

# Expressible Meibomian Glands Have Occult Fixed Obstructions: Findings From Meibomian Gland Probing to Restore Intraductal Integrity

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**Purpose:** To describe and quantify findings of intraductal obstruction during probing expressible and nonexpressible meibomian glands (MGs) in patients with obstructive meibomian gland dysfunction using a 1-mm intraductal MG probe.

**Methods:** A retrospective study of probe findings from 108 consecutive patients. Nonparametric tests using SPSS software 25.0 to explore relationships between expressibility and probe findings.

**Results:** Of 11,776 probed glands of 404 lids, 84% showed mechanical resistance (MR) and 16% showed no resistance (NR). Fixed, firm, focal unyielding resistance (FFFUR) occurred in 79.5% of obstructed glands, and nonfixed, nonfocal easily yielding soft resistance (SFT) in 20.4%. FFFUR was characterized by an audible and tactile “firm pop” (FP) or “firm gritty” (FG) sensation. No significant difference in MR and FFFUR for lids between 0% and >90% gland expressibility was observed. FP correlated with increased expressibility ( $P = 0.011$ ), lid tenderness ( $P = 0.045$ ), and complete proximal obstruction ( $P = 0.037$ ), whereas SFT correlated with reduced expressibility ( $P = 0.016$ ). Upper lids showed greater incidence of MR ( $P < 0.001$ ), FFFUR ( $P < 0.001$ ), and FG ( $P < 0.001$ ), whereas lower lids showed greater expressibility ( $P < 0.001$ ) and NR ( $P < 0.001$ ).

**Conclusions:** FFFUR was the most common probe finding in a large series of consecutively probed MGs, with an incidence of 67% of glands and 80% of obstructed glands. FFFUR was independent of gland expressibility, demonstrating expressible glands harbor FFFUR deep to at least one acinus. FP was associated with expressible gland occult obstruction and lid tenderness. SFT correlated with reduced

expressibility, perhaps related to altered duct/duct contents. Upper lids correlated with increased MR, FFFUR, and FG and lower lids with increased expressibility and NR, possibly reflecting contrasting anatomy and blink-related microtrauma.

**Key Words:** meibomian gland probing, meibomian gland dysfunction, dry eye, meibomian glands, Lipiflow, intense pulsed light

(*Cornea* 2019;38:880–887)

Obstructive meibomian gland dysfunction (o-MGD) is considered to be the most frequent cause of dry eye in the world.<sup>1,2</sup> If untreated, o-MGD can lead to lid and ocular surface inflammation with subsequent meibomian gland (MG) atrophy as noted on infrared meibography.<sup>3</sup> The traditional explanation and treatment for gland obstruction is focused on thickened viscous meibum or keratinized lumen debris,<sup>4,5</sup> yet results are inconsistent and often times inadequate, leading to dissatisfaction and frustration for patient and physician alike.

To better understand this disease, this author (S.L.M.) developed a meibomian gland probing (MGP) technique to probe obstructed MGs that had been refractory to traditional treatments. During this procedure, sterile stainless steel wire probes are inserted through the natural gland orifice and into the intraductal space.<sup>6</sup> This author’s (S.L.M.) report in 2010 revealed the unexpected finding of fixed, firm, focal, unyielding resistance (FFFUR) within the duct, which has since been related to periductal fibrosis.<sup>4,7–9</sup> This resistance was relieved by using increased probing pressure to advance the probe and relieve tight bands of fibrosis contracting around and pinching the external duct wall, causing a secondary loss of intraductal integrity from luminal strictures while obstructing meibum flow (Fig. 1). Immediate release of meibum along the wire probe to exit the orifice was noted as intraductal pressures (IDPs) equilibrated with restoration of intraductal integrity. Patient symptom relief was immediate and dramatic.

Fixed obstructions may occur distal to all acini and immediately proximal to or within the orifice, which we have proposed to be called complete distal obstruction (CDO).<sup>7</sup> Alternatively, the fixed obstruction may occur proximal to at least one acinus, which we proposed to be called complete proximal obstruction (CPO) (Fig. 2). In the setting of CPO type of FFFUR, heat and pressure may increase delivery of meibum from in front of or distal to the fixed obstruction. However, in the absence of restoring normal intraductal anatomic integrity, increased external pressure such as with therapeutic gland

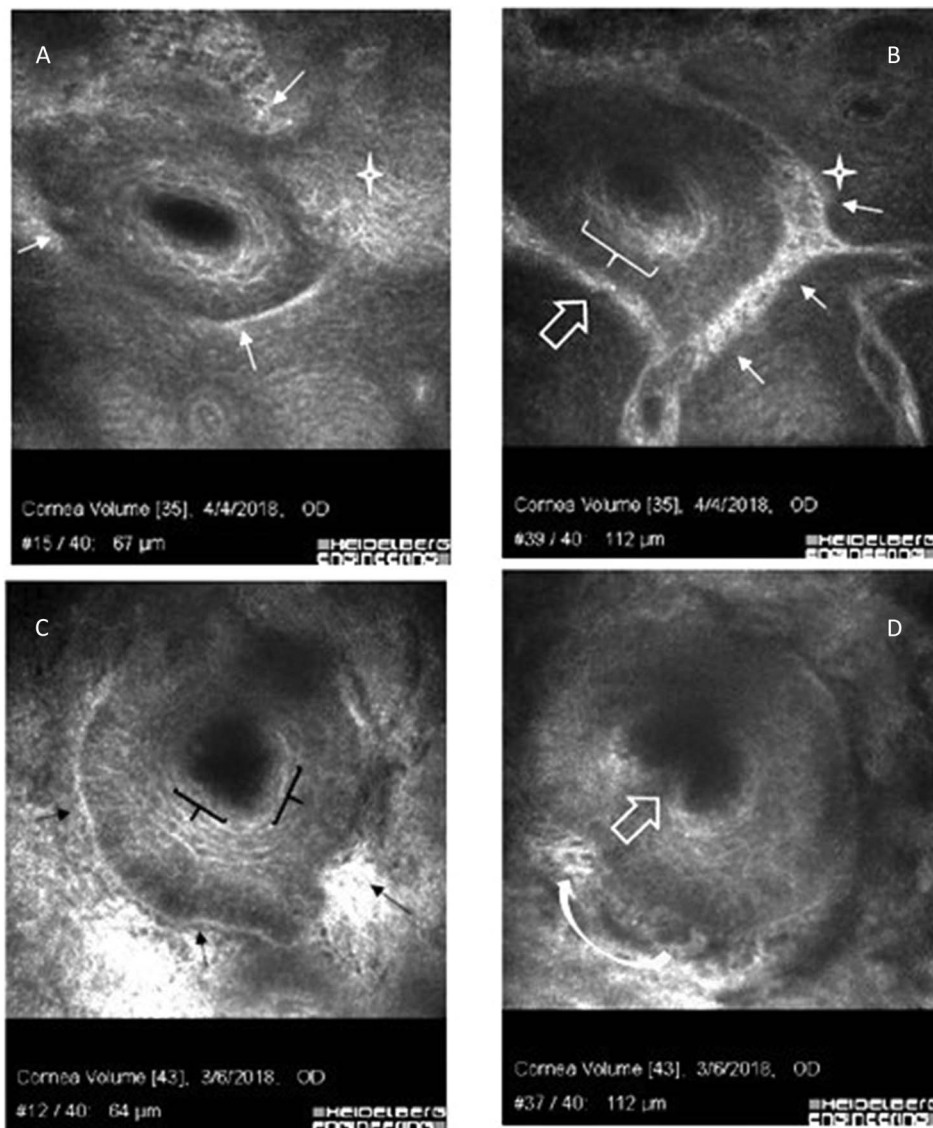
Received for publication November 16, 2018; revision received February 21, 2019; accepted March 1, 2019. Published online ahead of print XX XX, XXXX.

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S. L. Maskin holds patents on the use of jojoba anesthetic ointment and instrumentation and methods for intraductal diagnosis and treatment of meibomian gland disease. S. Alluri received an educational stipend from Ocular Surface Research and Education Foundation.

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**FIGURE 1.** Representative examples of periductal fibroses and corresponding internal lumen stricture and altered diameters using confocal microscopy: (A and B) are images of the same gland orifice at different depths. A, shows an oval lumen at 67  $\mu\text{m}$  depth with apparent fibroses (arrows), including a fibrotic sheet (star) which appears in (B) at 112  $\mu\text{m}$  as a tight periductal fibrotic band (star and arrows) surrounding and pinching the external duct wall. B, also shows an oval lumen with the flattest border (bracket), corresponding to the tightest area of fibroses (open arrow). (C and D) are views of the same gland orifice at 64 and 112  $\mu\text{m}$  depth (different gland orifice than A/B). C, shows scalloping and pinching of the external duct wall from apparent fibroses (arrows), with flattening of oval lumen at corresponding meridians (brackets). D, shows indentation of the external wall (arc), with corresponding lumen stricture (open arrow).

expression presents a risk of excessively increasing IDP behind the obstruction. This elevated IDP leads to possible adverse sequelae with cystic deformation, gland atrophy, and intolerable levels of pain in some patients.<sup>10</sup>

MGP has been shown to be a successful treatment for o-MGD and can restore glandular intraductal anatomic integrity with positive physical proof.<sup>6,7,11–17</sup> In our hands, from a group of 541 tender lids with o-MGD, probing eliminated tenderness in 86.1% of 144 lids at 1 week, 82.3% of 215 lids at 3 to 6 months, and 58.4% of 113 lids at 1 year. From a total of 271 nonfunctional lids that were probed [with 4 or less expressible glands (EGs) per lid], 93.8% of 64, 92.2% of 102, and 73.9% of 46 nonfunctional lids remained functional at 1-week, 3 to 6 months, and 1-year follow-up, respectively.<sup>7</sup> Separately, in 25 preprobing nonfunctional lids, the average number of EGs was 2.8 ( $\pm 1.1$ ) glands per lid, with a significant increase in the number of postprobing EGs per lid to 14.4 ( $\pm 6.4$ ) (412% increase,  $P <$

0.0001) at a mean follow-up of 2.4 months.<sup>7</sup> Using visual analog scale studies to evaluate the postprobing reduction in symptoms of o-MGD [except lid tenderness (LT)] such as photophobia and burning, we found in 7 patients and 19 lids an immediate 35% improvement, with 66.1% improvement by 1 month and 80.2% improvement by 3 to 6 months.<sup>8</sup>

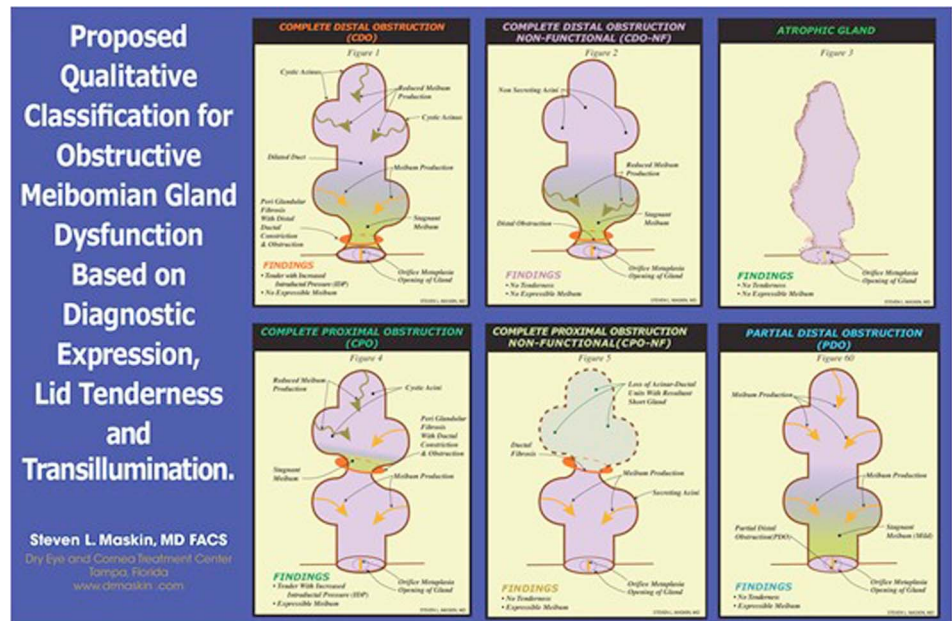
This study was performed to quantify probe findings of nearly 12,000 glands of 108 consecutive patients probed over a 34-month span to restore intraductal integrity through relief of fixed unyielding obstructions. We were interested in identifying and quantifying physical characteristics of the intraductal MG space to better understand the extent of occult disease.

## MATERIALS AND METHODS

### Study Design and Patient Selection

We conducted a review of the medical charts for all 108 patients who received their first MG probing (by S.L.M.)

**FIGURE 2.** The top row of images represents a fixed obstruction or FFFUR (indicated by the orange ring around the gland duct) of the MG distal to all acini. This type of obstruction will initially present with LT because meibum is being produced without an escape, leading to the buildup of pressure behind the obstruction (this obstruction is termed CDO, as depicted in the first image of the top row). Eventually, the buildup of pressure will result in a loss of function of the gland (termed CDO-NF, as depicted in the middle image of the top row), ultimately resulting in MG dropout as the entire gland atrophies (top row, right). No meibum will be expressed from this gland. The first 2 images in the bottom row represent a fixed proximal obstruction or FFFUR (indicated by the orange ring around the more proximal gland



duct) of the MG, in which 1 or more acini are in communication with the central duct and orifice. LT will be present because meibum is being produced without an escape, leading to the buildup of pressure behind the obstruction. However, this classification of MGs will have expressible meibum because the acini located distally to the obstruction still remains in communication with the central duct and orifice (this obstruction is termed CPO, as depicted in the first image of the bottom row). Eventually, the buildup of pressure will result in a loss of function of the gland proximal to the obstruction, ultimately resulting in a truncated MG (middle image, bottom row). The final classification of PDO (as depicted in the bottom row, right), is the result of a partial distally obstructed gland, such as orifice squamous metaplasia. This gland presents with no LT because there is not a complete obstruction and meibum is able to be expressed at the orifice. [Adapted from: Maskin S. Intraductal Meibomian Gland Probing: A Paradigm Shift for the Successful Treatment of Obstructive Meibomian Gland Dysfunction. In: Tsubota K, ed. Diagnosis and Treatment of Meibomian Gland Dysfunction. Tokyo, Japan: Kanehara & Co, Ltd; 2016:157 (Figure 6). Maskin SL, Testa WR. Growth of Meibomian gland tissue after intraductal Meibomian gland probing in patients with obstructive Meibomian gland dysfunction. *Br J Ophthalmol*. 2018;102:59–68.]. Adaptations are themselves works protected by copyright. So in order to publish this adaptation, authorization must be obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

within the 34-month period from September 16, 2015, to July 19, 2018. Five patients received a probing session elsewhere at an average 42.6 months previously. All patients had o-MGD diagnosed clinically by signs including lid margin or tarsal hyperemia, lid margin telangiectasia, thickening or irregularity, and MG orifice metaplasia, as well as symptoms of o-MGD. Neither LT nor a specific number of EGs were required for a positive diagnosis of o-MGD. Fluorescein clearance test,<sup>18</sup> infrared video meibography,<sup>7</sup> and confocal microscopy<sup>19–21</sup> were also performed in addition to microbiology evaluation when clinically indicated but will not be reviewed in this article. All procedures adhered to the principles of the Declaration of Helsinki, and all patients provided informed consent. This study received an institutional review board exempt review determination by an independent institutional review board.

## Patient Examination

### MG Analysis of Expressibility and LT

During routine slit-lamp examination within 1 week before MGP, the number of expressible MGs per lid was

counted while applying mild to moderate pressure with a cotton-tipped applicator (Henry Schein, Melville, NY) to the upper and lower lids over the MGs to manually express meibum oil. The presence or absence of LT was evaluated in a qualitative manner and recorded as previously reported.<sup>7</sup> A diagnosis was assigned for each lid depending on the number of EGs and the presence of tenderness. Tender lids were categorized as either CDO or CPO, where CDO lids have less than or equal to 4 EGs and CPO have more than 4 EGs. Nontender lids were categorized into CDO-nonfunctional (CDO-NF) or partial distal obstruction (PDO), where CDO-NF lids have less than or equal to 4 EGs and PDO lids have greater than 4 (Fig. 2).<sup>7</sup>

### MGP: Firm Versus Soft: Pop Versus Gritty

MGP was performed as previously described by the first author.<sup>7</sup> In brief, one drop of topical 0.5% tetracaine hydrochloride (Bausch and Lomb, Tampa, FL) was placed in the inferior fornix, followed by placing a bandage contact lens over the cornea. Topical anesthetic ointment consisting of 8% lidocaine with 25% jojoba in a petrolatum ointment base (O'Brien Pharmacy, Mission, KS) was applied to the inferior

lid margin. The eye was closed for 15 minutes. One additional drop of topical tetracaine was then placed in the eye. The patient was then positioned at the slit lamp. The MG orifices were then visualized and examined. A 1-mm long stainless steel sterile intraductal MG probe (Rhein Medical, a division of Katena Products, Denville, NJ) was then inserted into each orifice, perpendicular to the lid margin using a dart-throwing motion to find the angle of entry. As the probe passed through the orifice lumen and into the distal duct, there typically was resistance to the probe. The resistance was characterized as FFFUR, which required additional probing force to relieve, analogous to relief of punctal fibrosis with a canalicular probe. Opening the obstruction created a tactile sensation of pressure release and audible firm pop (FP) and firm gritty (FG) (multiple pops) sounds heard by the patient and physician as the tight band of contracting periductal fibrosis was released and resistance gave way, allowing sudden advancement of the probe, which was then able to freely pass to and fro within the duct. Accompanying an audible FP was a single focus of pressure release, whereas accompanying a FG were multiple foci. There was variation in the intensity level of tactile intraductal resistance which was consistent with the audible volume generated by relief of the obstruction, at times heard across the room by family members and thought to correlate with severity of obstruction. The FP and FG were sudden bursts of quick, not prolonged sounds. For FG, the multiple individual FP sounds could occur immediately after each other in rapid succession or after a short delay where the probe advanced through an interim nonstricted course of the duct lumen.

Less commonly, a mild back pressure or “soft” resistance (SFT) was noted, which was not fixed, not firm, and easily yielding. SFT was felt but allowed the probe to pass without significant additional mechanical pressure. Passing through SFT did not generate an audible sound. It can be thought of as providing “drag” on the “to and fro” movement of the wire probe. SFT was not focal in contrast to the FFFUR which characteristically was focal or multifocal. Infrequently, there was a lack of resistance designated as no resistance “(NR)” where the probe entered the orifice and duct without any resistance or drag.

### Data Collection and Analysis

During MGP, MG lid margin template maps were used to record the orifice gland position relative to the probe findings of each gland, including total glands probed and individual gland probing characteristics such as “NR,” “SFT,” and “FFFUR” including FP or FG, as well as upper or lower lid. These probing data were matched with EG and LT data obtained within the week before MGP, with 83% of lids examined on the day of probing before MGP and 94% of lids examined within 1 day before MGP.

### Statistical Analysis

Data were analyzed using IBM SPSS Statistics software version 25.0. Mann–Whitney *U* tests were conducted to

assess the relationship of probe findings [mechanical resistance (MR), FFFUR, FP, FG, SFT, and NR] with LT. A bivariate correlation (Spearman correlation) test was conducted to explore the correlation of the probe findings on the expressibility of the lid. Kruskal–Wallis tests were conducted to assess the intergroup variability of probe findings correlation with MGD classification to compare CPO and PDO lids. Mann–Whitney *U* tests were again performed to evaluate the significant presence of obstruction and probe findings between upper and lower lids. All tests performed were nonparametric tests, and the level of statistical significance was set at  $P < 0.05$ .

## RESULTS

### Patient Demographics

There were 108 patients and 404 lids probed for their initial time (by S.L.M.) between September 16, 2015, and July 19, 2018. Of these 404 lids, there were expressibility data for 357 lids. Basic demographics are presented in Table 1. There were 23 probed patients with previous LipiFlow thermal pulsation, 7 had previous Intense Pulsed Light, and 4 patients had both procedures previous to their probing session, adding up to 31.5% of total patients in this study.

### Probe Findings

During the course of this study, there were 11,776 glands probed with an average of 29.1 glands per lid. There were 9886 glands with intraductal MR (84%) and 1890 glands without resistance (16%) at a ratio of 5.25:1. Of the glands with resistance, there were 7864 (79.5%) glands with FFFUR, with 2022 (20.4%) glands with SFT at 3.88:1 ratio. Of the glands with FFFUR, there was a FP noted in 5467 (69.5%) glands and FG noted in 2396 (30.5%) glands at a ratio of 2.28:1 (Table 2).

### Expressibility as Function of MGP Findings

Table 3 shows the frequency of probe findings of intraductal obstruction stratified, by using decile with at least 10 glands per decile, according to the percentage of lid glands that showed expressible meibum. This excludes 3 lids, each from the 80% to 90% and >90% expressibility groups to avoid an outlier effect on statistical analysis. The percentage of glands within a single lid showing MR ranged from 80.9 to 87.6, with a mean of 83.9. The percentage of glands showing

**TABLE 1.** Basic Demographics

Total Patients	108
Lids probed	404
Expressibility data	357
Gender	
M	36
F	72
Mean age	56.4 (±16.8)

**TABLE 2.** Probe Findings Using a 1-mm Maskin Probe From 404 Lids

Probe Findings From	Total (404 Lids)
TGP	11,776 (29.1 glands/lid)
NR	1890 (16%)
Total glands with resistance: (MR)	9886 (84%)
Soft (SFT)	2022 (17.2% of TGP and 20.4% of MR)
Firm (FFFUR)	7864* (67% of TGP and 79.5% of MR)
Pop (FP)	5467 (46.4% of TGP, 55.3% of MR and 69.5% of FFFUR)
Gritty (FG)	2396 (20.3% of TGP, 24.2% of MR, 30.5% of FFFUR)

\*One gland with a missing pop or gritty value.  
TGP, total glands probed.

FFFUR ranged from 62 to 73.1, with a mean of 66.6 (mean obtained for obstructed glands was 79.3). There was no statistically significant difference among any decile of expressibility from 0% to <80% expressibility for MR and FFFUR, showing that each decile had similar levels of overall resistance and fixed unyielding resistance within the intraductal space. Interestingly, if we added back the 6 outlier lids representing 80% to 90% and >90% expressibility, there would still be no statistical significance difference in MR or FFFUR. There was the same likelihood of total and fixed intraductal obstruction for lids showing greater than 90% gland expressibility and lids showing less than 10% expressibility.

FP was present in a range from 41% to 56.8% of single lid glands, with a mean of 47.3. FP was correlated with increased expressibility by Spearman Rho at  $P = 0.011$ . SFT ranged from 6.7% to 23.1%, with a mean of 17.3%, and was correlated with decreased expressibility by Spearman Rho at  $P = 0.016$ . Scatter plots (Figs. 3A, B) show a statistically significant positive and inverse relationship of FP ( $P = 0.011$ ) and SFT ( $P = 0.016$ ), respectively, on expressibility.

### Probe Finding Correlations With Tender Lids

FP was present in 49.1% ( $\pm 17.8$ ) of tender glands, whereas FP was present in only 44.7% ( $\pm 20.5$ ) of nontender glands ( $P = 0.045$  by Mann–Whitney  $U$  test). No other variable showed significance between tender and nontender lids.

### Probe Finding Correlations With MGD Classification

When compared between CPO and PDO lids, the presence of FP was significantly higher in CPO lids than in PDO lids. There were 290 lids for this analysis, with 180 CPO lids and 110 PDO lids. FP was found in 50.3% ( $\pm 17.1$ ) of glands in CPO lids and 44.9% ( $\pm 20.3$ ) of glands in PDO lids ( $P = 0.037$  by Kruskal–Wallis test).

### Probe Findings as Function of Upper Versus Lower Lids

To analyze differences in upper versus lower lids, we evaluated the 351 lids used for analysis in Table 3. Expressibility was greater in the lower lids, with 38.8% ( $\pm 18.3$ ) of all lower lid glands showing expressibility, whereas upper lids showed expressibility in 30.6% ( $\pm 17.5$ ) of all glands ( $P < 0.001$  by Mann–Whitney  $U$  test) (Table 4).

There were 10,240 glands that were probed. MR was found in 8611 (84.1%) glands. MR with obstruction was found in 5110 (87.5%) upper lid and in 3501 (79.6%) lower lid glands ( $P < 0.001$  by Mann–Whitney  $U$  test). FFFUR was found in 81.7% of MR of upper lids and in 75.9% ( $P < 0.001$  by Mann–Whitney  $U$  test) of lower lids. FG was noted in 33.3% of upper lid FFFUR, with 23.1% of lower lid FFFUR ( $P < 0.001$  by Mann–Whitney  $U$  test). NR and combination of NR+SFT were more frequently found in the lower lids than in the upper lids. This was statistically significant for both values ( $P < 0.001$  by Mann–Whitney  $U$  test).

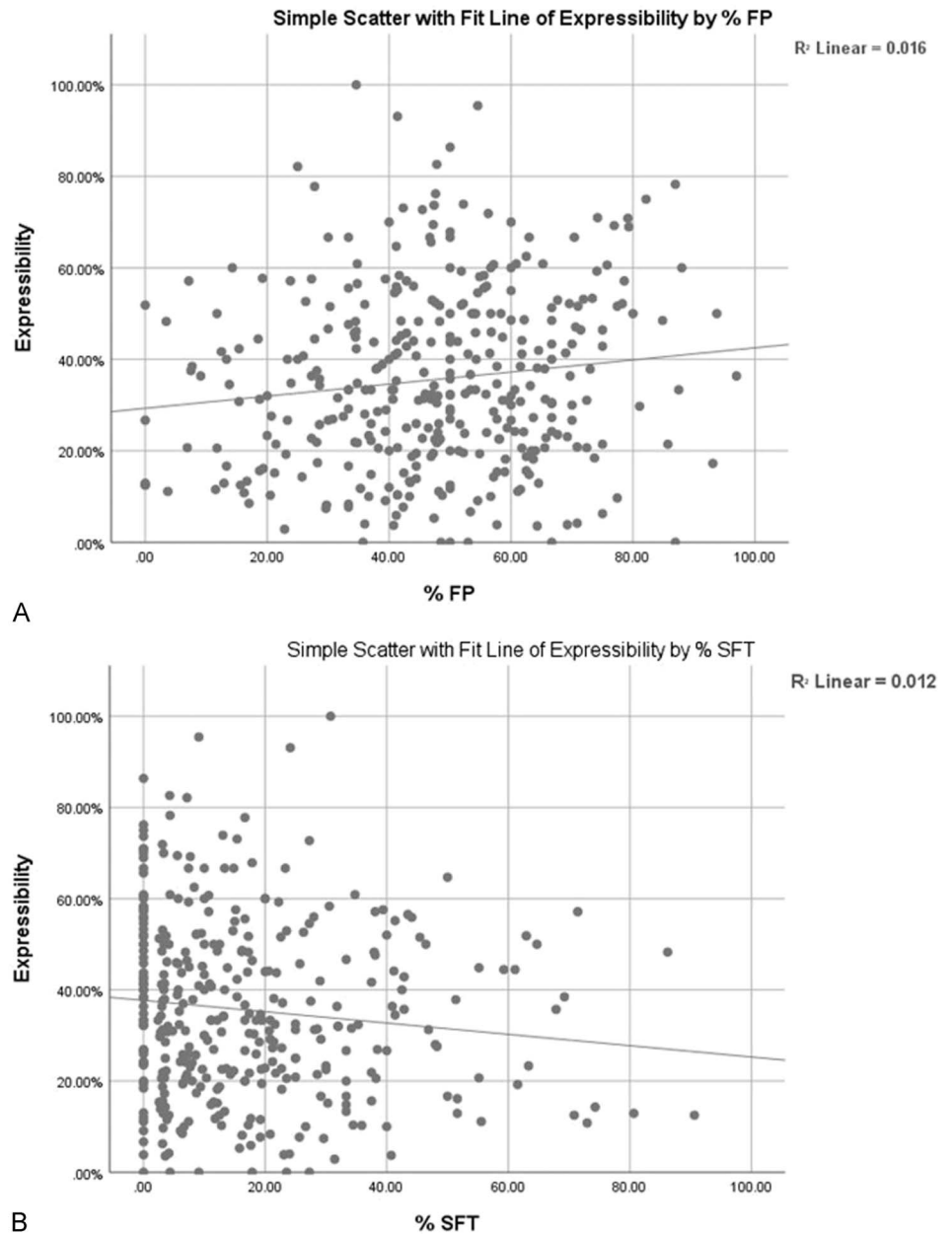
**TABLE 3.** Expressibility is Statistically Independent of Intraductal MR and FFFUR\*

Expressibility [(EG/TG) × 100]	N (Lid Count)	Avg No. of Glands per Lid	% Glands NR	% Glands MR	% Glands SFT	% Glands FFFUR	% Glands FP	% Glands FG
0% to <10%	25	28.8	12.4 ( $\pm 9.8$ )	87.6 ( $\pm 9.8$ )	14.9 ( $\pm 11.6$ )	72.7 ( $\pm 16.8$ )	48.7 ( $\pm 18.2$ )	23.9 ( $\pm 14.7$ )
≥10% to <20%	55	30.6	14.8 ( $\pm 11.7$ )	85.2 ( $\pm 11.7$ )	23.1 ( $\pm 23.9$ )	62 ( $\pm 23.9$ )	41 ( $\pm 20.9$ )	20.9 ( $\pm 17$ )
≥20% to <30%	69	29.2	16.9 ( $\pm 13.3$ )	83.1 ( $\pm 13.3$ )	16.9 ( $\pm 14.4$ )	66.1 ( $\pm 22.2$ )	46.9 ( $\pm 17.4$ )	19.2 ( $\pm 17.5$ )
≥30% to <40%	64	30.4	15.4 ( $\pm 12.6$ )	84.5 ( $\pm 12.6$ )	17.1 ( $\pm 16.1$ )	67.4 ( $\pm 20.2$ )	46.9 ( $\pm 18.6$ )	20.6 ( $\pm 17.2$ )
≥40% to <50%	54	29.8	19.7 ( $\pm 17.6$ )	80.3 ( $\pm 17.6$ )	16.9 ( $\pm 18.9$ )	63.4 ( $\pm 23.5$ )	46.5 ( $\pm 18.1$ )	16.9 ( $\pm 14$ )
≥50% to <60%	49	27.1	15.1 ( $\pm 10.8$ )	84.8 ( $\pm 10.8$ )	18.3 ( $\pm 19.4$ )	66.6 ( $\pm 23.1$ )	50.3 ( $\pm 19.8$ )	16.2 ( $\pm 15.8$ )
≥60% to <70%	23	28.1	15.4 ( $\pm 12.5$ )	84.6 ( $\pm 12.5$ )	11.5 ( $\pm 12.3$ )	73.1 ( $\pm 15.9$ )	54.8 ( $\pm 17.5$ )	18.2 ( $\pm 13.7$ )
≥70% to <80%	12	23.9	17.2 ( $\pm 10.9$ )	82.8 ( $\pm 10.9$ )	6.7 ( $\pm 9.2$ )	76.1 ( $\pm 16.4$ )	56.8 ( $\pm 19.1$ )	19.4 ( $\pm 15.7$ )
Total	351	29.2	16.1 ( $\pm 13.1$ )	83.9 ( $\pm 13.1$ )	17.3 ( $\pm 17.7$ )	66.6 ( $\pm 21.7$ )	47.4 ( $\pm 19$ )	19.2 ( $\pm 16.1$ )

FFFUR: fixed, firm, focal, unyielding resistance (FP + FG); MR: mechanical resistance (SFT + FFFUR).

\*We required at least 10 lids in a decile to include in statistical analysis derived from Table 3 to avoid an outlier effect on this analysis. There was no significant difference in MR and FFFUR from 0% to <80% expressibility. If added back, the 6 additional lids from 80% to 90% and >90% expressibility still showed no statistically significant difference among all deciles for MR and FFFUR.

TG, total glands noted by counting orifices.



**FIGURE 3.** A, Scatter plot showing positive correlation between the percentage of FP and percentage expressibility observed in a lid by Spearman Rho at  $P = 0.011$ . B, Scatter plot showing negative correlation between the percentage of soft (SFT) obstruction and percentage expressibility observed in a lid by Spearman Rho at  $P = 0.016$ .

**Probe and Expressibility Findings According to Gender**

There were 233 female and 118 male lids probed. We found statistically significant increases in FG ( $P < 0.001$ ) and FFFUR ( $P = 0.007$ ) for female lids and an increase in SFT for male lids ( $P = 0.005$ ).

**DISCUSSION**

The purpose of this study was to understand the nature of the physical characteristics of MG obstruction within the intraductal space in a large-scale study. The frequent intraductal fixed unyielding obstructions are consistent with clinical slit-lamp findings and confocal microscopy findings suggestive of periglandular fibro-

sis.<sup>4,8,9,20,21</sup> These probe findings offer a compelling hypothesis for the cause of ductal obstruction. For many years, the obstruction in MGD was thought to be from altered ductal contents, which could be heated and squeezed out through the orifice. However, traditional therapies have not been satisfactory, suggesting that at the very least, these concepts were incomplete.

To understand this disease, this author (S.L.M.) probed the first MGs in the mid-2000s. These initial probing sessions revealed for the first time the presence of FFFUR, now believed to be the breakthrough finding, bringing together previous slit-lamp observations described in the 1990s, with the longstanding difficulty controlling this vexing disease.

This study of nearly 12,000 glands over a 34-month period provides quantitative answers to help understand this

**TABLE 4.** Probe Data for Total, Upper, and Lower Lids Represented in Table 3 (351 Lids)

Probe Findings From	Upper Lids (180 Lids)	Lower Lids (171 Lids)	Total (351 Lids)
TGP	5843 (32.5 glands/lid)	4397 (25.7 glands/lid)	10,240 (29.2 glands/lid)
NR	733 (12.5%)	896 (20.4%)	1629 (15.9%)
Total glands with resistance: (MR)	5110 (87.5)	3501 (79.6%)	8611 (84.1%)
Soft (SFT)	936 (16% of TGP and 18.3% of MR)	846 (19.2% of TGP and 24.2% of MR)	1782 (17.4% of TGP and 20.7% of MR)
Firm (FFFUR)	4174* (71.4% of TGP and 81.7% of MR)	2655 (60.4% of TGP and 75.83% of MR)	6829* (66.7% of TGP and 79.30% of MR)
Pop (FP)	2781 (47.6% of TGP, 54.4% of MR, and 66.6% of FFFUR)	2041 (46.4% of TGP, 58.3% of MR, and 76.9% of FFFUR)	4822 (47.1% of TGP, 56% of MR, and 70.6% of FFFUR)
Gritty (FG)	1392 (23.8% of TGP, 27.2% of MR, and 33.3% of FFFUR)	614 (14% of TGP, 17.5% of MR, and 23.1% of FFFUR)	2006 (19.6% of TGP, 23.3% of MR, and 29.4% of FFFUR)

\*One gland with a missing pop or gritty value. TGP, total glands probed.

disease. Using a 1-mm probe, nearly 85% of all glands had some resistance to probe passage, but the remarkable, unexpected finding was that 67% of all glands had fixed, unyielding resistance. By targeting fixed, unyielding resistance and restoring intraductal integrity, we expect to help prevent elevated IDP with subsequent progressive gland atrophy of tissue proximal (or deep) to this occult obstruction.

Even more revealing is that lids showing variable percentages of gland expressibility from 0% to more than 90% all have *statistically insignificant* differences of percent FFFUR (Table 3). Glands that are expressible have occult fixed resistance. *Expressible glands were just as likely to have occult obstruction as nonexpressible glands to have obvious obstruction.* This suggests a significant incidence of obstruction proximal (deep) to at least one acinus in the case of lids with intact expressibility. This further suggests that EGs may yet develop elevated IDP behind the obstruction with subsequent atrophy. Therefore, seemingly healthy and expressible MGs may not be completely healthy. Furthermore, interventions to force meibum through such fixed obstructions using pressure and heat could similarly further elevate IDP, leading to possible exacerbation of inflammatory MGD and dry eye.

FP has been shown to correlate with LT and increased expressibility. This finding demonstrates the fundamental dynamic that occult obstructive disease can exist in the setting of lids with EGs. Furthermore, FP obstructions exist along with LT, suggesting elevated pressure behind FFFUR. A single FP would suggest an increased IDP generated from meibum secretion of many acini. Not surprisingly, FP was also correlated with CPO and not PDO,<sup>7</sup> where CPO was used to depict an EG with LT thought secondary to proximal or deep FFFUR with elevated IDP.

SFT correlated with decreased expressibility. This type of resistance was possibly an effect of altered duct or ductal contents such as thickened, viscous meibum or perhaps tissue edema which created drag on the probe as suggested by animal models of MGD.<sup>22–24</sup> This may present as a nonfixed nonfocal easily yielding SFT to an advancing probe.

Although our study reports findings using a 1-mm probe, we have recently started documenting probe findings

using longer 2 and 4 mm probes. We found that in glands labeled as SFT with a 1-mm probe, there were additional foci of FFFUR uncovered with deeper probing. In 17 additional lids using a 1-mm probe, we found 65% of all glands and 71% of glands with MR have FFFUR, yet immediate and subsequent probing of all glands with 2-mm probes revealed 79.3% of all glands and 90.3% of glands with MR have FFFUR at this deeper level. In a separate small study of 6 lids to evaluate selective 2-mm probing of all SFT or NR glands found with the 1-mm probe, we found a cumulative total of more than 93% of all glands had FFFUR at 1 or 2 mm. In a recent case, there was SFT probing through 1-mm and 2-mm probes up to 4-mm, which yielded a FP and sudden release of a micro hordeolum. It may be that nearly all glands are susceptible and harbor occult FFFUR along the length of the duct. Different probe findings at different depths may indicate variable pathologies and suggest potential differential analysis by probing gland depth. For example, the most distal 1-mm may reflect tear film and orifice pathology, whereas 2-mm to 4-mm may reflect periglandular pathology.

We also found the upper lid to have greater MR, FFFUR, and FG. The contrasting anatomy to the lower lids may be the explanation. The upper lid glands are typically greater in numbers, longer, and thinner.<sup>25–27</sup> Gritty implies multiple depths, so longer glands may have increased risk of fixed unyielding obstruction in a multifocal manner at variable depths along the course of the duct. The relatively greater upper lid movement across the globe with not only blinking but also with saccadic and pursuit eye movements may increase friction-related microtrauma, leading to increased FFFUR and lid wiper epitheliopathy of the upper lid.<sup>27–29</sup> We found the lower lids to show increased expressibility and increased NR. This may be related to increased lumen diameter<sup>26</sup> with shorter glands and, possibly, wider orifice opening.

We also found an increased FFFUR and FG in women compared with men and an increased SFT in men compared with women. A recent study by Suzuki et al<sup>30</sup> showed a gender difference in inferior lid orifice diameters and gland width (0.5 mm proximal to the orifice by meibography) in

healthy eyes. They found men had greater orifice diameters than premenopausal women and greater gland width than premenopausal and postmenopausal women. This suggests a possible natural predisposition for women to develop o-MGD with fixed obstructions.

Another interesting observation is that probed lids showed an average of 29 glands per lid, despite 84% of all glands showing obstructive disease and 67% of all glands having FFFUR. This finding is consistent with our understanding that o-MGD progresses in a gradual manner before whole-gland atrophy occurs (with hordeolum being the exception). This also suggests the benefit of introducing MGP early on before progression to whole-gland atrophy because glands with expressible and nonexpressible o-MGD have already developed FFFUR.

There are few limitations with this study. Characterizing probe findings is not a difficult task between FP and FG. However, differentiating SFT from NR may require experience to feel the difference as neither SFT nor NR has audible sensations. Neither SFT nor NR has a release of pressure as the probe passes through. The probe passes through at an unchanged velocity compared with the release of pressure and sudden advancement of the probe accompanied with relief of a FP or FG.

This study reveals significant and frequent occult fixed and unyielding blockages within the intraductal space of expressible and nonexpressible MGs in the setting of o-MGD. These occult lumen changes bring together subjective and objective findings of this elusive disease that help explain the frustrating clinical experience of treating this disease. The frequent findings of fixed obstructions in nearly 80% of obstructed glands within reach of a 1-mm probe placed into the orifice and more than 90% of obstructed glands within reach of a 2-mm probe are consistent with slit-lamp findings discussed in the late 1990s by Cher and later by Foulks,<sup>4</sup> in addition to confocal microscopy findings. Taken together, these findings may also help explain how therapies that thin meibum may provide palliative improvement but not address the loss of intraductal integrity, thereby allowing further elevated IDP. Ultimately, the relief of FFFUR and restoration of intraductal integrity from Meibomian Gland Probing (MGP) will enable the use of complimentary procedures and therapies to provide optimal treatment of obstructive MGD.

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