

Comparison of a new portable digital meniscometer and optical coherence tomography in tear meniscus radius measurement

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Abstract

Purpose: Non-invasive measurement of tear meniscus radius (TMR) is useful in the assessment of tear volume for dry eye diagnosis. This study investigates the agreement between a new, portable, slit-lamp mounted, digital meniscometer (PDM) and Optical Coherence Tomography (OCT) in the measurement of human TMR.

Methods: Images of the tear meniscus at the centre of the lower lid of 30 normal subjects (8M, 22F; mean age 27.5 SD±9.6 years), were taken using the PDM and the OCT. On the PDM and OCT images, TMR was measured using ImageJ 1.46b software. The meniscus on the OCT images was sub-divided vertically into three equal sections and the radius calculated for each: bottom (BTMR), centre (CTMR) and top (TTMR). The relationship between PDM and OCT measurements was analyzed using Spearman's Rank Coefficient, and differences between PDM and OCT sub-section measurements were evaluated using Bland-Altman plots.

Results: TMR measured with the PDM ($0.25\pm 0.06\text{mm}$) and OCT ($0.29\pm 0.09\text{mm}$) were significantly correlated ($r=0.675$; $p<0.001$). The mean differences between TMR using the PDM and the sub-sections from OCT showed that TMR measured with PDM was greater for BTMR (0.07mm ; CI 0.05 to 0.10; $p<0.001$), similar for CTMR (-0.01mm ; CI -0.04 to 0.02; $p=0.636$), and steeper for TTMR (-0.07mm ; CI -0.10 to -0.04; $p<0.001$).

Conclusions: PDM and OCT measurements of the TMR are significantly correlated, suggesting that the new PDM is a useful surrogate for OCT in this respect. The PDM appears to measure the radius of the central section of the tear meniscus.

Key words: Portable digital meniscometer, reflective meniscometry, tear meniscus radius, optical coherence tomography, tear volume

Introduction

The tear fluid on the ocular surface is present in the exposed area between the lids, in the conjunctival sac of the upper and lower lids, and in the tear menisci along the lid margins. However the tear menisci hold approximately 75% to 90% of the overall tear fluid volume and serve as reservoirs, supplying tears to the pre-corneal tear film (Holly 1985; Wang et al. 2006; Gaffney et al. 2009). The measurement of the anterior curvature radius of the tear meniscus (TMR) is an indicator of tear film volume and has been found to have good dry eye diagnostic accuracies (Mainstone et al. 1996; Bron et al. 1998; Yokoi et al. 1999; Oguz et al. 2000; Yokoi et al. 2000; Shen et al. 2009). When TMR measurement is done in a non-invasive way, this method has great advantages over other invasive tests to evaluate aqueous tear production or volume. These invasive tests, like the Schirmer and Phenol red thread tests, are variably influenced by reflex tearing and show large variations in the test results (Cho & Yap 1993; Tomlinson et al. 2001).

TMR can be measured using a slit-lamp microscope image capture system (Mainstone et al. 1996; Golding et al. 1997; Johnson & Murphy 2006), optical coherence tomography (OCT) (Wang et al. 2006; Palakuru et al. 2007; Wang et al. 2008; Wang et al. 2008; Shen et al. 2009; Li et al. 2012), or reflective meniscometry (Yokoi et al. 1999; Oguz et al. 2000; Yokoi et al. 2000; Yokoi & Komuro 2004; Yokoi et al. 2005; Oguz 2008).

With the slit-lamp biomicroscope, the radius of the meniscus can be observed in cross-section. TMR is normally assessed on the captured image by determining the radius of a circle that best fits the curved anterior meniscal face, with sodium fluorescein instilled in the tear film to improve visibility of the anterior border of the

meniscus, although the addition of fluorescein dye will increase tear volume and influence tear meniscus radius (Mainstone et al. 1996; Golding et al. 1997; Creech et al. 1998; Johnson & Murphy 2006). Indeed, the values of TMR obtained from this image capture technique with fluorescein are typically larger than those reported with reflective meniscometry or OCT (Table 1).

In contrast, reflective meniscometry is a non-invasive technique that measures TMR by projecting a target, usually consisting of black and white bands, onto the meniscus at the lower lid margin. The tear meniscus acts as a concave mirror and creates an image of the grating that, when captured by a digital camera, can be analysed using software. Reflex tearing is not stimulated using this technique as a reasonably low level of illumination is sufficient. The original meniscometer was a hand-held device, developed by Yokoi et al. (1999), and later refined by Oguz et al. (2000) into a free-standing version, called the Video Meniscometer (VM). However, only three versions of the VM currently exist worldwide and the instrument is no longer produced.

Anterior segment OCT of the ocular surface also permits a non-invasive examination of the tear meniscus (Bitton et al. 2007; Wang et al. 2008; Le et al. 2009). OCT provides cross-sectional high-resolution images of the meniscus and can be applied to the diagnosis and evaluation of dry eye disease (Fercher ; Ibrahim et al. ; Savini et al. 2006; Shen et al. 2008; Chen et al. 2009; Shen et al. 2009; Ibrahim et al. 2010; Li et al. 2012). Although OCT is useful for tear meniscus measurements, it has not found wide application among clinicians, mainly because it is considered to be too expensive (Savini et al. 2008). On an OCT image, TMR can be measured using the three-point method to fit a circle, thereby producing the tear meniscus radius (Wang et al. 2008), although there are some issues in determining the accuracy of these

measurements, due to the assumptions made in the instrument image processing algorithms. As with the slit-lamp image capture system, the anterior profile of the meniscus on the cross-sectional OCT images is treated as part of a circle with just one radius from the top to the bottom. However, it is likely that the profile of the meniscus has a more complex shape (Bron et al. 2011). Using slit-lamp image capture to analyse changes in TMR after a blink, Johnson and Murphy (2006) subdivided TMR into two radii, one at the top and one at the bottom of the meniscus. A more detailed description of the radii at the anterior surface of the meniscus has not been addressed in other OCT studies.

Based on the technique of reflective meniscometry for measuring TMR, a new portable, slit-lamp mounted, digital meniscometer (PDM) was recently introduced by the authors (Bandlitz et al. in press). The PDM uses a novel method using an iPod or iPhone screen to produce an illuminated target of parallel black and white bands which is then projected onto the meniscus at the lower lid margin. The PDM technique has been shown to be accurate and reliable, and is able to provide similar values for TMR to the existing non-portable video-meniscometer (VM) (Bandlitz et al. in press). Since the costs for the PDM are relatively low in comparison to the VM and OCT, it is suggested for use in both research and clinical practice.

Whilst VM and PDM both use reflective meniscometry to measure TMR, OCT uses a different technique. A more detailed description of the shape of the meniscus using a cross-sectional OCT image might therefore help in our understanding of the reflection-based principle of the PDM, specifically the region of the tear meniscus that the PDM image is reflected from. So, the aims of this study were (i) to investigate the agreement between the new PDM and OCT in the measurement of the TMR, and (ii)

to analyse the location on the tear meniscus from which the PDM image is being reflected.

Material and methods

Subjects

Thirty healthy subjects (male = 8, female = 22) were randomly selected from the staff and students of the Höhere Fachschule für Augenoptik Köln, (Cologne School of Optometry), Cologne, Germany. The mean age was 27.5 years (standard deviation, ± 9.3 years; range, 20 to 65 years). Subjects were excluded if they were pregnant or breast-feeding; had a current or previous condition known to affect the ocular surface or tear film; had a history of previous ocular surgery, including refractive surgery, eyelid tattooing, eyelid surgery, or corneal surgery; had any previous ocular trauma, were diabetic, were taking medication known to affect the ocular surface and/or tear film, and/or had worn any types of contact lenses less than two weeks prior to the study. Subjects with a history of dry eye, defined by either an item-weighted McMonnies questionnaire score >14.5 or a fluorescein tear break-up time <10 seconds, were excluded. All subjects gave written informed consent before participating in the study. All procedures obtained the approval of the Cardiff School of Optometry and Vision Sciences Human Ethics Committee and were conducted in accordance with the requirements of the Declaration of Helsinki.

Instruments

The portable digital meniscometer (PDM), based on a conventional iPod-touch (Apple Inc., Cupertino, CA, USA) with a 3.5" multi-touch-display 7.5 x 5.0 cm (480 x 320 Pixel), was fixed to a digital photo slit-lamp biomicroscope (BQ900 with IM900 digital imaging module, Haag-Streit, Koeniz, Switzerland) (Fig.1). Imaging of the

reflection was captured via a digital camera (RM 01 CCD-camera, 1600 x 1200 pixel, Haag-Streit, Koeniz, Switzerland) incorporated into the slit-lamp biomicroscope, and relayed to image-grabbing software (EyeSuite Imaging, Haag-Streit, Koeniz, Switzerland) within a computer. The computer screen had a resolution of 1280 x 1024, producing a total magnification of about 100x, which was the best compromise in terms of resolution and brightness of the image (Bandlitz et al. in press). The iPod-touch projects a grating target consisting of a series of white and black bands onto the tear meniscus. With the tear meniscus acting as a concave mirror, the reflected image of the lines was photographed and then analysed using ImageJ 1.46 software (Rasband, W.S., ImageJ, U. S. National Institutes of Health, Bethesda, Maryland, USA, <http://imagej.nih.gov/ij/>, 1997-2012) (Fig.2). The detailed construction of the PDM has been previously described (Bandlitz et al. in press).

The OCT images were obtained using a Cirrus HD-OCT (Carl Zeiss Meditec, Jena, Germany). This instrument uses spectral domain OCT (SD-OCT), with a wavelength of 840nm to achieve an axial resolution of 5 μ m. The cross-sectional images of the tear meniscus in this study were taken using the anterior segment five lines raster method (Fig.3). In this mode, five parallel vertical lines of 3mm length and a line distance of 0.25mm were scanned; each line was composed of 4096 A-scans. Since the anterior segment ruler function of the Cirrus HD-OCT is calibrated to measure in a vertical direction within corneal tissue, the images were rotated 90° before measuring the tear meniscus radius.

Sample calibration

To ensure that on-screen images represented curvature of known dimensions, the inner surface of five glass capillary tubes (radii 0.100mm to 0.505mm; Hilgenberg

GmbH, Malsfeld, Germany) were used as a model for the tear meniscus. The inner diameters of the glass capillaries were confirmed by use of a hole-gauge before cutting them in half. Three OCT scans were taken for each glass capillary. The OCT images were then exported to ImageJ software. Within the ImageJ software, a circle of the confirmed radius of the capillaries was used as a template onto which the OCT image was stretched or compressed until it matched with the circle (Fig.4). A regression line was then calculated to form a calibration curve, from which all OCT images of the tear meniscus were adjusted before analysis.

Procedures

The study was conducted in a room with controlled temperature (20 to 23°C) and humidity (44% to 53%). PDM and OCT images were taken of the lower tear meniscus of the right eye in primary gaze, directly below the pupil centre in a random order by a single observer. To minimize diurnal and inter-blink variation, measurements were taken in the morning between 10 and 12 o'clock, and 3 to 4 seconds after a normal blink. For both techniques the total measurement time was approximately two minutes, with a break of one minute between the two instruments.

Using ImageJ software, the width of the three bands on the PDM reflected images obtained was measured, and the radius of the meniscus calculated using the concave mirror formula. On the OCT images, the three-point circle fit technique was applied to calculate the radius (Fig.5). In addition, the meniscus on the OCT images was sub-divided vertically into three equal sections and the radius calculated for each sub-section: top (TTMR), centre (CTMR) and bottom (BTMR) (Fig.6).

Statistical analyses

Data were tested for normality using the Shapiro-Wilk test and appropriate statistical tests applied. The data were analyzed using SigmaPlot 12 (Systat Software Inc., Chicago, USA) and BiAS 10 (epsilon-Verlag, Darmstadt, Germany). The correlation between PDM and OCT measurements was assessed using Spearman's Rank coefficient, and differences between PDM and OCT sub-section measurements evaluated using paired t-testing and Bland-Altman plots.

Results

The mean values and standard deviations plus minimum and maximum values of the lower tear meniscus radius for each of the different measurements are summarized in Table 2. The radii obtained from the sub-sections suggest a parabolic curve for the tear meniscus, where the upper portion is flatter and becomes progressively steeper in the central and lower portions.

TMR measured with the PDM (0.25 ± 0.06 mm) and OCT (0.29 ± 0.09 mm) was significantly correlated (Spearman's Rank coefficient; $r=0.675$; $p < 0.001$). The mean differences between PDM and sub-sections of the OCT images showed that TMR measured with PDM was similar to that measured in the central region by the OCT (-0.01 mm; CI -0.04 to 0.02 ; paired t-test; $p=0.636$; Fig.8), but was significantly less for the TTMR (-0.07 mm; CI -0.10 to -0.04 ; $p < 0.001$; Fig.7), and significantly increased for the BTMR (0.07 mm; CI 0.05 to 0.10 ; $p < 0.001$; Fig.9).

Discussion

The PDM is an alternative way to non-invasively measure TMR and this study has demonstrated that it has a high measurement correlation to the existing OCT technique. The PDM therefore has useful potential for TMR measurements that are considered useful in the diagnosis of dry eye, the determination of tear film distribution, and in evaluation of the effectiveness of dry eye treatments.

Using OCT or reflective meniscometry, average TMR values of the lower central meniscus of normal subjects in previous studies have been reported to range from 0.24 ± 0.05 mm to 0.46 ± 0.40 mm (Table 1). The results from this study are within this range. This is important, since non-invasive measurement of lower TMR has showed good diagnostic accuracy (92% sensitivity and 87% specificity; cut-off value 0.18 mm) in the diagnosis of aqueous-deficient dry eye (Shen et al. 2009). In contrast, the average TMR found using the invasive, slit-lamp fluorescein technique ranges from 0.48 ± 0.21 mm to 0.55 ± 0.26 mm (Table 1), which gives with a cut-off value of 0.35 mm (80% sensitivity and 87% specificity), as suggested by (Mainstone et al. 1996).

Kato et al. (2010) reported a significant linear correlation between TMR values measured with VM (0.34 ± 0.21 mm) and OCT (0.35 ± 0.26 mm) in a mixed group consisting of 14 normals, 25 dry eye and 14 epiphora subjects. In their study they used the RTVue-100 OCT (Optovue, Fremont, USA), which is also SD-OCT with an axial resolution of $5 \mu\text{m}$, similar to the OCT used in this study. With the Cirrus HD-OCT we were able to measure TMR by the help of an external image analysing software.

However, there is a significant problem with using the OCT to describe the TMR shape. The dimensions of the images produced by an OCT suffer from distortions in the images paths that cannot be assessed easily. One of these distortions is the "fan-distortion". It is conditioned by the design of the scanner, and the arrangement and design of the mirror and the collimator lens (Ortiz et al. 2011; Siedlecki et al. 2012), but it has the effect that a flat surface appears to be bent. Further distortions, called "optical distortions", are caused by variations in the refractive indices of the tissue that is being measured (Ortiz et al. 2011; Siedlecki et al. 2012). The higher the refractive index of the tissue, the longer the light takes to go through the tissue: this has the result that a measuring scale calibrated to measure corneal thickness, for instance, cannot be used to measure other tissue structures. In order to perform reliable measurements with the OCT despite the resulting distortions, specialist algorithms are required to eliminate these errors (Westphal et al. 2002; Dunne et al. 2007). However, such algorithms are part of the OCT software and are not disclosed to the users of the instrument. In this study, the Cirrus HD-OCT (Carl Zeiss Meditec, Jena, Germany) was used. Within its anterior eye module, the ruler measures only vertical distances, with the scale factor calibrated for measuring corneal tissue only. Since the tear meniscus images are produced in air, the 'in-tissue' algorithm corrections were no longer appropriate, and so all OCT images were analyzed within separate software programs. To calibrate the distances and curvatures on the images, OCT images of glass-capillaries with known radii were used, and then stretched or compressed until no distortions were observed for the first interface. In contrast, there was no need to equalize the PDM images, which made the analyzing process easier. The PDM digital images can be directly used and, with the known pixel/mm ratio, distances in all directions can be measured without any transformation.

Our study showed, that the PDM measures the radius of the central section of the tear meniscus. To our knowledge, this is the first OCT study in which the meniscus was sub-divided into three different sections for detailed analyses. As might be expected from a casual perusal of the tear meniscus cross-sections, the steepest TMR was found in the bottom third and the flattest TMR in the top third of the meniscus. In a study by Johnson and Murphy (2006), where they used the slit-lamp image capture technique to measure changes in TM after a blink, the TMR was calculated at the top (TMR_t) and at the bottom (TMR_b) of the meniscus. On eye opening, they found (TMR_t) and (TMR_b) to be similar, indicating an approximately circular meniscus profile, while only one second later the radius of the top section was 0.19 mm than that of the bottom section. Thereafter, this difference in radii stabilized.

In this study, the measurements were completed 3 to 4 seconds after a blink and the TMR of the top third was found to be 0.14 mm flatter than that of the bottom third of the meniscus. Although a non-invasive technique was used, and three sub-sections instead of two, their findings of a flatter TMR at the top of the meniscus were confirmed by this study.

During the first 1.5 sec following the blink, Johnson and Murphy (2006) suggested that TMR increases by about 20%, while others observed the lower TMR to be stable during the inter-blink period (Yokoi et al. 1999; Johnson & Murphy 2006; Palakuru et al. 2007). This discrepancy is most likely the result of the different techniques used, or might be due to the observation that only some parts of the meniscus change, while other parts stay stable following a blink (Johnson & Murphy 2006). To

investigate this further, the iPod touch or iPhone used as a target in the PDM can be tilted. This will enable the positioning of the reflection of the white and black bands at different locations on the meniscus profile and may help make analysis of changes in TMR more detailed in the future.

Conclusions

PDM and OCT measurements of the TMR are significantly correlated. Since with the PDM no image calibration is needed, it seems to be a quick and non-invasive technique for evaluation of tear fluid quantity. The PDM appears to measure the radius of the central section of the tear meniscus.

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Conflict of interest

None

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Figures:

Figure 1. PDM instrument mounted on a digital imaging slit-lamp (BQ900 with IM900 digital imaging module, Haag-Streit, Koeniz, Switzerland).

Figure 2. Reflected image of the PDM lines on the concave central tear meniscus.

Figure 3. Tear meniscus cross sectional imaging with the anterior segment 5 line raster of the Cirrus HD-OCT.

Figure 4. OCT image of a glass capillary before (left) and after (right) image adjustment.

Figure 5. Tear meniscus radius measured on the OCT-image using the 3-point line-fit technique in ImageJ.

Figure 6. Best fitted radius for (A) the bottom-section of the tear meniscus (BTMR), for (B) the centre-section of the tear meniscus (CTMR) and for (C) the top-section of the tear meniscus (TTMR).

Figure 7. Differences between PDM and OCT in the top-section.

Figure 8. Differences between PDM and OCT in the centre-section.

Figure 9. Differences between PDM and OCT in the bottom-section.

Tables:

Table 1: Mean \pm standard deviation of central lower tear meniscus radius (TMR) values [mm] of normal subjects reported in the literature using reflective meniscometry, optical coherence tomography and slit lamp image capture technique.

Table 2: Mean \pm standard deviation and minimum and maximum values [mm] of the lower tear meniscus radius for each of the different measurements of central lower tear meniscus radius.