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ORIGINAL ARTICLE

Evaluation of lacrimal punctum and tear meniscus in dry eye syndrome: a comparative spectral domain OCT study

Murat Kaşıkcı,[1] Özgür Eroğul,[2] Hamidu Hamisi Gobeka,[2] Cansu Kaya[3]

[1]Ophthalmology Clinic, Muğla Education and Research Hospital, Mugla, Türkiye
[2]Department of Ophthalmology, Afyonkarahisar Health Sciences University, Faculty of Medicine, Afyonkarahisar, Türkiye
[3]Ophthalmology Clinic, Muğla Sitki Kocman University School of Medicine, Mugla, Türkiye

Abstract

Purpose: The aim of the study was to evaluate lacrimal punctum and tear meniscus using anterior segment-optical coherence tomography (AS-OCT), and compare the results among dry eye syndrome (DES) patients with aqueous-deficient dry eye (ADDE) and evaporative dry eye (EDE) subtypes, and healthy individuals.

Methods: We included 62 eyes of 31 ADDE subtype DES patients (Group 1), 62 eyes of 31 EDE subtype DES patients (Group 2), and 62 eyes of 31 healthy individuals (Group 3). All participants underwent a thorough ophthalmic examination, including a non-anesthetic Schirmer test for DES confirmation and detailed assessment of the cornea, as well as the conjunctiva, globe, and tear film for increased reflex secretion. The lacrimal punctum and tear meniscus were then measured using a spectral domain OCT system with high-resolution scanning software.

Results: Mean ages in Groups 1, 2, and 3 were 49.06±11.24, 46.74±11.68, and 45.48±9.17 years, respectively, (P=0.420). DES patients had significantly lower non-anesthetic Schirmer test (P<0.001), outer punctal diameter (P=0.012), punctal depth (PD) (P<0.001), tear well depth (P<0.001), and punctal reserve (P<0.001) than Group 3. Group 1 had significantly lower Schirmer test (P<0.001), PD (P=0.005), and tear well depth (P=0.003) than Group 2. Tear meniscus height (P=0.463), area (P=0.891), and angle (P=0.266) did not differ significantly among groups, nor did IOP (P>0.05).

Conclusion: AS-OCT could potentially be a useful optical diagnostic technique for in vivo lacrimal punctum microstructural and tear meniscus quantitative evaluation. It could also enable DES classification, leading to a better understanding of the underlying pathology and the avoidance of unnecessary tear drops.

Keywords: Anterior segment optical coherence tomography; dry eye syndrome; lacrimal punctum; meibomian gland dysfunction; schirmer test; tear meniscus.

Dry eye syndrome (DES) is a common ocular surface condition affecting millions of people globally, with varying degrees of severity.[1] It is a catch-all term for different symptoms and signs caused by a reduction in quality or quantity of tears on the ocular surface. An accurate DES diagnosis and classification of its severity as well as subtypes are necessary for implementation of an appropriate therapy. The first step in diagnosing and treating DES is finding out its presence, followed by a presenting subtype, which may be aqueous-deficient dry eye (ADDE) or evaporative

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Correspondence: Murat Kaşıkcı, M.D. Mugla Sitki Kocman University Education and Research Hospital, Mugla, Türkiye
Phone: +90 252 214 13 26 **E-mail:** drmuratk10@gmail.com
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dry eye (EDE).[2] These subtypes can both cause increased evaporation and decreased tear film stability, as well as similar symptoms. Despite the fact that EDE is the most common subtype, affecting 35–45% of patients, in most severe conditions, both subtypes of DES coexist.[3-6]

Lacrimal punctum is where the tears enter the nasolacrimal system and is typically larger in the lower than the upper eyelids in adults.[7,8] Despite the general assessment of the lower lid punctum, a lack of consensus on imaging modalities for the proximal lacrimal system has resulted in a paucity of punctum studies.[7,9] Punctal disease is commonly diagnosed using clinical and/or slit-lamp examinations. The latter enables easy lacrimal punctum visualization; however, it is highly subjective and insufficient for determining lacrimal punctum size. Further, while ultrasound biomicroscopy of the proximal lacrimal system has been proposed, the images obtained have lower resolution than those obtained with optical coherence tomography (OCT).[10]

OCT a relatively new painless, non-invasive, and non-contact optical diagnostic technology that employs infrared radiation can capture high-resolution images with strong tissue microstructural penetration, as well as fast cross-sectional image acquisition.[11,12] In addition to providing detailed in vivo cross-sectional images of the retina, it can be used in the anterior segment (AS), including cornea, iridocorneal angle, and conjunctiva. However, only a few studies, have focused on imaging the punctum and canaliculi, and the anatomical parameters currently measured by OCT are lacking.[13]

In the current study, the lacrimal punctum and tear meniscus were evaluated and compared in ADDE and EDE subtypes of DES patients and healthy individuals using AS-OCT.

Materials and Methods

Study Design

This observational study, which was conducted at Mugla Sitki Kocman University Training and Research Hospital between March 2020 and March 2021, included 62 DES patients and 31 age- and gender-matched health individuals. Patients were newly diagnosed individuals who did not previously received medical treatment. All participants were divided into three groups.

Group 1 (Primary Sjogren's Syndrome-sicca group) consisted of 31 patients with aqueous tear insufficiency. None of these were cases that did not receive artificial tears treatment. The tear film break-up time (TBUT) score of this group was ≤5 seconds and the Schirmer test result was ≤5 mm/5 min. There was also intense ocular surface fluorescein staining. Participants had mild-to-moderate ocular surface complaints.

Group 2 (EDE Group) consisted of 31 patients with meibomian gland dysfunction and increased evaporation. It included newly diagnosed patients who were not treated for dry eyes. The TBUT score was between 5 (or 6?) and 10 s but >5 seconds (range 5–10 seconds) and the Schirmer test result was between 6 and 10 mm/min. There was also mild-to-moderate ocular surface fluorescein staining. Group 2 participants had more ocular surface complaints than Group 1.

Group 3 included 31 healthy patients who did not have dry eye disease and came to the outpatient clinic primarily for refractive issues. The TBUT score was >10 seconds and the Schirmer test result was >10 mm/5 min. Group 3 participants had no ocular surface complaints and no ocular surface staining.

The Clinical Research Ethics Committee of Mugla Sitki Kocman University Training and Research Hospital reviewed and approved the study protocol, which abided to the principles of the Helsinki Declaration (Decision date: February 17, 2021, No. 4/II). All participants gave their written informed consents for the AS-OCT measurements and clinical note analysis.

Preliminary Ophthalmic Examination and Participant Recruitment

A preliminary comprehensive ophthalmic examination was performed on all participants, which included Logarithm of the Minimum Angle of Resolution (LogMAR) best-corrected visual acuity (BCVA) measurements and Goldmann applanation tonomtery, as well as anterior-posterior slit-lamp biomicroscopy (Inami, Japan). Additional tests were performed, including an examination of the cornea for any potential pathological conditions, as well as the conjunctiva, globe, and tear film for increased reflex secretion. Canthal ligament laxity, eyelid position, and punctal opening and position were also assessed. In addition to TBUT analysis, all participants underwent a non-anesthetic Schirmer test for DES confirmation. However, to avoid any potential influence of the study results, OCT measurements were performed before the Schirmer test. Following that, the Schirmer and TBUT tests were carried out.

Patients with bilateral EDE subtype who presented with clinical findings and high Schirmer test plus TBUT, as well as those diagnosed with MGD-related ADDE were included in the study. Other subtypes of MGD-unrelated EDE

patients with dry eye symptoms due to excessive evaporation, punctum, and/or canaliculi inflammation, as well as those with glaucoma, cataracts, corneal, and retinal disorders, were excluded from the study. The lacrimal drainage system was checked after AS-OCT measurements were made in all groups. Individuals with completely open lacrimal drainage systems were included in each group, while those with clogged lacrimal drainage systems were excluded from the study. Furthermore, participants in each group were asked if they were in menopause, taking systemic and topical medications, pregnant, or breastfeeding.

AS-OCT Acquisition

All lacrimal punctum and tear meniscus measurements were performed by an experienced technician using a spectral domain OCT system (Heidelberg Engineering GmbH, Heidelberg, Germany) with customized software (software version 1.8.6.0, Heidelberg Engineering) capable of high-resolution scanning, which was performed between 09:00 and 16:00. The technique involves placing the patient's chin against the OCT chin support and his/her forehead against the upper support. All participants had both their eyes scanned. None of the participants used eye drops an hour before the test, which could have influenced the study results.

The lower eyelid was turned slightly outward with a cotton swab placed under the punctum long enough to bring the punctum to a plane perpendicular to the light source while the participants' eyes were open. Before image acquisition, participants were asked to blink 2–3 times. They were also instructed to look straight at a fixation light with no background illumination, though spontaneous blinking was permitted. Each eye was examined independently, and the contralateral eye remained open during scanning. The average temperature and humidity level in the test room were 23±3°C and 41±5%, respectively. The ambient room light remained constant, as well. The medial lower eyelid was held slightly outward to expose the punctum to the OCT scanner, with great care taken not to distort the anatomy within the applicable range. The puncta were visualized to the mucocutaneous junction using a horizontal scan line, the lower lid tear meniscus height was then measured from the cornea-meniscus junction to the lower eyelid-meniscus junction using a scan line perpendicular to the mucocutaneous junction. Each patient was examined twice and all images were reviewed by an experienced ophthalmologist.

The widest and deepest punctal image with the maximum values was chosen as the final parameters. The final outer punctal diameter (OPD) was measured as the distance between the highest points of the punctal papilla. Punctal depth (PD) was calculated by measuring distance between OPD and the punctum base. The pool of tears standing in the punctum was referred to as a tear well. While tear well diameter represented the length of the tear well, tear well depth represented the distance from the surface of the tear film to the punctum base. Punctal reserve (PR) was defined as the difference between PD and tear film depth, and PR rate as the ratio of PR to PD (Fig. 1).

Furthermore, tear meniscus height measurements were performed under the same conditions, with an OCT pattern of a 6-mm vertical line placed at a central point being

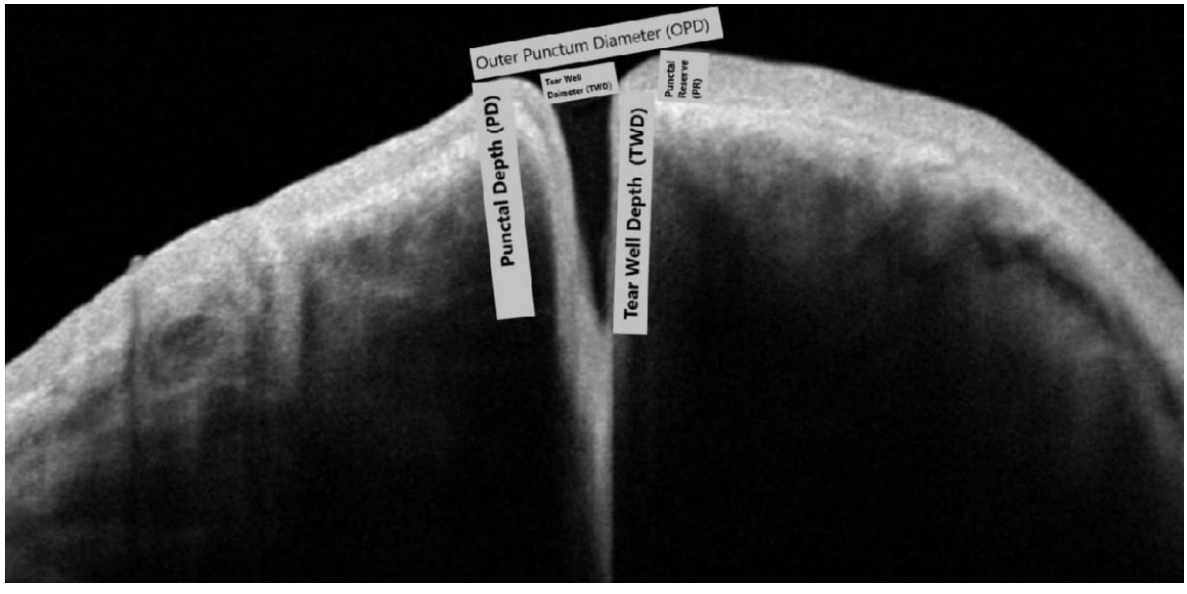

Fig. 1. An illustrative AS-OCT measurement of the lacrimal punctum parameters

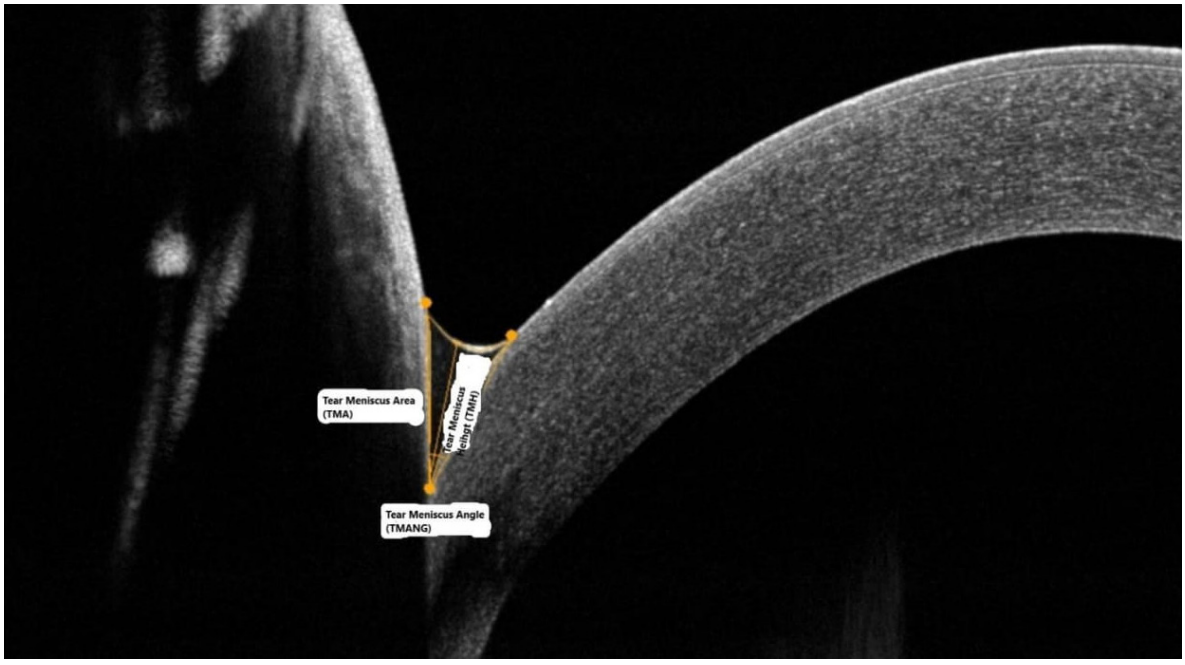

Fig. 2. An illustrative AS-OCT tear meniscus analysis, including tear meniscus height, area, and angle measurements

used to scan the tear meniscus. This central point was determined by intersecting the vertical axis of the central cornea with the lower eyelid (Fig. 2). Aside from the lacrimal punctum and tear meniscus measurements, demographic characteristics of all participants were recorded for statistical purposes.

Statistical Analysis

A Statistical Package for the Social Sciences (SPSS Inc., version 22.0, Chicago, IL, USA) was used for statistical analysis. The Kolmogorov–Smirnov test was used to assess data distribution. The one-way ANOVA test was used for data comparison. The Chi-square test was used to analyze qualitative data. The Pearson Correlation test was used to determine data correlation. P<0.05 were deemed statistically significant.

Results

The mean ages in Groups 1, 2, and 3 were 49.06±11.24, 46.74±11.68, and 45.48±9.17 years, respectively (p=0.42). The female to male ratios were 26:5 in Group 1, 24:7 in Group 2, and 25:6 in Group 3 (p=0.81). The logMAR BCVAs for Groups 1, 2, and 3 were 0.8±0.2, 0.7±0.2, and 0.9±0.1, respectively. Groups 1, 2, and 3 had intraocular pressure (IOP) of 17±6, 18±5, and 18±5 mm/Hg, respectively.

Lacrimal Punctum and Lower Lid Tear Meniscus Analyses

In comparison to Group 3, DES patients (Groups 1 and 2) had statistically significantly lower non-anesthetic Schirmer test (P<0.001), OPD (P=0.012), PD (P<0.001), tear well depth (P<0.001), and PR (P<0.001). Intragroup analysis of DES patients revealed statistically significantly lower non-anesthetic Schirmer test (P<0.001), PD (P=0.005), and tear well depth (P=0.003) in Group 1 than Group 2 (Fig. 3). Tear meniscus height (P=0.463), tear meniscus area (P=0.891), and tear meniscus angle (P=0.266) did not differ statistically significantly among groups (Table 1). There was no significant correlation between lacrimal punctum parameters and age or gender in any of the groups.

Discussion

DES is a serious ocular pathology with a multifactorial etiology that plays a role in the pathogenesis of chronic immunological processes characterized by immune cell infiltration in the lacrimal glands, as well as increased tear inflammatory cytokines and immune cell density. In the current study, DES patients had significantly lower OPD, PR, tear well depth, and PD compared to healthy individuals, probably due to the inflammatory processes associated with DES clinical manifestation. Further, intragroup analysis of DES patients revealed that ADDE subtype had significantly lower PD and tear well depth, as well as non-anesthetic Schirmer test measurements, than EDE subtype. This finding was unsurprising given that the inflammatory processes in ADDE subtype of DES is anticipated to be more severe than in EDE subtype. ADDE is characterized by reduced aqueous tear secretion by the lacrimal glands, leading to a hyperosmolar tear film and ocular surface desicca-

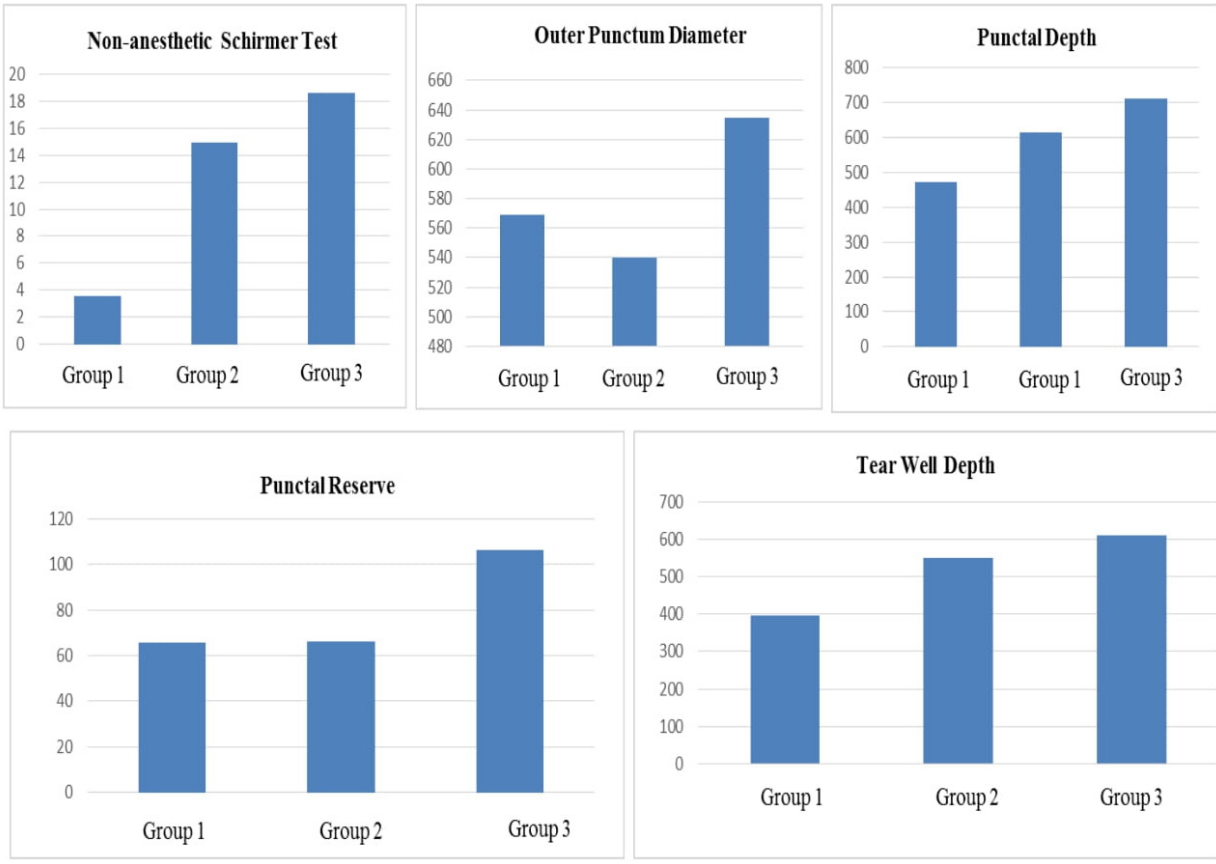

Fig. 3. A graphical representation of the lacrimal punctum parameters, which were found to be significantly lower in all DES patients when compared to healthy individuals

tion. EDE, on the other hand, is typically caused by MGD, which is characterized by altered lipid secretion needed to control evaporation and preserve a normal tear film.[14]

The use of AS-OCT lacrimal punctum measurements for early diagnosis and treatment follow-up in DES patients without a clear clinical manifestation is presumed to expand clinicians' perspectives.[15] In the current study, while the tear meniscus height and area were lower in ADDE subtype compared to EDE subtype and healthy individuals, the differences were not statistically significant, most likely due to the small number of patients and, consequently, the small number of eyes measured. The lacrimal punctum parameters did not correlate with age or gender in any of the study groups, as well.

While there is currently no in vivo method for evaluating disorders of the lacrimal punctum and canalicular structures, AS-OCT, pioneered by Izatt[16] in 1994, has emerged as a relatively novel non-invasive optical diagnostic technique for AS imaging. It is believed to have a significant future application value, and has been proposed for use in early diagnosis and treatment of severe DES patients. Because of its numerous benefits, this imaging technique has been widely used in clinical practice, most recently in evaluation of the proximal lacrimal system.[9] It has also been used to measure the lacrimal microstructural anatomical parameters, evaluate the punctoplasty effectiveness, and examine the lacrimal lesions.[9,17] Furthermore, this technique aids in the diagnosis and treatment of punctal lesions such as punctal stenosis, punctal obstruction, punctal tear, punctal atresia, and punctal mass by providing accurate imaging and measurement of punctal size. It may also be used to monitor the effect of surgery or drugs on punctal size, which could be useful in the future studies of the proximal lacrimal system's physiological functions and mechanisms.[17]

Several studies used OCT to assess the lacrimal microstructures of only healthy individuals, with varying results.[9,18-22] Despite the fact that the measurements were restricted to healthy individuals, OCT reliability and reproducibility were thoroughly investigated.[23] Vertical single-line AS-OCT scans have recently been used to assess lower eyelid tear meniscus height.[24,25] AS-OCT has also been used in normal healthy individuals for lacrimal punctum visualization, punctal parameter measurement, and determining

Table 1. Quantitative analysis of the lacrimal punctum and lower lid tear meniscus values in patients with dry eye syndrome and healthy individuals

	Group 1, n=31 (Aqueous type)	Group 2, n=31 (Evaporative type)	Group 3, n=31 (Healty Individuals)	P-value
Non-anesthetic schirmer test	3.52±2.25 mm/5 min	14.92±4.48 mm/5 min	18.60±4.39 mm/5 min	<0.001
				0.00021
Outer punctal diameter	568.71±143.49 µm	540.13±110.1 µm	634.45±88.03 µm	0.012
Punctal depth	471.95±273.38 µm	613.41±274.24 µm	710.46±234.82 µm	<0.001
				0.00012
Tear well depth	395.98±255.69 µm	549.79±275.97 µm	609.42±249.86 µm	<0.001
Tear well diameter	216.56±98.32 µm	188.84±56.59 µm	201.19±87.02 µm	0.446
Punctal reserve	65.52±40.55 µm	66.19±34.89 µm	106.37±75.21 µm	<0.001
				0.00018
Tear meniscus height	270.31±138.30 µm	321.68±194.98 µm	308.16±200.39 µm	0.463
Tear meniscus area	0.049±0.05 µm2	0.081±0.12 µm2	0.071±0.12 µm2	0.891
Tear meniscus angle	56.48±11.18°	57.35±10.19°	57.81±5.88°	0.266

the amount of tear meniscus around the punctum.[18,19,26] The authors believe, on the other hand, that the current AS-OCT study is the first to comparatively evaluate quantitative measurements of the lacrimal punctal microstructures and tear meniscus in both ADDE and EDE subtypes of DES patients, as well as healthy individuals to determine the correlations between lacrimal punctum and tear meniscus measurements.

The current study's mean OPD was consistent with Sung et al.,[18] and Timlin et al.,+ but not with Allam et al.,[22] Kamal et al.,[21] and Wawrzynski et al.[9] Further, Wang et al.,[19] reported an OCT study with mean OPD of 548.4±130.5 µm and mean inner punctal diameter of 262.8±120.8 µm. This discrepancy could be ascribed to different definitions of the punctal measurement range used by various studies and/or the presence of different measurements as a result of various OCT brands and models, as well as the participants' ages and ethnic backgrounds. Allam et al.,[22] and Kamal et al.,[21] used OCT RTVue for measurements, whereas Sung et al.,[18] and Timlin et al.,[20] used Heidelberg Spectralis OCT, as in the current study.[18] As far as the measurement range is concerned, there is currently no unified standard for OPD. The mean OPD was 620 µm in one study of healthy Koreans published in 1997.[27] Overall, the current study, which included healthy individuals, yielded results that were consistent with many prior studies in this circumstance.

Various definitions have been proposed for AS-OCT punctal parameters.[9,16] The definitions of OPD, PD, and tear well depth in the current study matched those of Timlin et al.,[20] and Sung et al.,[18] resulting in consistent findings. Further, AS-OCT measurements of PDs ranging from 252 to 890 µm have recently been reported.[9,16,18,20] Hwang et al.[28] reported as higher PD as 1110 µm in a cadaver study published in 2005. On the other hand, the current study, in which the longest PD was measured at 945.28 µm, found a mean PD of 710.46 µm in health individuals, which was in line with the majority of prior reported ranges. This correlation could be explained by the fact that the mean ages of participants in prior studies were comparable. Even so, there have been no prior studies on racial differences in punctal diameter as well as PD measurements.

The current study did not evaluate eyes with nasolacrimal duct obstruction presenting with a tear meniscus volume <100 µm and epiphora. This is because punctal images of these patients would show punctal tear flow and low PR in the patient's microenvironment granulomas.[18] These contradictory findings could make it difficult to measure the lacrimal punctum and tear meniscus, especially in patients with complicated conditions like DES and nasolacrimal duct obstruction.[29] Furthermore, when epiphora occurs in patients who have minor complaints, the diagnostic value of tear meniscus height may be diminished. These patients may eventually benefit from punctal AS-OCT, which can detect pathology in the lacrimal punctum through PR measurements. In the current study, DES patients had significantly lower mean PR than healthy individuals, which could be due to a reduction in tear secretion caused by pronounced inflammation in ADDE subtype. A low PR in EDE subtype, on the other hand, could be a result of increased tear osmolarity.

There are limitations to the current study. To examine the lacrimal punctum more clearly, turn the eyelid outward. Despite the fact that all participants were examined twice by an experienced technician and then thoroughly reviewed by the experienced ophthalmologist, direct measuring by the ophthalmologist could reduce technician-caused errors. The current study had a relatively narrow age range of 18–55 years, as well as a relatively small number of study participants, the majority of whom were females. Thus, the authors believe that large-scale studies involving patients and healthy individuals of various ages, gender, and ethnic backgrounds would be useful in determining the normal range of OCT values around the world and across races.

Conclusion

The current study demonstrated that using AS-OCT for lacrimal punctal microstructural visualization could help us understand its anatomy, allowing us to better understand diagnosis, follow-up, and severity of DES. It is worth noting that the lacrimal punctum microstructures not only changed significantly in DES patients compared to healthy individuals, but they were also correlated with tear meniscus measurements. The use of AS-OCT could also aid in the differentiation of DES subtypes, providing a better understanding of the underlying pathology and avoiding the use of unnecessary tear drops. Consequently, AS-OCT could be a useful optical diagnostic technique for quantifying in vivo lacrimal punctum microstructures and tear meniscus parameters.

Ethics Committee Approval: This study was approved by Mugla Sitki Kocaman University Faculty of Medicine Ethics Committee 17/02/2021 date; number: 4/II

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