Dry Eye Disease: Clinical Pearls and Practical Applications of New Technologies

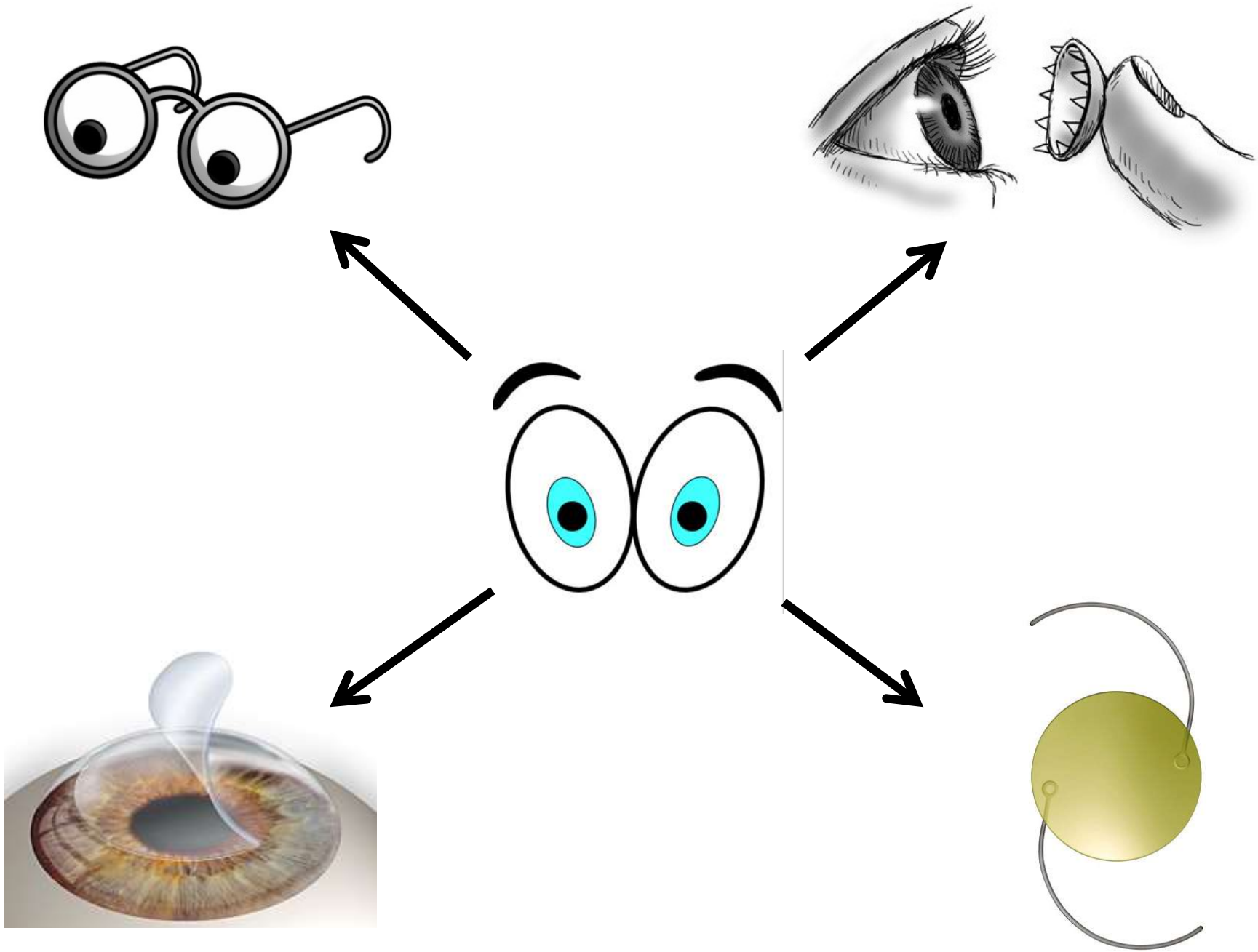
Mile Brujic, OD, FAAO

Disclosure

Unfortunately, the speaker has no financial or proprietary interest in any of the products that are mentioned

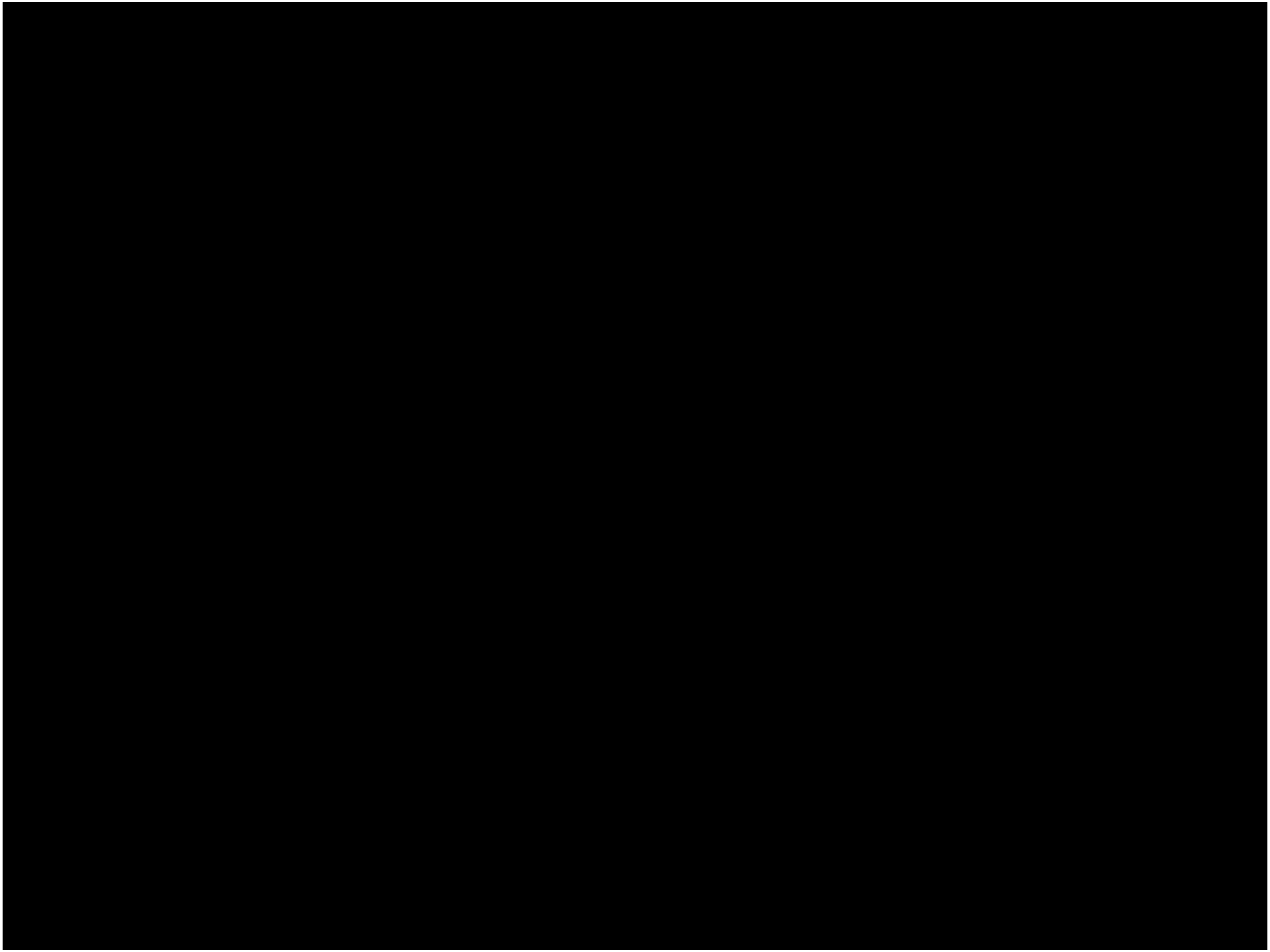
Co-Owner Optometric Insights with Dr. Dave Kading

I have received honoraria in the past 2 years for speaking, writing, participating in an advisory capacity or research from: ABB Optical, Akorn, Alcon Laboratories, Allergan, Art Optical, Bausch + Lomb Health, Contamac, CooperVision, CSEye, Euclid, Eyevance, Johnson & Johnson Vision Care, Luneau, Novartis, Oculus, Optovue, Sight Sciences, Sun Pharma, Tangible Science, TelScreen, Thea, TruForm Optics, Valley Contax, Visionary Optics, VMax Vision, Walman Optical, Weave, Zeiss and ZeaVision

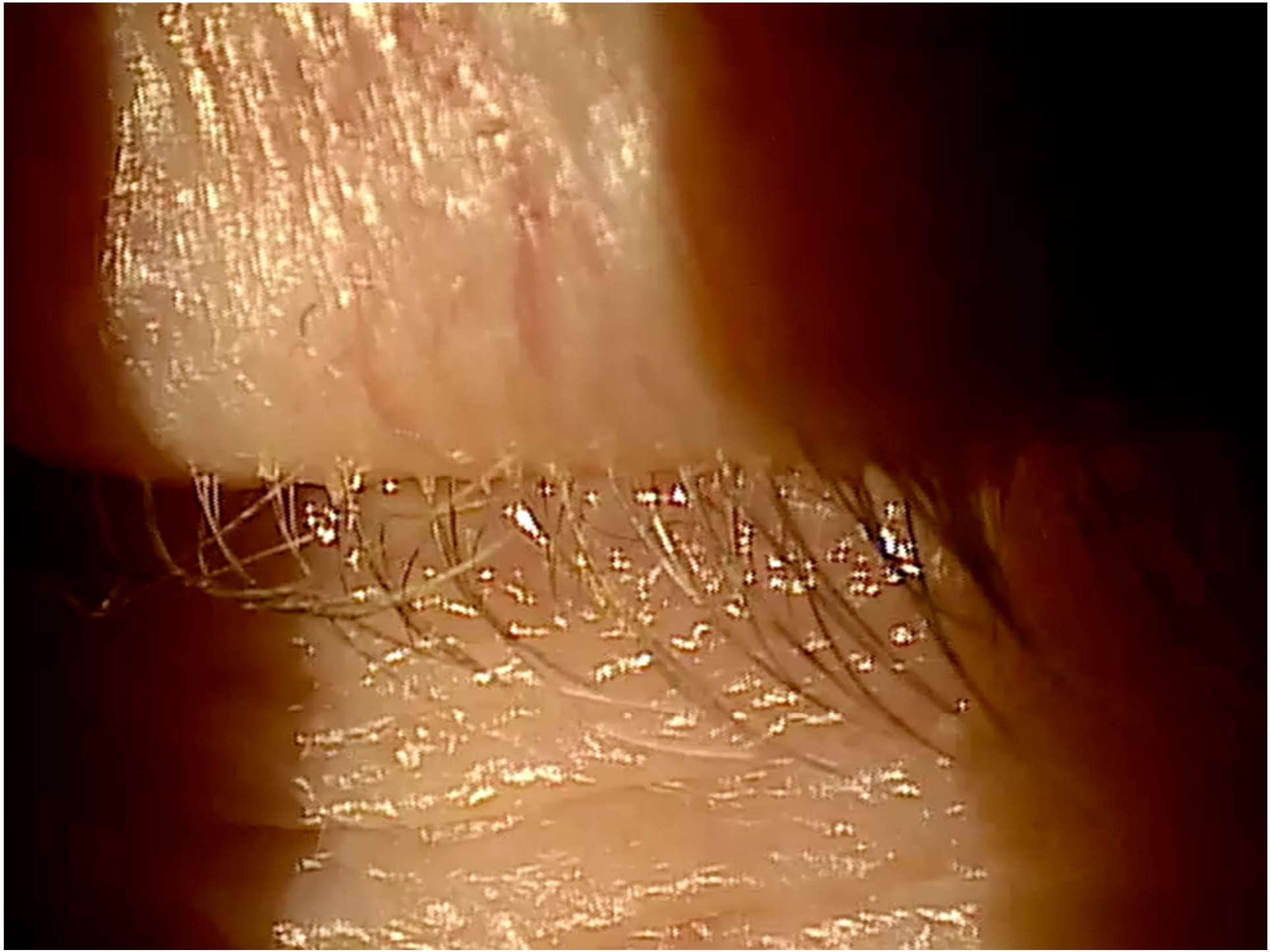


www.tearfilm.org

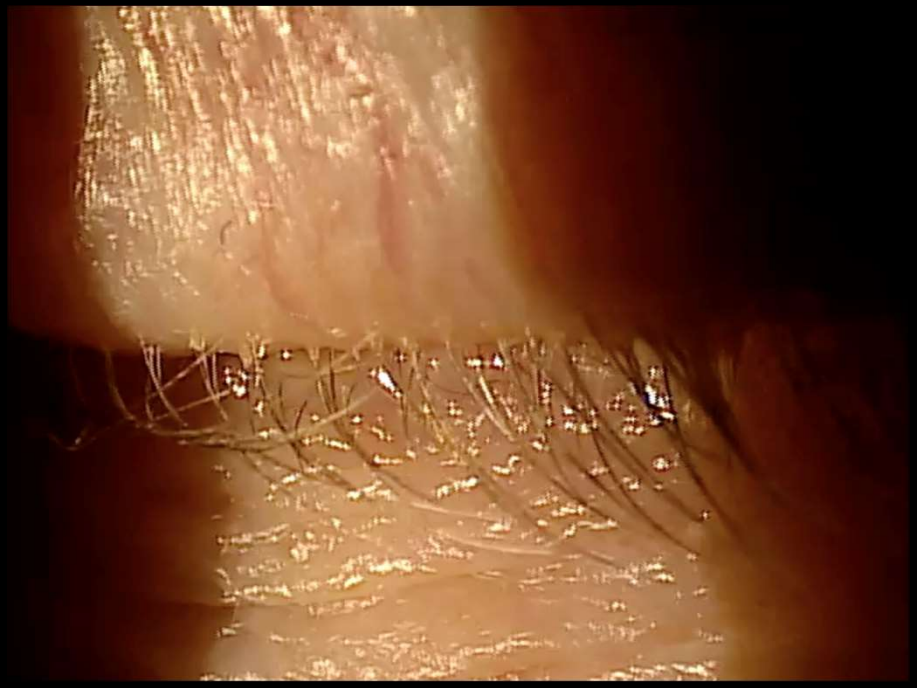
1) DEWS Report (2007)
2) DEWS II Report (2017)
3) International Workshop on Meibomian Gland Dysfunction
4) International Workshop on Contact Lens Discomfort



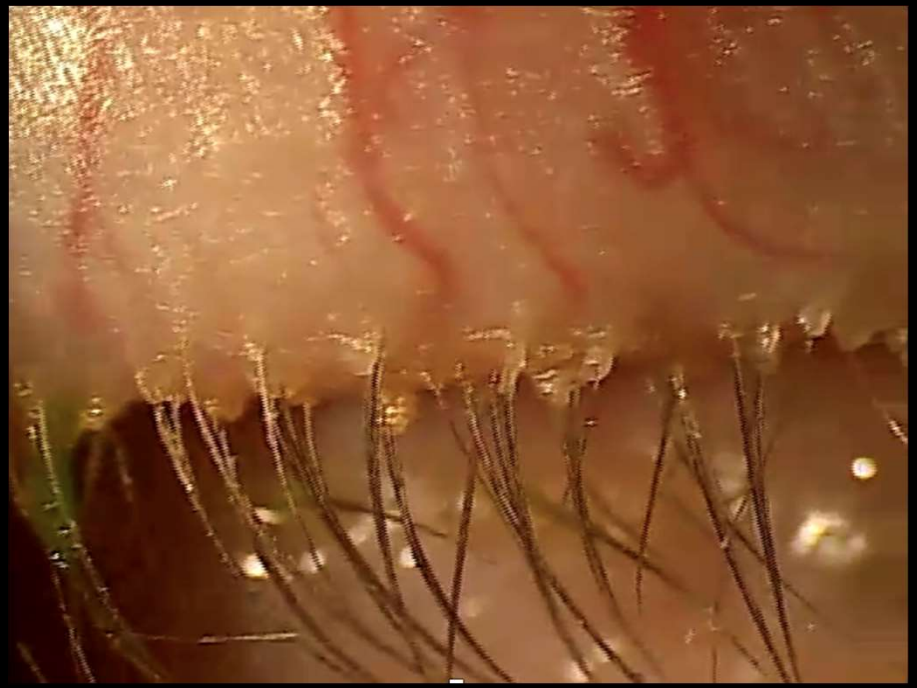
Diagnosis



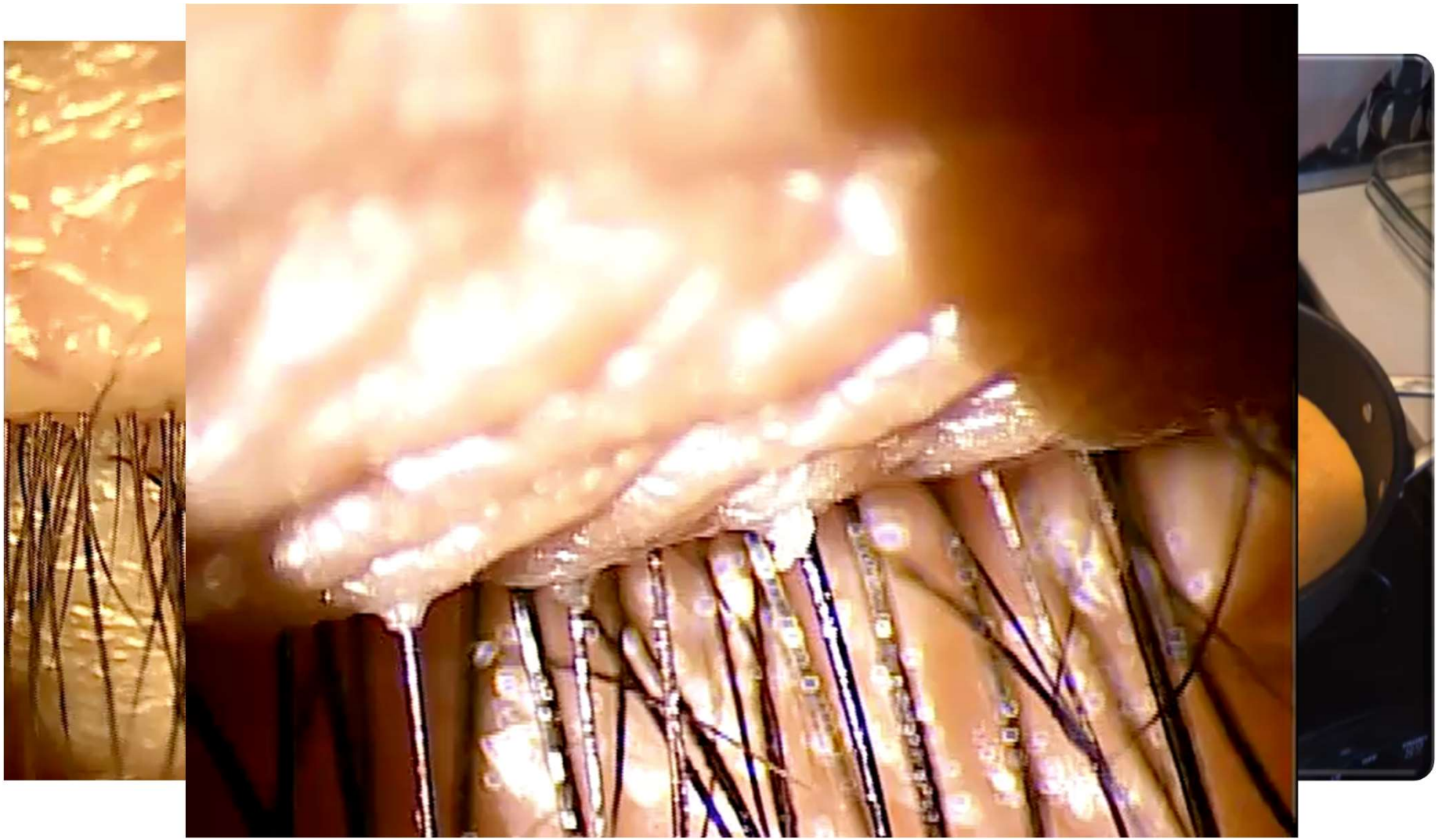
Collarettes at base of lashes



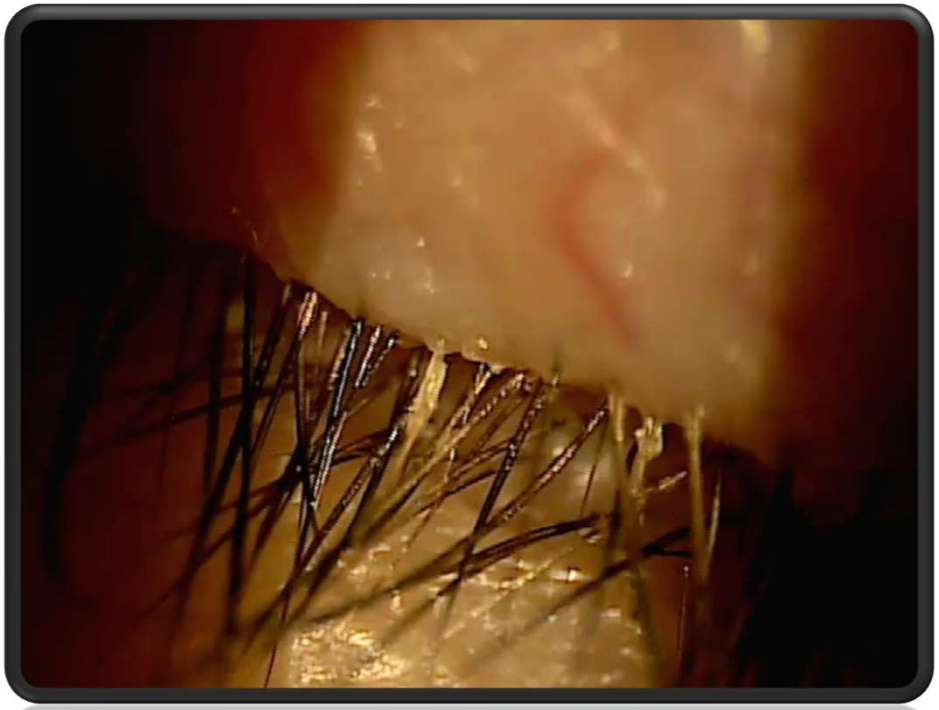
Low Mag



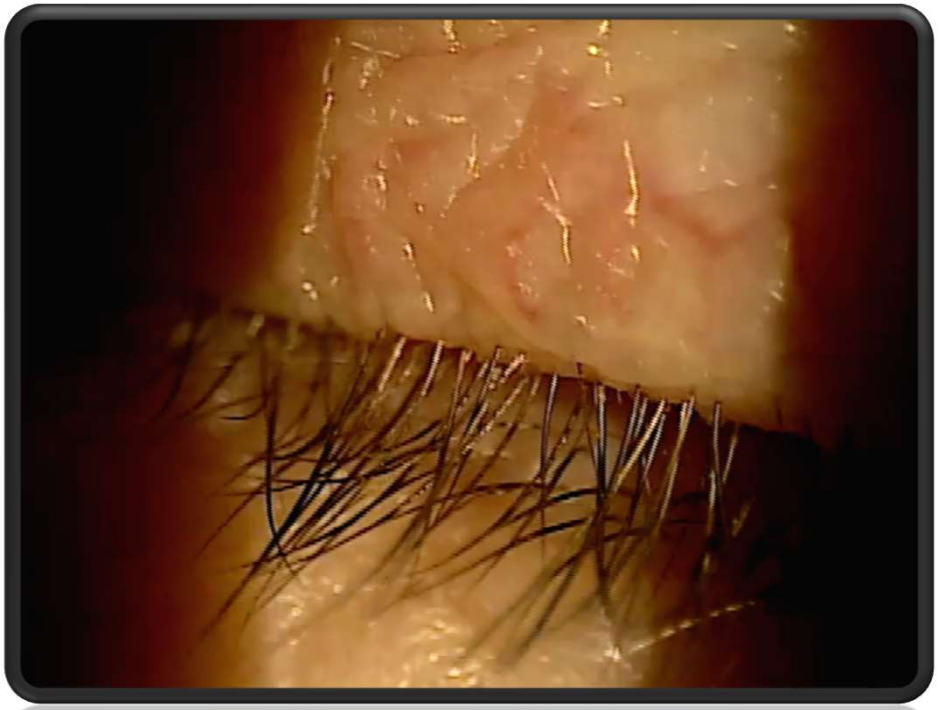
High



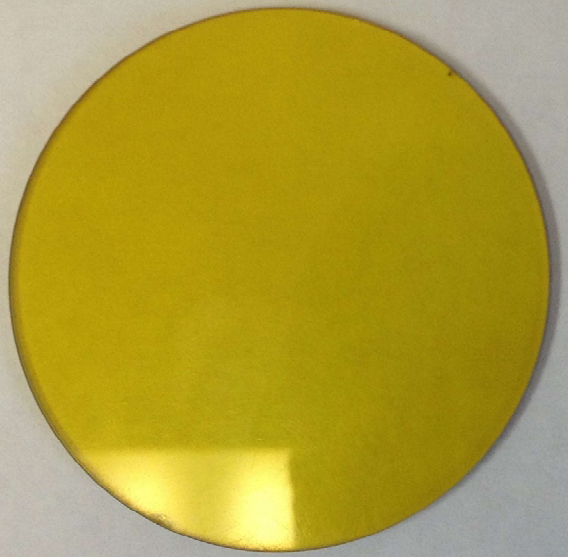
Before Treatment



After Treatment



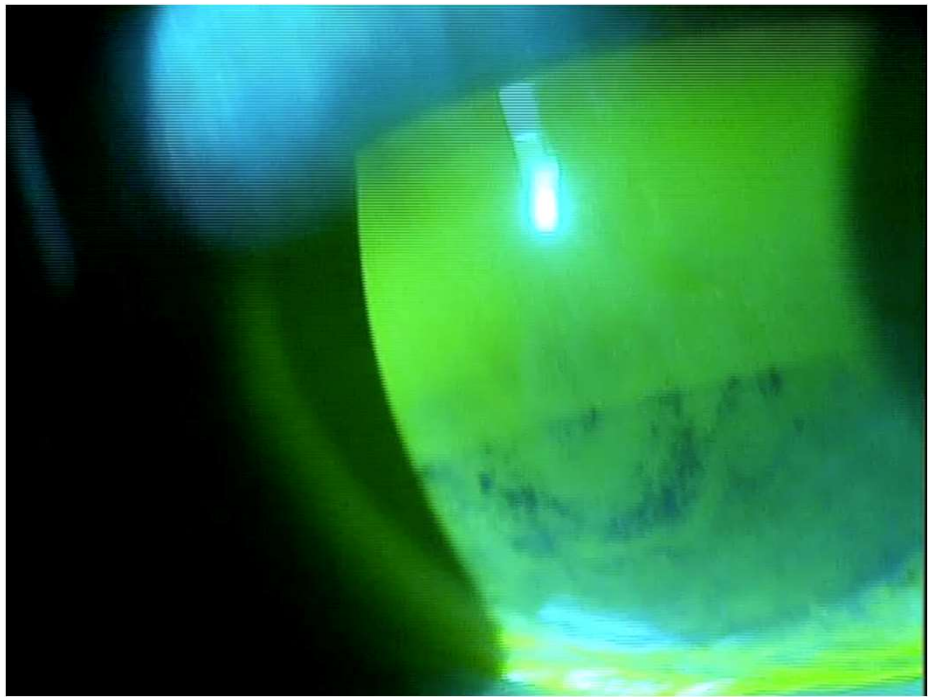
Wratten #12 filter

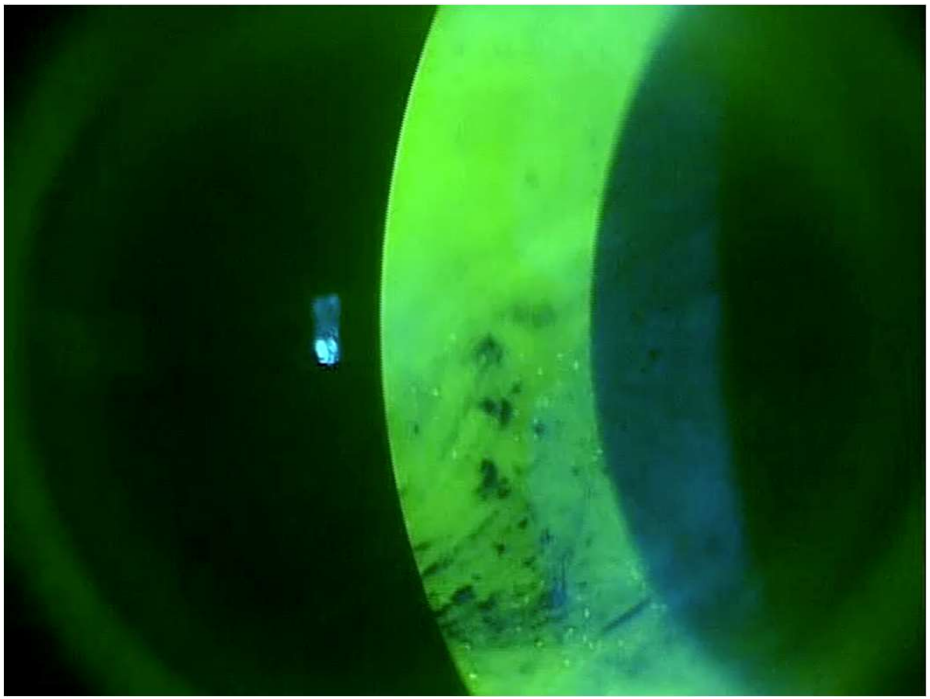


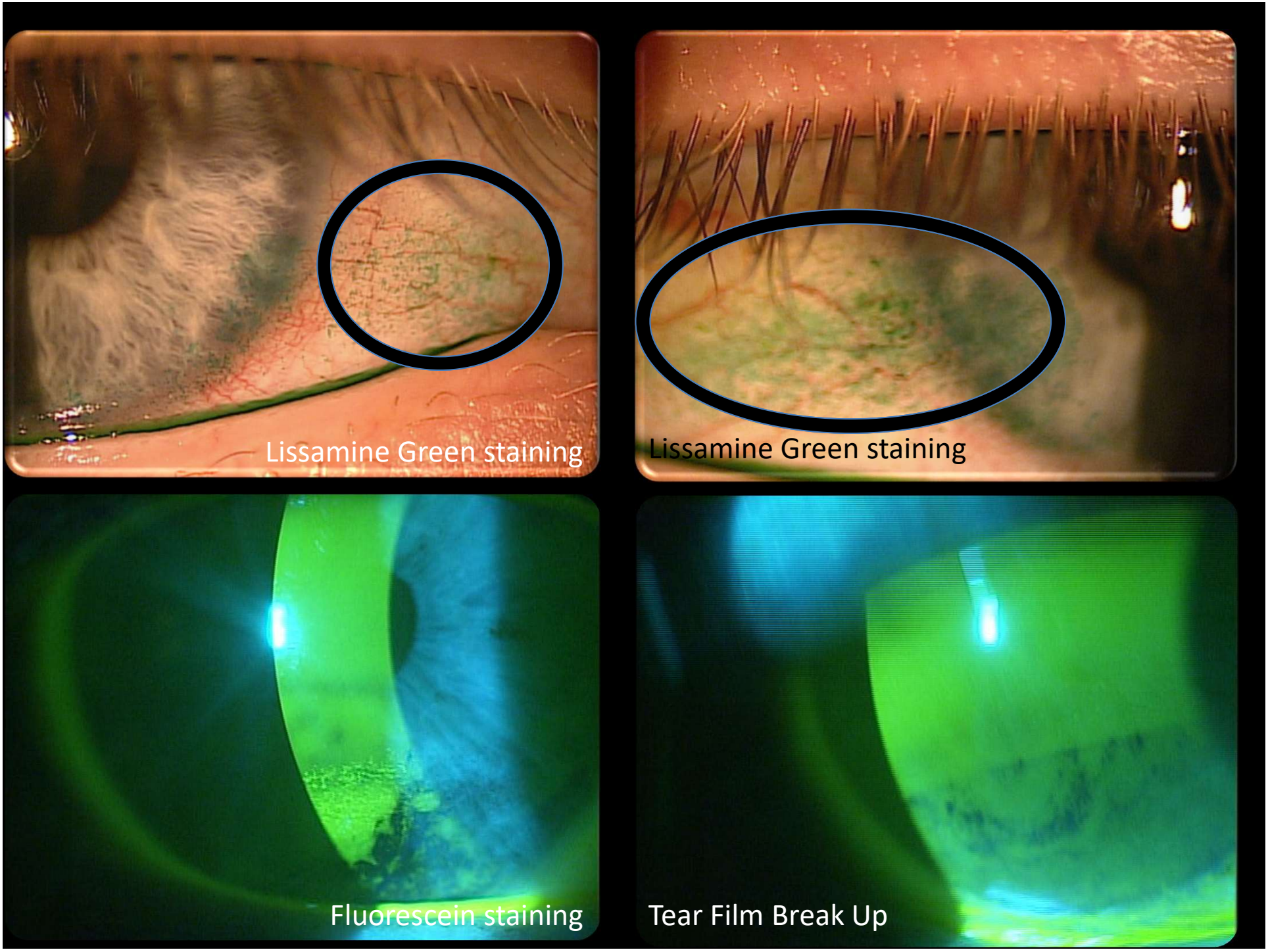
Fluorescein strip

TBUT – Normal range
(best viewed with fluorescein)

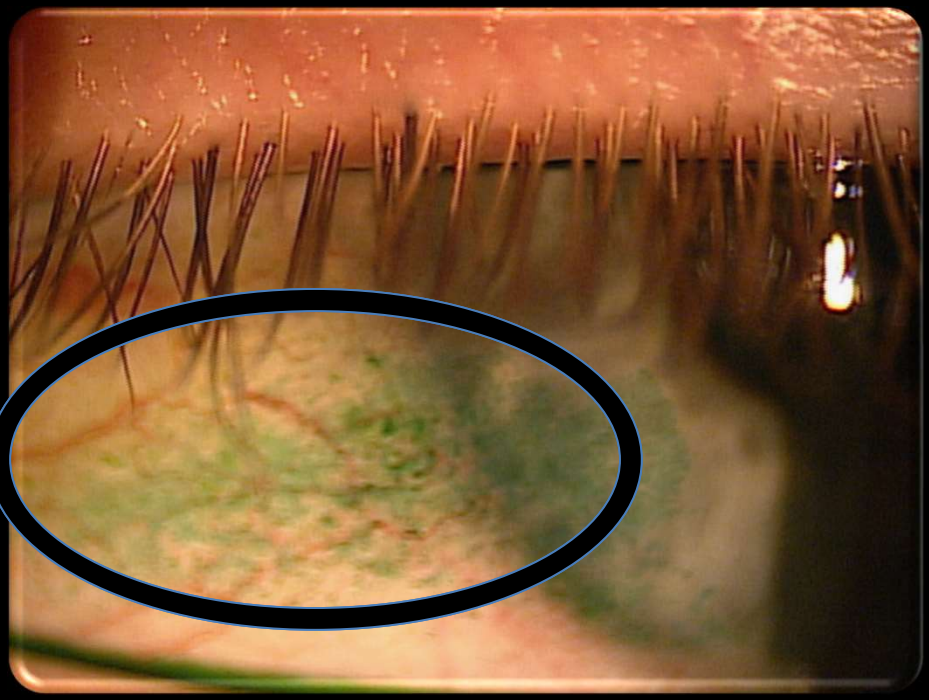
> 10 seconds



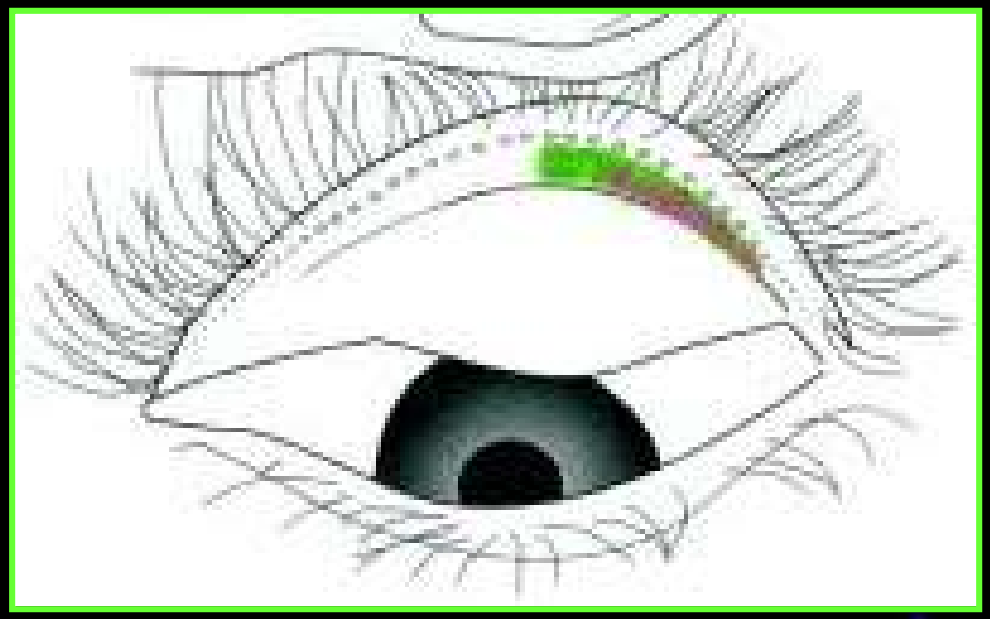


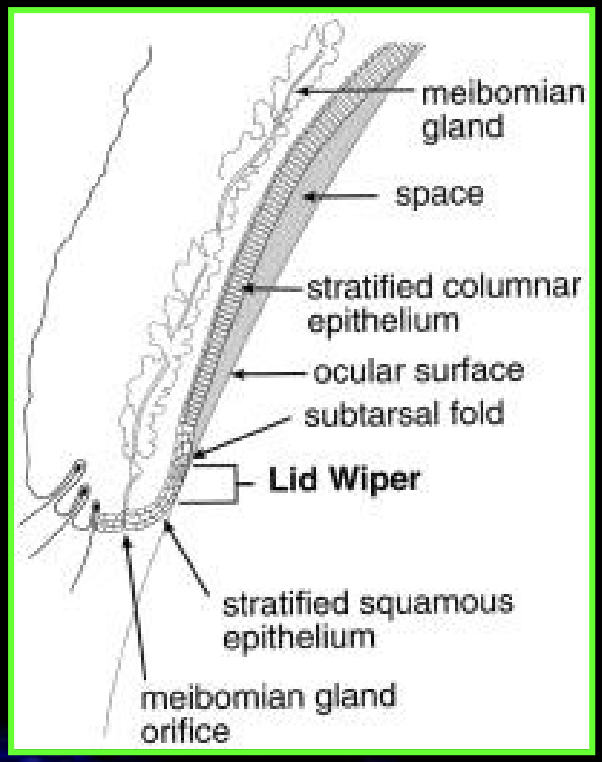

Lissamine Green staining
Lissamine Green staining
Fluorescein staining
Tear Film Break Up

Lissamine green is viewed best at low light levels



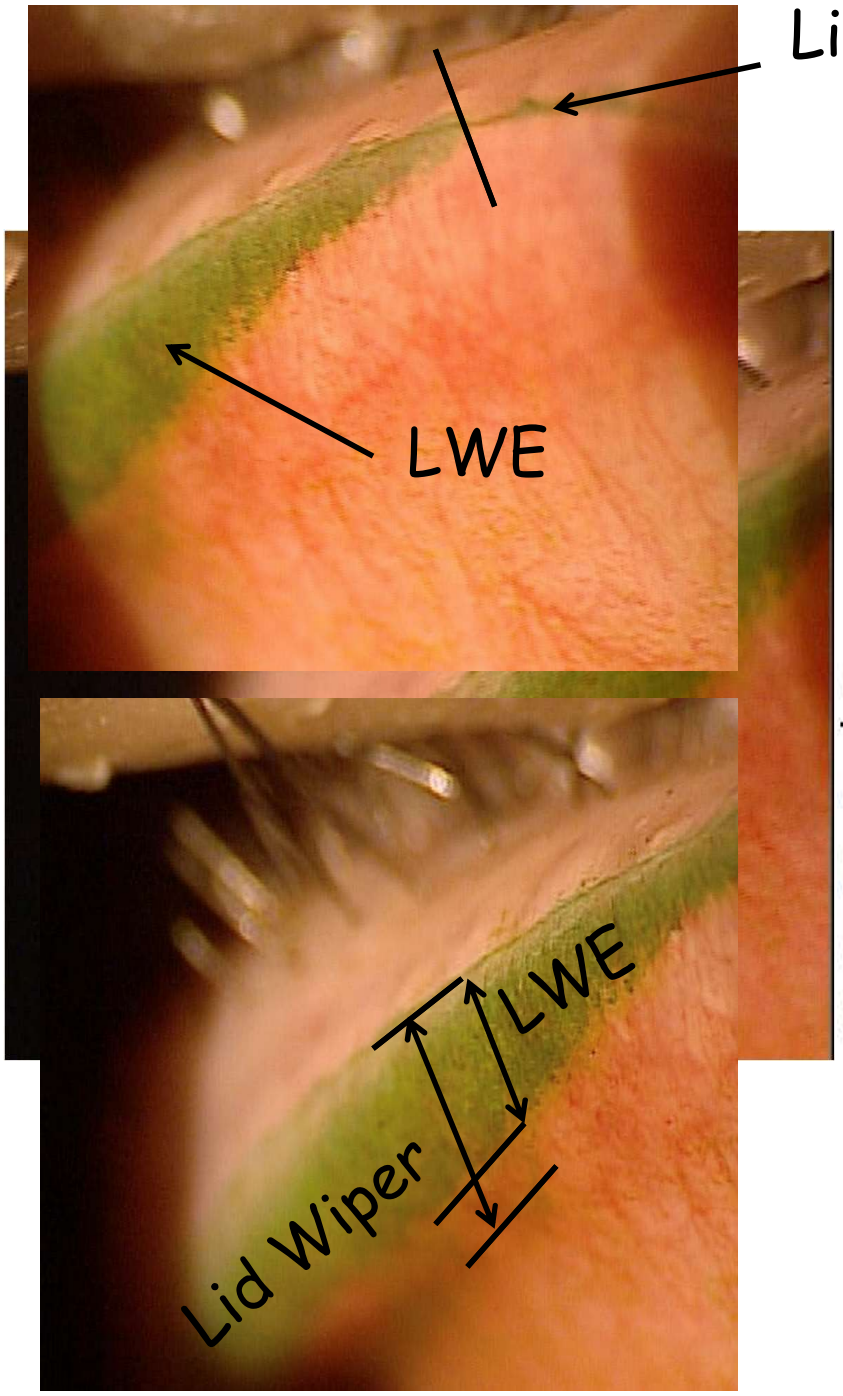
Lid Wiper Epitheliopathy





80% of symptomatic CL wearers

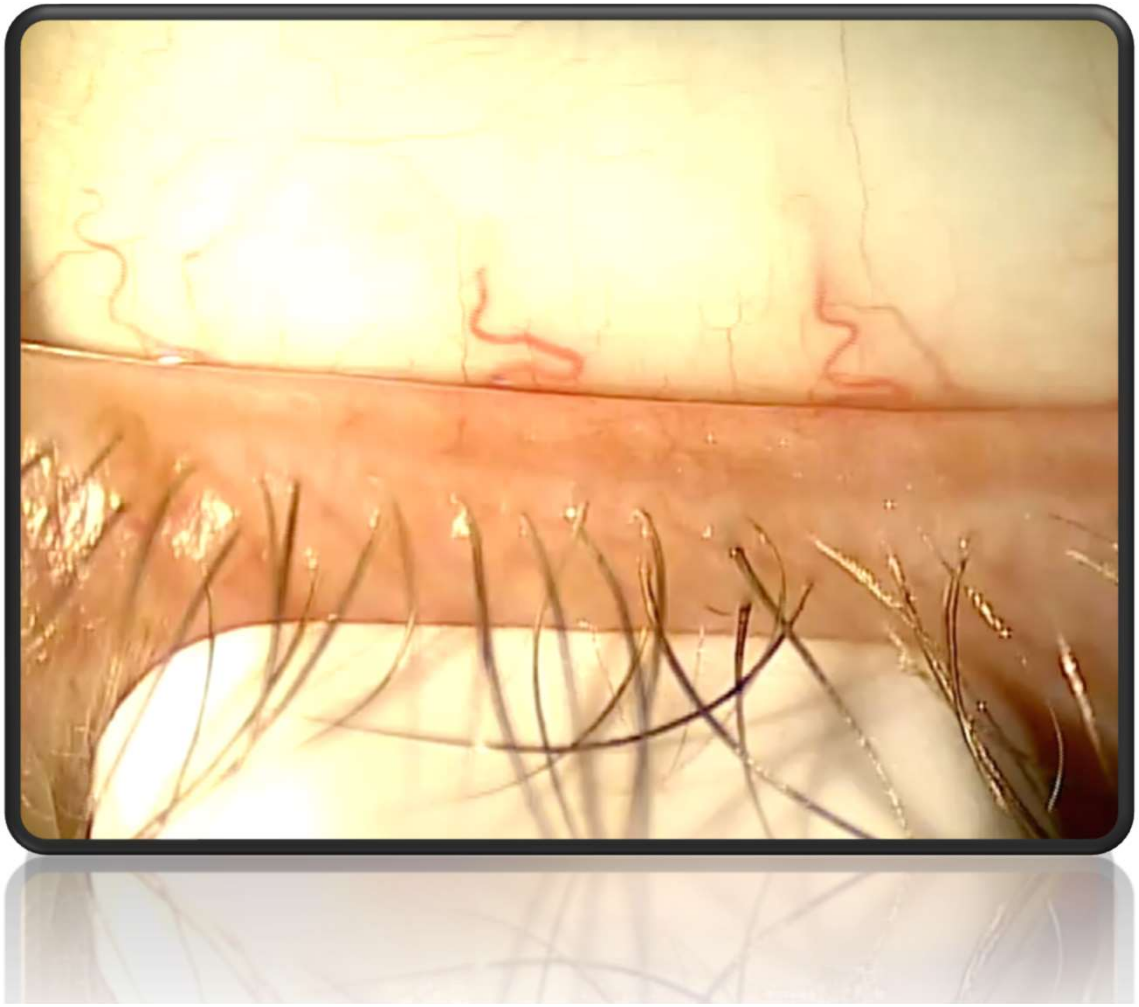
13% of asymptomatic CL wearers

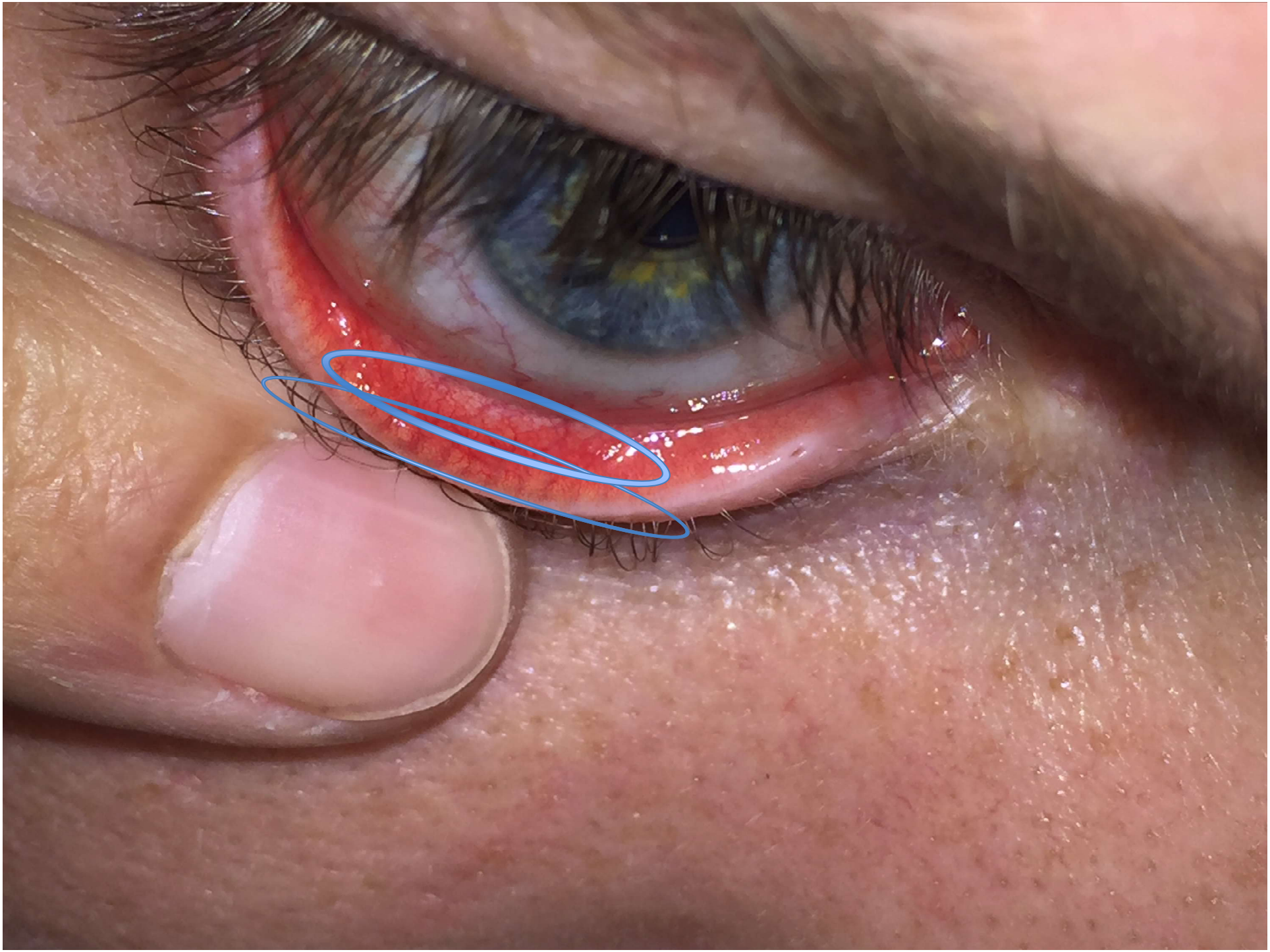


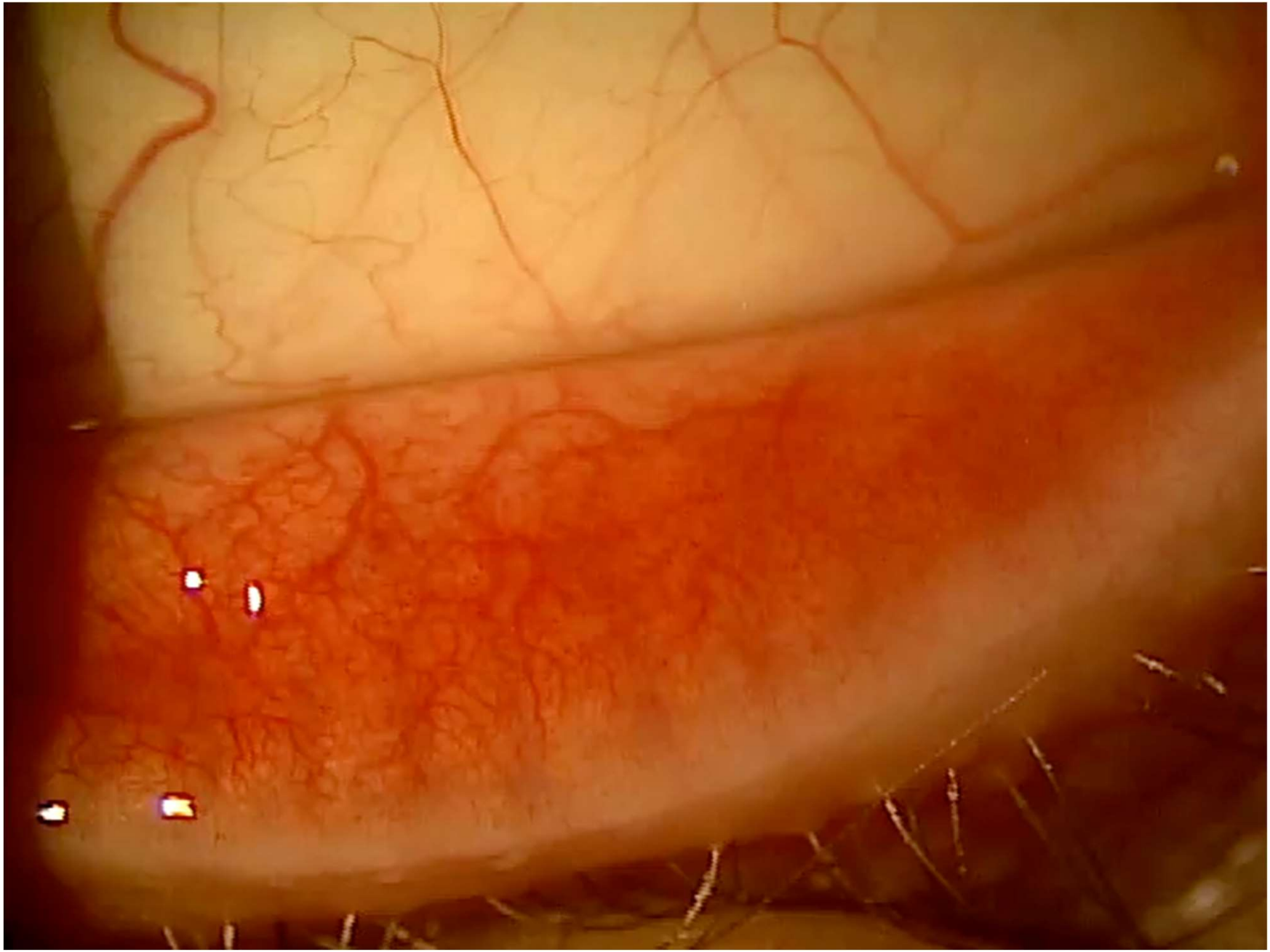
Horizontal length of staining	Grade
<2 mm	0
2-4 mm	1
5-9 mm	2
>10 mm	3

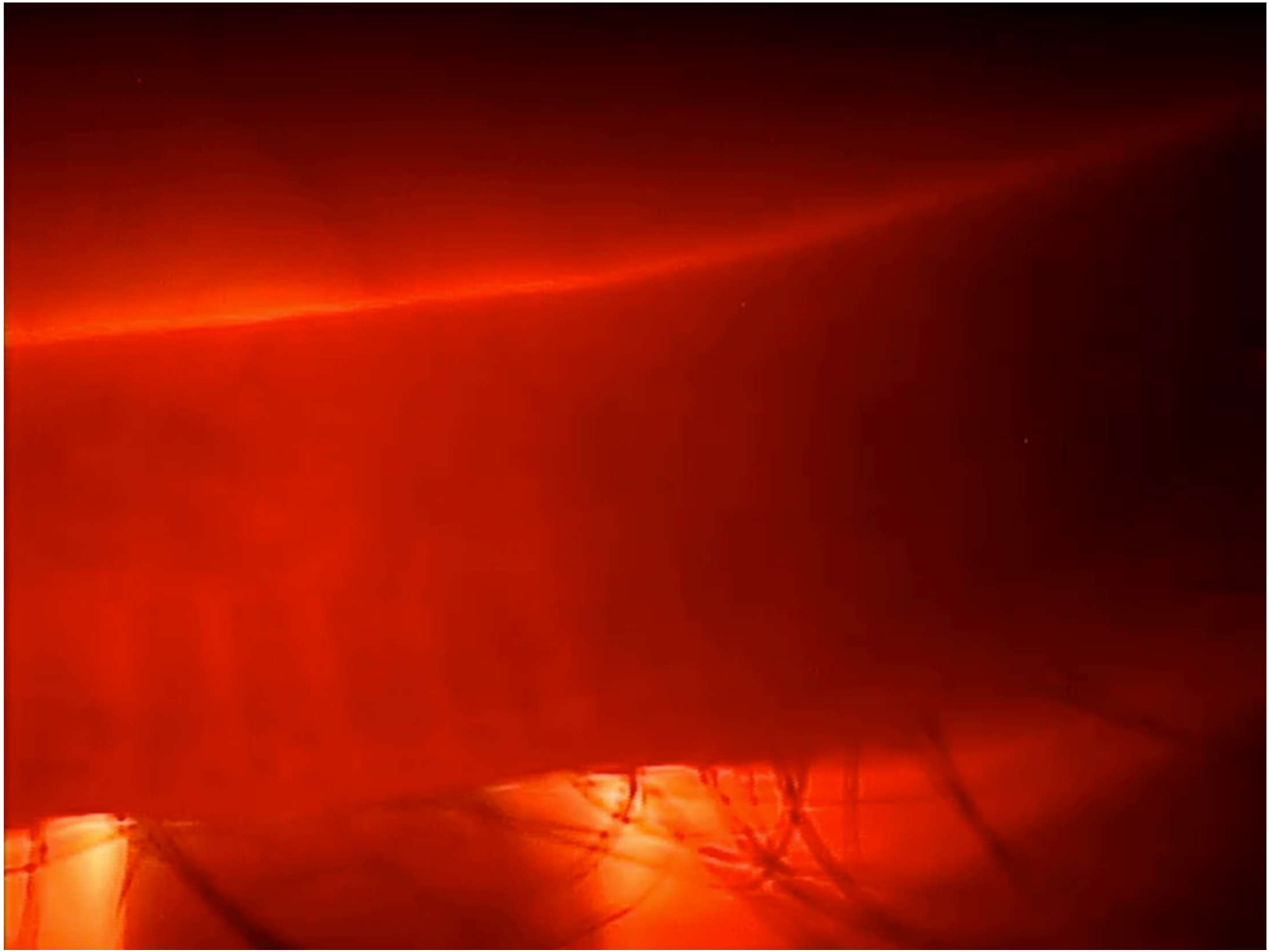
Sagittal width of staining	Grade
<25% of the width of wiper	0
25%-<50% of the width of wiper	1
50%-<75% of the width of wiper	2
≥75% of the width of wiper	3

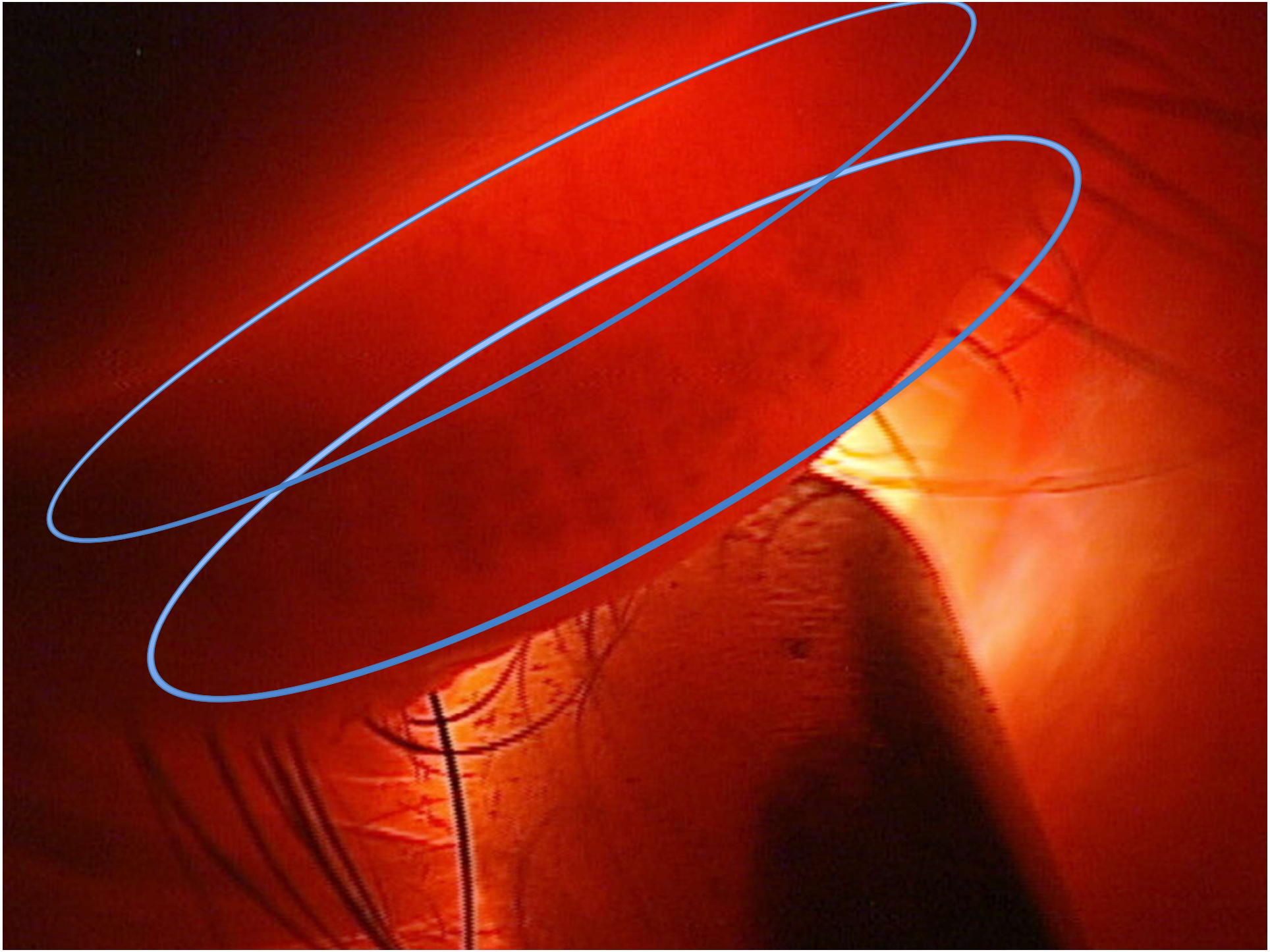
Most common form of MGD – Non obvious



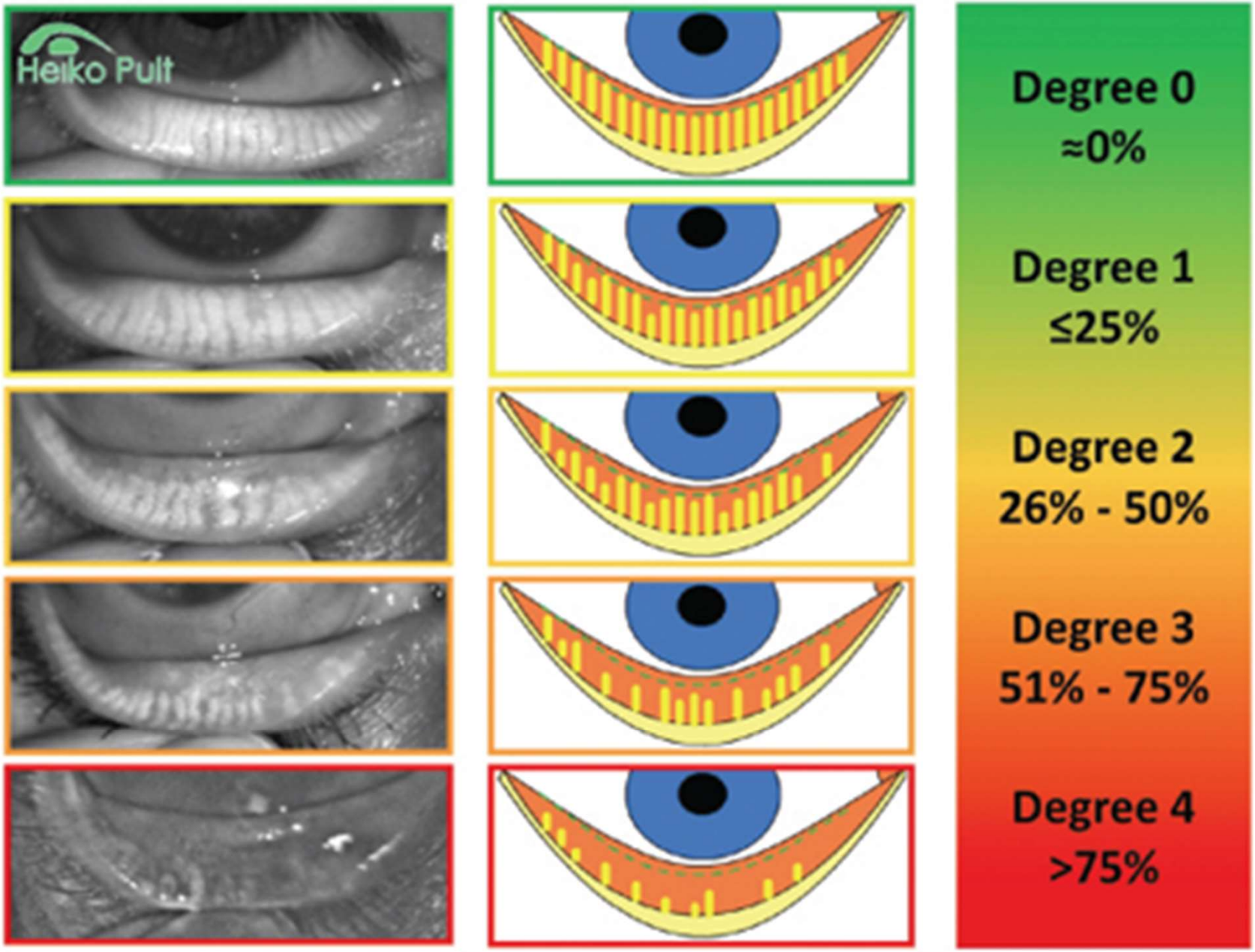


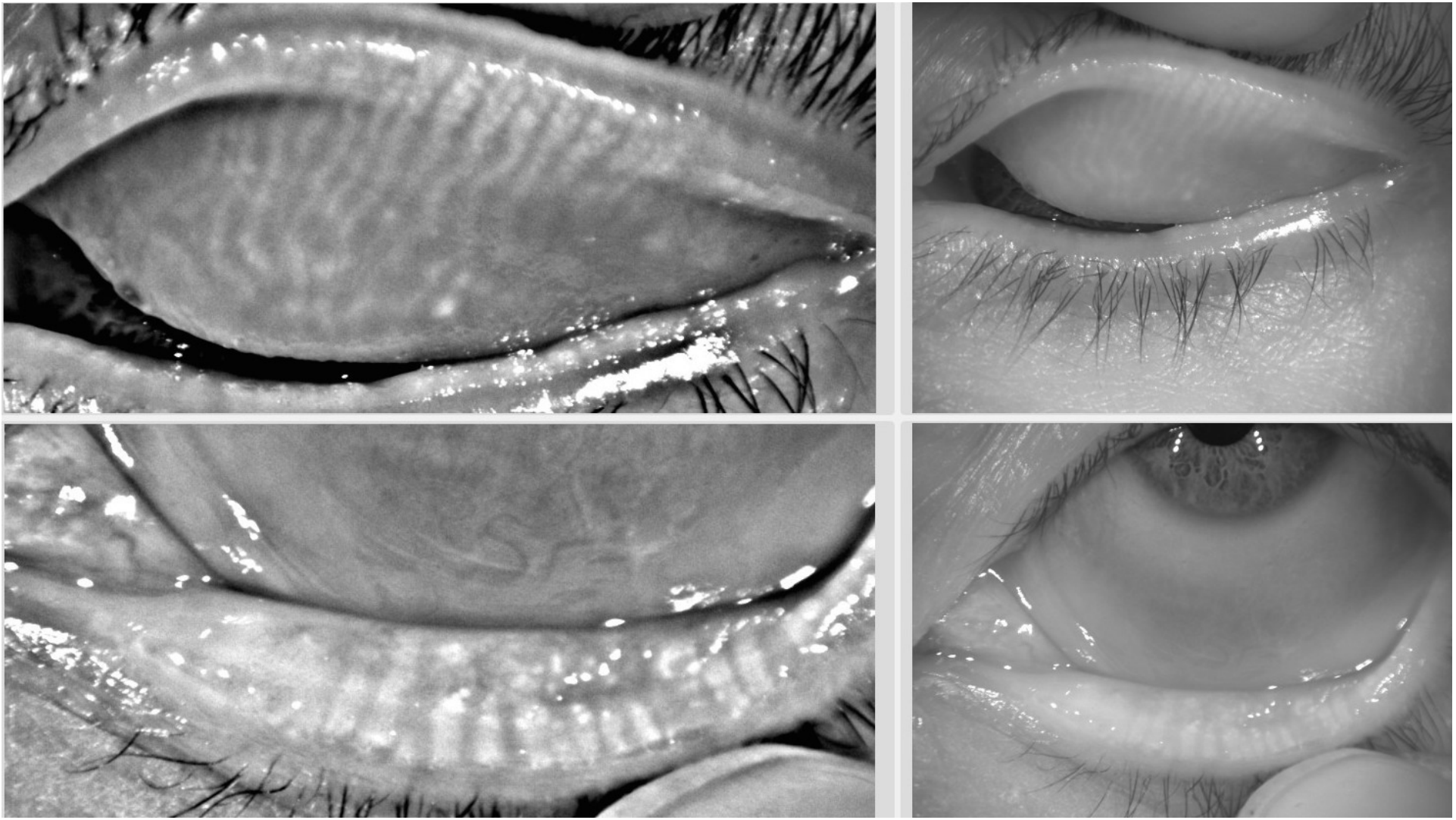






Meiboscale





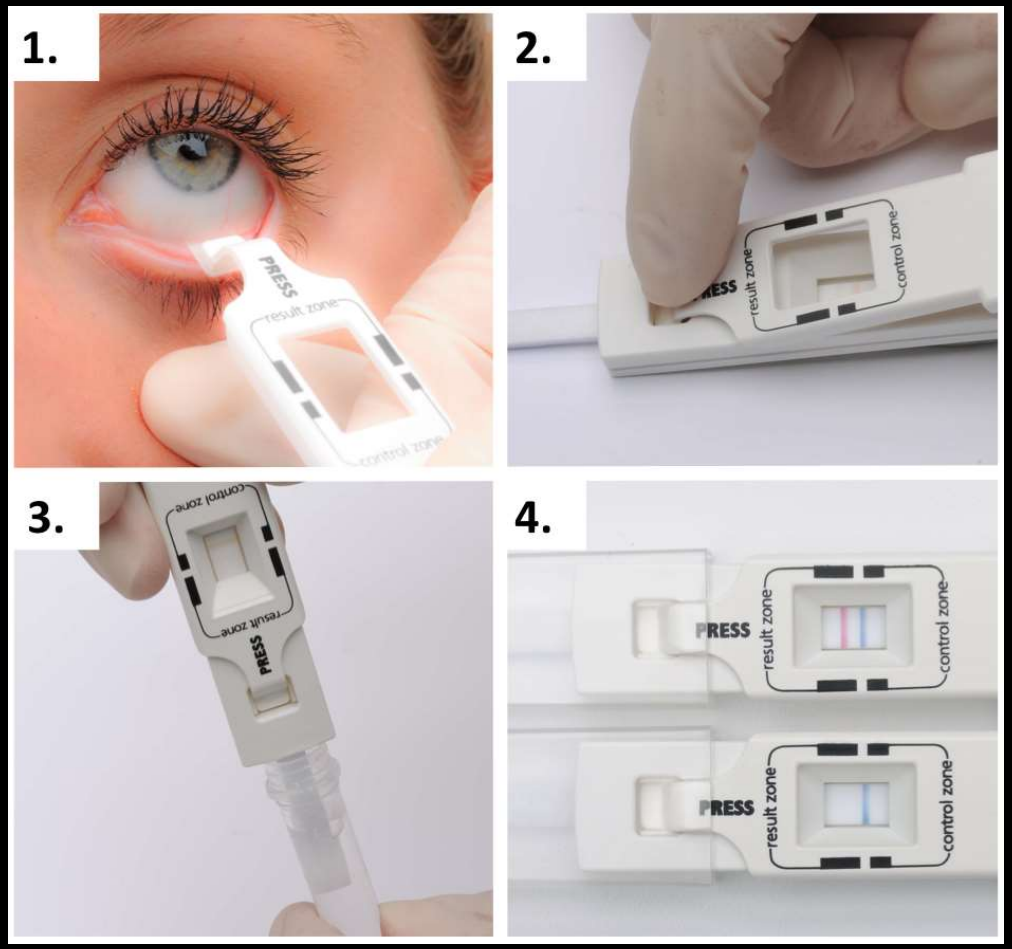
Images compliments of Dave Kading, OD, FAAO

InflammaDry

- Detects elevated levels of MMP-9 in tear fluid
- Rapid – 10 minute results
- Easy to use – can be performed by a nurse or technician
- In-office (point of care) test
- Low cost – no additional equipment required
- One time use – disposable
- Accurate – high sensitivity and specificity

InflammaDry is CE Marked and commercially available in Europe. At this time InflammaDry is pending 510(k) review by FDA and is not commercially available in the U.S.

How to Use InflammaDry: Four-step Process



1. Gently dab the Sample Collector in 6-8 locations on the palpebral conjunctiva (lower eyelid) to collect a tear sample. Do not use a dragging motion.
2. Snap the sample collector into the test cassette and press firmly where indicated.
3. Dip the test cassette into the provided buffer vial for 20 seconds. Replace the cap.
4. Read the results: 2 lines (1 **red**, 1 **blue**) = positive, 1 line (**blue**) = negative

Making Matrix Metalloproteinase-9 Levels More Meaningful

Mile Brujic, OD, FAAO, David Kading, OD, FAAO

Introduction

Dry eye, and more broadly ocular surface disease, is a complex yet intriguing condition. In this condition, we know that there are a number of changes that occur to the glands. These changes affect the quality of tears as well as cause chronic changes to occur to the ocular surface that the tear film supports. These micro-environmental changes can affect both comfort and visual quality of both contact lens and also non-contact lens wearers.

There are several inflammatory markers that are increased in the tear film of approximately 50% of dry eye patients. Chotikavanich et al showed that MMP-9 levels increase with increasing severity of dry eye disease.[1] A new point of care diagnostic technology that detects an elevation of matrix metalloproteinase-9 (MMP-9) in the tear film is becoming an increasingly utilized test in eye care practice to help manage routine dry eye patients and contact lens wearers experiencing discomfort with their lenses.

It is a qualitative test that exhibits a red result line indicative of a positive result when the MMP-9 concentration in the tears is 40 ng/mL or higher. Although this gives us important qualitative information on the concentration of MMP-9 in the tear film, the signal strength of the red result line is directly proportional to the concentration of MMP-9 in the tears and can be used to estimate the relative amount of MMP-9 present. We have seen this clinically and we use it as a gauge of how our treatment is influencing the MMP-9 levels.

While the test cannot quantitate the exact level of MMP-9 in the tear film, this poster proposes a semi-quantitative method of grading the intensity of the Inflamma Dry test result line signal to assist clinicians in monitoring the success or failure of treatments with their patients.

Methods

Contrived samples of differing concentrations of MMP-9 were created and tested using the Inflamma Dry test to produce positive results of varying strengths. The following concentrations of MMP-9 were tested:

8 ng/mL
34 ng/mL
66 ng/mL
101 ng/mL
381 ng/mL

Based on the varied intensities of the result lines, a proposed signal strength classification was developed.

Results

The test result signal intensity was found to increase proportionally to the increasing concentration of MMP-9 present in the sample. This linear relationship allows for the grading of the signal strength. A proposed signal strength classification was developed into one of five categories:

Negative (8 ng/mL)– no red result line is present and the level of MMP-9 is below 40ng/mL

Trace positive (34 ng/mL)– the red result line is just detectable. This is at the lower limit of the Inflamma Dry test.

Weak positive (66 ng/mL)– the red result line is a faint signal but stronger than the trace positive classification

Positive (101 ng/mL)– this red result line is relatively solid and easily visible

Strong positive (381 ng/mL)– this red result line is a strong signal and may appear vibrant

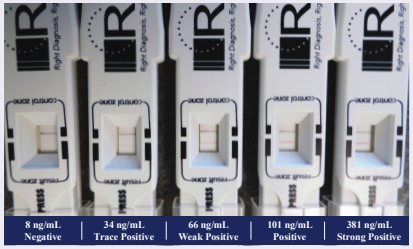


Figure 1.
Five Inflamma Dry tests showing the variation in responses of the red line when tested against various concentrations of MMP-9. From left to right, the concentration of MMP-9 that was used for the respective tests were: 8 ng/mL, 34 ng/mL, 66 ng/mL, 101 ng/mL and 381 ng/mL.

Discussion

Understanding the relative concentration of MMP-9 levels in the tear film facilitates a more robust understanding of the dry eye disease state as well as enhancing clinical decisions. Prior to this proposed classification system, the test simply provided a positive or negative result depending on whether the red result line was present or absent. This essentialy indicates the presence of either greater or less than 40 ng/mL of MMP-9 in the tears. Thus, if treating a patient for dry eye, improvements in MMP-9 measurements wouldn't be appreciated unless the levels went from a positive to a negative.

There may be improvements in MMP-9 levels during treatment that can be graded by the intensity of the red line result. Although this doesn't quantify the absolute concentration, it does provide perspective on an additional measure to follow over time to demonstrate the success or failure of treatment. The concentrations were placed right beside the categories proposed above as a gauge as to the approximate concentrations. Saying that, it is impossible to infer the concentration of MMP-9 to that level of accuracy based on the subjective grading scale presented here.

What was also interesting is that although the published minimum detected threshold of the Inflamma Dry test is 40 ng/mL, a trace positive was actually detected at 34 ng/mL. The approach of interpreting a semi-quantitative result arms the clinician with additional information. This classification system provides basic scientific assist to use the signal strength from a contemporary point of care test to guide the treatment of dry eye patients and those with contact lens comfort issues.

References

1. Chotikavanich S, de Paiva CS, Li de Q, et al. Invest Ophthalmol Vis Sci 2009; 50(7): 3203-3209.

Special Thanks

To RPS Diagnostic for providing support for this poster.

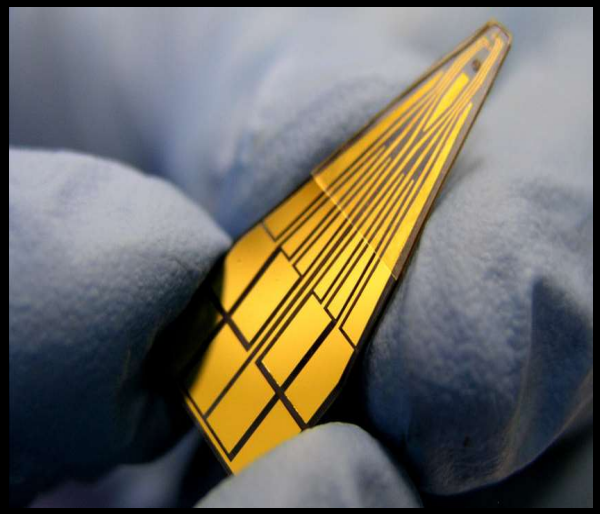
8 ng/mL Negative	34 ng/mL Trace Positive	66 ng/mL Weak Positive	101 ng/mL Positive	381 ng/mL Strong Positive

Signal Strength

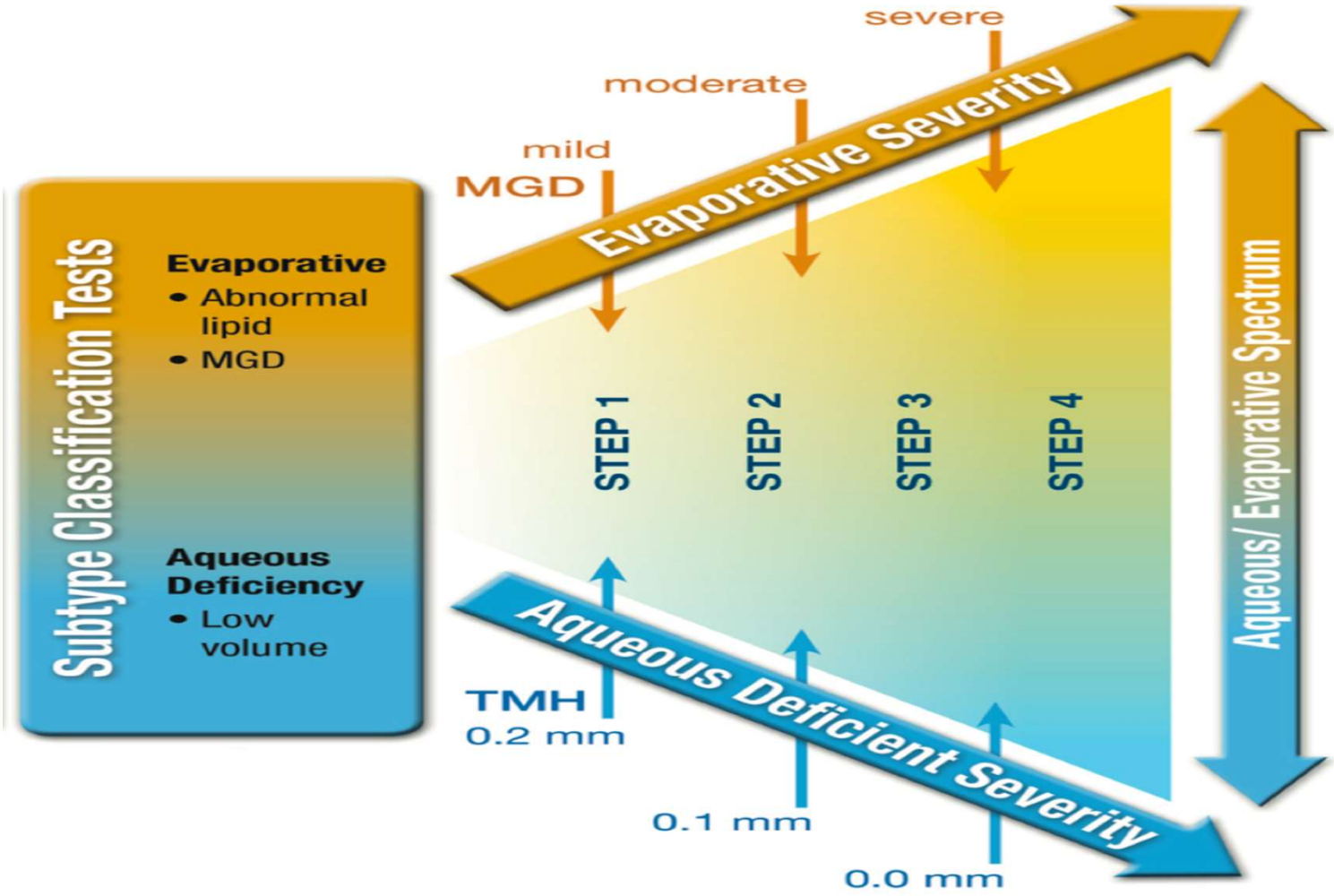
InflammaDry Clinical Trial

N = 206		Clinical Criteria	
		+	–
InflammaDry	+	121	4
	–	22	59
Sensitivity		**85%** (121/143)	
Specificity		**94%** (59/63)	
Overall Agreement		**87%** (180/206)	

307
Ready
11:22:56 AM
mOsms/L
OK



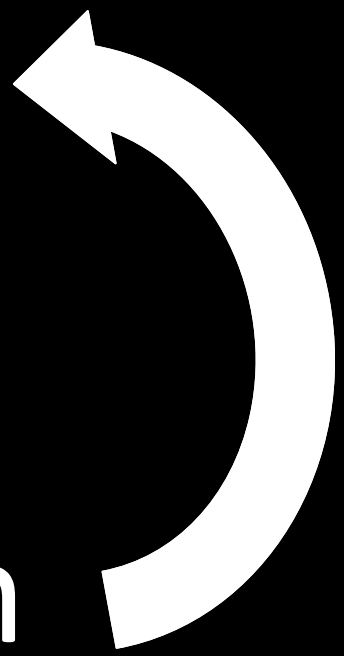
Treatment


Subtype Classification Tests
Evaporative
• Abnormal lipid
• MGD
Aqueous Deficiency
• Low volume
mild
MGD
moderate
severe
Evaporative Severity
STEP 1
STEP 2
STEP 3
STEP 4
Aqueous/ Evaporative Spectrum
Aqueous Deficient Severity
TMH
0.2 mm
0.1 mm
0.0 mm

Provide Relief

+

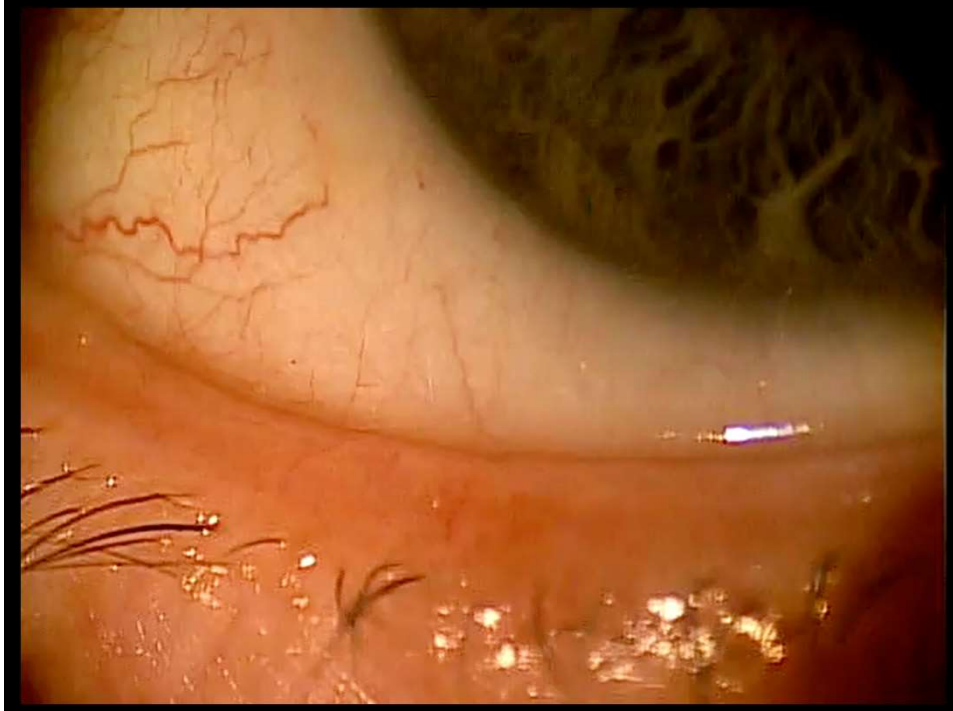
Improve function

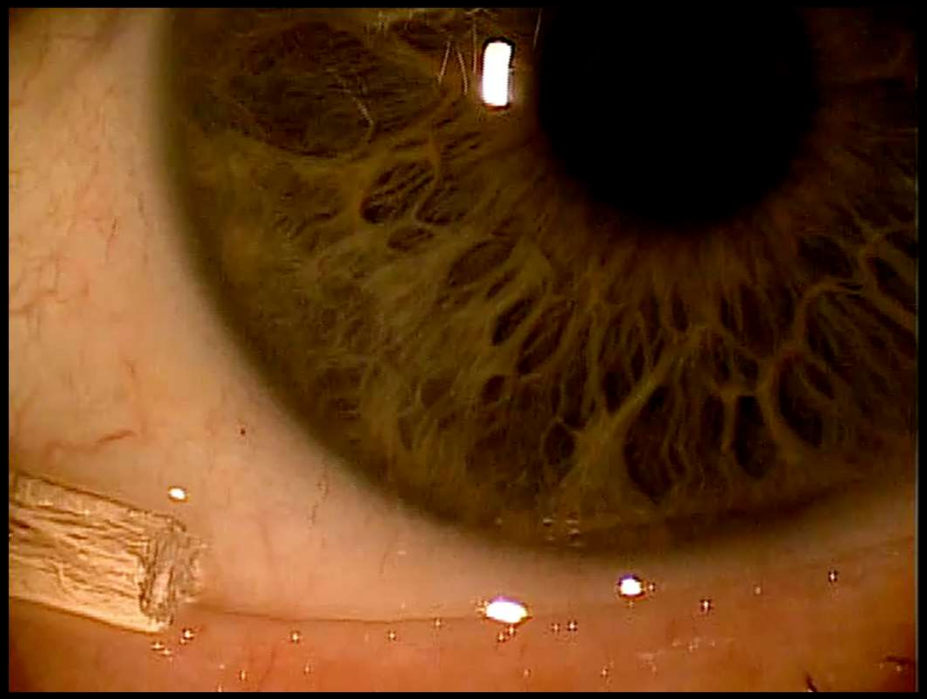



equate
sterile
artificial
tears
LUBRICANT EYE DROPS
• Soothing Relief
STERILE
0.5 FL OZ (15 mL)
Walgreens
Artificial
Tears
Lubricant Eye Drops
Relieves Dry,
Irritated Eyes
Sterile
1 FL OZ (30 mL)
DRY EYE
RELIEF
NATURAL TEARS FORMULA*
Sterile
Visine
TEARS
DRY EYE RELIEF
LUBRICANT EYE DROPS
Moisturizes
& Soothes
Protects against
irritation
1/2 FL OZ (15 mL)
STERILE
Artificial
Tears
LUBRICANT
EYE DROPS
• Soothing Relief
• For Dryness
and Irritation
0.5 FL OZ
(15 mL)


ATON
60 STERILE OPHTHALMIC INSERTS
LACRISERT®
(HYDROXYPROPYL CELLULOSE
OPHTHALMIC INSERT)
5 mg
CONTAINS NO PRESERVATIVE

Lacriserts dissolve in 24 hours





Clinical Ophthalmology

Dovepress
open access to scientific and medical research

Open Access Full Text Article

HYPOTHESIS

DEBS – a unification theory for dry eye and blepharitis

James M Rynerson[1]
Henry D Perry[2]

[1]BlephEx, LLC, Alvaton, KY, [2]Department of Ophthalmology, Nassau University Medical Center, Hofstra University School of Medicine, East Meadow, NY, USA

Abstract: For many years, blepharitis and dry eye disease have been thought to be two distinct diseases, and evaporative dry eye distinct from aqueous insufficiency. In this treatise, we propose a new way of looking at dry eye, both evaporative and insufficiency, as the natural sequelae of decades of chronic blepharitis. Dry eye is simply the late form and late manifestation of one disease, blepharitis. We suggest the use of a new term in describing this one chronic disease, namely dry eye blepharitis syndrome (DEBS). Bacteria colonize the lid margin within a structure known as a biofilm. The biofilm allows for population densities that initiate quorum-sensing gene activation. These newly activated gene products consist of inflammatory virulence factors, such as exotoxins, cytolytic toxins, and super-antigens, which are then present for the rest of the patient's life. The biofilm never goes away; it only thickens with age, producing increasing quantities of bacterial virulence factors, and thus, increasing inflammation. These virulence factors are likely the culprits that first cause follicular inflammation, then meibomian gland dysfunction, aqueous insufficiency, and finally, after many decades, lid destruction. We suggest that there are four stages of DEBS which correlate with the clinical manifestations of folliculitis, meibomitis, lacrimalitis, and finally lid structure damage evidenced by entropion, ectropion, and floppy eyelid syndrome. When one fully understands the structure and location of the glands within the lid, it becomes easy to understand this staged disease process. The longer a gland can resist the relentless encroachment of the invading biofilm, the longer it can maintain normal function. The stages depend purely on anatomy and years of biofilm presence. Dry eye now becomes a very easy disease to understand. We feel that dry eye should be treated and prevented by early and routine biofilm removal through electromechanical lid margin debridement.

Keywords: biofilm, quorum-sensing gene activation, Demodex, MGD, meibomian gland disease, aqueous insufficiency

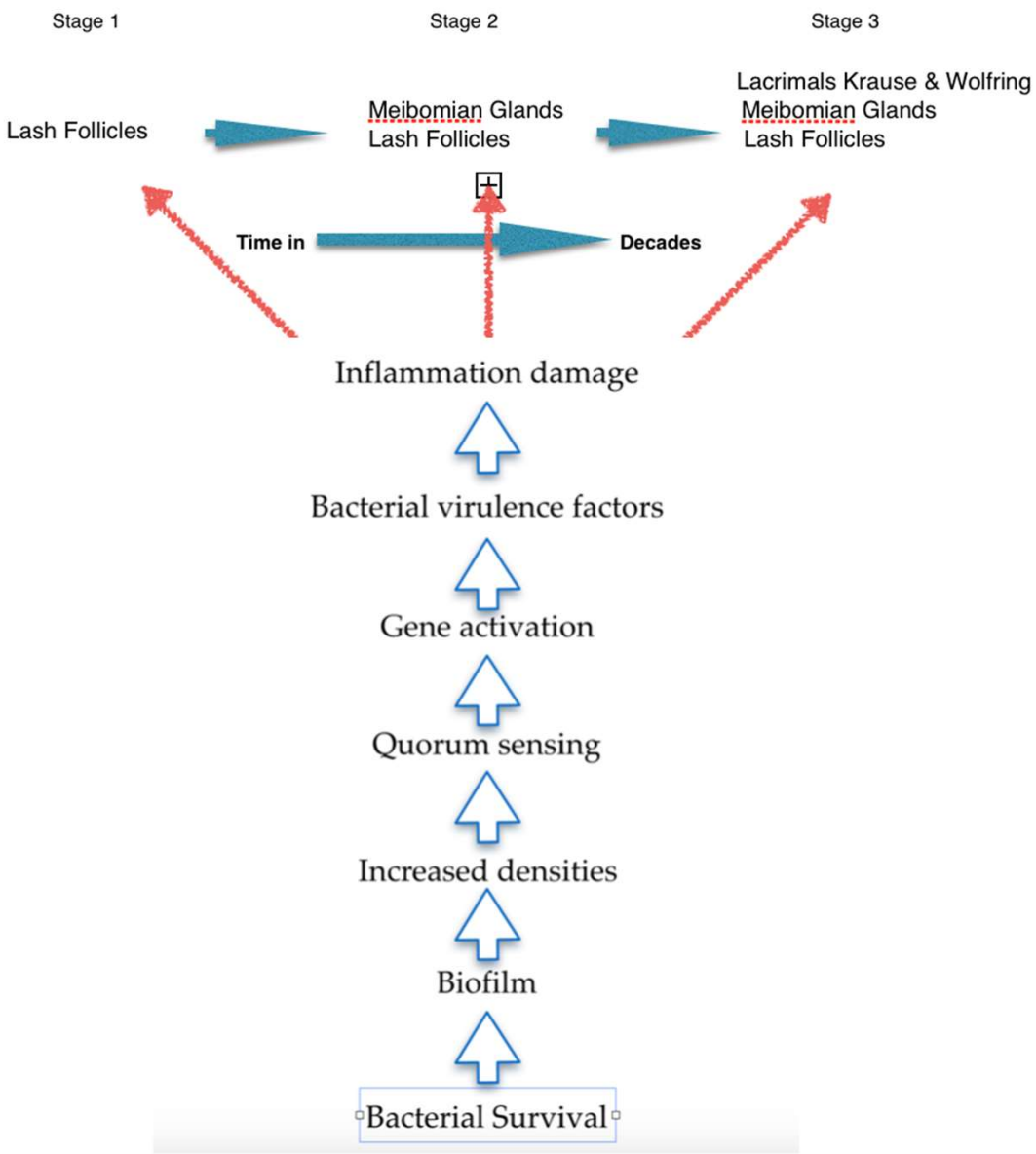
Introduction

In 1684, Antonie van Leeuwenhoek presented to the Royal Society of London and commented on the number of "animicules" noted within the scurf of a man's teeth.[1] This is the first known microscopic observation of a biofilm. For over 300 years, little was known about biofilms, and research was uncommon. Biofilm implications in all of human disease were vastly underappreciated.[2] In the past 20 years, however, biofilm research has burgeoned, with complicated but fascinating interactions between bacteria, host, and their environment now being revealed.[2,3] In a similar vein, the term "blepharitis" first appears in the literature in the 1800s, but like biofilm research, little progress was made over the subsequent 100+ years in terms of understanding or treating this disease.[4] While we have made some strides since the days of "Great German Eye Water" to treat "weak or inflamed eyes", blepharitis remains a poorly defined disease, with the use of confusing and inaccurate terminology and considerable

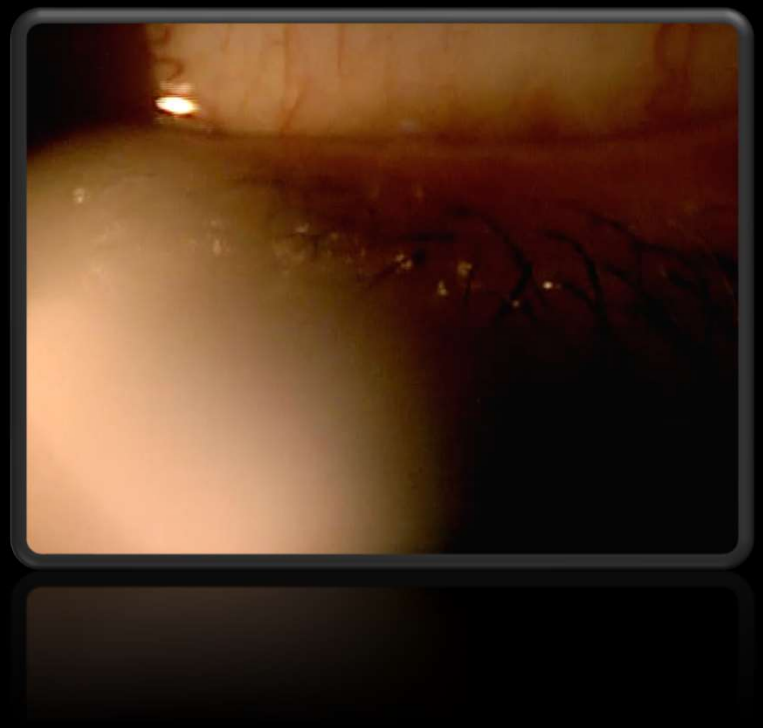
Correspondence: James M Rynerson
BlephEx, LLC, 275 Booth Drive, Alvaton, KY 42122, USA
Tel +1 270 779 3806
Fax +1 270 780 9544
Email docjmrmd@gmail.com

http://dx.doi.org/10.2147/OPTH.S114674

Rynerson Theory of DEBS



MICROBLEPHAROEXFOLIATION (MBE)



Clinical Effectiveness of Lid Debridement with BlephEx Treatment

Daniel Mulder, Kirsti Kyser, Bonnie Rosenberg, Charles Connor, Christopher Choat, Srihari Narayanan
University of the Incarnate Word, Rosenberg School of Optometry, San Antonio, Texas

ABSTRACT

Purpose: Eyelid disease is a common cause of evaporative dry eye. Lid scrubs and warm compresses done consistently will address this problem but poor compliance makes an office based procedure desireable. Korb found the debridement-scaling of the lower lid margin provides statistically significant symptom relief and improvement in the meibomian gland (MG)function. The Bleph Ex provides a method of accomplishing lid debridement without using a surgical instrument. This study compares signs and symptoms before and after BlephEx treatment.

Methods: Twenty subjects all with MG dysfunction were examined at baseline using a biomicroscope using the Efron scale for grading. Subjects also had a TBUT and OSDI performed. The subjects were then treated with the BlephEx according to manufacturer's directions. 4 weeks later all testing was repeated. Data was analyzed by a t-test with post hoc test for significance.

Results: Subjects TBUT improved from 3.31+/-1.3 to 5.47+/-4.3 p=0.05. Blepharitis on the Efron scale improved from 1.24+/-0.69 to 0.575+/-0.54 p=0.01. MG dysfunction also dramatically improved from 1.65+/-0.5 to 0.76 +/- 0.59 p=0.01. Symptoms also improved based on the OSDI which went from 43.74+/-14.27 to 20.33+/-14.35 p=0.01.

Conclusions: This study suggests BlephEx is a viable alternative to lid scrubs and warm compresses. Statistically significant improvement was observed in signs and symptoms of the subjects treated. Eyelid functions improved based on TBUT increase, reduced inflammation and enhanced MG function. Subjects were 50% less symptomatic after treatment. BlephEx appears to be a reasonable clinical approach for use non-compliant MG dysfunction patients.

BACKGROUND

Rynerson introduced a new instrument in 2014 that aims at reducing the effects of blepharitis. The minimal invasiveness of the instrument makes it ideal for use by optometrists.

This study examines changes in the signs and symptoms of the ocular surface before and after treatment with BlephEx.

METHOD

20 subjects with MGD and dry eye symptoms participated in a prospective randomized study.

All subjects underwent an initial baseline examination.

All subjects then received the BlephEx treatment according to the manufacturer's directions.

Outcome measures obtained at baseline and 4 weeks post-treatment included:

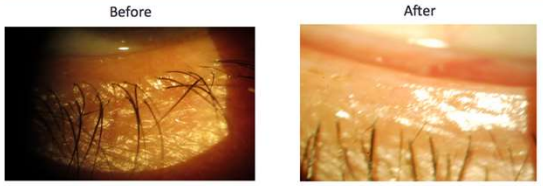
Biomicroscope examination using the Efron Grading Scale to grade MGD and Blepharitis severity

Ocular Surface Disease Index (OSDI)

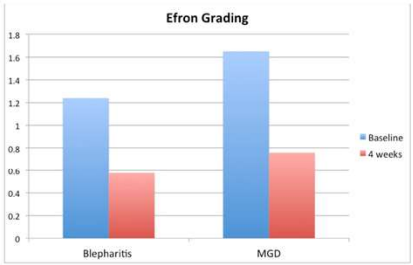
Tear Break-Up Time

Data was analyzed by a t-test with post hoc test for significance.

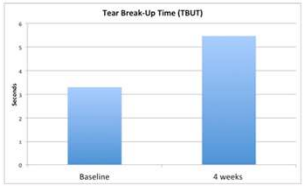
EFRON GRADING SCALE



Inferior lid margin OS; pre-treatment blepharitis rated 2+ (moderate), 4 weeks post-treatment rated 0 (normal).



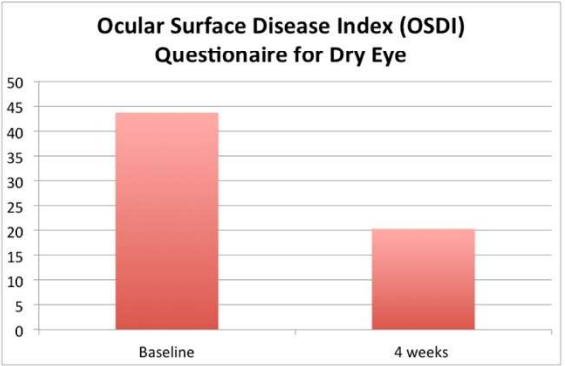
Efron grading scale for Blepharitis and MGD



RESULTS

- TBUTS significantly improved 4 weeks after treatment (p= 0.05)
- Blepharitis on the Efron Scale significantly improved 4 weeks after treatment (p=0.01)
- MG Dysfunction drastically improved 4 weeks after treatment (p=0.01)
- Symptoms also improved based on the OSDI 4 weeks after treatment (p=0.01)

EYELID DEBRIDEMENT



CONCLUSIONS

- BlephEx is a viable alternative to the conventional treatment (lid scrubs and warm compresses) for blepharitis
- Statistically significant improvement in signs & symptoms 4 weeks after treatment
- Increased TBUT, decreased inflammation, and increase in MG function after treatment
- Subjects were 50% less symptomatic after treatment

59% of symptomatic CL patients were converted to asymptomatic after just one treatment

A Comfortable Eye Needs Fats

Jaya Sowjanya Siddireddy, Jacqueline Tan-Showyin, Ajay Kumar Vijay, Mark Willcox
School of Optometry and Vision Science, University of New South Wales, Sydney, Australia

Introduction

- 140 million people wear contact lens worldwide and at least 50% of them experience discomfort.
- Comfort is the number one reason why people stop wearing contact lenses.

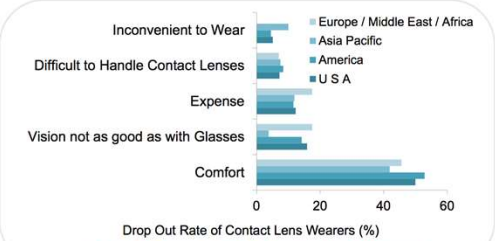
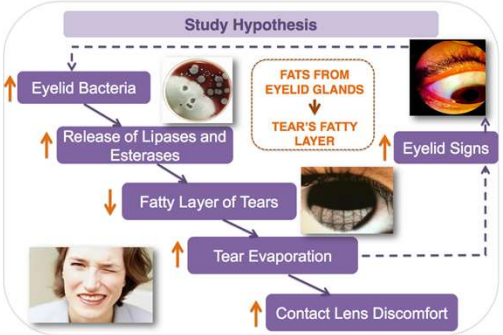


Figure 1: Dropout Rate of Contact Lens Wearers

- No clear consensus on precise reason for development of contact lens discomfort to date.

Purpose

- To evaluate the role of eyelids and tears in contact lens discomfort



Methods

Results

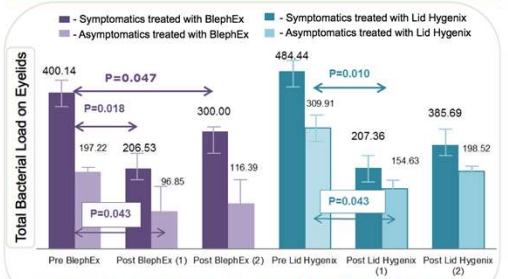


Figure 2: Reduction in Eyelid Microbes Post BlephEx Treatment

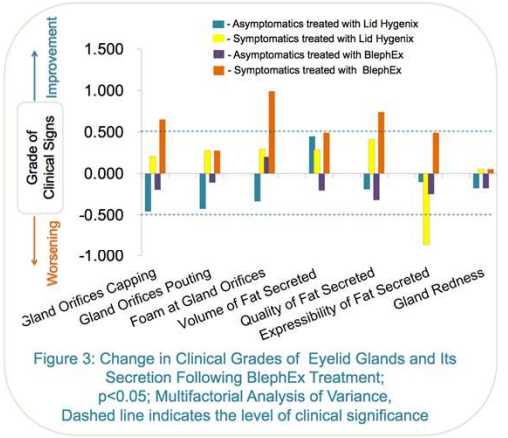


Figure 3: Change in Clinical Grades of Eyelid Glands and Its Secretion Following BlephEx Treatment;
$p<0.05$; Multifactorial Analysis of Variance,
Dashed line indicates the level of clinical significance

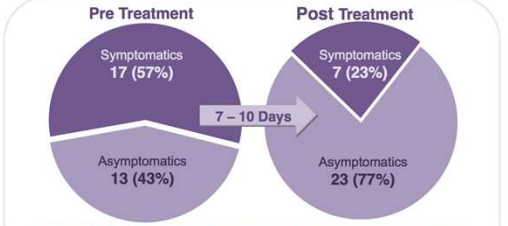


Figure 4: Post BlephEx Treatment 10 Contact Lens Wearers Convert from being Symptomatic to Asymptomatic.

Conclusion

- Symptomatic contact lens wearers had higher number of eyelid bacteria.
- Reduction in eyelid bacteria with BlephEx treatment improved signs of 'fat-producing' eyelid glands and tear's fatty layer; and comfort in symptomatic contact lens wearers.
- 59% of symptomatic lens wearers converted to asymptomatics post BlephEx treatment.

OPEN ACCESS
ARVO Annual Meeting Abstract | June 2017

Reduction in inflammatory marker matrix metalloproteinase-9 following lid debridement with BlephEx

Charles G Connor; Srihari Narayanan; William Miller

+ Author Affiliations & Notes

Investigative Ophthalmology & Visual Science June 2017, Vol.58, 498. doi:

Abstract

Purpose : Meibomian Gland Disease (MGD) is a common cause of evaporative dry eye. Lid scrubs and warm compresses can address this problem but poor compliance makes an office based procedure desirable. Korb found the debridement-scaling of the lower lid margin provides statistically significant symptom relief and improvement in MG function. The BlephEx provides a method of accomplishing lid debridement without using a surgical instrument. Ocular surface inflammation is well documented in dry eye patients. The RPS InflammaDry recognizes elevated levels of MMP-9, an inflammatory marker that is consistently

-Ten MGD patients with evaporative dry eye and tested positive with InflammaDry
-OSDI, NIBUT, meibography and InflammaDry were measured before and after BlephEx treatment (4 week post treatment)
- OSDI – 26 (pre-treat) and 10.66 (post-treat)
-NIBUT – 6.99 (pre-treat) and 9.53 (post-treat)
-Meibography – no change
-InflammaDry – positive (pre-treat) and negative (post-treat)

Hypochlorous Acid

- **Pure hypochlorous acid (HOCl) released from neutrophils**
- **Essential part of body's immune response**
- **In the body, Hypochlorous Acid:**
  - **Kills microorganisms**
  - **Neutralizes inflammatory toxins released from pathogens**
  - **helps suppress the body's inflammatory response**
  - **Prevents biofilm formation**

Hypochlorous Acid

- Avenova (0.01%)
- HyClear (0.01%)
- HypoChlor (0.02%)
- Theratears Sterilid Antimicrobial Eyelid Cleanser (0.01%)
- Bruder Hygienic Eyelid Solution (0.02%)
- Heyedrate Lid and Lash Cleanser (0.015%)

NuLids Works

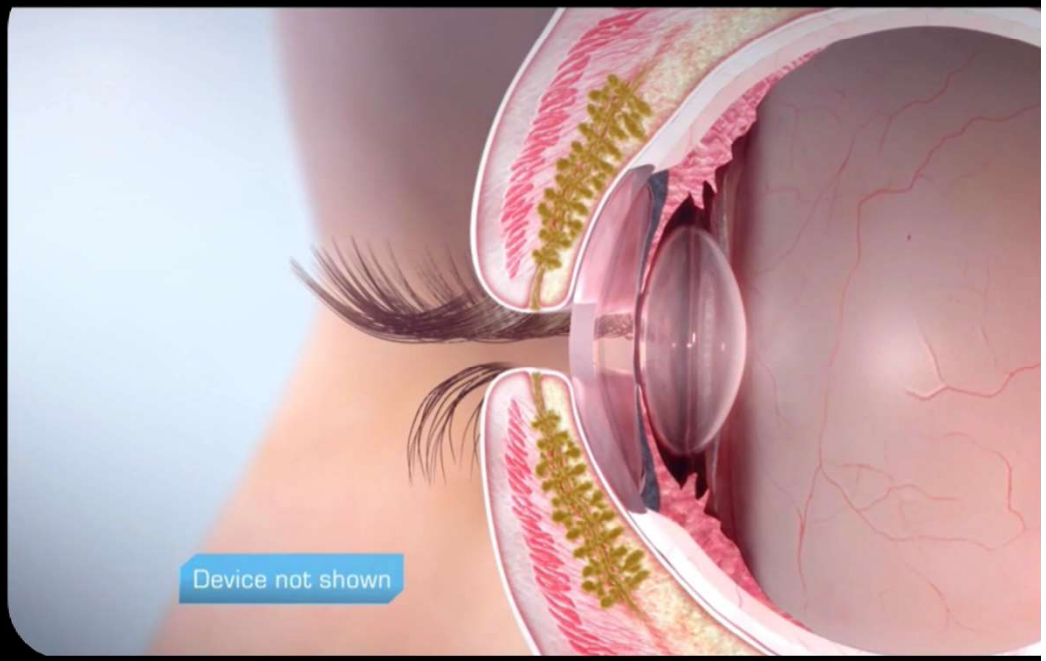
- The NuLids Starter Kit includes a rechargeable cordless handpiece, one charger plug and charger cord, and an initial 30-day supply of NuLids Daily Disposable Soft Tips
- Before each treatment, a new sterile Soft Tip is attached to the handpiece
- A small amount of lubricating gel or cleaner is applied to the edge of the Soft Tip [i.e. ZocuShield Gel/Systane /Hypochlorous acid]
- The handpiece is then powered on and the Soft Tip begins oscillating back and forth in a 15° arc pattern
- The Soft Tip is then gently placed on the eyelid margin and smoothly moved back and forth across the entire lid margin for approximately 30 seconds, and then repeated for the fellow eye

Tea Tree Oil

- Tea tree oil, or melaleuca oil
- Taken from the leaves of the Melaleuca alternifolia
- Is native to Southeast Queensland and the Northeast coast of New South Wales, Australia
- Toxic when taken by mouth, but is widely used in low concentrations in cosmetics and skin washes

Lipid Based Products

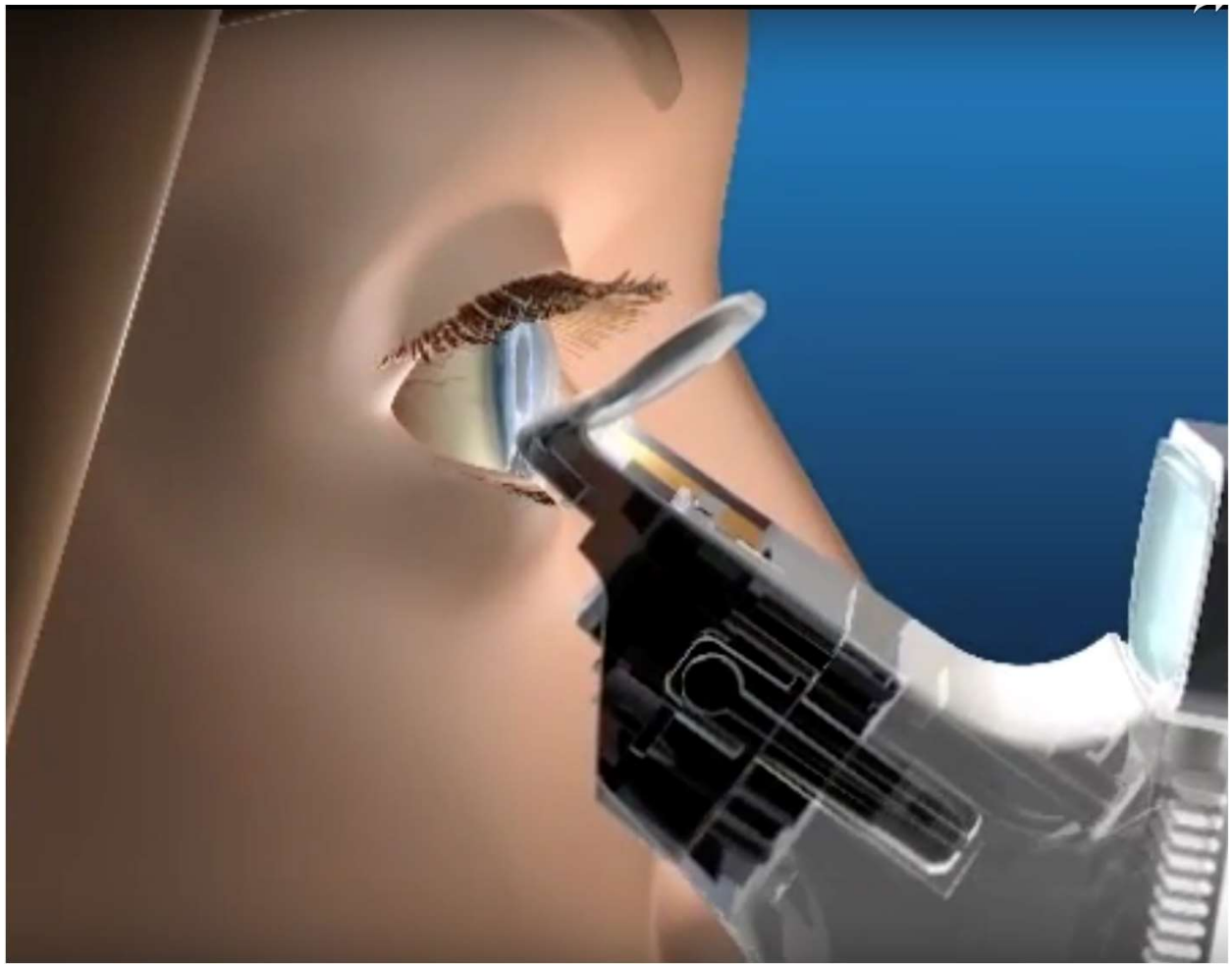
Lipiflow



- 3x gland improvement
- 2x symptom improvement
- Improvement seen beyond 9-months
- Safe
- Well Researched

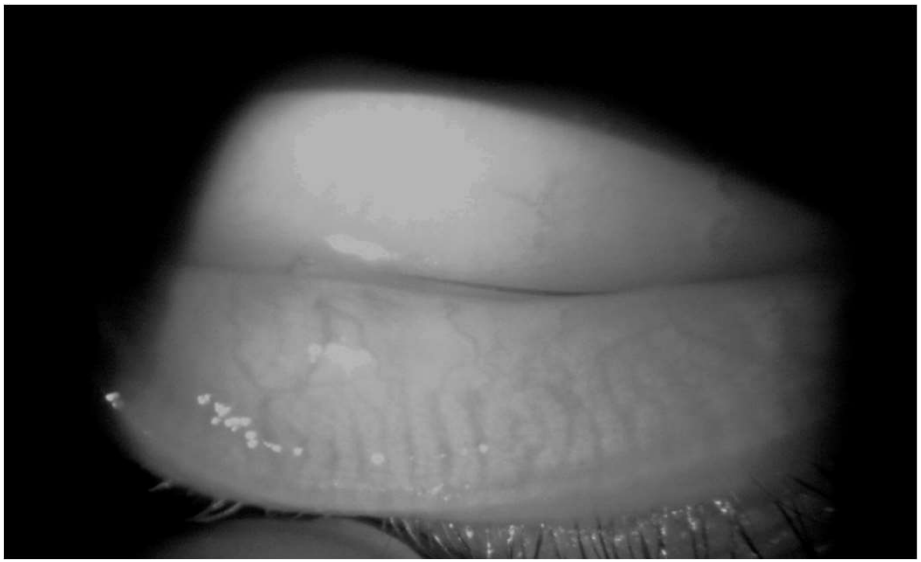
Alcon
iLux Device

Alcon
iLux Device



Sight Sciences
Tear Care System

Sight Sciences - Tear Care System



Traditional Thoughts – Treat Topically

Why Do Omega 3's Work?

Eicosapentaenoic acid / Docosahexaenoic acid
(EPA/DHA)

Cyclooxygenase

Prostaglandin - 3
(Anti-inflammatory)

IMPORTANT:

≠

Fish Oil

EPA/DHA

>70%

Cyclosporine Ophthalmic Emulsion 0.05%

- Manufacturer: Allergan, inc
- Active Ingredients: Cyclosporine 0.05%
- Inactive Ingredients: Glycerin, Castor Oil, Polysorbate 80, Carbomer 1342, and purified water
- Preservation: None (unit-dose vile)


Xiidra
(lifitegrast
ophthalmic solution) 5%
For Topical Application to the Eye
Rx Only
60 Single-Use Containers:
12 pouches x 5 single-use containers (0.2 mL each)
NDC-54092-606-02
Shire


NDC 47355-508-96
For topical use in the eye
Sterile, Preservative-Free
Cequa™
(cyclosporine ophthalmic solution) 0.09%
60 SINGLE-USE VIALS
6 pouches x 10 single-use vials (0.25 mL each)
Rx only
Keep out of reach of children.
Not child resistant.
SUN PHARMA

What if they have rosacea?



Meibomian Gland Dysfunction Treatment

- Oral Antibiotics
- Doxycycline
  - 20 to 200 mg bid po x 1-2 months, then taper

The effect of low-dose doxycycline therapy in chronic meibomian gland dysfunction

Korean J Ophthalmol. 2005 Dec;19(4):258-63.

Yoo SE1, Lee DC Chang MH.

-Patients with meibomian gland dysfunction unresponsive to eyelid hygiene

-150 patients randomized to 20 mg bid p.o. or 200 mg bid p.o.

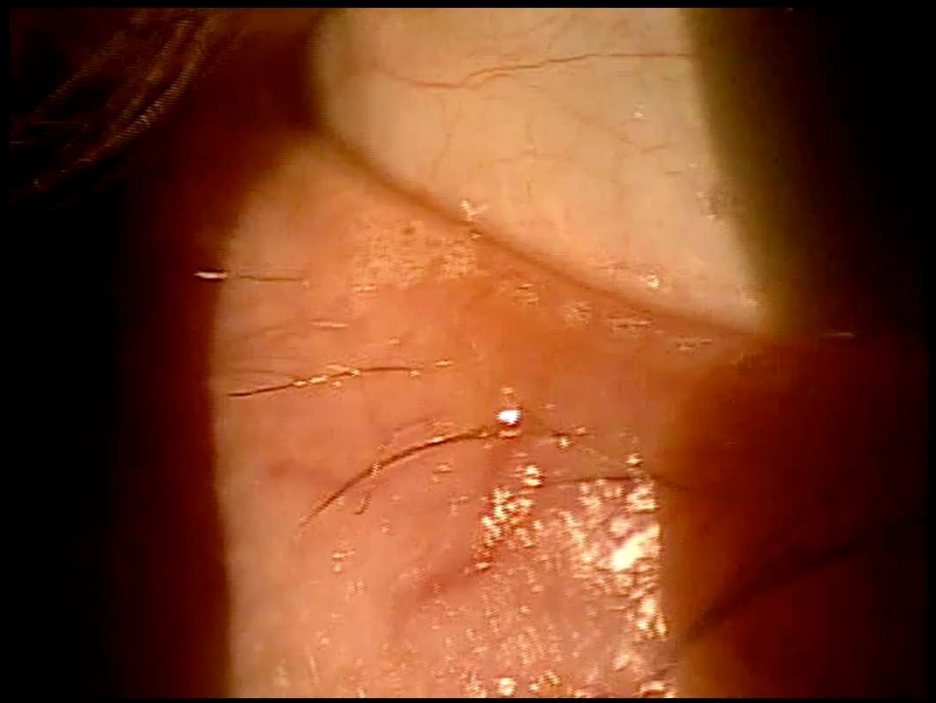
-Identical effectiveness

-39% of high dose experienced side effects vs. 17% of low dose

Meibomian Gland Dysfunction Treatment

- Oral Antibiotics
- Side Effects
  - Gastrointestinal upset
  - Yeast infections
  - Photosensitivity
  - Do not prescribe to children and pregnant women
  - Shouldn’t be taken with milk or dairy products

Entering Presentation



Day 45

Published in final edited form as:
Cornea. 2013 January ; 32(1): 44–53. doi:10.1097/ICO.0b013e318254205f.

Topical Azithromycin and Oral Doxycycline Therapy of Meibomian Gland Dysfunction: A Comparative Clinical and Spectroscopic Pilot Study

Gary N Foulks, MD[1], **Douglas Borchman, PhD**[2], **Marta Yappert, PhD**[3], and **Shelley Kakar**[4]
[1]Department of Surgery, Robley Rex Veterans Affairs Medical Center, Louisville, KY
[2]University of Louisville Department of Ophthalmology and Vision Science
[3]University of Louisville Department of Chemistry
[4]University of Louisville Department of Physiology

Abstract

Purpose—Meibomian gland dysfunction (MGD) is a common clinical problem that is often associated with evaporative dry eye disease. Alterations of the lipids of the meibomian glands have been identified in several studies of MGD. This prospective, observational, open label clinical trial documents the improvement in both clinical signs and symptoms of disease as well as spectroscopic characteristics of the meibomian gland lipids after therapy with topical azithromycin ophthalmic solution and oral doxycycline treatment.

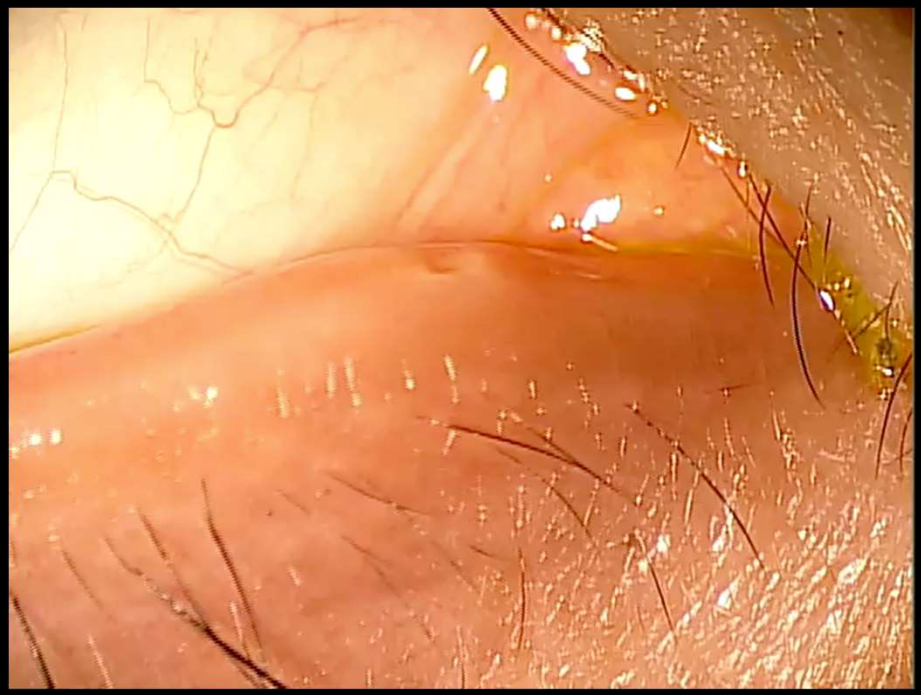
Methods—Subjects with symptomatic MGD were recruited. Signs of MGD were evaluated with a slit lamp. Symptoms of MGD were measured by the response of subjects to a questionnaire. Meibum lipid-lipid interaction strength, conformation and phase transition parameters, and meibum protein content were measured using Fourier transform infrared spectroscopy (FTIR) and principal component analysis (PCA). Terpenoids, short chain CH_3 moieties, lipid oxidation, wax, cholesterylesters and glycerides were measured with a proton nuclear magnetic resonance (^{1}H-NMR) spectrometer.

Results—Topical therapy with azithromycin and oral therapy with doxycycline relieved signs and symptoms and restored the lipid properties of the meibomian gland secretion towards normal. Compared to 4 weeks of azithromycin treatment reported in our previous study, oral doxycycline treatment was slightly less effective in improving foreign body sensation and the signs of plugging and secretion. In subjects with clinical evidence of MGD, changes in ordering of the lipids and phase transition temperature were brought closer to normal with azithromycin treatment than doxycycline treatment. Treatment with doxycycline but not azithromycin restored the FTIR PCA scores and relative area of the ^{1}H-NMR resonance at 1.26 ppm. Both doxycycline and

Corresponding author: Douglas Borchman, Ph.D., 301 E Muhammad Ali Blvd, Louisville, KY 40202, 502-852-7435 (phone) 502-852-7450 (fax), borchman@louisville.edu.

Doxycycline hyclate 100mg bid p.o. vs. topical Azithromycin 1% bid for 2 days then qd for 2 months

Punctal Occlusion



8 ng/mL Negative	34 ng/mL Trace Positive	66 ng/mL Weak Positive	101 ng/mL Positive	381 ng/mL Strong Positive

Signal Strength

Jewelers Forceps

Punctal Plugs

Permanent

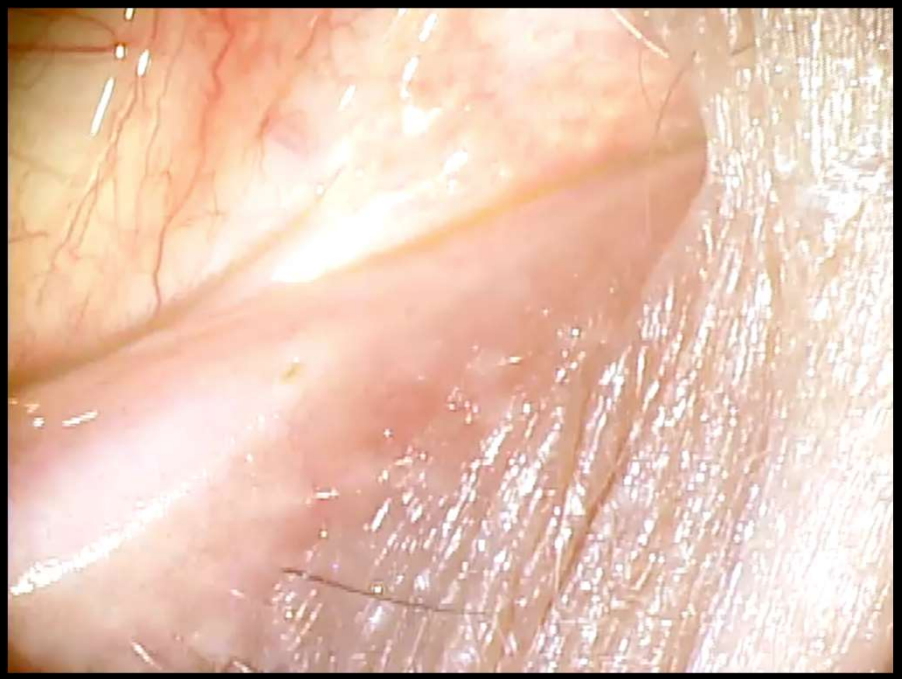
Pedi-Plug
X-Small
Small
Medium
Large
X-Large

Temporary

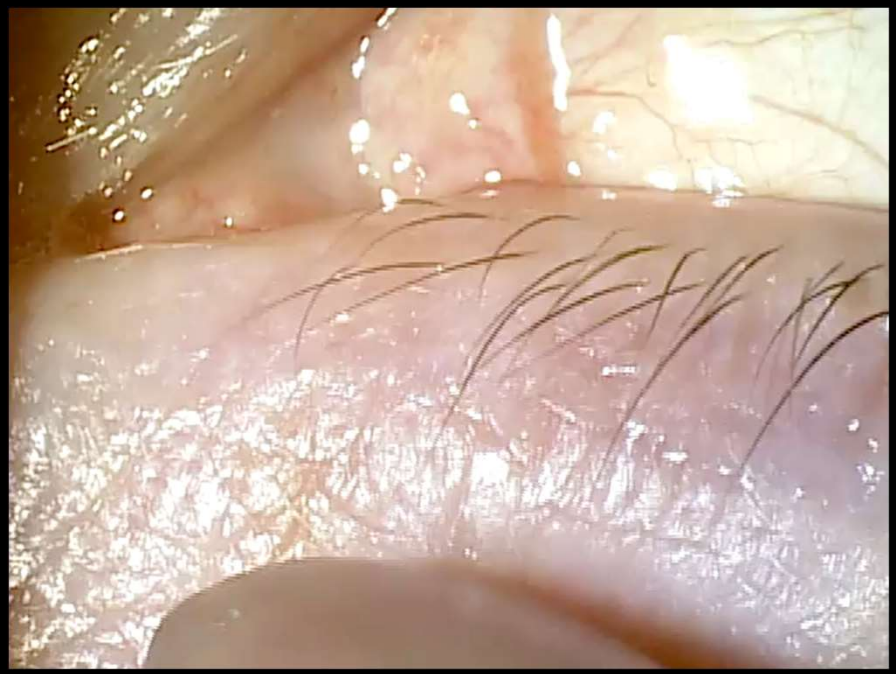
- Collagen (10-14 days)
  - 0.2 mm
  - 0.3 mm
  - 0.4 mm
- 3 month
  - 0.2 mm
  - 0.3 mm
  - 0.4 mm
  - 0.5 mm
- 6 month
  - 0.3 mm
  - 0.4 mm
  - 0.5 mm

Recently Became Available

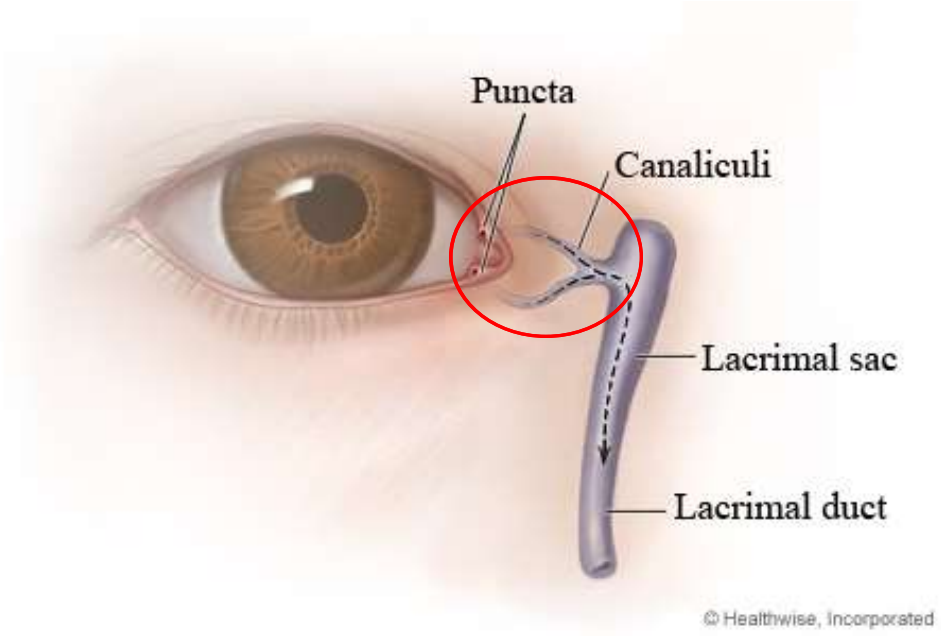
Various Size Puncta

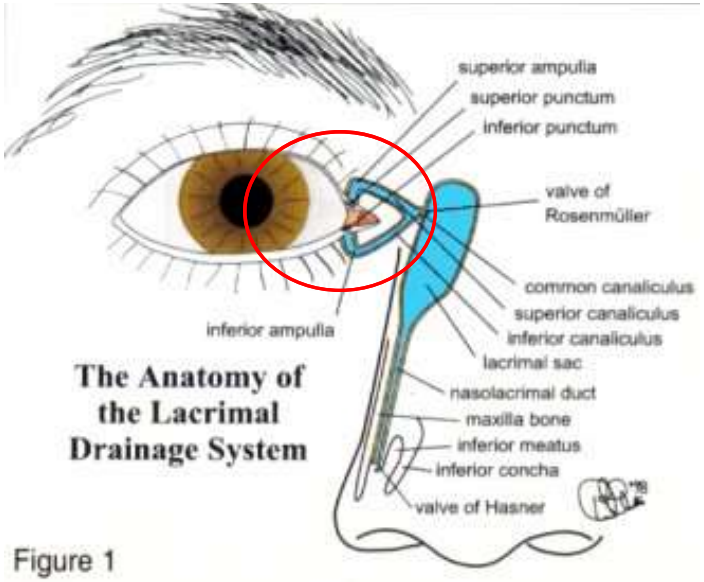


0.2 mm 3 month



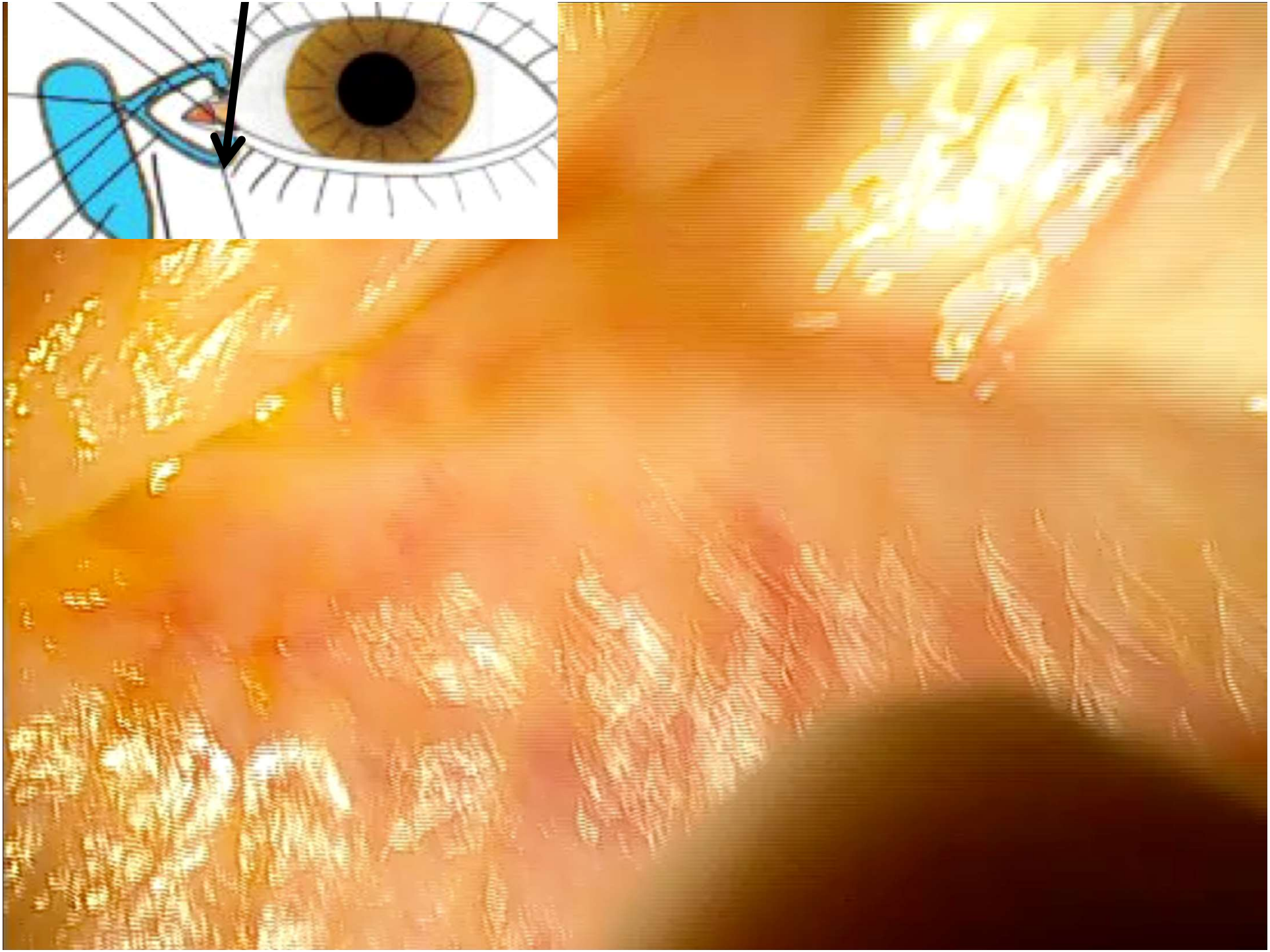
0.4 mm collagen

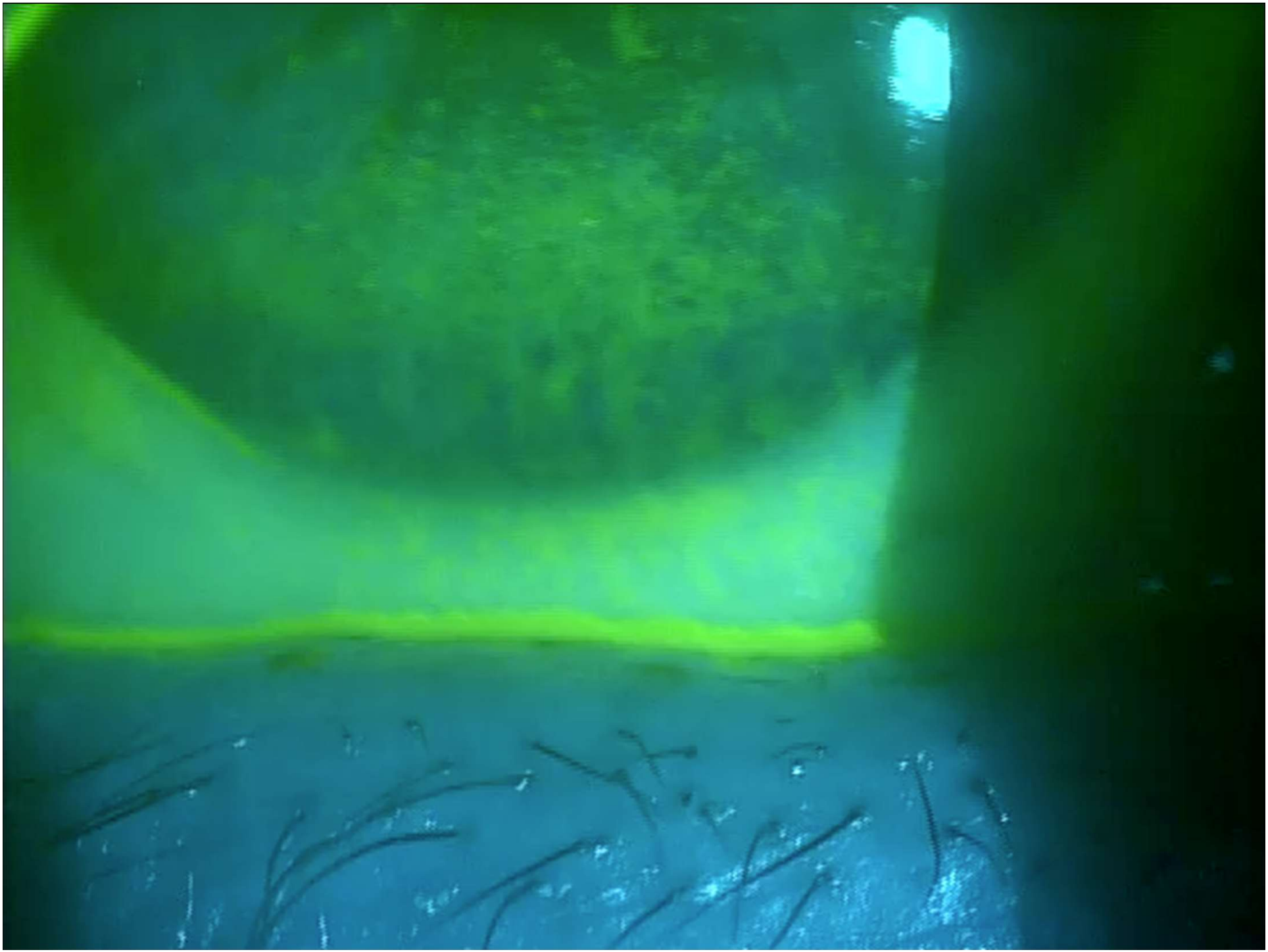




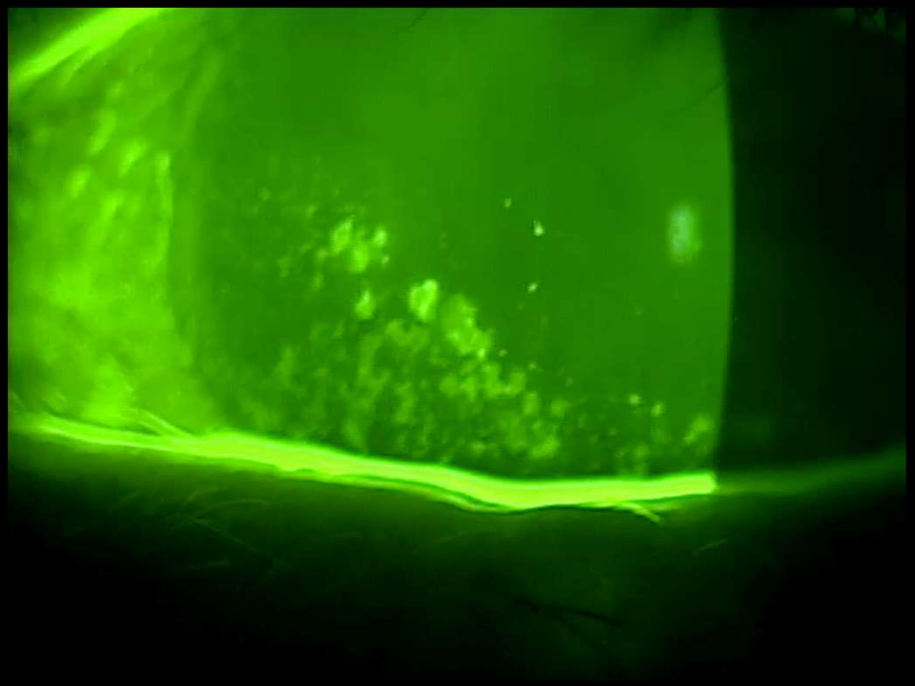
http://www.academy.org.uk/tutorials/dilate1.jpg

http://www.uofmhealth.org/sites/default/files/healthwise/media/medical/hw/h9991911_001.jpg

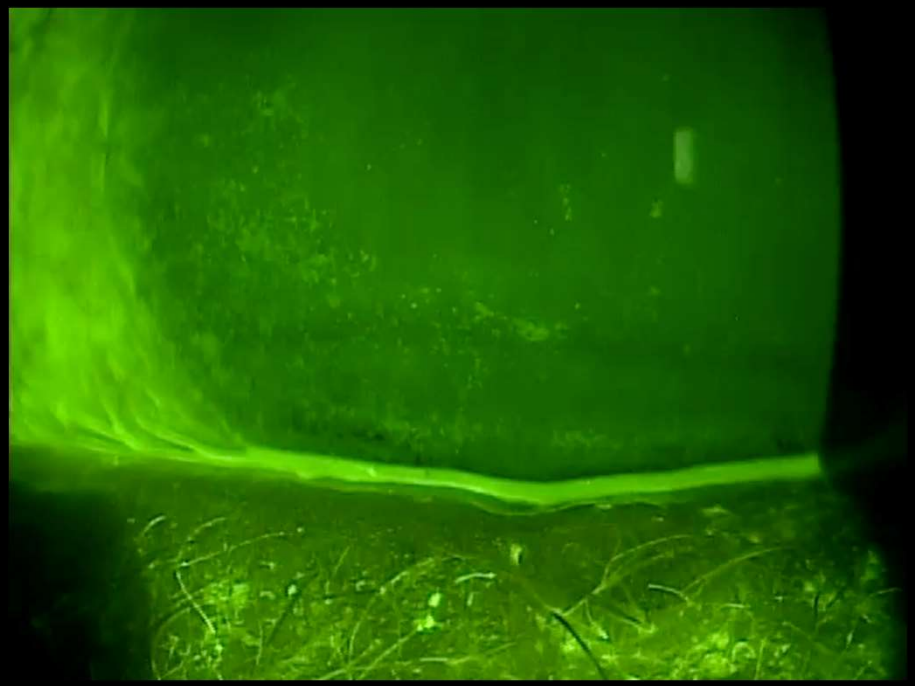




Before Plugs

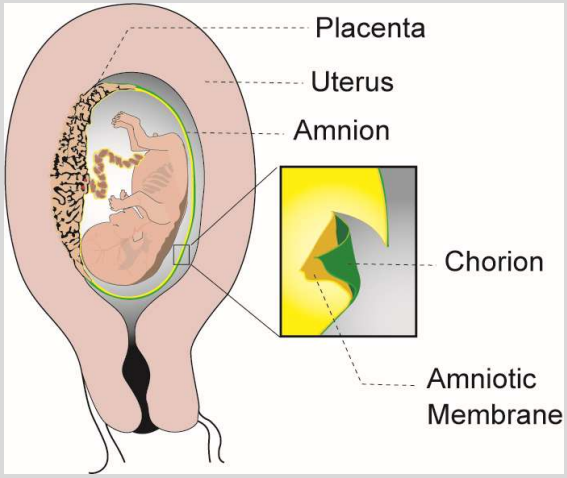


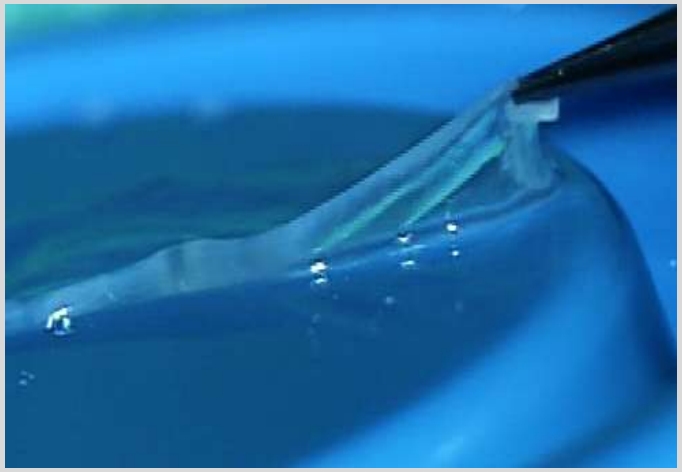
2 weeks

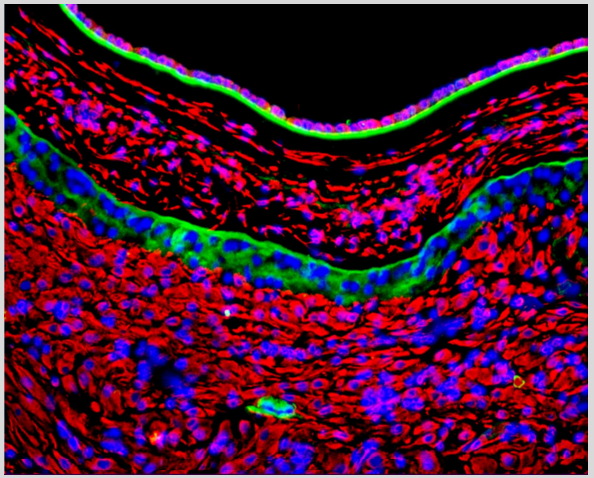


The Amniotic Membrane

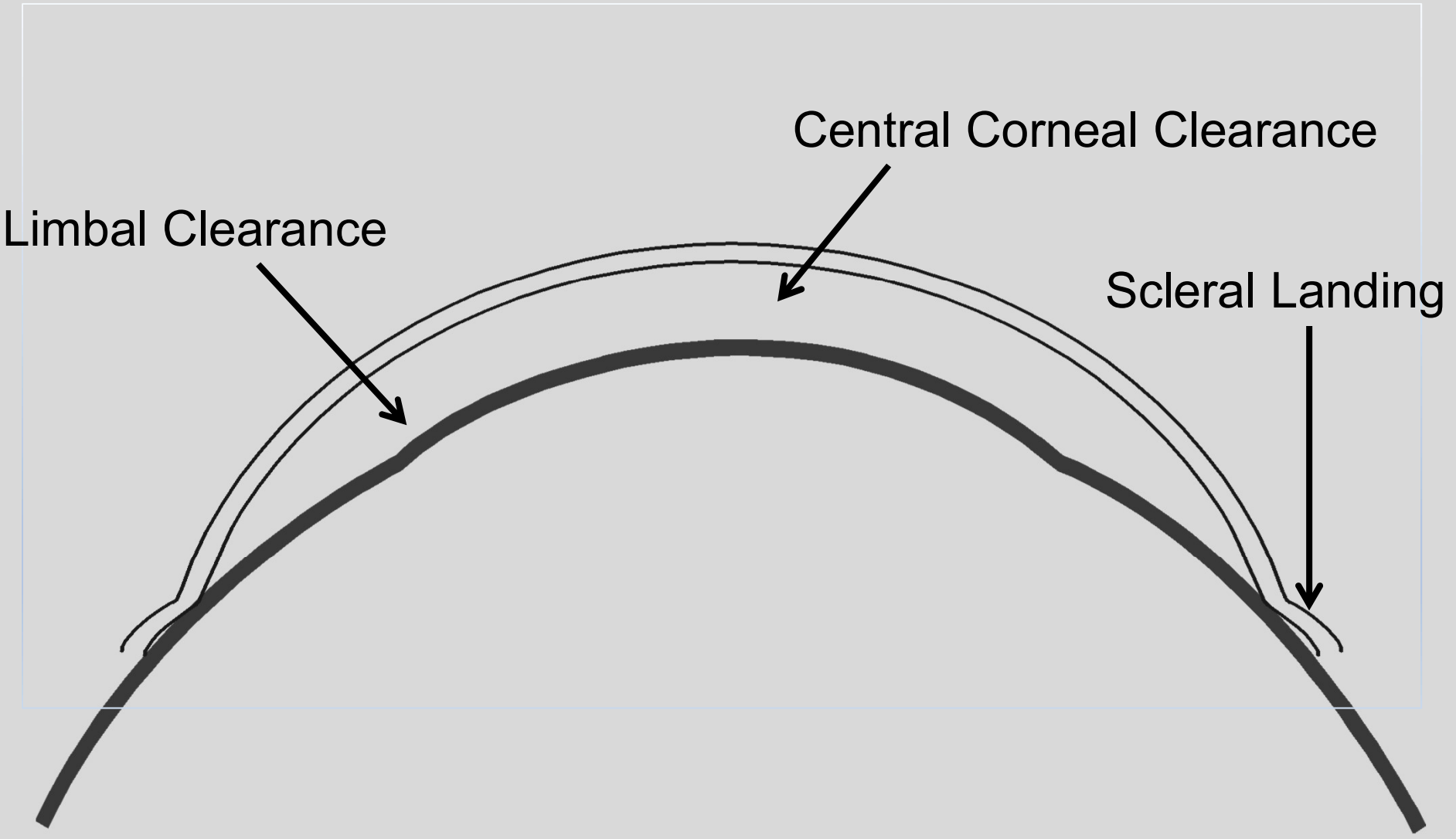
- The amniotic membrane is the innermost lining of the placenta (amnion)
- Amniotic membrane shares the same cell origin as the fetus
  - Stem cell behavior
- Structural similarity to all human tissue







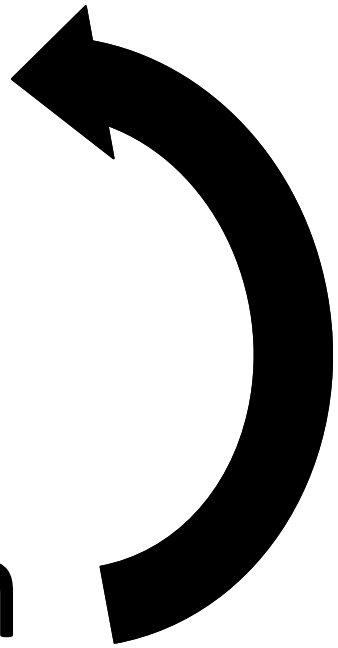
The Fitting Philosophy



Provide Relief

+

Improve function



Provide Relief?

Lipid Based

Aqueous Based

Gels

Ointment

Mechanical

1. MG Function

2. Retain Tears

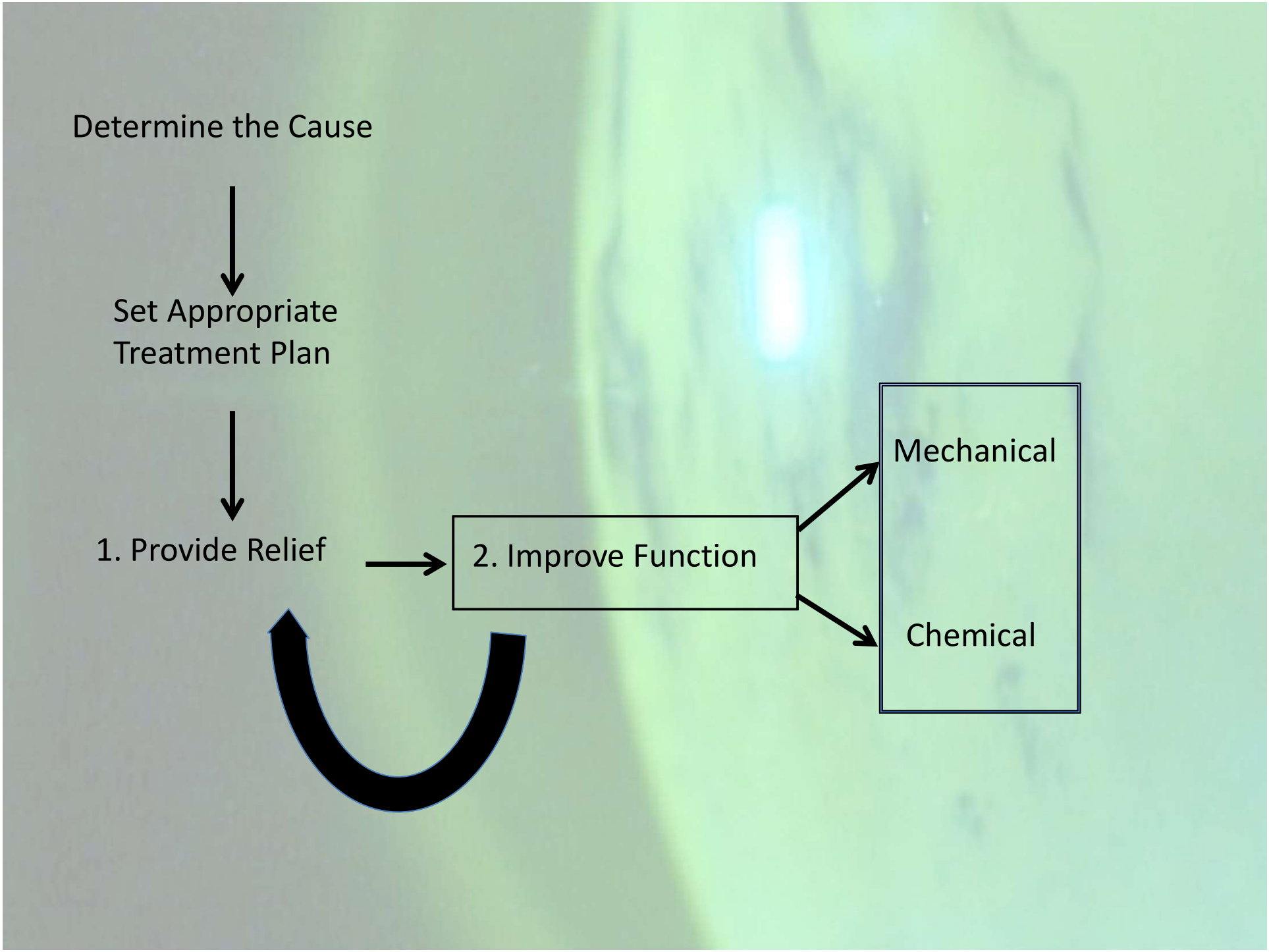
3. Clean lids

BlephEx™

Chemical

Topical

Oral


Determine the Cause
Set Appropriate Treatment Plan
1. Provide Relief
2. Improve Function
Mechanical
Chemical

Dry Eye Work-up / Follow-up

1) History
    a. Ocular Surface Disease Index
    b. SPEED Questionnaire
2) Tear film break up time
    a. Less than 10 seconds is low
3) Tear film break up pattern
4) Corneal staining - fluorescein
5) Conjunctival staining - fluorescein
6) Corneal staining – Lissamine green/rose bengal
7) Conjunctival staining - Lissamine green/rose bengal
8) Lid Wiper epitheliopathy

Horizontal length of staining	Grade
<2 mm	0
2-4 mm	1
5-9 mm	2
>10 mm	3
Sagittal width of staining	**Grade**
<25% of the width of wiper	0
25%-<50% of the width of wiper	1
50%-<75% of the width of wiper	2
≥75% of the width of wiper	3

9) Lid laxity/elasticity
10) Lid margin assessment
    a. Hyperemia; presence of debris at base of lashes
    b. Irregularity that is present at the margin
    c. Line of Marx
11) Quality of meibum expressed from glands
    a. Meibomian gland evaluator
12) Structure of Meibomian glands (eyelid transillumination); infrared imaging
13) InflammaDry (strong positive, weak positive, negative)
14) Phenol red thread test
    a. Thread is left in place for 15 seconds
    b. Less than 10mm suggests a tear deficiency

Premier Vision Group

1222 Ridgewood Drive, Bowling Green, OH, 43402
419-352-2502

○ Artificial tears
Type: Systane Complete / Systane Balance / Refresh Optive Advanced / Fresh Kote
Other: _____
Directions: 1-2 drops, _____ times per day

○ Thermal therapy
Bruder Heat mask
Other: _____

○ Ocular nutrition
EZ Tears – 2 capsules once per day before meal
Other: _____

○ Topical antibiotics
Azasite, Erythromycin
Other: _____
Directions: _____

○ Restasis / Xiidra
Directions: 1 drop twice a day
Other: _____

○ Steroids
Lotemax / FML / Flarex
Other: _____
Directions: _____

○ Doxycycline
Directions: _____

○ 3% testosterone cream
Directions: _____

○ Other: _____

Thank You

mile.bruijc75@gmail.com