Development of computer methods in the investigations of ocular surface temperature by infrared thermography

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**DEVELOPMENT OF COMPUTER METHODS IN THE
INVESTIGATIONS OF OCULAR SURFACE
TEMPERATURE BY INFRARED THERMOGRAPHY**

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DEVELOPMENT OF COMPUTER METHODS IN THE INVESTIGATIONS OF OCULAR SURFACE TEMPERATURE BY INFRARED THERMOGRAPHY

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ABSTRACT

Ocular surface temperature (OST), which nowadays is primarily captured using infrared (IR) thermography on human subject, refers to the temperature measured at the ocular surface enclosed by palpebral fissure. Hitherto, numerous ocular physiologies and pathologies were unveiled by the investigations in ocular surface temperature despite the absence of sophisticated and consistent analytic methods in the field.

The analyzing measures developed in literature on ocular surface temperature are monotonous and inconsistent. First-order spatial statistical analysis was widely adopted in investigations, and ocular surface was fragmentally studied. Corneal center was subjectively located, and with that temperatures of a number of points or regions were picked up to perform statistical analysis. The inconsistency in anatomical localization and the monotony in analysis have admittedly constrained the capability ocular thermography could have achieved.

In this report, second order spatial statistical analysis—one of the textural analysis—was introduced to extract thermal texture and looked

into the aging effect. Ocular surface was entirely investigated using a warping technique to reveal the role of aging physiologies on the surface temperature, and estimate the tear evaporation rate based on the recorded ocular thermographic sequence. Eyelashes were removed to improve data quality, and automated ocular, corneal localization were developed in the attempt to substitute manual localization, or introduce consistency in the determination of corneal region.

Elder subjects were determined to exhibit dissimilar thermal texture with younger subjects, and their ocular surfaces were cooler as a consequence of weaker corneal sensitivity; also, the corneal tear evaporation of the elderly was observed to be higher. Tear film was found to play a major role in the temporal topographical variation, and the absence of this thin layer might result in warmer ocular surface. Automated localizing algorithms for both thermal image and thermographic sequence achieved considerable accuracy in the delineation of ocular and corneal area, and were feasible alternatives to manual localization. The application of computer methods to the study of ocular surface temperature has been illustrated in this report to have

x

substantially expanded the capability of ocular thermography in the revelation of ocular physiologies.

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NOMENCLATURE

ε	emissivity
μ_{ocular}	mean OST of a warped thermographic sequence (unit: °C)
μ_{ocular}^f	mean ocular surface temperature (OST) at the frame f (unit: °C)
$\mu_{\sigma_{ocular}}$	mean $\sigma_{ocular,f}$ over the warped thermographic sequence (unit: °C)
$\phi(x[n]; \varepsilon)$	Gaussian mixture
$\rho_{i,j,f-r}$	reductive ratio in temperature of a point in the ocular surface at frame f
$\rho_{ocular-r}$	mean OST reductive ratio
Σ	energy (from ${}_cP_d(i, j)$)
σ_S	Stefan Boltzmann constant (unit: $Wm^{-2}K^{-4}$)
$\sigma_{ocular,f}$	standard deviation of the OST at frame f (unit: °C)
$\mathbf{C}(s)$	snake initial contour
${}^v\mathbf{C}(s)$	converged snake
$C_d(i, j)$	co-occurrence matrix
${}_cC_d(i, j)$	cross co-occurrence matrix
Co	contrast (from ${}_cP_d(i, j)$)
C_p	specific heat (unit: JK^{-1})
dA	element area (unit: m^{-2})

$E(x, y, t)$	the rate of tear evaporation in energy form (unit: Wm^{-2})
$\mathbf{E}_{avg}$	average ocular tear evaporation rate (unit: Wm^{-2})
$cor\mathbf{E}_{avg}$	average corneal tear evaporation rate (unit: Wm^{-2})
$cor\mathbf{E}_{avg}$	average sclera tear evaporation rate (unit: Wm^{-2})
${}_e^rE$	relative mean tear evaporation rate of an element (unit: Wm^{-2})
F_{tt}	target tracing function
f_e	edge map
f_G	Gabor filter
H	homogeneity (from ${}_cP_d(i, j)$)
$\bar{h}$	mean heat transfer coefficient (unit: $Wm^{-2}K^{-1}$)
${}_dh_b$	difference histogram
h_{amb}	convection coefficient in ambient environment for ocular surface (unit: $Wm^{-2}K^{-1}$)
$I(x, y)$	arbitrary image
$I(i, j)$	arbitrary image in discrete form
$I(i, j, f)$	a particular frame in a thermographic sequence in which blinking frames are removed
${}^nI_\epsilon(i, j)$	differential image
${}^nI_\epsilon(i, j)$	differential image (discrete form)
I_{sc}	scaled f_e in the range of 0~1
$m_{\neq g}$	moment (shape descriptor)

m_g	moments (from ${}_cP_d(i, j)$)
m	mass (unit: kg)
${}_o^w n_f$	total number of $t_{i,j,f}$ in an ocular thermal frame
n_F	total number of frames in a thermographic sequence
${}_cP_d(i, j)$	probability matrix derived from cross co-occurrence matrix
Q_{in}	inflow heat to control volume (unit: J)
Q_{out}	outflow heat leaving the control volume (unit: J)
$\ddot{q}$	heat flux (unit: Wm^{-2})
$\bar{R}$	total mean thermal resistance (unit: KW^{-1})
r_c	corneal radius (unit: $pixel$)
S_y	symmetry (from ${}_cP_d(i, j)$)
S	total ocular surface area (unit: m^{-2})
SP	total number of snake points
$T(x, y, t)$	ocular surface temperature of point (x, y) at time t (unit: $^{\circ}C$)
$T(t)$	corneal surface temperature after a blink (unit: $^{\circ}C$)
T_{amb}	ambient temperature (unit: $^{\circ}C$)
T_b	body temperature (unit: $^{\circ}C$)
$t_{i,j,f}$	temperature of a point (i, j) on the particular frame f in a warped thermographic sequence $T(i, j, f)$ in which blinking frames are removed, and the point (i, j) falls on the ocular surface and does not form any part of eyelashes in the frame f (unit: $^{\circ}C$)

$\mathbf{v}(x, y)$	gradient vector flow field (GVF)
$\mathbf{x}(s)$	snake curve, $\mathbf{x}(s) = [x(s) \ y(s)]$

CHAPTER 1. INTRODUCTION

1.1. BACKGROUND

Temperature has been used to investigate the physiological and pathological changes in human body since 400 B.C. with a number of techniques. Galileo invented the thermoscope in 17th century, and that evolved into modern mercury-in-glass thermometer, radiometers for middle-ear temperature and disposable sterile thermocouple which is widely adopted these days. Liquid crystals such as cholesteric esters (found in 1877) which exhibit the property of changing color with temperatures, are employed to display temperature distribution at skin topographically. Though inexpensive, such detectors have relatively short life span and may alter the surface temperature due to large area of contact. Except Schlieren photography, which enables researcher to see the convection current surrounding the body (Ring 1998), most of the methods developed in the past bear limitations of either requiring contact with subject or incapable of displaying distribution of temperature.

Infrared (IR) thermography is a non-contact and non-intrusive temperature measuring technique, with an advantage of no alteration in the surface temperature and capable of displaying real-time surface

temperature distribution. It has revolutionized the field of temperature measurement in the last 50 years and is widely adopted nowadays. For example, infrared thermography was applied to measure convective heat fluxes, and for the comprehension of fluid dynamics phenomena on the flow field behaviour over complicated body shapes (Meola, et al. 2004). Also, to study the process of ice nucleation and ice propagation in flowers of fruit trees and other frost sensitive plants (Wisniewski, et al. 1997); to measure the size, depth and thermal resistance of materials and components (Meola, et al. 2004), and also for environmental monitoring such as sea, river pollution, information about indoor climate (Cehlin, et al. 2000), inspection of plants and assistance in the reduction of maintenance cost of mechanical as well as electrical equipment (Meola, et al. 2004).

As for medical field, it was first introduced by Lawson in 1956 to investigate the feasibility and the potential of using infrared thermography as a tool to study breast lesions (Lawson 1957). Since then, this non-invasive temperature measuring technique is used for a variety of purposes in both medical research and clinical applications. For example, it has been used to assist in decision making in open heart surgery due to its ability to provide real-time information (Ruddock 2003), to manage

neuropathic pain (Hooshmand, et al. 2001a, b) or to assess patient response to chiropractic care by measuring the temperature gradient in clinical setting (Stillwagon, et al. 1998). Besides, it also serves as an diagnostic tool on breast cancer (Ng, et al. 2006a, Ng 2008), rheumatism (Ring 1998), skin lesion (Kalili, et al. 1996), fever (Ng, et al. 2008a), impotence (Merla, et al. 2007, Ng, et al. 2009) and thyroid gland disease (Helmy, et al. 2008).

In ophthalmology, the advances in this technology for the past few decades are translated into the abandon of invasive temperature measuring practice, and the adoption of thermography in the measurement of ocular surface temperature. Mapstone (Mapstone 1970) and Wachtmeister (Wachtmeister 1970) pioneered this method in the measuring of ocular surface temperature, and inspired a number of researchers looking into thermal asymmetry or anomalies in thermal distribution, both on the eyes and region surrounded the eyes, in the attempt to establish diagnostic criteria based on these asymmetry and anomalies. But these efforts and results were proved to be incorrect. The eye on thermogram was not clearly discernible at that time due to poor resolution in the thermal image, and hence the proposition of diagnostic

criteria was not possible. As the infrared technology advances, more detailed thermal distribution of the anterior eye is obtained. The better technology has prompted researchers to focus their studies on the thermographic pattern of the ocular anterior surface, instead of the orbito-ocular region. Hitherto, it is widely utilized to perform investigations such as inflammation of human lacrimal drainage system (Rosenstock, et al. 1983), dry eye (Morgan, et al. 1996), carotid artery stenosis (Morgan, et al. 1999a), glaucoma (Tokuoka, et al. 1990), unilateral exophthalmos (Bourjat, et al. 1975), Tolosa-Hunt syndrome (Hannerz 1985), ophthalmic postherpetic neuralgia (Cardona, et al. 1996), also diagnosis of retinoblastoma in children (Bogdasarov, et al. 1985) and vascular neuritis (Eremenko 1990) of the optic nerve.

A typical eye thermogram of normal right eye is shown in **Figure 1.1**.

FIGURE 1.1: TYPICAL OCULAR THERMOGRAM

1.2. MOTIVATION FOR RESEARCH

Investigations on ocular surface temperature (OST) by infrared thermography are no doubt fruitful, however issues such as ocular and corneal localization, absence of robust analytic methods remained unresolved (Tan, et al. 2009a). Each pixel in an ocular thermal image (ocular thermogram) denotes a temperature value, thus the image itself portrays the topographical temperature variation in the orbito-oculo region. The nature of this imaging modality makes it deeply dissimilar with optical image captured at the respective region, primarily manifested

in two aspects. First, cornea-sclera boundary is indiscernible in the ocular thermogram; second, the edge of palpebral fissure is not apparent in some cases, and has to be observed in conjunction with eyelashes, which exhibit far lower temperature.

These dissimilarities have profound consequences. The absence of cornea-sclera boundary and the unclear palpebral fissure in ocular thermogram deter any consistent anatomical localization, and hence coherent and comprehensive analysis. However, most of the investigations carried out on ocular thermogram need consistency in anatomical localization, especially the corneal center. Hence cornucopia approaches were proposed to detour the above obstacles, although many of them were dissatisfactory.

In the beginning, subjective assessment was the primary measure to look into ocular thermogram. Researchers of 80s, 90s studied the ocular surface temperature based on temperature values of a few points. Corneal center was estimated by subjective judgment (Tan, et al. 2009a). Followed by this were investigations which examined ocular surface temperature by getting a mean temperature over a pool of temperature values located within a box or a circle; some others performed the above on several

boxes or circular regions. They too approximated corneal center by subjective judgment. And either by points, boxes or circles, these measures and their ensued statistical investigations were in fact first-order spatial statistical analysis (Tan, et al. 2009a).

The aforesaid approaches have modestly provided useful information on ocular physiology and pathology, however they did not suffice for advanced analysis. Subjective assessment does not provide quantitative data that allows further processing, and the conclusion reached might vary among examiners. Investigations based on temperature values of a few points have given quantitative data about the ocular surface temperature, but they are sensitive to local thermal fluctuation. The mean temperature over some enclosed regions were the most evaluated first-order spatial statistics to get a “middle” or “expected” temperature on those sites, nevertheless they were insufficient, incomprehensive and unable to provide details on the physiology at ocular surface, and serve for diagnosis usage (Tan, et al. 2009a). Also, both corneal surface temperature and ocular surface temperature are vaguely defined in literature.

Hence a consistent, better defined measure in both ocular and corneal localizations would serve a great deal to facilitate investigation on ocular surface temperature. This can be achieved in some manual approaches and also by some automated methods. And some better analytic methods are needed to unveil relationships among surface temperature and other ocular physiologies. Computer methods in image analysis such as textural method could be introduced to extract subtle details, instead of utilizing only first-order textural analysis. Besides, the surface temperature should also be looked into as a whole instead on some of its fragments: by looking at the surface temperature in its entirety, we can in some extent detour the obstacle posed by the indiscernible cornea-sclera boundary.

This study intends to look into the abovementioned problems, and develops respective algorithms to resolve them. Several measures would be proposed to locate ocular surface and analyze the surface temperature. Particularly, the developed methods would be used to investigate the aging effect on ocular surface temperature.

1.3. OBJECTIVES AND SCOPES

The current research aims to develop algorithms that are capable of providing consistent and comprehensive analysis to unveil unknown ocular physiologies on normal subjects. Computer methods are employed to achieve the above objective in this study, and the developed algorithms would consist not only of methods analyzing ocular thermal images, but also ocular thermographic sequences. These algorithms aim to achieve the scopes of:

1. To reduce the uncertainties involved in the selection of region of interest (the region contained in palpebral fissure)
2. To provide in-depth analysis other than just first-order statistical textural analysis.
3. To remove eyelashes that fall on ocular surface.
4. To enable automated ocular and corneal localizations and the subsequent analysis.
5. To investigate the aging effect on ocular surface temperature.
6. To determine the rate of tear evaporation based on the ocular thermographic sequence

1.4. ORGANIZATION OF THESIS

The organization of this thesis is laid out as follow. Chapter 2 presents the literature review on investigations performed on ocular surface temperature, looks into the nature of the ocular surface temperature, the methodologies devised and the primary findings in previous investigations. Textural analysis, algorithm on removal of eyelashes are developed in Chapter 3, and automated ocular, corneal localization, which are achieved by snake algorithm, is detailed in Chapter 4. Both chapters work on ocular thermal images. For chapter 5, it sets to look into the determination of tear evaporation rate based on the thermographic sequences and the first law of thermodynamics. In that chapter, the ocular surface is wholly captured and transformed into a standardized shape to facilitate analysis, by using a technique termed 'image metamorphosis'. Chapter 6 uses the same technique to localize ocular surface in thermographic sequences, however it looks into the topographical variation in the surface temperature among the young, the elder and the contact lens wearer. Automated ocular localization in thermographic sequences, which again uses the snake algorithm but with the other edge map and target tracing function due to different data

modality, is elaborated in Chapter 7. Lastly the report concludes in Chapter 8; the possible future work is also accounted at there.

CHAPTER 2. LITERATURE REVIEW

Generally, infrared thermography refers to the recording of temperature of some areas by capturing infrared radiated from some surfaces, forming an image called thermogram. This two dimensional thermogram presents the distribution of temperature distinctly, unlike infrared thermometry, which gives only a single temperature value. Infrared thermography also differs with infrared photography, where the latter records infrared radiation reflected back from objects in the presence of some external infrared energy sources. The principle behind infrared ocular thermography involves the physics of radiation and the measurement of OST. These concepts, together with the applications of thermography in ophthalmology and their measures in the acquisition of OST are discussed in the following sections.

2.1. THE PRINCIPLES OF INFRARED THERMOGRAPHY ON HUMAN EYE

2.1.1. THE PHYSICS OF INFRARED RADIATION

Any object, when its temperature is above absolute zero, emits electromagnetic radiation, called thermal radiation. In physics, the amount

of electromagnetic waves radiated by an object is quantified by the term spectral radiance. It describes the amount of electromagnetic waves emitted from a particular surface on the basis of per unit solid angle. The idea of black body radiation forms the basis of the physics of thermal radiation, though behaviours of many objects deviate from the ideal black body extensively.

When a black body is in equilibrium at temperature T in environment, it absorbs and emits a specific continuous spectrum of wavelengths and intensities. The profile of the emitted spectrum by a black body depends only on the temperature at equilibrium in an environment and therefore the temperature of a black body is directly related to the wavelengths of the light that it emits. According to Planck's law, the spectral radiance, J (in watts per steradian per square metre) of electromagnetic radiation at all wavelengths λ , at temperature T from a black body as a function of wavelength is given by

$$J(\lambda, T) = \frac{2\pi hc^2}{\lambda^5} \frac{1}{e^{\frac{hc}{\lambda kT}} - 1} \text{Wcm}^{-2}\mu\text{m}$$

(1)

where k is the Boltzmann constant (1.381×10^{-23} J/K), h is the Planck constant (6.626×10^{-34} Js), c is the speed of light (2.998×10^8 m/s) and T is the absolute temperature (K). Differentiating Planck's law with respect to λ to look for the maximum radiation intensity, the Wien's displacement law is obtained

$$\lambda_{\max} = 2898 \mu\text{mK} / T \quad (2)$$

which mathematically illustrates a common observation: as the temperature of an object rises, the color of light emitted varies from infrared to red to orange. Given human body temperature of 37°C , the emitted light peaks at $9.35 \mu\text{m}$ which falls into the infrared region.

Consider a small flat body radiating outward into a half-sphere under an temperature-equilibrium environment, one can deduce Stefan-Boltzmann's law from (1) and get

$$j^{(r)} = \sigma T^4 \quad (3)$$

which states that for a black body the total energy radiated per unit surface area in a unit time is directly proportional to the fourth power of the absolute temperature of the black body.

In reality, real objects are rarely a black body, though in certain spectral intervals they may behave closed to the ideal black body. In most cases real object emits only part of the radiation a black body emits at the same temperature and same wavelength. Denote the amount of radiation emitted by real object as E_λ and $E_{b\lambda}$ for the amount of radiation emitted by black body, the emissivity is defined as

$$\varepsilon = \frac{E_\lambda}{E_{b\lambda}} \quad (4)$$

And expression (3) can be rewritten for grey body with the knowledge of emissivity as

$$j^{(r)} = \varepsilon \sigma T^4 \quad (5)$$

2.1.2. THE INFRARED THERMOGRAPHIC SYSTEM

Planck's law, Wien's displacement law, Stefan-Boltzmann's law and the concept of emissivity is the physics behind the working principle of an infrared thermography system. An infrared thermography system in general consists of a camera (as shown in [Figure 2.1](#)), with some detachable optics, and a personal computer that controls the camera. In the camera there is an infrared detector, which absorbs the infrared shining by the lenses and converts the infrared signal into electrical voltage or current for processing. The way a desired field of view is projected and recorded on IR detector within the camera, is determined by the imaging system.

Generally, there are two main sorts of imaging system available to the infrared thermography: scanner (scanning array) and focal plane array. The focal plane array is superior to scanning array in almost every aspect in terms of performance. Scanning array consists of linear arrays, rastered across the desired field of view using 1 detector, 2 lenses, 1 horizontal and 1 vertical deflection mirrors, to construct a 2-D image as illustrated in [Figure 2.2\(a\)](#). Its working principle is analogous to a person looking at a view through narrow slit, rastering both his/her head and slit

in the direction perpendicular to the slit to build up 2-D image. Focal plane array images a desired field of view without scanning, and it works similar to a typical camera, in which the film captures the 2-D image directly projected by the lens at image plane (Figure 2.2(b)).

FIGURE 2.1: A TYPICAL INFRARED CAMERA

(VarioTHERM® head II,

http://www.infratec.de/fileadmin/downloads/pdf/Flyer_Variotherm_head_en_mail.pdf)

Detectors of infrared thermography consist of an array of elements reactive to infrared. In the broader field of infrared thermology there are two types of IR detectors: thermal and photonic. Thermal detectors such as microbolometer, pyroelectric detectors and Golay cells detect heat

generated by incidence of IR radiation and are not wavelength dependent. They are commonly used in bolometers such as thermocouple and thermopile, and show slow response time and low detection capability without the need for cooling. The photonic detectors like quantum well infrared photodetector (QWIP) and mercury-cadmium-telluride, are wavelength dependent, and can detect the temperature of a remote object's surface by measuring the amount of IR incidence of a specific range. Unlike thermal detectors, they offer quicker response time and better detection performance, and therefore are favourite as IR detector for focal plane array imaging system.

FIGURE 2.2: (A) SCANNING ARRAY: 1. DETECTOR 2. LENS 3. HORIZONTAL DEFLECTION MIRROR 4. VERTICAL DEFLECTION MIRROR 5. LENS 6. OBJECT 7. MEASURING SPOT (B) FOCAL PLANE ARRAY: 1. OBJECT WITH MEASURING SPOTS 2. LENS 3. DETECTORS.

Most of the photonic detectors operate only at cryogenic temperature, otherwise the detected signal would be swamped by thermal noise. The IR thermography utilizing imaging system of focal plane array can be of cooled or uncooled type. Most of these detectors are cooled evaporatively, either by liquid helium, liquid nitrogen, thermal-electric cooler or Stirling cycle refrigerator. Though not common, in the latest

technologies microbolometer is used in focal plane array, which have lower cost and require no cooling.

IR spectrum can be subdivided into a few bands (Miller 1994, Miller, et al. 2004): Near IR (NIR), from $0.7 - 1\mu\text{m}$, Short-wave IR (SWIR), from $1 - 3\mu\text{m}$, Mid-wave IR (MWIR), from $3 - 5\mu\text{m}$, Long-wave IR (LWIR), from $7 - 14\mu\text{m}$, Very long-wave IR (VLWIR), from $12 - 30\mu\text{m}$. NIR and SWIR are used in fiber optics telecommunications and long-distance communications respectively; guided missiles technology making use of infrared heat is used in MWIR. Presently in the medical field infrared thermography captures thermogram at wavelength range of $8 - 12\mu\text{m}$, which falls in the region of long-wave IR (LWIR). The LWIR is the region of “thermal imaging” which does not require external thermal source to obtain a passive isotherm of the outside world. The infrared thermography used for measurement of OST obtains thermogram in LWIR.

2.1.3. THE MEASURED OCULAR SURFACE TEMPERATURE

In ophthalmology, the temperature of ocular surface is of great interest. However, as thermal imager determines a surface temperature according to the amount of infrared radiation detected, the opacity and the transmissive properties of various ocular tissues are of significant

importance. Since, it is possible for a thermal imager to receive radiation of an ocular tissue posterior to ocular surface if tissues around anterior chamber are transparent to infrared.

The absorption bands of ocular tissues is reported almost equal to that of water, opaque to far infrared (Hartridge, et al. 1915, Mapstone 1968c). The emissivity of water is 1, and it behaves similar to black body radiator on IR spectral above $3\mu\text{m}$. For ocular tissues, the radiated spectrum falls in between $1 - 30\mu\text{m}$ with a maximum emission at $9\mu\text{m}$ under normal circumstances (32°C). Hence, the spectrum radiated by any ocular tissues is to be absorbed entirely by ocular tissues anterior to it.

The transmission in between cornea and tear film takes place in a different way. On spectrum above $3\mu\text{m}$, water generally behaves similar to black body. But for thin water layer, the thickness of the layer determines the degree of absorption. For layer thickness of around $10\mu\text{m}$, the transmittance on spectrum $8\mu\text{m}$ to $13\mu\text{m}$ is about 30%; that value approximates to zero when the layer thickness is $40\mu\text{m}$ or above (Plyler, et al. 1954, Hamano, et al. 1969). And tear film thickness is determined to be around $40\mu\text{m}$ (Prydal, et al. 1992). The spectrum emitted by cornea is fully absorbed by tear film. Therefore, the measured OST by IR thermography

was the temperature of tear film (Hamano, et al. 1969, Fatt, et al. 1980, Morgan, et al. 1993).

A recent study (Purslow, et al. 2007) has verified the above idea. The OST is determined to be mainly related to tear film stability, instead of other parameters such as corneal curvature, central corneal thickness or depth of anterior chamber (Purslow, et al. 2007).

In clinical thermography, when a curved anatomical surface is viewed at angle beyond 90° , the measured temperature will be 4°C less or more, since emissivity varies with angle of viewing (Watmough, et al. 1970). The amount of thermal radiation of other sources reflected from an anatomical surface also increases when the angle of viewing is greater, resulting greater error in the measured temperature. But the resultant error is negligible when angle of view falls within $\pi/4$ (Watmough, et al. 1970). In practice, the error incurred due to the above factors is negligible for the recording of OST, since it is assumed that, the angle of viewing on an eye with respect to thermography is within $\pi/4$. As a result, the recorded OST can be seen as temperature of tear film.

2.2. METHODOLOGIES IN THE INVESTIGATIONS OF OST

Ocular thermogram is an image either stored in the form of gray-scale or RGB colour palette. It consists not only of temperature values but also their distribution over the ocular surface. As RGB thermogram provides better visual representation of temperatures, it is often adopted for manual inspection; thermogram of grayscale on the other hand is mainly for quantitative analysis.

The boundary in between cornea and sclera is not discernible in thermogram. Often in literature OST refers to the temperature of a specific location or some defined regions on the ocular surface (Mapstone 1970, Wachtmeister 1970, Bourjat, et al. 1975, Fielder, et al. 1981, Rosenstock, et al. 1983, Murphy, et al. 1999). So far there are two types of approach proposed in the investigations of OST: manual measure, and semi-auto methods. And these approaches are discussed below and summarized in **TABLE 2.1.**

2.2.1. MANUAL MEASUREMENT

Efron et al. measured surface temperature at every 0.5mm increments on either side of corneal surface horizontally (Efron, et al. 1989) , as illustrated in Figure 2.3(a). There are 11 points running across

the anterior surface, and the sixth point coincides with the estimated geometric centre of cornea. Horizontal temperature profile of OST was determined and expressed in terms of regression polynomial

$$\Delta T = ax^2 + bx + c$$

(6)

where $a = 0.01\text{ }^{\circ}\text{C}/\text{mm}^2$, $b = 0.003\text{ }^{\circ}\text{C}/\text{mm}$, $c = 0.01^{\circ}\text{C}$. x is the distance from the geometric centre of cornea in mm .

(A)

(B)

FIGURE 2.3: METHODOLOGY IN THE INVESTIGATION OF OST BY (A) EFRON *ET AL.* (EFRON, ET AL. 1989). (B) TAN *ET AL.* (TAN, ET AL. 2009C)

TABLE 2.1: SUMMARY OF METHODS USED TO ESTIMATE OST.

Studies	Types of OST acquisition	Methods	Main findings
Efron et al. (Efron, et al. 1989)	manual	11 points running across the anterior surface	average difference in temperature between the geometric center of cornea (GCC) and the limbus is 0.45°C
Morgan et al. (Morgan, et al. 1993, Morgan, et al. 1995, Morgan, et al. 1999a)	manual	5 10x10 boxes placed in 5 different anatomical locations along horizontal meridian running across the estimated centre of cornea	<p>In (Morgan, et al. 1999a), a significant negative correlation was found between OST and the degree of carotid artery stenosis (CAS) (Morgan, et al. 1999a)</p> <p>In (Morgan, et al. 1993), 95% normal subjects were found to have interocular temperature differences between -0.57 and 0.62°C (Morgan, et al. 1993)</p> <p>In (Morgan, et al. 1995), dry eye patients were found to have greater mean OST than normal subjects, and radial temperature difference (RTD) was also found to be greater in dry eye group (Morgan, et al. 1995)</p>
Galassi et al. (Galassi, et al. 2007, Galassi, et al. 2008)	manual	5 points placed on centre of cornea, internal and external canthus, half-way from the internal canthus and nasal limbus, half-way from the temporal limbus and external canthus	<p>For all 5 points temperature of patients of primary open-angle glaucoma (POAG) are lower than temperature of healthy control group (Galassi, et al. 2007)</p> <p>A negative correlation between postoperative changes in ophthalmic artery resistivity index and corneal surface temperature was observed 3 months after deep sclerectomy and trabeculectomy surgeries.</p>
Sodi et al. (Sodi, et al. 2007)	manual	5 points equally placed along a horizontal line running through centre of cornea, connecting medial and lateral canthi	In central retinal vein occlusion (CRVO) eyes and in fellow, non-affected eyes, OST values were lower than in controls (Sodi, et al. 2007)

Murphy et al.(Murphy, et al. 1999), Betney et al.(Betney, et al. 1997)	manual	a squared 10x10 pixels box placed at the centre of cornea	<p>In (Murphy, et al. 1999), The principal mode of corneal nerve stimulation, by the non contact corneal aesthesiometer (NCCA) air pulse, was the rate of temperature change of the corneal surface (Murphy, et al. 1999)</p> <p>In (Betney, et al. 1997), no correlation was demonstrated between the surgical parameters and either absolute temperature of relative temperature changes (Betney, et al. 1997)</p>
Mori et al.(Mori, et al. 1997)	manual	a squared 20x20 pixels box placed at the centre of cornea	the rate of decline in corneal temperature for normal blinking in patients with dry eye was significantly less than that in normal subjects (Mori, et al. 1997)
Chiang et al. (Chiang, et al. 2006)	manual	an encircled region of 4.4mm diameter (22 pixels)	diagnostic of dry eye using infrared thermal imager system has reached a sensitivity of 79.3%, a specificity of 75 (Chiang, et al. 2006)
Ng et al.(Ng, et al. 2008b)	manual	a small circle placed at the centre of cornea	OST was found to decrease with age at a rate of 0.0383°C per year (Ng, et al. 2008b)
Cardona et al. (Cardona, et al. 1996), Purslow and Wolffsohn (Purslow, et al. 2007), Craig et al.(Craig, et al. 2000)	manual	a circular region centred at the corneal centre	<p>In (Cardona, et al. 1996), patients with Herpes Zoster Ophthalmicus (HZO) in acute stage were found to show high inter-ocular temperature differences, with the affected side being warmer than the other side (Cardona, et al. 1996)</p> <p>In (Purslow, et al. 2007), strong positive correlations were found in between initial OST and both body (forehead) temperature and tear film stability (Purslow, et al. 2007)</p> <p>In (Craig, et al. 2000), dry eye patients were found to have lower central cornea</p>

			temperature and higher mean osmolality (Craig, et al. 2000)
Purslow et al. (Purslow, et al. 2005a)	manual	23 points placed across the anterior eye	OST is greater with hydrogel and greater still with silicone hydrogel contact lenses in situ, regardless of modality of wear (Purslow, et al. 2005a)
Tan et al. (Tan, et al. 2009c)	manual	20 points placed across the anterior eye, lined up in the shape of “+”	Vertical OST profile was noted to be a 'spoon-shaped'; for Chinese the average difference in temperature between the GCC and the limbus is 0.23°C ~0.43°C (Tan, et al. 2009c)
Chang et al. (Chang, et al. 2008)	manual	acquire local temperatures of lateral orbit, upper eyelid, caruncle, medial conjunctiva, lateral conjunctiva, lower eyelid and cornea	Temperature difference between lateral orbit and 3 other target areas (caruncle, medial conjunctiva, lateral conjunctiva and lower eyelid) of Graves' ophthalmopathy (GO) patients were found significantly higher than those of normal subjects (Chang, et al. 2008)
Acharya et al. (Acharya, et al. 2008)	Semi-auto	image was manually cropped to consist only of eye, the cornea was then detected by algorithm developed	average OST and temperature deviation across the cornea decreases with age (Acharya, et al. 2008)

A similar measurement was developed recently, (Tan, et al. 2009c) in which they determined not only the horizontal temperature profile but also the vertical profile. The approach recorded temperatures of 20 points across the anterior eye, and they are (estimated) geometric centre of cornea, three points inferiorly and four points superiorly at 2mm separation, six points nasally and temporally at 2mm separation,

respectively (Tan, et al. 2009c) (Figure 2.3(b)). Apparently, these points form a look like crosshair, for the purpose of producing horizontal and vertical temperature profiles (Tan, et al. 2009c).

On the other hand, Purslow et al. have devised a method which also seems like a crosshair, but more as an extension of the shape (Purslow, et al. 2005a). As illustrated in Figure 2.4(a), they recorded 23 temperature data points over the anterior ocular surface, and grouped into 5 regions (central, superior, inferior, nasal and temporal) for subsequent analysis (Purslow, et al. 2005a) to investigate the effect of contact lens wear on dynamic surface temperature.

(A)

(B)

FIGURE 2.4: METHODOLOGY IN THE INVESTIGATION OF OST BY (A) PURSLOW *ET AL.* (PURSLOW, ET AL. 2005A). (B) GALASSI *ET AL.* (GALASSI, ET AL. 2007, GALASSI, ET AL. 2008).

Besides, there were some other approaches looking into temperature of fewer sites. Galassi et al. (Galassi, et al. 2007, Galassi, et al. 2008) and Sodi et al. (Sodi, et al. 2007) measured only temperature of 5 anatomical locations along the horizontal meridian, although the measuring scheme of each method was slightly dissimilar with one another. For Galassi et al., they measured the centre of cornea, internal and external canthus, half-way from the internal canthus and nasal limbus, half-way from the temporal limbus and external canthus (**Figure 2.4(b)**) (Galassi, et al. 2007, Galassi, et al. 2008). For the other (Sodi, et al. 2007), they recorded temperatures on 5 equally spaced sites along a horizontal line running through the centre of cornea, connecting medial and lateral canthi.

Also, instead of using points as the above, research groups such as Morgan et al. (Morgan, et al. 1993, Morgan, et al. 1995, Morgan, et al. 1999a) adopted small squared boxes to measure OST. Five 10x10 pixels boxes were placed at separate anatomical locations along the horizontal meridian running across the estimated centre of cornea (as shown in **Figure 2.5**): one at the estimated centre of cornea, two at the limbal position, and another two at the nasal and temporal conjunctiva (2mm from the limbus). For some other investigations, either a square of 10x10

pixels (Betney, et al. 1997, Murphy, et al. 1999), a 20x20 pixels box (Mori, et al. 1997) with an actual area of 3.3mm^2 , an area of 4mm^2 (Morgan, et al. 1996), an encircled region with a diameter of 4.4mm (Chiang, et al. 2006), or a small circle (Ng, et al. 2008b) were placed at the centre of cornea to investigate OST. Chang et al. (Chang, et al. 2008) proposed otherwise: it looked into local temperatures within circular regions of lateral orbit (reference region), upper eyelid, caruncle, medial conjunctiva, lateral conjunctiva, lower eyelid and cornea.

FIGURE 2.5: METHODOLOGY BY MORGAN *ET AL.* (MORGAN, ET AL. 1993, MORGAN, ET AL. 1995, MORGAN, ET AL. 1999A).

2.2.2 SEMI-AUTOMATED MEASUREMENT

Acharya et al. developed a semi-auto method to investigate OST on thermogram using a standard procedure (Acharya, et al. 2008). In their algorithm, the user at first manually crops a rectangle which contains the

eye, as illustrated in **Figure 2.6**, and cornea is located by the algorithm. Corneal radius is pre-defined to be one-fourth of the palpebral fissure's width, and horizontal temperature profile at the middle of cornea is produced by the algorithm (illustrated in **Figure 2.7**). Besides, they proposed a feature termed temperature deviation along cornea (TDC), which wrote:

(7)

FIGURE 2.6: METHODOLOGY BY ACHARYA *ET AL.* IN THE ACQUISITION OF OST
(ACHARYA, ET AL. 2008).

FIGURE 2.7: HORIZONTAL TEMPERATURE PROFILE ACROSS CORNEA.

2.3. APPLICATIONS OF INFRARED THERMOGRAPHY ON OCULAR STUDIES

OST is volatile and easily affected by factors other than changes in ocular physiology and pathology. A rise in 1°C room temperature is possibly leading to an increase of 0.15°C to 0.2°C in OST (Mapstone 1968b, Morgan 1994). An increase in air flow decreases OST (Freeman, et al. 1973). Therefore, during data acquisition uniform temperature, air flow and humidity are maintained in most studies to minimize discrepancies in the final outcome.

Generally, investigations in thermal imaging by infrared on OST can be classified into three categories: studies of ocular physiologies, of ocular diseases and surgery and of non-ocular diseases. Previous research indicated that, the presence of ocular diseases may significantly alter surface temperature. It was studied by many investigators, that a large interocular difference in OST possibly indicates the presence of ocular diseases (Morgan, et al. 1993).

2.3.1. ON OCULAR PHYSIOLOGIES

Thermal imager was introduced to the field of ophthalmology by Mapstone, who first utilized Bofor infrared camera system to obtain ocular thermogram and delineated thermographic patterns of normal, ischaemic and hyperaemic eyes (Mapstone 1970). Wachtmeister conducted a similar study which investigated both normal and diseased eyes (Wachtmeister 1970). The affected eye was said to be warmer than normal eye for both anterior and posterior diseases.

After that, there were a number of researchers looking into the use of infrared thermal imager as a diagnostic tool to detect ocular diseases based on thermal asymmetry (Alio, et al. 1982b). They have investigated orbito-ocular region and concluded that, ocular diseases were present if

interocular difference in temperature was at least 0.5°C . However, this was illustrated to be incorrect (Alio, et al. 1982b). An investigation which involved 96 normal subjects showed that only 50% normal subjects exhibited asymmetry at orbito-ocular region (Alio, et al. 1982b). Hence symmetry itself is insufficient to discriminate diseased eye from normal one.

The introduction of wide-field color-coded thermal imager to the field in late 80s has enabled research on OST with greater ease. Efron et al. employed the imaging device to observe variation in temperature over ocular surface and the temporal stability of central cornea temperature (Efron, et al. 1989). Temperature apex was determined to be slightly inferior to the geometric center of cornea, surrounded by ellipsoidal isotherms (Efron, et al. 1989). Limbus was said to be 0.45°C warmer than that of the geometric center of cornea (Efron, et al. 1989).

On the other hand, the limbus was found to be $0.23^{\circ}\text{C}\sim 0.43^{\circ}\text{C}$ warmer than that of the geometric center of cornea in one recent work which recruited only Chinese origin subjects. (Tan, et al. 2009c). They found that, tear volume and tear stability was lower in Chinese eyes compared to the Caucasian eyes (Patel, et al. 1991, Cho, et al. 1992, Cho, et

al. 1993a, Cho, et al. 1993b) and also a lower temperature at limbus in brown eyes compared to blue eyes (Tan, et al. 2009c).

Other than the above, there were also investigations by infrared thermal imager on human lacrimal drainage system and the effect of non-contact corneal aesthesiometer (NCCA) air stimulus (Murphy, et al. 1999). As a common practice, clinicians and workers examine the anatomy and patency of human lacrimal drainage system using radionucleotide lacrimal scanning and dacryocystography. However, these techniques expose subjects to radiations. Raflo et al. proposed to use thermal imager in conjunction with lacrimal irrigation to visualize tear ducts in control and patients with obstructive epiphora (Raflo, et al. 1982).

Traditionally, corneal nerve function was assessed by nylon thread of fine wire, and during assessment this nylon thread would cause trauma to cornea. Non-contact corneal aesthesiometer was devised to avoid this problem, and stimulate corneal nerves with controlled air pulse.

Murphy et al. have discovered the principal mode of stimulation on cornea by non-contact corneal aesthesiometer is the rate of change in corneal surface temperature (Murphy, et al. 1999). In their research, corneal surface temperature was measured by dynamic IR imaging after

exposure to air-pulse stimulus, in a sequence of 32 images with an interval of 0.25s in between each image (Murphy, et al. 1999).

The examinations on relationships between OST and physical parameters of anterior eye such as corneal thickness, corneal topography, bulbar hyperaemia, and tear film stability were carried out using dynamic infrared thermography (Purslow, et al. 2007). The ocular surface temperature at the time immediately after a blink was determined to be correlated to body temperature and tear film stability (Purslow, et al. 2007).

2.3.2. ON OCULAR DISEASES AND SURGERY

Exophthalmos is a medical condition often observed in severe thyroid eye disease (Graves' ophthalmopathy). It is an auto-immune inflammatory disorder that affects the ocular orbit in patients with or without thyroid disorder.

In an early investigation, the assessments on left endocrinal exophthalmos, metastasis of left orbit were carried out by infrared thermal imager (Bourjat, et al. 1975). But statistical analysis was not performed as the number of subjects in each case was too small (Bourjat,

et al. 1975). In a recent study, the inflammatory state in patients with Graves' ophthalmopathy and the follow-up effect of methylprednisolone pulse therapy were examined by infrared thermal imager by (Chang, et al. 2008). Temperature differences in between lateral orbit and other target areas (caruncle, medial conjunctiva, lateral conjunctiva and lower eyelid) were determined to be higher in Graves' ophthalmopathy (Chang, et al. 2008). The difference in the sum of temperatures before and after treatment was positively correlated to the change in clinical activity score (Chang, et al. 2008).

Ocular surface of dry eye patients was determined to be warmer (Morgan, et al. 1995). Although it cools and evaporates faster (Rolando, et al. 1983a, Mathers, et al. 1993b), the conjunctival hyperaemia associated with it outweighs the cooling effect, leading an increase in surface temperature (Morgan, et al. 1995). But the above findings disagreed with that of Craig et al (Craig, et al. 2000), which showed cooler cornea (at the corneal center) in dry eyes; furthermore, temperature variation factor and mean osmolality were observed higher in dry eyes, and temperature variation factor was inversely correlated to central corneal temperature.

Ocular surface temperature decreases exponentially immediately after the eye opens. Such decrease asymptotically approaches a constant value after some time (Mori, et al. 1997), and can be modeled by the following formula:

$$T(t) = (T_o - T_\infty)e^{-kt} + T_\infty \quad (8)$$

where T is the corneal surface temperature after the eye opens for a period of t ; T_o is the temperature immediately after the eye opens; k is the temperature coefficient and T_∞ is the corneal surface temperature at equilibrium.

The mean k value in the above expression for both normal subjects and dry eye patients was determined in one investigation. The OST was measured using a box of 20x20 pixels, or $3.3mm^2$, placed at the centre of cornea for a period of 30seconds (Mori, et al. 1997). For normal blinking, the mean k value in dry eye patients (5.6 ± 2.9 per second) was significantly less than that of normal control subjects (9.3 ± 5.0 per second) (Mori, et al. 1997). The k value was deemed to reflect tear film stability (Hamano, et al. 1969).

In a later research, the above principle was adopted to diagnose dry eye. OST was measured by an encircled region having diameter of 4.4mm (22 pixels) positioned at the center of eye (Chiang, et al. 2006). The study illustrated a sensitivity of 79%, specificity of 75% with 0.841 area under ROC (receiver operating characteristics) curve (Chiang, et al. 2006). Also on dry eye, IR thermography was used in conjunction with acupuncture to determine the treatment effect on this ocular disease (Nepp, et al. 2002). The middle of the cornea was reported to be cooler after the treatment (Nepp, et al. 2002).

OST is determined to be correlated with ocular blood flow. In monkeys, intraocular pressure (IOP) was observed inversely related to ocular perfusion pressure and ocular temperature (Auker, et al. 1982); for human, corneal temperature was positively correlated to the ipsilateral values of end diastolic velocity (in left and right eyes respectively) and the resistivity index (of left and right eyes respectively). The interocular difference was indicated to be positively correlated with the difference in end diastolic velocity, and negatively correlated with resistivity index (Gugleta, et al. 1999). These findings however, were obtained with IR thermometer instead of IR thermal imager (Gugleta, et al. 1999).

Recently, Galassi et al. evaluated the OST of both the patients with primary open-angle glaucoma (POAG) and normal group through thermal imaging [46]. The correlations between OST, IOP and retrobulbar haemodynamics were investigated in conjunction with the use of Colour Doppler Imaging (CDI). Temperatures of 5 anatomical points (internal and external canthus, half-way from the internal canthus and nasal limbus, centre of the cornea, half-way from the temporal limbus and external canthus) of primary open-angle glaucoma patients were said to be lower than that of healthy control group, and these temperatures were significantly correlated to resistivity index (Galassi, et al. 2007). The influence of retrobulbar haemodynamics on OST was highlighted in their results (Galassi, et al. 2007). On the other hand, in another study patients with central retinal vein occlusion (CRVO) was found to show warmer ocular surface compared to normal subjects, and OST in ischemic CRVO eyes was lower compared to nonischemic ones (Sodi, et al. 2007).

Besides the correlation between ocular blood flow and OST, there was also investigation on the effects of two glaucoma surgeries (deep sclerectomy and trabeculectomy) on bulbar hemodynamics and corneal surface temperature using IR thermography (Galassi, et al. 2008). Corneal

surface temperature was observed to increase in both type of surgeries three month after operations, and postoperative changes in ophthalmic artery resistivity index were negatively correlated to corneal surface temperature and was observed for both types of surgeries (Galassi, et al. 2008).

Simiarly, in cataract various cataract surgery procedures based on the phacoemulsification system were compared and analyzed. In these studies, the amount of heat generated during surgery (Olson, et al. 2005), the thermal impact on eye (Corvi, et al. 2006), and the intraoperative thermal levels at wound site (Rose, et al. 2006) produced by various phacoemulsification system were assessed by IR thermal imager. Thermal imaging by IR in these studies was effective for the analysis on the outcome of cataract surgery with phacoemulsification.

2.3.3. ON NON-OCULAR DISEASES

In one study, correlation between OST and the degree of carotid artery stenosis (CAS) was examined using color-coded infrared ocular thermography (Morgan, et al. 1999a). They were observed to be negatively correlated, and so was the relative variation in CAS (CAS of right eye minus that of left eye) and the interocular difference in OST. The

circle of Willis and the other anastomoses within the brain were said to be unable to compensate for the reduction in blood flow, hence led to a cooler eye on the affected side (Morgan, et al. 1999a).

CHAPTER 3. TEXTURAL ANALYSIS ON OCULAR THERMAL IMAGE

In literature, investigations in ocular surface temperature by infrared thermography mainly employed either one of the two methods: subjective assessment and first-order spatial statistics of texture analysis (Tan, et al. 2009a). Most of the time researchers determined the mean value on temperature of one or several regions over the anterior ocular surface, and subsequently performed statistical analysis. This monotony and insufficiency in the methods of analysis has profoundly confined the capability of ocular thermogram.

Second-order spatial statistics of texture analysis was suggested for further analysis of ocular IR image (Tan, et al. 2009a). In many image problems, this method was utilized to enable the machine to recognize certain signal in a scene, like character recognition, weather forecasting from satellite images and target discrimination (Tsatsanis, et al. 1992). In medical imaging, it has been used in applications such as tumor detection and blood cell count (Tsatsanis, et al. 1992).

Image texture in simplicity can be considered as a function of spatial variation in pixel intensities (Tuceryan, et al. 1993). There are a number of perceived qualities and properties which are important in delineating texture, and they are roughness, coarseness, uniformity, density, directionality, direction, frequency, phase, regularity and linearity (Laws 1980).

Numerous approaches have been proposed to deal with image texture, and in general they can be categorized into four classes: statistical methods, geometrical (structural, syntactic) methods, model based methods, and signal processing methods (Tuceryan, et al. 1993). Statistical methods study the spatial distribution of gray levels, and derive a set of statistics on top of that. Geometrical methods view texture as being composed of many textural elements (called “texel” or primitives), and compute some statistics on the geometrical properties of a textural element, or extract the placement rule that forms a texture. In model based methods an image model, the parameters of which capture some essential perceived qualities of a texture, can be used not only to delineate a texture but also to synthesize it (Tuceryan, et al. 1993). Signal processing methods perform texture analysis using signal processing techniques, by

computing a number of features on the filtered images (Tuceryan, et al. 1993).

Analysis of image texture has played an important role in a number of medical applications, to perform a variety of classification tasks, such as discriminating normal tissue from abnormal one. For example, three texture features acquired on the basis of isotropic contrast measure, directional contrast measure and Fourier domain energy sampling were used to pick up diseased lungs from normal lung (Sutton, et al. 1972). Different types of white blood cells were differentiated using various first-order and second order statistics (Landeweerd, et al. 1978). Moments of responses to multiscale filter bank were used as texture feature to detect abnormalities in frontal chest radiographs (Ginneken, et al. 2002). First-order statistics, spatial grey-level dependence matrix (second-order) and neighborhood gray-tone-difference matrix (Amadasum, et al. 2009) (higher-order) were utilized to extract texture features from co-registered fluoro-deoxy-glucose (FDG) positron emission tomography/computed tomography (PET/CT) images to distinguish tumor from normal tissue in head and neck (Yu, et al. 2009).

In this chapter, cross co-occurrence matrix (Schaefer, et al. 2009) was employed along with first-order statistics, difference histogram and moments to extract texture features from ocular thermogram. It aims to study and determine if normal subjects of different age group exhibit dissimilar texture due to variations in metabolic rate. Besides, it also attempts to determine relationships among features of cross co-occurrence matrix, first-order statistics and age of subjects. Such findings may serve as a reference in future for the establishment of diagnosis criteria for ocular disease. The computational complexity for the cross co-occurrence matrix is $O(h^2)$ (Gadkari 2004).

3.1. DATA COLLECTION AND OST ACQUISITION

3.1.1. DATA COLLECTION

Ocular thermograms analyzed in this section were collected from normal subjects ranging from age 14 to 76, as summarized in [Table 3.2](#). The data collection was approved by ethic committee (NHG DSRB A) and informed consent was obtained from each participant. Subjects were asked to relax for 10 minutes and participants who have the following conditions are excluded (Morgan, et al. 1999b):

- I. Hot drinks, rubbing of eyes, use of tear drops

- II. Current eye disease.
- III. History of serious eye diseases
- IV. History of ocular or facial surgery
- V. Poor general health
- VI. Recent usage of tear drop or medications.

Conditions II and III were imposed to ensure subjects were of normal and had healthy eye. Rubbing of eyes and hot drinks consumed 2 hours before data taking were forbidden due to the fact that these actions may lead to unusual temperature level and distribution. In contrast, usage of tear drop or medications may bring down OST and therefore were excluded. Any subject with poor general health or history of either ocular or facial surgery may exhibit unusual OST, and hence not accepted into this study.

Infrared thermal images were obtained using VarioTHERM, JENOPTIK Laser (Germany) (URL: <http://www.jenoptik-ir.com/>), and thermogram were captured 50cm away from the chin-rest. The camera specification is tabulated in Table 3.1. Environmental conditions of the room where this study taking place was controlled, in which temperature and mean humidity were maintained at 25 ± 1 °C and $70 \pm 4\%$

respectively. The captured images were stored in *irbis* format which consists of temperature values. These *irbis* data were exported to *jpeg* format with an image size of 256x256 pixels using post-processing software installed with the camera for further processing.

The data collection was conducted in Biomedical Centre, Ngee Ann Polytechnic, Singapore. All the instrumental setup, environmental control and data collecting procedures performed follow the recommended guidelines laid out in the journal papers by Ring et. al. and relevant ISO standards (Ring 1998, ISO 2008, 2009, Ring, et al. 2010)

TABLE 3.1: INFRARED CAMERA SPECIFICATION

Spectral range	(3, 4 ... 5) μm , optionally (2 ... 5) μm
Frame size (no. of pixels)	256 $\times$ 256, 24 μm detector pitch
Detector type	PtSi-Focal plane array (cooled)
Temperature measurement range	(−25 ... + 1200) $^{\circ}C$
Measuring accuracy	$\pm 2K$, $\pm 2\%$
Thermal resolution power @ 30 $^{\circ}C$	Better than 0.1K
IR-frame rate	50Hz
Standard object lens, FOV, IFOV, min. focus	12.5mm, (14 $\times$ 14) $^{\circ}$, 1.0mrad, 0.4m

TABLE 3.2: AGE GROUPS OF THIS STUDY.

Age Group	Number of Subjects
35 and below	35
Above 35	45
Total	80

3.1.2. OST ACQUISITION

The method of acquisition of OST in this study is a semi-automated algorithm, proposed by Acharya et al. (Acharya, et al. 2008). The thermogram stored in *irbis* format was exported to monotone-RGB *jpeg* image (black $\rightarrow$ white), and converted into 256 grey-level image. The ocular grey-level image was cropped to have eye positioned at the centre of the region of interest, leaving other details behind (as illustrated in [Figure 2.6](#)). The resultant image was then standardized to a size of 400x200 pixels.

Cornea is known to be circular. Since the cropped image consists only of eye, the width and the height of an eye in the image equal to the width and the height of the image matrix. Corneal region was identified by a

circle, the centre and radius of which is at the centre of cropped image and is one-fourth of the width of eye (Acharya, et al. 2008). Temperature values within the circular region were extracted for further analysis.

In each thermogram, the darkest grey-level and the brightest grey-level correspond to 28°C and 36°C respectively.

3.2. STATISTICAL FEATURES EXTRACTION

3.2.1. FIRST-ORDER SPATIAL STATISTICS

First-order spatial statistics are the simplest features that describe the temperature distribution on an eye. However in this study, the differences in between left and right eyes for each statistic are of interest. Therefore interocular differences in absolute values for the following statistics were acquired as features: mean, median, standard deviation and 90th-percentile.

3.2.2. MOMENTS

The use of moments as shape descriptor was proposed by Hu (Hu 1962), and in the context of this study they were defined as:

$$m_{\phi\psi} = \sum_{i=1}^M \sum_{j=1}^N i^{\phi} j^{\psi} I(i, j)$$

(9)

where $M \times N$ is the image size and i and j define the pixel location. These moment-based shape descriptors were proved to be information preserving (Hu 1962). Zeroth order moment (e.g. m_{00}) is equivalent to the area of shape; first order moments (e.g. m_{10}) are used to obtain the coordinates of center of mass; second order moments (dubbed moment of inertia) can be used to compute the principal axes of shape (Loncaric 1998).

In this chapter interocular difference (in absolute value) on m_{10} and m_{01} were computed. For each eye, there is a distance in between geometrical center and center of mass obtained from first order moments. The interocular difference in the above distance was of interest and calculated, in horizontal and vertical directions respectively.

3.2.3. DIFFERENCE HISTOGRAM

Mathematically, a histogram h_b counts the amount of observations which falls into some disjoint categories known as bin. It is a sort of

mapping having a total number of n observations and k number of bins, and meets the following condition:

$$n = \sum_{b=1}^k h_b \quad (10)$$

In this study, the number of bin is 256 and the bin width is 1 grey-level. A difference histogram is obtained by subtracting the number of observations in each bin of the right eye histogram from the counterpart of the left eye histogram. Based on this, five features were evaluated in absolute values: the maximum number of observations in one bin, the number of zero crossing, the amount of bin exceeding certain threshold (in our case, a bin having more than 100 observations), energy and the difference in between the number of bins having positive and negative values.

The formula for energy (Tan, et al. 2010a) is:

$$E_{_d h_b} = \sum_{b=1}^k {}_d h_b^2 \quad (11)$$

Where ${}_d h_b$ denotes the difference histogram.

3.2.4. SECOND-ORDER SPATIAL STATISTICS

Co-occurrence matrix is widely used in literature to extract texture features. In this work we employed cross co-occurrence matrix (Schaefer, et al. 2009, Tan, et al. 2010a) instead. Given an $M \times N$ image, the co-occurrence matrix can be obtained by

$$C_d(i, j) = |\{(p, q), (p + \Delta x, q + \Delta y) : I(p, q) = i, I(p + \Delta x, q + \Delta y) = j\}|$$

(12)

In which $(p, q), (p + \Delta x, q + \Delta y) \in M \times N$, $d = (\Delta x, \Delta y)$ and $|\cdot|$ denotes the cardinality of a set. Then given a grey level i in an image, the probability that a pixel at a $(\Delta x, \Delta y)$ distance away is j is:

$$P_d(i, j) = \frac{C_d(i, j)}{\sum C_d(i, j)}$$

(13)

In our study, the size of both left and right cropped image is equal, and the corneal matrix for both eyes is of size of 200 x 200, the cross co-occurrence matrix is thus given by

$$_cC_d(i, j) = |\{(p, q), (p + \Delta x, q + \Delta y) : I_L(p, q) = i, I_R(p + \Delta x, q + \Delta y) = j\}|$$

(14)

and

$${}_cP_d(i, j) = \frac{{}_cC_d(i, j)}{\sum {}_cC_d(i, j)} \quad (15)$$

Where I_L and I_R denote corneal matrix for left and right eyes respectively. The displacement vector is set to be $d = (1, 0)$. Based on this, eight features were computed (Tan, et al. 2010a):

$$\text{Energy: } \Sigma = \sum_i \sum_j {}_cP_d(i, j)^2 \quad (16)$$

$$\text{Contrast: } Co = \sum_i \sum_j |i - j| {}_cP_d(i, j) \quad (17)$$

$$\text{Homogeneity: } H = \sum_i \sum_j \frac{{}_cP_d(i, j)}{1 + |i - j|} \quad (18)$$

$$\text{Symmetry: } Sy = 1 - \sum_i \sum_j |{}_cP_d(i, j) - {}_cP_d(j, i)| \quad (19)$$

And moments m_1, m_2, m_3 and m_4 using the following formula:

$$m_g = \sum_i \sum_j (i - j)^g {}_cP_d(i, j) \quad (20)$$

3.2.5. PRIMARY FINDINGS

Hypothesis testing on means of two independent samples was applied to study features of different age groups, and some of the results were tabulated in **Table 3.3**. In the table only statistical results with p values less than 0.08 were reported. The average mean OST for subjects aged 35 and below was $33.95^{\circ}C$, $33.48^{\circ}C$ for subjects aged above 35. The average interocular differences in median for two age groups were significantly different.

TABLE 3.3: STATISTICAL ANALYSIS ON FEATURES EXTRACTED BASED ON
DIFFERENT AGE GROUP

Features	Aged 35 and below	Aged above 35	<i>p</i>
Mean OST	$33.95 \pm 0.719^{\circ}\text{C}$	$33.48 \pm 0.689^{\circ}\text{C}$	0.0044
Interocular difference in median Energy (difference histogram)	$0.16^{\circ}\text{C}(0^{\circ}\text{C}\sim 0.53^{\circ}\text{C})$	$0.23^{\circ}\text{C}(0.03^{\circ}\text{C}\sim 0.91^{\circ}\text{C})$	0.0506
Homogeneity	185.87	277.15	0.0742
Contrast	0.096	0.081	0.0206
Moment 2	4.361	5.435	0.0211
Moment 3 (absolute value)	78.01	117.625	0.026
	1720.76	3393.02	0.0776

TABLE 3.4: LINEAR CORRELATION AMONG FEATURES OF INTEREST
ILLUSTRATED BY R^2 STATISTICS ($P < 0.00001$).

ONLY CORRELATIONS WITH R^2 VALUE ABOVE 0.5 ARE TABULATED. FEATURES OBSERVED TO HAVE CORRELATION WITH THE OTHERS ARE: INTEROCULAR DIFFERENCE IN MEDIAN (DMED), INTEROCULAR DIFFERENCE IN MEAN (DMN), MAXIMUM FOR DIFFERENCE HISTOGRAM (MAX), AMOUNT OF BIN EXCEEDING THRESHOLD (BET); E (H), ENERGY (DIFFERENCE HISTOGRAM), INTEROCULAR DIFFERENCE IN m_{10} (DM10), INTEROCULAR DIFFERENCE IN m_{01} (DM01), HOMOGENEITY (HOMO); CON, CONTRAST; SYM, SYMMETRY; M2, MOMENT 2; M3(ABS), MOMENT 3 IN ABSOLUTE VALUE; M4, MOMENT 4. (+) STANDS FOR POSITIVE CORRELATION AND (-) FOR NEGATIVE CORRELATION.

[illegible]

The average interocular difference in mean OST for subject group aged 35 and below was 0.17°C , and for subject group aged above 35 the corresponding value was 0.22°C , however the differences in these two values were found to be statistically insignificant ($p < 0.155$). Besides, for subjects having value of “maximum” (the maximum number of observations in one bin, a feature from difference histogram) 1000 and below, the average interocular difference in 90 percentile is 0.14°C , and the corresponding value for subjects having “maximum” value above 1000 is 0.29°C . The difference was found to be significant ($p < 0.002$).

Table 3.4 illustrated correlations among features investigated in this study, and only correlations between two features having R^2 value above 0.5 ($p < 0.00001$) were shown in the table. The interocular difference in median was found to be highly correlated with interocular difference in mean, giving an R^2 value of 0.9291. And the R^2 value for the correlation in between moment 1 and interocular difference in mean is 1. Features interocular difference in median and moment 1 were omitted in **Table 3.4**, since these two features were highly correlated with interocular difference in mean, any feature that was correlated with the interocular

difference in mean OST was bound to be correlated with both of the features.

Several linear regressions were listed in Table 3.5, and Figure 3.1, Figure 3.2, Figure 3.3 illustrated linear regression of interocular differences in median versus interocular differences in mean OST, moment 2 versus contrast, contrast versus interocular difference in m_{10} respectively. For Table 3.5, only correlations with R^2 value above 0.75 were listed. The units in x and y axis of Figure 3.1 are temperature instead of grey-level.

TABLE 3.5: SEVERAL LINEAR REGRESSIONS ON FEATURES EXTRACTED FROM OCULAR THERMOGRAM.

Predicted value (y)	Predictor (x)	Slope (b)	Intercept (c)	R^2
Interocular difference in median	Interocular difference in mean OST	0.9777	0.0062	0.93
Interocular difference in m_{01}	Interocular difference in mean OST	1.5299×10^3	3.9696	0.91
Moment 2	Contrast	36.09	-164.63	0.83
Interocular difference in m_{10}	Interocular difference in mean OST	1.2678×10^3	72.4048	0.77
Moment 3 (absolute value)	Moment 2	47.2319	-4.331×10^3	0.76
Contrast	Interocular difference in m_{01}	0.00005	6.2549	0.76
Contrast	Interocular difference in mean OST	21.3929	6.1235	0.75

FIGURE 3.1: INTEROCULAR DIFFERENCE IN MEDIAN VERSUS INTEROCULAR DIFFERENCE IN MEAN OST

FIGURE 3.2: MOMENT 2 VERSUS CONTRAST

FIGURE 3.3: CONTRAST VERSUS INTEROCULAR DIFFERENCE IN m_{01}

In summary, a total of 21 features, in which 4 of them from first-order spatial statistics, 4 of them from moment, 5 of them from difference histogram and another 8 of them pertained to the second-order spatial statistics based on cross co-occurrence matrix were studied. Some of them were found to be useful and discriminative for different age groups. Textures on ocular thermograms of younger subjects were more homogenous compared to elder subjects; hence textures of elder subjects should have more contrast. Moment 2 was observed to be lower in

younger subjects, but moment 3 (in absolute value) was higher in that subjects group and the above findings were statistically significant.

Interocular difference in mean OST was considered as an indicator of the state of ocular health. Mapstone revealed that acute unilateral anterior uveitis produces corneal temperature relatively higher to its normal counterpart (Mapstone 1968a). Interocular difference in mean OST was determined to fall within the range of -0.57°C and $+0.62^{\circ}\text{C}$ for 95% normal subjects, and no difference in ocular temperature is demonstrated between two eyes (Morgan, et al. 1993). Subject with *acanthamoeba* keratitis was reported to exhibit interocular difference in mean OST of up to 1.17°C (Morgan, et al. 1993), and patients with Herpes Zoster Ophthalmicus in acute stage were observed to have OST of one eye 0.5°C higher than the normal counterpart (Cardona, et al. 1996).

Cornea is avascular and its temperature is formed and determined mainly due to posterior vascularized limbal area, ocular blood flow, corneal thickness (Morgan 1994), and environment air flow (Freeman, et al. 1973). The presence of upper and lower eyelids heat up the upper and the lower parts of cornea, resulting elliptical isotherms instead of circular isotherms as simulated by FEM analysis (Ng, et al. 2007). Such heating

may introduce artifacts, and when temperatures of the corneal region are averaged, the obtained value may not accurately reflect the activities occurred in the ocular posterior segments.

Given the above situations, interocular difference in median may be a better feature in certain scenarios as illustrated in this study. When human grows older it is possible that their metabolism degrades and asymmetric growing in tissues of two eyes occurs. Interocular difference in median has captured this physiological difference in different age groups where interocular difference in mean OST did not occur .

Differences in values of some features were demonstrated with respect to age group. Besides interocular difference in median, energy (difference histogram), homogeneity, contrast, moment 2 and moment 3 were the other features having this relationship. However, it was found that age had no linear correlation with any other features investigated in the current study.

From [Table 3.4](#), it was observed that interocular difference in mean OST had the most number of linear correlations with other features, and they are in total 8 of them: 1 from first-order spatial statistics (D90P), 2 from difference histogram (BET and E (H)), 2 from interocular difference

in moments (DM10 and DM01), and 3 from second-order spatial statistics (Homo, Con, Sym). Besides, interocular differences in moments were found to be significantly correlated with features from cross co-occurrence matrix such as homogeneity, contrast, symmetry but not energy. The interocular difference in distance between geometrical center and center of mass obtained from first order moments, expressed in horizontal and vertical directions, had no correlation with other features.

Cross co-occurrence matrix compares each pixel in the left corneal region with the pixel one cell next to its counterpart horizontally in the right corneal region, since in this study we set $d = (1,0)$ and both corneal matrices are of equal size. The matrix records spatial distribution of grey-level among two image matrices. The similarity between two corneal matrices is demonstrated by the feature homogeneity, the larger the value the higher is the similarity. Feature contrast reveals something opposite to homogeneity, however not necessarily the larger the value of contrast, the lower the value of homogeneity as seen in [Table 3.4](#). In fact contrast has stronger correlation with interocular difference in m_{01} than homogeneity.

This study did not try to depict ocular thermographic texture for normal subject in general, nor it is possible to do so. However, it has set up

a number of linear regressions, obtained several statistics to illustrate relationships among features, and the possible outcome of other features if values of one or a few of them are known.

It is possible to bundle these linear regressions and statistics into a linear model, which says about the texture of normal ocular thermogram. This linear model can serve as a reference for the diagnosis of ocular disease. If these features for a particular thermogram deviate significantly from the model's prediction, then the subject's eye may not be healthy. And how those values deviate may vary among ocular diseases.

CHAPTER 4. AUTOMATED OCULAR LOCALIZATION AND REMOVAL OF EYELASHES

Hitherto, no technique of automated ocular and corneal localization is reported to investigate ocular thermal image. In this chapter we proposed a fully automated algorithm to achieve the aforesaid purpose, by utilizing snake algorithm, gradient vector flow field, genetic algorithm and target tracing function. After these, eyelashes that fall on the cornea are removed to improve data quality. This is also an automated procedure, followed immediately after the localization.

Snake (of snake algorithm) is sensitive to the initial conditions set before the algorithm actually runs. It must be put near to the object of interest, and of appropriate shape in order to correctly locate the object of interest. In fact, deformable template matching techniques such as snake, spline-based shape matching, diffusion snakes, and active shape models, are local optimizers which require good initial position or clear image to avoid local minima (Schindler, et al. 2008). Such restriction implies that the user needs to intervene beforehand to mark out the contour and the appropriate region for the snake to converge into feature of interest.

In our algorithm, the abovementioned restriction is overcome by the introduction of target tracing function. It is a function designed to produce a minimum for a particular category of image only if the snake accurately localizes the feature of interest (the eye). A search for minimum on the function is performed over the possible regions and shapes, to find for the snake with the best initial position and shape that would result in an accurate localization. And based on the snake that has localized the eye, the proposed algorithm derives the corneal center and diameter.

4.1. SNAKE ALGORITHM AND GRADIENT VECTOR FLOW FIELD

4.1.1. SNAKE

Snake, proposed by Kass et al. (Kass, et al. 1988), is an active deformable model which can adapt itself on a given image data. It is an energy-minimizing spline when in discrete form, comprising a series of disconnected point, and guided by its spline internal energy, derived image force and external constraint forces. The rationale behind this method can be traced back to Montanari (Montanari 1971) and Martelli (Martelli 1972), where in these works optimization of curve contrast and smoothness were adopted (Blake, et al. 1992). Several variants were proposed after the snake seminal paper, for example B-snake (Menet, et al.

1990), Fourier snake (Staib, et al. 1989), finite element snake (Cohen, et al. 1990), in the attempt to resolve issues such as initialization sensitivity, noise, selectivity for some object classes (Liang, et al. 2006). Nevertheless, there is yet a comprehensive solution developed to address all these issues (Liang, et al. 2006).

Mathematically, for a single image snake is a curve $\mathbf{x}(s) = [x(s) \ y(s)]$, $s \in [0, 1]$ defined in the image domain (Kass, et al. 1988), and moves across the image spatial domain under a group of forces, in order to minimize the below energy functional

$$\mathfrak{E} = \int_0^1 \left\{ \frac{1}{2} [\alpha |\mathbf{x}'(s)|^2 + \beta |\mathbf{x}''(s)|^2] + E_{ext}(\mathbf{x}(s)) \right\} ds \quad (21)$$

where $\mathbf{x}'(s)$ and $\mathbf{x}''(s)$ are the first and second derivatives with respect to s , controlled by the parameters α and β respectively. Since $\mathbf{x}'(s)$ and $\mathbf{x}''(s)$ refer to the length and rigidity of snake, one can determine the elasticity of snake primarily by the two parameters (Xu, et al. 1998). E_{ext} refers to the external energy function. By Euler equation, we can reduce the above functional (equation (20)) into

$$\alpha \mathbf{x}'(s) - \beta \mathbf{x}''(s) - \nabla E_{ext} = 0 \quad (22)$$

and $\nabla E_{ext} = [f_x(x, y) \ f_y(x, y)]$. One can view $\alpha \mathbf{x}'(s) - \beta \mathbf{x}''(s)$ as internal force and $-\nabla E_{ext}$ as external potential force. It can be seen that while snake progresses to reach its minimum in energy, the external potential forces tends to pull/push snake into nearby edges and the internal forces discourage stretching and bending of snake during its way to localize feature (Xu, et al. 1998). And the solution to the equation is

$$\begin{cases} x_t = (A_s + \gamma I)^{-1} [\gamma x_{t-1} - f_x(x_{t-1}, y_{t-1})] \\ y_t = (A_s + \gamma I)^{-1} [\gamma y_{t-1} - f_y(x_{t-1}, y_{t-1})] \end{cases} \quad (23)$$

where A_s is a pentadiagonal banded matrix, and I the identity matrix; γ is step-size.

4.1.2. GRADIENT VECTOR FLOW FIELD

For a single gray-level image, there are several appropriate external forces available to enable snake moving into feature of interest, such as

$$E_{ext}^{(1)} = -|\nabla I(x, y)|^2 \quad (24)$$

$$E_{ext}^{(2)} = -|G_{\sigma}(x, y) * \nabla I(x, y)|^2 \quad (25)$$

However, in actual practice there are several issues associated with the above external forces. First, the snake must be placed near to the feature of interest, or it would converge to undesired feature otherwise. Second, with the above external forces, snake often cannot progress into boundary cavity. Although several remedies were developed, they do not provide satisfactory solution (Xu, et al. 1998).

Gradient vector flow (GVF) field is adopted in this work as the external energy function. It is developed by Xu and Prince (Xu, et al. 1998), and has satisfactorily resolved the abovementioned issues without giving other difficulties. They first defined an edge map,

$$f_e(x, y) = -E_{ext}^{(i)}, \quad i = 1 \text{ and } 2 \quad (26)$$

which has primarily three properties: 1) it gives an ∇f_e of which it has vectors pointing toward and normal to the edges. 2) vectors values are large only in region where edges exist. 3) in homogenous region the vectors value are near to zero. The first property is highly desired, as it gives a force field pulling/pushing the snake into edges of interest.

However, for the second and third, they constrain the snake capture range, leading it unmovable in homogenous region. Therefore, GVF field is proposed to solve these issues by keeping the edge map first property, and extending the gradient map into homogenous region through computational diffusion process (Xu, et al. 1998).

Let the GVF be $\mathbf{v}(x, y) = [u(x, y) \ v(x, y)]$, and $-\nabla E_{ext} = \mathbf{v}(x, y) = [u(x, y) \ v(x, y)]$. It is a dense vector field that minimizes the following functional

$$\varepsilon = \iint [\mu(u_x^2 + u_y^2 + v_x^2 + v_y^2) + |\nabla f_e|^2 |\mathbf{v} - \nabla f_e|^2] dx dy \quad (27)$$

in which μ is the parameter that regularizes the first and the second terms in above integrand, and is suggested to set to a higher value on a noisy image. On the case where $|\nabla f_e|$ is small, the partial derivatives of the vector field would dominate, generating a slow varying field. On the contrary, the $|\nabla f_e|^2 |\mathbf{v} - \nabla f_e|^2$ dominates, giving a $\mathbf{v}$ almost equal to the gradient of the edge map, and at the same time generating slow varying field in homogeneous region. By Euler equation, from (27) one can get

$$\begin{cases} \mu \nabla^2 u - (u - f_{e_x}) (f_{e_x}^2 + f_{e_y}^2) = 0 \\ \mu \nabla^2 v - (v - f_{e_y}) (f_{e_x}^2 + f_{e_y}^2) = 0 \end{cases} \quad (28)$$

By treating u and v as functions of time, the solution is

$$\begin{cases} u_t(x, y, t) = \mu \nabla^2 u(x, y, t) - [u(x, y, t) - f_{e_x}(x, y)] [f_{e_x}^2(x, y) + f_{e_y}^2(x, y)] \\ v_t(x, y, t) = \mu \nabla^2 v(x, y, t) - [v(x, y, t) - f_{e_y}(x, y)] [f_{e_x}^2(x, y) + f_{e_y}^2(x, y)] \end{cases} \quad (29)$$

In actual practice, GVF snake is often observed trapped in image border, due to artifacts arisen in the calculation of Gaussian blur and GVF force field (Tan, et al. 2008, Tan, et al. 2009b). This is resolved through the expansion of image matrix, achieved by a number of the following iterative calculations. Assume A is an image matrix with a size of $M \times N$, B is the expanded image after each iteration having the size of $(M + 2) \times (N + 2)$ (Tan, et al. 2008, Tan, et al. 2009b):

$$A = \begin{bmatrix} a_{1,1} & a_{1,2} & \dots & a_{1,n} \\ a_{2,1} & a_{2,2} & \dots & a_{2,n} \\ \vdots & \vdots & \ddots & \vdots \\ a_{m,1} & a_{m,2} & \dots & a_{m,n} \end{bmatrix}, \quad B = \begin{bmatrix} b_{1,1} & b_{1,2} & \dots & b_{1,n+1} & b_{1,n+2} \\ b_{2,1} & b_{2,2} & \dots & b_{2,n+1} & b_{2,n+2} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ b_{m+1,1} & b_{m+1,2} & \dots & b_{m+1,n+1} & b_{m+1,n+2} \\ b_{m+2,1} & b_{m+2,2} & \dots & b_{m+2,n+1} & b_{m+2,n+2} \end{bmatrix}$$

then the expand function is

$$B = \mathbf{F}_{ex}(A) =$$

$$\left\{ \begin{array}{l} (b_{i,j})_{2 \leq i \leq m+1; 2 \leq j \leq n+1} = (a_{i,j})_{1 \leq i \leq m; 1 \leq j \leq n} \\ b_{1,j} = a_{1,j-1} - \mu \left(a_{1,j-1} - \frac{a_{1,1} + a_{1,2} + \dots + a_{1,n}}{n} \right), \text{ for } j = 2, 3, \dots, n+1 \\ b_{m+2,j} = a_{m,j-1} - \mu \left(a_{m,j-1} - \frac{a_{m,1} + a_{m,2} + \dots + a_{m,n}}{n} \right), \text{ for } j = 2, 3, \dots, n+1 \\ b_{i,1} = a_{i-1,1} - \mu \left(a_{i-1,1} - \frac{a_{1,1} + a_{2,1} + \dots + a_{m,1}}{m} \right), \text{ for } i = 2, 3, \dots, m+1 \\ b_{i,n+2} = a_{i-1,n} - \mu \left(a_{i-1,n} - \frac{a_{1,n} + a_{2,n} + \dots + a_{m,n}}{m} \right), \text{ for } i = 2, 3, \dots, m+1 \\ b_{1,1} = \frac{b_{1,2} + b_{2,1}}{2}, b_{1,n+2} = \frac{b_{1,n+1} + b_{2,n+2}}{2}, b_{m+2,1} = \frac{b_{m+1,1} + b_{m+2,2}}{2}, b_{m+2,n+2} = \frac{b_{m+1,n+2} + b_{m+2,n+1}}{2} \end{array} \right.$$

(30)

and for our application the edge map $f_e(x, y)$ is defined as

$$f_e = -\{|\nabla[G_{\sigma_1}(x, y) * I(x, y)]| + r_e \cdot G_{\sigma_2}(x, y) * |\nabla_{\text{sob}} I(x, y)|\}$$

(31)

where r_e is a control parameter; ∇_{sob} refers to the Sobel gradient operator. G_{σ_1} and G_{σ_2} denote the Gaussian blur functions having standard deviations of σ_1 and σ_2 respectively (Tan, et al. 2008, Tan, et al. 2009b). The edge map proposed in equation (31) is designed to combine two types of external forces, in order to preserve the subtle intensity level difference in the lower eyelashes region.

4.2. TARGET TRACING FUNCTION AND GENETIC ALGORITHM

4.2.1. TARGET TRACING FUNCTION

The snake algorithm in this work starts with a contour consisting of two parabolas (Tan, et al. 2008, Tan, et al. 2009b), as illustrated in [Figure 4.1](#). They are generated by

$$\mathbf{C}(x_c, y_c, p_1, p_2, w) = [C_u(s) \quad C_l(s)]^T = \mathbf{C}(s) \quad (32)$$

Where

$$\begin{cases} C_u(s) = [y_u(s) \quad x_u(s)] = \left[\frac{(x_u(s) - x_c)^2}{-4p_1w} + (y_c + p_1w) - (h_u - y_c) \quad x_u(s) \right], & \text{for } 0 < s \leq 0.5 \\ C_l(s) = [y_l(s) \quad x_l(s)] = \left[\frac{(x_l(s) - x_c)^2}{4p_2w} + (y_c - p_2w) - (h_l - y_c) \quad x_l(s) \right], & \text{for } 0.5 < s \leq 1 \end{cases}$$

And

$$p_1 = \frac{a_u}{w}, p_2 = \frac{a_l}{w}, h_u = \frac{(w/2)^2}{-4p_1w} + (y_c + p_1w), h_l = \frac{(w/2)^2}{4p_2w} + (y_c - p_2w)$$

FIGURE 4.1: INITIAL CONTOUR FOR THE SNAKE ALGORITHM

$\mathbf{C}(s)$ in the equation (32) is $\mathbf{x}(s) = [x(s) \ y(s)]$ in discrete form. These snake points deform under equation (23) until equation (21) reaches minimum. To speed up convergence time and produce desired shape, equal-distant redistribution algorithm (see [Appendix I](#)) is applied

on snake points after each iteration of equation (23). And we denote ${}^v\mathbf{C}(s) = {}^v\mathbf{C}(x_c, y_c, p_1, p_2, w)$ as the snake deformed from contour $\mathbf{C}(s) = \mathbf{C}(x_c, y_c, p_1, p_2, w)$, and of which its energy in equation (21) reaches minimum.

Snake is sensitive to initialization. Ideally, disregard to which values the x_c, y_c, p_1, p_2 and w are the snake should accurately locate the object of interest (in our studies, the eye). However in practice this is not the case. The values of x_c, y_c, p_1, p_2 and w determine if the snake can converge to the right target. And the algorithm does not know in advance for any thermal images what the correct x_c, y_c, p_1, p_2 and w values are likely to be. To overcome this issue we have developed target tracing function (Tan, et al. 2008, Tan, et al. 2009b), which is designed to produce the minimum only when the ${}^v\mathbf{C}(s)$ accurately locates the object of interest. It is defined as:

$$\begin{aligned}
 y_{ft} &= F_{tt}(x_c, y_c, p_1, p_2, w) \\
 &= \int \left[\left\| \frac{d^2}{ds^2} I_{sc} \left({}^v\mathbf{C}(s) \right) \right\| \times c_1 + I_{sc}^2 \left({}^v\mathbf{C}(s) \right) + \left| {}^v\mathbf{C}'(s) \right| \right. \\
 &\quad \left. \times c_2 \right] ds + c_3 \times \frac{\int I_{sc}^2 \left({}^v\mathbf{C}(s) \right) ds}{\int \left| {}^v\mathbf{C}'(s) \right| ds}
 \end{aligned} \tag{33}$$

In which

$$I_{sc} = \frac{f_e(x, y) - \min f_e}{\max f_e - \min f_e}$$

$$\frac{d^2}{ds^2} I_{sc} \left({}^v\mathbf{C}(s) \right) \approx I_{sc} \left({}^v\mathbf{C}(s_{n+1}) \right) - 2 \cdot I_{sc} \left({}^v\mathbf{C}(s) \right) - I_{sc} \left({}^v\mathbf{C}(s_{n-1}) \right)$$

Where I_{sc} is the f_e scaled in the range of $0 \sim 1$. c_1, c_2, c_3 are control parameters.

FIGURE 4.2: A CONVERGED SNAKE LYING ON A TWO DIMENSIONAL MANIFOLD.

Figure 4.2 illustrates a two-dimensional manifold spreading across the spatial domain of an image. In the figure, both x and y axes refer to the

x and y directions as defined in the snake equation; and z denotes I_{sc} . The dark solid line that falls on the elliptical-like lower region is a snake which has correctly localized the eye. From [Figure 4.2](#), it can be observed that, as a snake on its way converges to the object interest under the combination of internal and external forces, it is in fact sliding along the manifold derived from I to reach the minimum of its total potential energy, $I_{sc}^2 \left({}^v\mathbf{C}(s) \right)$.

For most cases, the edge of the palpebral fissure in an ocular thermogram generates an elliptical dark ring in I_{sc} . This dark ring is a low and relatively level region on the two-dimensional manifold, as illustrated in [Figure 4.2](#). The term $I_{sc}^2 \left({}^v\mathbf{C}(s) \right)$ represents the total potential energy of all snake points, and $\left\| \frac{d^2}{ds^2} I_{sc} \left({}^v\mathbf{C}(s) \right) \right\|$ determines the flatness of the region of the manifold where a snake stays, with respect to x-y plane. Hence, for a snake which has converged and stayed on the edge, it would give a minimum value for the term $\left\| \frac{d^2}{ds^2} I_{sc} \left({}^v\mathbf{C}(s) \right) \right\|$ and $I_{sc}^2 \left({}^v\mathbf{C}(s) \right)$ of the target tracing function.

FIGURE 4.3: INCORRECT LOCALIZATION OF LOWER EYELID BY SNAKE (OCCASIONALLY).

However, in actual practice, the problem as illustrated in [Figure 4.3](#) appears occasionally. Hence, the term $\frac{\int I_{sc}^2(v\mathcal{C}(s))ds}{\int |v\mathcal{C}'(s)|ds}$ is added to promote the selection of the snake falling on the preferred region, and $\int |v\mathcal{C}'(s)|ds$ in the added term is input to prevent the snake from growing larger than palpebral fissure.

4.2.2. GENETIC ALGORITHM

The search for minimum on equation (33) is performed by genetic algorithm, a stochastic searching technique in which sampled points are determined based on stochastic sampling instead of groups of decision

rules laid down beforehand. Its working principle mimics the mechanism of Darwinian natural selection and the idea of genetics. The algorithm at first generates a fixed number of individuals, each of them denotes a potential solution to the objective function of interest, and the variable values are encoded in the individual chromosome. In each generation, the fitness of every individual is evaluated. Chromosomes of individual with reasonable fitness are selected to survive in the upcoming generation. Among the selected chromosomes, a few of them will be mutated, and some other chromosomes will be applied cross-over operation in the attempt to produce better individual. After these, a pool of chromosomes (or individuals) is ready, and the algorithm begins the next generation. Again the fitness of individuals is evaluated, chromosomes are selected, mutated and cross-overed. These procedures are carried out iteratively, until the best solution is observed.

In our application, genetic algorithm is coupled with snake algorithm to search for the eye. In the first generation, genetic algorithm randomly generates a fixed number of contour $\mathbf{C}(\mathbf{s})$ over variables x_c, y_c, p_l, p_c and w (the individuals). These contours deform respectively by equation (23) (the snake algorithm) until each of them reaches minimum in equation

(21). Genetic algorithm follows to evaluate the fitness of each ${}^u\mathbf{C}(s)$ using equation (33). For individuals observed with reasonable fitness, their variable values, expressed in chromosomes, are chosen to survive in this round of natural selection. Operations of mutation and cross-over are performed on some chromosomes before the start of next generation. These procedures are carried out in a finite iteration until the correct solution is determined.

FIGURE 4.4: AUTOMATED OCULAR AND CORNEAL LOCALIZATION

The automated ocular and corneal localization algorithm is illustrated in [Figure 4.4](#).

4.3. LOCATING CORNEA

Since snake points ${}^v\mathbf{C}(s) = [{}^x\mathcal{C}(s) \quad {}^y\mathcal{C}(s)]$ are equal-distant, we assume cornea to be circular in shape, therefore corneal center can be obtained through

$$\begin{cases} x_{cc} = \frac{1}{SP} \sum_s {}^x\mathcal{C}(s) \\ y_{cc} = \frac{1}{SP} \sum_s {}^y\mathcal{C}(s) \end{cases} \quad (34)$$

Where SP denotes the total number of snake points. Let the radius of cornea be r_c , then

$$r_c = rt \times dX \quad (35)$$

Define

$$dX = \max {}^x\mathcal{C}(s) - \min {}^x\mathcal{C}(s) \quad (36)$$

$$dY = \max {}^yC(s) - \min {}^yC(s) \quad (37)$$

For a snake correctly converges to the edge of the palpebral fissure, its dX and dY as defined in equations (36) and (37) are almost equal to the width and the height of the eye. Corneal radius was said to be approximately about 0.25 times of the width of the palpebral fissure for most cases (Yuille, et al. 1989), so the dX/dY for the eye would be 2 (assume the cornea touches the upper and lower eyelid). And rt is 0.25 in this case for equation (35) to be true (see [Figure 4.5](#)).

When a snake only converges to the edge of cornea, in this case the dX/dY is 1 since cornea is assumed to be circular, and rt is 0.5 for equation (35) to be true. From these two cases we propose a formula to adaptively determine the corneal radius solely from the points of a converged snake. Based on simple interpolation

$$\frac{2 - 1}{0.25 - 0.5} = \frac{dX/dY - 1}{rt - 0.5}$$

and we get

$$rt = \left(\frac{dX}{dY} - 1 \right) (-0.25) + 0.5 \quad (38)$$

With rt calculated, r_c is simply determined by equation (35). As palpebral fissure size varies among individuals, equations (36)-(38) allow the algorithm to adaptively determine corneal diameter on the basis of ${}^v\mathbf{C}(s)$.

FIGURE 4.5: (a) A SNAKE CORRECTLY DELINEATES THE EDGE OF PALPEBRAL FISSURE (b) A SNAKE CONVERGES TO CORNEA

4.4. REMOVAL OF EYELASHES

Alonso-Caneiro *et al* have estimated corneal surface topography with videokeratoscopy, by identifying strong interference signal due to factors such as narrow palpebral apertures, nystagmus and long eyelashes (Alonso-Caneiro, et al. 2008). We have modified this technique for the identification of eyelashes in ocular thermogram and their subsequent removal.

After the above ocular localization, our algorithm generates a square matrix, the width of which is the size of corneal diameter. The square matrix is resized to 300x300 pixels after using linear interpolation to give a better identification of eye lashes (usually the size of square matrix before resize is not more than 100x100 pixels). Then a series of concentric rings are superimposed to the resized square matrix, with the rings' center coincide to the matrix center. The detailed procedures are illustrated in the following steps.

4.4.1. SUPERPOSITION OF CONCENTRIC RINGS

Figure 4.6 shows the before and after of the superposition of the alternative bright and dark concentric rings. Each of the stripe (or ring) has a width of 2.8 pixels. The pixels in brighter rings are 0.04 higher in intensity level before superposition; and 0.04 lower before superposition in darker rings (at this stage of processing, value of 0 corresponds to the darkest and value of 1 corresponds to the brightest pixel intensity level). The combined width of one bright ring and one dark ring forms the wavelength for Gabor filter processing.

(A)

(B)

FIGURE 4.6: SQUARE MATRIX (A) BEFORE SUPERPOSITION (B) AFTER SUPERPOSITION.

4.4.2 NORMALIZATION

The superimposed image forms a 2D matrix $I(i, j)$, with $i = 1, 2, \dots, N$ and $j = 1, 2, \dots, M$, and is divided into non-overlapped blocks of equal size. Let W denotes block width and $\lfloor \cdot \rfloor$ as floor operator, for an image block centered at (i_b, j_b) :

$$\begin{aligned}
& I_{block}(i_b, j_b) \\
&= \begin{bmatrix} \left(i_b - \frac{W}{2} + 1, j_b - \frac{W}{2} + 1\right) & \cdots & \left(i_b - \frac{W}{2} + 1, j_b\right) & \cdots & \left(i_b - \frac{W}{2} + 1, j_b + \frac{W}{2}\right) \\ \vdots & & \vdots & & \vdots \\ \left(i_b, j_b - \frac{W}{2} + 1\right) & & (i_b, j_b) & & \left(i_b, j_b + \frac{W}{2}\right) \\ \vdots & & \vdots & & \vdots \\ \left(i_b + \frac{W}{2}, j_b - \frac{W}{2} + 1\right) & \cdots & \left(i_b + \frac{W}{2}, j_b\right) & \cdots & \left(i_b + \frac{W}{2}, j_b + \frac{W}{2}\right) \end{bmatrix}
\end{aligned}
\tag{39}$$

where

$$\begin{aligned}
i_b &= \frac{W}{2}, \frac{W}{2} + W, \frac{W}{2} + 2W, \dots, \frac{W}{2} + \left(\left\lfloor \frac{N}{W} \right\rfloor - 1\right)W \\
j_b &= \frac{W}{2}, \frac{W}{2} + W, \frac{W}{2} + 2W, \dots, \frac{W}{2} + \left(\left\lfloor \frac{M}{W} \right\rfloor - 1\right)W
\end{aligned}$$

The block size in this study is set to 6x6 pixels, since the width of stripe is 2.8 pixels, such size of block is sufficient to contain information for identification of eye lashes. Statistical block normalization with zero mean and unit variance is applied to remove background, in order to ensure further image processing is not affected by the variation in temperature in ocular thermogram.

4.4.3. GABOR FILTERING

A Gabor filter is defined (Alonso-Caneiro, et al. 2008) as

$$f_G(i, j; \theta, \lambda, \sigma_i, \sigma_j) = \exp \left[-\frac{1}{2} \left(\frac{R_1^2}{\sigma_i^2} + \frac{R_2^2}{\sigma_j^2} \right) \right] \cdot \exp \left(\sqrt{-1} \cdot \frac{2\pi R_1}{\lambda} \right) \quad (40)$$

where

$$R_1 = i \cos \theta + j \sin \theta, R_2 = -i \sin \theta + j \cos \theta$$

θ and λ refer to the orientation and the wavelength of sinusoidal wave respectively; σ_i and σ_j are standard deviations for Gaussian function along i and j directions.

Gabor filter in this technique is used to determine if a block has any specific orientation. The presence of interference such as eyelashes often associates with no specific orientation in a block after Gabor filter processing. In other words, given an image convoluted with a bank of Gabor filter having K different orientations, outputs of all these filters would give similar values for the blocks where eye lashes were present (Alonso-Caneiro, et al. 2008).

Thus, equation (40) is rewritten to obtain output of k -th Gabor filter

$$g(i, j; \theta_k, \lambda, \sigma_i, \sigma_j) = I(i, j) * f_G(i, j; \theta_k, \lambda, \sigma_i, \sigma_j) \quad (41)$$

The block sample mean of each of the filter outputs is given by

$$G_k = \frac{1}{W^2} \sum_{i_b} \sum_{j_b} g_{block}(i, j; \theta_k, \lambda, \sigma_i, \sigma_j) \quad (42)$$

In which $g_{block}(i_b, j_b)$ is part of the filter output of (42) corresponding to $I_{block}(i_b, j_b)$. For each image block we could get a vector $\mathbf{G} = [G_1, G_2, \dots, G_K]$ and derive the sample standard deviation for the vector $\mathbf{G}$, $\hat{s}(i_b, j_b)$ (Alonso-Caneiro, et al. 2008). In the presence of eyelashes, the sample standard deviation of the vector $\mathbf{G}$ would be low since the filter outputs of various orientations provide similar values.

In this study $K = 8$ is selected for Gabor filter, and the value of λ is set to 5.6, the combined width of a bright and dark stripes. $\sigma_i = \sigma_j$ is chosen since the rings pattern is regular and consistent, and both are fixed at 0.5λ in order to achieve a good localization of eyelashes (Alonso-Caneiro, et al. 2008).

4.4.4. IMAGE SEGMENTATION

After Gabor filtering, the matrix $\hat{s}(i_b, j_b)$ is normalized into range of 0 (non-oriented pattern) to 1 (maximally oriented pattern). All the columns of the normalized matrix are concatenated to form the block orientation vector, and the probability density function of this vector exhibits a bimodal distribution which can be approximately modeled as Gaussian mixture:

$$\phi(x[n]; \varepsilon) = (1 - \varepsilon)\phi_{signal}(X) + \varepsilon\phi_{noise}(X) \quad (43)$$

In which ε is the mixture parameter, and $0 < \varepsilon < 1$; ϕ_{signal} and ϕ_{noise} correspond to the Gaussian probability density functions of the oriented and non-oriented blocks (Alonso-Caneiro, et al. 2008).

The parameters of the Gaussian mixture $\hat{\mu}_{signal}, \hat{\sigma}_{signal}, \hat{\mu}_{noise}, \hat{\sigma}_{noise}$ are estimated using Expectation-Maximization (EM) algorithm (Moon 1996). The threshold, which is used to distinguish between areas of interference (eyelashes) and areas of corneal surface, is set to $\hat{\mu}_{signal} - \hat{\sigma}_{signal}$ as suggested (Alonso-Caneiro, et al. 2008). Thus, for blocks having the sample standard deviation of the vector $\mathbf{G}$ lower than

$\hat{\mu}_{signal} - \hat{\sigma}_{signal}$ are recognized as interference. The entire procedure is illustrated in **Figure 4.7**.

FIGURE 4.7: REMOVAL OF EYELASHES

4.4.5. ESTIMATION OF REMOVAL EFFECTS OF EYELASHES

The introduction of eyelashes removal has prevented reading in or inclusion of temperatures which are lower in nature compared to corneal surface temperature. The effect of this introduction can be estimated with the use of two statistics. For a study which has a number N_c of corneas, Mn

and Mx denote the minimum and maximum temperature of n th cornea, then we have

$$D_{Mn} = \frac{1}{N_c} \sum_{i=1}^{N_c} |Mn_{m_i} - Mn_{a_i}| \quad (44)$$

$$D_{Mx} = \frac{1}{N_c} \sum_{i=1}^{N_c} |Mx_{m_i} - Mx_{a_i}| \quad (45)$$

where subscripts m and a stand for manual and automated corneal localization methods respectively.

In summary, equation (44) calculates the average difference in between the minimum temperature obtained using automated method and the minimum temperature acquired using manual method on all corneas. Equation (45) instead calculates the average difference in between the maximum temperatures obtained using those two methods.

4.5. PERFORMANCE EVALUATION

The performance of the automated cornea localization method after eyelashes removal was compared against a manual measure to evaluate the feasibility of the proposed algorithm. Procedures in data collection is

similar to that detailed in chapter 3.1.1., however only thermal images of 67 subjects aged 14 to 68 are evaluated in this chapter (see [Table 4.1](#)). Manual corneal localization was carried out using a built-in software IRBIS plus 2.2 provided by Jenoptik. In the software, ocular thermal image was displayed in RGB colors, and a circle was drawn to approximately delineate the cornea and avoid the inclusion of eyelashes as much as possible (Acharya, et al. 2008). Average, minimum, maximum and spanning temperature within the circular region are evaluated using the software as shown in [Figure 4.8](#).

FIGURE 4.8: MANUAL CORNEAL LOCALIZATION AND THE AUTOMATED CORNEAL LOCALIZATION ON A THERMOGRAM

TABLE 4.1: DETAILS ON SUBJECTS RECRUITED FOR THE PERFORMANCE EVALUATION

Age Group	Number of Subjects
Below 30	32
30 ~ 50	19
After 50	16
Total	67

The snake algorithm was found to achieve a success rate of 90% on corneal localization (a case was said 'success' when the localized cornea fell approximately on the corneal center, and the circle touched the upper and lower eyelid) (Tan, et al. 2009b). The parameters α and β in equation (21) were set to value of 1 and 2 to achieve the above results. These values were selected by trial and error, but the underlying rationales behind these settings were to prevent unnecessary extension or shrinkage of snake, and also to avoid snake to develop corner during its convergence, since the shape of the eye is pretty straightforward. And it was observed that, the parameter σ in equation (25) also had a significant effect on the localization outcome. When σ was set to a lower value, the snake was found easily trapped or disturbed by local minima; on the other hand, if the value of σ was large, the image would be over blurred and the snake would shrink into a smaller area than the palpebral fissure. By extensive searching, it was determined that a value of 10 for σ worked out the best.

As for the time complexity of the localization algorithm, in each iteration the snake algorithm took about 0.012s on a typical dual core computer, and generally it took approximately 15 iterations for the snake to reach its minimum. The genetic algorithm in average searched over 250

potential solutions to minimize the target tracing function; gradient vector flow field on the other hand was set to run 20 iterations, with each iteration costing about 0.42s. So in total, the localization algorithm used up approximately 53s to accurately delineate the eye.

Table 4.2 tabulates some basic statistical parameters evaluated using automated and manual corneal localizations. Average corneal temperature from both methods were close to each other: $34.01 \pm 0.64^{\circ}\text{C}$ for automated and $33.99 \pm 0.63^{\circ}\text{C}$ for manual localization. The dispersion of temperature within a single cornea is determined by the standard deviation. Both the automated and manual corneal localization methods gave similar results, although for the youngest subject group the automated method gave higher values as compared to manual measure, as observed in **Table 4.3**.

TABLE 4.2: BASIC STATISTICAL FINDINGS BY AUTOMATED AND MANUAL LOCALIZATIONS

Parameters	Automated	Manual
Average corneal surface temperature	$34.01 \pm 0.64^{\circ}\text{C}$	$33.99 \pm 0.63^{\circ}\text{C}$
Standard deviation in temperatures within localized cornea	$0.24 \pm 0.08^{\circ}\text{C}$	$0.24 \pm 0.10^{\circ}\text{C}$
Average interocular difference in corneal surface temperature	$0.22 \pm 0.21^{\circ}\text{C}$	$0.21 \pm 0.18^{\circ}\text{C}$

As there is no widely accepted population mean for ocular surface temperature, we did not perform hypothesis test on mean. Also, we did not consider the values obtained by manual measure as the population mean, hence no statistical test is performed against them. As a result, there would be no statistical analysis on confidence limits on the mean, and therefore no confidence interval and confidence level are reported. However, we did perform statistical analysis on the hypothesis $H_0: \mu_A - \mu_M = 0$ for all statistical results, where subscript A denotes automated method and subscript M for manual method. At the significance level of 95%, we failed to reject the hypothesis for all the statistical findings.

TABLE 4.3: DETAILED FINDINGS ON EACH AGE GROUP BY BOTH LOCALIZATIONS

Parameters	Age Groups	Automated	Manual
Average corneal surface temperature	Below 30	$34.19 \pm 0.66^{\circ}\text{C}$	$34.15 \pm 0.68^{\circ}\text{C}$
	30 ~ 50	$33.88 \pm 0.61^{\circ}\text{C}$	$33.88 \pm 0.58^{\circ}\text{C}$
	After 50	$33.82 \pm 0.51^{\circ}\text{C}$	$33.81 \pm 0.47^{\circ}\text{C}$
Standard deviation in temperatures within localized cornea (average)	Below 30	$0.24 \pm 0.08^{\circ}\text{C}$	$0.24 \pm 0.09^{\circ}\text{C}$
	30 ~ 50	$0.24 \pm 0.08^{\circ}\text{C}$	$0.25 \pm 0.01^{\circ}\text{C}$
	After 50	$0.23 \pm 0.05^{\circ}\text{C}$	$0.23 \pm 0.07^{\circ}\text{C}$
Average interocular difference in corneal surface temperature	Below 30	$0.23 \pm 0.21^{\circ}\text{C}$	$0.17 \pm 0.13^{\circ}\text{C}$
	30 ~ 50	$0.26 \pm 0.27^{\circ}\text{C}$	$0.25 \pm 0.19^{\circ}\text{C}$
	After 50	$0.23 \pm 0.1^{\circ}\text{C}$	$0.23 \pm 0.24^{\circ}\text{C}$

Figure 4.9 presents the histogram of average corneal surface temperature obtained by both automated and manual corneal localizations; for Figure 4.10 the histogram plots on average interocular difference in corneal surface temperature instead. Similar trends were observed between the two methods , as found in the Figure 4.9 and Figure 4.10.

FIGURE 4.9: HISTOGRAM OF AVERAGE CORNEAL SURFACE TEMPERATURE VERSUS NUMBER OF CORNEAS ON METHODS OF (a) AUTOMATED AND (b) MANUAL CORNEAL LOCALIZATION.

Figure 4.11 plots the average corneal surface temperature against age for the two methods. Both the obtained linear regressions showed a downward trend, i.e. average corneal surface temperature decreased as age of subject increased, although the correlations were not significant ($R^2=0.08$ and $R^2=0.07$ respectively for automated and manual methods).

The ocular localizing algorithm was reported to deliver a 90% of rate of success (Tan, et al. 2008, Tan, et al. 2009b). In most cases this automated algorithm (including localization of eye, also removal of eye lashes and thermogram analysis) took less than 2 minutes (on a PC having Intel core duo) to complete the analysis. The proposed target tracing

function (equation (33)) has enabled fully automation in localization without the need of any human intervention for the snake's initialization and the subsequent monitor on its convergence, which are often required in many other snake applications.

FIGURE 4.10: HISTOGRAM OF INTEROCULAR DIFFERENCE (LEFT-RIGHT) IN CORNEAL SURFACE TEMPERATURE VERSUS NUMBER OF SUBJECTS ON METHODS OF (a) AUTOMATED AND (b) MANUAL CORNEAL LOCALIZATION.

From Table 4.2 and Table 4.3, we can see that both the findings by manual and automated measures agree well with each other methods. Consider the normalized root mean squared error (NRMSE) between the

corneal surface temperature obtained by manual and automated methods, according to

$$NRMSE = \sqrt{\frac{\sum_{i=1}^{N_c} (T_{m_i} - T_{a_i})^2}{\sum_{i=1}^{N_c} T_{m_i}^2}} \times 100 = 0.46\%$$

Where T_{m_i} denote the i th corneal surface temperature obtained manual method; T_{a_i} denote the i th corneal surface temperature acquired by automated method. The low NRMSE value suggests our proposed automated algorithm could be used as a substitution for the manual method in the investigation of ocular surface temperature. Besides, this automated algorithm could also be explored for applications such as computer-based diagnostic tool for early detection of ocular diseases.

FIGURE 4.11: AVERAGE CORNEAL SURFACE TEMPERATURE VERSUS AGE ON BOTH CORNEAL LOCALIZATION METHODS.

The eyelashes were removed in thermal images, although its effect was not apparent in Table 4.2 and Table 4.3, nor in Figure 4.9 to Figure 4.11. But it is possible to see its importance by equations (44) and (45). D_{Mn} was calculated to be 0.62, and 0.18 for D_{Mx} , which implied that similar maximum temperatures were obtained by the two methods. But the 0.62 in D_{Mn} indicates that, the removal of eyelashes has avoided substantially cooler temperatures due to eyelashes to be taken in as part of the corneal surface temperature.

The mean ocular surface temperature was determined to be 34.01°C in this chapter, 0.79°C lower than the reported mean by Mapstone on 70 subjects (Mapstone 1968c). It is also 0.29°C cooler compared to the

temperature at geometric centre of cornea determined by Efron et al. (Efron, et al. 1989). Girardin et al. reported average corneal surface temperature of 33.7°C on 266 subjects, but how they defined corneal surface temperature was not mentioned (Girardin, et al. 2007). Exact temperature measurement at limbus was not performed in this chapter, instead, the standard deviation in temperature within the localized cornea was provided to give an idea on the degree of temperature dispersion over the region of interest (it is 0.24°C). The average interocular difference in corneal surface temperature is 0.22°C. And there were 3% subjects having the above difference exceeding 0.75°C, which was similar to the previous reported result (Morgan, et al. 1993).

Corneal surface temperature reduces as the age increases (Alio, et al. 1982a), although age was said not a good predictor of central corneal surface temperature (Morgan, et al. 1999b). In present work no significant correlation was observed in between corneal surface temperature and age, which agrees well with the finding by Morgan et al (Morgan, et al. 1999b).

CHAPTER 5. EVALUATION OF TEAR EVAPORATION

Evaporation of tear from ocular surface is one of the major topics often studied in tear dynamics. The primary motivation behind investigations was to improve understanding on dry eye, an ocular disease that has affected a number of elder adults. For women age between 35 and 60, almost half of them had occasional dry eye symptoms; 10 to 15% of elder population was affected by this disease (McMonnies, et al. 1987, Bjerrum 1997, Schein, et al. 1997, Caffery, et al. 1998, McCarty, et al. 1998, Mathers, et al. 2002). Diagnosis of this abnormality is mainly achieved by tests such as tear break-up time, Schirmer's test or ocular surface staining. However, they are at times unreliable and invasive (Tan, et al. 2009a).

The rate of tear evaporation in general is determined to be higher in patients suffering from dry eye disease, although it is not consistent among literature in regard to the above finding (Mathers 2004). It was suggested that such disagreement among reports may be due to the selection of subject rather than physiology, measurement techniques or instrumentation (Mathers 2004). Furthermore, the reported values on the

rate of tear evaporation for both normal and dry eye subjects are also incongruent between existing studies.

The tear evaporation measurement was first performed on rabbits using a chamber fixed around their corneas (Von Bahr 1941), and the evaporative rate was found to be $41.6 \times 10^{-7} gcm^{-2}s^{-1}$. Two other similar studies were performed (Mishima, et al. 1961, Iwata, et al. 1969), which gave the values of $7.8 \times 10^{-7} gcm^{-2}s^{-1}$ (Mishima, et al. 1961) and $10.1 \times 10^{-7} gcm^{-2}s^{-1}$ (Iwata, et al. 1969) respectively. For evaporation in normal human eye, in vivo measurement was at first conducted by Hamano et. al. (Hamano, et al. 1980), and followed by Rolando and Refojo, whose instruments set-up consisted of a tightly fitted goggle with its chamber pumped with dry air (Rolando, et al. 1983b, Mathers 2004). The reported values were $26.9 \times 10^{-7} gcm^{-2}s^{-1}$ for Hamano et. al. and $4.07 \times 10^{-7} gcm^{-2}s^{-1}$ for the other research group (Rolando, et al. 1983b).

The devices developed in the above mentioned investigations had shortcomings. The modified tightly-fitted goggle of Rolando and Refojo was unable to evaluate evaporation at a specific relative humidity and temperature (Mathers 2004). In addition, petroleum jelly was used to

cover skin enclosed within the goggle, in the attempt to reduce skin-contributed evaporation (Rolando, et al. 1983b).

Techniques of evaporation measurement were enhanced in a number of investigations performed during the 90s of the last century. The rate of evaporation in several studies was approximated in the following fashion. Evaporation of tear was recorded twice, or the recording and analysis was made of two parts: one while eyes opened (blinking allowed) and another while the eyes closed (continuously). The rationale behind these arrangements was to eliminate contribution to the detected evaporation from skin area enclosed by the closed chamber, which can be a goggle, an eye cup or etc. This method was first carried out by Tsubota and Yamada who reported a value of 16.2×10^{-7} in the unit gs^{-1} for normal subject (Tsubota, et al. 1992). Tomlinson et al. investigated tear evaporation by employing servomed evaporimeter, reporting values ranging from $2.7 \times 10^{-7} \sim 19.4 \times 10^{-7} gcm^{-2}s^{-1}$ (Tomlinson, et al. 1991). They took first set of 30 readings at 2s interval with subject's eye closed, followed by 5 sets of 30 readings at the same interval with eye open. Mathers et al. measured water evaporation from skin and eyelid (eye closed) for a 2-minute period, and proceeded to measure tear evaporation

with eyes open and blinking allowed (Mathers, et al. 1993a). The final corrected tear evaporation was obtained by subtracting the value with eye closed from the value with eye open. They reported $14.7 \times 10^{-7} gcm^{-2}s^{-1}$ for normal evaporation. Recently, Goto et al. recorded tear evaporation using a evaporimeter with greater responsivity. The measurement is made based on the changes in frequency shift due to relative humidity change (Goto, et al. 2003), and one set of measurement is acquired on the subject's eye closed, and another on the subject's eye open with natural blinking allowed. The final rate is calculated by subtraction between the value obtained while the eye opens and the eye closed.

Besides the above investigations, there were also estimations on tear evaporation derived from the measurement of tear flow using fluorophotometry or other devices. The estimated values in those studies fall in the range of $10 \times 10^{-7} \sim 40 \times 10^{-7} gcm^{-2}s^{-1}$ (Mathers 2004), around 10% of the tear produced (Mathers, et al. 1993a). In another study, the evaporation rate was determined to be $14.7 \times 10^{-7} mg cm^{-2}h^{-1}$ (Adler, et al. 1970), or equivalently $100Wm^{-2}$ (the power loss per area) (Scott 1988).

In this chapter we propose a novel technique to measure tear evaporation based on dynamic/functional infrared (IR) thermography. So far ocular thermal image or thermographic recording/sequence has not been used to estimate tear evaporation, although there were several investigations by thermography on dry eye. Craig et al. has determined that temperature variation factor and mean osmolality of dry eye patients were higher compared to normal subjects (Craig, et al. 2000) and central corneal temperature was inversely correlated to temperature variation factor (Craig, et al. 2000). Also, there were attempts in modeling the changes in corneal surface temperature after an eye opens, in the form of $T(t) = (T_o - T_\infty)e^{-kt} + T_\infty$, and further utilized to diagnose dry (Tan, et al. 2009a).

We determine the tear evaporation based on the first law of thermodynamics using the OST. At the ocular surface, the heat exchange in that region consists of 5 components: heat loss due to convection, radiation, tear evaporation, the heat produced/absorbed by the ocular surface (the control volume) and the inflow of heat from human body through eyeball. If thermal properties at ocular surface are known, it is possible to determine the heat loss due to convection, radiation and the

heat produced/absorbed by the control volume. Furthermore, the inflow of heat can be estimated based on a 3D model developed for finite element analysis (Ng, et al. 2007), given the body temperature and the ambient temperature. With these values in hand, we can determine the tear evaporation across the entire eye, and monitor its variation with respect to time.

5.1. DATA ACQUISITION

Ocular thermographic sequence of normal subjects aged 17 to 70 years old were recorded in this study, as summarized in [Table 5.1](#). Participants were asked to relax for 10 minutes before recording. Subjects who suffer eye disease, poor in health, or have a history of serious eye disease were excluded. Participants were not allowed to consume hot drink, rub their eye or apply tear drop 20 minutes before the recording of sequence.

TABLE 5.1: DETAILS ON RECRUITED SUBJECTS

	No. of subjects	(Age) Mean $\pm$ Std
Age below 35	30	18.9 $\pm$ 0.8
Age above 35	30	47 $\pm$ 8.4
	60	33 $\pm$ 15.3

Infrared thermographic sequence was acquired using the same instrument detailed in chapter 3.1.1. Environment conditions of the room such as humidity, air flow and temperature were maintained. The room temperature was controlled at 22.5 ± 1 °C, and humidity at $70 \pm 4\%$. In each sequence, 25 sequential shots were taken for one second and such recording was carried out for 20 seconds. Four sequences were acquired for each subject: two for right eye and another two for the left. These sequences were stored in *irbis* format and exported to *jpeg* format using post-processing software installed with the camera for further processing.

The data was collected at Biomedical Centre, Ngee Ann Polytechnic, Singapore, and all the instrumental setup, environmental control and data collecting procedures performed followed the recommended guidelines laid out in the journal papers by Ring et. al. and relevant ISO standards (Ring 1998, ISO 2008, 2009, Ring, et al. 2010).

5.2. METHODS ON EVALUATION OF TEAR EVAPORATION

In this proposed algorithm, every image in a thermographic recording is warped to an image in which the region of interest is transformed to a standard form and size. Such procedure allows the algorithm to approximate the corneal and sclera region, also to compare

ocular surface data of various ocular sizes on a common basis. Temperature data within region of interest is read and calculation is performed, using the first law of thermodynamics, to determine the tear evaporation rate of an eye.

5.2.1. IMAGE WARPING

Generally, there are two approaches available for image warping: forward mapping and reverse mapping (Wolberg 1990). The former approach goes through source image pixel by pixel, and puts them into appropriate locations on destination image; while the latter scans through destination image pixel by pixel, and samples the relevant pixels of source image (Beier, et al. 1992). The method adopted in this studies was proposed by Beier and Neely (Beier, et al. 1992), using reverse mapping. The warping algorithm starts with a number pairs of lines defined on a source image ($Q'_{q_{i+1}} Q'_{q_i}$) and its corresponding destination image ($Q_{q_i} Q_{q_{i+1}}$). For each line $Q_{q_i} Q_{q_{i+1}}$,

$$u = \frac{(D - Q_{q_i}) \cdot (Q_{q_{i+1}} - Q_{q_i})}{\|Q_{q_{i+1}} - Q_{q_i}\|^2} \quad (46)$$

$$\mathbf{v} = \frac{(\mathbf{D} - \mathbf{Q}_{q_i}) \cdot \text{perpendicular}(\mathbf{Q}_{q_{i+1}} - \mathbf{Q}_{q_i})}{\|\mathbf{Q}_{q_{i+1}} - \mathbf{Q}_{q_i}\|} \quad (47)$$

$$\mathbf{D}' = \mathbf{Q}'_{q_i} + \mathbf{u} \cdot (\mathbf{Q}'_{q_{i+1}} - \mathbf{Q}'_{q_i}) + \frac{\mathbf{v} \cdot \text{perpendicular}(\mathbf{Q}'_{q_{i+1}} - \mathbf{Q}'_{q_i})}{\|\mathbf{Q}'_{q_{i+1}} - \mathbf{Q}'_{q_i}\|} \quad (48)$$

Where $\mathbf{D}$ and $\mathbf{D}'$ are coordinates of destination image pixel and source image pixel respectively, as illustrated in [Figure 5.1](#). $\text{perpendicular}()$ gives the vector perpendicular to and equal to the input vector. Then on the case of multiline, the algorithm is as follow:

For each pixel $\mathbf{D}$ in destination image

DSUM = 0

weightsum = 0

For each line $\mathbf{Q}_{q_i} \mathbf{Q}_{q_{i+1}}$

Get $\mathbf{u}, \mathbf{v}$ determined on $\mathbf{Q}_{q_i} \mathbf{Q}_{q_{i+1}}$

Get $\mathbf{D}'_{q_i}$

Calculate $\mathbf{Ds}_{q_i} = \mathbf{D}'_{q_i} - \mathbf{D}$

dist = *shortest distance from $\mathbf{D}$ to $\mathbf{Q}_{q_i} \mathbf{Q}_{q_{i+1}}$*

$$\mathbf{weight} = \left(\frac{\|\mathbf{Q}_{q_i} \mathbf{Q}_{q_{i+1}}\|^{c_1}}{(c_2 + \mathbf{dist})} \right)^{c_3}$$

$$\mathbf{DSUM} += \mathbf{Ds}_{q_i} \cdot \mathbf{weight}$$

$$\mathbf{weightsum} += \mathbf{weight}$$

$$\mathbf{D}' = \mathbf{D}_{q_i} + \mathbf{DSUM} / \mathbf{weightsum}$$

$$\mathbf{destinationImage}(\mathbf{D}) = \mathbf{sourceImage}(\mathbf{D}')$$

The shortest distance from $\mathbf{D}$ to $\mathbf{Q}_{q_i} \mathbf{Q}_{q_{i+1}}$ is $\mathbf{abs}(v)$ if $0 < \mathbf{u} < 1$; if $\mathbf{u} \leq 0$, that value equals to the straight-line distance between $\mathbf{D}$ and $\mathbf{Q}_{q_i}$; if $\mathbf{u} \geq 1$, it is equal to the straight-line distance between $\mathbf{D}$ and $\mathbf{Q}_{q_{i+1}}$, and is illustrated in [Figure 5.2](#).

FIGURE 5.1: ILLUSTRATION ON A SINGLE LINE PAIR BETWEEN SOURCE IMAGE
AND DESTINATION IMAGE

In our application, from the first thermogram of any length of sequence we determine eight points, which form eight lines that approximately encloses the entire eye, as illustrated in Figure 5.3. Four points Q'_1 , Q'_3 , Q'_5 and Q'_7 are to be determined at first, as seen in Figure 5.3(a); these points correspond to the medial canthus, middle upper edge, lateral canthus and middle lower edge of a left eye (similarly, these points correspond to the lateral canthus, middle upper edge, medial canthus and middle lower edge of a right eye). Then Q'_2 falls on the location somewhere middle in between Q'_1 and Q'_3 along the edge of an eye. Similar principle applies to Q'_4 , Q'_6 and Q'_8 (Figure 5.3(a)). For the corresponding points and lines in destination image, they are illustrated in Figure 5.3(b). The destination image has a size of 75 x 150 pixels.

FIGURE 5.2: THREE CASES ON THE SHORTEST DISTANCE FROM D to $Q_{q_i} Q_{q_{i+1}}$

After warping, temperature values within the region enclosed by Q_1 to Q_8 will be acquired for the calculation of tear evaporation.

FIGURE 5.3: POINTS AND LINES IN SOURCE AND DESTINATION IMAGE DEFINED IN THIS APPLICATION. (a) Q'_1 , Q'_3 , Q'_5 AND Q'_7 ARE FIRST DETERMINED, AND DOTTED BROWN LINES CONNECTING THESE POINTS APPEAR AFTER THE POINTS SELECTION TO FACILITATE THE DETERMINATION OF POINTS Q'_2 , Q'_4 , Q'_6 AND Q'_8 . (b) THE PIXEL LOCATION IN EACH POINT IS IN THE FORM OF (I, J).

5.2.2. TEAR EVAPORATION

Previous investigations have indicated that, the temperature values recorded in ocular thermogram are of tear film (Tan, et al. 2009a), which mainly consists of three layers: an outer lipid layer, middle aqueous layer and mucous layer (illustrated in Figure 4). It has a thickness of around 7 to 10 μm , in which aqueous layer accounts for 90% thickness (Remington 2004); lipid layer is approximately 100 nm thick (Craig, et al. 1997). However, in literature it is a common practice to regard those temperature captured in ocular thermogram as the temperature of corneal and conjunctival surface. In this work we consider the temperatures recorded in ocular thermography as corneal and conjunctival surface temperature, and derive respective equations by setting the region as the control volume of interest.

FIGURE 5.4: TEAR FILM LAYER AND THE CONTROL VOLUME OF INTEREST

Consider a small-piece element on the corneal or conjunctival epithelium with an area of dA , as illustrated in [Figure 5.5](#). When an eye opens after a blink, from the first law of thermodynamics, during a short period of time $\Delta t = t_2 - t_1$, on that element we get

$$\left(Q_{in} + W_{in} + \sum m_i h_i\right) - \left(Q_{out} + W_{out} + \sum m_e h_e\right) = m C_p (T_2 - T_1)$$

(49)

FIGURE 5.5: THE CONTROL VOLUME AND THE HEAT LOSS PRESENT IN EACH ELEMENT

And there are three types of heat losses occurring on the small-piece control volume within the inter-blink period: tear evaporation, convective and radiative heat transfer. The element has a thickness of $d = d_2 - d_1$ such that it satisfies both of the following conditions:

$$T(x, y, t, d_2) \approx T(x, y, t, d_1) \approx T(x, y, t)$$

$$mC_p(T_2 - T_1) \approx 0 \quad \text{or} \quad mC_p(T_2 - T_1) \text{ is negligible in calculation}$$

(50)

T_2, T_1 are element temperature at time t_2, t_1 respectively. The conditions stated in (50) require the thickness of the element to be very fine and the $T_2 - T_1$ to be small, so that $mC_p(T_2 - T_1)$ can be considered negligible when compared to the other values in the left hand side of equation (49). If we consider the thickness d to be about the thickness of lipid layer, which is around 100nm or less than that, the conditions can be comfortably satisfied (see [Appendix II](#)). Moreover, ocular surface temperature fluctuates over a very narrow range during inter-blink period, hence during a short time period Δt the net change in internal energy is in fact negligible. Since $\sum m_i h_i = 0, \sum m_e h_e \rightarrow$ tear evaporation, no work on the system and by the system, i.e. $W_{in} = W_{out} = 0$, from these we can get

$$\begin{aligned} \int_{t_1}^{t_2} \ddot{q}(x, y, t) dA dt - \int_{t_1}^{t_2} h_{amb} [T(x, y, t) - T_{amb}] dA dt \\ - \int_{t_1}^{t_2} \sigma_s \varepsilon [T(x, y, t)^4 - T_{amb}^4] dA dt - \int_{t_1}^{t_2} E(x, y, t) dA dt = 0 \end{aligned} \quad (51)$$

Where h_{amb} is the convection coefficient in ambient environment for ocular surface, and its value is $10 W m^{-2} K^{-1}$ (Emery, et al. 1975). ε is emissivity, 0.975 for cornea (Ng, et al. 2007) and ocular surface; σ_s is Stefan Boltzmann constant ($5.67 \times 10^{-8} W m^{-2} K^{-4}$). $T(x, y, t)$ is the ocular

surface temperature at the location of (x, y) (the coordinates definition is in line with **Figure 5.3(a)**) and T_{amb} is the ambient temperature, which remains constant. $E(x, y, t)$ is the rate of tear evaporation in energy form. Then the total amount of heat transferred out of the entire anterior surface during that period is

$$Q_{out} = \int_{t_1}^{t_2} \left\{ h_{amb} \int_S [T(x, y, t) - T_{amb}] dA + \sigma_s \varepsilon \int_S [T(x, y, t)^4 - T_{amb}^4] dA \right\} dt + \int_{t_1}^{t_2} \int_S E(x, y, t) dA dt \quad (52)$$

Where S is the total ocular surface area. And

$$Q_{in} = \int_{t_1}^{t_2} \int_S \ddot{q}(x, y, t) dA dt$$

Where $\ddot{q}(x, y, t)$ is heat flux, get

$$\begin{aligned}
& \int_{t_1}^{t_2} \int_S \ddot{q}(x, y, t) dA dt \\
& - \int_{t_1}^{t_2} \left\{ h_{amb} \int_S [T(x, y, t) - T_{amb}] dA \right. \\
& \left. + \sigma_s \varepsilon \int_S [T(x, y, t)^4 - T_{amb}^4] dA \right\} dt - \int_{t_1}^{t_2} \int_S E(x, y, t) dA dt \\
& = 0
\end{aligned}$$

Rearrange,

$$\begin{aligned}
& \int_{t_1}^{t_2} \int_S E(x, y, t) dA dt \\
& = \int_{t_1}^{t_2} \int_S \ddot{q}(x, y, t) dA dt \\
& - \int_{t_1}^{t_2} \left\{ h_{amb} \int_S [T(x, y, t) - T_{amb}] dA \right. \\
& \left. + \sigma_s \varepsilon \int_S [T(x, y, t)^4 - T_{amb}^4] dA \right\} dt
\end{aligned} \tag{53}$$

Divide the above equation by $S\Delta t$ and let

$$\mathbf{E}_{12} = \int_{t_1}^{t_2} \int_S E(x, y, t) dA dt / S\Delta t$$

$$\begin{aligned}
& \mathbf{L}_{12} \\
& = \int_{t_1}^{t_2} \left\{ h_{amb} \int_S [T(x, y, t) - T_{amb}] dA + \sigma_s \varepsilon \int_S [T(x, y, t)^4 - T_{amb}^4] dA \right\} dt / S\Delta t
\end{aligned}$$

$$\mathbf{Q}_{12} = \int_{t_1}^{t_2} \int_S \ddot{q}(x, y, t) dA dt / S \Delta t$$

Then

$$\mathbf{E}_{12} = \mathbf{Q}_{12} - \mathbf{L}_{12} \quad (54)$$

Where $\mathbf{E}_{12}$, $\mathbf{Q}_{12}$, $\mathbf{L}_{12}$ are the mean tear evaporation rate, mean heat flux (into an element), mean heat loss (due to convection and radiation) across the anterior ocular surface during the time period $\Delta t = t_2 - t_1$.

In thermogram, the temperature of a point can be regarded as the temperature of an element, therefore in discrete form,

$$\begin{aligned} & \left\{ h_{amb} \int_S [T(x, y, t) - T_{amb}] dA + \sigma_s \varepsilon \int_S [T(x, y, t)^4 - T_{amb}^4] dA \right\} / S \\ & \approx \left\{ h_{amb} \sum_i \sum_j [T(i, j, t) - T_{amb}] dA + \sigma_s \varepsilon \sum_i \sum_j [T(i, j, t)^4 - T_{amb}^4] dA \right\} / n_p dA \\ & \approx \left\{ h_{amb} \sum_i \sum_j [T(i, j, t) - T_{amb}] + \sigma_s \varepsilon \sum_i \sum_j [T(i, j, t)^4 - T_{amb}^4] \right\} / n_p \end{aligned} \quad (55)$$

Where n_p is the number of points pertained to anterior ocular surface, and $S = n_p \cdot dA$. With (55), $\mathbf{L}_{12}$ can be approximated using trapezoidal rule

L₁₂

$$\begin{aligned}
&= \int_{t_1}^{t_2} \left\{ h_{amb} \int_S [T(x, y, t) - T_{amb}] dA + \sigma_s \varepsilon \int_S [T(x, y, t)^4 - T_{amb}^4] dA \right\} dt / S \Delta t \\
&\approx \frac{1}{\Delta t \cdot n_p} \\
&\cdot \frac{1}{2} \left[\left\{ h_{amb} \sum_i \sum_j [T(i, j, t_1) - T_{amb}] + \sigma_s \varepsilon \sum_i \sum_j [T(i, j, t_1)^4 - T_{amb}^4] \right\} \right. \\
&\quad \left. + \left\{ h_{amb} \sum_i \sum_j [T(i, j, t_2) - T_{amb}] + \sigma_s \varepsilon \sum_i \sum_j [T(i, j, t_2)^4 - T_{amb}^4] \right\} \right] \Delta t \\
&\approx \frac{1}{2n_p} \left[\left\{ h_{amb} \sum_i \sum_j [T(i, j, t_1) - T_{amb}] + \sigma_s \varepsilon \sum_i \sum_j [T(i, j, t_1)^4 - T_{amb}^4] \right\} \right. \\
&\quad \left. + \left\{ h_{amb} \sum_i \sum_j [T(i, j, t_2) - T_{amb}] + \sigma_s \varepsilon \sum_i \sum_j [T(i, j, t_2)^4 - T_{amb}^4] \right\} \right] \\
&\hspace{15em} (56)
\end{aligned}$$

Human being maintains body temperature by homeostatic regulation, and generates heat to preserve the level of body temperature, especially as the external environment is much cooler than their core body temperature. In other words, human body produces heat in response to ambient temperature, hence the amount of heat generated is mainly

dependent on the external temperature. For human eye, ocular globe is constantly warmed primarily by ocular blood flow and several tissues' metabolism. The amount of heat brought to the ocular globe through blood flow and metabolism (and hence the heat transferred out to the external environment) is likely to remain constant, as long as there are no major changes in internal and external environment and no presence of other stimulants (this assumes the subject has adapted to the environment, staying there for sometime, i.e. thermal equivalent with steady state condition). Under this condition, the heat is flowing uniformly across the entire ocular globe, and the total heat transferred into the cornea over time can be taken as constant, i.e.

$$\mathbf{Q} = \mathbf{Q}_{12} = \mathbf{Q}_{23} = \mathbf{Q}_{34} = \dots = \text{constant} \quad (57)$$

And the rate of heat transferred into the entire anterior surface can be given by

$$\mathbf{Q} \cdot S = \int_{\Delta t} \int_S \ddot{q}(x, y, t) dA dt / \Delta t = \frac{1}{R} \{T_b - T_{amb}\} \quad (58)$$

Where T_b is the body temperature. Since body temperature remains fairly constant over a period of time, the heat transferred into the control volume can be conceived as a heat flow from core body to the control volume, passing through a number of tissues. The conductivity is not the same in most of the tissues, and some convection may play a role in the heat flow to control volume. However, all of these transfer of heat can be lumped into a single formula as illustrated above, which is an analogy to $I = \frac{\Delta V}{R}$. $\bar{R}$ is the total mean thermal resistance, which denotes the total resistance in the above heat transfer. The product of the thermal resistance and ocular surface area, which in simplicity is the inverse of overall heat transfer coefficient, is assumed to be fairly constant in different subjects, since

$$R \cdot A_r = \frac{L}{K_{tc} A_r} \cdot A_r = \frac{1}{U}$$

Where L, A_r, K_{tc} , are the length, heat transfer area, and thermal conductivities of an object of interest. U is the overall heat transfer coefficient (detailed explanation can be located in (Cengel 1996)). It is more useful to determine the heat flux, as ultimately we are interested in tear evaporation rate per area, so

$$\mathbf{Q} = \frac{T_b - T_{amb}}{\bar{R} \cdot S} = \bar{\mathbf{h}}(T_b - T_{amb}) \quad (59)$$

Where $\bar{\mathbf{h}}$ is the mean heat transfer coefficient, which is not known.

Previous studies have reported a myriad of values on tear evaporation rate, mainly falling in $9Wm^{-2} \sim 100Wm^{-2}$ and none of these works reported OST, hence their result cannot be utilized to determine the value of $\bar{\mathbf{h}}$. However, we can determine the $\bar{\mathbf{h}}$ by referring to an ideal 3D ocular model, which was developed by Ng and Ooi (Ng, et al. 2007).

In the 3D model, the entire system is in steady-state, so the rate of heat transfer of both into and out of the system is time-independent at this stage, hence

$$\dot{Q}_{in} = \dot{Q}_{out}$$

Then equation (53) is reduced to

$$\begin{aligned} \int_S \ddot{q}(x, y) dA - h_{amb} \int_S [T(x, y) - T_{amb}] dA \\ - \sigma_s \varepsilon \int_S [T(x, y)^4 - T_{amb}^4] dA - \int_S E(x, y) dA = 0 \end{aligned} \quad (60)$$

Divide the above equation by S

$$\left[\int_S \ddot{q}(x, y) dA \right] / S - \left\{ h_{amb} \int_S [T(x, y) - T_{amb}] dA \right\} / S \\ - \left\{ \sigma_s \varepsilon \int_S [T(x, y)^4 - T_{amb}^4] dA \right\} / S - \left[\int_S E(x, y) dA \right] / S = 0$$

And

$$\left[\int_S \ddot{q}(x, y) dA \right] / S = \frac{T_b - T_{amb}}{R \cdot S} \approx \bar{h}(T_b - T_{amb}) \\ \left\{ h_{amb} \int_S [T(x, y) - T_{amb}] dA \right\} / S \\ \approx \left\{ h_{amb} \sum_i \sum_j [T(i, j) - T_{amb}] dA \right\} / n_p dA \\ \approx \frac{h_{amb}}{n_p} \sum_i \sum_j [T(i, j) - T_{amb}] \\ \left\{ \sigma_s \varepsilon \int_S [T(x, y)^4 - T_{amb}^4] dA \right\} / S \\ \approx \left\{ \sigma_s \varepsilon \sum_i \sum_j [T(i, j)^4 - T_{amb}^4] dA \right\} / n_p dA \\ \approx \frac{\sigma_s \varepsilon}{n_p} \sum_i \sum_j [T(i, j)^4 - T_{amb}^4] \\ \left[\int_S E(x, y) dA \right] / S \approx \left\{ \sum_i \sum_j E(i, j) dA \right\} / n_p dA \approx \frac{1}{n_p} \sum_i \sum_j E(i, j)$$

(61)

Rearrange and we get

$$\begin{aligned}
 \bar{h}(T_b - T_{amb}) &= \frac{h_{amb}}{n_p} \sum_i \sum_j [T(i, j) - T_{amb}] + \frac{\sigma_s \varepsilon}{n_p} \sum_i \sum_j [T(i, j)^4 - T_{amb}^4] \\
 &\quad + \frac{1}{n_p} \sum_i \sum_j E(i, j) \\
 \bar{h} &= \frac{1}{T_b - T_{amb}} \\
 &\quad \cdot \left\{ h_{amb} \left[\frac{\sum_i \sum_j T(i, j)}{n_p} - T_{amb} \right] + \sigma_s \varepsilon \left[\frac{\sum_i \sum_j T(i, j)^4}{n_p} - T_{amb}^4 \right] \right. \\
 &\quad \left. + \frac{1}{n_p} \sum_i \sum_j E(i, j) \right\}
 \end{aligned}
 \tag{62}$$

The central corneal temperature was determined to be 34.48°C (Ng, et al. 2007) in this study and limbus (which is 6.44mm from the geometric centre of cornea) was found 1.07°C lower than central corneal temperature, but no value on each $T(i, j)$ was provided.

FIGURE 5.6: OST DERIVED FROM THE IDEAL 3D OCULAR MODEL (UNIT IN °C)

Nevertheless, from the reported results, it is observed that the differences in temperature between a particular point on ocular surface and the corneal center form a paraboloid of revolution, which can be approximated by:

$$z = \frac{x^2}{a^2} + \frac{y^2}{b^2}$$

$a = b$ for paraboloid of revolution, then

$$z = \frac{x^2 + y^2}{a^2}$$

(63)

TABLE 5.2: DIFFERENCE IN TEMPERATURE BETWEEN CENTRAL CORNEAL TEMPERATURE AND POINT $x^2 + y^2$, EXTRACTED FROM (Ng, et al. 2007)

$x^2 + y^2$	z
0.001^2	0.01
0.00125^2	0.02
0.002^2	0.055
0.0025^2	0.09
0.003^2	0.14
0.0035^2	0.19
0.004^2	0.25
0.0045^2	0.34
0.005^2	0.445
0.0055^2	0.58
0.006^2	0.76
0.00644^2	1.07

Variable z stands for the temperature difference in between a particular point (x, y) and the corneal center (the coordinates defined on x - and y -axis in the above are in line with the coordinates defined in [Figure 5.3](#)). a and b are semi-major and semi-minor axis respectively. On limbus

region, $x^2 + y^2 = 0.00644^2 \text{ (m}^2\text{)}$ and $z = 1.07 \text{ (}^\circ\text{C)}$, and further values pair $(x^2 + y^2, z)$ can be interpolated from the paper's reported results, as tabulated in [Table 5.2](#). These values pairs form an overestimated system, which are solved using least square method and get

$$z = 20992(x^2 + y^2) \quad (64)$$

From the above equation, we derive [Figure 5.6](#) and obtain the mean OST over the entire eye, which is 35.31°C . Besides, the studies adopted a tear evaporation rate of 40 W m^{-2} in their simulation, so we know

$$\frac{1}{n_p} \sum_i \sum_j E(i, j) = 40 \text{ W m}^{-2}$$

$$\left[\sum_i \sum_j T(i, j) \right] / n_p = 35.31^\circ\text{C}$$

By calculation

$$h_{amb} \left[\frac{\sum_i \sum_j T(i, j)}{n_p} - T_{amb} \right] = 103.1$$

$$\sigma_s \varepsilon \left[\frac{\sum_i \sum_j T(i, j)^4}{n_p} - T_{amb}^4 \right] = 63.57$$

From (62),

$$\bar{h} = \frac{103.1 + 63.57 + 40}{37 - 25}$$

$$\bar{h} = 17.22 \text{ (K}^{-1}\text{Wm}^{-2}\text{)}$$

Together with (54), (57) and (59), we have

$$\mathbf{E}_{12} = 17.22(T_b - T_{amb}) - \mathbf{L}_{12}$$

And derive the following equation

$$\mathbf{E}_{t_k \rightarrow t_{k+1}} = 17.22(T_b - T_{amb}) - \mathbf{L}_{t_k \rightarrow t_{k+1}}$$

Where

$$\begin{aligned} \mathbf{L}_{t_k \rightarrow t_{k+1}} = \frac{1}{2n_p} & \left[\left\{ h_{amb} \sum_i \sum_j [T(i, j, t_k) - T_{amb}] \right. \right. \\ & + \sigma_s \varepsilon \sum_i \sum_j [T(i, j, t_k)^4 - T_{amb}^4] \Big\} \\ & + \left\{ h_{amb} \sum_i \sum_j [T(i, j, t_{k+1}) - T_{amb}] \right. \\ & + \sigma_s \varepsilon \sum_i \sum_j [T(i, j, t_{k+1})^4 - T_{amb}^4] \Big\} \Big] \end{aligned}$$

Finally, we get the average tear evaporation rate by

$$\mathbf{E}_{avg} = \frac{1}{n_t} \sum_{k=1}^{n_t} \mathbf{E}_{t_k \rightarrow t_{k+1}}$$

(65)

Besides, we can also acquire the tear evaporation rate on cornea and sclera:

$$\text{cor}\mathbf{E}_{t_k \rightarrow t_{k+1}} = \text{cor}\mathbf{Q}_{t_k \rightarrow t_{k+1}} - \text{cor}\mathbf{L}_{t_k \rightarrow t_{k+1}} \quad (66)$$

$$\text{scl}\mathbf{E}_{t_k \rightarrow t_{k+1}} = \text{scl}\mathbf{Q}_{t_k \rightarrow t_{k+1}} - \text{scl}\mathbf{L}_{t_k \rightarrow t_{k+1}} \quad (67)$$

Since the total heat transferred to the control volume is taken as constant, and the heat is considered uniformly flowing across the ocular globe, then

$$\text{cor}\mathbf{Q}_{t_k \rightarrow t_{k+1}} = \text{scl}\mathbf{Q}_{t_k \rightarrow t_{k+1}} = \mathbf{Q}_{t_k \rightarrow t_{k+1}} = \bar{h}(T_b - T_{amb})$$

For the mean heat loss for corneal region, it can be obtained by integrating the heat loss across the corneal area over the time Δt , and divided by the product of corneal area and time period Δt . The mean heat loss for sclera region can be calculated in similar way. Hence

$$\begin{aligned}
\mathbf{corL}_{t_k \rightarrow t_{k+1}} &= \frac{1}{2n_p} \left[\left\{ h_{amb} \sum_i \sum_j [T(i, j, t_k) - T_{amb}] \right. \right. \\
&\quad \left. \left. + \sigma_s \varepsilon \sum_i \sum_j [T(i, j, t_k)^4 - T_{amb}^4] \right\}_{cor} \right. \\
&\quad \left. + \left\{ h_{amb} \sum_i \sum_j [T(i, j, t_{k+1}) - T_{amb}] \right. \right. \\
&\quad \left. \left. + \sigma_s \varepsilon \sum_i \sum_j [T(i, j, t_{k+1})^4 - T_{amb}^4] \right\}_{cor} \right] \\
\\
\mathbf{sclL}_{t_k \rightarrow t_{k+1}} &= \frac{1}{2n_p} \left[\left\{ h_{amb} \sum_i \sum_j [T(i, j, t_k) - T_{amb}] \right. \right. \\
&\quad \left. \left. + \sigma_s \varepsilon \sum_i \sum_j [T(i, j, t_k)^4 - T_{amb}^4] \right\}_{scl} \right. \\
&\quad \left. + \left\{ h_{amb} \sum_i \sum_j [T(i, j, t_{k+1}) - T_{amb}] \right. \right. \\
&\quad \left. \left. + \sigma_s \varepsilon \sum_i \sum_j [T(i, j, t_{k+1})^4 - T_{amb}^4] \right\}_{scl} \right]
\end{aligned}
\tag{68}$$

Furthermore, for each element, from (51), we divide the equation by dA and Δt , then we can get the mean tear evaporation of that element during that period of time:

$$\begin{aligned}
& \frac{1}{dA \cdot \Delta t} \int_{t_1}^{t_2} E(x, y, t) dA dt \\
&= \frac{1}{dA \cdot \Delta t} \int_{t_1}^{t_2} \ddot{q}(x, y, t) dA dt \\
&\quad - \frac{1}{dA \cdot \Delta t} \int_{t_1}^{t_2} h_{amb} [T(x, y, t) - T_{amb}] dA dt \\
&\quad - \frac{1}{dA \cdot \Delta t} \int_{t_1}^{t_2} \sigma \varepsilon [T(x, y, t)^4 - T_{amb}^4] dA dt
\end{aligned}$$

Let

$$\begin{aligned}
{}_eE &= \frac{1}{dA \cdot \Delta t} \int_{t_1}^{t_2} E(x, y, t) dA dt \\
{}_eQ &= \frac{1}{dA \cdot \Delta t} \int_{t_1}^{t_2} \ddot{q}(x, y, t) dA dt \\
{}_eL &= \frac{1}{dA \cdot \Delta t} \int_{t_1}^{t_2} h_{amb} [T(x, y, t) - T_{amb}] dA dt \\
&\quad + \frac{1}{dA \cdot \Delta t} \int_{t_1}^{t_2} \sigma_s \varepsilon [T(x, y, t)^4 - T_{amb}^4] dA dt
\end{aligned}$$

Then

$${}_eE = {}_eQ - {}_eL \quad (69)$$

Where ${}_eE$ is the mean tear evaporation of that element during Δt .

From (69), we equate ${}_eQ$ to (59), and get the relative mean tear evaporation of that element:

$$r_e E = 17.22(T_b - T_{amb}) - eL \quad (70)$$

5.3. PRIMARY FINDINGS ON EVALUATION OF TEAR EVAPORATION

FIGURE 5.7: TEAR EVAPORATION OF A SUBJECT IN A PERIOD OF 20S

FIGURE 5.8: TEAR EVAPORATION RATES AT OCULAR SURFACE, CORNEAL AND SCLERA REGION. 'A' DENOTES THE GROUP IN WHICH SUBJECT AGES ABOVE 35, WHILE 'B' DENOTES THE GROUP WHERE SUBJECT AGES BELOW 35.

Figure 5.7 shows the variation in tear evaporation of a subject in a period of 20s. The main findings of our current investigations on different age groups are tabulated in Table 5.3. In that table, E_{avg} denotes the average tear evaporation rate at the ocular surface (including corneal and sclera region) during the recording period. Figure 5.8 demonstrates the distributions in values of tear evaporation at ocular surface, corneal and sclera region. For the group in which subject ages above 35, the value is 55.82Wm^{-2} and 58.9Wm^{-2} for the group aged below 35, though the difference is not statistically significant. However, the difference in the

average of corneal tear evaporation ${}_{\text{cor}}\mathbf{E}_{\text{avg}}$ between the two age groups is significant (58.1Wm^{-2} for age group above 35 and 61.94Wm^{-2} for age group below 35). The variation in evaporation rate at different time during the 20s period is captured in the terms ‘Standard deviation of $\mathbf{E}_{t_k \rightarrow t_{k+1}}$ ’ for the entire eye, ‘Standard deviation of ${}_{\text{cor}}\mathbf{E}_{t_k \rightarrow t_{k+1}}$ ’ and ‘Standard deviation of ${}_{\text{scl}}\mathbf{E}_{t_k \rightarrow t_{k+1}}$ ’ for corneal and sclera region. Among these terms, only the difference in sclera region is statistically significant.

FIGURE 5.9: $\mathbf{E}_{\text{avg}}$ VS BODY-AMBIENT TEMPERATURE DIFFERENCE ON AGE GROUP ABOVE 35

Figure 5.9 and Figure 5.10 illustrate the linear regressions between the $\mathbf{E}_{\text{avg}}$ and the body-ambient temperature difference on the two age groups. For age group above 35, the R^2 value is 0.14; the corresponding

value for the age group below 35 is 0.31. It seems the difference in body-ambient temperature plays a more important role in the determination of tear evaporation in younger subjects compared to the elder counterpart. Besides, on both groups, $\mathbf{E}_{avg}$ is observed to be positively correlated with the body-ambient temperature difference.

TABLE 5.3: MAIN RESULTS OF CURRENT STUDIES. THE UNIT FOR THE VALUES IS WM^{-2} EXCEPT THE NUMBER OF BLINKS.

	Below 35	Above 35	p
$\mathbf{E}_{avg}$	55.82±12.44	58.9±12.94	0.19
Standard deviation of $\mathbf{E}_{t_k \rightarrow t_{k+1}}$	1.14±0.55	1±0.65	0.2
$\text{cor}\mathbf{E}_{avg}$	58.1±12.66	61.94±13.08	0.11
Standard deviation of $\text{cor}\mathbf{E}_{t_k \rightarrow t_{k+1}}$	1.12±0.59	1.06±0.67	0.61
$\text{scl}\mathbf{E}_{avg}$	52.03±12.22	53.93±12.96	0.41
Standard deviation of $\text{scl}\mathbf{E}_{t_k \rightarrow t_{k+1}}$	1.31±0.69	1.06±0.85	0.08
$\min_k \mathbf{E}_{t_k \rightarrow t_{k+1}}$	53.03±12.06	56.54±12.87	0.13
$\max_k \mathbf{E}_{t_k \rightarrow t_{k+1}}$	58.8±12.91	61.18±13.23	0.32
The number of blinks in 20s	6.35±4.48	4.73±3.65	0.03

According to a study by Doughty, the rate of spontaneous eye-blinking for human being (primary gaze) is around 10 times per minutes (Doughty 2002). In other words, for a normal subject he/she blinks around 3.3 times in a period of 20s. Based on this, on each age group we further divide the subjects into two categories-----subjects who blinks more than 4 times as one category, those who blinks less than or equal to 4 times another category-----and perform another round of statistical analysis. The findings are tabulated in **Table 5.4**. In the age group below 35, it seems the number of blinks has relationships with the variation in tear evaporation at the regions of the whole eye ($\mathbf{E}_{t_k \rightarrow t_{k+1}}$), cornea ($\text{cor}\mathbf{E}_{t_k \rightarrow t_{k+1}}$) and sclera ($\text{scl}\mathbf{E}_{t_k \rightarrow t_{k+1}}$). However, for the age group above 35 the number of blinks has only a relationship with the variation in corneal tear evaporation.

FIGURE 5.10: E_{avg} VS BODY-AMBIENT TEMPERATURE DIFFERENCE ON AGE
GROUP BELOW 35

The relative mean tear evaporation of each element on the ocular surface at the first second after a subject blinked is shown in [Figure 5.11](#). From the illustration, it can be deduced that tear evaporation is likely to peak at the central cornea region.

TABLE 5.4: SOME STATISTICAL RESULTS ANALYZED BASED ON THE NUMBER OF BLINKING WITHIN 20-SECOND THERMOGRAPHIC RECORDING.

		No. of blinks > 4	No. of blinks $\leq$ 4	p
Age below 35	Standard deviation of $\mathbf{E}_{t_k \rightarrow t_{k+1}}$	1.25 $\pm$ 0.55	0.95 $\pm$ 0.53	0.04
	Standard deviation of $\text{cor}\mathbf{E}_{t_k \rightarrow t_{k+1}}$	1.24 $\pm$ 0.6	0.92 $\pm$ 0.53	0.04
	Standard deviation of $\text{scl}\mathbf{E}_{t_k \rightarrow t_{k+1}}$	1.43 $\pm$ 0.69	1.12 $\pm$ 0.68	0.1
Age above 35	Standard deviation of $\text{cor}\mathbf{E}_{t_k \rightarrow t_{k+1}}$	1.25 $\pm$ 0.73	0.93 $\pm$ 0.6	0.1

In this investigation, we have determined that for normal subjects the rate of tear evaporation in average is $57.36 \pm 12.73 \text{Wm}^{-2}$, or equivalently $25.38 \pm 5.63 \times 10^{-7} \text{gcm}^{-2} \text{s}^{-1}$ (assume the water latent heat of evaporation is 2260kJ kg^{-1}). This reported value falls in the range of $10 \times 10^{-7} \sim 40 \times 10^{-7} \text{gcm}^{-2} \text{s}^{-1}$, a range consolidated based on a number of investigations (Mathers 2004). The technique developed in this article approaches the estimation of tear evaporation from the thermodynamics

point of view, instead of on the basis of relative humidity measurement as in the conventional approaches.

FIGURE 5.11: IMAGE FORMED BASED ON THE RELATIVE MEAN TEAR EVAPORATION OF EACH ELEMENT (UNIT IN WM^{-2})

By functional IR thermography, we estimate tear evaporation on a sequence of thermal images. In frames where blinking happens, the corresponding thermal data is removed and not included in our analysis, as illustrated in [Figure 5.7](#). Together with the method of image warping discussed in section 3.1, investigators are provided with full control over the evaluation of tear evaporation, as they can easily exclude both the non-ocular region by properly selecting the region of interest, and also the moments where an eye blinks. Application of petroleum jelly on skin around the eye is not necessary, nor the two-part recording and the

elimination of the contribution to evaporation by the skin. In many studies, the final values on the rate of tear evaporation were estimated by subtracting the rate acquired with eye open and natural blinking allowed, from the rate obtained with eye fully closed. While an eye is closed, both the skin around the eye and eyelid evaporate. However, during the time an eye opens, eyelid is retracted and does not evaporate. Hence the subtraction in evaporation rate may underestimate the true value.

For most of the investigations in literature, a closed chamber is fixed around subject's eye in order to collect data on evaporation. In at least one of the studies the air inside the closed chamber was trapped within, allowing the humidity within to rise. In other words, there is no constant flow of dry air in and out of the closed chamber. Under this setup, the rise in humidity within the chamber in fact retards tear evaporation, and the values obtained may not truthfully represent the actual evaporation of tear under a normal, stable environment conditions. Furthermore, it is not sure if the application of closed chamber around an eye has any effect to the ocular physiologies.

Our proposed method has few weakness. In some cases, the presence of eyelashes at the ocular anterior surface slightly pushes up the rate

obtained than it should be. However, this issue can be resolved by applying eyelashes removal algorithm proposed by Tan et al. (Tan, et al. 2010c) and also, a better, refined 3D ocular model would give a better estimation on mean heat transfer coefficient $\bar{h}$, thus lead to a more accurate evaluation on evaporation. Nevertheless, our method does not have the above mentioned issues present in the conventional methods based on humidity measurement. Furthermore, our approach enables us to monitor the tear evaporation both in each inter-blink period, and the variation among a few inter-blink periods, or observes the differences arisen in different sort of eyeblink. The image generated based on the relative mean tear evaporation of each element provides an approximate but intuitive visualization to the evaporative conditions at ocular surface.

For human beings, tear film covers the ocular anterior surface, keeping it moist and functioning as a primary source of atmospheric oxygen for the cornea (Remington 2004). Its outmost lipid layer retards the evaporation of tear, if not according to an estimate, pure water at 34°C is to evaporate at the rate 170ml min^{-1} , which will immediately lead to dry eye (Mathers 2004). However, the lipid layer structure and its evaporation-retarding mechanism so far remain poorly understood

(Mathers 2004). Findings in previous literature suggested that, in the down-phase of blinking lipid layer is compressed and re-stretched (or reformed) in the up-phase of blinking. During the up-phase blinking, lipid layer moves up rapidly although it lags behind the movement of eyelid (which finishes its retraction in 300 ms), completes its traverse across the entire anterior surface in about 1 second (Bron, et al. 2004). This may explain the decrease in tear evaporation after an eye opens in some of our observations, which could also be seen in [Figure 5.7](#). Furthermore, although lipid layer remains stable and stationary after it completes its traverse across anterior surface (except when a subject changes its gaze position), there is still a continuous secretion and delivery of meibomian lipid to the layer, which explains the fluctuation in evaporation rate. Besides, as Benedetto has pointed out, forced blinking produces thicker lipid layer and pre-corneal tear film in compared to light or complete blinking (Benedetto, et al. 1984). Hence, the observed different evaporative patterns between several inter-blink intervals in our studies may be due to the variations in blinking duration or the degree of forcing.

In this study, tear evaporation of the entire anterior surface is found to be unaffected by age, in conformed to the finding by Craig (Craig 1995).

However, in the corneal region our investigation shows that, overall speaking tear evaporation is slightly higher in subjects aged above 35. Evaporative variation along time at sclera region (Standard deviation of $_{scl}E_{t_k \rightarrow t_{k+1}}$) for elder subjects, in contrast is smaller than their younger peers, and they also blink less compared to young adults.

Besides, the relationship between blink rates and tear evaporation was determined not significantly in our current investigations, which is in agreement with the study conducted previously by Tsubota and Nakamori (Tsubota, et al. 1995). Nevertheless, the evaporative variation along time differs significantly between the subgroup in which the subjects blink less and the other which blink more, especially for the younger adults. In the younger age group, it seems those who have a greater fluctuating magnitude in evaporation at both corneal and sclera region also blinks more (see [Table 5.4](#)). Craig and Tomlinson (Craig, et al. 1997) have observed some subjects who had poor tear stability but with normal evaporation rate. No restrictions of blinking were instructed in their experiment, and hence they explained, the subjects were able to maintain the lipid layer before it broke up by frequent blinking. Furthermore, normal involuntary blinking is said to be related to tear film stability (Yap

1991). The fluctuating magnitude in evaporation investigated in this report might be related with tear film stability, and thus if the rate of evaporation of a subject climbs too fast, which could be a sign of instability in tear film, then it would stimulate involuntary blinking of both eyes. This might especially be the case for corneal region, since the corresponding evaporative variation between the two subgroups differs significantly in both age groups.

The findings reported in this chapter indicate that it is possible to measure tear evaporation on a sequence of thermal images. The proposed method has no contact with any part of an eye, nor it places any devices around the eye. Repeated measurement is possible since it does not interfere with any part of the ocular surface. The data is easily captured and the procedure is simple. Once the thermographic sequence is recorded, the worker needs only to select the region of interest and the algorithm would generate all the relevant values and plots. Thermal data was captured at the rate of 25 frames per second in this experiment for the purpose of study, however, for daily diagnosis the frames rate could be captured at far lower value so that the handling time could be speed up to

meet hectic workload. This technique is likely to be handy for clinicians in assisting dry eye diagnosis.

CHAPTER 6. THE TOPOGRAPHICAL VARIATIONS IN OCULAR SURFACE TEMPERATURE

Ocular surface temperature and its determinants concern many other physiologies and research. The lower corneal surface temperature drives the flow in anterior chamber (Kumar, et al. 2006), and plays a part in the tear film thinning (Braun, et al. 2003). On meibomian lipid, its fluidity is dependent on the temperature of the ocular surface where the lipid layer sits on (Bron, et al. 2004). Modellers examine and refine their ocular models in accordance to reported corneal surface temperature (Ng, et al. 2007). Furthermore, warmer ocular surface under some circumstances is a manifestation of sick eye (Tan, et al. 2009a).

By infrared thermography, a number of correlations are determined between several ocular diseases and ocular surface temperature, such as dry eye, exophthalmos, glaucoma and etc (Tan, et al. 2009a). And there were attempts to diagnose ocular diseases such as retinoblastoma, vascular neuritis of optic nerve based solely on the temperature (Tan, et al. 2009a). Effects of acupuncture on dry eye, or even the outcome of some

glaucoma surgeries were examined from the ocular surface temperature point of view (Tan, et al. 2009a).

Despite these research, there are two issues remained scarcely touched on the ocular surface temperature. First, most of the studies in past focused mainly on corneal region, and their analytic methods remained relatively simple and incomprehensive. Ocular surface temperature has never been looked into as a whole, but only fragments of it. We believe in this problem, part of the obstacle lies in the indiscernible cornea-sclera boundary, and the myriad shapes of palpebral fissure. Second, aging effect and its corresponding topographical/spatial variation in ocular surface temperature are understudied in literature, which in some extent are the consequence of the above obstacle . Age is demonstrated to negatively correlate to the surface temperature in literature (Purslow, et al. 2005b), although there was also finding illustrating no relationship between them (Morgan, et al. 1993). And nothing more on aging effect is reported.

TABLE 6.1: DETAILS ON RECRUITED SUBJECTS: THE NUMBER OF SUBJECTS AND
THE MEAN AGE IN EACH GROUP

	No. of subjects	(Age) Mean $\pm$ Std
Young subjects	30	18.9 $\pm$ 0.8
Elder subjects	30	47 $\pm$ 8.4
Contact lens wearers	29	18.4 $\pm$ 1

Hence, in this chapter we attempt to look into these issues and provide satisfactory solutions to the problems. First, we record ocular thermographic sequences of the youth, the elderly and the contact lens wearer. The recording procedures follow the accounts in [Section 5.1](#), and the subjects' details are tabulated in [Table 6.1](#). Second, for each subject we warp the temperature data within the subject's palpebral fissure into a standard form, as detailed in [Section 5.2.1](#) and illustrated in [Figure 6.1](#). Such transformation promotes consistent analysis. Third, eyelashes are removed in every thermographic frame to prevent inclusion of unnecessary temperature in the latter analysis. After these steps we examine the aging effect and the topographical variations.

FIGURE 6.1: IMAGE METAMORPHOSIS: (a) BEFORE AND (b) AFTER. BOTH THE THERMAL IMAGES ARE DISPLAYED IN CONTOUR PLOT, WHICH GIVE VERY CLEAR ILLUSTRATION ON TEMPERATURE DISTRIBUTION.

6.1. REMOVAL OF EYELASHES

Let $I(i, j, f)$ denote a particular frame in a thermographic sequence in which blinking frames are removed, and the i and j refer to the spatial domain whereby f refers to the number of a particular frame. Consider the

thermographic sequence of interest has n_F of frames, and we further divide the sequence into a number of subsequences, for each subsequence it has n_{S_q} of frames (except the last subsequence if n_F/n_{S_q} is not an integer) and a differential image (Tan, et al. 2010b) is given by

$$^n I_{\epsilon}(i, j) = \frac{I_{\epsilon}(i, j) - \min I_{\epsilon}(i, j)}{\max I_{\epsilon}(i, j) - \min I_{\epsilon}(i, j)} \cdot 255 \quad (71)$$

and

$$I_{\epsilon}(i, j) = \frac{1}{n_{S_q}} \sum_{i_{\epsilon}} \frac{1}{1 + \|I(i, j, i_{\epsilon}) - I(i, j, i_{\epsilon} + i_{df})\|}, \quad i_{\epsilon} = f_{df}, f_{df} + 1, f_{df} + 2, \dots, n_{S_q} \quad (72)$$

where $\|\cdot\|$ denote absolute value and f_{df} denote the number of the beginning frame for the subsequence. As discussed and observed in previous study (Tan, et al. 2010b), in differential image the larger the variation in temperature of a site over a period of time, the darker the image pixel; and generally eyelashes temperature varies greater compared to ocular surface and orbital skin. Furthermore, the differential image has an image histogram showing approximately a bimodal distribution (with

image intensity level 255 excluded), and hence can be modeled by a Gaussian mixture

$$\phi(x[n]; \varepsilon) = (1 - \varepsilon)\phi_{signal}(X) + \varepsilon\phi_{noise}(X) \quad (73)$$

Where ε is the mixture parameter, and $0 < \varepsilon < 1$; ϕ_{signal} and ϕ_{noise} correspond to the Gaussian probability density functions of the non-eyelashes and eyelashes regions.

The Gaussian mixture parameter $\hat{\mu}_{signal}, \hat{\sigma}_{signal}, \hat{\mu}_{noise}, \hat{\sigma}_{noise}$ are estimated using Expectation-Maximization (EM) algorithm in this investigation, and the threshold is set to $\hat{\mu}_{signal} - 3\hat{\sigma}_{signal}$ to distinguish eyelashes from the rest of orbito-ocular region. Therefore on each differential image, pixels having image intensity level lower than the threshold are identified as eyelashes, and these pixels are given a new but very high intensity value (e.g., 1×10^6). After these, the differential image is warped according to the algorithm introduced in section 3.1, and in the resultant destination image eyelashes are manifested as pixels with image intensity level beyond value 255. For each thermal image within the subsequence, the eyelashes in their corresponding destination images are

marked according to the warped differential image, and temperature data on those pixels are excluded in later analysis (as illustrated in **Figure 6.2**).

FIGURE 6.2: REMOVAL OF EYELASHES (OCULAR THERMOGRAPHIC SEQUENCE)

6. 2. STATISTICAL ANALYSIS

Let $t_{i,j,f}$ denotes the temperature of a point (i,j) on the particular frame f in a warped thermographic sequence $T(i,j,f)$ in which blinking frames are removed, and the point (i,j) falls on the ocular surface and does not form any part of eyelashes in the frame f . By this the mean ocular surface temperature (OST) at the frame f is obtained by

$$\mu_{ocular}^f = \frac{1}{w_o n_f} \sum_{i,j} t_{i,j,f} \quad (74)$$

where $w_o n_f$ denote the total number of $t_{i,j,f}$ that meets the above definition. And the mean OST of the warped thermographic sequence is calculated by

$$\mu_{ocular} = \frac{1}{n_F} \sum_f \mu_{ocular}^f \quad (75)$$

The standard deviation of the OST at frame f is

$$\sigma_{ocular,f} = \sqrt{\frac{1}{w_o n_f} \sum_{i,j} (t_{i,j,f} - \mu_{ocular}^f)^2} \quad (76)$$

And the mean $\sigma_{ocular,f}$ over the warped thermographic sequence is

$$\mu_{\sigma_{ocular}} = \frac{1}{n_F} \sum_f \sigma_{ocular,f} \quad (77)$$

Similarly we determine μ_{cornea} , $\mu_{\sigma_{cornea}}$, μ_{sclera} , in the same spirit as equations (74), (75), (76), and (77) for corneal and sclera regions.

Besides the above statistics, we propose a statistic that takes into account of the factors body temperature and ambient temperature. Such

statistic, termed reductive ratio, is dimensionless and aims to provide an indication on how warm an ocular surface is in comparison to the population. Let T_b, T_{amb} denote body and ambient temperature respectively, the difference in temperature between a point (i, j) on the ocular surface at a particular frame f and the environment is

$$\Delta_{i,j,f-amb} = t_{i,j,f} - T_{amb} \quad (78)$$

Where $t_{i,j,f}$ meets the above definition. And we further denote

$$\Delta_{b-amb} = T_b - T_{amb} \quad (79)$$

As $\Delta_{b-amb} > \Delta_{i,j,f-amb}$, it can be said that there is a reduction in temperature difference from Δ_{b-amb} to $\Delta_{i,j,f-amb}$, so the reductive ratio in temperature of a point in the ocular surface at frame f is defined as

$$\rho_{i,j,f-r} = \frac{\Delta_{b-amb} - \Delta_{i,j,f-amb}}{\Delta_{b-amb}} = \frac{T_b - T_{amb} - (t_{i,j,f} - T_{amb})}{T_b - T_{amb}}$$

$$\rho_{i,j,f-r} = \frac{T_b - t_{i,j,f}}{T_b - T_{amb}} \quad (80)$$

Based on this, we get

$$\rho_{ocular-r}^f = \frac{1}{w_o n_{i,j}} \sum_{i,j} \rho_{i,j,f-r}$$
(81)

And

$$\rho_{ocular-r} = \frac{1}{n_F} \sum_f \rho_{ocular-r}^f$$
(82)

Where $\rho_{ocular-r}$ is the mean OST reductive ratio. Again, we can also determine $\rho_{cornea-r}$, $\rho_{sclera-r}$ in the same spirit as equations (80), (81), and (82) for corneal and sclera region.

Mathematically speaking, reductive ratio refers to the amount of reduction per °C difference in Δ_{b-amb} . By equation (80), we have transformed the concern of how warm an ocular surface is as compared to the population, into the problem asking what is the amount of reduction per °C difference in Δ_{b-amb} for the particular subject; and the lower the value, the warmer the surface appears to be.

6.3. PRIMARY FINDINGS

Table 6.2 illustrates some of the main findings in various subject groups, and the respective statistical significances are determined by ANOVA. Among these groups young subject had the warmest OST (μ_{ocular}), and contact lens wearer had the coolest. Similar pattern was also observed in the statistics mean corneal (μ_{cornea}) and sclera (μ_{sclera}) temperature. These observations were statistically significant. Besides, contact lens wearer was determined to have greater variation in OST ($\mu_{\sigma_{ocular}}$), followed by elder subject and their younger peer. The average number of blinks, ambient and body temperature of young and elder subject groups were tabulated in [Table 6.3](#).

TABLE 6.2: BASIC STATISTICS ON VARIOUS SUBJECT GROUPS

	Elder subjects	Young subjects	Contact lens wearers	p
μ_{ocular}	33.81±0.63°C	34.34±0.59°C	33.55±0.84°C	< 0.00001
$\mu_{\sigma_{ocular}}$	0.42±0.12°C	0.36±0.09°C	0.48±0.19°C	< 0.00001
μ_{cornea}	33.61±0.67°C	34.17±0.59°C	33.31±0.89°C	< 0.00001
$\mu_{\sigma_{cornea}}$	0.27±0.09°C	0.22±0.07°C	0.31±0.14°C	< 0.00001
μ_{sclera}	34.14±0.6°C	34.66±0.58°C	33.97±0.79°C	< 0.00001
$\rho_{ocular-r}$	0.1900±0.0562	0.1642±0.0508	0.2212±0.0607	< 0.00001
$\rho_{cornea-r}$	0.2047±0.0590	0.1763±0.0511	0.2381±0.0631	< 0.00001
$\rho_{sclera-r}$	0.1650±0.0528	0.1421±0.0507	0.1916±0.0585	< 0.00001

TABLE 6.3: THE AVERAGE NUMBER OF BLINKS, AMBIENT AND BODY TEMPERATURE OF YOUNG AND ELDER SUBJECT GROUPS

	Young subjects	Elder subjects	p
Body temperature	36.7°C	36.45°C	< 0.02
Ambient temperature	22.43±0.61°C	22.51±1.27°C	< 0.69
The number of blinks in 20s	6.35±4.48	4.73±3.65	< 0.03

TABLE 6.4 THE AVERAGE TEMPERATURE AT GEOMETRIC CORNEAL CENTER (GCC), AND THE AVERAGE TEMPERATURE DIFFERENCE BETWEEN LIMBUS AND GEOMETRIC CORNEAL CENTER (LIMBUS - GCC)

	Limbus - GCC	GCC
Young subjects	0.32±0.11°C	33.99°C
Elder subjects	0.48±0.10°C	33.35°C
Contact lens wearers	0.53±0.10°C	33°C

TABLE 6.5: AVERAGE OCULAR SURFACE TEMPERATURE PROFILE APPROXIMATED BY PARABOLOID OF REVOLUTION ($T(x, y) = A + B(x^2 + y^2)$).

RMSE DENOTES ROOT-MEAN SQUARED ERROR

	A	B	R^2	RMSE
Young subjects	33.99	0.33	0.9	0.0843
Elder subjects	33.43	0.38	0.92	0.0867
Contact lens wearers	33.09	0.47	0.92	0.104

TABLE 6.6: AVERAGE OCULAR SURFACE TEMPERATURE PROFILE

APPROXIMATED BY PARABOLOID OF REVOLUTION

$$(T(x, y) = A + [Bx^2 + C(y - D)^2] + [Ex^4 + F(y - G)^4] + Hx^2y).$$

	A	B	C	D	E	F	G	H	R^2	RMSE
Young subjects	33.95	0.44	0.11	-0.33	-0.04	0.14	0.1	-0.16	0.98	0.038 ₃
Elder subjects	33.11	0.53	0.13	-1.21	-0.06	0.09	0.85	-0.16	0.99	0.023
Contact lens wearers	33.95	0.63	-0.13	2.89	-0.06	0.12	0.99	-0.28	0.99	0.045 ₁

Also, we have consolidated the average ocular surface temperature profile (AOSTP) for all subject groups, as illustrated in [Figure 6.3](#). The average ocular surface temperature profile in each subject group was determined by compiling the warped thermographic sequence of every subject in the group. Besides, we also approximated these profiles by equations of the following forms using non-linear least square

$$T(x, y) = A + B(x^2 + y^2) \quad (83)$$

$$T(x, y) = A + [Bx^2 + C(y - D)^2] + [Ex^4 + F(y - G)^4] + Hx^2y \quad (84)$$

where $(0, 0)$ is defined to be the corneal center, and the unit of x and y for both equations is R , the corneal radius. The coefficients for respective equations, and their fitness, which accounted by R^2 and root-mean squared error, are tabulated in [Table 6.5](#) and [Table 6.6](#).

From [Figure 6.3](#), several important observations can be made in regard to the AOSTP. First, the corneal central region of elder subjects is cooler than their younger peer's but warmer than contact lens wearer's; however, unlike elder subjects, in contact lens wearers the temperature at

their corneal peripheral region does not rise as the elder subject's does when it gradually approaches limbus. Second, for all groups the temperature at the vicinity near to lower eyelid is higher than the one close to upper eyelid. Third, temperature apex (coolest point) is slightly inferior to the geometric corneal center (GCC) regardless of groups, although inferior limbus is warmer compared to its superior counterpart.

FIGURE 6.3: SUBFIGURE A, C, E ARE THE ACTUAL AVERAGE OCULAR SURFACE TEMPERATURE PROFILE (AOSTP) OF ELDER, YOUNG AND CONTACT LENS WEARER SUBJECT GROUPS RESPECTIVELY. FOR SUBFIGURE B, D, F, THEY ARE AOSTP GENERATED BY THE APPROXIMATED EQUATIONS (EQUATION (84)) FOR EACH RESPECTIVE SUBJECT GROUP (ELDER, YOUNG, AND CONTACT LENS WEARER).

In literature, limbus was reported to be 0.23~0.45°C warmer than GCC (Efron, et al. 1989, Tan, et al. 2009c), however that value was determined by comparisons between two limbal sites and GCC. Since limbus is a circular stripe which encloses the cornea, that determinations were not of sufficient representative. We have instead produced the temperature difference between every limbal site and GCC respectively (as illustrated in [Figure 6.4](#)), and obtained the mean difference for each group as tabulated in [Table 6.4](#).

FIGURE 6.4: LIMBUS - GCC PROFILE, THE TEMPERATURE DIFFERENCE BETWEEN EVERY LIMBAL SITE AND GCC, STARTING FROM 0 DEGREE (3 O'CLOCK DIRECTION) IN ANTI-CLOCKWISE TILL 360 DEGREE. THESE PROFILES ARE PLOTTED BASED ON THE APPROXIMATED EQUATIONS INSTEAD OF THE ORIGINAL AOSTP

Lastly, we have observed no significant interocular variation on μ_{ocular} , μ_{cornea} , and μ_{sclera} for all subject group. **Figure 6.5** and **Figure 6.6** illustrate horizontal and vertical temperature profiles of the three subject groups.

FIGURE 6.5: HORIZONTAL TEMPERATURE PROFILE (FROM Q_1 TO Q_5) OF EACH SUBJECT GROUP. THESE PROFILES ARE PLOTTED BASED ON THE APPROXIMATED EQUATIONS INSTEAD OF THE ORIGINAL AOSTP

Ocular surface temperature is determined by a number of factors. Warmer ambient environment heats up ocular surface, and stronger air flow on the contrary is likely to cool the ocular surface, due to greater heat transfer (Purslow, et al. 2005b). A double in humidity can double lipid layer thickness, although how it varies OST remains unclear (Purslow, et al. 2005b). Besides these external factors, there were also investigations on determinants such as lid retraction and closure, blinking, and tearing to

unveil their underlying correlations with the surface temperature (Mapstone 1968b). Age is reported to play part of the role, and so is the case for body temperature (Purslow, et al. 2005b).

FIGURE 6.6: VERTICAL TEMPERATURE PROFILE (FROM Q_3 TO Q_7) OF EACH SUBJECT GROUP. THESE PROFILES ARE PLOTTED BASED ON THE APPROXIMATED EQUATIONS INSTEAD OF THE ORIGINAL AOSTP

For tear film, it is said to be the layer where its temperature is captured by infrared thermographer during measurement based on a number of assumptions (particularly the tear film thickness) (Purslow, et

al. 2005b, Tan, et al. 2009a). However, its formation after a blink and the following variation in the determination of surface temperature are constantly overlooked in literature. For example, a tear film is likely to drop at least 6.6°C within the first second after a blink if ocular surface does not provide any heat into the water layer, and furthermore, only convective heat loss is accounted for in this simple calculation (see [Appendix III](#)). In the other words tear film does not warm the ocular surface as it was thought previously, although its initial temperature is claimed to approximate that of the body core (Schwartz 1965). In fact, it draws heat on ocular surface. This is especially the case when we consider evaporation on the ocular surface: it works similar to sweat which cools skin.

Therefore, ocular surface would be warmer if pre-ocular tear film never exists, despite an extreme case rarely observed in most subjects. On the other hand, a similar circumstance but far from the extreme would be clinical dry eye, an ocular disease mainly characterized by insufficient tear. In literature dry eye is determined to give warmer ocular surface (Morgan, et al. 1995), although the provided explanation on the hotter cornea is due to associated conjunctival hyperemia in dry eye. We think however, the

better, plausible reason is due to less tear and evaporation, and hence less cooling. The justification on this reasoning can be observed in the investigation by Mori et al., which demonstrated smaller variation and falling in corneal temperature after a blink in dry eye subject (Mori, et al. 1997). Their finding implies, the smaller variation and falling are the consequence of lower evaporation, and therefore possibly lead to warmer corneal surface due to lower decrement in corneal temperature over time.

Evidently, tear film plays a larger role than we have conceived in the determination of OST. In fact immediately after a blink, both the temporal and topographical variations in the surface temperature are mainly determined by the tear film formation during a blink, and its following variation. And ocular surface is warmed primarily by the closure of eyelid.

In this investigation we did not adopt the common practice in the recording of thermographic sequence, in which subject is asked to shut his/her eye for sometime before the data acquisition. Since prolonged eyelid closure definitely produces warmer ocular surface, such a consequence may introduce artifacts in the coming recording. Also, warmer ocular surface is likely to change the fluidity of meibomian lipid in

tear film, and consequently varies the lipid distribution and its functional performance (Bron, et al. 2004). Under this circumstance, tear film behaviour after the eyelid retraction is likely to deviate from its usual one, and hence leading to undesirable temporal and topographical OST profile, given the influence tear film has over the OST as abovementioned.

Besides, we too did not lift the subject's upper eyelid by a cotton bud during recording, a practice adopted by Tan et al (Tan, et al. 2009c). We think that practice may induce reflex tearing in subject, as observed by Mapstone who reported manipulation of eyelids by experimenter as one of the possible actions leading to the undesirable tearing (Mapstone 1968b). Instead, we developed eyelashes removal algorithm to improve the quality of our analysis.

The recording of ocular thermographic sequence in this investigation covers at least one interblink period in most subjects. These recordings deliver better, more comprehensive statistics in comparison to that of single static thermal image captured at a particular time. For example, mathematically speaking, μ_{ocular} is the expected temperature value of any ocular site (restricted to ocular surface) at any particular moment in the interblink period; similarly for other statistics. These

features provide a general picture on ocular surface in temperature, and facilitate better analysis. In particular, the colder ocular surface.

Ocular surface of the elderly is observed to be cooler, and one of the plausible explanations is their lower metabolism, as seen in [Table 6.3](#): young subject's body core is significantly warmer than their elder peers. Assume lower metabolism is the only factor that makes ocular surface of the elderly cooler, and mean OST reductive ratio $\rho_{ocular-r}$ is similar regardless of age, we can determine the expected μ_{ocular} for elderly based on their lower body core temperature using equation similar to (80)

$$\rho_{ocular-r} = \frac{T_b|_{elder} - \mu_{ocular}|_{elder}}{T_b|_{elder} - T_{amb}} \quad (85)$$

as mean OST reductive ratio is assumed to be similar for all ages, we take $\rho_{ocular-r} = \rho_{ocular-r}|_{younger} \approx 0.16$ (since human proceeds from young to old). And with $T_b|_{elder} = 36.45^\circ C$, $T_{amb} = 22.51^\circ C$ we get

$$0.16 = \frac{36.45 - \mu_{ocular}|_{elder}}{36.45 - 22.51}$$

$$\mu_{ocular}|_{elder} = 34.22^\circ C \quad (86)$$

The expected $\mu_{ocular|elder}$ is 0.41°C higher than the reported μ_{ocular} of the elderly (33.81°C) in Table 6.2. Such comparison indicates that there are factors other than metabolism leading to cooler ocular surface in the elderly. Closer examination on Table 6.3 will observe another important fact within the data: the elderly also blinks less during measurement. In the other words, elder subject performs fewer blinks even though his/her ocular surface is cooler, which is somewhat unusual, since spontaneous blinking rate in normal subject is reported to exhibit modest increase, rather than decrease with age (Sun, et al. 1997).

In fact, there are two probable situations that would lead to cooler ocular surface manifested in lower μ_{ocular} in this investigation given the data modality. First, the ocular surface is in nature cooler, or second, it has longer exposure to external, cooler ambience. For the elderly, it seems their ocular surface experience the both: they are in nature cooler due to lower metabolism, and they blink less leading to longer exposure. But it remains unclear why they allowed their ocular surface to be cooler and did not blink more to preserve its warmth as their younger peers did.

The only conceivable explanation is the decrease in corneal sensitivity in the elder people, due to the loss of corneal nerve. Corneas of

the elderly are reported not as sensitive as those of young people (Millodot 1977), and hence the former is likely to be more susceptible to injury without any awareness (Millodot, et al. 1984). In our case, lower corneal sensitivity is manifested as delayed sensation of coolness in ocular surface, and hence less blinks.

And not only the surface temperature relates to corneal sensitivity, but also other physiologies. In anterior chamber, aqueous humour flows in some patterns and is drained through Trabecular meshwork. The in-chamber fluid dynamic is driven by buoyant force, as a consequence of the temperature gap between iris and cornea ($2\sim 4^{\circ}\text{C}$) (Kumar, et al. 2006). Hence, in the computational simulation of aqueous humour flow corneal surface temperature (or OST) is one of the key factors in producing the desired understanding of the flow mechanism . And this understanding will facilitate better apprehension of glaucoma, since this ocular disease is often connected to obstruction of aqueous humour outflow (Kumar, et al. 2006). On the other hand, in the modeling of tear film the temperature at the ocular surface serves as one of the parameters in the determination of tear film thinning (Braun, et al. 2003). These modeling led to further

understanding on blinking and tear film drainage mechanism, and possibly dry eye.

Given that, the above simulations and other similar attempts may yield better findings if the surface temperature and its distribution can be defined by a single equation. To serve this purpose, we have approximated AOSTP of each subject group to give the corresponding mathematical description in the forms of equation (83) and (84), as tabulated in **Table 6.5** and **Table 6.6**. Furthermore, we have also approximated the average ocular reductive ratio profile of the three groups in the form similar to equation (84), as tabulated in **Table 6.7** to provide flexibility in modeling. Since

$$\rho(x, y) = A + [Bx^2 + C(y - D)^2] + [Ex^4 + F(y - G)^4] + Hx^2y \quad (87)$$

And

$$\rho(x, y) = \frac{T_b - T(x, y)}{T_b - T_{amb}} \quad (88)$$

With $\rho(x, y)$ known, experimenters can perform simulation in various scenarios by manipulating T_b and T_{amb} .

On the other hand, we provided approximations in the form of equation (83), which generates a paraboloid of revolution, for other intention. Computational modelling of the human eyeball, which attempted to predict temperature profile on the ocular sagittal plane under various internal or external conditions, were performed to simulate the biological nature of the human eye (Ng, et al. 2007). And these investigations must be verified and benchmarked to determine the model's accuracy. Since in most results the temperature profile at the ocular surface (on sagittal plane) resembles parabola (Scott 1988, Ng, et al. 2006b) and also, they assumed rotational symmetry in the model (Ng, et al. 2007), hence their surface temperature profile at the ocular surface is in fact a paraboloid of revolution. Our AOSTP approximations by paraboloid of revolution revealed an R^2 around 0.9. To benchmark their models, we find that the maximum predictability these models can reach on young subject is 90%, with an expected error of 0.08°C on any site at the ocular surface; for the elderly the predictability is slightly higher, 92%, but the expected error rises to 0.09°C (Table 6.5).

TABLE 6.7: AVERAGE OCULAR SURFACE REDUCTIVE RATIO PROFILE
 APPROXIMATED BY $\rho(x, y) = A + [Bx^2 + C(y - D)^2] + [Ex^4 + F(y - G)^4] + Hx^2y$

	A	B	C	D	E	F	G	H	R^2	RMSE
Young subjects	0.1914	-0.031	-0.0093	-0.2658	0.0028	-0.0098	0.3891	0.0105	0.98	0.0027
Elder subjects	0.232	-0.0398	-0.0144	-0.6243	0.0042	-0.007	0.7473	0.0114	0.99	0.0016
Contact lens wearers	0.1819	-0.0446	0.0071	3.467	0.0042	-0.009	0.9494	0.0194	0.99	0.0032

CHAPTER 7. AUTOMATED OCULAR LOCALIZATION IN THERMOGRAPHIC SEQUENCE

In chapter 4 an automated algorithm in the ocular and corneal localization was developed, however, the algorithm worked primarily on a single static ocular thermal image. For this chapter we propose an efficient algorithm to locate the ocular area and the cornea in thermographic sequences. It is capable of localizing the eye and cornea for all the sequential thermal images (of one recording) in once, without going through and performing snake algorithm in every image.

The algorithm at first determines the differential image, a single variational image derived from all the sequential thermal images of a recording. The differential image is later expanded, and manipulated to form an edge map for the calculation of gradient vector flow (GVF) field. With GVF as the external force field, a search for minimum on target tracing function is performed by genetic algorithm coupled with the snake algorithm, in the way similar to the algorithm detailed in chapter 4. However, as the subject of investigation are not the same (i.e., thermographic sequence versus single static thermal image), we propose a

new target tracing function in this chapter to accommodate the dissimilarity.

7.1. DIFFERENTIAL IMAGE AND TARGET TRACING FUNCTION

7.1.1. DIFFERENTIAL IMAGE

Let $I(x, y, f)$ denotes a particular frame in a thermographic sequence, where the x and y refer to the spatial domain, and f to the number of the particular frame. Consider the thermographic sequence of interest has n_F of frames, then

$$^n I_\epsilon(x, y) = \frac{I_\epsilon(x, y) - \min I_\epsilon(x, y)}{\max I_\epsilon(x, y) - \min I_\epsilon(x, y)} \cdot 255 \quad (89)$$

and

$$\begin{aligned} I_\epsilon(x, y) &= \sum_{i_\epsilon} \frac{1}{1 + \|I(x, y, i_\epsilon) - I(x, y, i_\epsilon - f_{df})\|}, \quad i_\epsilon \\ &= f_{df} + 1, f_{df} + 1 + i_{df}, \dots, f_{df} + 1 + n i_{df}, n_F \end{aligned} \quad (90)$$

where $\|\cdot\|$ denote absolute value and

$$i_{df} \geq f_{df} \quad (91)$$

Figure 7.1 illustrates a typical differential image. Equation (89) basically relates the variation in temperature over a period of time with image intensity level. The larger the variation, the darker the image pixel. From Figure 7.1, it can be observed that the anterior ocular surface in general varies in the same degree with orbital skin, except eyelashes. Such phenomenon allows the snake to move into the region of anterior ocular surface, and follow the eyelashes to delineate the shape of eye. It is also observed that, the number of eyelashes at lower eyelid and their variation in temperature in usual are smaller in amount in compared to its upper counterpart.

FIGURE 7.1: TYPICAL DIFFERENTIAL IMAGE (THE EXPANDED REGION DUE TO EQUATION (92) IS OMITTED IN THIS FIGURE)

After these, the differential image is expanded after ${}^e n_i$ iteration according to equation (30) and give

$${}^e I_\epsilon = \mathbf{F}_{ex}^{e n_i}({}^n I_\epsilon) \quad (92)$$

Substituted (92) into equation (31) and obtain the edge map for both the GVF and snake algorithm:

$$f_e = -\{|\nabla[G_{\sigma_1}(x, y) * {}^e I_\epsilon(x, y)]| + r_e \cdot G_{\sigma_2}(x, y) * |\nabla_{\text{sob}} {}^e I_\epsilon(x, y)|\} \quad (93)$$

7.1.2. TARGET TRACING FUNCTION FOR THERMOGRAPHIC SEQUENCES

For each snake point in ${}^v \mathbf{C}(s)$ we denote it as

${}^v C_1, {}^v C_2, \dots, {}^v C_{sp}, \dots, {}^v C_{SP}$, and get the corresponding

${}^n f_{e_1}, {}^n f_{e_2}, \dots, {}^n f_{e_{sp}}, \dots, {}^n f_{e_{SP}}$ by

$${}^n f_{e_{sp}} = {}^n f_e({}^v C_{sp}) \quad (94)$$

where

$${}^n f_e(x, y) = \frac{f_e(x, y) - \min f_e(x, y)}{\max f_e(x, y) - \min f_e(x, y)} \quad (95)$$

SP refers to the total number of snake points. And we rank ${}^n f_{e_1}, {}^n f_{e_2}, \dots$, ${}^n f_{e_{SP}}$ from the least to the greatest, define the percentile correspond to the sp -th value by

$$p_{sp} = \frac{100}{SP} \left(sp - \frac{1}{2} \right) \quad (96)$$

The value ${}^n f_e$ corresponds to a percentile p_{rc} is obtained by finding an integer k such that

$${}^n f_{e_{p_{rc}}} = {}^n f_{e_k} + \frac{SP}{100} (p_{rc} - p_k) ({}^n f_{e_{k+1}} - {}^n f_{e_k}), \quad p_k \leq p_{rc} \leq p_{k+1} \quad (97)$$

Finally, the target tracing function in this study is defined as:

$$y_{ft} = F_{tt}(x_c, y_c, p_1, p_2, w) = \frac{c_1}{\int |{}^v \mathbf{C}'(s)| ds} + ({}^n f_{e_{p_{rc}}})^2 \quad (98)$$

c_1 refers to a control parameter.

${}^n f_{e_{sp}}$ is in fact the gray-scale intensity level of a particular snake point ${}^v C_{sp}$ in the normalized edge map ${}^n f_e(x, y)$. Equations (96), (97) determine the gray-scale intensity level which correspond to a particular

percentile based on all the snake points. In our case, the percentile (p_{rc}) is set to 40th. As abovementioned, the eyelashes at lower eyelid has smaller temporal variation in temperature compared to the upper-eyelid eyelashes, as a result they frequently appear as some dark spots around the lower eyelid in differential image. Occasionally, this also happens in upper-eyelid eyelashes (as illustrated in [Figure 7.2](#)). Hence, such configuration ($p_{rc} = 40$) makes the target tracing function to select the converged snake that has crossed these regions—regions which roughly indicate the location and the shape of the eye. A minimum in target tracing function would require only 40% of the ${}^n f_{esp}$ to be as low as possible, and this would disregard whatever values the rest of the ${}^n f_{esp}$ are and pick up the snake that stays in these dark spots instead of the one which is entirely immerse in a ring of dark region (not an often encountered situation in ocular ${}^n f_e(x, y)$). The term $\frac{c_1}{\int |{}^v \mathbf{C}'(s)| ds}$ discourages ${}^v \mathbf{C}(s)$ to be short in length and hence small in area. It is to avoid the target tracing function to select snake that locates the tail end of the upper-eyelid eyelashes instead of the upper eyelid where eyelashes originate from (see [Figure 7.2](#)).

FIGURE 7.2: TWO NORMALIZED EDGE MAPS. (c), (d), (g), (h) ARE DARK SPOTS THAT STAY IN LOWER EYELID. OCCASIONALLY, THIS ALSO HAPPENS IN UPPER EYELID, AS IN (II). THE EYELASHES IN UPPER EYELID OF (II) DO NOT FORM A DARK BAND AS IN (I), BUT INSTEAD AS A FEW DARK SPOTS SUCH AS (e) AND (f). REGION (a) CORRESPONDS TO THE TAIL-END OF THE UPPER-EYELID EYELASHES; REGION (b) IS THE AREA WHERE THE UPPER EYELID SITUATES.

7.1.3. MEASURES FOR DELINEATION QUALITY

The delineation quality in this study is measured by two of the following parameters: 1) the overlap

$$q(A_{ac}, A_{gt}) = \frac{A_{ac} \cap A_{gt}}{A_{gt}} \quad (99)$$

and 2) the remainder

$$r(A_{ac}, A_{gt}) = \frac{A_{ac} - (A_{ac} \cap A_{gt})}{A_{ac}} \quad (100)$$

where A_{ac} denotes the area enclosed by ${}^v\mathbf{C}(s)$, and A_{gt} denotes the ocular area delineated manually using polygon by eight distinct points as detailed in [Section 5.2.1](#) (as illustrated in [Figure 5.3](#)), serving as a ground truth reference. The overlap illustrates how much the true ocular area is covered by the area encircled by snake. The region where the snake covers but is not part of the true ocular area is indicated in the remainder. It is important to note that, however, due to delineation by polygon, even the snake perfectly encircles the eye, the remainder is not likely to be zero in value. Consider an octagon that delineates a round circle with a radius R as illustrated in , the octagon area is given by $A_{oct} = 2\sqrt{2}R^2$ (since R is the octagon circumradius), and the remainder is

$$r(A_{cir}, A_{oct}) = \frac{A_{cir} - (A_{cir} \cap A_{oct})}{A_{cir}} = \frac{\pi R^2 - 2\sqrt{2}R^2}{\pi R^2} = 0.1$$

Hence, as there is an inherent incomplete delineation on smooth curve by polygon, for a perfect snake delineation on the object of interest, the

remainder value is likely to fall around 0.1, depending on the shape of the object.

FIGURE 7.3: CIRCUMCIRCLE OF AN OCTAGON

7.2. LOCALIZATION OUTCOME

A total of 72 normal ocular thermographic sequence were analyzed in this work, 36 of them were recorded on subjects younger than 35 years old, and the rest on subjects aged above 35. Procedures in data collection are detailed in [Section 5.1](#). The delineation qualities for the 72 thermographic sequences are tabulated in [Table 7.1](#) and [Table 7.2](#). [Figure 7.4](#) illustrates ocular and corneal localization in some of the thermographic sequences, on a particular frame in each sequence. The mean value of the overlap and remainder measures for thermographic sequences of normal subjects aged above 35 are 0.92 and 0.12

respectively; for the sequences of subjects aged below 35, the two measures have a mean value of 0.92 and 0.1 respectively. In overall, our algorithm achieves a 0.92 for overlap measure and a 0.11 for the remainder in all the 72 sequences.

TABLE 7.1: DELINEATION QUALITIES FOR THERMOGRAPHIC SEQUENCES
RECORDED ON NORMAL SUBJECTS AGED ABOVE 35

Case	$q(A_{ac}, A_{gt})$	$r(A_{ac}, A_{gt})$	Case	$q(A_{ac}, A_{gt})$	$r(A_{ac}, A_{gt})$
1	0.94	0.07	19	0.85	0.10
2	0.92	0.09	20	0.90	0.05
3	0.91	0.08	21	0.96	0.19
4	0.90	0.07	22	0.98	0.17
5	0.91	0.09	23	0.94	0.06
6	0.92	0.09	24	0.91	0.08
7	0.96	0.20	25	0.90	0.03
8	0.88	0.09	26	1.00	0.24
9	0.99	0.23	27	0.96	0.15
10	0.99	0.19	28	0.93	0.11
11	0.93	0.04	29	0.92	0.05
12	0.89	0.14	30	0.96	0.28
13	0.92	0.16	31	0.81	0.05
14	0.91	0.15	32	0.92	0.17
15	0.97	0.10	33	0.92	0.14
16	0.94	0.09	34	0.95	0.19
17	0.83	0.07	35	0.94	0.08
18	0.85	0.05	36	0.92	0.25

Previously, there were several investigations carried out based on ocular thermographic sequence. Efron *et al.* recorded the temperature of geometric corneal center, which was a single point, at 5s interval, lasting to the stage when the subject blinked (Efron, et al. 1989). In a later investigation which measured corneal temperature at a rate of 60 times per second, a 20x20 pixels box was placed at the center of cornea, and for each frame the mean temperature of that region was calculated. That investigation attempted to model the variation in corneal temperature of both normal and dry eye subjects in the form of $T(t) = (T_0 - T_\infty)e^{-kt} + T_\infty$, and found that for normal blinking parameter k was in average higher in dry eye subjects (Mori, et al. 1997). A similar experiment was conducted, however, to diagnose dry eye based on the parameter k (Chiang, et al. 2006). The experiment recorded corneal temperature on an encircled region with an area of $4.4mm^2$ (22 pixels). On the other hand, Purslow *et al.* determined the possible changes on OST during and immediately after a lens wear, by continuously recording temperatures of 23 points across the anterior eye at a frame rate of 30Hz (Purslow, et al. 2005a).

TABLE 7.2: DELINEATION QUALITIES FOR THERMOGRAPHIC SEQUENCES
RECORDED ON NORMAL SUBJECTS AGED BELOW 35

Case	$q(A_{ac}, A_{gt})$	$r(A_{ac}, A_{gt})$	Case	$q(A_{ac}, A_{gt})$	$r(A_{ac}, A_{gt})$
1	0.86	0.01	19	0.97	0.15
2	0.92	0.12	20	0.96	0.09
3	0.95	0.17	21	0.93	0.16
4	0.88	0.12	22	0.99	0.14
5	0.97	0.14	23	0.97	0.15
6	0.95	0.09	24	0.96	0.16
7	0.89	0.15	25	0.90	0.07
8	0.88	0.07	26	0.94	0.14
9	0.86	0.10	27	0.87	0.00
10	0.86	0.08	28	0.99	0.19
11	0.88	0.12	29	0.90	0.17
12	0.95	0.11	30	0.94	0.13
13	0.90	0.07	31	0.94	0.02
14	0.99	0.19	32	0.97	0.10
15	0.90	0.11	33	0.86	0.01
16	0.87	0.04	34	0.91	0.06
17	0.92	0.03	35	0.87	0.05
18	0.85	0.04	36	0.93	0.11

None of the above investigations use semi-automated or automated ocular localizations, and corneal region is subjectively located. Since subject's head position can be easily maintained unchanged when it rests on chin rest, it is indeed possible to locate all the ocular area in every

thermal images by just analyzing any one of them, using the method detailed in chapter 4. However, the availability of a number of sequential thermal images provide an opportunity to derive another sort of edge map, and facilitate a better ocular localization. The primary advantage of the presently proposed algorithm over the previous method is that the edge map proposed in this chapter captures the variation in temperature of every pixel with respect to time, whereas the former captures the gradient in temperature of every pixel in a single static image. As some subjects exhibit irregular orbito-ocular thermal pattern, the former edge map may not provide a proper external guide for snake to locate the eye under these circumstances. However, the variation in temperature with respect to time were observed to be more consistent in orbito-ocular region among normal subjects, and hence produces a cleaner edge map.

FIGURE 7.4: SOME LOCALIZATION RESULTS OF OUR ALGORITHM

The localized ocular region in our proposed algorithm in average cover 92% of the true anterior region, and non-anterior region covered in average account for 11% of the localized area. As discussed in section 4.4, the inherent error in the remainder measure is around 0.1, or 10%, depending on the shape of object of interest. Using 10% as the yardstick, in our case the actual non-anterior region covered can be comfortably said to be less than 5%.

To sum up, the proposed target tracing function performs well in the selection of x_G , y_G , p_l , p_c and w , enables fully automation without any manual assistance. Our algorithm takes in any thermographic sequence and generates the localization result without any pre-selection on region

of interest. In average, the algorithm takes less than 1 minute to complete localization on a PC equipped with Intel Core 2 Duo processor.

CHAPTER 8. CONCLUSION & FUTURE WORK

8.1. CONCLUSION

In this thesis several computer methods were applied to investigate ocular surface temperature. Second-order spatial statistical analysis together with difference histogram, moments were used to extract thermal textural properties within the cornea. These methods have been proved to be feasible alternatives that have unveiled further useful details on ocular surface temperature in compared to the previous methodologies.

Altogether 21 textural features were extracted from the corneal thermogram, eight of which were features derived from cross co-occurrence matrix. The reported findings showed that these features were effective in delineating the variations in ocular thermal texture among various age groups, and a number of correlations among those features were described. Further textural investigations on diseased ocular thermogram should provide better and deeper understandings in ocular physiology and diseases, and serve for diagnostic usage.

On the other hand, investigations in the surface temperature in its entirety have prompted inspiring discoveries. Warping thermal data

within the palpebral fissure into a standardized format spares us from the discrimination between cornea and sclera—the corneal localization is automated once the palpebral fissure is delineated by polygon. And the standardized data allowed ample consistent comparisons among subjects and age groups. Topographical variations among subject groups were pointed out (clearly illustrated in [Figure 6.3](#)), and the rationales behind these variations were accounted: the behaviour of tear film predominately determines the temporal topographical variations in ocular surface temperature after a blink, and elder subjects' ocular surfaces were cooler as a consequence of their weaker corneal sensitivity and lower metabolism.

In addition to the above, the warping methodology has also made evaluation of tear evaporation rate by infrared thermography possible. Previous developments in literature on the acquisition of tear evaporation rate were made mostly based on the measurement of relative humidity. They fixed a closed chamber around subject's ocular area, measured the relative humidity within and derived the rate of tear evaporation. In this thesis the evaporation rate was evaluated based on the ocular thermographic sequences. Region of interest was selected at first and the

encircled region within all the sequential thermal images were warped into a standard form. Calculations were performed using the thermal data and equations derived based on the first law of thermodynamics to obtain the evaporation rate. The mean tear evaporation rate determined for all subjects was $25.38 \times 10^{-7} gcm^{-2}s^{-1}$, and the corneal tear evaporation was higher in elder subjects. Also, corneal rate of evaporation was observed to fluctuate in a larger magnitude in subjects who blinked more than average.

Rigorous investigation in the surface temperature needs not only sophisticated analytic technique, but high standard in data quality. Eyelashes are noises in ocular thermal data. Although they were far cooler, eyelashes were not attended to in the past as both corneal and ocular surface were rarely looked into in their entireties, except one investigation in which upper eyelid was lifted to prevent reading of eyelashes temperature (Tan, et al. 2009c).

Algorithms for removal of eyelashes were developed in this thesis to address the abovementioned, and there were two of them: one for static ocular thermal image, another for thermographic sequence. The former utilized Gabor filter and the latter used differential image to achieve the

task. Both of them however employed Expectation-Maximization to determine the threshold, which served as a criteria for the discrimination of eyelashes. The removal outcome was consolidated in the parameter D_{Mn} for static thermal image; on thermographic sequence, though no statistics was devised to determine the effect, average ocular surface temperature profile (AOSTP) would not be possible if removal of eyelashes were absence.

Automated ocular and corneal localizations on the other hand, were devised to substitute manual effort in the determination of ocular and corneal area. These automated methods provided an alternative to introduce consistency in the localization of cornea, although at current state some further refinements are necessary to achieve stringent robustness.

Snake algorithm and gradient vector flow field were utilized in this study to achieve automated localization both in the static thermal image and thermographic sequence. But snake algorithm and other deformable template matching techniques are local optimizers that are sensitive to initialization, and snake algorithm can utmost achieve only semi-automated localization as manual intervention is needed to achieve

acceptable feature delineation. This defect was overcome by coupling snake algorithm and genetic algorithm, and utilizing target tracing function as the discriminating function in this thesis: a search was performed on target tracing function by genetic algorithm, to look for the snake that would produce a minimum; and target tracing function was designed in the way such that only the snake which accurately delineates the feature gives the minimum in that function. And to account variations in data modalities between single thermal image and thermographic sequence, two target tracing functions were developed in this study.

In summary, the objectives of this thesis laid down in chapter 1.3 were all achieved, each by one or several novel applications of existing methodologies. Cross co-occurrence matrix was employed to provide in-depth analysis; image metamorphosis was used to reduce uncertainty in the selection of region of interest, and facilitate the investigation of the aging effect on ocular surface temperature; combination of Gabor filter and expectation maximization algorithm has enabled eyelashes removal in static thermal image; for thermographic sequence, that was achieved by differential image and again expectation maximization algorithm; tear evaporate rate was the first time evaluated by infrared thermography

instead of humidity sensor; finally, the proposed target tracing functions made automated localization possible. These novel applications of existing computer methods to the ocular thermography have in some extent enriched the capabilities of ocular thermal images.

8.2. FUTURE WORK

In this thesis, only first and second order textural analysis were introduced to look into ocular thermal texture, though the findings on aging are satisfactory, it is far from complete. Other textural methods, such as run length, texture spectrum, or fractal analysis should yield further insights both on ocular physiology and pathology when they are applied to analyze normal and diseased ocular thermogram, coupled with the technique discussed in [Section 5.2.1](#). Besides, it is possible and insightful to look into the temporal textural variations, by examining each of the texture features on frame-by-frame basis in the ocular thermographic sequences.

Tear film completes its formation within the first two second after a subject opens his/her eyes during a blink. The temperature data and its variation within this short period, especially during the first second, may unveil important behaviours or characteristics both of tear film and ocular

surface. However in this thesis, most of the temperature data within the first second was not acquired and analyzed. This is due to the fact, during the short period, the eye is opening and the shape of palpebral fissure keeps varying. And therefore thermographic sequences in that period of time were considered as part of the blinking frames and consequently removed for the ease of analysis. In future, it is possible to acquire these data, by using the technique detailed in [Section 5.2.1](#), to mark out the ocular area on each of the eye-opening thermographic sequences and perform the necessary analysis.

The algorithm elaborated in [Chapter 5](#), which evaluates the rate of tear evaporation based on ocular thermographic sequences, was applied only on normal subjects in this study. It can be further investigated on dry eye subjects, together with the eyelashes removal algorithm developed in [Chapter 6](#), to look into dry eye patients' tear evaporation rate and their corresponding temporal variation. It is possible to propose a preliminary guideline in dry eye diagnosis based on the obtained tear evaporation rate and some other parameters derived from the observed temporal variation in the rate of tear evaporation.

The thermographic sequences in this study were recorded at a rate of 25 frames per second; for clinical usage, that number can be far lower to speed up analysis. However, some preliminary investigations must be conducted with the lower rate of recording to ensure no compromise in the quality of analysis. Furthermore, it is feasible to look into dry eye from textural point of view, and feed the relevant features, together with tear evaporation rate into classifier to perform semi-automated diagnosis. For fully automated diagnosis, however, a more robust automated ocular localization algorithm is required.

Both the proposed automated localization algorithms in [Chapter 4](#) and [Chapter 7](#) are satisfactory, but not sufficiently robust to meet clinical usage. They can be refined in mainly two ways: 1) to propose a better edge map , and 2) to design a better target tracing function. It is believed that, there are plenty rooms for improvements in both aspects, and hence in future work it is possible to deliver a more accurate delineation of palpebral fissure in ocular thermal image. Furthermore, the idea which combines snake algorithm, genetic algorithm and target tracing function to localize an object of interest can be extended to other fields, such as breast cancer diagnosis.

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APPENDIX I: EQUAL-DISTANT REDISTRIBUTION ALGORITHM

The ultimate target of this algorithm is to get SNAKE points equally distributed while conserving the shape

Consider first three points in this example. let counter for SNAKE points before redistribution as n , counter for SNAKE points after redistribution as n_p

- The straightline distance for SNAKE points are equal among $n_p = 1, 2, 3 \dots$

- for $n_p = 1$, its x and y positions are same as SNAKE points $n = 1$. Then $n_p = n_p + 1$, $n = n + 1$

- for $n_p = 2$, examine if its cumulative distance is larger than cumulative distance of $n = 2$, also if it is larger than cumulative distance of $n = 3$. If it is not larger than cumulative distance of $n = 3$, then point $n_p = 2$ lies in between points $n = 2$ and $n = 3$. So point $n = 2$ can be made used to determine the position of $n_p = 2$

The formula to get point's position $n_p = 2$:

$$x'_{n_p=2} = \frac{x_{n=3} - x_{n=2}}{Cl_{n=3} - Cl_{n=2}} \cdot dl + x_{n=2}$$

$$y'_{n_p=2} = \frac{y_{n=3} - y_{n=2}}{Cl_{n=3} - Cl_{n=2}} \cdot dl + y_{n=2}$$

where Cl is the cumulative distance of a point seen from the first SNAKE point, $n = 1$

- The rest of points $n_p = 3, 4, 5 \dots$ can be determined by the same idea

APPENDIX II: JUSTIFICATION ON ASSUMPTION IN EQUATION (50)

The following illustration is to show that $mC_p(T_2 - T_1)$ is negligible in equation (50). From observation in literature (Efron, et al. 1989) and our data, on ocular surface it is found that the value of $T_2 - T_1$ hardly beyond 0.2°C in 1s. For convenience, we assume $\Delta t = t_2 - t_1 = 1\text{s}$, $T_2 - T_1 = 0.2^\circ\text{C}$; and $\rho = 1050\text{kgm}^{-3}$, $C_p = 4278\text{Jkg}^{-1}\text{C}^{-1}$ for cornea, $d = d_2 - d_1 = 100\text{nm}$. $E(x, y, t)$ and $T(x, y, t)$ are considered to be constant within the time Δt and throughout the area dA . The change in energy within the control volume during a period of 1s is given by $mC_p(T_2 - T_1)$, and divide the term by the area dA we get the change in energy per area per second:

$$\begin{aligned} \frac{mC_p(T_2 - T_1)}{(dA \cdot \Delta t)} &= \frac{\rho \cdot dA \cdot d \cdot C_p \cdot (T_2 - T_1)}{dA \cdot 1} \\ &= 1050 \cdot 4278 \cdot 100 \times 10^{-9} \cdot 0.2 = 0.089\text{Wm}^{-2} \end{aligned}$$

From literature, the reported tear evaporation rate (per area) falls in the range of $9\sim 100\text{Wm}^{-2}$ (Adler, et al. 1970, Morgan, et al. 1995, Mathers 2004). Hence, it can be seen that the contribution of the change in energy per area (control volume) to the tear evaporation rate is negligible. Furthermore, the sum of heat loss per area per second due to convection and radiation is

$$\begin{aligned}
& \frac{h_{amb}[T(x, y, t) - T_{amb}]dA\Delta t}{dA \cdot \Delta t} + \frac{\sigma\varepsilon[T(x, y, t)^4 - T_{amb}^4]dA\Delta t}{dA \cdot \Delta t} \\
&= 10 \cdot [(273 + 35.31) - (273 + 25)] + 5.67 \times 10^{-8} \cdot 0.975 \\
&\quad \times [(273 + 35.1)^4 - (273 + 25)^4] \\
&= 103.1 + 63.54 \\
&= 166.64\text{Wm}^{-2}
\end{aligned}$$

, which is 1800 times the value of $mC_p(T_2 - T_1)$, therefore the term $mC_p(T_2 - T_1)$ can comfortably be neglected in our calculation. The maximum error is $0.089\text{Wm}^{-2}/9\text{Wm}^{-2} = 0.0099$, less than 1%.

APPENDIX III: JUSTIFICATION ON THE AMOUNT OF CONVECTIVE HEAT LOSS PROPOSED IN CHAPTER 6

The tear film is a fine layer which has its anterior surface exposed to external environment, and its posterior surface joint by ocular surface. Under this circumstance, we consider only convection and no heat exchange takes place at the posterior surface. Hence the heat transfer at the layer can be modelled by the following:

$$hA(T_{\infty} - T)dt = mC_p dT \quad (\text{AIII.1})$$

Since T_{∞} the ambient temperature is constant, the above equation can be arranged as

$$\frac{d(T - T_{\infty})}{T - T_{\infty}} = -\frac{hA}{\rho V C_p} dt \quad (\text{AIII.2})$$

where h is the convection heat transfer coefficient, A is the tear film surface area, V the tear film volume, ρ the water density, C_p the water specific heat, and T is the tear film temperature at a particular time. Integrate the above equation from $t = 0$ at $T = T_i$ to any time t and get

$$\ln \frac{T(t) - T_{\infty}}{T_i - T_{\infty}} = -\frac{hA}{\rho V C_p} dt$$

then

$$\frac{T(t) - T_{\infty}}{T_i - T_{\infty}} = e^{-\frac{hA}{\rho V C_p} t}$$

(AIII.3)

We assume $T_i = 37^{\circ}\text{C}$ the body core temperature, and get $A = 168 \times 10^{-6} \text{m}^2$ (Johnson, et al. 2006), $V = 0.5 \times 10^{-9} \text{m}^3$ (Johnson, et al. 2006), $\rho = 1000 \text{kgm}^{-3}$, $C_p = 4200 \text{J/kg} \cdot \text{K}$, $h = 10 \text{Wm}^{-2} \text{K}^{-1}$ (Emery, et al. 1975), $T_{\infty} = 25^{\circ}\text{C}$, hence

$$\frac{T(t) - 25}{37 - 25} = e^{-\frac{10 \times 168 \times 10^{-6}}{0.5 \times 10^{-9} \times 1000 \times 4200} t}$$

(AIII.4)

And the tear film temperature at the first second is given by

$$T(1) = 30.39^{\circ}\text{C}$$

It can be seen that, the tear film temperature drops from 37°C to 30.39°C within the first second, giving a loss of 6.6°C in that period of time.

RELATED PUBLICATIONS FROM THIS THESIS

JOURNAL

Tan, J.-H., Ng, E. Y. K., Rajendra Acharya, U., and Chee, C. (2010a), "Study of Normal Ocular Thermogram Using Textural Parameters," *Infrared Physics & Technology*, 53, 120-126.

Tan, J. H., Ng, E. Y. K., and Acharya, U. R. (2010b), "An Efficient Automated Algorithm to Detect Ocular Surface Temperature on Sequence of Thermograms Using Snake and Target Tracing Function," *Journal of Medical Systems*, DOI:10.1007/s10916-10010-19552-10916.

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Tan, J. H., Ng, E. Y. K., Acharya, U. R., and Chee, C. (2010c), "Automated Study of Ocular Thermal Images: Comprehensive Analysis of Corneal Health with Different Age Group Subjects and Validation," *Digital Signal Processing*, 20, 1579-1591.

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Tan, J. H., Ng, E. Y. K., and Acharya, U. R. (2010), "Evaluation of tear evaporation from ocular surface by functional infrared thermography," *Medical Physics* 37, 6022

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CONFERENCE PROCEEDINGS

Tan, J. H., Ng, E. Y. K., and Rajendra, A. U. (2008), "Detection of Eye and Cornea on Ir Thermogram Using Genetic Snake Algorithm," in *9th International Conference on Quantitative Infrared Thermography*, Krakow, Poland, pp. 143-150.