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Screening for dry eye disease using infrared ocular thermography

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ABSTRACT

Purpose: To evaluate the efficacy of infrared (IR) ocular thermography in screening for dry eye disease (DED).
Methods: IR ocular thermography was performed on 62 dry eye and 63 age- and sex-matched control subjects. Marking of ocular surface and temperature acquisition was done using a novel 'diamond' demarcation method. 30 static- and 30 dynamic-metrics were studied and receiver operating characteristic curves were plotted. Efficacy of the temperature metrics in detecting DED were evaluated singly and in combination in terms of their area under the curve (AUC), Youden's index and discrimination power (DP).
Results: Absolute temperature of the extreme nasal conjunctiva 5 s and 10 s after eye opening were best detectors for DED. With threshold value for the first metric set at 34.7 °C, sensitivity and specificity was 87.1% (95% CI: 76.2–94.3%) and 50.8% (95% CI: 37.9–63.6%) respectively. With threshold value for the second metric set at 34.5 °C, sensitivity and specificity was 77.6% (95% CI: 64.7–87.5%) and 61.9% (95% CI: 48.8–73.9%) respectively. The two metrics had moderate accuracy and limited performances with AUC of 72% (95% CI: 63–81%) and 73% (95% CI: 64–82%); Youden index of about 0.4 and DP of 1.07 and 1.05 respectively. None of the dynamic metrics was good detector for DED. Combining metrics was not able to increase the AUC.
Conclusions: This work suggests some utility for the application of IR ocular thermography for evaluation of dry eye patients.

1. Introduction

Dry eye disease (DED) is a commonly encountered condition in clinical practice and affects up to 12.3% of the population in Singapore [1] with a world prevalence range of 5–38% [2]. The condition has remarkably impact on daily social and physical functioning, work place productivity and quality-of-life [3–6]. Diagnosing the disease can be a tedious and challenging task [7] and been hampered by the lack of objective tests with sufficient sensitivity and specificity, adequate repeatability, ease of performance, and suitability for the clinical practice setting particularly in early or mild cases [8]. Due to its multifactorial nature, DED potentially requires a broad spectrum of test measures in the monitoring of its diagnosis and treatment [9]. While there are many clinical tests for DED, the diagnostic values can be inconclusive [10,11] and may not be repeatable and/or reliable because of variable results, poor reproducibility and low sensitivity [12–15]. Determining the cause of dry eye when minimal clinical signs are present is difficult and the diagnosis is complicated further when there is a lack of correlation between its signs and symptoms [11,16–22].

Tear film stability is a key test in screening and diagnosing DED [8]. It has been reported that capturing ocular surface temperature (OST) changes using infrared (IR) ocular thermography reflects the nature of the tear film [23,24] and its stability [25] and can be used to screen DED [26,27]. However, temperature metrics available from ocular thermography to screen DED were limited and remain unclear. Most studies on OST and dry eye have evaluated the temperature of the geometric center of the cornea [23,26,28–30]. A small number of studies evaluated other metrics such as the

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relative differences in temperature across the ocular surface [31,32], mean ocular surface temperature [32,33], temperature at the nasal and temporal conjunctiva [26] and temperature difference and compactness values of the OST [27]. Two reports on dry eye screening using ocular thermography were done using temperature of the geometric center of the cornea [26] and temperature difference and compactness values of the OST [27].

The current study was devised to evaluate the efficacy of IR ocular thermography as a diagnostic tool for DED and to determine the most effective temperature metrics, applied singly or in combination.

2. Methods

2.1. Subjects

The research protocol was approved by the Singapore National Health Group (NHG) Domain-Specific Review Board (DSRB) and the Singapore Polytechnic ethics review committee and the work adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from each subject at study enrolment. Sixty-two dry eye (48 ± 10 years; 14 Male and 48 Female) and 63 age- and sex-matched control subjects (46 ± 7 years; 16 Male and 47 Female) completed the study with the age matching range of ± 2 years. This study included mild or moderate dry eye subjects. They were classified based upon a composite disease severity index, derived from the Dry Eye Workshop severity scale [34]. The inclusion criteria for the dry eye subjects were as described previously [35]: use of tear replacement therapy and had either a fluorescein tear break-up time of 10 s or less [36], or a Schirmer I test result of less than 10 mm in 5 min [31] along with presence of corneal or conjunctiva staining. All dry eye patients were screened and diagnosed by an ophthalmologist at Khoo Tech Puat Hospital eye clinic. Control subjects were those not using tear replacement therapy or any topical medication and without signs or symptoms of dry eye. All subjects were required to be noncontact lens wearers for at least two years prior to enrolment. Subjects were excluded from control group if they had Schirmer I test result of less than 10 mm in 5 min or fluorescein tear break-up time of 10 s or less. Subjects with any anterior ocular anomalies (e.g. current ocular infection, allergy or ptosis), those undergone surgery or taking any medication that could affect the tear film or who were currently pregnant or breastfeeding were also excluded.

2.2. Procedures

The procedures were the same as described previously [35]. Subjects were asked to refrain from using their eye-drops or eye make-up on the day of measurement. Ocular thermography was performed in real time using an Infrared thermo-tracer (NEC TH9420) with resolution of 640 (H) × 480 (V) pixels, operational sensitivity of 0.06 °C and frequency of 30 frames per second, detecting infrared radiation between 8 and 14 μm. The emissivity of 0.98 was assumed [37]. A standard examination protocol as reported in the literatures [23,25,26,32] was adopted. All the measurements were performed from 9 am to 2 pm in the same room with controlled room temperature (24.06 ± 0.41 °C) and humidity (49.76 ± 2.61%), with no air drifts and same brightness (380 lux). Subjects were adapted to the room for 20 min prior to ocular thermography as previous work has shown that this period was necessary to achieve ocular temperature stabilisation [38]. OST was recorded under the conditions described by Morgan and associates: the subjects blinked normally, closed for 3 s and the first image was recorded just after the eyes had opened [32,39]. 0 s was recorded as the time upon eye opening. 300 frames of real time thermal images reflecting OST changes at the ocular surface were captured over 10 s sustained eye opening. The measurement was done three times on right eye followed by left eye. At any time if subject blinked or changed fixation before 10 s, the measurement was discounted and repeated.

A novel 'diamond' method was used to mark the ocular surface using a custom-designed OST Analysis V2 software (developed using MatLab Simulink 7.11.0, R2010b). The region of interest (ROI) formed by five anatomical points (labelled as 1–5) shaped like a diamond (Fig. 1). This method has the advantages of (1) overcome problems of truncated image by upper lids [40] and (2) minimize possible inconsistency in OST acquisition due to variation in palpebral aperture size and (3) enable study of the inferior zone of the ocular surface that reported to be a predictive area in detection of dry eye subtypes [41]. Each point marked represents an area of 3×3 pixels so that temperature was an average of nine pixels:-

1) Temporal limbus (LT)
2) Nasal limbus (LN)
3) Extreme temporal conjunctiva (T1)
4) Extreme nasal conjunctiva (T4)
5) Most inferior point of the ocular surface

Once the marking of ROI was completed, OST acquisition and processing was performed automatically by double clicking the last point marked (point 5) to activate the OST Analysis V2 program and process all the 300 frames. All frame marking and data processing were undertaken by a single examiner (LL). Ten OST indices of the ocular surface were generated as shown in Table 1. In this study, GCC denotes the temperature of the geometric center of the cornea, obtained midway between LT and LN. The OST indices were selected to document the whole inferior zone of the exposed ocular surface within ROI and to include as far as possible, all the reported temperature metrics [23,26–33]. All the ten OST indices extracted by the 'diamond' method has shown to be highly repeatable in assessing healthy and dry eyes [35] in terms of inter-image, inter-examiner and intra-examiner variability.

2.3. Data analysis

Data on all 62 dry eye subjects and 63 controls were tabulated and analysed. The ten OST indices were studied in two aspects: static and dynamic measures. To prevent difficulties arising when non-independent data were collected from both eyes, only data obtained from right eye were used in the analysis [42].

Static measures were study of absolute OST at t = 0 s, 5 s and 10 s (3 static attributes) after eye opening. Data were obtained directly from the raw data. As we had ten OST indices, 30 static

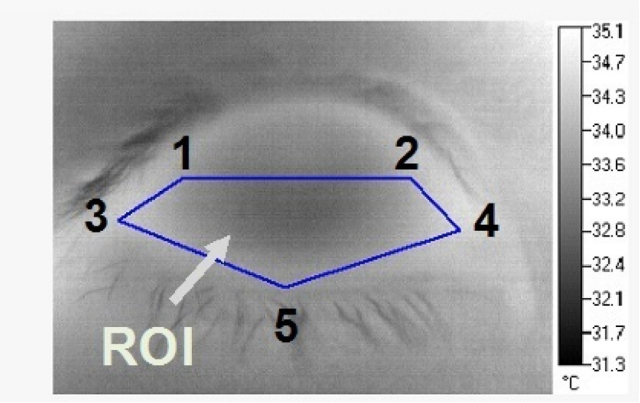

Fig. 1. The 'diamond' method in marking the ocular surface and OST acquisition. ROI = region of interest.

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