



# Thermographic evaluation of tear film break-up time to study tear film stability



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## ABSTRACT

Tear film instability is one of the major characteristics of dry eye syndrome. However, traditional diagnostic method like fluorescein tear film break-up time (FTBUT) test is limited by its invasiveness, the necessity to use fluorescein sodium and thus variable result. In this study, we proposed a noninvasive method to demonstrate thermal break-up area (Thermal BUA) by thermography, and defined its appearance as thermal break-up time (Thermal BUT). Among 31 normal controls and 42 dry eye patients enrolled in this study, Thermal BUT was significantly lower in dry eye patients ( $P < 0.001$ ). Further, dry eye patients showed faster increase in Thermal BUA. The correlation between Thermal BUT and FTBUT was also significant ( $r = 0.56$ ;  $P < 0.001$ ) in dry eye patients. Using 4 s as the cut-off value, Thermal BUT had high sensitivity and specificity to screen dry eye patients (0.80 and 0.89, respectively). These results indicate that thermography can be used to evaluate tear film stability and assessing the status of dry eye syndrome.

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## 1. Introduction

Tear film is composed of 3 layers: lipid, aqueous, and mucus layers [1]. An imbalance in any of these layers reduces the tear film stability, which may cause dry eye syndrome. Dry eye syndrome is one of the most common eye diseases in developed countries, and its incidence continues to increase [2]. The manifestations of dry eye syndrome include ocular fatigue, irritation, redness, and blurred vision [3]. The lack of lubrication on the ocular surface may eventually lead to its damage [4].

The diagnosis of dry eye syndrome is based on tear film stability, the tear production rate, and meibomian gland functionality [4]. Among various diagnostic tests, fluorescein tear film break-up time (FTBUT) test, Schirmer test with anesthesia, and meibomian gland dysfunction (MGD) test is the most common used in clinical setting. However, these tests have notable limitations, for results are often variable, and performing the procedures need to instill eye drops or

even contact the patients, which may lead to discomfort and further increase the variability of the results. Therefore, a noninvasive diagnostic tool for dry eye syndrome is warranted.

Recently, thermography has been used to evaluate tear film quality and stability through detecting the temperature change in ocular surface. Tear film evaporation is the major cause of unstable tear film, which subsequently reduces the ocular surface temperature [5–7]. As a result, detecting the change in ocular surface temperature may reflect the stability of tear film [8–10]. Previous studies have demonstrated that patients with MGD showed a higher tear evaporation rate and thus more temperature reduction compared with normal controls [11]. Moreover, ocular surface temperature reduction was also more obvious in elderly people due to excessive tear evaporation [12,13]. Compared with other diagnostic methods, thermography exhibits high sensitivity and specificity due to its non-contact nature, and can be used to detect temperature changes in the entire ocular surface in real time fashion [14–19].

In this study, we aimed to use thermography to detect changes in the ocular surface temperature. Through analyzing the temperature change, we defined thermal break-up area (Thermal BUA) and thermal break-up time (Thermal BUT). In addition, the correlation between Thermal BUT and FTBUT, and the screening potential of Thermal BUT for dry eye syndrome were also evaluated.

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## 2. Method

The Institution Review Board of Far Eastern Memorial Hospital approved the experimental protocol. Informed consent was obtained from each participant before the procedure. In this study, we included 31 eyes of 31 normal participants (13 men and 18 women) and 42 eyes of 42 patients with dry eyes (16 men and 26 women). Data from only the right eye were used for analysis. The diagnosis of dry eye was made if participants fulfill the following criteria: Schirmer I test value  $\leq 5$  mm, FTBUT  $\leq 5$  s, and MGD  $\geq$  Grade 1 [4]. The control group was defined as Schirmer I test value  $> 5$  mm, FTBUT  $> 5$  s, MGD in Grade 0, and no other signs of dry eye syndrome. Exclusion criteria included signs of ocular surface abnormalities, history of ocular surface surgery, or fluorescein allergies. None of the participants received any eye drop instillation at least 6 h before measurement. The measurements were performed in an examination room at a stable temperature ( $25 \pm 3$  °C) and humidity ( $50\% \pm 10\%$ ), with standard indoor levels of illumination and no air drafts. We performed ocular surface thermography examination on all participants first, followed by FTBUT, MGD grading, and Schirmer I test.

### 2.1. Ocular surface thermography

We used a customized ocular surface thermography device (IT-85, United Integrated Services Co., Taiwan) to measure thermal radiation (Fig. 1A). Thermographic images were constructed by converting the digital value to temperature value by a third-order polynomial. The transfer function in this study was  $T = aI^3 + bI^2 + cI + d$ , where  $T$  was the temperature,  $I$  was the digital level recorded by the thermographic camera, and  $a$  to  $d$  were the response coefficients ( $a = 7.93181 \times 10^{-10}$ ,  $b = -4.57262 \times 10^{-6}$ ,  $c = 0.02987$ , and  $d = 9.97763$ ) in the temperature range of 10–40 °C. The nonlinear relationship between the digital value and temperature was shown in Fig. 1B. The device was designed to record the thermographic images of the ocular surface at a rate of 30 frames per second, and the resolution of each frames is  $320 \times 240$  pixels. The germanium lens transmitted an 8–12  $\mu\text{m}$  infrared spectrum, with a noise-equivalent temperature difference of 0.07 °C. The device broadcasted a sequence of instructions for the participants, who opened or closed their eyes as instructed.

### 2.2. Thermographic measurement

All of the thermographic measurements were performed by a single technician. Each measurement contained 4 cycles. In each cycle, the participants were instructed to close their eyes for 9 s, then open their eyes for approximately 6 s during the recording,

and then blink right after opening the eye. An audio recording was used to deliver prerecorded instructions to the participants.

### 2.3. Thermal break-up area (thermal BUA)

As aforementioned, the machine captured the thermographic images at a rate of 30 frames per second. Average of frames was used to obtain a reliable data. Thus, images taken at each 0.1 s were the average of the previous 3 frames captured. Fig. 2A demonstrated the first image taken at 0.1 s, which served as the reference image. Subsequent images were taken (Fig. 2B), and the reference image intensity was subtracted to obtain the temperature difference image (Fig. 2C). The temperature range was further reduced from 3.6 °C to 0.5 °C by using a contrast stretching method (Fig. 2D). Furthermore, mosaic picture was constructed by using an image mosaic method, and each mosaic was calculated by averaging of 25 pixels (Fig. 2E). The threshold of thermal break-up was set at 0.2 °C, and the areas with temperature differences more than 0.2 °C were defined as Thermal BUA, which were illustrated and quantitated for further analysis (Fig. 2F). In this study, we found averaging of 25 pixels and setting threshold at 0.2 °C had the best sensitivity and specificity. The change of thermal break up areas with time under different pixels per mosaic and threshold were shown in Supplementary Fig. 1.

### 2.4. Thermal break-up time (thermal BUT)

After obtaining the change of Thermal BUA with time, we defined the beginning of thermal tear break-up as the appearance of the first 3 consecutive increase in Thermal BUA, and Thermal BUT was defined as the first of these 3 dots showing a temperature reduction of 0.2 °C (Fig. 3). We then sampled the next 5 dots, and constructed the regression line according to these 8 dots. The angle of the regression line in dry eye and normal groups were calculated and compared, which indicates the rate of increase in Thermal BUA and thus tear film evaporation rate (Fig. 3).

### 2.5. Fluorescein tear film break-up time

A standard FTBUT test procedure was performed. Each participant was administered with 2  $\mu\text{L}$  of 2% sodium fluorescein sodium drops onto the bulbar conjunctiva by using a micropipette. The participant was instructed to blink several times, which allowed the fluorescein sodium to uniformly cover the ocular surface. The FTBUT was recorded using a slit lamp, and was measured 4 times for each eye. The average of these 4 values was used for further analysis.



**Fig. 1.** Customized ocular surface thermography. A. Photograph of the customized ocular surface thermography. B. Third-order polynomial transfer function used to convert digital value into temperature value.

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