**Quantitative Assessment of Pain
Through
Clinical Digital Infrared Thermal Imaging**

by

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A thesis submitted to

The Faculty of Graduate Studies and Research

In partial fulfilment of the requirements for the degree of

Master of Applied Science

in Electrical Engineering

Ottawa-Carleton Institute for Electrical and Computer Engineering

Department of Systems and Computer Engineering

Carleton University

Ottawa, Ontario, Canada

August 2002

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A handwritten signature in cursive script, appearing to read 'Monique Frize', written over a horizontal line.

Dr. Monique Frize, Thesis Supervisor

A stylized handwritten signature, possibly 'S. P.', written over a horizontal line.

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September 2002

To Françoise and Jean-Yves, for their long-distance support.

To Myriam and Isabelle, who believe in dreams...

To Diana.

And to all my friends and relatives on both sides of the Atlantic.

Acknowledgements

I would like to thank my thesis supervisor, Dr. Monique Frize, for giving me the opportunity to expand my engineering horizons, for her enthusiastic support and her dedication to research.

Thank you as well to Dr. Delphine Rossille for her invaluable advice, her effective supervision and co-supervision and for debating with me about the subtleties of the universe.

Thank you to François for helping me with the boring stuff...

A big thank you to all the students, assistants and contractors for cheering up this gloomy office.

And thank you to Laurent for pushing me to finish (almost) on time so that we can go camping.

Abstract

This thesis focuses on the computerised assessment of pain in infrared thermal images. Medical infrared thermography is the recording of skin temperature distribution and is believed to give valuable information on the functioning of the autonomous nervous system (ANS) that regulates the temperature of the body. Many types of pain affect the ANS and may be indirectly visualised by infrared thermography. Qualitative techniques to assess pain in thermal images are highly subjective and proposed quantitative or computerised techniques still require multiple intervention from the user, thereby increasing the risk of error. We propose an automated approach to the assessment of medical thermal images focusing on the preprocessing, the identification of the regions of interest as well as the statistical analysis to determine whether a region is thermally abnormal, which may be associated with pain. Original denoising and background extraction techniques are considered, as well as an automatic delimitation of regions of interest. Finally, a new approach using distance measures between histograms are used to classify the region as normal or abnormal.

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Chapter 1

Introduction

1.1 Motivation

It is now well known that thermoregulation of the human body is affected by a wide range of factors including pathological abnormalities. The recording of temperature distribution of the human body can therefore provide valuable information about the underlying physiological processes that cause those abnormalities. Human skin plays a major role in thermoregulation by dissipating or preserving heat. The dissipation of heat through the skin is mainly radiative and occurs in the infrared part of the spectrum, which makes infrared detectors particularly suitable for the recording of skin temperature distribution and by extension of whole body core temperature distribution [4] [28].

The assessment of pain is a difficult task since pain is a combination of various phenomena, some of which are still not fully understood. Pain has many subjective aspects that are linked to the person that experiences it and thus hard to quantify. Current ways of evaluating pain rely on the ability of patients to formulate their

pain through words, facial expressions or to point out its level of pain on specific scales, which may be complicated for people with impairments or younger children or infants. However pain also exhibits characteristic physiological or anatomical changes that may be studied in a more objective manner. One physiological change associated with many types of pain is an alteration of the thermoregulation of the human body.

Clinical infrared thermography or infrared thermal imaging is defined as the recording of the temperature distribution of the human body using infrared radiation emitted by the surface of that body i.e. the skin [33]. Many studies have been carried out on the assessment of thermal imaging for various medical applications since its introduction in the early fifties. The results of these studies were not always in favour of a clinical use of thermography, usually due to poor protocols, poor quality control, poor training and generally a lack of understanding of the proper role and scope of thermography [7]. Despite growing scepticism, interest in this technique remained high and the development of quantitative infrared thermal imaging techniques helped to overcome many of the initial difficulties. Computerised infrared thermal imaging, dynamic thermography and advances in infrared camera technology now provide adequate tools to reassess the value of medical thermography.

1.2 Thesis Objectives and Definition of the Problem

Many attempts to quantify the analysis of thermal images were proposed in the literature. Among the various applications of medical infrared thermal imaging, oncology and particularly breast cancer detection have been the most thoroughly explored

and are still under review by many recent studies [18] [37] [51]. Pain management and assessment is another prolific area of application of thermography. Thermal dysfunction associated with pain was investigated in many past and recent publications but most papers provide general quantification techniques and to our knowledge, none so far proposed to apply comprehensive computerised techniques to the assessment of static thermal images of persons experiencing pain.

In this thesis, two major aspects of the digital processing of thermographic images are addressed while keeping in perspective the overall goal, which consists of automating and computerising as much as possible the assessment of thermal images, in order to facilitate the physician's task. The first objective will be to identify the regions of interest for the thermal analysis of the images. A first step will consist of preprocessing the thermal images in order to reduce the noise introduced during the initial acquisition and storage of the images. In addition, extraction of the background irrelevant for the subsequent analysis will be performed, for an optimal selection of the regions of interest.

We then identify regions that exhibit large variations of temperature, in particular regions with extreme temperature variations. A selection of symmetrical regions of interest will be performed whenever possible, since an important feature of the thermal distribution of a healthy human body is its contralateral symmetry. The process of defining regions of interest will be automated as much as possible to eliminate potential artefacts introduced by a manual selection by the user, however standard delimitation of regions of interest based on a mapping of skin areas with specific part of the nervous system will also be considered in order to compare with temperature asymmetry values published in the literature.

The second main objective of this thesis is to determine whether the selected regions of interest may be deemed thermally abnormal and if the answer is yes, how well it correlates to the sensation of pain. The analysis of the regions of interest will be achieved through statistical comparisons between symmetrical regions of interest as well as comparisons with the difference statistics available in the literature and from our own control population. The results from the statistical analysis will be compared with the actual diagnosis for each thermal image, if it is available.

1.3 Thesis Outline

This section describes briefly the organisation of the remaining of this discussion. Chapter 2 gives an overview of the various concepts necessary to the proper understanding of the issues faced by a computerised approach to the analysis of images obtained from medical thermography. A review of pain mechanisms and their relationship to the thermal distribution in the human body is given, followed by the technical aspect of medical thermal infrared imaging.

A literature review on the assessment of medical thermal images is given in the first section of Chapter 3. It is followed by a discussion on the limitations of current approaches and the need for new solutions.

Chapter 4 presents the definition of the problem studied in this thesis. The first part explains the requirements necessary for an efficient analysis of thermal images for the assessment of pain. Then, required processing tasks are exposed and discussed in light of the solutions proposed in the current literature on processing of medical thermographic images.

Chapter 5 describes the proposed integrated approach. It gives a statistical anal-

ysis of the results obtained for the overall system and compares the results from the thermal images of pain patients with their clinical outcomes. The thesis results are also validated with a control population of persons that do not experience any thermal dysfunction triggered by pain.

Finally, chapter 6 summarises the results of the thesis, highlighting the contributions of this work and its potential applications. Future work will be identified.

Chapter 2

Background

This chapter describes the concepts behind the assessment of pain through medical thermography. It presents a brief overview of the physiology of pain in section 2.1 with an emphasis on pain processes and thermoregulation of the human body. Section 2.2 focuses on the physics, the technology and the practical aspects of medical thermography.

2.1 Physiology of Pain

2.1.1 Pain Processes

Pain is a complex multidimensional phenomenon whose different mechanisms are still not fully understood. The very definition of pain may vary slightly among health care workers involved in the assessment and management of pain. Pain is defined by the International Association for the Study of Pain (IASP) as [56]

an unpleasant sensory and emotional experience associated with actual or

potential tissue damage, or described in terms of such damage.

Although pain usually results from stimuli triggered by pathophysiological causes, it is important to emphasise that pain is subjective by nature and therefore the perception of pain, *i.e.* its intensity, localisation and quality, is linked to the person that experiences it, hence the difficulty of pain assessment.

Pain processes typically involve three anatomical and physiological layers. The first layer implies peripheral nerve fibres called nociceptors. Nociceptors have endings located in body tissue and are sensitive to physical, chemical and thermal stimuli. Any noxious stimulus activates local nociceptors, which translate the stimulus into electrical activity. This process is referred to as transduction. The information is then transmitted in the form of electrical impulses to the central nervous system through the spinal cord, which forms the second layer. Finally the message reaches the brain regions underlying pain perception through ascending relay neurons.

Pain perception does not only depend on the intensity or localisation of the noxious stimuli but is also greatly affected by a neural process called modulation that reduces activity in the transmission system. Modulation can be induced by administrated analgesic drugs or by equivalent chemicals released by the brain. In addition, pain perception has an important non-physiological subjective component, which varies according to behavioural, psychological and emotional factors specific to the person experiencing pain [31].

2.1.2 Pain Classification and Complexity of Pain Assessment

Several classification systems are available in the pain literature according to the aspect or aspects of pain one is interested in, which might include physiological, etio-

logical, temporal characteristics of pain [63] [8] [56]. However, due to the complexity and multidimensionality of most pain syndromes, there are no universally undisputed system, so far, among the various proposed ones and they are merely guiding tools for pain assessment and management specialists. Since we are interested in the physiological causes and implications of pain, we will only focus on a pathophysiological approach to the classification of pain, which has the advantage of being quite simple and fairly undisputed.

From a physiological perspective, pain can be divided in two general categories: nociceptive and neuropathic pain [46] [47]. Nociceptive pain results from the direct stimulation of nerve endings due to tissue damages and is proportionate to the actual degree of damage. It is considered most of the time as the normal protective response of an healthy or intact nervous system to potentially damaging stimuli according to the mechanisms described in section 2.1.1. It can be further sub-categorised as somatic or visceral pain. Somatic pain arises from body tissue other than viscera, such as bone, joint, muscle, skin or connective tissue. It is typically well localised and described as sharp, aching, throbbing or pressure-like. Visceral pain arises from visceral, internal organs such as pancreas and the liver. It can be diffuse and cramping or fairly well-localised and aching depending on the cause of the pain.

Neuropathic pain is defined as any pain syndrome that results from the processing of anomalous sensory signals in the peripheral or central nervous system. In other words, neuropathic pain can occur with mild stimuli that normally would not lead to a response or without any stimulus. The cause of the painful sensation is no longer tissue damage as it is for nociceptive pain but rather damage or irritation to the nervous system itself. The mechanisms underlying neuropathic pain are not yet clear

and the many different pathologies that can be classified as neuropathic pain make the task of decrypting the essential and relevant mechanisms even more difficult.

Neuropathic pain is also commonly subdivided into pain generated by the central nervous system, which comprises deafferentation pain and Complex Regional Pain Syndrome (CRPS) (sympathetically maintained pain), and pain generated by the peripheral nervous system, which comprises painful mono- and poly-neuropathies [46].

Pain is also qualified according to its time course as acute or chronic. Acute pain is pain that lasts or is expected to last less than one month. The definition of chronic pain varies among authors and can refer to pain that lasts more than one, three or six months. Nociceptive pain is usually acute but may also be chronic as in cancer pain or arthritis. Neuropathic pain is mostly chronic but may also be associated with acute pain conditions.

Finally, it is worth mentioning psychogenic pain and idiopathic pain, which used to be diagnosed by default when no obvious cause was found and are now encountered less frequently thanks to a better knowledge of pain mechanisms. Psychogenic pain is a physical pain caused mostly by a psychological problem and no or very little physiological or anatomical abnormalities [63]. Idiopathic pain is pain that has no apparent physiological, anatomical or psychological cause.

Despite the different aspects of pain used for classification, it is usually not straightforward to categorise pain conditions in a particular and definite category. A good example is cancer pain, which exhibits a complex association of nociceptive, neuropathic, acute and chronic pain [63].

2.1.3 Pain and Thermoregulation of The Human Body

The autonomic nervous system is more of a functional rather than anatomical system that consists of motor neurons located in both the central and peripheral nervous systems. The autonomic nervous system is responsible for the regulation and co-ordination of the internal environment of the body in a more or less autonomic manner. In other words, it controls basic functions of the body that do not require a conscious or voluntary intervention, such as the heart beat, blood flow, digestion, breathing, or more complex mechanisms such as thermoregulation of the body, which relies on one or more of those basic functions.

The human body temperature is kept more or less constant by a combination of heat production and heat loss. The core body temperature remains constant at about 310 degrees Kelvin ($^{\circ}\text{K}$) or 37 degrees Celsius ($^{\circ}\text{C}$) in normal situations thanks to the heat generated by internal organs or cells during and after digestion *i.e.* metabolism and by flexing of muscles. Contrary to the core body temperature, the skin surface temperature can vary substantially due to heat exchange in the form of radiation, conduction, natural and forced convection, exhalation and evaporation of sweat. The skin temperature may also vary significantly from one area of skin to another [5]. The heat from core body organs is conveyed to peripheral parts of the body such as skin by blood flow through the circulatory system. Blood vessels in the lower layer of the skin can constrict or dilate to regulate blood flow and lose heat to the upper layer when necessary. Specialised neurones act as thermoreceptors to keep track of the temperature of the blood and transmit this information to the brain, which in turn may activate neurons of the autonomic nervous system that regulates temperature [33].

A wide range of external and internal stimuli may trigger autonomic activity. In particular, variations of body temperature due to excessive external temperature, abnormal variations of vital signs and distress applied to the immune system will lead to a response of the autonomic nervous system in the form of increase or decrease of the production of heat, elevation of pulse and blood pressure, and more obvious responses including swelling, spontaneous bruises of skin and fever [26].

Any painful stimulus can induce a response of the autonomic nervous system. However pain syndrome such as neuropathic pain is more likely to exhibit signs of autonomic activity since it involves nerve damage and dysfunction that can provoke inflammation or simply impair the autonomic nervous system [74] [27].

2.2 Medical Thermography

2.2.1 Thermal Radiation

All objects heated at temperatures above absolute zero (zero degree Kelvin ($^{\circ}\text{K}$) or -273 degrees Celsius ($^{\circ}\text{C}$)) emit electromagnetic radiation. The emissive power of the surface of an object is the total energy transferred from the object to its surroundings. It is proportional to the emissive power $E_{b\lambda}$ of a black body, defined as an ideal body that absorbs all incident radiation and radiates in a continuous spectrum according to Planck's law:

$$E_{b\lambda} = \frac{2\pi hc^2}{\lambda^5 (\exp(\frac{hc}{\lambda kT}) - 1)} \quad (2.1)$$

where $E_{b\lambda}$ is the emissive power of a black body in watts per steradian per square metre per micron for a particular wavelength λ and temperature T , h is Planck's constant, c is the velocity of light, k is the Boltzmann's constant.

The integration of Planck's law yields the total emissive power E_b of a black body over all frequencies, which is referred to as Stefan-Boltzmann's law and is given by the following equation:

$$E_b = \sigma T^4 \quad (2.2)$$

Where σ is the Stefan-Boltzmann's constant. Then the emissive power E_λ of an object or a body at a wavelength λ is given by the following relationship (Khirschhoff's law):

$$E_\lambda = \alpha_\lambda E_{b\lambda} = \epsilon_\lambda E_{b\lambda} \quad (2.3)$$

where α_λ is the absorption coefficient of the object and ϵ_λ is the emissivity of the object. The emissivity in equation (2.3) is assumed to be constant over the temperature range and direction of radiation.

In reality, the emissivity of an object is not constant and depends on temperature, wavelength and direction. However, it may be considered as a constant within a certain bandwidth, range of temperature and cone of direction, which simplifies greatly the determination of the emissive power or other related quantities. The amount of energy reflected by an object is determined by the reflectivity coefficient ρ_λ , which is given by the simple relationship:

$$\rho_\lambda = 1 - \epsilon_\lambda \quad (2.4)$$

Note that the reflectivity of a blackbody is null. If a gradient of temperature is applied to a black body and if only radiative heat transfer is considered, the Stefan-Boltzmann's law becomes:

$$E_b = \sigma(T_b^4 - T_s^4) \quad (2.5)$$

where T_b is the temperature of the body and T_s is the temperature of the surroundings. It is also interesting to notice that the emissive power reaches a maximum at a wavelength λ_{max} given by Wien's law:

$$\lambda_{max}T = 0.002898 \quad (2.6)$$

where λ_{max} is the wavelength (in metres) of the maximum emissive power at temperature T (in °K).

Equations (2.1) and (2.3) provide a direct link between the measured radiative energy of a body with the temperature of that body for a specific wavelength. Thus, the accuracy of the measurement of the temperature of an object or a body depends on the ability to measure the radiative energy correctly. If an object has an emissivity less than unity and consequently a reflectivity that is not zero, the total energy radiated from that body will be the sum of the energy emitted by the body itself and the energy that is reflected by that body but comes from the surroundings or other bodies present at the time of the measurement. In such a case, the relationship between measured radiative energy and temperature has to be adjusted to take into account the reflectivity. It is therefore desirable to have an emissivity as close to unity as possible in order to have a high accuracy of temperature measurement [4]. The correction needed to account for the reflectivity of the skin is generally relatively small, especially if the environment has a temperature somewhat lower than that of skin and if the angle of viewing of the measurement is less than $\pi/4$, which is usually the case in clinical settings [4] [33].

2.2.2 Basics of Medical Thermography

The human body is typically at temperatures ranging from 300 °K to 315 °K and therefore emits energy in the form of electromagnetic waves. A major part of the energy radiated by the human body goes through the skin and occurs in the infrared part of the electromagnetic spectrum [28]. In particular, it has been found that the emissive power radiated by the skin reaches a peak around $9.5\mu\text{m}$ and it is very significant in the ranges $3 - 5\mu\text{m}$ and $8 - 14\mu\text{m}$ compared to the rest of the spectrum, although it should be noted that the average radiative power levels of the skin are low with respect to typical radiative power values in the visible range of the electromagnetic spectrum [4]. Also, an interesting characteristic of human skin is its high emissivity in the $8 - 14\mu\text{m}$ range, typically 0.97 to 0.98, which makes skin temperature measurements in that range particularly accurate. The emissivity of skin in the $3 - 5\mu\text{m}$ range is somewhat lower than that in the $8 - 14\mu\text{m}$ range and this range of the electromagnetic spectrum is also more prone to environmental artifacts according to Anbar [4]. As a result, measurements of skin temperature should be carried out in the $8 - 14\mu\text{m}$ region in order to obtain better accuracy and more reliable results.

2.2.3 Medical Infrared Imaging Technology

Historically, two types of infrared imaging systems were used for medical applications. The older infrared imaging system used a thermochromic liquid crystal plate that was put in contact with the part of the body that was to be imaged. The liquid crystal takes different colours according to its temperature and therefore provides a straightforward means of obtaining a thermal distribution of the body. The other type of medical infrared thermographic equipment uses a single non-contact infrared sensor

or detector that scans an object on a pixel-by-pixel basis, by means of a combination of electronic, optical and mechanical elements, comparable to those used in a regular camera. Linear detector array and two-dimensional (focal) plane array cameras use multiple detectors to scan a line at a time or a two-dimensional region at a time respectively, allowing faster rates of acquisition [4].

Contact thermography should not be recommended for most of the medical applications of thermography since it does not meet requirements in terms of thermal sensitivity, resolution and rapidity of acquisition. Furthermore, the contact with the liquid crystal plate induces changes in the temperature distribution of the body and therefore reduces the accuracy of the measurement [3]. Therefore this study focusses on the technology used in non-contact thermal imaging equipment only.

Before presenting the most common infrared detectors used and their main characteristics, let us define the main figures of merit that characterise infrared detectors [30][82][13]. The responsivity $\mathcal{R}$ is defined as the ratio of the detector output, usually a voltage or a current, to the incident radiant power, and is a function of the wavelength of the incident radiation. However, the responsivity does not take into account the effect of noise on the response of the detector and therefore does not reflect the true sensitivity of the detector. Another figure called the Noise Equivalent Power (NEP) attempts to remedy this lack of specificity of the responsivity. NEP is defined as the minimum incident radiant power necessary to give an output signal equal to the detector noise level, *i.e.* a signal-to-noise ratio of one at the output. Since the detector noise level is dependent on the observation bandwidth and the area of the detector, so is the NEP. The NEP can also be seen as the output noise divided by the responsivity $\mathcal{R}$. The inverse of the NEP is called the detectivity D .

The detectivity is usually normalised to unit area and bandwidth and is then called D^* . The detectivity is commonly preferred to the NEP figure since it increases with the performance of the detector.

Infrared sensors are generally classified in two categories: thermal detectors and photodetectors (or photon detectors). Thermal detectors are sensitive to the variation of temperature induced by the incident radiant energy, which changes some electrical characteristics of the detector such as resistance, capacitance or polarisation, voltage or current. Since their response is directly related to the variation of temperature, thermal detector characteristics are constant over a wide range of wavelengths and can be considered constant over the infrared spectrum in particular. Three major types of thermal detectors may be identified: bolometers, pyroelectrics and thermopiles. Other thermal detectors using thermopneumatic properties such as Golay cells are not commonly encountered in infrared thermal imaging.

Bolometers consist of a thermistor placed in a measuring circuit such as a Wheatstone bridge [13][84][35]. The resistance value R of the thermistor sensor varies according to the temperature as follows:

$$R = R_0(1 + \alpha\Delta T) \quad (2.7)$$

where R_0 is the resistance at nominal temperature, α is the temperature coefficient of resistance of the thermistor ($\%/^{\circ}\text{K}$), ΔT is the temperature difference ($^{\circ}\text{K}$). The greater the temperature coefficient of resistance, the larger the variation of voltage with respect to temperature variation.

Pyroelectric detectors are made from ferroelectric materials, whose polarisation varies with temperature, and detect the rate of change of temperature rather than the

change of temperature itself, which makes them immune to interference from constant background radiation [13][35]. The charge Q and the current i measured across the capacitance with charge Q are given by:

$$\begin{aligned} Q &= p\Delta T \\ i &= p \frac{d\Delta T}{dt} \end{aligned} \tag{2.8}$$

where p is the pyroelectric coefficient ($C/^{\circ}K$).

Finally, thermopiles use several thermocouple junctions, which consist of two different metal wires connected in a loop [13][84]. The difference of temperature between the two wires creates a voltage of proportional magnitude depending on the thermoelectric coefficient S ($C/^{\circ}K$) of the junction:

$$V = S\Delta T \tag{2.9}$$

Photodetectors convert the incident radiated energy into a measurable change of voltage or conductance, through the excitation of electrons, or other charge carriers, by the incident flux of photons. They use either the photovoltaic, photoconductive or photoemissive effect exhibited by various semiconducting materials or compounds of the latter.

Photoemissive detectors do not cover the infrared spectrum of interest for medical thermography, *i.e.* the range $3\mu m - 14\mu m$, and thus will be omitted from this discussion [13][84].

Photovoltaic detectors are semiconductor devices that generate a voltage across a p-n junction when incident photons with an energy greater than the energy gap of the

junction excite charge carriers. Since the energy of a photon depends on its associated wavelength, the response of the detector will vary according to the wavelength of the incident radiation. Typically, a photodetector detectivity reaches a maximum at a wavelength λ_{max} before decreasing sharply, with λ_{max} given by:

$$\lambda_{max} = \frac{hc}{E_g} \quad (2.10)$$

where h is Planck's constant, c is the velocity of light and E_g the band gap of the semiconductor junction.

Photoconductive detectors have a conductance that varies according to the incident flux of photons. Incident photons are absorbed and free charge carriers are released, which increases the conductance of the detector material. The change in conductance is measured by means of a bias voltage applied across the photoconductive element [13][35][59].

Thermal detectors typically exhibit a slow response rate and their detectivity is relatively low compared to that of photodetectors. However, they represent a low cost alternative to more costly photodetectors and can be used over a wide spectral range. In addition, they do not require cooling. Most photodetectors must operate at cryogenic temperature to achieve best performance as this reduces the various types of intrinsic and extrinsic noises that affect the photodetector [13][30].

Until recently, the detectors of choice for medical thermography were either photoconductive or photovoltaic, since they provide high detectivity and fast response and can be tailored to the ideal part of the infrared spectrum required for skin temperature measurements. New micro-bolometer technology seems to achieve much better detectivity and response rate in the spectral range of interest, although developments in

photodetectors, especially those using Quantum Well technology, have also improved their performance dramatically [16].

2.2.4 Noise Considerations

Predominant noise types for infrared detectors are 1/f noise (also called excess or flicker noise), thermal noise, shot noise, generation-recombination noise, photon noise and temperature noise [13][35][82][84].

1/f noise occurs in most devices and is thought to be linked with a wide range of phenomena such as bad contacts or leakage currents. The current noise spectrum is usually expressed as:

$$i_n^2 = \frac{KI^\alpha \Delta f}{f^\beta} \quad (2.11)$$

where K is a constant dependent on the detector, I is the current, α is a constant typically between 1.25 and 4, Δf is the noise (or observation) bandwidth, f is the frequency and β is a constant typically between 0.8 and 3.

Thermal noise comes from the random motion of charge carriers in resistive materials. The mean-square thermal noise voltage v_n^2 is given by:

$$v_n^2 = 4kTR\Delta f \quad (2.12)$$

where k is Boltzmann's constant, T is the temperature ($^{\circ}\text{K}$), R is the electrical resistance and Δf is the noise or observation bandwidth. Equivalently and with the same notation, the mean-square thermal noise current i_n^2 is given by:

$$i_n^2 = \frac{4kT\Delta f}{R} \quad (2.13)$$

It is interesting to note that thermal noise can be reduced efficiently by lowering the temperature at which the detector operates.

Shot noise is caused by the random and discrete nature of the generation of charge carriers in a photodetector submitted to photons excitation, which cause random fluctuations in the motion of charge carriers when they cross a barrier of potential. Assuming that each generation of charge carriers is independent of each other, the current flowing through the device follows a Poisson distribution and its mean value or dc value i is given by the relationship:

$$i = qr \quad (2.14)$$

where r is the average rate of charge carriers generated and q is the charge; r is a function of the incident radiant power and the quantum efficiency. The mean-square shot noise current is derived from equation (2.14) and is expressed as:

$$i_n^2 = 2qi\Delta f \quad (2.15)$$

using previous notation.

Generation-recombination noise (G-R noise) comes from the random character of generation, recombination and trapping of charge carriers in a semiconductor, which induces fluctuations of the conductivity or resistance of the material. As a result, it will have a significant effect only when a bias voltage is applied to the device as it is the case for photoconductors. G-R noise is frequency dependent and its contribution to the overall noise of the system is negligible at high frequencies.

Photon noise comes from the random fluctuation of the incident radiation, *i.e.*

the background or the signal itself. Photon noise has been shown to exhibit Poisson statistics. A photodetector that is primarily affected by photon noise is said to operate in background-limited infrared photodetection (BLIP) mode, which represents the ultimate performance achievable by the detector.

Finally, temperature noise accounts for the temperature fluctuations of the background and is the ultimate limiting factor for thermal detectors.

Other sources of noise arising from the electronic circuit that amplifies and transmits the electrical signal to a video display or a recording device may degrade further the overall performance of infrared systems. Typical significant additional noises are thermal noise from the amplifier, quantisation noise or readout noise in the case of charge-coupled devices (CCD). However, careful design and integration of the infrared systems generally enables to reduce these additional forms of noise below the level of the detector noise.

2.2.5 Clinical Infrared Thermography

Clinical infrared thermography or infrared thermal imaging is defined as the recording of the temperature distribution of the human body (or body areas) using infrared radiation emitted by the surface of that body *i.e.* the skin [33]. In other words, medical thermography gives a picture, or a sequence of pictures, of the temperature distribution of the surface of the body. It can therefore give valuable information on the physiology of the human body since it provides an accurate representation of the human body thermoregulation, which is itself controlled by the autonomic nervous system and therefore related to the proper functioning of various structures of the body. It is important to keep in mind that medical thermography is a functional

test and therefore cannot be expected to provide a direct diagnosis of anatomical or structural pathologies. It can however suggest location and/or cause of dysfunctions of an anatomical or neurological nature [3].

The definition of medical thermography is sometimes extended to the study of media other than the skin, for instance arteries during bypass surgery [33]. Medical infrared thermography may be static or dynamic. Static thermography means that a single thermal image is taken for each subject and the analysis is carried-out on this single image. Dynamic thermography indicates that several thermal images of the same subject have been taken, which allows comparison between thermograms and temporal characterisation of temperature distribution. Dynamic thermal imaging may also imply a thermal stress test in order to study the return to equilibrium of the area under examination. Since, medical thermography looks at functional aspects of the human body, dynamic medical thermography is believed to provide a more complete picture of temperature distribution and related physiological processes [4]. However, many older databases of thermographic images currently available consist of static images and their quantitative analysis may still prove to be very valuable.

Medical infrared imaging requires to follow strict protocols and standards in order to achieve accurate measurements [33][67]. In particular, the control of the environment (temperature, humidity, reflectivity) and of the thermal characteristics of the skin on the other side are critical.

Advocates of medical thermography often put forward that it is non-invasive, low cost and that it has a wide range of applications in neurology, vascular disorders, rheumatic diseases, oncology, neonatology or ophthalmology, among others. However, the sensitivity, *i.e.* the amount of false-negative results, and the specificity,

i.e. amount of false-positive results, of the technique vary greatly depending on the applications considered. The explanation for the variation in performance of thermographic examination as a diagnostic aid mostly lie in the interpretation of thermograms (*i.e.* thermographic or thermal images), which remains difficult due to the complexity of the phenomena involved and to the necessity to understand all the underlying processes that lead to changes in the thermal distribution of the human body [3].

Chapter 3

Assessment of Thermal Images: Literature Review

3.1 State of the Art

3.1.1 General Considerations

The skin temperature distribution of healthy human body exhibits a contralateral symmetry in part due to the symmetry of the autonomic nervous system that controls thermoregulation of the human body and therefore of the skin temperature to a great extent. Temperature distribution that shows asymmetrical patterns is usually a strong indicator of abnormality [22][73], but the converse is not always true since some pathological conditions may exhibit bilateral thermal dysfunction and in such cases other signs of abnormalities in the temperature distribution have to be found [27].

A main part of the literature on medical thermography focuses on qualitative interpretation of thermograms. It involves the determination of abnormal thermal

variations of the skin by means of a visual assessment of pseudo-coloured or grey-level thermograms with the help of isothermal displays, visual localisation of hot or cold spots and visual detection of asymmetries [15][21][27][29][38][39][70]. And yet, the task of decrypting thermograms and of extracting useful and reliable information appears very complex, even for highly trained medical thermographers, since it relies upon the subjectivity of the human visual ability to distinguish between more or less large variations of intensity levels representing temperature distribution in thermograms. The use of pseudo-colours for mapping the temperatures of a thermogram has also been criticised for its subjectivity due to the psychological effect of certain colours, which may skew the observer's performance [3].

In an attempt to quantify thermographic findings and increase their objectivity and reliability, some researchers studied the limits for normal thermal asymmetry of the human body. Goodman *et al.* found that thermal symmetry (or asymmetry) for the back and extremities on 31 patients was independent of age (between 20 and 50 years), sex, body proportions and percentage of body fat [22]. The back and extremities were divided into boxes of variable sizes and statistics to the fourth order were computed for each box and then compared with its symmetric counterpart. The authors found that thermal symmetry was stable within 0.2°C across regions as small as $2.5\text{cm} \times 2.5\text{cm}$ over the back, although larger areas resulted in better confidence intervals. They also noted that thermal symmetry was stable over a two-week interval, which was later confirmed by Uematsu's work over a longer period of time [73].

Uematsu *et al.* [72] [74] used a similar method of decomposition of the body and published normal values of thermal asymmetry for 90 normal subjects ranging in age from 19 to 59 years. The temperature differences between one side of the body and

its contralateral part were found to be small (typically less than 0.5 °C except for extremities such as toes or fingers) and reproducible over a 5-year period [73]. Normal temperature asymmetries helped to set up standards and protocols for the analysis of thermograms and improve their interpretation.

3.1.2 Statistical Analysis

Regions of Interest (ROIs) within thermograms must be chosen carefully in order to be able to link the results from the thermal analysis with physiological processes. For instance, Montoro and Anbar suggested to follow anatomical areas or areas controlled by specific parts of the nervous system, when choosing ROIs. Furthermore, they criticised the simple approach that consists in comparing the mean and standard deviation of ROIs with arbitrary sizes and shapes, even though the temperature distributions within each ROI may not follow a Gaussian law, which is often the case when the ROIs enclose hot or cold spots [48].

Anbar identified two methods of extracting ROIs from a thermal image [3]. The first method implied the delimitation of a ROI on one side of the body by an operator and the corresponding contralateral ROI was obtained by basic reflection across a vertical line of symmetry. The second method was similar to that used by Goodman in [22] and consisted of a grid of squares or rectangles superposed to the thermal image.

Lipari and Head selected breast contour as ROIs for the detection of breast tumours and decomposed each breast into four smaller ROIs (quadrants) using anatomical reference points or directions [25] [41]. The division of the breasts in quadrants was based on the observation that different parts of the breasts had different thermal

dynamics. Analysing the quadrants separately could therefore provide additional information and point out more precisely the origin of abnormalities, if any exist. The authors compared statistical differences between the whole breasts, between each quadrants and also the sum of the differences for each quadrants and found that it correlated well with the outcomes from a trained thermographer.

Frize *et al.* recently reassessed and improved the methods used by Lipari and Head for breast thermograms. They obtained a high correlation between thermographic findings and clinical outcomes [18]. In a subsequent paper [17], they also found that only one of the three methods proposed by Lipari and Head worked well for a slightly larger population. They also adjusted the threshold used to differentiate between normal and abnormal breast thermograms and obtained a better classification rate.

Several authors also suggested stretching and mapping techniques applied to ROIs to allow a more efficient comparison between different ROIs in dynamic thermography, especially when ROIs are not simple geometric shapes [19] [48] [50] [78]. More complex methods of boundary or edge detection can also be implemented to define adequate ROIs [9] [62] [51].

Common statistical parameters are then computed for each ROI: mean value, standard deviation and skewness of the temperature distribution. Maximum, median and minimum temperature along with the area in pixels may also provide additional information. Montoro and Anbar also suggested using a "heat content index", which they defined as the product of the mean temperature with the area, for a better comparison between two ROIs with very distinct temperature distributions [48] [49].

Another useful statistical tool is the histogram that represents the temperature distribution over a discrete range of values. Hot (or cold) spots are easily detected by

setting thresholds on the histogram. Montoro also mentioned the use of histograms for the analysis of thermograms with comparable temperature distributions but with different mean temperatures as it might be the case for thermograms taken at different times or under slightly different conditions [48] [49]. Some authors varied the size of ROIs to further investigate the effect of scaling on temperature asymmetries and improve the statistical accuracy of temperature differences [22] [41].

Mabuchi *et al.* proposed an image processing program to evaluate and display the temperature difference distribution between one healthy side of the body and the contralateral healthy side [43]. Temperature differences were computed on a pixel-by-pixel basis inside trapezoids of various sizes that divided symmetrically the human body. The authors noted that their method works only for pathologies that do not affect both sides of the body.

Vavilov *et al.* [80] studied the left-right thermal asymmetry of breasts, thorax and ankles of subjects previously classified as 'practically healthy'. They computed the signal-to-noise ratio, the Z-statistics and the Kolmogorov-Smirnov statistics of contralateral small rectangular regions of interest chosen manually by an operator to quantify thermal asymmetries. Their results suggest that it is possible to distinguish between normal and pathological thermal distributions with an appropriate choice of thresholds for each of the statistical parameters, although they underlined the need for test procedures that are more specific to the area investigated.

3.1.3 Spatial Methods

Qualitative assessment of thermograms by trained and qualified physicians focused mainly on the detection of hyperthermia or hypothermia. This was done by looking at

the whole thermogram, comparing two symmetric areas or by a combination of those two after a stress test [76]. In an attempt to quantify their findings, thermographers studied indexes based on specific scoring systems.

Head *et al.* proposed an infrared index that ranged from 0 to 8 by adding individual scores for each abnormality found according to their type and characteristics, *i.e.* size of hot spots, location of heat patterns [24].

Gautherie *et al.* [20] developed an interpretation method for more objective and efficient detection of breast cancer by thermography. Their method used both qualitative and simple quantitative findings and scores were attributed to each thermal sign according to the significance of the corresponding pathological phenomenon. The sum of all individual scores was classified into five levels with increasing probability of the presence of cancer [34]. Similar methods using grading of qualitative and quantitative abnormalities were also investigated by Keyserlingk [36] [37].

Contrary to previous authors, Usuki *et al.* [76] did not find that quantitative findings were discriminatory enough to be included in standard criteria for breast thermography. They suggested to use qualitative findings only.

The detection and interpretation of thermal asymmetries were greatly facilitated by looking at isothermal contours that define areas of same temperature. By varying the thermal sensitivity of the measurement of isotherms, one can notice hot spots or disrupted and asymmetric thermal patterns [23] [49].

Collins *et al.* introduced a thermal index to quantify isothermal changes and the index was subsequently applied to assess inflammatory conditions and rheumatoid

diseases [11] [6]. The thermal index is given by the following formula:

$$TI = \sum \frac{\Delta t \times a}{A} \quad (3.1)$$

Where Δt is the difference between the mean temperature of each of the isotherms measured at 0.5°C intervals within the ROI and the baseline temperature of the ROI, a is the area of each of the isotherms and A is the area of the ROI. The index was shown to be fairly consistent under specific standardised thermographic examination [64] [65] [66].

Another objective criterion that provides spatial information is a temperature profile line, which displays temperatures as a function of distance. Montoro and Anbar argued that temperature profiles gave more information than simple isotherms because they are not quantised. Temperature profiles should be drawn between anatomically defined points in order to be able to compare findings from different thermograms. The spatial temperature distribution along the line allows an easy detection of hot spots or thermal asymmetries [48].

Montoro and Anbar also suggested computing the derivative of temperature profiles with respect to distance to evaluate the rate of change of temperature profiles and detect fast changes of temperature gradients like edges or blood vessels [48].

3.1.4 Temporal Characterisation

Since thermography is an image representing thermal patterns that reflect permanent anatomical aberrations, as well as time-varying physiological processes, it is legitimate to consider the evolution of temperature distributions with time [49] [4]. Dynamic

thermography will not improve the detection of permanent hot or cold spots resulting from anatomical problems but it can bring valuable temporal or frequency information that may lead to a better diagnosis.

In order to highlight the temporal changes of thermal patterns, a stress test is usually performed, which consists of exposing the area of the patient to be studied to cold or hot stimuli. The evolution and the final state of the response to thermal stimuli are then analysed by several methods that are described below.

Dynamic thermographic changes can be revealed by simple subtraction of two sequential images or of images taken prior and after the test. The detection of hot or cold spots in the resulting thermogram or positive heat patterns in a dynamic sequence of thermograms are likely to be the result of vascular and thermal abnormalities [54] [55].

Ring [65] [66] applied a cold stress test to patients suffering from Raynaud's phenomenon and compared temperature differences between the mean temperature of the fingers and that of the back the hand, before and after the cold stress. This comparison provided an objective indication of normal or abnormal condition. The index based on the comparison of two temperature differences was also used successfully with patients suffering from Reflex Sympathetic Dystrophy (RSD) now called Complex Regional Pain Syndrome (CRPS).

Parisky [58] submitted 117 female patients to a cold stress and recorded hundreds of infrared thermal images before, during and after the cold stress. After the definition of ROI over the breasts, several features were defined and estimated for all but one image of the sequence of thermograms, using an expectation maximisation algorithm, and the left-out thermogram was then declared abnormal or not according to the

outcome of a set of Bayesian classifiers based on these features.

Ohashi and Uchida [54] [55] proposed to model thermal recovery after a cold stress test by a monoexponential function of the time with parameter μ . The μ values of each pixel from sequential thermograms were recombined to form a new thermogram, called the μ -thermogram, which was expected to give additional information about physiological abnormalities.

The oscillatory nature of human thermoregulation and the time-varying nature of physiological phenomena suggest that an analysis of thermograms in the frequency domain can reveal hidden pathological disorders.

Montoro and Anbar computed the Fast Fourier Transform (FFT) of time profiles (temperature of a single pixel or average temperature of a group of pixels as a function of time) taken from ROIs located in the back of an asymptomatic subject and extracted characteristic frequencies of temperature oscillations after removal of slow trends [49]. They also argued that static thermography cannot diagnose reliably temperature asymmetries of less than 0.1°C because the variation of temperature asymmetries over a short period of time can be of the order of that limit or even higher. Similarly hot spots from static thermography may also be the result of temporary desynchronised oscillations between two symmetrical areas and therefore disappear a while later [3] [49].

The same authors identified global, regional and local thermoregulatory frequencies (TRFs) across the back ranging from 2 to 50 mHz. However, they were unable to determine if all their frequencies were fundamental physiological frequencies or artefacts created by reflected higher frequencies. Preliminary studies also found that TRFs respected the symmetry observed with spatial thermal patterns for healthy

patients whereas patients with spinal cord injury exhibited asymmetrical distribution of the TRFs across the spine [4]. Anbar mentioned several methods for an objective analysis of TRFs, such as cluster analysis, feature extraction algorithm, or autocorrelation analysis [4].

Another original method to analyse a sequence of thermograms is the use of the Karhunen-Loeve Transform (KLT). The KLT is an orthogonal transformation that achieves perfect decorrelation and is therefore an optimal data compression transform in a mean square error sense. In the case of sequential thermograms, it reduces the temporal and spatial information contained in the sequence in a small number of significant eigen-images, with specific weights to take into account the time dimension. Unser *et al.* [75] claimed that the analysis of the main eigenvalues enabled an easier detection of abnormalities because all the relevant information was present with reduced noise. Two equivalent (or dual) KLT expansions relying on spatial or temporal models, allow to favour a spatial or temporal interpretation of the results. Static and dynamic components were distinguished by subtraction of the average image of the sequence, which favours a spatial interpretation.

Varga and DeMuyne [77] used a similar method to process sequential thermograms but used a unique colour coding scheme on the first three resultant eigen-images and summed the three resulting images to improve the discriminatory value of the final image.

Finally, Varga and Hanka [79] proposed a complex method of classification of the response to a cold stress test for normal and abnormal conditions of the hands. The images were standardised and presented as a dual representation before being processed by KLT in order to identify ROI for the feature extractor, which was based

on Kittler and Young transformation. A 7-Nearest Neighbour classifier was then used and the results were presented as a colour-coded image.

3.1.5 Image Processing Approaches

The processing of thermographic images has seen new developments in recent literature. More elaborate methods of image processing have been applied to the detection and a better display of thermal abnormalities.

Snyder *et al.* [68] proposed an algorithm to increase the resolution of thermal infrared images by a factor of two while removing noise and preserving edges. The idea was to find an optimal interpolation using an algorithm similar to a maximum a posteriori (MAP) algorithm to estimate the missing data while removing the noise and blur. The optimisation was performed on a cost function, using a Mean-Field-Annealing method. The cost function modeled the degradation from the acquisition process with an estimate of the Point Spread Function derived from camera measurements. An additive Gaussian noise model was used. The authors tested the algorithm on infrared breast images with satisfactory results.

Feature or object extraction by boundary detection and image segmentation were investigated by Qi *et al.* and Ng *et al.* [51][62] for the detection of breast cancer.

These authors presented an automated asymmetry analysis of breast thermograms. Their approach used a Canny edge detector and a Hough transform to detect global edges of the image and breast boundaries. Then they compared the curvature of the curves of smoothed versions of the histograms of the two segmented breasts in order to determine the degree of asymmetry of the temperature distribution of the breasts.

Ng *et al.* presented a method of extracting breasts shapes from breast thermograms. Gradients of thermograms were computed using the Robert cross-gradient operator in order to detect edges and boundaries. Gradient images were enhanced by contrast stretching and median filtering and then divided into 25 regions before being submitted to a thresholding rule.

Chan and Pearce applied image processing techniques to enhance the visualisation of subcutaneous vessels in thermograms after a stress test [9]. They compared the results for two different methods. The first method used a 9x9 median filter followed by a Frei-Chen edge detector and thresholding. The second method filtered the images with a rule-based adaptive window-size filter. A 9x9 median filtered version of the resulting images was subtracted from it and a root image derived by successive median filtering. The vascular patterns were then extracted by thresholding.

Finally, Wu *et al.* [83] tried to map cerebral cortex of small animals using computerised dynamic thermography and image enhancement techniques. A stress test was performed on the subjects and the first image was subtracted from the rest of the sequence in order to enhance weak response signal. The resulting sequence was spatially averaged and activated regions of the cortex were detected using an iterative image threshold and object searching procedure based on spatial and temporal correlation between pixels. An optimisation procedure was then implemented to further refine the detection of activated regions of the cortex.

3.2 Discussion

It has been mentioned in previous sections that a desirable goal for the assessment of infrared thermal images of the human body is to increase as much as possible the

objectivity of the assessment by automating the processing of the images and by providing quantitative results to the medical specialist responsible for the interpretation of the images, thereby reducing the chances of a misdiagnosis.

Section 3.1 presented the various alternatives proposed in the literature on medical thermography that deal with the quantitative assessment of infrared thermal images. Many of these alternatives provided only automated processing of specific aspects of the assessment. For instance, many authors rely on the ability of the operator to define accurately the regions of interest for the asymmetry analysis [25][41][43][48][80], although many also suggest that a more automated approach would be desirable since it would increase the objectivity of the assessment.

Anbar and Goodman's method of extracting ROIs has the merit of being semi-automated and adapted to thermal images of various body areas, although the use of a grid may not prove to be very flexible [3][22].

The statistical analysis following the delimitation of ROIs is limited in many papers to first-orders normal descriptive statistics, *i.e.* mean, standard deviation and sometimes skewness and kurtosis. The evaluation of the statistical difference between two regions is also usually reduced to a comparison between means and standard deviations. Such a comparison is unable to fully capture the statistical nature of most regions of interest, whose distribution is not Gaussian, as Montoro and Anbar noted [3][48]. They used the heat-content index mentioned in section 3.1.2 to compare non-Gaussian temperature distributions.

The so-called thermal index proposed by Collins, Ring, Cosh and Bacon was an attempt to summarise the information contained in isothermal regions of thermal images by means of a area-weighted sum of mean temperature differences between

isothermal regions. The thermal index was investigated primarily on thermal images of arthritic joints (in knees or hands) and uses only limited statistical information.

More interesting statistical techniques were proposed by Vavilov *et al.*. They overcame the problem of non-Gaussian distribution by using the non-parametric Kolmogorov-Smirnov test to compare histograms of contralateral regions. They also argued that a decision making threshold could easily be set to differentiate between normal and pathological asymmetries, without mentioning any and they only produced a few pathological examples to back up their claims [80].

The automated asymmetry analysis of breast thermograms by Qi *et al.* suggested an interesting method to identify abnormalities in breast thermograms by looking at the curvature of the temperature distribution of each breast [62]. However, their method relied heavily on the specific shape (assumed to be parabolic) and characteristics of the breast and would be difficult to transpose to other parts of the body with more varying shapes. The use of profile lines or equivalently the curvature of curves seems nevertheless to be a fairly good and relatively simple indicator of asymmetry and may be worth considering as part of the asymmetry analysis.

The preprocessing of medical thermal images is rarely mentioned as part of the assessment. However, automating the process of delimitation of the ROIs or implementing a registration procedure for the thermal images could be greatly improved by applying noise removal techniques as well as extracting a global region of interest from unwanted areas constituting the background. Snyder *et al.*'s [68] method was claimed to increase the resolution while removing the noise and preserving the edges. However, they modeled the noise as an additive Gaussian process, which may not be always true since medical thermal images may exhibit signal-dependent non Gaus-

sian noise. Also it seems to be directed towards a visual interpretation of the thermal images, since they focused on optimal interpolation of subsampled images.

Furthermore, the papers that proposed integrated approaches such as in [41][51][62][68] are specific to a particular pathology, namely breast cancer, and the methods cannot be fully translated to our problem of interest *i.e.* the assessment of pain.

Finally, several other interesting methods for assessing thermal images only apply to dynamic thermography and rely on the temporal characterisation of the thermal changes as exposed in section 3.1.4.

Chapter 4

Pain Assessment Through Computerised Digital Infrared Thermal Imaging

This chapter states in greater detail the problem of assessing thermographic images of patients with pain-related thermal dysfunction. The first section deals with the specific issues associated with the analysis of thermal images and proposes a solution for each of those issues in accordance with our integrated approach for the digital processing of thermal images. Section 4.2 presents the database of images, which consists of two separate sets of images. The last section exposes our methods in greater details.

4.1 Methodology for Data Analysis: Problem Statement

The problem tackled in this thesis will be twofold.

The first issue is to find among the existing quantitative analysis techniques the methods best suitable for the assessment of pain in infrared thermal images. Also, we wish to identify new techniques, if needed, that could improve the performance of the assessment.

The next task consists of automating as much as possible the processing of infrared images after the data acquisition and before applying a decision-support system.

Preprocessing of clinical thermal images is usually overlooked by most researchers, although it may well be beneficial to the proper identification and delimitation of regions of interest or any other advanced image processing task.

As a result, preprocessing methods adapted to our database of thermal images are identified. They will satisfy the following requirements:

1. remove most of the acquisition noise while preserving the useful information that is the temperature distribution and its statistical properties. The characteristics of the image itself should be preserved as well, for instance the edges and contours of the regions of interest.
2. separate the useful areas of the body from the background.

The identification of regions of interest is a necessary step for the interpretation of thermal images and the medical thermographic literature proposes several distinct methods to achieve this. However, the automation of the identification of the best

regions that will enable to differentiate between normal and pathological thermal images, as far as the assessment of pain is concerned, still remains to be accomplished successfully. This work includes the development of an automated identification of ROIs.

Similarly, although many statistical analysis strategies are proposed in the literature in order to provide an input to any type of decision system, be it computerised or human, many of them are either non specific enough to pain assessment or are conceptually not adapted to the task they are supposed to perform. Defining the discriminatory features derived from the statistical analysis will constitute our next objective.

Finally, if one of the goals of a computerised assessment of pain in thermal images is to produce a decision support aid to medical experts, it would be useful to give a clear outcome of the computerised assessment not only with characteristic figures but also with a visual map of the identified areas of abnormalities, if any.

4.2 Data Collection

Two distinct databases of images were available for our analysis. A great deal of images were recorded in the early eighties at the Pain Clinic of the Moncton Hospital by Monique Frize and her team. They consisted mostly of patients experiencing various types of pain. However, only the thermal images were available to us and we did not have access to patients file or recording information, which means that we did not have any knowledge of the clinical outcome at the time of the analysis.

For comparison purposes we took a new series of images of normal subjects using the same equipment as that of the images from the Pain Clinic. Details on the two

databases are given in sections 4.2.2 and 4.2.3.

4.2.1 Equipment

The infrared thermographic system used for both series of thermal images was a first generation infrared camera AGA Thermovision Model 680 Medical, from AGA corporation, and corresponding video display system AGA Thermovision Display Main Frame 102C. The thermovision 680 camera system uses an Indium Antimonide (InSb) photovoltaic detector cooled to 77°K by liquid nitrogen. The detector operates in the $2\mu\text{m} - 5.6\mu\text{m}$. A series of lenses and rotating prisms transfer the incident optical radiation from the Germanium collimating lens to the detector. The aperture used was $f/1.8$, which gives a scanned area of $23\text{cm} \times 23\text{cm}$ at 0.6m [1].

The electrical signal coming from the detector is amplified using a low-noise direct-coupled preamplifier, which was designed in a way not to introduce any additional significant noise to the signal coming from the detector. A rotary chopper covers the detector for a fraction of the scanning period, which gives the preamplifier a reference temperature every scanning period therefore reducing any undesirable temperature drift. Also, the optical modulation induced by the chopper makes the contribution of the $1/f$ noise from the infrared detector negligible with respect to other sources of noise by increasing the frequency to about 300Hz. Generation-recombination noise being also negligible for photovoltaic detectors, the only significant source of noise at these intermediate frequencies is the photon noise from the background; the cooling of the detector further ensures that the detector functions near the BLIP limit [30].

The user is responsible for selecting the appropriate range of temperatures for each specific object to be imaged, by varying the middle temperature level control and sensitivity settings, thus allowing the best thermal resolution for each image.

The images are produced quasi instantaneously by the camera thanks to the fast response rate of the InSb detector. Then they are transferred to the video display unit. The images consist of seven interlaced frames of 64×128 pixels. However, only two frames are kept for the digital image, which gives a usable resolution of 128×128 or 16384 pixels. Each pixel has a resolution of 8 bits or 256 possible grey-levels [2].

The digital images are stored on magnetic tape by means of the AGA Offline System for Computer Access and Recording (OSCAR). They may be transferred to a computer in the form of ASCII files through a simple interface and then processed through an imaging software to produce a more usable format. For each image transferred from the tape recorder to the computer, we kept a version in the original ASCII format and another one as a Tag-Based Image File Format (TIFF) image.

Calibration of the camera was achieved by means of a temperature reference source, which consisted of a thermostatically controlled heated blackened plate, whose emissivity was assumed to be close to that of a blackbody.

4.2.2 Control Population

The control population consisted of fifteen healthy volunteers, 9 males and 6 females, with age ranging from 21 to 47. A person was considered healthy for the purpose of the test if he or she had no known history of significant dermatological, orthopedic, or neurological problems nor any systemic vascular, rheumatological or endocrine disease that could affect the thermal distribution of their body.

The tests took place at Carleton University in the Department of Systems and Computer Engineering, Minto Centre, room 7047, between June 17, 2002 and June 23, 2002. The protocol followed the commonly accepted thermographic guidelines [60]

and was approved by the Carleton University Research Ethics Committee. The information letter detailing the protocol that was given to each volunteer is provided in Appendix A.

For each volunteer, a series of images were taken of different parts of their body: head, arms, legs, back and chest. Eleven images of the whole back and whole chest were obtained and fifteen images for the remaining parts of the body. The images were stored on magnetic tapes and on a personal computer, according to the procedure and format described in the previous section (128×128 pixels, 8 bits).

For each patient, the investigator recorded the middle temperature level, sensitivity settings, the room temperature and the temperature of thermistor probe placed on the skin at a specific location (forehead or chest) prior to the recording. The room temperature ranged between 22°C and 25°C and was kept more or less constant during the actual test. The middle temperature levels ranged from 30°C to 34°C depending of the part of the body studied. The sensitivity setting used was either 0.5 or 1, which gives a temperature range between 29.5°C and 34.5°C or 27°C and 37°C respectively for a middle temperature level of 32°C.

4.2.3 Actual Medical Cases

The database of actual medical cases was constituted in the early eighties by Dr. Monique Frize, Dr. Gilbert Quartey, neurosurgeon at the Moncton Hospital, New Brunswick, Canada and Denis Lapalme, psychologist at the Pain Clinic in Moncton.

The thermal images were available on magnetic tapes and about 700 images were transferred to the hard drive of a personal computer for more accessible use. Within those 700 or more images, about 140 images were thermal images of the back (upper

back, lower back or neck), approximately 220 images were thermal images of the legs (upper legs or lower legs, front or back), about 30 images represented the chest or the abdomen, about 60 images were thermal images of the head (front and sides), about 100 images were thermal images of the arms (front, back and sides) and the remaining were thermal images of hands and feet as well as images of all these areas from other angles of view.

We were unable to find any records of the experimental settings used for each of these images, *i.e.* middle temperature level, sensitivity, room temperature, although it was suggested that the sensitivity had been set to 1 for most of the pictures. Assuming a sensitivity of 1 gives a temperature range of 10°C and allows us to convert the grey-level intensity differences back into temperature differences, which is our parameter of greatest interest for the asymmetry analysis.

4.3 Proposed Computerised Assessment of Pain in Thermal Images

4.3.1 The preprocessing of thermal images

Enhancing thermal images consists mostly of reducing the noise since the protocol and equipment required for medical thermography should ensure that the images produced are not blurred or that they do not have poor contrast other than that resulting from noisy measurements. This was observed in the great majority of our available images.

Noise model

The overall system noise analysis should include any additional noise coming from signal processing electronics, such as thermal (or Johnson) noise in resistive elements, as well as possible quantisation noise arising from the Analog-to-Digital converters. Assuming an ideal infrared system where all the noise types inherent to the design are minimised, the only significant source of noise remaining becomes the photon noise. We have seen in section 2.2.4 that photon noise follows Poisson statistics and is signal-dependent, contrary to the common model of additive Gaussian noise. If the infrared system is not ideal, the total noise of the system has to include an additive term, to take into account the thermal noise. This extra term can be assumed to follow a Gaussian distribution [30]. The quantisation noise may be considered negligible with respect to the other types of noise present.

From the previous paragraph a general noise model for infrared imaging system could be of the following form [32]:

$$\eta(k, l) = h(s(k, l)) \times \eta_1(k, l) + \eta_2(k, l) \quad (4.1)$$

where $\eta(k, l)$ is the noise at pixel (k, l) ; $s(k, l)$ is the intensity level at pixel (k, l) for the noiseless signal¹; $h(\cdot)$ is a nonlinear operator; η_1 is zero-mean, unit-variance Gaussian white noise process and η_2 is a zero-mean Gaussian white noise accounting for thermal noise and independent from η_1 .

¹The image $s(k, l)$ is usually a version of the original image degraded or blurred by the Point Spread Function associated with the optical part of the imaging system.

The observed image $f(k, l)$ can therefore be represented as follows [52]:

$$f(k, l) = s(k, l) + \eta(k, l) \quad (4.2)$$

where $f(k, l)$ will have a Poisson probability distribution with mean value $s(k, l)$.

The difficult task resides in the removal of the signal-dependent part of the noise, since the additive Gaussian white noise, if present, can be efficiently removed using common efficient noise removal methods such as Wiener or Wavelet-domain filtering.

For high intensity values, *i.e.* a high number of incident photons, the probability distribution of f can be approximated by a Gaussian distribution, according to the Central Limit Theorem. Many authors use this simplification and then use the well-known noise removal techniques based on additive Gaussian noise assumption, although this might not always be justified due to the signal-dependence and therefore spatially variant nature of the noise.

Another technique consists of taking the operator $h(\cdot)$ as a $\sqrt{(\cdot)}$ (or equivalent) in order to make the distribution approximately Gaussian while stabilising the noise variance, which is proportional to the signal [52]. The noise removal procedure would therefore consist in first taking the square root of the noisy image, then use a denoising filter and take the square of the result to obtain a denoised version of the image.

A recurrent problem in the denoising of images is a tendency to smooth the fine details of the original image such as edges or contours. This can be damageable for the correct interpretation of medical images and should be minimised as much as possible. Many denoising methods work in a transform domain where coefficients corresponding to the signal are high and usually concentrated around the origin while those corresponding to the noise are low and usually spread out. The fourier domain

provides such a framework and is based on the projection of the signal or image onto a basis of sines and cosines, therefore differentiating the signal according to its frequency [32].

Wavelet transform overview

The wavelet transform is a more useful decomposition than the Fourier transform since it projects the signal onto a basis of dilated and translated functions called wavelets, which are well localised in both time and frequency, unlike the sines and cosines of the Fourier transform. The Wavelet bases allow a decomposition of the time-frequency plane more adapted to the type of signal, therefore providing a better analysis of the details of various size orders or in other words, at different resolutions or scales [45] [81].

A simple wavelet ψ is a normalised function whose first moment is zero (using Mallat's notations [45]):

$$\begin{cases} \int_{-\infty}^{+\infty} \psi(t) dt = 0 \\ \int_{-\infty}^{+\infty} \psi(t) \psi^*(t) dt = 1 \end{cases} \quad (4.3)$$

Where $*$ denotes the complex conjugate.

For any one-dimensional signal $f(t) \in \mathbf{L}^2(\mathbb{R})$, the Wavelet transform Wf of f is defined as [45]:

$$Wf(u, s) = \langle f, \psi_{u,s} \rangle = \int_{-\infty}^{+\infty} f(t) \frac{1}{\sqrt{s}} \psi^* \left(\frac{t-u}{s} \right) dt \quad (4.4)$$

Where $\langle f, . \rangle$ is the inner product, $u \in \mathbb{R}$ is a translation parameter, $s \in \mathbb{R}^+ - \{0\}$ is a scale parameter. The wavelet transform may also be seen as a convolution by a

time-reversed, scaled complex conjugate function $\frac{1}{\sqrt{s}} \psi^* \left(\frac{-t}{s} \right)$.

The continuous Wavelet transform defined in (4.4) is of little use to our current application and it is necessary to define a discrete form equivalent. This discrete wavelet transform theory has been covered extensively in the literature and the most significant results will be discussed.

The discrete wavelet transform may be presented as a continuous wavelet transform whose scale and translation parameters have been made discrete [45]. A common way of doing this is achieved by sampling the scale parameter along a dyadic sequence² (*i.e.* $s = 2^j$, $j \in \mathbb{Z}$), and sampling the translation parameter uniformly (*i.e.* $u = n$, $n \in \mathbb{Z}$), yielding a family of wavelets:

$$\left\{ \psi_{j,n}(t) = \frac{1}{\sqrt{2^j}} \psi \left(\frac{t - 2^j n}{2^j} \right) \right\}_{(j,n) \in \mathbb{Z}^2} \quad (4.5)$$

If the wavelet is chosen appropriately³, the family created may form a basis of $\mathbf{L}^2(\mathbb{R})$ and the signal f may be projected onto this basis as:

$$f(t) = \sum_{j=-\infty}^{+\infty} \sum_{n=-\infty}^{+\infty} \langle f, \psi_{j,n} \rangle \psi_{j,n}(t) = \sum_{j=-\infty}^{+\infty} d_j(t) \quad (4.6)$$

where

$$d_j(t) = \sum_{n=-\infty}^{+\infty} \langle f, \psi_{j,n} \rangle \psi_{j,n}(t) \quad (4.7)$$

may be interpreted as the details of the function f at a particular resolution 2^{-j} ,

²Other discretisation methods are of course also possible.

³For a discussion on the properties of common wavelets and wavelet bases, please refer to the literature and in particular to [45] [12].

inverse of the scale parameter, and

$$d_{j,n} = \langle f, \psi_{j,n} \rangle \quad (4.8)$$

are the wavelet coefficients. The function f is equal to the sum of all its details at all resolutions.

Note that it is possible to break the infinite sum over the j 's into two terms:

$$\begin{aligned} f(t) &= \sum_{J+1}^{+\infty} d_j(t) + \sum_{-\infty}^J d_j(t) \\ &= A_J(t) + \sum_{-\infty}^J d_j(t) \end{aligned} \quad (4.9)$$

where $A_J(t)$ represents the approximation of $f(t)$ up to the scale 2^J (or equivalently, up to the resolution 2^{-J}) and $\sum_{-\infty}^J d_j(t)$ represents the finer details. $A_J(t)$ and $d_J(t)$ are related in the following manner:

$$A_{J-1}(t) = A_J(t) + d_J(t) \quad (4.10)$$

Equations (4.9) and (4.10) have obvious similarities with a multiresolution representation of the signal f , especially if the basis is made orthogonal, which allows unique decomposition and reconstruction of the signal. It can indeed be linked to the mathematical multiresolution framework proposed by Mallat [44], which projects a function f onto a sequence of embedded subspaces of $\mathbf{L}^2(\mathbb{R})$ resulting in multiple approximations of f at various resolutions. At each scale 2^j or approximation level j corresponds a space $\mathbf{V}_j$ of $\mathbf{L}^2(\mathbb{R})$. The family $\{\mathbf{V}_j\}_{j \in \mathbb{Z}}$ is called a multiresolution

approximation if it follows a set of properties described in [44]. In particular the spaces $\mathbf{V}_j$ are such that

$$\mathbf{V}_j \subset \mathbf{V}_{j-1}$$

for all $j \in \mathbb{Z}$. If we call $\mathbf{W}_j$ the orthogonal complement of space $\mathbf{V}_j$ then we get the following relationship:

$$\mathbf{V}_{j-1} = \mathbf{W}_j \oplus \mathbf{V}_j \quad (4.11)$$

This formalises the intuitive idea that an approximation of a signal f at a resolution $2^{-(j-1)}$ is the sum of the approximation at a lower resolution 2^{-j} and a detail term corresponding to the projection of f on the space $\mathbf{W}_j$.

The final step consists of identifying the spaces $\mathbf{W}_j$ and $\mathbf{V}_j$. From our initial discussion and equations (4.6) and (4.7), the basis of wavelets up to the scale 2^j seems to be a reasonable candidate to span $\mathbf{W}_j$. As for the space $\mathbf{V}_j$, it is possible to find a family of dilated and translated functions $\{\phi_{j,n}\}_{n \in \mathbb{Z}}$ that is an orthonormal basis of $\mathbf{V}_j$. The function ϕ is referred to as the scaling function and has been shown to have a close relationship with the wavelet function ψ [45].

More specifically, the scaling function and wavelet function satisfy the following equations:

$$\frac{1}{\sqrt{2}} \phi(t/2) = \sum_{n=-\infty}^{+\infty} h[n] \phi(t - n) \quad (4.12)$$

$$\frac{1}{\sqrt{2}} \psi(t/2) = \sum_{n=-\infty}^{+\infty} g[n] \phi(t - n) \quad (4.13)$$

Where $h[n]$ and $g[n]$ are discrete-time low-pass and high-pass filters (respectively). Finding the scaling and wavelet function simplifies to finding two related discrete-time

filters.

From the preceding discussion, we can re-decompose the function $f(t)$ as:

$$f(t) = \sum_{n=-\infty}^{+\infty} a_{(J,n)} \phi_{(J,n)}(t) + \sum_{j=-\infty}^J \sum_{n=-\infty}^{+\infty} d_{(j,n)} \psi_{(j,n)}(t) \quad (4.14)$$

where

$$a_{(J,n)} = \langle f, \phi_{J,n} \rangle \quad (4.15)$$

are the approximation or scaling coefficients at scale 2^J (or resolution 2^{-J}). From equations (4.8), (4.12), (4.13) and (4.15), we get the following recursions:

$$a_{(j+1,p)} = \sum_{n=-\infty}^{+\infty} h[n-2p] a_{(j,n)} \quad (4.16)$$

$$d_{(j+1,p)} = \sum_{n=-\infty}^{+\infty} g[n-2p] a_{(j,n)} \quad (4.17)$$

which may be implemented efficiently in a two-level filter bank, by successive convolutions with the reversed low-pass filter h and high-pass filter g and then subsampling by a factor 2.

The recursions require an initialisation step explained in [45], which reduces to $a_{(0,p)} = f(p)$, $p \in \mathbb{Z}$ for a discrete signal $f(p)$, $p \in \mathbb{Z}$. In addition, the infinite summations becomes finite in the case of a discrete signal since the number of samples and therefore the resolution is limited to $j_{max} = \log_2(N)$, with N the number of samples.

Also, the decomposition of signals defined over a finite interval raises border problems that may be dealt with by adapting the wavelet bases (making it periodic for instance). Finally, the discretisation of the wavelet transform and more specifically of

the translation parameter, makes the discrete wavelet transform lose its translation-invariance, which may be undesirable for the processing of images. Strategies may be implemented to restore the translation-invariance, such as no sampling or adaptive sampling of the translation parameter, or computing all the possible shifts of the wavelet transform of the signal and then averaging [45] [10]

Figure 4.1: Two stages of a one-dimensional wavelet decomposition, using a two-level filter bank.

These results may be generalised to an n -dimensional case in a relatively straightforward way. In particular, using separable wavelet bases allows fast implementations of n -dimensional cases.

Let us take the example of a two-dimensional discrete image $a_{(0,m,n)}$, where the 0 indicates the scale 0, or the initial best resolution. The recursions in (4.16) and

(4.17) become (assuming separable bases):

$$a_{(j+1,p,q)} = \sum_{m=-\infty}^{+\infty} \sum_{n=-\infty}^{+\infty} h[m-2p] h[n-2q] a_{(j,m,n)} \quad (4.18)$$

$$d_{(j+1,p,q)}^{vertical} = \sum_{m=-\infty}^{+\infty} \sum_{n=-\infty}^{+\infty} h[m-2p] g[n-2q] a_{(j,m,n)} \quad (4.19)$$

$$d_{(j+1,p,q)}^{horizontal} = \sum_{m=-\infty}^{+\infty} \sum_{n=-\infty}^{+\infty} g[m-2p] h[n-2q] a_{(j,m,n)} \quad (4.20)$$

$$d_{(j+1,p,q)}^{diagonal} = \sum_{m=-\infty}^{+\infty} \sum_{n=-\infty}^{+\infty} g[m-2p] g[n-2q] a_{(j,m,n)} \quad (4.21)$$

where the filters h and g operate successively and alternatively on rows and columns of the image. Each approximation level 2^j returns an approximation image at resolution $2^{-(j+1)}$ and three detail images.

Figure 4.2: One stage of a two-dimensional wavelet decomposition, using a two-level filter bank.

Figures 4.1 and 4.2 adapted from [45] show the wavelet implementation process

for one- and two-dimensional signals. The result is a set of wavelet and scaling coefficients.

Wavelet-Domain Filtering

Filtering in the Wavelet domain, where most of the energy is concentrated in a few coefficients, is similar to classical noise filtering in the Fourier domain except the filtering is adapted to the regularity of the original signal, or in other words adapted to the smoothness of the signal. The filtering therefore does not yield excessive smoothing as may be the case in the Fourier domain.

The goal of noise filtering in a transform domain, wavelet, fourier or other, is to identify the coefficients that correspond to noise from those that correspond to the desired original signal. It is reasonable to assume that the coefficients corresponding to the signal have higher energy (or value) than the coefficients corresponding to the noise. As a result, a simple thresholding procedure may be able to remove a great part of the noise coefficients in the transform domain [14]. However, finding an efficient threshold and thresholding technique may represent a difficult challenge, especially in the case of signal-dependent (non-additive) noise. Thresholding methods that adapt to the noise level at each scale are potentially good candidates for wavelet-domain removal of signal-dependent noise.

Nowak and Baraniuk [52] proposed an original thresholding method to filter out the Poisson noise in photon-limited images, in the wavelet domain. They considered the successive sub-images created at constant interval during the acquisition period of a single image. Those successive images have increasing intensity levels until the final image, since more and more photons are detected as the observation period

increases. Then the authors measured the error between a wavelet-domain filtered image accounting for all the sub-images but one, and this image and this for each sub-image. The sum of these errors forms a criterion called Predictive Sum of Squares (PRESS), which is dependent on the filter (or threshold) used. Minimising the PRESS criterion yields the optimal filter (or threshold) ⁴. The authors also proved that the sub-images were not required to compute the optimal threshold since as the number of sub-images goes to infinity, the filter (or threshold) reduces to:

$$\mathbf{h}^{(PRESS)} = \left(\frac{\theta^2 - \alpha \hat{\sigma}^2}{\theta^2} \right)_+ \quad (4.22)$$

where θ refers to the wavelet transform of the image, $\hat{\sigma}^2$ is the corresponding matrix of noise variance estimates, α is a regularisation parameter (the threshold is optimal for $\alpha = 1$), and $(.)_+$ sets to zero the negative thresholds.

The noise variance is estimated by projecting the image onto the square of the wavelet and scaling functions, yielding what Nowak and Baraniuk called Discrete Squared Wavelet Transform (DWST). The squared wavelet and scaling coefficients

⁴This technique consisting of using the prediction error based on the knowledge of a sequence of related signals or functions but one is called cross-validation

are obtained through the following recursion:

$$a_{(j+1,p,q,r,s)} = \sum_{k,l,m,n=-\infty}^{+\infty} h[k-2p] h[l-2q] h[m-2r] h[n-2s] a_{(j,k,l,m,n)} \quad (4.23)$$

$$d_{(j+1,p,q,r,s)}^{vertical} = \sum_{k,l,m,n=-\infty}^{+\infty} h[k-2p] h[l-2q] g[m-2r] g[n-2s] a_{(j,k,l,m,n)} \quad (4.24)$$

$$d_{(j+1,p,q,r,s)}^{horizontal} = \sum_{k,l,m,n=-\infty}^{+\infty} g[k-2p] g[l-2q] h[m-2r] h[n-2s] a_{(j,k,l,m,n)} \quad (4.25)$$

$$d_{(j+1,p,q,r,s)}^{diagonal} = \sum_{k,l,m,n=-\infty}^{+\infty} g[k-2p] g[l-2q] g[m-2r] g[n-2s] a_{(j,k,l,m,n)} \quad (4.26)$$

This recursion can also be implemented with filter bank in a similar manner as for the regular Discrete Wavelet Transform. An example is shown in figure 4.3. The initialisation of the recursion is done by placing the original image onto the four-dimensional diagonal $a_{(0,p,q,r=p,s=q)}$. The complexity of the computation is lowered by the extreme sparsity of the arrays involved. The authors showed that these estimates of the noise variance were unbiased, under a Poisson noise assumption.

The wavelet-based denoising of Poisson noise can therefore be carried out as follows:

1. Compute the wavelet coefficients θ by taking the Discrete Wavelet Transform (DWT) or Fast Wavelet Transform (FWT) of the noisy image.
2. Compute the variance estimates $\hat{\sigma}^2$ with the Discrete Squared Wavelet Transform (DWST) of the noisy image.
3. Compute the filter $\mathbf{h}^{(PRESS)}$ and threshold of the wavelet coefficients.
4. Compute the denoised image by taking the Inverse Discrete Wavelet Transform

(IDWT) or Inverse Fast Wavelet Transform (IFWT) of the thresholded wavelet coefficients.

Figure 4.3: One stage of a two-dimensional squared-wavelet decomposition, using a two-level filter bank.

The choice of the wavelet basis is important to preserve the original features of the image. Since thermal images and most real-world images are inherently smooth with localised fine details, wavelets that are well localised and have a certain degree of smoothness are usually required. Daubechies orthogonal wavelets are commonly suggested, although other wavelets such as Battle-Lemarié spline orthogonal wavelets have been applied successfully for medical images processing [52] [42].

The preservation of boundaries is necessary for a proper automated analysis of thermal images, since techniques of decomposition of thermal images into regions of interest of adapted sizes are based on identification of body shapes and proportions. This is especially true when anatomical landmarks are not easily distinguishable, as is the case in many images. Also, if one wants to apply pattern recognition techniques in

order to identify the abnormalities detected by the asymmetry analysis, it is desirable to preserve the fine details in the images. This is another factor supporting the choice of a wavelet-domain filtering of the Poisson noise for thermal images.

Background Extraction

The goal of background⁵ extraction consisted in facilitating the analysis of thermal images by removing any unwanted parts of the images such as clothing, background, hair etc.

The background in thermal images is usually relatively simple and even though it may consist of the many different parts mentioned in the previous paragraph, the overlapping between the intensity levels of the background and those of the parts of interest is usually limited. Also, the background extraction occurs after noise removal, which means that the delimitation of various regions in the thermal image is simplified.

As a result a background removal method that is based on thresholding should provide fairly good results for our analysis and more sophisticated segmentation techniques should not be needed. The advantage of thresholding techniques is their simplicity and computational efficiency. We considered in this thesis simple thresholding techniques based on optimal thresholding of the image. Optimal thresholding refers to the minimisation of the probability of error when trying to find a single threshold that separates the region of interest from the background.

The simplest optimal thresholding method can be found by taking the mean of the mean values for the background and the region of interest respectively. This is done

⁵Background is considered in a broad meaning and refers here and in the following to any unwanted signal, not only the background radiation.

iteratively with an arbitrary number of pixels (corners of the image for instance) set to be background pixels initially and applying the successive thresholds based on the means of background and region of interest, until stabilisation of the threshold [69]. A similar method that takes into account the variances of the two regions may give better results [57]. It consists of maximising the between-class variance that is the difference between the total variance of the image and a weighted sum of the variances of each regions, normalised by the total variance.

Both previous methods give similar results and work globally well for thermal images where the variation of intensity levels is fairly smooth over the region of interest. However, when colder regions are close to hotter ones, as is the case for thermal images of the lower back and buttock, where some parts of the buttock are usually colder, they are assimilated to the background. It is therefore necessary to have additional processing steps in order to restore the wrongly segmented parts.

We proposed a third approach to the background extraction in thermal images that combines optimal thresholding and morphological image processing steps in order to achieve a higher rate of good classification between background and region of interest. The first part of our method was adapted from Tsai's work [71], which implied smoothing the histogram of an image until the desired number of modes are achieved and then looking for the extrema of the resulting function. The choice of the threshold among the extrema obtained was not always satisfying and we devised a different scheme for the threshold selection. The resulting algorithm may be broken into several processing steps:

1. The histogram of the image was computed and smoothed with a Gaussian function to obtain a desired number of modes.

2. The extrema of the resulting function were then computed as well as their corresponding grey-level.
3. A first threshold was set to the strongest minimum, that is the last minimum remaining after successive smoothing with increasing variance of the Gaussian function.
4. A second threshold was selected to be the first stable minimum when the variance of the Gaussian function was increased, yielding a slightly more aggressive one than the simple absolute minimum.
5. The final threshold was then given by a weighted sum of the two thresholds.

The image was then thresholded, the background pixels were set to white and additional morphological steps were then performed to fill the possible holes created by an aggressive thresholding and to remove the unwanted regions remaining. Again, this was broken into several processing steps:

1. Isolated pixels (white pixels surrounded by grey-level pixels) wrongly labeled as background pixels inside the main region of interest were corrected.
2. The approximated boundaries of the image were superposed to the thresholded image and any holes created were filled⁶.
3. The remaining regions of interest were then roughly segmented and the smaller regions were discarded as they likely correspond to background items. The same procedure was performed on the background regions, with some additional

⁶Computing the boundaries directly and filling the interior pixels is not easily feasible due to the sometimes complex structure of thermal images that lead to an overestimation of the number of edges or the opposite, which makes the definition of exterior boundaries and interior pixels difficult.

logical steps that prevent the algorithm from discarding background regions around the border.

4. Finally, the remaining possible holes in the foreground regions were filled based on the size and shape of the regions.

4.3.2 Identification of Regions of Interest

Following the discussion in section 3.2, we automated the delimitation of regions of interest for their comparison using modified versions of existing methods.

First of all, in order to compare the results that were derived from our population of normal patients with the values published in the literature [73] [22], we divided the body into multiple squares or rectangles that other authors used. The manual division by Uematsu followed more or less the areas of the skin called dermatomes that are innervated by the major peripheral nerves. Being able to link the data from those regions of interest with the corresponding nervous system that feeds them is believed to be more meaningful for the assessment of the thermograms. Goodman used a grid of squares, for the back and front, and rectangles for the arms, legs and extremities. The grid was adapted to the bodily dimensions of each subject and could be moved around to cover any wanted areas. The statistics were computed for various number of slices or frames of the unit square or rectangle and results from their analysis compared to that of Uematsu's.

For comparison purpose, we devised a hybrid of the two divisions for the back, chest and legs, which consisted mostly in Uematsu's division with two additional regions in the back. Our algorithm first looked for some easily identifiable landmarks, namely the shoulders and the hips for the chest and back, the buttock cleft for the

back, the area around the knee for the legs. This was achieved by the following steps:

1. The vertical symmetry line separating contralateral parts of the body was first sought by detecting the edges and averaging the middle distance between the outer boundaries of the body.
2. For the right and left sides of the body, we defined the function corresponding to the distance between the outer boundaries and the symmetry line, thus obtaining two functions representing the left and right profiles of the body.
3. Then, we smoothed the profile resulting from averaging both left and right profiles with a Gaussian function and looked for extrema of the resulting function.
4. The first significative maximum was found to be representative of the extremity of the shoulder and the level corresponding to 80% of the maximum was used to find the coordinate of the extreme point for choosing the ROIs.
5. The flank level was found through a similar method for the upper back images but looking for the first significative minimum of the profile function instead of the maximum. For the lower back images, a search for the minimum distance between left and right sides, above the upper point of the buttock cleft, provided acceptable results.
6. The buttock cleft was found through an analysis of the horizontal profile lines across the lower part of the images, when a middle edge line was present. The distance between the lower point and higher points was computed for each profile lines, yielding a function of this distance. The first minimum of this

function was chosen to be approximately the upper extremity of the buttock cleft.

7. Finally, the knee was easily detected by looking at the minimal distance between each edge lines for both legs.

Based on the previous landmarks, the positioning of the sizes of the various boxes delimiting the ROIs defined by both Uematsu and Goodman was determined in a straightforward manner.

A second method was implemented to determine more specific regions of interest than dermatomes. It was based on an isothermal analysis of the entire image (without the background) to determine hotter and colder regions. The step for the computation of each isotherm was chosen according to the range of intensity values covered in the image, to provide some adaptivity to the generation of isotherms. It helped to limit the area of each isothermal regions to acceptable sizes, rather than having a region covering most of the body. In practice, the step was set to one tenth of the total range of intensity values. For instance, if the intensity values were ranging from 80 to 180, the corresponding step size would be $(180 - 80)/10 = 10$ and assuming a sensitivity of one, the isotherm range would be $10/255 = 0.039^\circ\text{C}$. Also, whenever the sensitivity setting was available, we looked for isothermal regions at regular intervals of 0.5°C , for comparison with common isothermal analysis found in the literature.

The first isotherm was ranging from the minimum intensity/temperature up to the minimum intensity/temperature plus the step, the second isotherm was ranging from the minimum intensity/temperature plus one step up to two steps and so on. The same rule was applied for the hotter regions, starting from the maximum and subtracting successive increments of the step. Typically, only the first two to three

steps were necessary to yield significant regions. As the isotherm was getting closer to the mean intensity/temperature, the regions were getting bigger, covering most of the image.

In addition, the smaller regions, typically less than 10 pixels, were discarded by thresholding the areas of the regions returned by the previous isothermal computation. Statistical comparisons with regions smaller than the threshold area would have limited significance in most cases. If two regions of very different sizes (one large and one small) were found to be too close to each other, they were merged into one bigger region. The positions and pixels in the remaining regions were kept for the statistical analysis.

Finally, in order to avoid artefact regions located around the contour of the body area of interest, as may be the case if the background extraction algorithm was not able to remove some of the clothing around the body for instance, the image was eroded along the boundaries using a simple morphological operator.

A simple algorithm was used to compute the reflection of the regions of interest with respect to the vertical line of symmetry, for all methods, allowing us to assess the asymmetry of the resulting intensity/temperature distribution.

4.3.3 Asymmetry Analysis and statistical considerations

Following our discussion in section 3.2 on the limitations of current and past statistical measures that were devised to compare symmetric ROIs or assess asymmetries in the temperature distribution of the body, we attempted to provide a more powerful and efficient comparison of regions of interest. We first considered a comprehensive set of statistical features that may be able to capture more completely the nature of the

distributions in the regions of interest. Those features include the classical moments (mean, variance, skewness and kurtosis), the extrema, the area, the heat content as defined by Montoro and Anbar and finally the entropy of the region, which may be approximated as:

$$E = - \sum_{k=1}^L p_k \log_2(p_k) \quad (4.27)$$

where p_k is the number of pixels in each grey-level $k \in [1 \ L]$.

The outcome for a particular region of interest usually relies on the computation of the difference of statistics between this region and its contralateral counterpart. Some authors also considered the statistics of the pixel-by-pixel difference between two comparable regions [43]. However, we felt that both these approaches were omitting important parameters of the temperature distribution of ROIs, since they looked at a few statistical features derived from assumptions on the nature of this distribution. As a result, we proposed a new statistical approach using distances between histograms of comparable ROIs in order to assess their degree of similitude as it is extensively used in image registration and pattern recognition.

The following distance measures were considered: Manhattan or absolute distance, Euclidian distance, maximum distance, chi-squared distance, Jeffrey-divergence distance and Mallows distance [61][40]. The first three distances are simply the first three moments of the classical Minkowski distance based on the metric of the same name. The general formula for the Minkowski distance is:

$$D(H, G) = \left(\sum_{i=1}^L |H(i) - G(i)|^p \right)^{1/p} \quad (4.28)$$

where H and G denote the histograms, L is the number of bins, which we chose

to be 256 *i.e.* a regular-, fixed-bin histographic representation; and $p = 1$ for the Manhattan distance, $p = 2$ for the Euclidian distance and $p = \infty$ for the maximum distance.

The chi-square distance is given by:

$$D_{chisquare}(H, G) = \sum_{i=1}^L \frac{\left(H(i) - \frac{H(i)+G(i)}{2}\right)^2}{\frac{H(i)+G(i)}{2}} \quad (4.29)$$

The Jeffrey divergence is defined by:

$$D_{JD}(H, G) = \sum_{i=1}^L H(i) \log \frac{H(i)}{\frac{H(i)+G(i)}{2}} + G(i) \log \frac{G(i)}{\frac{H(i)+G(i)}{2}} \quad (4.30)$$

The Mallows distance is:

$$D_{Mallows}(H, G) = \left(\frac{1}{L} \sum_{i=1}^L |H_{(i)} - G_{(i)}|^p \right)^{1/p} \quad (4.31)$$

where $H_{(i)}$ and $G_{(i)}$ are the sorted histogram values and p was chosen to be 2.

In addition, we also calculated the Kolmogorov-Smirnov statistic, which is defined as the maximal distance between two cumulative distributions:

$$D_{Kolmogorov-Smirnov}(H, G) = \max_i |H_{cum}(i) - G_{cum}(i)| \quad (4.32)$$

where H_{cum} and G_{cum} are the cumulative histograms corresponding to H and G respectively.

The Kolmogorov-Smirnov test derived from this statistic was performed for each pair of symmetric regions of interest, since it showed encouraging results in Vavilov

et al.'s paper [80]. This test has the advantage of being non-parametric, that is it does not assume that the population of pixels within each region follows a specific distribution.

Chapter 5

Results

This chapter presents the main results of this thesis. The first section focuses on the efficiency of the techniques described in Chapter 4 for the processing of thermal images. The next section applies the computerised automated analysis framework to both our databases.

5.1 Extraction of the Regions of Interest

The analysis described in Chapter 4 was implemented in Matlab (©The MathWorks Inc.) on a PC (pentium II at 400Mhz, 128MB of memory and pentium III at 1.2GHz with 512MB of memory).

5.1.1 Performance of the denoising method

The Discrete Wavelet Squared Transform (DWST) was implemented in a relatively straightforward manner using the one-dimensional and two-dimensional wavelet transforms available in the Wavelab library from the department of Statistics of Stanford

University. The brute force algorithm requires a large amount of memory (typically 2 Gigabytes for a 128×128 image) since it stores four-dimensional arrays temporarily. Nowak and Baraniuk noted that these arrays were sparse and therefore the computational complexity is comparable to that of a two-dimensional wavelet transform, while the memory requirements are reduced. Since the manipulation of sparse multi-dimensional arrays was not supported when we implemented the algorithm, we chose to decompose each 128×128 thermal image into four 64×64 sub-images and remove the noise from each of these sub-images.

In practice, it was found that some artifacts affect the quality of the resulting image at the border of each sub-image. In order to reduce these artifacts we increased the number of sub-images to nine partially overlapping 64×64 images and we kept the areas away from the interior borders for each sub-image (see figure 5.1). This division into sub-images does not eliminate completely the border effect but reduces it to an acceptable level that does not affect the subsequent analysis. A DWST applied to the whole image would remove most of these border artifacts or limit them to background areas. Also, a translation invariant DWST may provide a good alternative although it would increase the computational complexity. In addition, we assumed that our subdivision kept the signal-dependence and Poisson nature of the noise.

A few wavelet bases were investigated on thermal images from our database with various noise levels. We then performed the Poisson Noise removal technique exposed in Chapter 4. Nowak and Baraniuk [52][53] suggested to use a simple Haar basis or a Daubechies wavelet basis for nuclear medicine images. Our tests on thermal images showed that the best results quantitatively (based on the reduction in noise variance) and visually (presence of artifacts and ringing effect for instance) were achieved with

a Battle-Lemarié spline wavelet basis of the 3rd order.

Figure 5.1: Decomposition of the original image into 9 sub-images. The plain lines delimit the sub-images considered in each case.

Furthermore, we varied the parameter α in equation 4.22 and found that $\alpha > 1$ yielded better denoising results. In particular, $4.5 < \alpha < 7.5$ consistently produced the best tradeoff between reduction of noise and conservation of the image structure.

Since the computation of mean square errors between original images and denoised images was not readily available, the performance of the denoising was assessed in terms of percentage of edges and contours remaining after denoising for comparable signal-to-noise ratio or rather comparable noise level. It was found that the resulting images from the Press-optimal wavelet-domain filter retained the contours and edges of the thermal images better than when a fourier domain Wiener filter or a wavelet-

domain filter¹ applied to the square root of the image were used.

In order to determine the percentage of edges remaining after denoising we summed the total number of pixels returned by a Canny edge detector for increasing threshold level, up to a level where no edge can be detected. We assumed that the Canny edge detector was not affected significantly by the noise and therefore we normalised the number of pixels to that of the noisy image. Table 5.1 shows the results for ten randomly picked images from our database.

Image	Press-optimal	Wiener	Threshwave
pain6120	83.7 %	78.4 %	73.1 %
pain6089	80.9 %	76.4 %	77.9 %
pain6052	84.5 %	80.0 %	67.1 %
pain6017	90.1 %	85.5 %	81.2 %
pain0085	94.4 %	79.9 %	80.6 %
pain0034	80.8 %	77.3 %	77.8 %
npain9143	86.4 %	85.4 %	81.1 %
knownpat1009	63.6 %	67.2 %	57.4 %
knownpat1091	92.0 %	85.0 %	85.4 %
npain9049	85.6 %	77.0 %	76.8 %
Mean	84.2 %	79.2 %	75.8 %
Std. Dev.	8.1 %	5.2 %	7.8 %

Table 5.1: Percentage of edges preserved after denoising for Wiener filtering, wavelet-domain filtering and PRESS-optimal filtering.

5.1.2 Background extraction efficiency

The background extraction method exposed in section 4.3.1 was applied on both denoised and original (noisy) thermal images from our database. The thresholding technique proved to be efficient enough on its own for many images. However, we also

¹Translation invariant, soft-thresholding wavelet-based denoising function from the Wavelab library

found that it could create small holes inside a region of interest, especially when the intensity level inside the region was close to that of the background, which consisted most of the time of clothing with intensities comparable to that of the regions of interest. The limitations of the thresholding technique was partially overcome by the morphological and logical processing steps mentioned in section 4.3.1.

In addition, the ratio of the number of images whose background was properly extracted, to the total number of images was slightly higher for the denoised images, as shown in table 5.2. A correct background extraction according to our criteria means that only the region targeted when the image was taken is present, for instance the upper-back, the lower-back or the legs in our study. The quality of the background extraction was assessed visually and thermal images not properly segmented were discarded manually. An automated quality assessment of the background extraction would be worth considering although the complexity of such a task was beyond the scope of this thesis. Figures 5.2, 5.3 and 5.4 show thermal images before and after preprocessing (including denoising and background extraction).

The results from table 5.2 confirms our initial assumption that an efficient denoising could improve the subsequent processing of thermal images. The overall percentage of images whose background was correctly extracted was 88% for the denoised images and 81% for the noisy images. However, it appeared that the thresholding part of our background extraction was less affected by the noise than the corrective morphological processing. Therefore, a more complex thresholding strategy may yield similar results for noisy and denoised thermal images.

Figure 5.2: Original, denoised and final thermal image of legs. Black is hot and white is cold.

(a) Original image

(b) Denoised image

(c) Denoised image without background

Figure 5.3: Original, denoised and final thermal image of upper-back. Black is hot and white is cold.

Figure 5.4: Original, denoised and final thermal image of upper-back. Black is hot and white is cold.

	With Denoising	Without Denoising
Lower Back images	9/72	22/72
Upper Back images	12/85	15/85
Legs	22/205	30/205

Table 5.2: Rate of incorrect background extraction for images of the lower-back, upper-back and legs. The first figure indicates the number of images whose background was incorrectly extracted. The second figure is the total number of images.

5.1.3 Automated selection of ROIs

The selection of regions of interest followed the discussion of section 4.3.2. At this stage, a proper removal of the background is necessary since the method proposed uses the contours of the body as well as intensity surfaces by means of profile lines (for instance to find buttock's limits). The automated selection of ROIs using a compromise between Uematsu's division and the more complete one by Goodman gave fairly good results as far as the automation was concerned. The determination of the limits for the ROIs based on the shape of the body and on its intensity distribution enabled us to place the boxes corresponding to each ROI approximately. A simple iterative procedure was performed on the boxes to make sure they do not contain any background pixels (white pixels in our images). A division of the thermal images of figures 5.2, 5.3 and 5.4 into predetermined ROIs is shown in figure 5.5 to illustrate a successful attempt. However, the difference of body shapes and the lack of symmetry of body areas in some thermal images made it difficult to adapt the ROIs to cover the best area.

Furthermore, we assumed that thermal images would be symmetrical with respect to a vertical line of symmetry. This was verified in most thermal images but some thermal images showed areas of the body bent towards one side of the border of

Figure 5.5: Predetermined division of the legs, lower-back and upper-back.

the image or another, or rotated. As a result, even if the limits for the ROIs were correctly identified, the final ROIs did not cover the wanted areas. It may therefore be necessary to consider alternative symmetry curves and define a proper reflection method to get corresponding pixels from contralateral regions.

In addition, we found that the division in rectangular boxes based on the dimension of the body may fail to include an abnormality if the latter happens to be in the middle of two boxes.

This outlines the necessity for a complementary ROI delimitation method that works well for asymmetric images and targets potential abnormalities, such as the isothermal analysis. The hottest and coldest regions of interest were obtained using both isothermal steps mentioned in section 4.3.2. They produced similar results in most cases, that is targeted ROIs over possible abnormalities in the thermal pattern distribution in the form of hot or cold spots. ROIs covering both contralateral parts of the body and ROIs along the line of symmetry were flagged for later analysis, so that the assessment does not fail to detect bilateral abnormalities. A strong gradient

of temperature between a flagged region and its surrounding indicated an abnormality according to our procedure.

We also compared the ROIs produced by the isothermal analysis of fully preprocessed images and of the noisy images with the background extracted. We found that noisy images tend to identify a greater number of smaller ROIs that are merged into bigger ROIs in the isothermal analysis of denoised images. However, smaller regions may not necessarily reflect a true elevation or decrease of temperature but instead indicate spurious, noisy pixels. That is why we chose to discard regions smaller than 20 pixels. In addition, statistical comparisons of very small samples may not be significant, which justifies further our decision.

5.1.4 Some Performance Aspects of the Thermographic Analysis

The performance of our quantitative analysis of thermal images in terms of complexity and CPU time was greatly affected by the denoising stage and by our choice of the PRESS-Optimal filter. For instance the DWST theoretically required $O(21^3 \times 128^2)$ computations per resolution level, but our implementation using smaller sub-images also increased the complexity significantly. The average CPU time to process a single image using a pentium III at 1.2GHz with 512MB of memory was about 4 minutes. In comparison, the rest of the analysis (background extraction, identification of ROIs, asymmetry analysis) required typically less than 3 seconds. Although it is difficult to assess the overall complexity of the thermographic analysis, it is certainly heavily weighted by the denoising step.

The other denoising techniques considered required less CPU time than the PRESS-

Optimal method, but they also performed worse. If we assumed that the CPU time is a decisive factor for the analysis of large database of thermal images, it would be desirable to improve the implementation of the PRESS-Optimal method or investigate other denoising methods that perform equally well.

5.2 Processing of the Databases of Thermal Images

5.2.1 Thermal Asymmetry of the Control Population

We selected images of the back and legs from our control population of normal healthy subjects and performed the preprocessing steps and the selection of regions of interest. In order to validate the normality of the population as far as pain is concerned, we first divided each image using the predetermined grid from Uematsu *et al.*'s and Goodman *et al.*'s paper and compared the statistics derived from these ROIs with the published normal values of thermal asymmetry. Our results are presented in table 5.3.

ROIs	Number of Cases	Mean Temperature Difference $\pm$ Standard Deviation
Thoracic (medial)	12	0.09 ± 0.09
Shoulder (posterior)	12	0.12 ± 0.10
Thoracic (lateral)	12	0.09 ± 0.09
Thigh (anterior)	13	0.15 ± 0.11
Thigh (posterior)	14	0.11 ± 0.09
Knee (anterior)	13	0.12 ± 0.13
Knee (posterior)	14	0.15 ± 0.12
Leg (anterior)	13	0.15 ± 0.12
Leg (posterior)	14	0.10 ± 0.06

Table 5.3: Mean Temperature Difference plus or minus standard deviation for our control population of healthy volunteers.

All the values of the mean temperature differences are well within the limits for normal values from Uematsu and Goodman. Our values are in fact significantly lower, of the order of 0.1°C lower, which may be explained partly by the relatively small number of cases in our control population. This certainly had an effect on the standard deviation of the mean temperature differences. Another reason for these low values may be the size of the regions of interest, which was smaller than that of the previous authors for practical reasons. However, we felt that following the strict protocol for medical thermography given in Appendix A ensured the accuracy of our results to the same extent as for previously mentioned authors and therefore we validated our control population.

Based on this assumption, we pursued our assessment by computing the various distances of section 4.3.3 on all our ROIs and for noisy images and denoised images (without background). Table 5.4 and 5.5 summarise the results and give the mean, standard deviation, and upper 99% confidence interval of the mean for the distances between the temperature distribution of ROIs of the back and legs. We did not differentiate between specific regions of the back or legs since we are interested in deriving one threshold for all regions, which would thus be applicable to the ROIs returned by the isothermal analysis, although the approach consisting of defining a threshold for each region is also valid. For each distance, we chose the upper 99% confidence interval as the threshold for determining whether or not a region is abnormal.

Results from noisy and denoised images did not differ significantly and confidence intervals were overlapping. This confirms also that the denoising does not affect the statistical properties of thermal images and thus does not induce a loss of critical

Distance results: noisy image							
	Mahn. dist.	Eucl. dist.	Max. dist.	Chi sq. dist.	JD dist.	Mallows dist.	KS dist.
Mean	0.492	0.083	0.032	0.110	0.084	1.092	0.171
Std. dev.	0.152	0.025	0.013	0.057	0.048	0.571	0.103
Threshold (99%CI)	0.796	0.133	0.057	0.223	0.180	2.235	0.377
Distance results: denoised image							
	Mahn. dist.	Eucl. dist.	Max. dist.	Chi sq. dist.	JD dist.	Mallows dist.	KS dist.
Mean	0.565	0.105	0.042	0.142	0.108	1.427	0.205
Std. dev.	0.180	0.039	0.020	0.070	0.060	0.798	0.111
Threshold (99%CI)	0.924	0.184	0.082	0.282	0.229	3.022	0.427

Table 5.4: Mean, standard deviation and threshold of distance measures for the back, for our control population.

Distance results: noisy image							
	Mahn. dist.	Eucl. dist.	Max. dist.	Chi sq. dist.	JD dist.	Mallows dist.	KS dist.
Mean	0.663	0.099	0.037	0.195	0.101	0.509	0.181
Std. dev.	0.150	0.022	0.013	0.075	0.030	0.247	0.091
Threshold (99%CI)	0.964	0.142	0.063	0.345	0.160	1.004	0.364
Distance results: denoised image							
	Mahn. dist.	Eucl. dist.	Max. dist.	Chi sq. dist.	JD dist.	Mallows dist.	KS dist.
Mean	0.694	0.106	0.038	0.206	0.109	0.528	0.192
Std. dev.	0.166	0.025	0.014	0.083	0.035	0.279	0.100
Threshold (99%CI)	1.027	0.155	0.066	0.373	0.178	1.086	0.392

Table 5.5: Mean, standard deviation and threshold of distance measures for the legs, for our control population.

information, while we showed it facilitated the previous analysis.

Using the threshold values from table 5.4 we assessed the efficiency of each distance measure to discriminate between normal and abnormal regions of interest, looking at the distances generated from a complete isothermal analysis² of thermal images of the back and legs, for our normal population. The distance with the least number of misclassifications may thus be seen as the more discriminative with respect to normal regions, that is the distance with the best specificity or the least number of regions identified as positive or abnormal.

Table 5.6 shows the specificity values for each distance measures. The specificity values are quite high as expected, since thresholds were applied to the same population from which they were extracted, although on different regions of interests. Table 5.6 may thus be seen as a preliminary validation results for the thresholds selected, showing their efficiency at identifying normal ROIs.

Specificity for thermograms of the back							
	Mahn. dist.	Eucl. dist.	Max. dist.	Chi sq. dist.	JD dist.	Mallows dist.	KS dist.
Specificity	0.95	0.95	0.93	0.95	0.94	0.95	0.86
Specificity for thermograms of the legs							
	Mahn. dist.	Eucl. dist.	Max. dist.	Chi sq. dist.	JD dist.	Mallows dist.	KS dist.
Specificity	0.97	0.99	0.98	0.97	0.98	0.98	0.95

Table 5.6: Specificity values of statistical distance measures considered, from a complete isothermal analysis of thermograms of the back and legs for our control population.

Finally, we noted that contrary to Vilavov *et al.* who found that the Kolmogorov-Smirnov statistics allowed to accurately classify normal regions from abnormal and

²A complete isothermal analysis means that all isothermal regions were considered. No regions were merged or discarded, except regions less than 20 pixels.

potentially pathological regions, our experiment suggested that other distance measures may be more suitable to the task. All the other distance measures have very similar specificity values.

5.2.2 Tests on Actual Cases

As mentioned in section 4.2.3, we did not have the records nor the clinical outcomes³ for the thermal images from our database of actual patients. In order to validate our approach and draw some conclusions on the performance of our novel statistical tool for the assessment of pain in thermal images, we therefore analysed first a set of 72 thermal images of the upper back with the fixed division into rectangular ROIs, after proper preprocessing. Then the common statistics were computed as well as distance between distributions of comparable ROIs. Out of 222 regions of interest identified (and their symmetric parts when available), 33 regions were classified as abnormal using the Mahnattan distance, 38 for the Euclidian distance, 27 for the Maximum distance, 36 for the Chi-square distance, 30 for the Jeffrey-Divergence distance, 39 for the Mallows distance and 37 for the Kolmogorov-Smirnov distance. The number of abnormal regions produced by the comparison of mean, variance, skewness, kurtosis, maximum and minimum was only 6. The abnormal regions were not necessarily consistent accross the distance measures. The abnormal regions produced by the Euclidian distance, the Chi-squared distance, the Kolmogorov-Smirnov distance and to a lesser extent those produced by the Mahnattan and Jeffrey-divergence distances were generally equivalent. The abnormal regions produced by the three other methods were typically relatively different.

³A proper clinical outcome would be based on the patient history and a complete clinical assessment.

It is interesting to note that the comparison of the mean, variance, skewness, kurtosis, maximum and minimum returned a very low number of abnormal regions as opposed to the distance measures. The threshold on the mean was based on the values of table 5.3. The other parameters were used to determine whether or not the comparison on the mean was meaningful.

Furthermore, we noted that the performance of the Mallows distance seemed to be dependent on the size of the sample, when the sample was less than a hundred pixels typically. This is especially problematic when used in conjunction with the isothermal analysis, which may return several small regions. The Jeffrey-Divergence suffered from a similar drawback and as a result we need to consider one of the other distances for very small samples. The Minkowski distances, the chi-square distance and the Kolmogorov-Smirnov distance performed equally well when tested on small samples returned by the isothermal analysis. The five distances identified correctly small abnormal regions for a series of 5 images with apparent abnormalities, while the Jeffrey-Divergence and Mallows distances missed 4 out of 5.

In addition, we compared the outcome from our analysis with the outcome of the assessment of 24 thermal images of the back and legs by Dr. Quartey, neurosurgeon at the Moncton Hospital and experienced thermographer. The images were visually assessed by the thermographer since no records or patient history were available. Figures 5.6, 5.7 and 5.8 show an isothermal display at 0.5°C intervals for the 24 images submitted to the thermographer. Original images are given in Appendix B. The sensitivity values⁴ and the specificity values⁵ for the 24 images are summarised in table 5.7.

⁴Number of false negatives with respect to the number of true positives

⁵Number of false positives with respect to the number of true negatives

	Mahn. dist.	Eucl. dist.	Max. dist.	Chi sq. dist.	JD dist.	Mallows dist.	KS dist.	Mean Temp. diff.
Sensitivity	0.67	0.78	0.33	0.72	0.67	0.55	0.71	0.5
Specificity	0.67	0.83	0.83	0.67	0.67	0.5	0.43	0.67

Table 5.7: Sensitivity and specificity values for thermograms of actual pain patients. Mean Temp. diff. refers to the comparison based on the mean, variance, skewness, kurtosis, maximum and minimum as outlined in a previous paragraph.

These results confirmed that the sensitivity of the Euclidian, Chi-square and Kolmogorov-Smirnov distance seemed to be significantly higher than that of other distances. Also the specificity of the Kolmogorov-Smirnov distance is the lowest one, again confirming the results from the analysis of the control population. Based on the assessment of these 24 images, the best distance appeared to be the Euclidian distance with a fairly high sensitivity and specificity. The Mahnattan distance, the Mallows distance and the method based on a comparison of basic statistics had relatively low sensitivity. This suggests they would dismiss a number of patients with actual pain as normal. Both Mahnattan distance and Mallows distance did not seem to perform as well as the results of table 5.6 would have suggested.

Finally, it is interesting to note that from our analysis it is possible to determine specific abnormal regions. In particular, the isothermal analysis allowed to localise these abnormal regions fairly well when tested on images of obvious abnormalities. This could provide a valuable visual aid for the medical doctor or specialist responsible for the assessment of the pain in a patient.

Figure 5.6: Pseudo-color isothermal display of thermograms of the upper-back. The colorbar on the right gives the range of temperature in $^{\circ}\text{C}$.

Figure 5.7: Pseudo-color isothermal display of thermograms of the lower-back. The color-bar on the right gives the range of temperature in $^{\circ}\text{C}$.

Figure 5.8: Pseudo-color isothermal display of thermograms of the legs. The colorbar on the right gives the range of temperature in $^{\circ}\text{C}$.

Chapter 6

Conclusion

6.1 Concluding Remarks and Summary of Contributions

In this thesis, the computerised assessment of pain through digital infrared thermal imaging was investigated. In particular, we looked at the overall digital processing of medical thermograms from the preprocessing requirements to the input to the decision-support system. In an attempt to increase the objectivity and to facilitate the assessment of pain by a medical specialist, we automating as much as possible the assessment of thermal images, starting from the preprocessing and the identification of the regions of interest, to finish with the statistical analysis and a set of features that can be used by a physician to make a diagnosis.

The preprocessing of thermal images had been overlooked in the literature on medical thermography, which focused a great deal on the statistical and asymmetry analysis. In order to make the identification of the regions of interest easier, we pro-

posed to apply denoising techniques to thermal images. We modeled the noise by a Poisson distribution with an additive Gaussian white noise component easily removed if present by classical denoising techniques. Then, we identified the need for a noise-removal method that takes the Poisson nature of the noise (and of the signal) into account. This was achieved through a Poisson noise removal technique in the Wavelet domain called PRESS-optimal, that was available and used for nuclear medicine images [52]. We showed that the resulting denoised image was processed more easily in the subsequent analysis, without any significant loss of statistical information.

The next problem was to remove the background in order to keep the area of interest only, thereby once again facilitating the following identification of the regions of interest for the statistical comparison. We proposed a simple yet efficient histogram thresholding technique with additional morphological and logical steps, which performed well on both our databases of thermal images.

The identification of the regions of interest consisted of an automated division into a rectangular grid following Uematsu *et al.* and Goodman *et al.*'s papers [22][74] for comparison with our control population of normal healthy subjects. This was done by means of the identification of specific reference points on the body, through an analysis of contours and profiles across the image. In addition, an isothermal analysis was performed to determine specific and localised regions, especially the hotter and colder ones that may be indicative of abnormalities.

Finally, we proposed a new statistical tool for the classification of regions of interest as normal or abnormal, based on the computation of several distances between histograms of the ROIs. The results of the quantitative assessment of thermal images from our control population and from pain patients showed that the method based on

the Euclidian distance seemed to outperform the other statistical methods considered.

Overall, we covered many of the steps of importance in the computerised assessment of thermal images and removed the user input from each processing steps considered, thus providing with a highly automated assessment of pain in thermal images.

6.2 Future Work

Several aspects of a truly automated assessment of thermograms have been overlooked and are worth considering. First of all, it would be desirable to register the thermograms prior to the processing since many of the techniques presented in this work are specific on general areas of the body such as the back , the legs etc. An automatic classification would certainly be of interest and could be done through the various image registration methods currently available.

Similarly, the background extraction step could be fully automated by integrating a computerised assessment of the quality of the segmentation as mentioned in section 5.1.2. Other more sophisticated methods to identify the ROIs, such as region growing or split-and-merge methods, may also be implemented, which may increase the efficiency of the analysis. Also, the detection of the edges and contours when localising anatomical markers on the thermal images could be performed in the wavelet domain.

The PRESS-Optimal method chosen for our analysis should also be implemented more efficiently especially from a complexity and CPU time point of view. A greater number of denoising methods could also be investigated.

In addition, the validation of the performance of our computerised assessment

still remains to be done, for instance by obtaining the actual outcome from the pain patients of our database.

Furthermore, the development of the decision-support system that will enable to accurately predict whether or not the patient indeed experiences pain, its location and possibly its cause still remains a challenge. A starting point might be to build a scoring system on significant parameters from the statistical or asymmetry analysis such as the first statistical moments or our proposed Mallows distance.

Finally, we limited our assessment to specific regions of the body but our framework could certainly be applied and our techniques extended to various other regions of the body. A new type of population such as young children or babies may also benefit from this relatively simple yet powerful medical modality and bring new challenges to the field.

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Appendix A

RESEARCH SUBJECT INFORMATION**Carleton University**

Research Project and Title: Quantitative assessment of pain through clinical digital infrared thermal imaging.

Investigators/Researchers:

- 1. Main investigator:** Christophe Herry, M.A.Sc. EE. Candidate, Department of Systems and Computer Engineering, Carleton University
- 2. Supervisor:** Dr. Monique Frize, P.Eng., O.C., Professor in the Department of Computer and Systems Engineering, Carleton University

You are being asked to participate in a research study. This consent form provides you with information about the study. The Principal Investigator (the person in charge of this research) or his/her representative will also describe this study to you and answer all of your questions. Read the information below and ask questions about anything you don't understand before deciding whether or not to take part.

Your participation is entirely voluntary and you can refuse to participate without penalty or loss of benefits to which you are otherwise entitled. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

What is the purpose of this study?

This research study is undertaken as part of a Master's thesis research. The purpose of this study is twofold:

1. To obtain the thermal distribution of a group of healthy subjects, which will enable to generate a standard thermal distribution of healthy subjects in a comparable format to that of our current database of thermograms or infrared thermal images.
2. To record the mid-level temperature and specificity level of the thermograms of healthy subjects in order to deduce empirically the mid-level temperature and specificity level of our currently available thermograms or infrared thermal images.

What will be done if I take part in this research study?

If you decide to take part in this research study, an infrared thermal image of parts of your body (back, forehead, legs, arms) will be recorded with an infrared camera. This procedure is called medical thermography. Medical thermography is a procedure that allows the investigator or doctor to have a record of the thermal distribution of your body or part of your body. The thermal distribution of a subject is closely related to underlying physiological processes and can provide valuable information about functional abnormalities or pathologies. Medical thermography can simply be viewed as an infrared picture of your body. As such, it does NOT send any radiation (such as X-Rays or radio waves) nor requires any invasive procedure prior to or following the taking of the infrared picture. Due to the extreme sensitivity of the thermoregulation process of the human body, you will be required to conform to the following rules prior to the thermographic test:

1. No talcum powder, lotions, medications or deodorants should be applied to the skin on the day of the examination.

2. Alcoholic beverages should not be consumed for 24 hours prior to the thermographic examination.
3. Hot beverages should not be consumed for 1 hour prior to the thermographic examination.
4. Procedures such as electromyography, acupuncture, nerve block, myelography, transcutaneous electric nerve stimulation, hot or cold packs use or any form of physiotherapy should be avoided for 24 hours prior to the examination.
5. Immobilisation devices (collars, braces...) should not be worn for 4 hours prior to the examination.
6. Sun exposure should be avoided for one week prior to the examination.
7. subjects should not smoke for at least two hours prior to the study.
8. subjects should not wear any any type of jewelry during the test.
9. subjects should not exercise for 4 hours prior to the examination.

The thermographic examination will take place in a room with the following characteristics:

1. No windows
 2. Uniform, constant temperature of $19^{\circ}\text{C} - 21^{\circ}\text{C}$.
 3. Constant humidity of $50 - 70\%$.
 4. Insulated walls, no shiny or smooth plastic floor
-

5. Fluorescent light.

The thermographic examination procedure is as follows:

The part of the body to be examined will be exposed to the ambient temperature ($19^{\circ}\text{C} - 21^{\circ}\text{C}$) for at least 15 minutes or cooled by a fan for 10 minutes. The subject will not touch the part of the body to be examined. After the equilibration period, one or several infrared images of the region of interest will be taken (back, legs, arms, head). The test will last 30 minutes approximately. The thermographic test will be performed by an investigator of the same sex than that of the participant when the subject is female in order to avoid any discomfort. The subjects will wear shorts during the test.

What are the possible discomforts and risks?

Infrared thermography is a non-invasive, non-radiative imaging procedure. We may find an abnormality after analysis of your thermal infrared pictures. However, our possible conclusions with respect to the normality of your thermal distribution will not constitute a medical diagnosis in any way because no physician or medical specialist will be involved in this part of the study. Since we are only interested in normal thermal distributions, should we detect any abnormality with the thermal distribution of your body, your record and all associated data collected for the purpose of this study will not be used and will be destroyed. If you have any questions regarding the thermographic test, please feel free to ask the investigator.

What are the possible benefits to me or to others?

You are not expected to receive any direct medical benefits from your participation

in the study, since you are considered healthy for the purpose of this study. However, your participation will help us develop a computer-aided analysis and classification of thermographic images in order to provide an objective tool for the diagnosis of subjects by qualified physicians. This may eventually help increase the objectivity, sensitivity and specificity of the diagnosis of pain-related pathologies.

Will it cost me anything?

No. Your participation to this research study is free and on a voluntary basis.

Will I be paid?

No. You will not receive any financial compensation.

How will my privacy and the confidentiality of my research records be protected?

Your identity in this study will be treated as confidential. The results of the study, including laboratory or any other data, may be published for scientific purposes but will not give your name or include any identifiable references to you. Although measures will be taken to ensure confidentiality, it cannot be fully guaranteed. Each participant will be assigned an identification number. Only this identification number and the information in the record will be accessible to the researchers. The record will consist of the following:

1. Identification number
2. Imaging date
3. Imaging facility name and address

4. Age
5. Sex
6. Mid-temperature level
7. Sensitivity
8. Thermographic images
9. Comments and relevant thermographic findings

The correspondence between identification numbers and names of the participants will be kept in a separate database and will only be made available to the supervisor (Prof. M. Frize). It will be destroyed when the study is completed.

How can you withdraw from this research study?

If you wish to stop your participation in this research study for any reason, you should contact Christophe Herry at (613) 520 2600 ext.5586 or Dr. Monique Frize at (613) 520 2600 ext. 8229. You are free to withdraw your consent and stop participation in this research study at any time. Throughout the study, the researchers will notify you of new information that may become available and that might change your decision to be in the study.

Your participation in this study may be ended by the main investigator without your consent at any time because:

1. You have not followed study instructions;
2. The supervisor has stopped the study; or

3. Administrative reasons.

Will you have access to your record? Will you be notified of the results of the study?

You will have access to your own record upon request. This study being part of a Master's thesis research, the results of the study will be presented in the final Master's thesis. The results might also be presented in scientific conferences or meetings.

Who would you call if you have any questions?

Should you have any questions about the study or your study participation, please contact:

Christophe Herry

Dr. Monique Frize

Phone: (613) 520 2600 ext. 5586 (613) 520 2600 ext. 8229

E-mail: cherry@sce.carleton.ca monique_frize@carleton.ca

If you have any questions about your rights as a research subject, you may contact:

Chair of the Carleton University Research Ethics Committee

Professor Klaus Pohle

Phone: 613-520-7434

Email: klaus_pohle@carleton.ca

Appendix B

Figure B.1: Original thermograms of the upper-back (submitted to the clinical thermographer).

Figure B.2: Original thermograms of the lower-back (submitted to the clinical thermographer).

Figure B.3: Original thermograms of the legs (submitted to the clinical thermographer).

Figure B.4: Some thermograms of the back from the control population.

Figure B.5: Some thermograms of the legs from the control population.