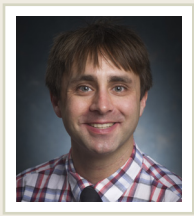
Contact Lens Update
CLINICAL INSIGHTS BASED IN CURRENT RESEARCH

Meibomian Gland Morphology Questions & Answers

February 16, 2021



Andrew D. Pucker, OD, PhD, FAAO, FSLS earned his OD, MS, and PhD degrees from The Ohio State University, and he is currently an Assistant Professor and Chief of the Myopia Control Clinic at the University of Alabama at Birmingham.

Meibography first emerged in the late 1970s.[1, 2] While this technology allowed for the observation of the meibomian glands in vivo for the first time, the technique required direct contact with the eyelids.[3] It was challenging to perform, and was poorly tolerated by patients because it was time-consuming and uncomfortable.[3] However, within my academic career, modern, non-contact meibography has emerged as common practice. This more recent method negates most of the pitfalls associated with contact meibography, which has allowed for the imaging of large groups of patients in a relatively short amount of time.[4, 5] This has subsequently allowed our understanding of meibomian gland morphology to explode. Since this field is ever-evolving, this article will address a number of commonly asked questions, so readers have the most up-to-date information for their clinical decision making.

How should we grade meibomian gland atrophy?

The community currently has a number of available methods for subjectively grading meibography images. Perhaps the most commonly used grading scale is the meiboscore grading system introduced by Arita et al. (2008) during their seminal report on non-contact meibography.[6] The meiboscore grading scale uses a 0 to 3 grading scale, with a grade of 0 representing no meibomian gland atrophy, with grades of 1, 2, and 3 representing 1% to 33%, 34% to 66%, and ≥67% of glands lost, respectively.[6] Pult *et al*.'s 0 to 4 grading scale is likewise commonly used.7 Much like the meiboscore scale, a grade of 0 represents no atrophy while grades of 1, 2, 3, and 4 represent <25%, 26% to 50%, 51% to 75%, and >75% glands lost, respectively.7 Both scales have been found to have good repeatability.[7, 8]

There are reports of objectively grading meibography images by assigning a percentage of glands loss with computer programs such as ImageJ (https://imagej.nih.gov/ij/).[5, 9] When Pult *et al*. used digital grading, the authors found that upper eyelid atrophy had a sensitivity of 0.889 and a specificity of 0.857 for diagnosing dry eye when a cutoff value of 16.9% was used, and they found that lower eyelid atrophy had a sensitivity of 0.818 and a specificity of 0.778 for diagnosing dry eye when a cutoff value of 28.7% was used.[9] Pucker *et al*. did not find objective grading to improve the rater's ability to diagnose dry eye disease when making a comparison to subjective grading.[5] Nevertheless, recent data suggests that digital grading may be preferred for tracking meibomian gland morphology over time, since small amounts of change in atrophy typically occur over the course of a clinical trial.[10-12] While digital image analysis may be valuable in the research laboratory, it may be too cumbersome for a clinician in routine practice since it typically requires investigators to export the meibography images and subsequently determine atrophy percentages with non-automated software.[5]

Evaluating meibomian gland tortuosity is also gaining popularity because Arita *et al*. have found gland tortuosity to be associated with gland function.[13] Halleran *et al*. (2016) have since introduced a descriptive grading scale that can be easily employed within the clinic.[14] The Halleran *et al*. grading scale specifically evaluates the number of

tortuous glands with grades of 0, 1, 2, 3, and 4 representing none, <25%, 26% to 50%, 51% to 75%, and >75%, respectively, of the glands being tortuous.[14] Pucker *et al*. have since used this scale to determine that worse upper eyelid meibomian gland tortuosity is associated with being more likely to drop out of contact lenses.[14] The Dry Eye Assessment and Management (DREAM) study has recently introduced a number of other meibomian gland morphology metrics (distorted, hooked, shortened, overlapping, ghost, and tadpoling glands); however, the utility of these metrics for diagnosing dry eye disease has yet to be fully explored.[15]

Is there a normal level of meibomian gland atrophy?

Some level of meibomian gland atrophy can be expected in both normal adults and normal children. Arita *et al*. found in their 2008 study of adults that 55% of their normal participants had at least some level of meibomian gland atrophy.[6] Wu *et al*., Tichenor *et al*., and Rojas-Carabali *et al*. have likewise provided evidence that it is common in normal children to have some level of meibomian gland atrophy.[16-18] Therefore, a grade 2 or more on either of the above-mentioned subjective grading scales may be the point that one might consider meibomian gland atrophy to be at a clinically significant level.

Are meibomian glands able to regenerate?

Atrophy can be defined as “a diminished volume of cells under certain pathologic conditions after normal development of cells and tissue”.[19] This degenerative process in meibomian glands has generally been thought to be irreversible; nonetheless, recent data calls this assertion into question. Arita *et al*. (n = 10) found that when participants with obstructive meibomian gland dysfunction were treated with topical diquafosol 3% ophthalmic solution that their visible area of meibomian glands increased by an average of 4.6% when analyzing upper and lower eyelids together after participants were treated for at least 4 months.[10] Maskin *et al*. (n = 28) found with a retrospective review that after performing intraductal meibomian gland probing on patients who had obstructive meibomian gland dysfunctionthat at 4.5 to 12.0 months post treatment that these patients had a 4.87% increase in glands. They also found at 12 to 25 months post treatment that participants had a 11.19% increase in meibomian glands.[11] Hura *et al*. (n = 43) lastly found with participants who were treated with a thermal pulsation system that 69% of the treated eyes showed an increase in visible meibomian glands at the 1 year visit compared to the baseline visit.[12] While the above changes of ~11% or less in meibomian gland atrophy over a clinical trial are unlikely to be clinically meaningful based upon conventional, subjective grading scales, these data overall suggest that meibomian glands can either regenerate after gland obstruction is removed, or that existing glands may become more visible on meibography after gland function/health improves. Nevertheless, the finding that glands may be able to regenerate is intriguing because it provides hope for patients who have severe meibomian gland atrophy, and because it suggests that it may be possible to create a treatment that specifically promotes gland regrowth. More research on this topic is still needed to confirm and fully understand what is occurring when glands become more visible on meibography.

Should clinicians screen for abnormal meibomian gland in asymptomatic patients?

Non-obvious meibomian gland dysfunction may have been first documented by Korb and Henriquez in 1980,[20] yet this condition has not become recognized by the greater community until relatively recently.[21] Non-obvious meibomian gland dysfunction is a condition where the patient is typically asymptomatic, lacks obvious signs of inflammation, and lacks obvious eyelid damage/obstruction; nevertheless, when a clinician attempts to express these patient’s meibomian glands, they fail to be able to express meibum or normal meibum.[21] Excessive blinking may indicate mild irritation and non-obvious meibomian gland dysfunction.[21] Blackie *et al*. indicate that non-obvious meibomian gland dysfunction may not become symptomatic until a patient stresses their ocular surface with a factor such as a contact lens;[21] thus, it may be best to screen (meibomian gland atrophy, meibomian gland expressibility) on a regular basis, such that a practitioner can catch and treat these early stage patients, to avoid them advancing into a pathological condition.

What is the typical meibomian gland morphology in children?

It has long been known that the level of meibomian gland atrophy present increases with age.[6] It has also historically been thought that childhood dry eye and meibomian gland atrophy is rare. However, recent prevalence data suggests that somewhere between 0.4% and 23.7% of children have dry eye.[22-24] Wu *et al*. (n = 70) have also found in normal children and adolescents that 28% of the participants in their study had some level of meibomian gland atrophy, finding a mean meiboscore of 0.39 ± 0.70; no difference in atrophy was found in this study between children and adolescents.[17] Tichenor *et al.* (n = 225) in a group of normal children later found a mean of 9.9% atrophy in the upper eyelids of participants and a mean of 8.5% atrophy in the lower eye lids of participants.[16] The authors also found that there was no difference in symptoms between participants with and without dry eye symptoms. Rojas-Carabali *et al*. (n = 60) lastly determined in their group of normal children that 37% of their participants had at least some level of meibomian gland atrophy.[18] Thus, clinicians need to be commonly screening children for dry eye, and they should consider initiating treatments in these patients when non-obvious meibomian gland dysfunction is found, because early treatment may delay or even prevent bothersome dry eye, and it may promote additional years of happy contact lens use.

How do contact lenses affect the meibomian glands?

One can easily hypothesize that a worn contact lens may result in meibomian gland damage/atrophy because the interaction between the blink and the meibomian glands may cause repeated mechanical insult to the glands throughout the wear day. Arita *et al*. provided one of the first large, cross-sectional studies investigating this issue by comparing a group of contact lens (n = 121) and non-contact lens (n = 137) wearers.[25] The authors of this study determined that with greater years of contact lens use there were greater amounts of meibomian gland atrophy.[25] This same study interestingly failed to find a difference in atrophy between soft and gas permeable contact lens wearers, which lends less credence to the mechanical insult theory. Alghamdi *et al*. (n = 100) later found that meibomian gland atrophy increased over the first two years of contact lens use and subsequently stabilized thereafter.[26] These two studies are in contrast to the majority of the other studies found in the literature. This is highlighted by Pucker *et al*. (n = 112) and Machalinska *et al*. (n = 75) who failed to find any association between atrophy and contact lens use in their matched pair studies that compared comfortable contact lens wearers to age- and sex-matched non-contact lens wearers.[5, 27] Pucker *et al.* (n = 112) later compared contact lens dropouts to participants who were comfortable contact lens wearers and failed to find an association with contact lens status and meibomian gland atrophy.[28] Llorens-Quintana *et al*. (n = 41) furthermore followed a group of daily disposable contact lenses wearers for 12 months, and found no change in meibomian gland atrophy at the 12-month visit compared to baseline when analyzing the group as a whole.[29] Uçakhan and Arslanturk-Eren (n = 190) and Gu *et al.* (n = 141) have since found a significant association between contact lens use and meibomian gland atrophy; however, these significant differences were not clinically meaningful.[30, 31] These data overall suggest that while there is a chance that contact lenses may negatively impact meibomian gland structure, this impact is likely limited and if it does occur, it most likely just occurs during the initial years of contact lens use.

Summary

Meibomian gland atrophy and dysfunction in general are common and are the primary source of dry eye disease.[32] With non-obvious meibomian gland dysfunction being common in both adults and children, eye care professionals should regularly be screening for meibomian gland function and morphology to catch any issues before they precipitate into significant damage and highly bothersome symptoms. While there is data suggesting that contact lens use may stress the meibomian glands, contact lens wear itself is unlikely to directly damage and promote progressive meibomian gland atrophy. All of these data together indicate that while contact lenses may have a minimal impact on meibomian gland morphology, these patients should be closely monitored, because contact lenses may stress the ocular surface, impede meibomian gland function, and eventually result in contact lens intolerance if the ocular surface is not treated appropriately in a timely manner.

REFERENCES

1. Molinari JF, Tapie R. Color photography of meibomian glands. *Am J Optom Physiol Opt* 1982;59:758-759.
2. Tomlinson A, Bron AJ, Korb DR, *et al*. The international workshop on meibomian gland dysfunction: report of the diagnosis subcommittee. *Investig Ophthalmol Vis Sci* 2011;52:2006-2049.
3. Wise RJ, Sobel RK, Allen RC. Meibography: A review of techniques and technologies. *Saudi J Ophthalmol* 2012;26:349-356.
4. Srinivasan S, Menzies K, Sorbara L, Jones L. Infrared imaging of meibomian gland structure using a novel keratograph. *Optom Vis Sci* 2012;89:788-794.
5. Pucker AD, Jones-Jordan LA, Li W, *et al*. Associations with Meibomian Gland Atrophy in Daily Contact Lens Wearers. *Optom Vis Sci* 2015;92:e206-213.
6. Arita R, Itoh K, Inoue K, Amano S. Noncontact infrared meibography to document age-related changes of the meibomian glands in a normal population. *Ophthalmology* 2008;115:911-915.
7. Pult H, Riede-Pult B. Comparison of subjective grading and objective assessment in meibography. *Cont Lens Anterior Eye* 2013;36:22-27.
8. Ngo W, Srinivasan S, Schulze M, Jones L. Repeatability of grading meibomian gland dropout using two infrared systems. *Optom Vis Sci* 2014;91:658-667.
9. Pult H, Riede-Pult BH, Nichols JJ. Relation between upper and lower lids' meibomian gland morphology, tear film, and dry eye. *Optom Vis Sci* 2012;89:E310-315.
10. Arita R, Suehiro J, Haraguchi T, *et al*. Topical diquafosol for patients with obstructive meibomian gland dysfunction. *Br J Ophthalmol* 2013;97:725-729.
11. 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.
12. Hura AS, Epitropoulos AT, Czyz CN, Rosenberg ED. Visible Meibomian Gland Structure Increases After Vectored Thermal Pulsation Treatment in Dry Eye Disease Patients with Meibomian Gland Dysfunction. *Clin Ophthalmol* 2020;14:4287-4296.
13. Arita R, Itoh K, Maeda S, *et al*. Meibomian gland duct distortion in patients with perennial allergic conjunctivitis. *Cornea* 2010;29:858-860.
14. Pucker AD, Jones-Jordan LA, Marx S, *et al*. Clinical factors associated with contact lens dropout. *Cont Lens Anterior Eye* 2019;42:318-324.
15. Daniel E, Maguire MG, Pistilli M, *et al*. Grading and baseline characteristics of meibomian glands in meibography images and their clinical associations in the Dry Eye Assessment and Management (DREAM) study. *Ocul Surf* 2019; 17:491-501.
16. Tichenor AA, Ziemanski JF, Ngo W, Nichols JJ, Nichols KK. Tear Film and Meibomian Gland Characteristics in Adolescents. *Cornea* 2019;38:1475-1482.
17. Wu Y, Li H, Tang Y, Yan X. Morphological Evaluation of Meibomian Glands in Children and Adolescents Using Noncontact Infrared Meibography. *J Pediatr Ophthalmol Strabismus* 2017;54:78-83.
18. Rojas-Carabali W, Uribe-Reina P, Munoz-Ortiz J, *et al*. High Prevalence of Abnormal Ocular Surface Tests in a Healthy Pediatric Population. *Clin Ophthalmol* 2020;14:3427-3438.
19. Obata H. Anatomy and histopathology of human meibomian gland. *Cornea* 2002;21:S70-74.
20. Korb DR, Henriquez AS. Meibomian gland dysfunction and contact lens intolerance. *American Optometric Association* 1980;51:243-251.
21. Blackie CA, Korb DR, Knop E, Bedi R, Knop N, Holland EJ. Nonobvious obstructive meibomian gland dysfunction. *Cornea* 2010;29:1333-1345.
22. Donthineni PR, Das AV, Basu S. Dry eye disease in children and adolescents in India. *Ocul Surf* 2020;18:777-782.
23. Titiyal JS, Falera RC, Kaur M, Sharma V, Sharma N. Prevalence and risk factors of dry eye disease in North India: Ocular surface disease index-based cross-sectional hospital study. *Indian J Ophthalmol* 2018;66:207-211.
24. Zhang Y, Chen H, Wu X. Prevalence and risk factors associated with dry eye syndrome among senior high school students in a county of Shandong Province, China. *Ophthalmic Epidemiol* 2012;19:226-230.
25. Arita R, Itoh K, Inoue K, Kuchiba A, Yamaguchi T, Amano S. Contact lens wear is associated with decrease of meibomian glands. *Ophthalmology* 2009;116:379-384.
26. Alghamdi WM, Markoulli M, Holden BA, Papas EB. Impact of duration of contact lens wear on the structure and function of the

meibomian glands. *Ophthalmic Physiol Opt* 2016;36:120-131.

27. Machalinska A, Zakrzewska A, Adamek B, *et al.* Comparison of Morphological and Functional Meibomian Gland Characteristics Between Daily Contact Lens Wearers and Nonwearers. *Cornea* 2015;34:1098-1104.
28. Pucker AD, Jones-Jordan LA, Marx S, *et al*. Clinical factors associated with contact lens dropout. *Cont Lens Anterior Eye* 2019;42:318-324.
29. Llorens-Quintana C, Garaszczuk IK, Szczesna-Iskander DH. Meibomian glands structure in daily disposable soft contact lens wearers: a one-year follow-up study. *Ophthalmic Physiol Opt* 2020;40:607-616.
30. Ucakhan O, Arslanturk-Eren M. The Role of Soft Contact Lens Wear on Meibomian Gland Morphology and Function. *Eye Contact Lens* 2018.
31. Gu T, Du B, Bi H, *et al*. Meibomian Gland Dropout, not Distortion, Can Distinguish Dry Eyes from Normal Eyes in Contact Lens Wearers. *Curr Eye Res* 2020;45:897-903.
32. Nichols KK, Foulks GN, Bron AJ, *et al*. The international workshop on meibomian gland dysfunction: executive summary. Investig *Ophthalmol Vis Sci* 2011;52:1922-1929.