

A Novel Quantitative Index of Meibomian Gland Dysfunction, the Meibomian Gland Tortuosity

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Received: February 27, 2020

Accepted: July 10, 2020

Published: August 21, 2020

Keywords: meibomian gland tortuosity; meibomian gland dysfunction; diagnosis; asymptomatic MGD; symptomatic MGD

Citation: Lin X, Fu Y, Li L, Chen C, Chen X, Mao Y, Lian H, Yang W, Dai Q. A novel quantitative index of meibomian gland dysfunction, the meibomian gland tortuosity. *Trans Vis Sci Tech.* 2020;9(9):34, <https://doi.org/10.1167/tvst.9.9.34>

Purpose: To quantitatively measure meibomian gland (MG) tortuosity in meibomian gland dysfunction (MGD) patients and normal controls and to observe the efficacy of evaluating MG tortuosity for the diagnosis of MGD.

Methods: This cross-sectional study enrolled 32 obstructive MGD patients and 28 normal volunteers. Clinical assessments were performed, including symptom questionnaires, tear meniscus height, tear break-up time (TBUT), corneal fluorescein staining, lid margin abnormality, MG expressibility, and meibography. The meibomian gland tortuosity and meibomian gland density were measured by VIA software.

Results: The mean age of the patients in the MGD group was 33.28 ± 9.28 years, and that of the normal controls was 25.25 ± 11.19 years. The average tortuosity of all MGs in the MGD patients was significantly larger than in the normal controls ($P < 0.05$). We further stratified the MGD patients into symptomatic MGD and asymptomatic groups. The average tortuosity of all MGs and of the central eight MGs was significantly higher in the symptomatic MGD patients than in the asymptomatic MGD patients ($P < 0.05$). Significant linear correlations were found between MG tortuosity and the lid margin score, meiboscore, meibum expressibility score, and TBUT ($P < 0.05$). When the diagnosis of obstructive MGD was based on the tortuosity of the central eight MGs of both eyelids, the sensitivity and specificity were 100% and 100%, respectively.

Conclusions: MG tortuosity is an effective index to delineate MG morphology and to diagnose MGD, especially for the diagnosis of early-stage MGD.

Translation Relevance: Calculating tortuosity quantitatively may play an important role in the diagnosis of MGD.

Introduction

Meibomian glands (MGs) are tarsal glands in the eyelids that secrete meibomian lipids to the orifices at the lid margin.¹ The lipids secreted by MGs are the main constituent of the lipid layer of the tear film that prevents tears from evaporating and maintains the stability of the tear film.² If the terminal ducts of MGs are obstructed and/or the quality or quantity of meibum changes, meibomian gland dysfunction (MGD) will develop, which has been widely accepted as the main cause of dry eye.³ The diagnosis of MGD

is based primarily on related symptoms, lid margin abnormalities, meibum quality and expressibility, and MG morphology. Changes in MG morphology are a leading cause of MGD.¹

Previous studies have found that the morphological characteristics of MGs are critical to distinguishing healthy and unhealthy MGs.⁴⁻⁶ It has been observed that the degree of MG atrophy was significantly correlated with the non-invasive break-up time (NIBUT) and lipid layer thickness.^{4,7} MG ductal length and MG width are decreased in MGD patients, and MG ductal length has been correlated with symptoms, as well as meibum and fluorescein staining scores.^{4,5} MG width

has been shown to be significantly correlated with tear film stability and lid margin abnormality.⁵ However, a more detailed analysis of MG morphology, such as tortuosity, is needed to further explore the role of MG morphological changes in ocular surface health. The study by Pult et al.⁷ reported that the bent degree of the most bent MG in the upper eyelid was correlated with the NIBUT; however, this method measures only the bent degree of a single MG, which does not represent the tortuosity of all of the MGs. In addition, the studies by Zhao et al.⁸ and Arita et al.⁹ divided MG tortuosity into three and five grades, a process that was semi-quantitative and subjective. New software was used in this study that can calculate the tortuosity of all MGs quantitatively and objectively. In our study, we quantitatively measured MG tortuosity in MGD patients and normal controls and observed the efficacy of evaluating MG tortuosity for the diagnosis of MGD.

Methods

Study Population

A total of 32 (53.3%) patients (16 males, 16 females; mean age, 33.28 ± 9.28 years) with obstructive MGD and 28 (46.7%) normal volunteers (11 males, 17 females; mean age, 25.25 ± 11.19 years) were included in the study. Only the right eyes of the enrolled subjects were included. Informed consent was obtained from all of the subjects before their inclusion in the study. This study was approved by the Investigational Review Board of the Eye Hospital of Wenzhou Medical University in Wenzhou, China. All procedures adhered to the tenets of the Declaration of Helsinki.

The patients were diagnosed with obstructive MGD by an experienced ophthalmologist based on ocular symptoms, lid margin abnormalities, and meiboscore. Patients were diagnosed with obstructive MGD if any two of the three following criteria were met: ocular symptom score ≥ 3 , lid margin score ≥ 2 , and meiboscore ≥ 3 . In accordance with the study by Arita et al.,¹⁰ the sensitivity and specificity for the diagnosis of obstructive MGD based on these criteria were 84.9% and 96.7%, respectively. The exclusion criteria for both groups were as follows: ocular inflammation, a history of ocular surgery, contact lens wear, trauma, the use of systemic medications that affect the function of meibomian glands, or any other ocular or systemic disease known to affect the tear film.

Subject Examination

Clinical assessments were performed sequentially as follows: symptom questionnaires, tear meniscus height (TMH), tear break-up time (TBUT), corneal fluorescein staining (CFS), lid margin abnormality, MG expressibility, and meibography. All of the subjects completed the Ocular Surface Disease Index (OSDI) questionnaire, and they were asked whether they had any of the 14 MGD-related ocular symptoms.¹⁰

The Keratograph 5M (K5M; Oculus, Wetzlar, Germany) was used to measure TMH and to perform the meibography scans. TMH was measured 5 seconds after blinking, and we measured the central TMH of the lower eyelid. TBUT was measured and CFS was performed after the instillation of fluorescein. TBUT was measured three times, and the mean value was recorded. CFS was graded using the Baylor grading scheme from 0 to 4.¹¹ Lid margin abnormalities were scored from 0 through 4 according to the following four parameters: anterior or posterior displacement of the mucocutaneous junction, vascular engorgement, plugged meibomian gland orifices, and irregularity of the lid margin. We assessed the meibum quality and quantity of the 15 glands on each lower eyelid. The MG expressibility score ranged from 0 to 45.^{12,13}

Images of both the upper and lower MGs were captured by the K5M. To assess the degree of MG atrophy, we used the method described by Arita et al.¹⁴ to calculate the meiboscore: 0, no atrophy; 1, atrophy of $<1/3$ of the total lid area; 2, atrophy of $1/3$ to $2/3$ of the total lid area; and 3, atrophy of $>2/3$ of the total lid area. The meiboscore results ranged from 0 to 6.

Parameters including MG density and MG tortuosity were calculated from the meibography images. We further analyzed the images using VIA 3 software (<http://www.robots.ox.ac.uk/~vgg/software/via/>).¹⁵ First, we created a grid over the whole tarsus of the eyelid and then marked out the boundaries of each MG point by point. These points were then transformed into pixel coordinates for further analysis. MG density was defined as the ratio of the sum of the area of MGs to the total area of the tarsus:

$$\text{MG density} = \frac{\text{Sum pixels of all MGs}}{\text{Total pixels of the tarsus}} \quad (1)$$

This study defined MG tortuosity as the ratio of the imaginary straight length between the two nodes and the actual length of each MG. A similar method was used previously to measure the vessel tortuosity of the

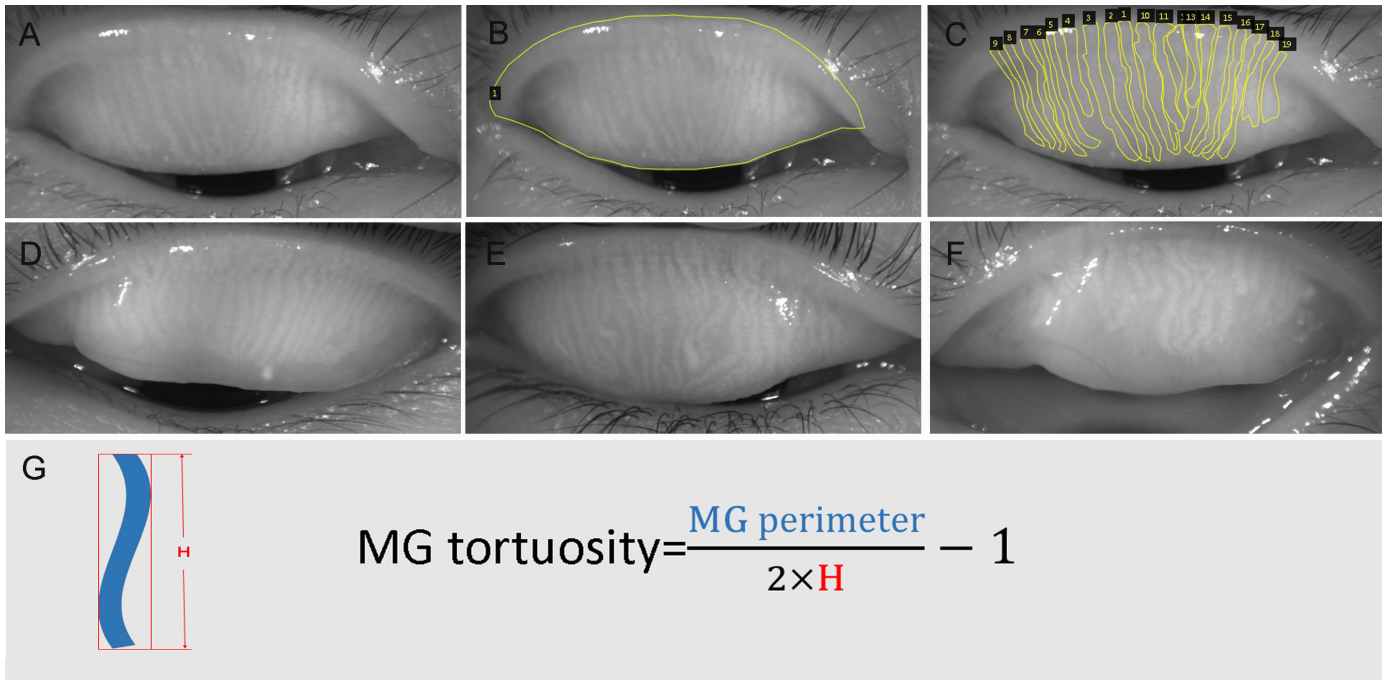


Figure 1. The method to calculate meibomian gland tortuosity. (A) An original MG image of the right eye of a 44-year-old female patient. (B) The “polygon region shape” function of the VIA software was used to draw the edge of the whole tarsus of the eyelid. (C) The boundaries of each MG were determined one by one. (D) Image of a healthy volunteer whose average MG tortuosity of the upper eyelid was 0.053. (E) Image of a healthy volunteer whose average MG tortuosity of the upper eyelid was 0.127. (F) Image of a MGD patient whose average tortuosity for all MGs was 0.262. (G) Method used to measure the height (H) of the minimum external rectangle of the MG and MG tortuosity.

retina.¹⁶ MG tortuosity was calculated as follows:

$$\text{MG tortuosity} = \frac{\text{MG perimeter}}{2 \times \text{height of the minimum external rectangle of the MG}} - 1 \quad (2)$$

The MG perimeter was the pixels at the edge of the MG. As the width of each MG was small, we used half of the MG perimeter to represent the actual length of the MG. Also, because the outlines of MGs are irregular and some MGs are tilted, the minimum external rectangle was used as the outline of the MG, and its height was calculated as the imaginary straight length (Fig. 1G). To start MG tortuosity at 0, the ratio minus 1 was recorded.

Repeatability and Reproducibility of MG Tortuosity and MG Density Measurements

To measure the repeatability and reproducibility of MG tortuosity measurements, 20 of the normal control subjects were randomly selected using a random number table. The meibography images of these patients were used for our analysis. To calculate intra-observer variation, the ranges of the whole tarsus and each MG were delineated two times by the same operator at two separate time points. To determine

any inter-observer differences, the ranges of the whole tarsus and each MG were delineated by two independent operators. The parameters of MG tortuosity and MG density were calculated by the same independent operator.

Classification of MGD Subgroups

The MGD participants were classified into symptomatic and asymptomatic MGD subgroups. Symptomatic MGD was diagnosed based on the following criteria: (1) OSDI ≥ 13 (based on the Dry Eye Workshop II Diagnostic Methodology report),¹⁷ AND (2) fulfilling the criteria for obstructive MGD.

Statistical Analysis

The normality of all datasets was tested by using the Kolmogorov–Smirnov test. The independent-samples *t*-test or the Mann–Whitney *U* test was used to compare differences between MGD patients and normal control subjects. Differences between symptomatic and asymptomatic MGD patients were also studied by using the independent samples *t*-test or the Mann–Whitney *U* test. As the difference in age between the MGD patients and normal controls was significant, analysis of covariance was used to

Table 1. Clinical Parameters of the Two Study Groups

Parameter	Normal (<i>n</i> = 28)	MGD (<i>n</i> = 32)	<i>P</i>	<i>P</i> *
Age (y), mean ± SD	25.25 ± 11.19	33.28 ± 9.28	0.004	–
Sex (male/female), <i>n</i>	11/17	16/16	0.409	–
Ocular Surface Disease Index (0–100)	6.89 ± 10.27	23.66 ± 18.94	<0.001	0.001
Symptom score (0–14)	1.74 ± 1.74	4.80 ± 2.93	0.002	0.007
Tear film break-up time (s)	7.14 ± 4.08	2.88 ± 1.99	<0.001	<0.001
Fluorescein score (0–20)	0.11 ± 0.42	0.75 ± 1.52	0.028	0.150
Tear meniscus height (mm)	0.19 ± 0.06	0.21 ± 0.06	0.201	0.371
Lid margin score (0–4)	0.46 ± 0.74	2.59 ± 1.50	<0.001	<0.001
Meiboscore (0–6)	1.46 ± 0.74	2.78 ± 1.24	<0.001	<0.001
Meibum expressibility score (0–45)	38.29 ± 7.99	17.19 ± 15.32	<0.001	0.035

**P* values adjusted for age by analysis of covariance.

Table 2. MG Tortuosity Parameters and MG Density of the Two Study Groups

Parameter	Mean ± SD		<i>P</i>	<i>P</i> *
	Normal (<i>n</i> = 28)	MGD (<i>n</i> = 32)		
MG tortuosity, upper eyelid				
Average tortuosity of all MGs	0.09 ± 0.02	0.13 ± 0.04	<0.001	0.002
Average tortuosity of central eight MGs	0.09 ± 0.02	0.14 ± 0.05	<0.001	<0.001
MG tortuosity, lower eyelid				
Average tortuosity of all MGs	0.20 ± 0.04	0.27 ± 0.07	<0.001	0.018
Average tortuosity of central eight MGs	0.19 ± 0.04	0.25 ± 0.08	<0.001	0.123
MG density				
Upper eyelid	0.42 ± 0.09	0.34 ± 0.10	0.002	0.321
Lower eyelid	0.39 ± 0.10	0.28 ± 0.09	<0.001	0.038

**P* values adjusted for age by analysis of covariance.

adjust for age for comparisons between the two groups. Correlations between MG tortuosity and the OSDI, TBUT, CFS, lid margin score, meiboscore, and meibum expressibility score were analyzed using Pearson's or Spearman's correlation analysis.

The χ^2 test was used to compare the sex ratios between groups. Student's *t*-test or the Mann–Whitney *U* test was utilized for MG tortuosity and density comparisons, depending on the data distribution. The correlations were analyzed by Spearman's rank-order correlation test. Receiver operating characteristic (ROC) curve analysis was used to determine the predictive value of MG tortuosity for the diagnosis of MGD. A two-sided *P* < 0.05 was considered statistically significant. The coefficient of variation (CoV) and within-subject standard deviation (Sw) between measurements were used to analyze repeatability and reproducibility. The CoV was the ratio of the Sw to the mean value. A lower CoV often indicated higher repeatability. All of the statistical analyses were performed using SPSS Statistics 21.0 (IBM, Armonk, NY).

To evaluate the agreement between two measurements, Bland–Altman analysis was performed using MedCalc version 19.0 (MedCalc, Ostend, Belgium). The 95% limits of agreement (LoA) were calculated as the mean difference ± 1.96 SD. Lower values of the 95% LoA indicated higher agreement between two measurements.¹⁸

Results

A total of 60 eyes of 60 patients were included in the study. The mean age of the patients in the MGD group was 33.28 ± 9.28 years, and that of the normal controls was 25.25 ± 11.19 years. No significant difference in sex was observed between the MGD patients and normal controls. The clinical parameters of the MGD patients and normal controls are shown in Table 1. Scores for MGD-related symptoms were significantly higher in the MGD patients than in the controls (*P* = 0.007).

Table 3. MG Tortuosity and MG Density in Symptomatic and Asymptomatic MGD Patients

	Mean ± SD		P
	Symptomatic (n = 20)	Asymptomatic (n = 12)	
MG tortuosity, upper eyelid			
Average tortuosity of all MGs	0.15 ± 0.05	0.12 ± 0.03	0.038
Average tortuosity of central eight MGs	0.16 ± 0.06	0.12 ± 0.04	0.047
MG tortuosity, lower eyelid			
Average tortuosity of all MGs	0.30 ± 0.06	0.21 ± 0.06	<0.001
Average tortuosity of central eight MGs	0.29 ± 0.07	0.19 ± 0.05	<0.001
MG tortuosity, both eyelids			
Average tortuosity of all MGs	0.45 ± 0.08	0.33 ± 0.06	<0.001
Average tortuosity of central eight MGs	0.45 ± 0.08	0.31 ± 0.04	<0.001
MG density			
Upper eyelid	0.31 ± 0.10	0.38 ± 0.08	0.030
Lower eyelid	0.25 ± 0.09	0.33 ± 0.08	0.024

Table 4. MG Tortuosity, Tear Film Functions, and MG Status

	OSDI	TBUT	CFS	TMH	Lid Margin Score	Meiboscore	Meibum Expressibility Score
MG tortuosity, upper eyelid							
Average tortuosity of all MGs	0.243	-0.249	0.062	-0.113	0.325*	0.489‡	-0.439‡
Average tortuosity of central eight MGs	0.164	-0.299*	0.040	-0.066	0.389†	0.426†	-0.435‡
MG tortuosity, lower eyelid							
Average tortuosity of all MGs	0.209	-0.339†	0.164	-0.080	0.303*	0.436†	-0.532‡
Average tortuosity of central eight MGs	0.094	-0.337†	0.110	-0.015	0.267*	0.437‡	-0.514‡
MG tortuosity, both eyelids							
Average tortuosity of all MGs	0.257*	-0.357†	0.148	-0.107	0.362†	0.529‡	-0.579‡
Average tortuosity of central eight MGs	0.153	-0.404†	0.103	-0.045	0.397†	0.542‡	-0.605‡

Spearman's rank correlation coefficient test.

*P < 0.05.

†P < 0.005.

‡P < 0.001.

The break-up time was significantly worse in the MGD patients than in the control group ($P < 0.001$). Lid margin scores, meibum expressibility scores, and meiboscores were obviously more severe in the MGD patients than in the normal controls ($P < 0.001$, $P = 0.035$, and $P < 0.001$, respectively).

Original and processed meibography images of both groups are shown in Figure 1. We calculated the average tortuosity of all of the MGs (average tortuosity of all MGs) and the average tortuosity of the central eight MGs (average tortuosity of the central eight). The results are shown in Table 2. The average tortuosity of all MGs was significantly increased in the MGD

patients compared to the normal controls. The average tortuosity of the central eight MGs of the upper eyelid was 0.14 ± 0.05 in the MGD patients, which was significantly higher than for the controls (0.09 ± 0.02 ; $P < 0.001$). However, the average tortuosity of the central eight MGs of the lower eyelid was not significantly higher in the MGD patients (0.25 ± 0.08) than in the normal controls (0.19 ± 0.04 ; $P = 0.123$). The MG density of the lower eyelid was significantly lower in the MGD patients compared to the corresponding eyelid in the normal controls ($P = 0.038$).

The average tortuosity of all MGs and the average tortuosity of the central eight MGs of the upper

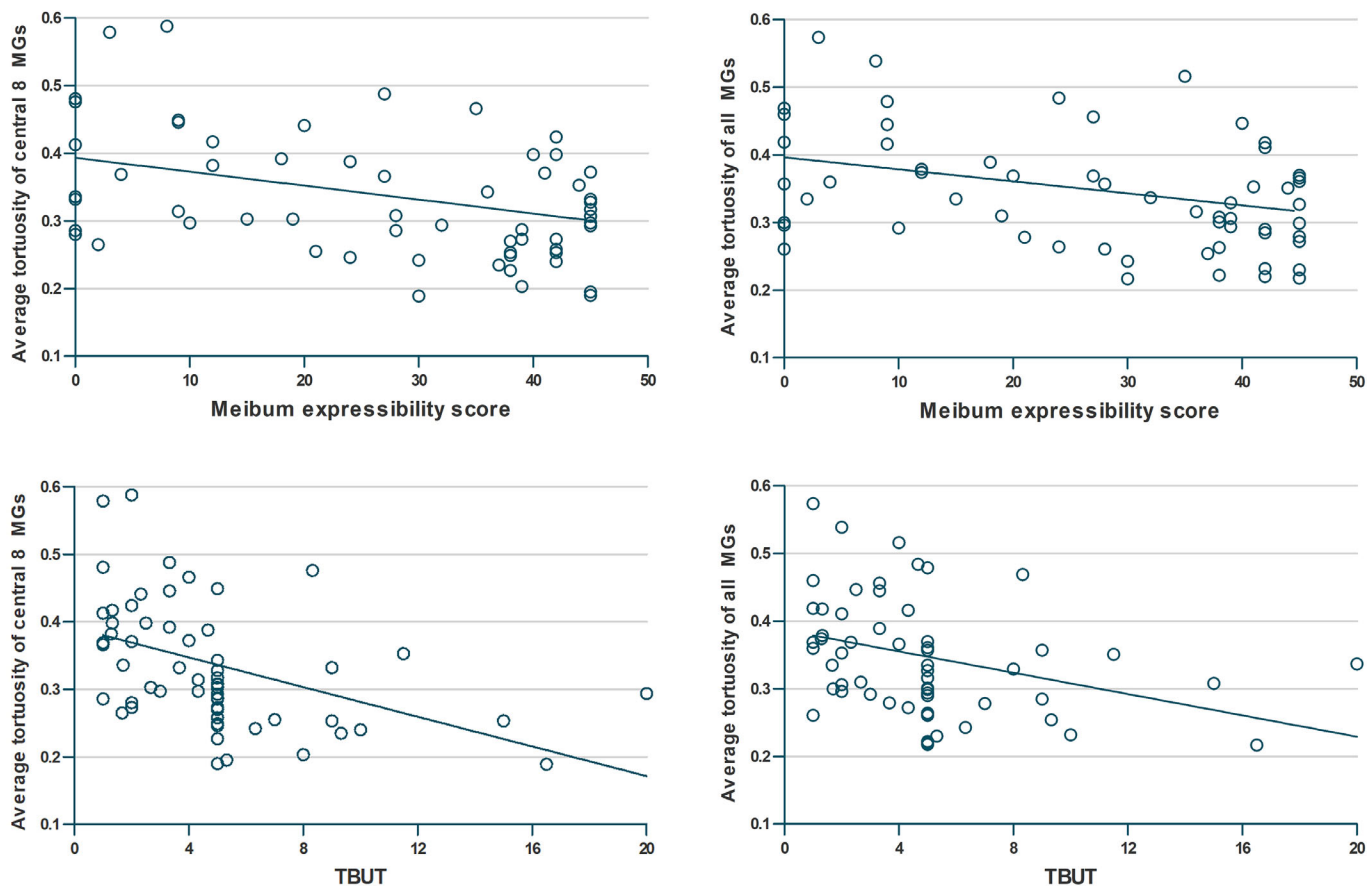


Figure 2. Correlations between MG tortuosity and meibum expressibility score and TBUT.

or lower eyelid were significantly higher in the symptomatic MGD patients than in the asymptomatic MGD patients ($P < 0.05$) (Table 3). MG densities of the upper eyelid and the lower eyelid were also significantly lower in the symptomatic MGD patients than in the asymptomatic MGD patients ($P < 0.05$).

We also compared MG tortuosity between the asymptomatic MGD patients and normal controls. The results showed that the average tortuosity of all MGs and the average tortuosity of the central eight MGs of the upper eyelid were all significantly higher in the asymptomatic MGD patients than in the normal controls ($P < 0.05$); however, there was no significant difference for MG tortuosity in the lower eyelids ($P > 0.05$).

There were significant positive correlations among MG tortuosity parameters, including the average tortuosity of all MGs and the average tortuosity of the central eight MGs, lid margin score, and meiboscore ($P < 0.05$). The same MG tortuosity parameters also showed a very significant negative correlation with the meibum expressibility score ($P < 0.001$). MG tortuosity showed a significant negative correlation with

TBUT ($P < 0.05$). The results were similar for the upper eyelid, lower eyelid, and sum of both eyelids. The results are shown in Table 4 and Figure 2.

Figure 3 shows the results of the ROC curve analyses, which indicate the sensitivity and specificity of MG tortuosity for the diagnosis of MGD. The areas under the curve (AUCs) were 0.975 and 0.962 for the average tortuosity of all MGs and the average tortuosity of the central eight MGs of the upper eyelid when the cutoff values were set at 0.085 and 0.109, respectively. The sensitivity and specificity were 90% and 100% for the average tortuosity of all MGs and 80% and 100% for the average tortuosity of the central eight MGs, respectively. For the lower eyelids, the AUCs were 0.787 and 0.663 for the average tortuosity of all MGs and the average tortuosity of the central eight MGs. The respective cutoff values were 0.202 and 0.204. The sensitivity and specificity were 70% and 100% for the average tortuosity of all MGs and 50% and 100% for the average tortuosity of the central eight MGs, respectively. When the tortuosity values for both eyelids were summed, the AUC was 1.000 for the average tortuosity of all MGs. The sensitivity and specificity were

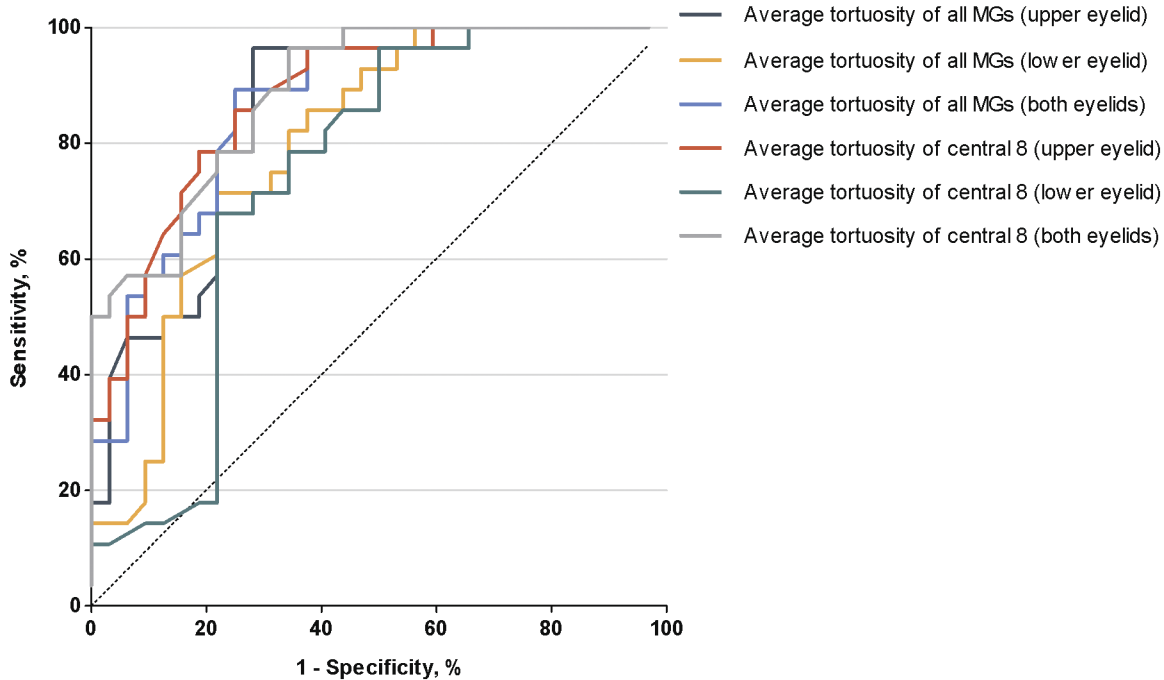


Figure 3. ROC curve analysis of MG tortuosity for the diagnosis of MGD.

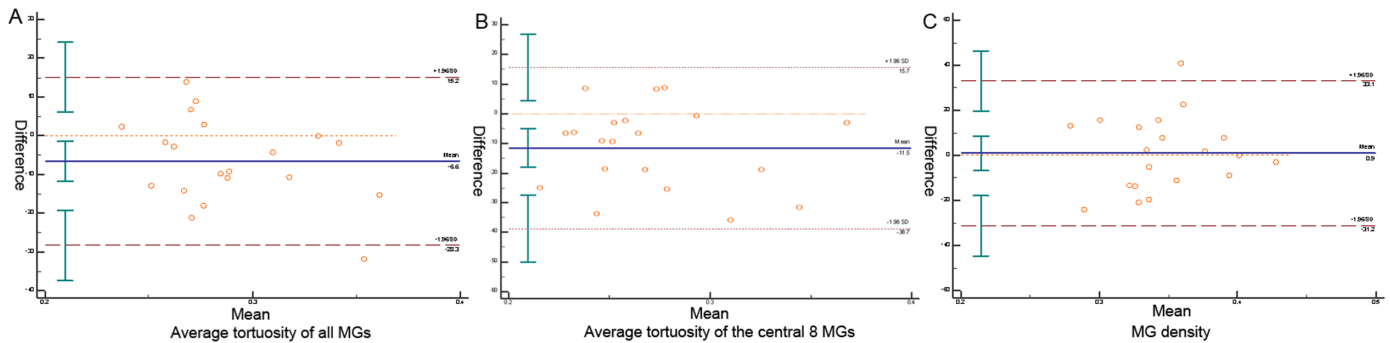


Figure 4. Bland–Altman plots showing intra-observer repeatability differences for all measured parameters.

80% and 100%, respectively. The AUC was 1.00 for the average tortuosity of the central eight MGs of both eyelids. The sensitivity and specificity were 100% and 100%, respectively, at the cutoff value of 0.269.

Figure 4 shows the Bland–Altman plots of the difference between the two measurements by the same observer. The 95% LoA for all parameters showed high agreement between the two measurements. Table 5 provides the Sw, 2.77Sw, and CoV values for the average tortuosity of all MGs, the average tortuosity of the central eight MGs, and MG density. The results indicate that the intra-observer repeatability was good, with a low CoV for all parameters. Figure 5 shows the Bland–Altman plots of the differences between the two measurements by two independent observers. The agreement between the two observers was high, as the

95% LoA for all parameters showed little variability. Also, the results in Table 6 indicate that the inter-observer reproducibility was good, with a low CoV for all parameters.

Discussion

In this study, we quantified MG tortuosity in normal controls and MGD patients and found that MG tortuosity was significantly higher in MGD patients than in controls. We further observed that MG tortuosity was significantly higher in symptomatic MGD patients than in asymptomatic MGD patients. Also, MG

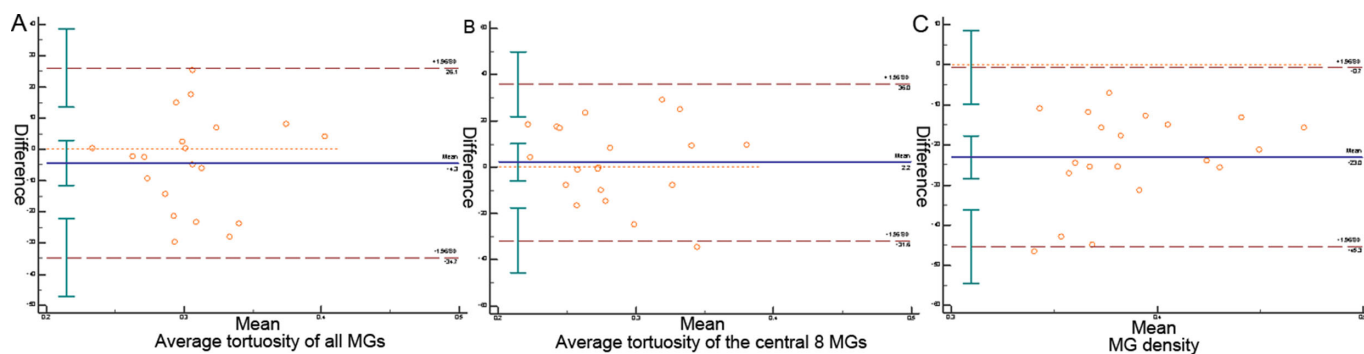


Figure 5. Bland–Altman plots showing inter-observer reproducibility differences for all measured parameters.

Table 5. Intra-Observer Repeatability Results of MG Tortuosity and MG Density

	Mean ± SD	Sw	2.77Sw	CoV
MG tortuosity, both eyelids				
Average tortuosity of all MGs	0.30 ± 0.05	0.001	0.003	0.003
Average tortuosity of central eight MGs	0.29 ± 0.05	0.002	0.006	0.007
MG density, both eyelids	0.35 ± 0.05	0.001	0.003	0.003

Table 6. Inter-Observer Reproducibility Results of MG Tortuosity and MG Density

	Mean ± SD	Sw	2.77Sw	CoV
MG tortuosity, both eyelids				
Average tortuosity of all MGs	0.31 ± 0.04	0.001	0.003	0.003
Average tortuosity of central eight MGs	0.28 ± 0.05	0.001	0.003	0.004
MG density, both eyelids	0.43 ± 0.04	0.005	0.014	0.012

tortuosity showed a significant correlation with other clinical parameters and MGD.

Previous studies have indicated that MG tortuosity is an important component of MG morphological changes, and a previous report has suggested that MG distortion is a first-stage morphological alteration that occurs in MGs.^{8,9,19} Most MG morphology studies, however, have focused on MG atrophy; few of them have discussed the characteristics of MG tortuosity. Moreover, accurate methods for evaluating tortuosity have not been available. Arita et al.⁹ defined MG tortuosity as the occurrence of tortuosity > 45° in one MG according to meibography results; they categorized tortuosity into three grades and suggested that increased MG tortuosity might influence meibum expression during blinking.

In another study, Pult et al.⁷ measured the bent angle of the most bent gland and suggested that the bent angle of the upper eyelid was negatively correlated with the NIBUT. In our previous study, we graded MG tortuosity according to the bent angle

and bent area; the results indicated that tortuosity was negatively correlated with lipid layer thickness in children.⁸ However, the findings mentioned here were all semiquantitative or subjective. The present study used an objective method to quantitatively measure MG tortuosity that is more accurate and reduces the interference of subjective factors. A similar method has been used previously to measure the vessel tortuosity of the retina, and the results showed that vessel tortuosity may be a useful and quantitative parameter for evaluating diabetic retinopathy progression.¹⁶

In accordance with the previous study, our study confirmed that ocular symptom abnormalities (i.e., tear film stability, lid margin abnormalities, MG expressibility, and MG atrophy) were more severe in MGD patients than in normal controls.^{20,21} Moreover, our results suggest that the average tortuosity values for all of the MGs and the central eight MGs were significantly higher in the MGD patients than in the normal controls. MG tortuosity showed a significant

correlation with lid margin score, meiboscore, and meibum expressibility score. These three parameters are important values for the diagnosis of MGD and determining its severity.^{10,17,22} Furthermore, when we combined the MG tortuosity of both eyelids, the correlation was more significant. We also found a significantly negative correlation between the average tortuosity of the central eight MGs and TBUT, which is in agreement with the findings of a previous study.⁷ As TBUT is an important parameter for the diagnosis of dry eye, this finding suggests that MG tortuosity may be correlated with dry eye.

To study the applicability of MG tortuosity parameters for the diagnosis of obstructive MGD, ROC curve analysis was used to measure sensitivity and specificity and their respective cutoff values. The efficacy of MG tortuosity of the upper eyelid for the diagnosis of MGD was much greater than that of the lower eyelid. Each MG tortuosity parameter of the upper eyelid revealed acceptable specificity and sensitivity. The MG tortuosity of both eyelids showed the best efficiency, sensitivity, and specificity for the diagnosis of MGD. Our results suggest that MG tortuosity can be an applicable diagnostic method for MGD.

Furthermore, we compared MG tortuosity differences in symptomatic and asymptomatic MGD patients. Asymptomatic MGD was documented as a preclinical stage of MGD with clinical changes of MGD but no lid-related symptoms.^{23,24} The diagnosis of this preclinical stage may require MG expression or meibography results. Our results showed that the average tortuosity and the average tortuosity of the central eight MGs were much higher in symptomatic MGD patients than asymptomatic patients. When MG tortuosity was compared between the asymptomatic MGD patients and normal controls, the results showed that MG tortuosity in the upper eyelid was significantly higher in the asymptomatic MGD patients than in normal controls; however, there was no significant difference in MG tortuosity in the lower eyelid. These results indicate that MG tortuosity may be a good method for diagnosing early stages of MGD, as early changes in MG tortuosity may occur in the upper eyelids.

Previous studies also found that MG tortuosity can occur in children. Shirakawa et al.²⁵ reported that the meiboscores of both eyelids were 0 in children under 3 years of age, but Zhao et al.⁸ found that every child had a distinct morphological change between 7 and 14 years of age. The reason for MG morphological changes in children is still unknown. Environmental aggravation or the popularity of electronics use may contribute to the results⁸; however, Wu et al.²⁶ suggested that meibomian gland dropout might be a physiological

phenomenon in children. A long-term observational study is needed to confirm the hypothesis.

This study also has limitations. The software used for the measurements cannot recognize MGs automatically, and the manual contouring of MGs may lead to varying quantification, although we applied a single standard when using the software. Also, the sample size was small. In future research, we will enroll a greater number of preclinical MGD patients, and various dry eye subgroups will also be enrolled to determine whether MG tortuosity can be a diagnostic tool for dry eye subgroups.

Conclusions

MG tortuosity is a novel quantitative index for diagnosing MGD and may be an efficient tool for the diagnosis of early-stage MGD.

Acknowledgments

Supported by grants from the Zhejiang Provincial Natural Science Foundation of China (LSY19H120001, LQ18H120007) and the Zhejiang Provincial Medical and Health Science, Technology Program of Health and Family Planning Commission (2019RC220, 2019PY049).

Disclosure: **X. Lin**, None; **Y. Fu**, None; **L. Li**, None; **C. Chen**, None; **X. Chen**, None; **Y. Mao**, None; **H. Lian**, None; **W. Yang**, None; **Q. Dai**, None

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