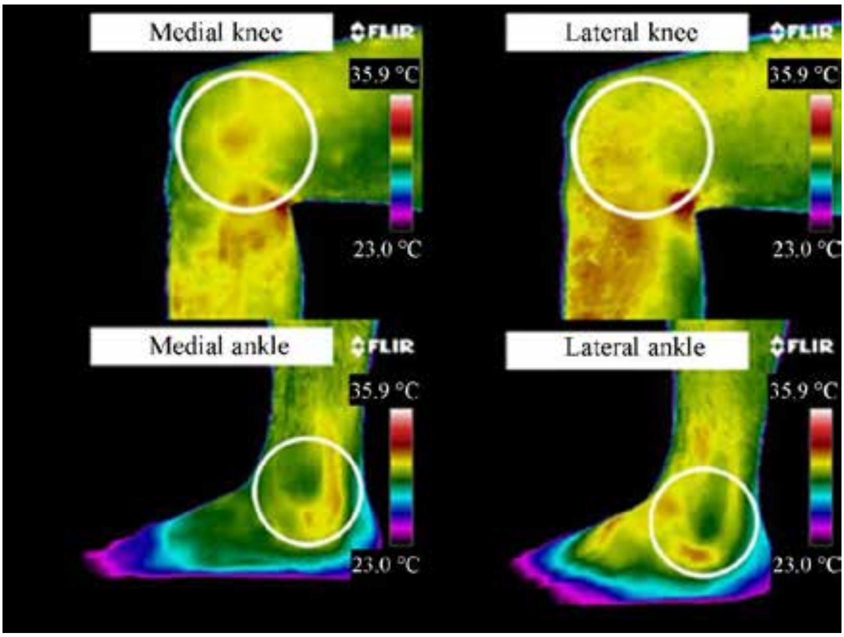

Figure 4.3. *ROIs used in Study II. In the knee joints, ROIs were placed to the midline of the patella and the popliteal cubital fold. In the ankle joints, ROIs were placed on the center of the malleolus. The sizes of the ROIs were maximized to fit within the joints.*

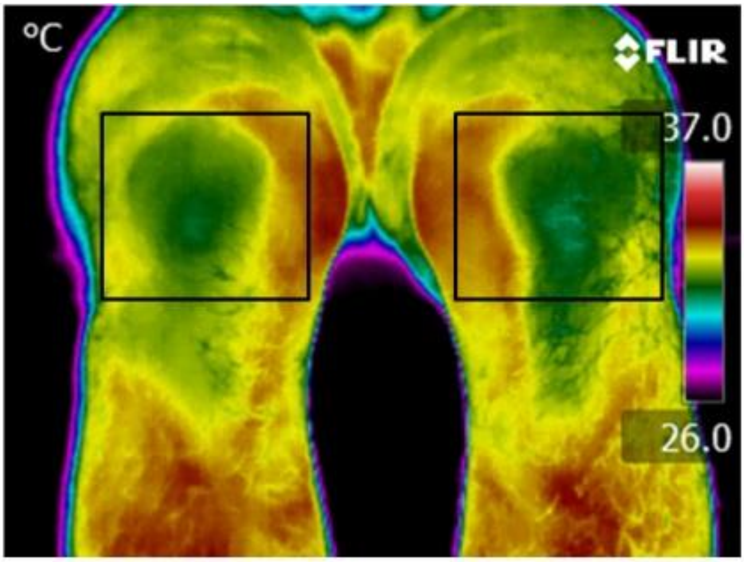

Figure 4.4. *To evaluate TI values from anterior knees, rectangular ROIs were placed on top of the knee joint with the patella approximately in the middle.*

In Study III, an 8 × 3 cm sized rectangular area was placed inside the gel area. The average temperature was recorded from this ROI. The reference temperature was recorded from two circular ROIs placed distally and proximally to the gel site (Figure 4.5). The diameter of the reference ROIs was 2 cm. The temperatures from the two reference ROIs were averaged and subtracted from the gel site temperature values to obtain the temperature decrease caused by the gel. Furthermore, median values for each gel version at each time point were calculated over all subjects. The locality of the cooling effect was tested by linear fitting of the temperatures of reference ROIs and at times 15 minutes before and after the application of the gel (Figure 4.5). The linear equations were then compared to evaluate whether the cold gel actually caused any decrease in temperature.

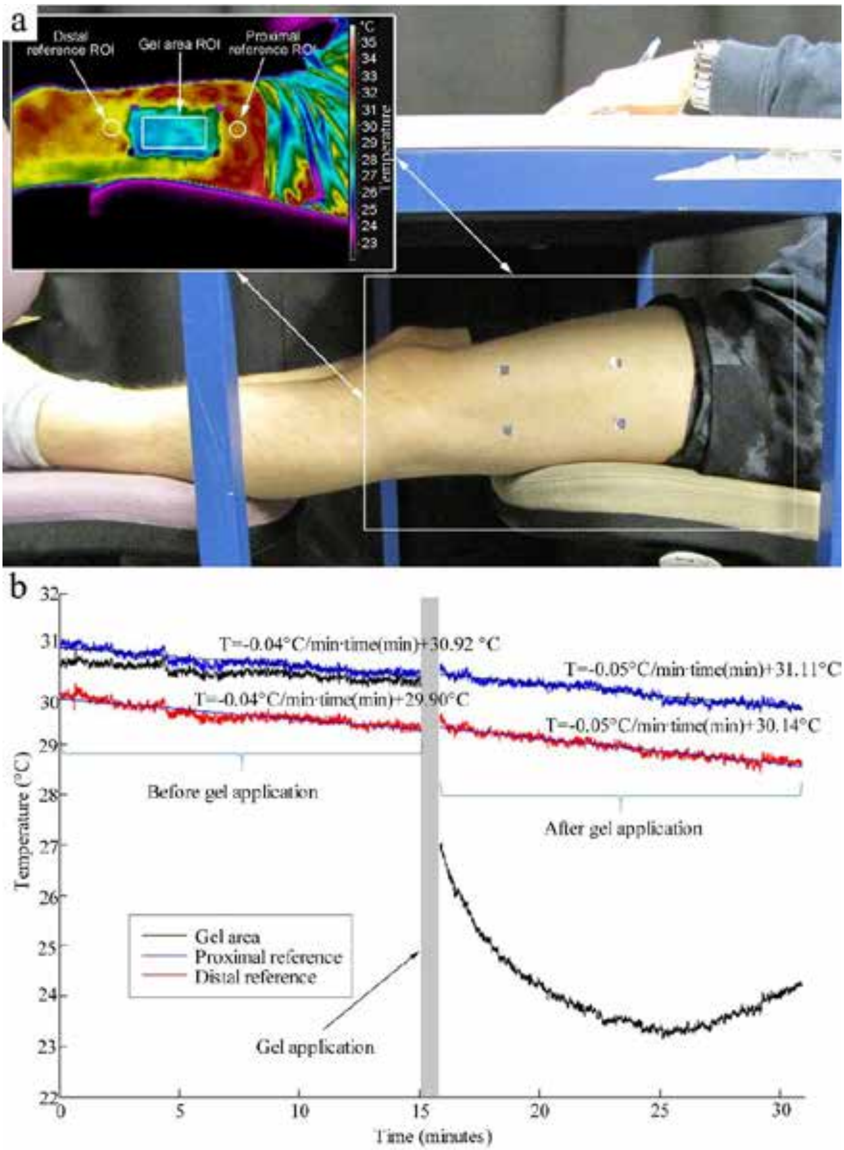

Figure 4.5 *(a) Measurement setting and ROIs used in Study III. (b) To evaluate the locality of the skin cooling, linear equations were fitted to reference point temperature data 15 minutes before and 15 minutes after the gel application. This data demonstrates the skin temperature in the gel area and reference points and is from one of the subjects.*

4.5 STATISTICAL TESTS

All statistical tests were performed with SPSS-software (Version 17, IBM Corporation, Somers, NY). The threshold level for statistical significance was set to $p < 0.05$.

In Study I, Wilcoxon's signed rank test was used to evaluate the differences in values gathered before and after the working day measurements for all of the variables. Kolmogorov-Smirnov test was used to test the normal distribution of the temperatures within the ROI.

In Study II, the significance of the difference in temperatures of non-inflamed and inflamed joints was tested with a linear mixed model. There were three fixed factors; aspect (anterior, medial or lateral), side (left of right) and diagnosis (inflamed or non-inflamed). As dependent variables, mean or maximum temperature, SD, HDI and TI were used. In the *post-hoc* analyses, due to the exploratory nature of the analyses, the least significant difference (LSD) adjustment was applied.

In Study III, One-Sample Wilcoxon signed rank test with zero as a test value was applied to determine the duration of statistically significant cooling. Two-Related Samples Wilcoxon signed rank test was applied for all other variables.

5 Results

5.1 IRT IN THE EVALUATION OF COMPUTER WORK ERGONOMICS

In study I, skin temperature at all electrode locations increased significantly ($p < 0.05$) with both postures during the working day. There were no significant differences in the muscle activity (*i.e.* sEMG) between the first and the last working hours when working with the traditional posture. However, when working with the upright posture, the muscle activity of left neck extensor ($p = 0.003$), left rhomboid ($p = 0.014$), right rhomboid ($p = 0.006$) and right trapezius muscles ($p = 0.025$) decreased significantly between the first and the last working hour.

The median temperatures in the upper back increased significantly ($p < 0.01$) with both postures (Figure 5.1a). However, in contrast to the situation with the traditional posture, there was a significant ($p = 0.008$) decrease in the MAD of the temperatures while working with the upright posture (Figure 5.1b). Furthermore, the NDI-value was significantly lower ($p < 0.003$) after participants had worked with the upright posture (Figure 5.2c).

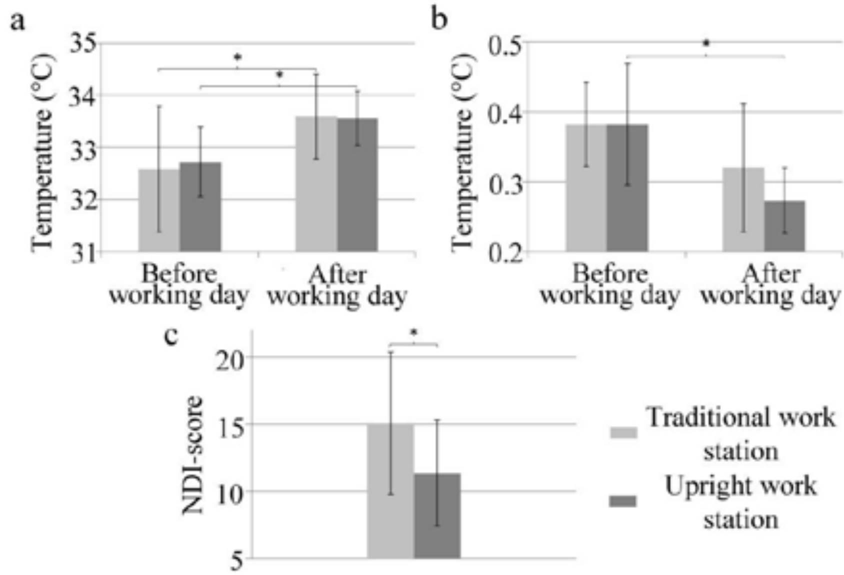

Figure 5.1. *Both postures increased upper back median temperatures significantly (p < 0.05) (a). With the upright posture, MAD of temperature in the upper back decreased significantly (p < 0.05) during the working day (b). NDI-scoring was decreased significantly (p < 0.05) after working with the upright posture (c). Significant differences are indicated with an asterisk.*

5.2 APPLICATION OF IRT IN THE DETECTION OF JOINT INFLAMMATION IN CHILDREN

5.2.1 Comparison of inflamed and non-inflamed joints

In Study II, 19/116 knee joints and 32/116 ankle joints were classified to be inflamed in the clinical examination. In inflamed ankle joints, skin temperature was significantly higher (p_{max} = 0.044, p_{mean} < 0.001) in non-inflamed ankle joints (Table 5.1). In knee joints, no significant differences in the skin temperature were observed (Table 5.1). Inflammation status did not correlate with SD, HDI or TI (Table 5.1).

Table 5.1: *Post-hoc analyses between inflamed and non-inflamed joints revealed significant ($p < 0.05$) differences between the maximum (T_{max}) and mean (T_{mean}) temperatures of inflamed and non-inflamed ankle joints. Temperature standard deviation (T_{SD}) or HDI did not display any significant correlation with inflammation status. In knee joints, no significant differences were observed between any of the variables. Statistical significance ($p < 0.05$) is indicated by bold font.*

	Non-inflamed versus inflamed	95 % confidence interval for difference (°C) Lower bound	Higher bound	*p*- and *F*-values	Mean difference (°C)
Ankles					
T_{max}		**0.009**	**0.629**	***p* = 0.044** **F = 4.12**	**0.319**
T_{mean}		**0.251**	**0.754**	***p* < 0.001** **F = 15.54**	**0.503**
T_{SD}		0.052	0.058	*p* = 0.908 F = 0.01	0.003
HDI		0.137	0.295	*p* = 0.908 F = 0.01	0.216
Knees					
T_{max}		0.641	1.206	*p* = 0.543 F = 0.37	0.283
T_{mean}		0.244	0.288	*p* = 0.870 F = 0.03	0.022
T_{SD}		0.057	0.121	*p* = 0.539 F = 0.38	0.089
HDI		0.114	0.242	*p* = 0.539 F = 0.38	0.178
TI		-0.180	0.353	*p* = 0.519 F = 0.42	0.087

5.2.2 Temperature comparison between medial and lateral aspects

Table 5.2: *No significant differences were observed in post-hoc analyses between the temperatures of medial and lateral aspects of ankle joints.*

		95 % confidence interval for difference (°C)			
	Medial versus lateral	Lower bound	Higher bound	p- and F-values	Mean difference (°C)
All ankles					
T_{max}		0.072	0.233	$p = 0.300$ F = 1.08	0.080
T_{mean}		0.070	0.174	$p = 0.400$ F = 0.0.71	0.052
Non-inflamed knees					
T_{max}		-0.164	0.148	$p = 0.917$ F = 0.011	0.008
T_{mean}		-0.054	0.144	$p = 0.368$ F = 0.818	0.045
Inflamed knees					
T_{max}		-0.076	0.410	$p = 0.173$ F = 1.926	0.167
T_{mean}		-0.101	0.226	$p = 0.445$ F = 0.595	0.062

No significant differences were observed between the medial and lateral aspects of the ankle joints (Table 5.2). The mean temperature of all knee joints and non-inflamed knee joints between lateral and medial aspect exhibited a statistically significant difference ($p < 0.005$) (Table 5.3) as the medial aspect had higher temperatures than the lateral aspect (Table 5.3).

Table 5.3: *Post-hoc analyses between medial and lateral aspects of knee joints exhibited significant (p < 0.05) differences in mean temperature. Furthermore, it was found that there was a difference between the mean temperatures of medial and lateral aspects of non-inflamed knee joints. Statistical significance (p < 0.05) is indicated by bold font.*

	Medial versus lateral	95 % confidence interval for difference (°C) Lower bound	Higher bound	*p*- and F-values	Mean difference (°C)
All Knees					
T_{max}		0.524	1.156	*p* = 0.459 F = 0.55	0.316
T_{mean}		**0.041**	**0.215**	***p* = 0.004** **F = 8.41**	**0.128**
Non-inflamed knees					
T_{max}		-0.230	1.041	*p* = 0.185 F = 1.771	0.419
T_{mean}		**0.039**	**0.178**	***p* = 0.002** **F = 9.575**	**0.109**
Inflamed knees					
T_{max}		-0.946	3.319	*p* = 0.264 F = 1.299	1.186
T_{mean}		-0.029	0.322	*p* = 0.098 F = 2.973	0.147

5.2.3 Repeatability of placing the ROIs

The short-term precision error of placing the ROIs was extremely small *i.e.* 0.00-0.17 % (Table 5.4).

Table 5.4: *Repeatability of placing the ROIs was found to be excellent.*

	Maximum temperature		Mean Temperature	
	Mean ± SD	CV (%)	Mean ± SD	CV (%)
Knees lateral	33.47 ± 0.01	0.08	32.10 ± 0.02	0.11
Knees medial	33.28 ± 0.02	0.09	32.24 ± 0.03	0.13
Ankles lateral	32.33 ± 0.03	0.15	30.86 ± 0.05	0.17
Ankles medial	32.03 ± 0.00	0.00	30.68 ± 0.04	0.14

5.3 EFFECT OF MENTHOL CONTENT IN A TOPICAL GEL ON SKIN TEMPERATURE

The median cooling time (± median absolute deviations) was 69 ± 16 min for 0.5 % gel, 56 ± 7 min for 4.6 % gel and 62 ± 20 min for 10.0 % gel. However, there were no significant differences ($p > 0.05$) between the cooling times or median temperatures between the gel versions (Figure 5.2). In three subjects, 4.6 % and 10.0 % gels caused the skin temperature under the gel to rise over the starting temperature after the gel effect had dissipated.

VAS-ratings showed that the 4.6 % gel caused a stronger cooling effect than 10.0 % and 0.5 % gels ($p < 0.05$) (Figure 5.3). Gels did not affect significantly ($p > 0.07$) the skin temperature in the reference ROIs.

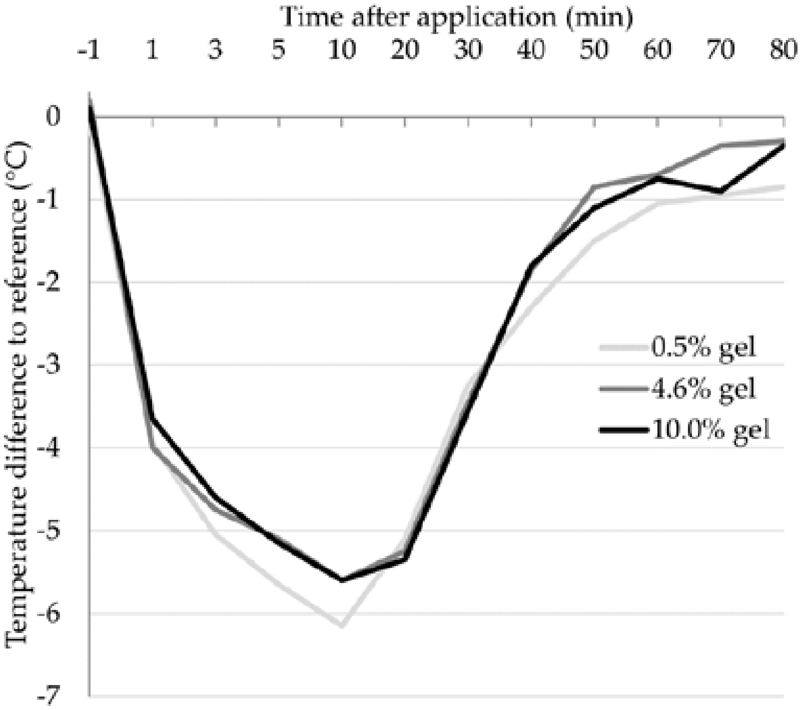

Figure 5.2. *Median temperature decrease with different gels.*

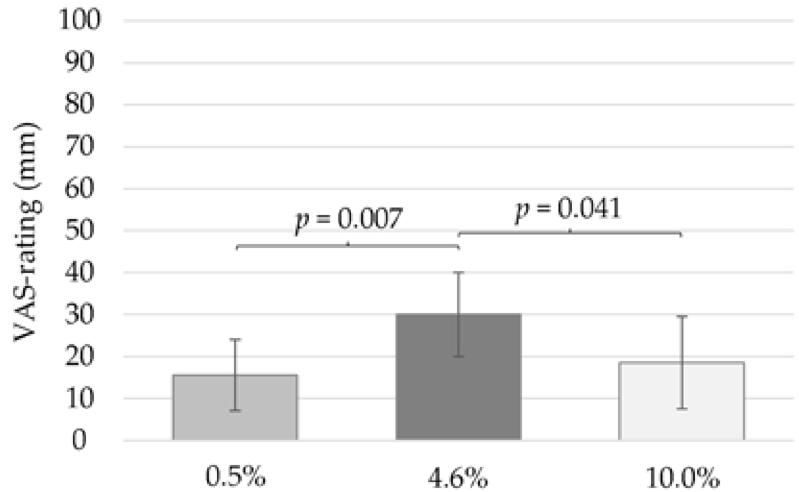

Figure 5.3. *VAS-rating medians and median absolute deviations. 4.6 % gel caused a statistically significantly stronger cooling sensation than either the 10.0 % or the 0.5 % gels.*

6 Discussion

6.1 IRT IN THE EVALUATION OF COMPUTER WORK ERGONOMICS

In Study I, the distribution of muscle activation in the subjects' neck and upper back was evaluated by IRT and sEMG when they were working either at upright and traditional working stations. Furthermore, the NDI-questionnaire was used for measuring subjects' self-evaluated neck pain related disability.

A statistically significant ($p < 0.05$) increase in skin temperature was observed with both postures in all electrode locations. This was not surprising as it is well-known that body temperature is at its minimum in the early morning and the maximum body temperature is reached in the early evening [179-182]. sEMG recordings revealed a significant ($p < 0.03$) decrease in upper back muscle activity when the secretaries were working with an upright posture between the first and the last working hours whereas with the traditional posture, no significant difference was observed. Furthermore, a statistically significant ($p < 0.008$) decrease in the spatial variation of skin temperature was seen only after working in upright posture. The NDI-questionnaire demonstrated that the subjects were experiencing neck-related symptoms before the first measurement which may have been related to poor work ergonomics. After one month of using the upright working station, the NDI-questionnaire detected that there had been a significant reduction in neck symptoms. As described in the methods, no attempt was made to optimize the traditional working station in any way and it was left in the position that the subjects had used it before these measurements. It was found that the upright posture, which had been optimized for each subject, decreased the computer work related muscle stress. The present findings indicate that IRT has potential benefits in evaluating work ergonomics and in the assessment of work related muscle stress. Previously, IRT has been found to be a sensitive way to assess changes in task loadings and demands [77, 78]. The present study differs from these reports as it was designed to measure the stress of a full working day. One good aspect of this intervention was that it assessed a real working day situation, especially the stress caused by actual working situations. However, with this type of trial design, it is difficult to control the intervention, *e.g.* the working tasks may well have varied between the measurement days, which may have introduced some variation into the results. Despite this limitation, it was possible to demonstrate that the values obtained with IRT correlated with those from the other measuring methods, emphasizing that the optimized upright working station had exerted a true favorable effect *i.e.* not only on both the self-evaluated neck-related symptoms but also on the objectively measured (sEMG) variables. Thus, IRT may be considered as a potential method for evaluating work ergonomics *e.g.* for providing an objective assessment to demonstrate improvements in work station designs and set-ups.

6.2 APPLICATION OF IRT IN DETECTION OF JOINT INFLAMMATION IN CHILDREN

In Study II, the potential of exploiting IRT for detecting joint inflammation was evaluated in children. Furthermore, the temperature differences were evaluated between medial and lateral aspects of inflamed and non-inflamed knee and ankle joints.

6.2.1 Comparison of inflamed and non-inflamed joints

This study examined a total of 58 volunteer child patients. From this subject group, 19/116 knee joints and 32/116 ankle joints were classified as being inflamed. The vast majority (55/58) of the patients had been diagnosed with rheumatic disease and were taking medication to treat this disease. In IRT analysis, a statistically significant (p_{max} = 0.044, p_{mean} < 0.001) correlation was observed between clinical evaluation and joint skin temperature in ankle joints. However, no significant correlation was observed in the knee joints. Joint inflammation enhances synovial blood flow [183] and increases the thickness of the synovium [184] and therefore it elevates temperature in the joint area, which can be detected by means of IRT. Previously, it has been shown that IRT can quantify the degree of inflammation in rat models [108, 110]. Furthermore, it has been reported that there is a correlation between skin temperature and the clinical evaluation of the severity of osteoarthritis in knee joints [109, 185]. However, the present study is the first performed in a pediatric patient population. Here, no correlation was detected between inflammation status and knee joint skin temperature. There are several possible reasons to explain this result. It has been reported that cutaneous temperature of the patellar region reflects intra-articular temperature and that it is accurate in its ability to localize inflamed synovial tissues [117]. It has been claimed that medical treatment affects significantly the joint skin temperature [186] and this may have had a major effect on the present results as almost all subjects were being treated with drugs to alleviate the symptoms of their rheumatic disease. Furthermore, only the standard clinical evaluation could be compared with the IRT assessment; *i.e.* there was no detailed knowledge on the actual state of the studied joints. For example, magnetic resonance imaging (MRI) could have revealed the true state of inflammation in the studied joints but unfortunately this procedure was not available when these patients were assessed. Thus, further studies should be directed at quantifying the states of joint inflammation in a more quantitative manner (*e.g.* with MRI) to obtain a better understanding of the association between joint inflammation and skin temperature.

There is one other reason why the knee joints exhibited non-significant findings in contrast to the ankle joints *i.e.* the anatomical geometry and skin contact with these joints is different. While the knee joint is surrounded by the large active muscles of the thigh, the ankle joint has less active surrounding temperature-insulating tissue. For this reason, the temperature in the knee joints is likely spread to the surrounding tissues more than the temperature in the ankle joints. Therefore, the temperature transfer within these joints and their interaction with the skin from which the temperature is measured with IRT is very likely to be different. These phenomena may well explain why the knee joints did not display such good potential for IRT as the ankle joints.

Inflammation status did not correlate with HDI, temperature SD or TI. In contrast, Spalding et al. [111] reported that HDI values of arthritic joint and control group were significantly different. Warashina et al. [185] reported that HDI correlated with joint swelling and tenderness but not with radiographic findings. The present study did not evaluate joint swelling or tenderness separately. HDI and SD are indices of variation and they should only be used for normally distributed data. There is no mention about testing the normality of distribution of the data by the authors reporting the correlation with HDI values [111, 118, 185]. It may be advantageous to test whether the assessment of MAD would be worthwhile in future studies as described by Leys et al. [177]. TI incorporates both the temperatures of the joint and the areas of each isotherm [117]. However, TI did not correlate with the clinical assessment in the present study. van Holsbeeck et al. measured the effect of intra-articular corticosteroid injections by means of clinical scores, sonography and thermography [187]. They reported that peak temperature correlated with the clinical status 10 days after the injection, as the temperature decreased significantly after the injection but they did not detect any significant correlation with TI. Unfortunately, there are not many studies which have used TI and thus it is difficult to compare their results with the present values. In a few studies [104, 188], HDI has been used instead of TI *e.g.* Salisbury et al. stated that HDI correlated better than TI with the clinical assessment [118]. In contrast, Warashina et al. reported that TI correlated better than HDI with clinical and radiographic parameters. Due to these discrepancies, the use of these indices and the effect caused by the medication need to be clarified.

6.2.2 Temperature of medial and lateral aspects of knee and ankle joints

No significant difference was found in skin temperature between the medial and lateral aspects of the ankle joints. However, in all knee joints and more specifically in non-inflamed knee joints, a statistically significant ($p < 0.005$) difference was detected between the medial and lateral aspects. Based on this study, no recommendation can be given on which aspect should be used for detecting joint inflammation. However, a few studies [118, 189] have preferred side aspects rather than the anterior aspect because in the anterior view, the patella acts as a kind of heat shield and this complicates the interpretation of IRT results.

6.2.3 Repeatability of placing the ROIs

The short-term precision of ROI placement was found to be excellent. The ROIs used here were originally described by Ammer [165] and they were adopted for their easy implementation as they fill the entire joint area and do not require much user dependent assessment of the location. However, in future studies, ROIs could be optimized *e.g.* by evaluating how the omission of the popliteal fossa area would affect the results. The temperature of the popliteal fossa area clearly stands out from the IRT images because it has an abundant blood flow. For this reason, the temperature of that area may not be related to joint inflammation and thus one can speculate that the optimization of the ROIs would be one way to enhance the sensitivity of IRT analyses.

6.3 EFFECT OF MENTHOL CONTENT IN A TOPICAL GEL ON THE SKIN TEMPERATURE

In Study III, the effect of the menthol concentration in cold gels on skin temperature was evaluated by means of IRT. Furthermore, the subjects evaluated the cooling sensation by providing a subjective VAS-rating. The locality (*i.e.* its spread to adjacent skin areas) of skin cooling was also evaluated by analyzing reference ROIs outside the area where cold gels were applied.

All gels caused skin cooling lasting for at least 40 minutes. However, there were no significant differences in the skin cooling effect of the gels with different menthol concentration although there were major differences in their menthol concentrations; the only other difference between the gels was in their water content.

Interestingly, the Voltaren® vehicle gel, which does not have any menthol, has been reported to possess similar skin cooling properties as the gels studied here [134]. In the study of Hug et al. [134], Voltaren® was reported to decrease skin temperature on average by 5.1 °C whereas in the present study, the median reduction in skin temperature was 6.2 °C (0.5 %), 5.7 °C (4.6 %) and 5.7 °C (10.0 %). Furthermore, with Voltaren®, the maximum skin temperature reducing effect was reached 10 minutes after gel application, which is the same as with the products evaluated in this thesis. Based on these findings, it seems that the skin cooling phenomenon is not menthol-related. The evaporation of the water in the gel may be the main factor involved in skin cooling. This was also concluded by Ring et al. [190]. In the present study, the gel that had the highest water content (0.5 % gel) cooled the skin for the longest time, which supports this proposal.

There was a significant ($p < 0.05$) gel-related difference in the cooling sensation felt by the participants *i.e.* the 4.6 % gel caused a stronger cooling sensation than the two other gels. This finding is interesting because it was hypothesized that the highest menthol concentration would evoke the most intense cooling sensation as described in the literature [191-193]. This discrepancy may be related to skin permeability. High menthol concentrations may not be absorbed as efficiently as lower levels. Only a few studies have compared menthol permeation through the skin [194-196] and in all of these studies, the ointments used have had differences in other adjuvants in addition to their menthol concentration, so results are inconclusive. In the study of Cal [196], the highest concentration ointment (10 % menthol, other menthol concentrations were 3 %, 0.4 % and 0.13 %) resulted in the highest menthol penetration. However, this particular ointment had also the highest terpene concentration, which may have affected the skin's barrier properties, increasing its permeability. The results emerging from the present study indicate that threshold levels for permeation of different menthol concentrations and the effect of exposure time need to be clarified.

None of the gels exerted any effect on the skin temperature in the reference ROIs. This indicates that their effect is restricted to the area where gels are applied. Other studies have shown that menthol can have an effect on skin blood flow [129, 130, 132, 133, 197] but here no effect was detected in the surrounding tissues. However, in three subjects, a rise in skin temperature was observed with 4.6 % and 10.0 % gels after the cooling effect of the gels had dissipated. This could imply that the present gels had some effect on blood circulation. One reason for the limited change in temperature in the surrounding skin areas may be due to small area where the gels were applied (50 cm^2). In those studies where menthol caused significant blood circulation changes, the gel was spread over much larger areas (800 cm^2 [131], 700 cm^2 [130, 132], 1600 cm^2 [133], 470 cm^2 [129]) and furthermore 1 ml of gel was used per 200 cm^2 whereas in the present study ~1.5 ml of gel was used per 50 cm^2, indicating that the area of application may have a more significant effect on vascular conductance than the amount of gel applied to the skin.

This study provided new insights into the effects of menthol gels used topically. However, it still leaves unanswered questions on the effect of menthol on skin cooling. As mentioned, the skin-cooling property seemed to be related to evaporation of the gels. Thus, in future studies, gels could be wiped off after immediate absorption onto the skin. In this manner, the evaporation of the gels would not be the main observable factor and the underlying effect might be visible and capable of being captured by IRT.

6.4 THERMAL CAMERA RELIABILITY

The measurement accuracy is an important factor with all medical measurement devices. With thermal cameras, the warm-up time may have an impact on the measured temperatures and if devices are being used for a long time without proper calibration, temperature drift and offset may occur [198, 199]. The effect of warm-up time was tested on the measured temperatures with the camera used in these studies. After 5 minutes of warm-up, camera stability was good. Thus, it can be concluded that if the camera is kept on for at least 5 minutes before imaging, as in the present studies, then the thermal readings will be reliable. In this thesis, no reference source was utilized during the experiments, which can be considered as a limitation. The camera manufacturer's calibration was valid and, thus it was decided to rely on that information that the measurements would be reliable. However, the ISO standard for screening thermographs [200] recommends the use of a reference source to ensure the acquisition of valid thermal readings. This is especially important if there are several thermal systems in use and the results from these different devices are being compared. In the present studies, measurements were always performed with the same camera rendering this limitation less critical.

6.5 FUTURE PROSPECTS OF IRT

The availability of high resolution thermal cameras has meant that IRT is today a potential medical imaging modality. Skin temperature changes in the presence of various musculoskeletal conditions and these changes are easily detectable with this method, since these devices can undertake a rapid screening of skin temperature. Currently, the potential of IRT is being investigated in almost every medical area. Due to its low cost and noninvasive character, IRT may have exciting prospects for basic healthcare applications. For example, IRT could be used as a screening tool and it could help to decrease the numbers of patients being directed to special healthcare. These kinds of inexpensive and portable screening tools are especially needed in the developing countries, where specialized healthcare facilities and sophisticated equipment are not available. For example, breast cancer could be screened with IRT and only suspicious cases would need to be directed for more detailed investigation [34]. Furthermore, the follow-up of the condition of the feet of diabetics could be conducted with IRT [29, 36] either by the patients themselves with consumer-friendly thermal cameras, *e.g.* attached to a smart phone, or by nursing professionals. Before being used for self-management, dedicated software would have to be developed so that the patients would not need to self-analyze the results. In specialized healthcare, IRT may have advantages over other imaging modalities in patient populations who are vulnerable to ionizing radiation, such as children or pregnant women. Furthermore, IRT could be used as an adjunct method to complement traditional imaging modalities (*e.g.* X-ray, MRI, US) and improve the sensitivity and specificity of the diagnosis. Although the prospects are promising, all medical applications of IRT still need scientific evaluation, refinement and development to ensure their diagnostic reliability. For this purpose, reliable quantitative imaging methods need to be developed. This can be achieved by means of standardized imaging protocols and advanced image analyzing methods together with multimodal approaches, such as combining information from other clinical parameters or imaging modalities. It is evident that this technique is becoming more common, but only the future will reveal, if IRT represents a real breakthrough in medical diagnostics.

7 Summary and conclusions

In this thesis, IRT was applied to investigate various musculoskeletal conditions. The potential of IRT in evaluation of computer work related muscle activity was tested by comparing the effect of upright and traditional work stations to neck and upper back skin temperature. Furthermore, the correlation between joint inflammation status and skin temperature was investigated in children. Finally, the effect of menthol concentration in cold gel to skin temperature was evaluated by means of IRT. The main findings and conclusions of this thesis are:

- IRT was found to have potential for evaluating computer work related muscle activity.

- IRT may have potential for detecting joint inflammation, especially in ankle joints in children with JIA or autoimmune disease with arthritis such as SLE.

- IRT is capable of detecting the skin cooling properties of topical gels. The menthol concentration did not correlate with skin cooling and the effect was localized only in the area where the gel had been applied.

Based on these results, it is concluded that IRT can be used to assess various skin-related conditions. IRT imaging is a relatively easy imaging method which is non-invasive and relatively cheap as compared to many other medical imaging modalities. However, the analyzing methods will need to be further improved to ensure their reliability before they can be widely applied in medical diagnoses.

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Roope Lasanen

Infrared thermography in the evaluation of skin temperature

As the healthcare costs are continuously spiraling, there is a clear demand for new low cost diagnostic imaging modalities. This thesis investigated the potential of IRT in diagnostics of various musculoskeletal conditions. IRT enabled detection of changes in skin temperature related to these conditions affecting tissues underneath the skin. Based on the present results, IRT may become a complementary tool to be used in a patient's clinical assessment and to help in therapeutic decision making.

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