Published in final edited form as:

Ophthalmic Surg Lasers Imaging. 2009 ; 40(5): 442–447. doi:10.3928/15428877-20090901-01.

Reproducibility of Tear Meniscus Measurement by Fourier-Domain Optical Coherence Tomography: A Pilot Study

Sheng Zhou, MD, Yan Li, PhD, Ake Tzu-Hui Lu, PhD, Pengfei Liu, MS, Maolong Tang, PhD, Samuel C. Yiu, MD, PhD, and David Huang, MD, PhD

Doheny Eye Institute and Department of Ophthalmology (SZ, YL, AT-HL, PL, MT, SCY, DH), University of Southern California, Los Angeles, California; the Department of Cornea & Refractive Surgery Center (SZ), State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, China; and the College of Biomedical Engineering & Instrument Science (PL), Zhejiang University, Hangzhou, China

Abstract

BACKGROUND AND OBJECTIVE—To study the reproducibility of tear meniscus measurement with high-speed high-resolution Fourier-domain optical coherence tomography (FD-OCT).

PATIENTS AND METHODS—Twenty normal participants were enrolled in this prospective study. The lower tear meniscus in the right eye of each subject was imaged by vertical scans centered on the inferior cornea and the lower eyelid using an FD-OCT system (RTVue; Optovue, Inc., Fremont, CA) with a corneal adaptor. The system performs 26,000 axial scans per second and has a 5-micron axial resolution. Each subject was examined at two visits 30 to 60 days apart. Each eye was scanned twice on each visit. The scans were taken 2 seconds after a blink. The lower meniscus height, depth, and cornea-meniscus angle were measured with a computer caliper. The cross-sectional area was calculated using a two-triangle approximation.

RESULTS—The between-visits coefficient of variation was 17.5%, 18.0%, 35.5%, and 12.2% for meniscus height, depth, area, and angle, respectively. The intraclass correlations for these parameters were 0.605, 0.558, 0.567, and 0.367, respectively.

CONCLUSION—FD-OCT measures lower tear meniscus dimensions and area with higher between-visits reproducibility than previous OCT instruments. FD-OCT may be a useful way to measure dry eye severity and treatment effectiveness.

INTRODUCTION

Dry eye is one of the most frequent ophthalmic diseases in older adults. It has been estimated that approximately 4.91 million Americans 50 years and older have dry eye.¹ A decrease in tear secretion and tear volume is an important component of dry eye.

The purpose of our study was to investigate the reproducibility of lower tear meniscus measurement by a commercially available Fourier-domain optical coherence tomography (FD-OCT) system. FD-OCT has much greater speed than conventional time-domain OCT. The speed improvement decreases motion error. The resolution of our FD-OCT system is higher than other commercially available anterior segment OCT systems, which may further improve measurement precision.

PATIENTS AND METHODS

Normal subjects without any history of eye diseases were enrolled in this prospective study. Slit-lamp examination was performed to exclude any corneal pathology. All measurements were performed by one technician. This study was in accordance with Health Insurance Portability and Accountability Act of 1996 regulations and was approved by the institutional review board of the University of Southern California. The lower tear meniscus in the right eye of each subject was imaged with FD-OCT on two visits scheduled between 30 and 60 days apart.

Imaging Procedure

An FD-OCT system (RTVue, software version 2.7; Optovue Inc., Fremont, CA) with a corneal adaptor module (CAM) was used. The system operated at an 830-nm wavelength and had an axial resolution in tissue of 5 microns. The CAM produced telecentric scanning for anterior segment imaging using either a wide-angle or high-magnification adaptor lens. We used the wide-angle lens, which provided a transverse resolution of 15 microns. The room temperature was set at 21°C. Patients were asked to look straight ahead at the fixating target within the OCT system. The OCT pattern used to scan the lower tear meniscus was a 6-mm vertical line centered on the inferior corneal limbus (Fig. 1). Subjects were instructed to blink and then count to 3 seconds. Images were taken at 2 seconds after blink. Two images were taken at each visit. Only right eye images were used for this study.

The OCT images were exported for computer caliper measurements of lower tear meniscus height, depth, area, and cornea-meniscus angle (α) (Fig. 2). The height was measured from the cornea-meniscus junction to the lower eyelid-meniscus junction. The depth was measured from the midpoint of the air-meniscus interface to the cornea-lower eyelid junction. The area was approximated by two triangles (Fig. 3). The cornea-meniscus angle was the angle between inferior cornea and lower tear meniscus surfaces. The saline group index of 1.342 at 830-nm wavelength was used to correct the refraction at the air-meniscus interface.^{2,3}

Statistical Analysis

A linear mixed model was used to compute within-visit and between-visits reproducibility for tear meniscus parameters. The variance components in the model were including subject (σ_s^2), visit (σ_b^2), and measurement error variation (σ_w^2) to account for repeated measurements from within and between visits. Based on the above model, the difference of two measurements has a variance of $2\sigma_w^2$ if they are measured within the same visit and a variance of $2(\sigma_w^2 + \sigma_b^2)$ if they are measured at different visits. The reproducibility was assessed by the pooled standard deviation (SD), coefficient of variation (CV), and intraclass correlation coefficient (ICC), in which CV (in %) was estimated by $100 * \text{pooled SD} \div \text{mean}$. For between-visits reproducibility,

pooled SD was estimated by $\sqrt{\sigma_w^2 + \sigma_b^2}$ and ICC was estimated by $\frac{\sigma_s^2}{\sigma_w^2 + \sigma_b^2 + \sigma_s^2}$.

Statistical analyses were performed using SAS 9.1 PROC MIXED procedure (SAS Institute Inc., Cary, NC).

RESULTS

The study included the right eye of 20 healthy subjects (9 men and 11 women; mean $\pm$ SD age: 37.3 ± 8.3 years; range: 20 to 53 years).

We were able to visualize the lower tear meniscus and make measurements from 65 of 80 images. Every study eye had at least one valid image per visit. Fifteen images were excluded from the study because of poor image quality (tear meniscus boundary invisible) or large debris shadowing the cornea-lower eyelid junction point. The air interface of the meniscus has a concave curve due to surface tension (Figs. 1 and 2).

The mean and population SD of meniscus parameters are shown in Table 1 by visit. The measurements were remarkably consistent between the two visits.

Between-visits and within-visit reproducibility were assessed by ICC, CV, and pooled SD (Table 2). The meniscus height and depth had good CV and ICC. The meniscus cross-sectional area has comparable ICC, but the CV is increased because the area combines error in both depth and height. The cornea-meniscus angle has a low CV but high ICC, which shows that the angle has a small population variance in normal eyes. The between-visits variance component is comparable to the measurement (within visit) variance. This suggests that averaging several measurements within a visit is a useful way to improve the precision of meniscus evaluation.

We performed a Medline search for previous literature on the measurement of tear meniscus. The mean and reproducibility of meniscus measurements in previous studies on normal eyes are summarized in Table 3. Some studies provided the SD of the difference between measurements on repeat visits,⁴ whereas others provided the 95% confidence interval.⁵ We converted all of these values to between-visits total CV that could be directly compared with the values listed in Table 2.

DISCUSSION

Dry eye (more generally tear film dysfunction) is assessed by a battery of tests that measures secretion, volume, stability, tonicity, epithelial damage, and inflammation. For the purpose of this article, we focus on the tear meniscus, which is a measure of tear volume. The clinician typically assesses the tear volume by slit-lamp examination of the tear film and meniscus. This is subjective and only provides a rough grading. Tear volume is closely related to secretion, drainage, and evaporation. There are no simple tests for drainage and evaporation, but secretion is commonly assessed by Schirmer's tests.

Since Dr. Otto Schirmer developed Schirmer's test based on the Koster test in 1903,⁶ Schirmer's tests have been used by ophthalmologists for more than 100 years. Despite its popularity in measuring the tear meniscus volume, Schirmer's tests have the disadvantage of creating artificial tear secretion due to the use of paper strips during measuring. The use of topical anesthetic drops reduces but does not completely eliminate this side effect. Other limitations of Schirmer's tests include sensitivity to the positioning of the filter paper in the eye, the completeness of fornix drying, and the influence of evaporation, temperature, and humidity.⁷ As a result, the reproducibility and accuracy of Schirmer's tests are poor.⁸ A study by Lamberts et al.⁸ demonstrated the CV of Schirmer's test I (with anesthetic) was 66% in normal eyes. In another study,⁹ the CV of multiple tests for 10 normal eyes of Schirmer's test I (with anesthetic) varied from 31% to 55%.

Prior to OCT, quantitative tear meniscus (height and depth) measurements have been performed by a variety of instruments such as optical pachymetry and videokeratography.^{5, 10–12} A previous study¹¹ had also demonstrated that tear meniscus height was significantly correlated with Schirmer's test volumes in dry eyes. Methods that use fluorescein to enhance contrast had the best reproducibility in normal eyes, with CV of meniscus height measurement between 9.3% and 18.0% (Table 3). However, fluorescein instillation introduces extrinsic volume to the tear meniscus and may also trigger reflex tearing. Methods that measure the

meniscus in its natural state are preferable. Optical pachymetry does not require fluorescein and has a good CV of 18.7% (Table 3). However, it is not able to measure the meniscus depth or volume due to limited depth resolution.

With its high depth resolution, OCT¹³ has the potential to improve the precision and completeness of tear meniscus evaluation.⁵ Some studies were performed using time-domain OCT retinal scanners, such as the OCT1 (Carl Zeiss Meditec, Dublin, CA). Tear meniscus imaging captured with these systems presents several potential problems. First, the scan length settings are calibrated for retinal scanning in the average eye and are likely to differ from the actual length when used for anterior eye imaging. Second, the slow speed of imaging (100 axial scans/sec for OCT1) means that the image frame is acquired in approximately 1 second. Eye and head motion on this time frame may reduce the accuracy of measurement. Despite these limitations, the mean of the lower tear meniscus height, depth, and area values agree well with our results.^{11,14} Savini et al.¹⁴ showed that the meniscus height and depth were roughly halved in patients with dry eye in comparison to normal subjects. Both tear meniscus height and depth were significantly correlated with the Schirmer's paper strip wetting length.

The OCT system used by Wang et al.¹⁵ was a time-domain OCT prototype (4,000 axial scans/sec)¹⁶ that was faster than OCT1 and was designed for anterior segment imaging with telecentric scan geometry and dewarping software. Based on these considerations, the results of Wang et al. should be more accurate than previous measurements based on the OCT1 retinal scanner. Wang et al. also measured central tear film thickness, but the method was indirect and involved imaging before or after artificial tear instillation. They also measured both the upper and lower tear menisci and found their post-blink dynamics to be similar. We found upper tear meniscus measurements to be more difficult due to interference by eyelashes. Therefore, we focused our FD-OCT study on the lower tear meniscus, which was easy to obtain and may be the most practical way to assess tear volume.

FD-OCT^{17–19} is capable of much higher speed and sensitivity compared to the older time-domain OCT technology. RTVue FD-OCT acquires 26,000 axial scans per second, which is 260 times faster than the OCT1, 13 times faster than the Visante time-domain OCT anterior segment scanner (Carl Zeiss Meditec), and 6.5 times faster than the time-domain OCT prototype used by Wang et al. The RTVue acquires a 1,000-line image in 0.04 second, whereas the OCT1 acquires a 100-line image in 1.00 second and the Visante time-domain OCT acquires a 512-line image in 0.26 second. Therefore, the effect of eye motion on the measurement should be much smaller with an FD-OCT instrument.

In addition, the RTVue-CAM has a telecentric (rectangular) geometry to reduce image distortion in anterior segment imaging. The RTVue-CAM also has software that dewarps image distortion due to air-tissue index difference and allows proper calibration and measurement of anterior segment structures. Furthermore, the RTVue-CAM has higher depth resolution (5 microns) than the previous OCT systems used for meniscus measurement. For all of these reasons, the RTVue-CAM should provide more accurate and precise tear meniscus measurement compared to those obtained with previous commercial OCT instruments. Our results (Table 2) showed better CV for meniscus height and area measurements than previous OCT results (Table 3).

The measurement of meniscus cross-sectional area is complicated by the curvature of the air-meniscus interface. Wang et al.²⁰ fitted this interface with a circular arc. We took a slightly different approach and fitted the interface with two equal line segments that divide the meniscus area into two triangles. Our scheme allows the determination of a cornea-meniscus angle (α) and an eyelid-meniscus angle (Fig. 3). The meniscus forms a concave air interface due to the hydrophilic surfaces of the cornea and lower eyelid (if the cornea and eyelid were hydrophobic,

then the meniscus would be convex). Thus, α is a measure of corneal surface hydrophilicity or wettability. We do not have any data on the clinical significance of α at this time, but theoretically it might be correlated with the quality of the mucin layer. Further investigation is needed to help us interpret the clinical meaning of this new parameter.

Our study demonstrated that FD-OCT can measure the lower tear meniscus with better reproducibility than previously used OCT instruments. It provides noncontact imaging of the tear meniscus in a small fraction of a second. This new instrument may be useful in the clinical evaluation of dry eye and its treatment.

Acknowledgments

Supported by NIH grants R01 EY018184, P30 EY03040, China Scholarship grant 2007U25183, a grant from Johnson & Johnson Vistakon, Inc., a grant from Optovue, Inc., and a grant from Research to Prevent Blindness, Inc.

Drs. Li, Tang, and Huang receive grant support and patent royalties from Optovue, Inc. Dr. Huang also has stock options in Optovue, Inc. Drs. Zhou, Lu, Liu, and Yiu have no financial or proprietary interest in the materials presented herein.

REFERENCES

1. Epidemiology Subcommittee of the International Dry Eye WorkShop. The epidemiology of dry eye disease: report of the Epidemiology Subcommittee of the International Dry Eye WorkShop. *Ocul Surf* 2007;2007;5:93–107. [PubMed: 17508117]
2. Lin RC, Shure MA, Rollins AM, Izatt JA, Huang D. Group index of human cornea at 1.3-microm wavelength obtained in vitro by optical coherence domain reflectometry. *Optics Letters* 2004;29:83–85. [PubMed: 14719668]
3. Drexler W, Hitzenberger CK, Baumgartner A, Findl O, Sattmann H, Fercher AE. Investigation of dispersion effects in ocular media by multiple wavelength partial coherence interferometry. *Exp Eye Res* 1998;66:25–33. [PubMed: 9533828]
4. Palakuru JR, Wang J, Aquavella JV. Effect of blinking on tear dynamics. *Invest Ophthalmol Vis Sci* 2007;48:3032–3037. [PubMed: 17591869]
5. Johnson ME, Murphy PJ. The agreement and repeatability of tear meniscus height measurement methods. *Optom Vis Sci* 2005;82:1030–1037. [PubMed: 16357644]
6. Murube J. The Schirmer test: celebration of its first centenary. *Ocul Surf* 2003;1:157–159. [PubMed: 17075647]
7. Tsubota K. The importance of the Schirmer test with nasal stimulation. *Am J Ophthalmol* 1991;111:106–108. [PubMed: 1985472]
8. Lamberts DW, Foster CS, Perry HD. Schirmer test after topical anesthesia and the tear meniscus height in normal eyes. *Arch Ophthalmol* 1979;97:1082–1085. [PubMed: 444137]
9. Patton TF. Reliability of the Schirmer tear test. *Can J Ophthalmol* 1980;15:101–102. [PubMed: 7378894]
10. Uchida A, Uchino M, Goto E, et al. Noninvasive interference tear meniscometry in dry eye patients with Sjogren syndrome. *Am J Ophthalmol* 2007;144:232–237. [PubMed: 17533107]
11. Kawai M, Yamada M, Kawashima M, et al. Quantitative evaluation of tear meniscus height from fluorescein photographs. *Cornea* 2007;26:403–406. [PubMed: 17457186]
12. Patel S, Alio JL, Artola A, Martinez MJ. Tear volume and stability after LASIK. *J Refract Surg* 2007;23:290–298. [PubMed: 17385296]
13. Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. *Science* 1991;254:1178–1181. [PubMed: 1957169]
14. Savini G, Barboni P, Zanini M. Tear meniscus evaluation by optical coherence tomography. *Ophthalmic Surg Lasers Imaging* 2006;37:112–118. [PubMed: 16583632]
15. Wang J, Aquavella J, Palakuru J, Chung S. Repeated measurements of dynamic tear distribution on the ocular surface after instillation of artificial tears. *Invest Ophthalmol Vis Sci* 2006;47:3325–3329. [PubMed: 16877398]

16. Radhakrishnan S, Rollins AM, Roth JE, et al. Real-time optical coherence tomography of the anterior segment at 1310 nm. *Arch Ophthalmol* 2001;119:1179–1185. [PubMed: 11483086]
17. Truong SN, Alam S, Zawadzki RJ, et al. High resolution Fourier-domain optical coherence tomography of retinal angiomatous proliferation. *Retina* 2007;27:915–925. [PubMed: 17891017]
18. Gerth C, Zawadzki RJ, Choi SS, Keltner JL, Park SS, Werner JS. Visualization of lipofuscin accumulation in Stargardt macular dystrophy by high-resolution Fourier-domain optical coherence tomography. *Arch Ophthalmol* 2007;125:575. [PubMed: 17420386]
19. Alam S, Zawadzki RJ, Choi S, et al. Clinical application of rapid serial Fourier-domain optical coherence tomography for macular imaging. *Ophthalmology* 2006;113:1425–1431. [PubMed: 16766031]
20. Wang J, Aquavella J, Palakuru J, et al. Relationships between central tear film thickness and tear menisci of the upper and lower eyelids. *Invest Ophthalmol Vis Sci* 2006;47:4349–4355. [PubMed: 17003425]

Figure 1.
Video image illustrating the 6-mm vertical scan path (arrowed line) of the optical coherence tomography beam used to image the lower tear meniscus.

Figure 2.
An optical coherence tomography vertical line scan cross-sectional image of the lower tear meniscus.

Figure 3. Magnified and cropped optical coherence tomography image of the lower tear meniscus showing the meniscus height and depth and two triangles approximating the lower tear meniscus cross-sectional area. The cornea-meniscus angle (α) was also measured.

TABLE 1

Mean and Population Standard Deviation of Low Tear Meniscus Parameters by Visit

Dimensions	Height (mm)	Depth (mm)	Area (mm ²)	α
Visit 1	0.29 $\pm$ 0.08	0.21 $\pm$ 0.06	0.027 $\pm$ 0.013	34.4° $\pm$ 4.2°
Visit 2	0.28 $\pm$ 0.08	0.20 $\pm$ 0.05	0.024 $\pm$ 0.012	34.0° $\pm$ 4.8°

TABLE 2

Reproducibility Estimation of Lower Tear Meniscus Measurements Using a Linear Mixed Model

Variance Components	Height	Depth	Area	α
Within-visit ^a				
Pooled standard deviation	0.040 mm	0.026 mm	0.006 mm ²	3.9°
Coefficient of variation (%)	14.1	12.6	23.9	11.3°
Between-visits component ^b				
Pooled standard deviation	0.029 mm	0.027 mm	0.007 mm ²	1.6°
Between-visits total ^c				
Pooled standard deviation	0.049 mm	0.037 mm	0.009 mm ²	4.2°
Coefficient of variation (%)	17.5	18.0	35.5	12.2
Intraclass correlation coefficient	0.605	0.558	0.567	0.367

^aThis represents the measurement variability or the reproducibility of repeat measurements taken in quick succession.

^bThis represents the change in tear meniscus between days.

^cThis represent the reproducibility of single repeat measurements taken on separate days, which combines both measurement variability and the change in tear meniscus between days.

TABLE 3
Between-Visits Reproducibility of Tear Meniscus Measurements in Normal Eyes Reported in the Literature

Author	Instruments	Height		Area	
		Mean (mm)	CV (%)	Mean (mm)	CV (%)
Palakuru et al. ⁴	TD-OCT	0.297	19.0	0.028	37.8
Wang et al. ²⁰	TD-OCT	0.259	23.8	0.024	35.4
Wang et al. ¹⁵	TD-OCT	0.259	24.0	0.024	36.0
Johnson & Murphy ⁵	OCT1	0.27	18.7	-	-
	PACH	0.33	14.2	-	-
	SL-F	0.31	10.7	-	-
	SL-X	0.38	18.0	-	-
	VC	0.34	9.3	-	-

CV = coefficient of variation of single repeat measurements taken on different days; TD-OCT = a time-domain optical coherence tomography prototype; OCT1 = a TD-OCT retinal scanner (Carl Zeiss Meditec, Dublin, CA); PACH = optical pachymetry in cross-section without fluorescence; SL-F = optical pachymetry en-face with fluorescence; SL-X = optical pachymetry in cross-section with fluorescence; VC = video (TK-1270; JVC, Tokyo, Japan) capture en-face with fluorescence.