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# Analysis of the relationship of the Central Tear Meniscus Area with the tear film symptomatology and stability

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## ABSTRACT

**Purpose:** Tear film meniscus evaluation offers a non-invasive indication of the total volume of the tear. The aim of this study was to analyse the relationship between the central tear meniscus area with symptomatology and tear film stability. **Material and methods:** 120 participants who completed an OSDI questionnaire were enrolled in the study. After fluorescein instillation, two videos were recorded by a digital camera attached to a slit-lamp. The first video recorded the lower central portion of the tear meniscus (6 o'clock) with a short light beam (3x5mm), and the second one recorded the complete ocular surface obtaining the Break-Up time (BUT) and Maximum Blink Interval (MBI). A self-design program (FWCapture) was used to acquire the videos while the participants were requested to keep the eye open for as long as possible three times. Images were extracted from each video by a masked observer. From de first video, Central Tear Meniscus Area with fluorescein (CTMAF) was "manually" measured by using ImageJ software (command ">>*freehand* tool"). From the second video, BUT and MBI were determined by counting video frames then converted in seconds; both parameters were averaging using only the two most similar measurements. **Results:** CTMAF showed a negative correlation with OSDI score (Spearman Rho: $p < 0.001$, $r = -0.372$). There was found a statistical difference in the CTMAF between OSDI subgroups (Kruskal-Wallis: $p = 0.001$). CTMAF showed a positive correlation with BUT/MBI (Spearman Rho: both $p \leq 0.003$, $r \geq 0.246$). **Conclusions:** Tear film volume showed a relationship with the symptomatology and tear film stability.

**Keywords:** Central Tear Meniscus Area, OSDI, Dry Eye Disease, Tear Film Stability, Break-up time, Optometry, ImageJ, FWCapture

## 1. INTRODUCTION

To maintain an adequate balance in the tear film volume by the secretion and elimination systems is essential for the ocular surface homeostasis [1]. Since it has been proposed that the tear meniscus holds around of the 75–90% of the total tear film volume, this structure offers a non-invasive indication of that tear film characteristics [2]. Assessment of the meniscus by slit-lamp biomicroscope is performed universally by eye care practitioners as part of routine ocular assessments [3, 4]; therefore, it has been proposed by the literature different parameter to evaluate the meniscus [5, 6].

On the other hand, evaporation-induced tear volume loss because of poor tear film stability is considered one of the core mechanisms and a hallmark of tear film diseases such as the dry eye [7, 8]. High evaporative rates and volume loss generates a tear film hyperosmolarity which set up a cascade of signalling events within surface epithelial cells, that leads to the release of inflammatory mediators and proteases [1]. All those processes ends in an epithelial injury on all ocular surface components that stimulate corneal nerve endings, leading to symptoms of discomfort, increased blink rate and potentially a compensatory reflex increase in lacrimal tear secretion [9]. The aim of this study was to analyse the relationship between the central tear meniscus area with symptomatology and tear film stability.

## 2. MATERIAL AND METHODS

### 2.1 Participants and procedure

For the present study a total of 120 participants (48 male and 72 female), with a mean age of 21.6 ± 5.5 years were recruited among patients attending to the Optometry Clinic of the Optometry Faculty (USC, Spain). All of them had good ocular and general health, not wearing contact lenses and were free of any disease or drug that could alter the data.

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Subjects were excluded if they had a history of conjunctival, scleral or corneal disease, prior eye surgery (including refractive surgery or eyelid tattooing), glaucoma, diabetes mellitus, or a thyroid disorder, were pregnant or breast-feeding, or had systemic inflammatory/autoimmune disease. No participant was under any type of medication or used artificial tears at the time of the testing session. The procedures followed the Declaration of Helsinki and the protocol was reviewed and approved by the Ethics committee of the Universidad de Santiago de Compostela.

Measurements were performed under similar conditions of light, temperature (20-23°C) and humidity (50-60%). Only the right eye was examined in order to avoid the effects of overstating the precision of statistical estimates [10]. Diurnal variations were minimized as measurements were performed at the same hour by the same investigator [11, 12].

### 2.2 Ocular Surface Disease Index (OSDI)

Prior to the tear film parameters recording, during a period of 5-10 minutes to adapt to the laboratory conditions, participants completed an OSDI questionnaire (Allergan Inc.) [13]. Answers were annotated by the interviewer for the subsequent numerical evaluation according to the published guidelines on a scale of 0 to 100, with higher scores representing greater disability [13, 14]. OSDI was considered in the study to evaluate the impact of dry eye with the following scores subgroups: Asymptomatic (OSDI score < 13), Mild symptomatic (OSDI score between 13 and 23) and Severe symptomatic (OSDI score ≥ 23) participants [13, 14].

### 2.3 Tear film parameters

Previously to tear film recording and storage, a 2-µl volume of non-preserved 2% sodium fluorescein was instilled in the inferior temporal bulbar conjunctiva using a micropipette [15, 16]. Participants were instructed to blink naturally during 30 seconds without squeezing in order to equally distribute the fluorescein over the ocular surface [15]. Then, participants were positioned at the chin rest and instructed to look at a target located to maintain primary eye gaze. For further analysis, two videos of the tear film parameters studied here were recorded: one video of the Central Tear Meniscus Area with fluorescein (CTMAF) and a second video of the complete ocular surface obtaining the Break-Up Time (BUT) and the Maximum Blink Interval (MBI). All videos were recorded by a Topcon DV-3 digital camera attached to a Topcon SL-D4 biomicroscope using a cobalt blue filter and a Wratten 12 yellow filter to enhance tear film visibility [15].

#### 2.3.1 Central tear meniscus Area

##### 2.3.1.1 Meniscus recording and image selection

First, the lower tear meniscus was videotaped with a natural blink under 40X. Following previous protocols, a short light beam of 5 mm height and 3 mm wide with moderate illumination was used to avoid reflex tearing because of the light shining directly into the pupil during measurements [17-19]. The settings for video capture were specific, following the procedure previously done [17, 18, 20]. Since the height of the tear meniscus varies along the length of the lower eyelid [18, 21], the video was recorded at the centre of the lower lid margin [18, 19, 22]: central meniscus was captured at the 6 o'clock position perpendicularly below the pupil centre, with the observation and illumination systems set at 0º and without tilt of the illumination column [18, 19, 21]. The 6 o'clock-centred short light beam was used as the “measurement area” in the CTMAF measurement protocols. Videos were stored by a connected computer via Topcon IMAGEnet i-base at a spatial resolution of 1024x768pixels in RGB colour space

One image from each video of each participant was extracted and stored on high resolution in a masked numerical order by a second masked investigator to evaluate the CTMAF. To avoid inter-blink variations, in all cases the meniscus image selection was captured when the meniscus was stable with minimal changes and completely expanded after 2 seconds of the blink [12, 21, 23].

##### 2.3.1.2 Evaluation of the CTMAF parameter by computer-assisted image analysis

For the CTMAF calculation, tear meniscus images were analysed by Java-based open source image processing software ImageJ software v1.45s (National Institutes of Health, Bethesda, MD; http://imagej.nih.gov/ij/) [17, 19, 24] following a previous proposed protocol [20], One investigator manually measured in a masked and randomized order the studied parameter in the short light beam illuminated area of the images. After the upload of the images to the software (Figure 1A), the >>*freehand* tool in the toolbar (Figure 1A and 1B, upper left in the image) which allows the user to set or create a continuous non-linear line with a free size and position was selected. Then the limits of the central tear meniscus area illuminated in the short light beam during tear meniscus recoding were marked by this tool, and with the command *Analyse* > *Measure* (Figure 1B, down right in the image) the size of the area was provided by the ImageJ. In order to obtain a conversion to mm$^2$ (the unit usually used in meniscus evaluation) for further statistical and data analysis, author's asses previous to the study with ImageJ that one millimetre in a rule captured by the Topcon DV-3 camera used here have a digital equivalent length of 300pixeles.

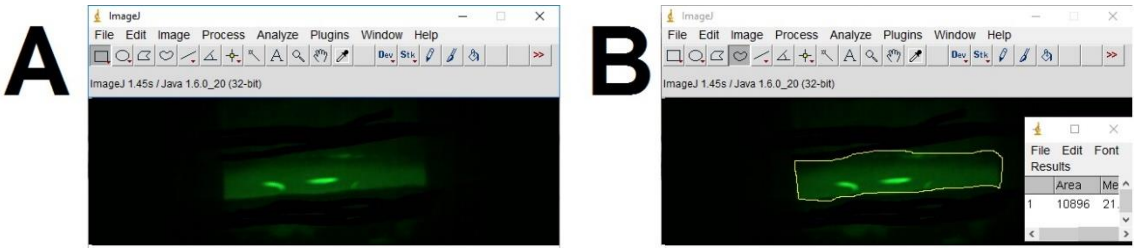


Figure 1. Measurement example of CTMAF with ImageJ by using the >>*freehand* tool in the pre-illuminated area (tool selected in the toolbar in the upper left part of the image), and the area value provided in a separate window (down right in the image).

### 2.3.2 Ter film stability

Second, the complete ocular surface was videotaped under 25X. Participants were asked to blink three times, and then to keep the experimental eye open for as long as possible [25, 26]. During this time, the tear film was recorded by a self-design program (FWCapture; Figure 2A). The process was repeated three times per experimental eye.

After the study session, another investigator quantified the BUT (defined as the time from the last blink to the first dark spot/line) and the MBI (defined as the time that the participant was able to keep the eye open before needing to blink) in a masked and randomized order on the video-recordings obtained [25, 26]. The procedure to analyse both parameters, BUT and MBI, was conducted under Linux using a program called BUTAnalysis (Figure 2B) also designed for this protocol. Using the program, a key is pressed [space, letter B and space, respectively]: when the test starts (last blink before keeping the eye opens); when the tear film breaks up; and when the test is over (first blink after keeping eye open). BUT was defined as the time between the start of the measurement and the appearance of the first tear film break. MBI was defined as the time the participant opens the eye to the first blink after keeping eye opens. Outputs for both variables with their corresponding frame numbers are provided by the software in a text document (Figure 2C), and then frames were converted into seconds (15 frames = 1 second).

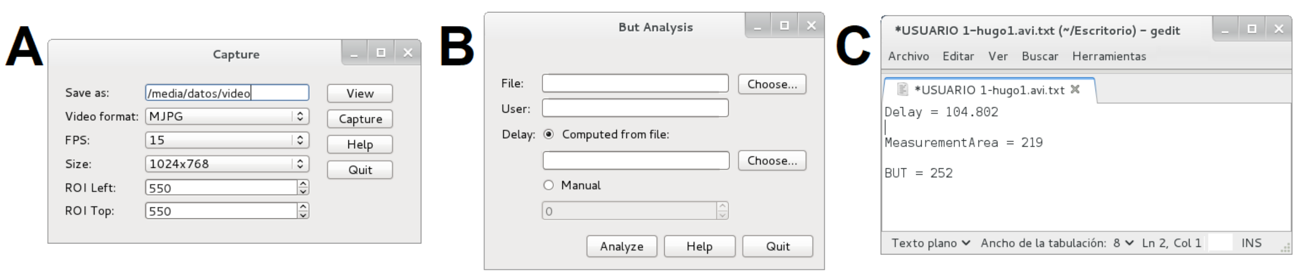


Figure 2. A) FWCapture software Control panel; B) BUT Analysis Main Window; C) Example of a .txt archive indicating in frames the three marks during the process video

## 2.4 Statistical analysis

SPSS statistical software v.19.0 for Windows (SPSS Inc., Chicago, IL) was used for data analysis. For all statistical tests, significance was set at a $p \leq 0.05$. Previous to analysis, the normal distribution of the data was checked using the Kolmogorov-Smirnov test [27]. All parameters showed a non-continuous distribution ($p \leq 0.015$). Since CTMAF showed a non-continuous distribution, differences of this parameter between subgroups generated by OSDI categories were assessed using the Mann-Whitney U and the Kruskal-Wallis for the analyses between various subgroups. Correlation between OSDI score, BUT, MBI and CTMAF was calculated using the Spearman rho Correlation. Correlations were categorized as weak (0.2–0.4), moderate (0.4–0.6), substantial (0.61–0.8), and almost perfect (0.8–1.0).

## 3. RESULTS

Table 1 showed the descriptive statistic for the parameter used in the study. While non-parametric descriptive statistics were showed (median, inter-quartile range (IQR)), mean and standard deviation (SD), as well as maximum and minimum, are also provided for comparisons with other studies.

Table 1. Descriptive statistics of the parameters studied. n = 120 subjects. SD = Standard Deviation. IQR = Interquartile Range. CTMAF = Central Tear Meniscus Area with fluorescein. BUT = Break-Up Time. MBI = Maximum Blink Interval.

| | Mean ± SD | Median | IQR | Minimum | Maximum |
|---|---|---|---|---|---|
| **CTMAF ($mm^2$)** | 55.94 ± 16.23 | 54.50 | 45.00 - 63.00 | 27.00 | 120.00 |
| **OSDI (Score)** | 10.54 ± 7.77 | 8.33 | 4.17 - 14.58 | 0.00 | 35.15 |
| **BUT (s)** | 9.49 ± 7.18 | 7.98 | 4.91 - 11.81 | 1.28 | 45.17 |
| **MBI (s)** | 14.84 ± 9.33 | 11.64 | 8.96 - 17.68 | 3.95 | 52.03 |

There was found a significant negative but weak correlation between CTMAF and OSDI score (Spearman Rho: $p < 0.001$, r =- 0.372; Figure 3): as tear volume decreases (represented by the CTMAF) the symptomatology complains raises (represented by the OSDI score). From all participants, 78 reported no relevant symptomatology (65.0 % of the total), 33 reported mild symptomatology (27.5 % of the total), and only 9 reported severe symptomatology (7.5 % of the total). There was found a statistical difference in the CMTAF parameter between groups when the sample was grouped by OSDI categories (Kruskal-Wallis test: $p = 0.001$; Table 2).

Table 2. Descriptive statistics and differences in the CMTAF between participants grouped by OSDI. SD = standard deviation. CTMAF = Central Tear Meniscus Area with fluorescein. *Kruskal-Wallis test.

| | | OSDI | | CTMAF ($mm^2$) | | |
|---|---|---|---|---|---|---|
| **OSDI score group** | **n** | **Mean ± SD** | **Median (IQR)** | **Mean ± SD** | **Median (IQR)** | **p** |
| Asymptomatic | 78 | 5.81 ± 3.09 | 6.25 (4.17 - 8.33) | 58.94 ± 14.57 | 59.00 (48.00 - 68.50) | 0.001 |
| Mild symptomatic | 33 | 16.85 ± 3.66 | 16.67 (13.54 - 20.83) | 51.42 ± 18.91 | 45.00 (40.00 - 56.00) | |
| Severe symptomatic | 9 | 28.40 ± 3.35 | 29.16 (25.00 - 30.03) | 46.56 ± 13.16 | 48.00 (33.50 - 54.00) | |

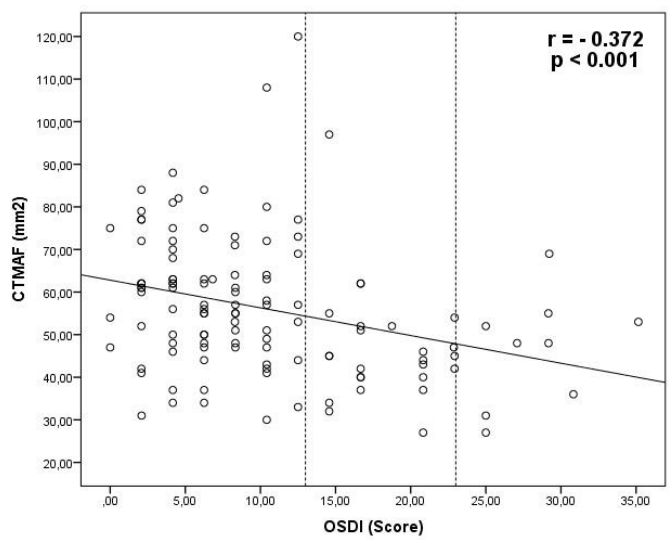


Figure 3. Spearman Rho Correlation between CMTAF and OSDI Score. Non-symptomatic, Mild and Severe symptomatic groups are segregated by the vertical dashed lines. n = 120. CTMAF = Central Tear Meniscus Area with fluorescein

The CTMAF parameter showed a significant positive but weak correlation both with both, BUT (Spearman Rho: $p < 0.001$, r = 0.271; Figure 4A) and MBI (Spearman Rho: $p = 0.003$, r = 0.246; Figure 4B): higher values in the tear film volume (represented by the CTMAF) were significantly correlated with higher values respectively in the tear film stability (represented by the BUT and MBI parameters).

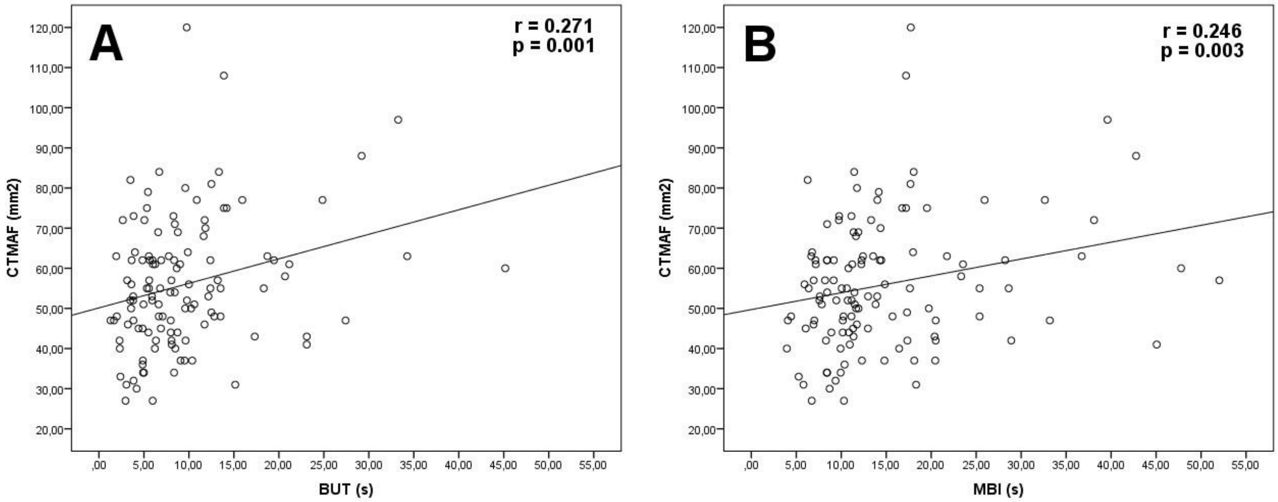


Figure 4. Spearman Rho Correlation between A) CMTAF vs. BUT, B) CMTAF vs. MBI. n = 120. CTMAF = Central Tear Meniscus Area with fluorescein. BUT = Break-Up Time. MBI = Maximum Blink Interval.

## 4. CONCLUSION

In the present study, CTMAF showed a correlation and differences with the different dry eye symptomatology status, as well as a correlation with the tear film stability parameters. Tear film production is a highly complex process [8, 28]. A good balance in its production, preservation, and elimination is vital for the tear film to be able to fulfil its numerous roles and for ocular surface health. The tear meniscus evaluation offers a non-invasive indication of the total volume of the tear film [2], an essential characteristic that allows the tear film functions. On the other hand, in clinical practice, tear film stability is usually assessed through measurement of the tear film BUT [29, 30]. Both parameters tear film stability and volume, has been established as essential in the physiopathology of some diseases such as the dry eye [7, 8]. It has been proposed that an imbalance in these processes end in an ocular surface inflammation that leads to symptoms and ocular discomfort. Confirming this hypothesis, in the present study it has been found a relationship between the tear film volumes with the symptomatology and tear film stability.

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