



Impact of meibomian gland width on successful contact lens use

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ARTICLE INFO

Keywords:

Meibomian gland width
Meibomian gland atrophy
Meibomian gland dysfunction
Contact lens dissatisfaction
Image analysis

ABSTRACT

Purpose: To evaluate meibomian gland (MG) width and determine its impact on successful contact lens (CL) use and ocular health.

Methods: A five-site study was conducted by recruiting 18- to 45-year-old subjects who had dropped out of CLs because of discomfort. CL dropouts were compared to age- and sex-matched successful CL wearers. Right eyes were evaluated for tear break-up time, tear meniscus height, MG expressibility, meibum quality, and meibography. Central MG widths were evaluated with a custom MATLAB program.

Results: CL dropouts (n = 56) and successful CL (n = 56) wearers had similar grades for upper (p = 1.0) and lower (p = 0.22) MG atrophy, upper (p = 0.07) and lower (p = 0.89) MG tortuosity, and upper (p = 0.92) and lower (p = 0.97) MG widths. Upper eyelid MG widths were narrower than lower eyelid MG widths (p = 0.03). Upper and lower MG tortuosity (p < 0.001) and widths (p = 0.03) were associated, but not atrophy (p = 0.42). Lower eyelid MG widths were associated with MG expressibility (p = 0.01), but MG widths were not with any other factors.

Conclusions: Successful CL wear does not appear to be clinically influenced by MG width or other measures of MG structural integrity. Lower eyelid MGs were wider than upper eyelid MGs and narrower lower eyelid MGs were associated with worse MG expressibility, suggesting that narrower MGs may produce abnormal meibum. Data also suggests that MG factors of both eyelids should be evaluated in practice.

1. Introduction

Meibomian gland dysfunction (MGD) is the most common cause of dry eye, a condition that affects millions of people around the world [1,2]. The meibomian glands (MG) are large sebaceous holocrine glands that are located within the tarsal plates of both the upper and lower eyelids [3,4]. The MGs are important because expression of these glands produces a mostly lipid secretion (meibum), that traverses to the ocular surface and forms the outer layer of the tear film [5,6]. A robust lipid layer promotes tear stability and minimizes tear evaporation [7,8]. If the meibum composition is altered or production is reduced, it can result in tear film destabilization [9,10]. This can ultimately lead to ocular discomfort, and in contact lens (CL) wearers, it could lead to CL

dropout [11,12]. While the full mechanism leading to MGD is unclear, MG atrophy is likely involved, because atrophy has been associated with altered tear lipid production and altered tear film stability [13–15].

MG atrophy can be captured and monitored with a technique called meibography, a method first described by Tapie in 1977 [16,17]. The original form of meibography, contact meibography, involves transilluminating an everted eyelid with a light probe, and the eyelids (MGs) are then typically imaged with a camera [16,18]. While contact meibography systems are able to obtain quality images, they are difficult to use and have a limited field of view [18]. Patients also generally find this method uncomfortable [18]. Together, these factors have inhibited contact meibography from being employed in clinical practice

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<https://doi.org/10.1016/j.clae.2019.06.004>

Received 26 January 2019; Received in revised form 8 May 2019; Accepted 17 June 2019

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[18]. Contact meibography has since given way to non-contact meibography [19]. The initial version of non-contact meibography (2008) used a modified slit-lamp biomicroscope coupled with an infrared camera to directly image the MGs, without the need for a transilluminator [19]. Non-contact meibography alleviates the disadvantages noted above [18]. Automated commercial meibography instruments have since been introduced, and trained technicians can now easily use these devices to obtain full-field MG images [20,21].

With the advent of a quicker, easier, and more patient-friendly meibography method, the technique has become much more clinically relevant, and it has begun to emerge as a routine clinical test for dry eye assessments. Clinicians can now use meibography to easily grade the amount of atrophy present, a metric that is typically assessed as the overall amount of MGs remaining compared to the hypothetical original amount of MGs; this information is then used to determine a patient's relative disease state and treatment plan [19,21]. With that said, the literature is still forming as to how MG atrophy and general MG structural integrity, as quantified by the amount of atrophy and tortuosity (gland deviation), is related to ocular surface disease and as to what potentiates these MG structural changes.

MG atrophy (structural changes) has been hypothesized to result from hyperkeratinization of the MG ducts, which then causes obstruction, pressure, and MG atrophy [22]. Alternatively, obstruction and subsequent MG atrophy may result from hyperproliferation of non-keratinized ductal epithelial cells, or MG atrophy could also result from stress-induced "early exhaustion of the progenitor or stem cells" needed to support the acini within the MGs [22]. Increasing amounts of MG atrophy has been correlated with increasing age and greater ocular symptoms [19,20,23,24]. There is also evidence that MG atrophy may be related to years of CL use [25,26], though this association has since been called into question [21,27]. Likewise, upper eyelid MG tortuosity has been found to be associated with an increased odds of dropping out of CLs [28].

While the literature on MG structural changes, primarily atrophy and tortuosity, is maturing, there is currently a dearth of information on how MG width (a potential new metric for MG health) is related to a patient's ability to wear CLs and its impact on dry eye signs and symptoms. This information is practically relevant to understanding mechanisms leading CL discomfort, a condition that has been associated with MG dysfunction [28]. Thus, the purpose of this study was to use a novel semi-automated MATLAB program to analyze mean MG width of the central MGs in the upper and lower eyelids, to determine if MG width has an impact on CL success and dry eye signs and symptoms. This was accomplished by comparing successful CLs wearers to subjects who have ceased wearing CLs due to discomfort. This information may help the community better understand the etiology of Contact Lens Discomfort [29].

2. Methods

2.1. Subjects

The general protocol for this study has been previously published [28]. This single-visit study competitively recruited participants from five clinical study sites, which included the University of Alabama at Birmingham, University of Waterloo, Marshall B. Ketchum University, JENVIS Research c/o Ernst Abbe University of Jena, and University of Houston. Subjects who had completed a comprehensive eye exam within the past two years and were between the ages of 18 and 45 years were recruited to participate in the study. Subjects who were older than 45 years were excluded, to decrease the chances of a subject discontinuing CL use because of presbyopia. Subjects were enrolled as cases if they self-reported CL dropout in the past six to twelve months because of ocular discomfort. A small CL dropout window allowed for a more direct comparison between the CL dropout and successful CL wearing groups. CL dropouts were age- and sex-matched to minimally

symptomatic CL wearers from the same site that the dropout was recruited from. Successful CL wearers were required to wear their CLs for 8 or more hours per day and 5 or more days per week; they were also required to be minimally symptomatic (CLDEQ-8 scores ≤ 10) [30]. Past gas permeable or specialty hard CL wearers were excluded. Subjects were also excluded if they had an autoimmune disease associated with altering tear film physiology, a recent history of eye surgery (≤ 12 months), a recent history of severe eye trauma, active eye infection or inflammation, were currently using isotretinoin-derivatives or ocular medications, or if they were pregnant or breast feeding [31]. Subjects who had mild corneal scarring (no corneal elevations changes and acuity better than 20/40) were allowed to participate. Artificial tear or rewetting eye drop users were allowed to participate if they agreed to not use these drops within two hours of the study visit.

2.2. Statistical analysis and sample size

MG atrophy (measured subjectively as meiboscores – described below) was used as the primary clinical outcome measure, on which the two cohorts were compared during the primary study [28]. A pre-calculated sample size estimate for MG width was not possible because of the lack of data on this factor. Data from Arita et al. were used to obtain estimates of variability in meiboscores [19]. Sample size calculations were performed using PASS 2005, assuming a two-sided *t*-test with $\alpha = 0.05$ and $\beta = 0.10$ (90% power). The aim was to observe a difference between the two cohorts that was similar to that of our previous study on MG atrophy (effect size = 0.55) [21]. Therefore, 74 total subjects (37 subjects in each arm) were required to make a comparison between successful CL wearers and CL dropouts.

2.3. Study protocol

CL dropouts were required to have dropped out of CLs because of discomfort within the past six to twelve months [11]. CL dropouts were age- and sex-matched to minimally symptomatic CL wearers (Contact Lens Dry Eye Questionnaire-8 scores of ≤ 10) [30]. All CL wearers were asked to report for the study visit without their CLs, to allow for a more direct comparison of the two study groups and to avoid any transient tear changes that may have been associated with CL removal. Each site obtained Human Subjects Institutional Review Board approval, and this study followed the tenants of the Declaration of Helsinki. Qualifying subjects were consented and asked to sign a health privacy document as deemed appropriate by each site's internal review board. Tests were administered in the least to most invasive order to avoid influencing subsequent tests [32].

An investigator-developed questionnaire was used to collect ocular, systemic, and CL history. Subjects were asked to complete the Standardized Patient Evaluation of Eye Dryness (SPEED) questionnaire to quantify common dry eye symptoms [33,34]. A multifunctional topographer (Keratograph 5 M, Oculus, Inc., Wetzlar, Germany) was used to determine the subject's non-invasive tear break-up times (NITBUT) and tear meniscus heights (TMH) [35]. NITBUT was measured by using a stopwatch to time the amount of time until the first Placido disc distortion was detected while TMH was calculated with the multifunctional topographer's imbedded software. Both NITBUT and TMH were measured in triplicate, and the mean of each measurement was reported. A slit-lamp biomicroscope was used to evaluate upper and lower eyelid blepharitis using a 0–4 grading scale, upper and lower MG expressibility with a 0–3 grading scale and upper and lower eyelid MG quality with a 0–4 grading scale [36]. Upper and lower MG atrophy was graded via meibography by imaging the MGs with the multifunction topographer and having two masked examiners subjectively grade each image with a 0–3 grading scale; the same images were graded with a 0–4 grading scale to determine MG tortuosity by the same two examiners [19,20,37,38]. The majority of discordant grades were resolved by having a third examiner regrade the images. All remaining

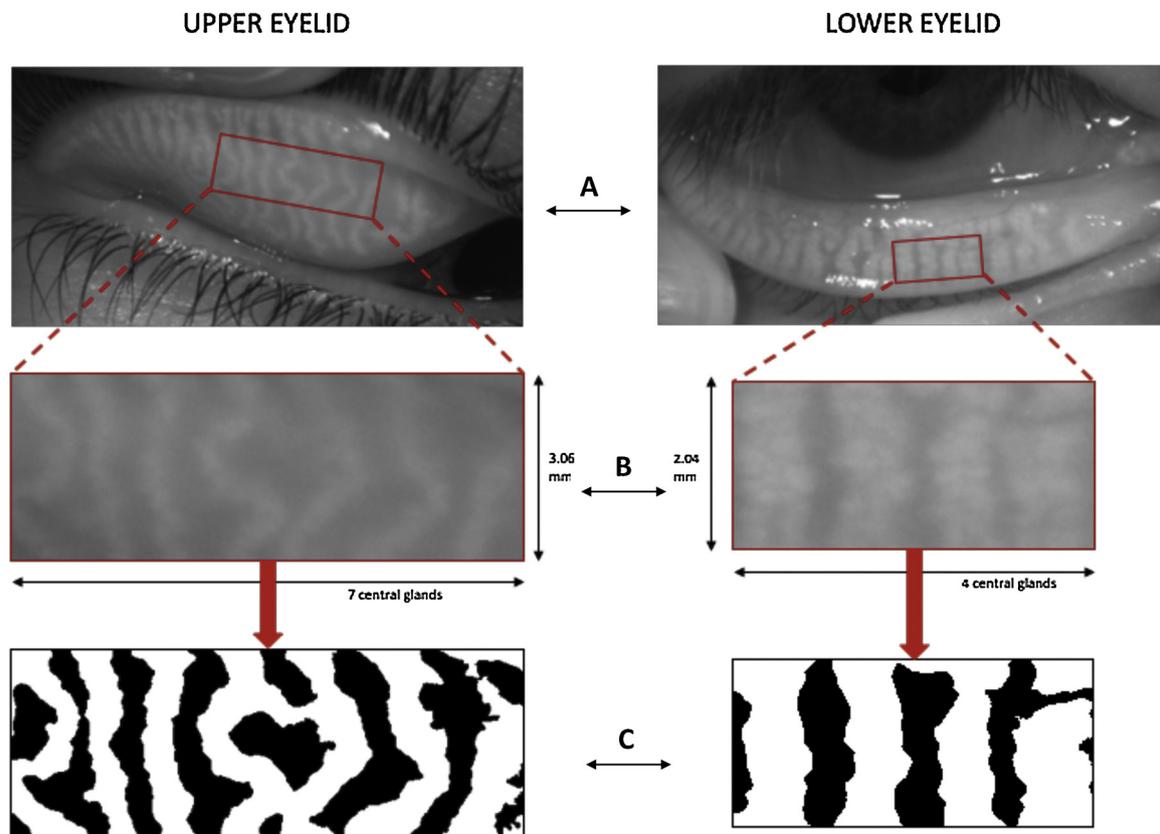


Fig. 1. Grading of upper (7 central meibomian glands) and lower (4 central meibomian glands) eyelid meibography images (OCULUS Keratograph 5 M) to determine MG width: Selection of meibomian glands (A); Enhanced binarized image of meibomian glands (B); Data extraction (C).

grades were resolved by discussion by the original two examiners. Upper (7 central MGs with a fixed box height of 3.06 mm) and lower (4 central MGs with a fixed box height of 2.04 mm) eyelid MG width was evaluated with a custom semi-automated MATLAB program, which yielded mean MG width of the central glands (Figs. 1). Dry eye was diagnosed if a subject had a SPEED score > 5.0 and a positive TMH (< 0.2 mm) test or NITBUT (< 10 s) [39].

2.4. Statistical analysis

The right eye was used in analysis, and SAS Version 9.3 was used to analyze the data. The primary outcome of this study was MG width differences between successful CL wearers and CL dropouts. Clustering was incorporated because successful CL wearers and CL dropouts were 1:1 matched on age (± 3 years) and sex. Means and standard deviations were used to describe general data trends. Between-group differences for continuous variables were evaluated with paired t-tests. McNemar's test for 2×2 tables and Bowker's Test of Symmetry for $n \times n$ tables were used to evaluate categorical variables because of the matched-pair study design. Correlations with mean MG width were performed using a Pearson's correlation coefficient for continuous data and a Spearman's correlation coefficient for categorical data.

3. Results

3.1. Subject demographics

A total 56 matched-pairs were recruited across all study sites with each site contributing between 8 and 14 subject pairs. The sample was 60.7% female. Successful CL wearers and dropouts had mean \pm SD ages of 28.5 ± 7.1 and 28.6 ± 7.0 years, respectively ($p = 0.66$). CL dropouts had worn CLs for 7.82 ± 6.74 years while successful CL

wearers had worn CLs for 10.86 ± 6.52 years ($p = 0.01$). CL dropouts (7.82 ± 6.74) wore their CLs significantly fewer hours per day compared to the successful CL wearers (13.47 ± 2.92 ; < 0.001). The majority of CL dropouts (67.3%) reported wearing their CLs for four or fewer days per week, while the majority of successful CL wearers (74.5%) reported wearing their CLs for six or more days per week ($p < 0.001$). CL dropouts (6.4 ± 5.0) had significantly higher ($p < 0.0001$) SPEED scores compared to the successful CL wearers (2.6 ± 2.7), and CL dropouts were significantly more likely to have diagnosed dry eye compared to the successful CL wearers ($p < 0.001$).

NITBUT ($p = 0.44$), TMH ($p = 0.31$), and upper ($p = 0.09$) and lower ($p = 0.05$) eyelid blepharitis did not significant differ between the CL dropouts and successful CL wearers (Table 1). CL dropouts and successful CL wearers had similar upper (0.91 ± 0.52 vs. 0.91 ± 0.29 ; $p = 1.0$) and lower (1.04 ± 0.74 vs. 0.89 ± 0.59 ; $p = 0.22$) MG atrophy grades and upper (1.76 ± 1.02 vs. 1.46 ± 0.74 ; $p = 0.07$) and lower (0.75 ± 0.67 vs. 0.75 ± 0.69 ; $p = 0.89$) MG tortuosity grades. CL dropouts and successful CL wearers did not differ with regards to upper (0.45 ± 0.08 vs. 0.45 ± 0.07 ; $p = 0.92$) or lower (0.61 ± 0.12 vs. 0.62 ± 0.10 ; $p = 0.97$) MG widths.

3.2. Ocular factors and associations meibomian gland width

Upper or lower MG widths were not significantly associated with SPEED scores ($p = 0.18$, $r = -0.14$ / $p = 0.21$, $r = -0.13$), being diagnosed with dry eye ($p = 0.98$, $r = 0.002$ / $p = 0.17$, $r = -0.14$), number of years of CL use ($p = 0.32$, $r = 0.10$ / $p = 0.18$, $r = 0.14$), hours of CL use per day ($p = 0.69$, $r = -0.04$ / $p = 0.49$, $r = -0.07$), NITBUTs ($p = 0.34$, $r = -0.10$ / $p = 0.62$, $r = 0.05$), or TMHs ($p = 0.98$, $r = 0.002$ / $p = 0.12$, $r = 0.16$). Upper or lower MG widths were not significantly associated with upper ($p = 0.47$, $r = 0.07$ / $p = 0.71$, $r = 0.04$) or lower ($p = 0.65$, $r = 0.05$ / $p = 0.41$, $r = 0.09$)

Table 1
Ocular Factors by Subject Group (Right Eye).

Test	Overall Group (Mean ± SD)	Successful Contact Lens Wearers (Mean ± SD)	Contact Lens Dropouts (Mean ± SD)	Successful Wearers vs. Dropouts (P-Value)
SPEED Score (units)	4.52 ± 4.40	2.62 ± 2.66	6.42 ± 4.96	< 0.0001
Diagnosed Dry Eye	18.8%	5.4%	32.1%	< 0.001
Non-Invasive Tear Break-Up Time (seconds)	12.06 ± 9.30	12.53 ± 9.93	11.58 ± 8.68	0.44
Tear Meniscus Height (mm)	0.29 ± 0.09	0.29 ± 0.09	0.28 ± 0.09	0.31
Blepharitis				
Upper Eyelid (0-4 scale)	0.58 ± 0.74	0.46 ± 0.66	0.70 ± 0.81	0.09
Lower Eyelid (0-4 scale)	0.29 ± 0.59	0.20 ± 0.52	0.39 ± 0.65	0.05
Meibomian Gland Expressibility				
Upper Eyelid (0-3 scale)	0.92 ± 0.95	0.61 ± 0.80	1.24 ± 0.98	< 0.001
Lower Eyelid (0-3 scale)	0.91 ± 0.98	0.73 ± 0.94	1.09 ± 0.99	0.04
Meibum Quality				
Upper Eyelid (0-4 scale)	1.00 ± 1.31	0.66 ± 1.01	1.35 ± 1.49	< 0.001
Lower Eyelid (0-4 scale)	0.79 ± 1.16	0.73 ± 1.18	0.85 ± 1.15	0.64
Meibomian Gland Atrophy (Meiboscore)				
Upper Eyelid (0-3 scale)	0.91 ± 0.42	0.91 ± 0.29	0.91 ± 0.52	1.00
Lower Eyelid (0-3 scale)	0.96 ± 0.67	0.89 ± 0.59	1.04 ± 0.74	0.22
Meibomian Gland Tortuosity				
Upper Eyelid (0-3 scale)	1.61 ± 0.89	1.46 ± 0.74	1.76 ± 1.02	0.07
Lower Eyelid (0-3 scale)	0.74 ± 0.68	0.75 ± 0.69	0.75 ± 0.67	0.89
Mean Meibomian Gland Width				
Upper Eyelid (mm)	0.45 ± 0.08	0.45 ± 0.07	0.45 ± 0.08	0.92
Lower Eyelid (mm)	0.61 ± 0.11	0.62 ± 0.10	0.61 ± 0.12	0.97

eyelid blepharitis, upper ($p = 0.16$, $r = -0.14$ / $p = 0.17$, $r = -0.14$) or lower ($p = 0.05$, $r = -0.20$ / $p = 0.28$, $r = -0.11$) eyelid meibum quality, upper ($p = 0.38$, $r = -0.09$ / $p = 0.15$, $r = -0.15$) eyelid MG expressibility, upper ($p = 0.17$, $r = 0.14$ / $p = 0.25$, $r = -0.12$) or lower ($p = 0.59$, $r = 0.05$ / $p = 0.29$, $r = 0.11$) eyelid MG atrophy, or upper ($p = 0.22$, $r = 0.12$ / $p = 0.62$, $r = -0.05$) or lower ($p = 0.42$, $r = 0.08$ / $p = 0.47$, $r = 0.08$) eyelid MG tortuosity. Upper ($p = 0.002$, $r = 0.38$) but not lower ($p = 0.24$, $r = 0.15$) MG widths were associated with the number of days of CL use per week. Lower eyelid MG expressibility was negatively correlated ($p = 0.01$, $r = -0.27$) with lower MG width suggesting that thinner MG widths were associated with decreased MG expressibility.

3.3. Differences between upper and lower eyelid factors

Subjects had significantly wider lower eyelid (0.61 ± 0.11) MGs than upper eyelid (0.45 ± 0.08) MGs ($p = 0.03$), and the subjects had significantly worse upper eyelid (1.61 ± 0.89) MG tortuosity grades than the lower eyelid (0.74 ± 0.68) MG tortuosity grades ($p < 0.001$). The subjects also had significantly higher upper eyelid blepharitis grades (0.58 ± 0.74) than lower eyelid (0.29 ± 0.59) blepharitis grades (< 0.001). No other significant between eyelid (upper vs. lower) differences were noted among the subjects (Table 2).

4. Discussion

MG health is of great concern, because MGD can lead to altered tear lipid production, increased ocular symptoms, and potential CL dropout [9–12]. One measure of MG health is the structural integrity of the MGs, which can now be evaluated in clinical practice with meibography [18,19,40]. While evaluation of MG atrophy and tortuosity with meibography is now becoming common-place within clinical practice because of its ease and utility for guiding clinical decision making (e.g., subjects with complete MG atrophy may be a poor candidate for thermal pulsation) [28,41,42], MG width has been largely ignored, likely because of the lack of methods for grading MG width. The current study begins to bridge this knowledge gap by using a custom developed

MATLAB program for evaluating MG width and using a clinical dataset to determine if MG width is an indicator of ocular disease or CL success.

Pult et al. has previously analyzed upper and lower eyelids MG width in a group of 20 normal subjects by using ImageJ (ImageJ Units) to measure the width of the “worst case gland” in the upper and lower eyelids [23]. Pult et al. overall found that the MGs of the lower eyelid were significantly wider than the upper eyelid MGs, and they found that the upper but not lower eyelid MG widths were associated with symptoms scores [23]. Uçakhan and Arslanturk-Eren have also previously analyzed MG width in a group of CL ($n = 87$) and non-CL ($n = 55$) wearing subjects by subjectively counting the number of “thickened” MG (MGs at least twice the width of the other MGs within the subject being analyzed) and assigning the subjects a severity score [43]. Uçakhan and Arslanturk-Eren found that CL wearers had significantly worse MG thickening scores in their upper eyelids than lower eyelids [43]. They also found that the upper and lower eyelids of CL wearers had worse MGs thickening scores than the corresponding eyelids of non-CL wearers [43].

The current study extends our understanding of MG width by automatic assessment of the mean width of the 7 selected central upper eyelid MGs and the 4 selected central lower eyelid MGs. The current study found that lower eyelid MGs were significantly wider than upper eyelid MGs and that narrower lower eyelid MG were associated with decreased MG expressibility, which suggests that MG health may be negatively correlated with narrower MG widths. The current study did not find a significant association between symptoms and MG width, which is in contrast to Pult et al., a difference that could be potentially attributed to methodical differences (e.g., measuring one vs. multiple MGs), sample size (20 subjects vs. 112 subjects), or subjects (non-CL vs. CL wearers) [23]. This study also did not find a difference in MG width between successful CL wearers and CL dropouts. The current MG width analysis would need to be repeated in a group of non-CL wearers to determine if the custom semi-automatic MATLAB program developed during this study produces data to support the subjective counting of thickened MGs in Uçakhan and Arslanturk-Eren’s study (CL induction of MG thickening) [43].

The current predominating theory of MG atrophy suggests that

Table 2
Upper and Lower Eyelid Comparison of Ocular Factors (Right Eye).

Test	Overall Group (Mean \pm SD)	Upper vs. Lower Eyelid Mean (P-Value)	Upper vs. Lower Eyelid Correlation (r)
Blepharitis			
Upper Eyelid (0-4 scale)	0.58 \pm 0.74	< 0.001	0.69
Lower Eyelid (0-4 scale)	0.29 \pm 0.59		
Meibomian Gland Expressibility			
Upper Eyelid (0-3 scale)	0.92 \pm 0.95	0.92	0.56
Lower Eyelid (0-3 scale)	0.91 \pm 0.98		
Meibum Quality			
Upper Eyelid (0-4 scale)	1.00 \pm 1.31	0.12	0.36
Lower Eyelid (0-4 scale)	0.79 \pm 1.16		
Meibomian Gland Atrophy (Meiboscore)			
Upper Eyelid (0-3 scale)	0.91 \pm 0.42	0.42	0.25
Lower Eyelid (0-3 scale)	0.96 \pm 0.67		
Meibomian Gland Tortuosity			
Upper Eyelid (0-3 scale)	1.61 \pm 0.89	< 0.001	0.09
Lower Eyelid (0-3 scale)	0.74 \pm 0.68		
Mean Meibomian Gland Width			
Upper Eyelid (mm)	0.45 \pm 0.08	0.03	0.23
Lower Eyelid (mm)	0.61 \pm 0.11		

wider MGs are worse/more diseased than narrower MGs, because wider MGs are thought to signify central MG duct dilation secondary to chronic MG blockage [44], though central MG duct dilation is likely only one stage in the MG atrophy process. The current and past data on MG width and tortuosity may provide some insight into the mechanism leading to MGD. These data specifically suggest that structural changes associated with increased MG tortuosity or MG narrowing may be leading to altered lipid production, which may subsequently promote decreased MG expressibility, which could then subsequently promote ocular symptoms [23,28]. This decreased MG expressibility and structural changes may precede central MG duct dilation and atrophy, or narrowing may occur after central MG duct dilation as part of the atrophy process. Additional research is still needed before this theory can be confirmed and before the mechanistic sequence of events leading to altered MG width, tortuosity, and atrophy is fully understood.

The current study also investigated if MG width was associated with CL success, and it found that MG width was not clinically significantly associated with being a successful CL wearer, at least when successful CL wearers are compared to subjects who had recently dropped out of CLs because of discomfort. This claim is supported by the only two significant differences between groups (upper eyelid MG expressibility [0.63 grade different] and upper eyelid meibum quality [0.69 grade different]) being less than one grade different. This result is not entirely unexpected, given the results of several recent studies [21,27,28,42]. While it is true that Arita et al. found in 2009 that increased years of CL use were associated with worse MG atrophy grades [25], the preponderance of data since this seminal study has failed to find an association between MG atrophy and CL use [21,27,28,42]. Therefore, a lack of association between CL use and MG width also seems reasonable. Nevertheless, there is still evidence that MG health (decreased MG expressibility with altered meibum secretions may promote CL intolerance) is clinically significantly important for successful CL use and that these factors should be evaluated during a standard clinical examination [28].

The current study also investigated upper and lower eyelid MGD signs with the intent of better understanding the necessity of grading both the upper and lower eyelids in clinical practice, which could potentially affect patient chair time. The current study overall found that upper and lower eyelid blepharitis grades, MG tortuosity grades, and MG width grades were significantly different from each other, with blepharitis and MG tortuosity grades being worse in the upper eyelid and MG widths being wider in the lower eyelid. Nevertheless, of these significant between eyelid variables, the only clinically significant

difference was for MG tortuosity (~1 grade difference). These results are in general agreement with past work from McCann et al., Yin et al., and Eom et al., who previously noted that the lower eyelid MGs had more atrophy than the upper eyelid MGs [45–47], and Pult et al. who found greater MG tortuosity in upper eyelids than the lower eyelids [23]. The current study also found a lack of association between upper and lower eyelids for MG atrophy, MG expressibility, and meibum quality. Past research has also noted that right and left eyelids are highly correlated [24]. Therefore, these data overall suggest that additional information can be gained by grading both upper and lower eyelids, though grading one eye may be sufficient for research and maybe even clinical practice. This recommendation is in agreement with Yin et al., who also suggested evaluating both the upper and lower eyelids for various dry eye factors [45].

This study found that lower eyelid MGs were wider than upper eyelid MGs and that narrower lower eyelid MGs are associated with decreased MG expressibility, which suggests that MG width may have an impact on the development of MGD. This study also found that MG width was not associated with CL success and, that while there were few between-eyelid differences for the commonly graded upper and lower eyelid MGD factors evaluated in this study, that it may be still worth evaluating each eyelid to gain a better clinical picture of the patient [45]. Moving forward, additional work is needed to better understand the stages and mechanisms leading to MG width alterations, tortuosity, and atrophy. Work is also needed to develop enhanced early diagnosis and treatment methods for MGD.

Financial support

Alcon Research Inc. supported this investigator-initiated study.

Commercial relationship disclosures

The authors have received financial and/or equipment research support from Advanced Vision Research (LJ, SS), Allergan (LJ, SS), Alcon (All), American Academy of Optometry (ADP, LAJ, JTK, SS), Bausch + Lomb (ADP, CMEK, LAJ, JTK), Contamac (ADP, CMEK, LAJ, LJ, JTK), Novartis (LJ, SS), CooperVision (DRP, LJ, SS, CMEK), Essilor (LJ, SS), Euclid (ADP), GL Chemtec (SS, LJ), Inflamax Research (LJ, SS), Johnson & Johnson Vision (SS, LJ), Kala (DRP), Menicon (LJ, SS), Nature's Way (SS, LJ), Novartis (SS, LJ), Ocular Dynamics (LJ, SS), Oculus, Inc. (ADP, LAJ, LJ, JTK, SS), Ophtecs (LJ), PentaVision (ADP), Safilens (LJ, SS), Santen (SS, LJ), Shire (DRP, LJ, SS), TearLab (LJ, SS),

and TearScience (LJ, SS) in the past three years.

Acknowledgments

Alcon Research, Inc. supported this investigator-initiated trial grant; however, they did not influence the outcomes of the study. REDCap data collection was supported by CTSA Grant UL1TR001070. CMEK and SS were employees at the College of Optometry, University of Houston and Centre for Ocular Research and Education (CORE), University of Waterloo during the execution of this study; they are currently employed at Alcon Research.

References

- [1] K.K. Nichols, G.N. Foulks, A.J. Bron, B.J. Glasgow, M. Dogru, K. Tsubota, et al., The international workshop on meibomian gland dysfunction: executive summary, *Invest Ophthalmol Vis Sci* 52 (4) (2011) 1922–1929.
- [2] M.A. Lemp, L.A. Crews, A.J. Bron, G.N. Foulks, B.D. Sullivan, Distribution of aqueous-deficient and evaporative dry eye in a clinic-based patient cohort: a retrospective study, *Cornea* 31 (5) (2012) 472–478.
- [3] J.V. Jester, N. Nicolaidis, R.E. Smith, Meibomian gland studies: histologic and ultrastructural investigations, *Invest Ophthalmol Vis Sci* 20 (4) (1981) 537–547.
- [4] J.S. Andrews, The Meibomian secretion, *Int Ophthalmol Clin* 13 (1) (1973) 23–28.
- [5] A.D. Pucker, J.J. Nichols, Analysis of meibum and tear lipids, *Ocul Surf* 10 (4) (2012) 230–250.
- [6] S.H. Brown, C.M. Kunnen, E. Duchoslav, N.K. Dolla, M.J. Kelso, E.B. Papas, et al., A comparison of patient matched meibum and tear lipidomes, *Invest Ophthalmol Vis Sci* 54 (12) (2013) 7417–7424.
- [7] S. Mishima, D.M. Maurice, The effect of normal evaporation on the eye, *Exp Eye Res* 1 (1961) 46–52.
- [8] J.P. Craig, A. Tomlinson, Importance of the lipid layer in human tear film stability and evaporation, *Optom Vis Sci* 74 (1) (1997) 8–13.
- [9] G.N. Foulks, The correlation between the tear film lipid layer and dry eye disease, *Surv Ophthalmol* 52 (4) (2007) 369–374.
- [10] C. Joffre, M. Souchier, S. Gregoire, S. Viau, L. Bretilon, N. Acar, et al., Differences in meibomian fatty acid composition in patients with meibomian gland dysfunction and aqueous-deficient dry eye, *Br J Ophthalmol* 92 (1) (2008) 116–119.
- [11] G. Young, J. Veys, N. Pritchard, S. Coleman, A multi-centre study of lapsed contact lens wearers, *Ophthalmic Physiol Opt* 22 (6) (2002) 516–527.
- [12] D.R. Korb, A.S. Henriquez, Meibomian gland dysfunction and contact lens intolerance, *J Am Optom Assoc* 51 (3) (1980) 243–251.
- [13] B.E. Jester, C.J. Nien, M. Winkler, D.J. Brown, J.V. Jester, Volumetric reconstruction of the mouse meibomian gland using high-resolution nonlinear optical imaging, *Anat Rec* 294 (2) (2011) 185–192.
- [14] C.J. Nien, J.R. Paugh, S. Massei, A.J. Wahlert, W.W. Kao, J.V. Jester, Age-related changes in the meibomian gland, *Exp Eye Res* 89 (6) (2009) 1021–1027.
- [15] B.S. Schuett, T.J. Millar, Lipid component contributions to the surface activity of meibomian lipids, *Invest Ophthalmol Vis Sci* 53 (11) (2012) 7208–7219.
- [16] J.F. Molinari, R. Tapie, Color photography of meibomian glands, *Am J Optom Physiol Opt* 59 (9) (1982) 758–759.
- [17] A. Tomlinson, A.J. Bron, D.R. Korb, S. Amano, J.R. Paugh, E.I. Pearce, et al., The international workshop on meibomian gland dysfunction: report of the diagnosis subcommittee, *Invest Ophthalmol Vis Sci* 52 (4) (2011) 2006–2049.
- [18] R.J. Wise, R.K. Sobel, R.C. Allen, Meibography: a review of techniques and technologies, *Saudi J Ophthalmol* 26 (4) (2012) 349–356.
- [19] R. Arita, K. Itoh, K. Inoue, S. Amano, Noncontact infrared meibography to document age-related changes of the meibomian glands in a normal population, *Ophthalmology* 115 (5) (2008) 911–915.
- [20] S. Srinivasan, K. Menzies, L. Sorbara, L. Jones, Infrared imaging of meibomian gland structure using a novel keratograph, *Optom Vis Sci* 89 (5) (2012) 788–794.
- [21] A.D. Pucker, L.A. Jones-Jordan, W. Li, J.T. Kwan, M.C. Lin, W. Sickenberger, et al., Associations with meibomian gland atrophy in daily contact lens wearers, *Optom Vis Sci* 92 (9) (2015) e206–13.
- [22] J.V. Jester, G.J. Parfitt, D.J. Brown, Meibomian gland dysfunction: hyperkeratinization or atrophy? *BMC Ophthalmol* 15 (Suppl. 1) (2015) 156.
- [23] H. Pult, B.H. Riede-Pult, J.J. Nichols, Relation between upper and lower lids' meibomian gland morphology, tear film, and dry eye, *Optom Vis Sci* 89 (3) (2012) E310–5.
- [24] D. Finis, C. Konig, J. Hayajneh, M. Borrelli, S. Schrader, G. Geerling, Six-month effects of a thermodynamic treatment for MGD and implications of meibomian gland atrophy, *Cornea* 33 (12) (2014) 1265–1270.
- [25] R. Arita, K. Itoh, K. Inoue, A. Kuchiba, T. Yamaguchi, S. Amano, Contact lens wear is associated with decrease of meibomian glands, *Ophthalmology* 116 (3) (2009) 379–384.
- [26] W.M. Alghamdi, M. Markoulli, B.A. Holden, E.B. Papas, Impact of duration of contact lens wear on the structure and function of the meibomian glands, *Ophthalmic Physiol Opt* 36 (2) (2016) 120–131.
- [27] A. Machalinska, A. Zakrzewska, B. Adamek, K. Safranow, B. Wiszniewska, M. Parafiniuk, et al., Comparison of morphological and functional meibomian gland characteristics between daily contact lens wearers and nonwearers, *Cornea* 34 (9) (2015) 1098–1104.
- [28] A.D. Pucker, L.A. Jones-Jordan, S. Marx, D.R. Powell, J.T. Kwan, S. Srinivasan, et al., Clinical factors associated with contact lens dropout, *Cont Lens Anterior Eye* 42 (3) (2018) 318–324.
- [29] J.J. Nichols, M.D. Willcox, A.J. Bron, C. Belmonte, J.B. Ciolino, J.P. Craig, et al., T.I.W.o.C.L.D. Members of the, the TFOS International Workshop on contact lens discomfort: executive summary, *Invest Ophthalmol Vis Sci* 54 (11) (2013) TFOS7-TFOS13.
- [30] R.L. Chalmers, C.G. Begley, K. Moody, S.B. Hickson-Curran, Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8) and opinion of contact lens performance, *Optom Vis Sci* 89 (10) (2012) 1435–1442.
- [31] B.D. Sullivan, L.A. Crews, B. Sonmez, M.F. de la Paz, E. Comert, V. Charoenrook, et al., Clinical utility of objective tests for dry eye disease: variability over time and implications for clinical trials and disease management, *Cornea* 31 (9) (2012) 1000–1008.
- [32] A.J. Bron, V.E. Evans, J.A. Smith, Grading of corneal and conjunctival staining in the context of other dry eye tests, *Cornea* 22 (7) (2003) 640–650.
- [33] W. Ngo, P. Situ, N. Keir, D. Korb, C. Blackie, T. Simpson, Psychometric properties and validation of the standard patient evaluation of eye dryness questionnaire, *Cornea* 32 (9) (2013) 1204–1210.
- [34] A.D. Pucker, B.E. Dougherty, L.A. Jones-Jordan, J.T. Kwan, C.M.E. Kunnen, S. Srinivasan, Psychometric analysis of the SPEED questionnaire and CLDEQ-8, *Invest Ophthalmol Vis Sci* 59 (8) (2018) 3307–3313.
- [35] E. Faber, T.R. Golding, R. Lowe, N.A. Brennan, Effect of hydrogel lens wear on tear film stability, *Optom Vis Sci* 68 (5) (1991) 380–384.
- [36] J.F. Meadows, P. Ramamoorthy, J.J. Nichols, K.K. Nichols, Development of the 4-3-2-1 meibum expressibility scale, *Eye Contact Lens* 38 (2) (2012) 86–92.
- [37] C. Halleran, J.T. Kwan, M.J. Hom, J. Harthan, Agreement in reading centre grading of meibomian gland tortuosity and atrophy, *Optom Vis Sci* (2016) 165079E-abstract.
- [38] R. Arita, K. Itoh, S. Maeda, K. Maeda, A. Furuta, A. Tomidokoro, et al., Meibomian gland duct distortion in patients with perennial allergic conjunctivitis, *Cornea* 29 (8) (2010) 858–860.
- [39] K. Asiedu, S. Kyei, S.N. Mensah, S. Ocansey, L.S. Abu, E.A. Kyere, Ocular surface disease index (OSDI) versus the standard patient evaluation of eye dryness (SPEED): a study of a nonclinical sample, *Cornea* 35 (2) (2016) 175–180.
- [40] W. Ngo, S. Srinivasan, L. Jones, Historical overview of imaging the meibomian glands, *J Optom* 6 (1) (2012) 1–8.
- [41] J. Qiao, X. Yan, Emerging treatment options for meibomian gland dysfunction, *Clin Ophthalmol* 7 (2013) 1797–1803.
- [42] R. Arita, K. Itoh, S. Maeda, K. Maeda, A. Tomidokoro, S. Amano, Association of contact lens-related allergic conjunctivitis with changes in the morphology of meibomian glands, *Jpn J Ophthalmol* 56 (1) (2012) 14–19.
- [43] O. Ucakhan, M. Arslanturk-Eren, The role of Soft contact Lens Wear on meibomian gland morphology and function, *Eye Contact Lens* (2018), <https://doi.org/10.1097/ICL.0000000000000572> [Epub ahead of print] PMID: 30608243.
- [44] E. Knop, N. Knop, T. Millar, H. Obata, D.A. Sullivan, The international workshop on meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland, *Invest Ophthalmol Vis Sci* 52 (4) (2011) 1938–1978.
- [45] Y. Yin, L. Gong, Uneven meibomian gland dropout over the tarsal plate and its correlation with meibomian gland dysfunction, *Cornea* 34 (10) (2015) 1200–1205.
- [46] Y. Eom, K.E. Choi, S.Y. Kang, H.K. Lee, H.M. Kim, J.S. Song, Comparison of meibomian gland loss and expressed meibum grade between the upper and lower eyelids in patients with obstructive meibomian gland dysfunction, *Cornea* 33 (5) (2014) 448–452.
- [47] L.C. McCann, A. Tomlinson, E.I. Pearce, C. Diaper, Tear and meibomian gland function in blepharitis and normals, *Eye Contact Lens* 35 (4) (2009) 203–208.