Meibography & Tear film lipid layer

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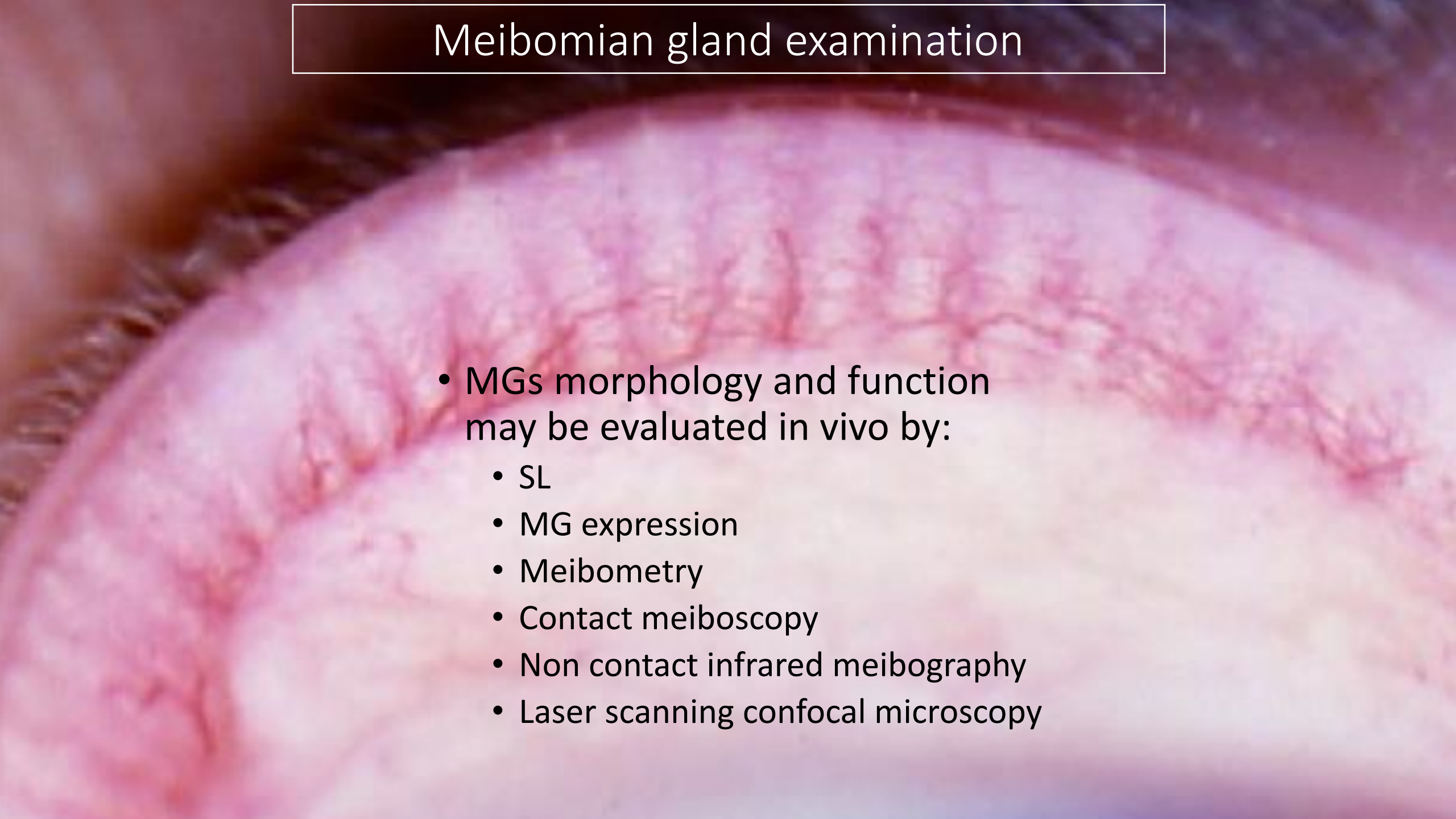
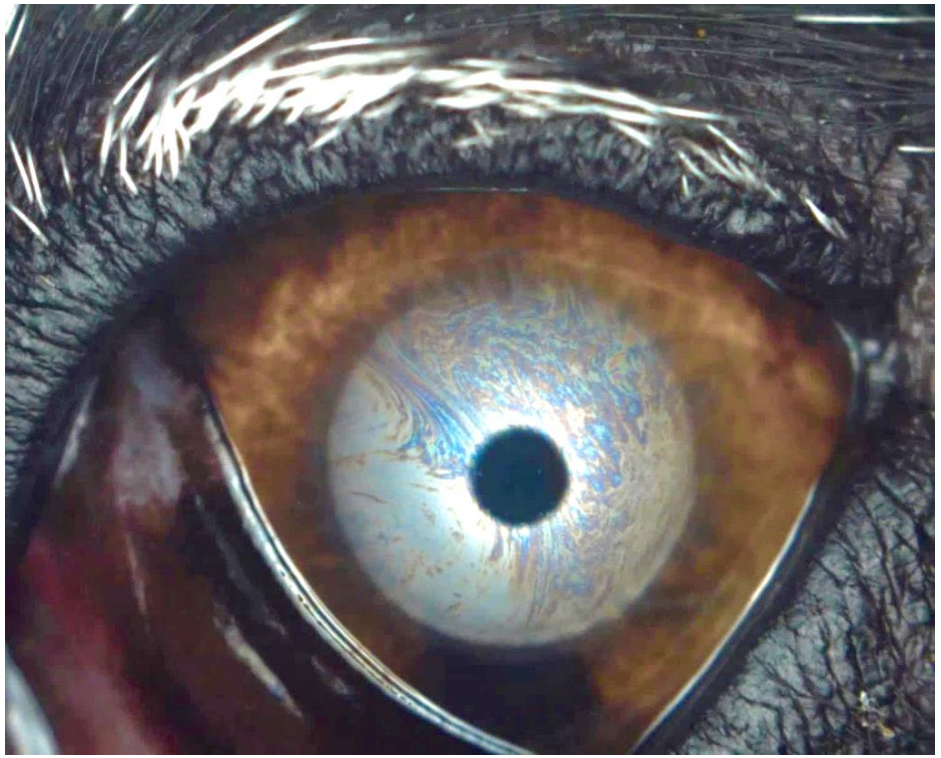
Meibomian gland examination



- MGs morphology and function may be evaluated in vivo by:
  - SL
  - MG expression
  - Meibometry
  - Contact meiboscopy
  - Non contact infrared meibography
  - Laser scanning confocal microscopy

Meibomian glands and tear film lipid layer



- Meibomian lipids are the main component of the superficial lipid layer of the TF, essential for the maintenance of ocular surface health and integrity
- LL examination may add important data to better assess MGs function and TF stability

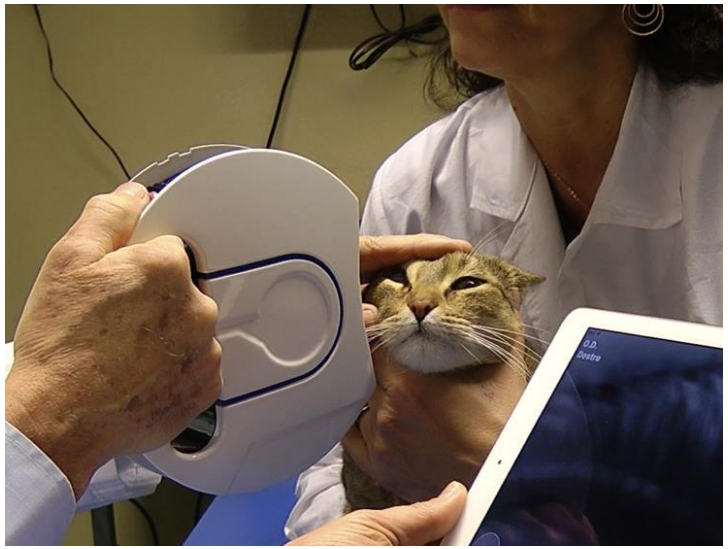
Non Contact Infrared Meibography - NCIM

- Non contact infrared meibography has been first described by Reiko Arita in 2008 to show the effects of ageing in a normal population[1]
- At the 2011 ACVO meeting Masanori Endo presented a poster on “Non contact infrared meibography in dogs and cats” by using a portable probe[2]
- At the 2015 4th COSDW in Tokyo, NCIM has been considered

1. Arita R, Itoh K, Inoue K, et al. Noncontact infrared meibography to document age-related changes of the meibomian glands in a normal population. Ophthalmology,115:911–915, 2008
2. Endo M, Horie A, Higaya Y. Noncontact infrared meibography in dogs and cats. ACVO Conference Proceedings, 11, Hilton Head, SC, USA, 2011

NCIM by hand held meibographs

- MGA-VET: hand held meibograph wi-fi connected to an iPad



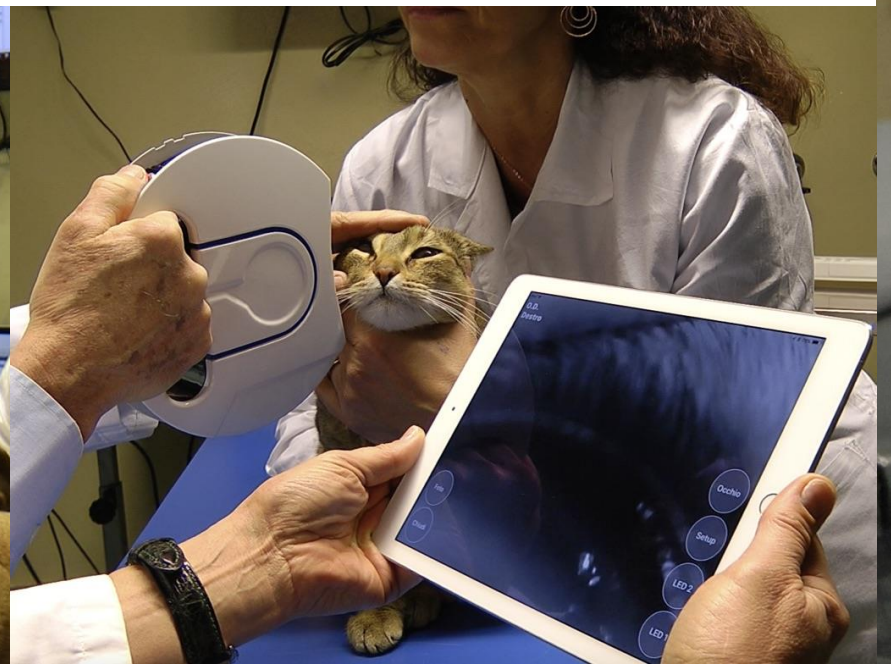
NCIM by hand held meibographs

- OSA-VET: hand held Ocular Surface Analyser cable connected to a computer

NCIM in dogs & cats

Feasibility

- The animal cooperative temper and the owner's compliance are essential requirements
- No need of specific restraint for dogs and cats if the owner and/or an assistant hold the head
- Short training period



NCIM in horses

- Most horses have been sedated with detomidine (10µg/Kg) and butorphanol (10 µg/Kg) and an auricolopalpebral nerve block has been carried out
- All exams were performed when clinical signs of deep sedation were evident by placing the animal's head on a support

D
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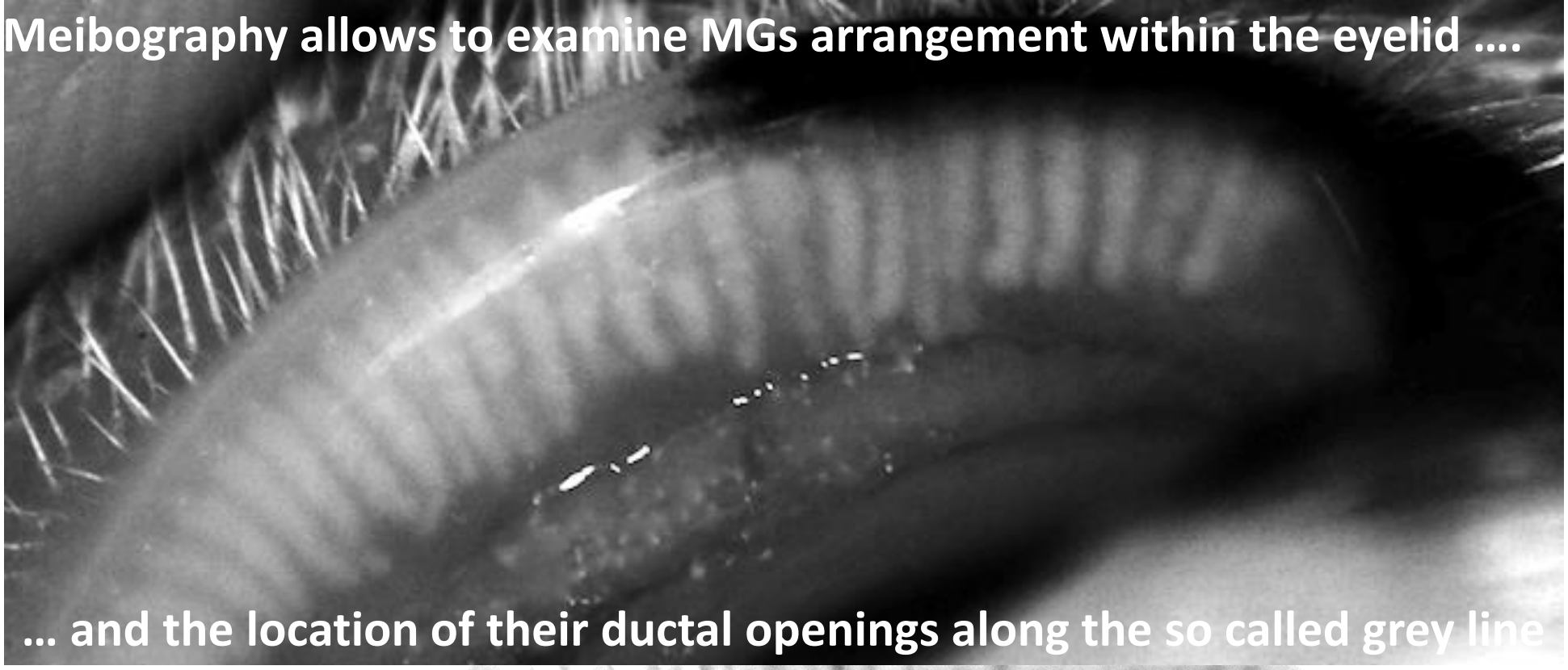
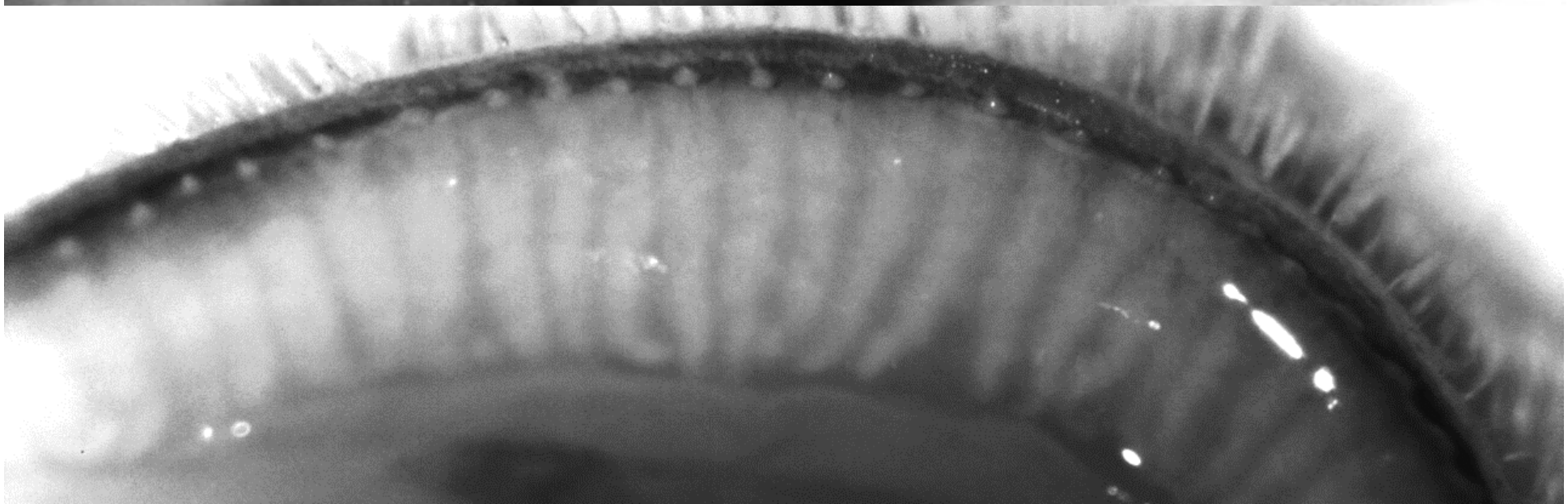
Meibography allows to examine MGs arrangement within the eyelid ….



… and the location of their ductal openings along the so called grey line



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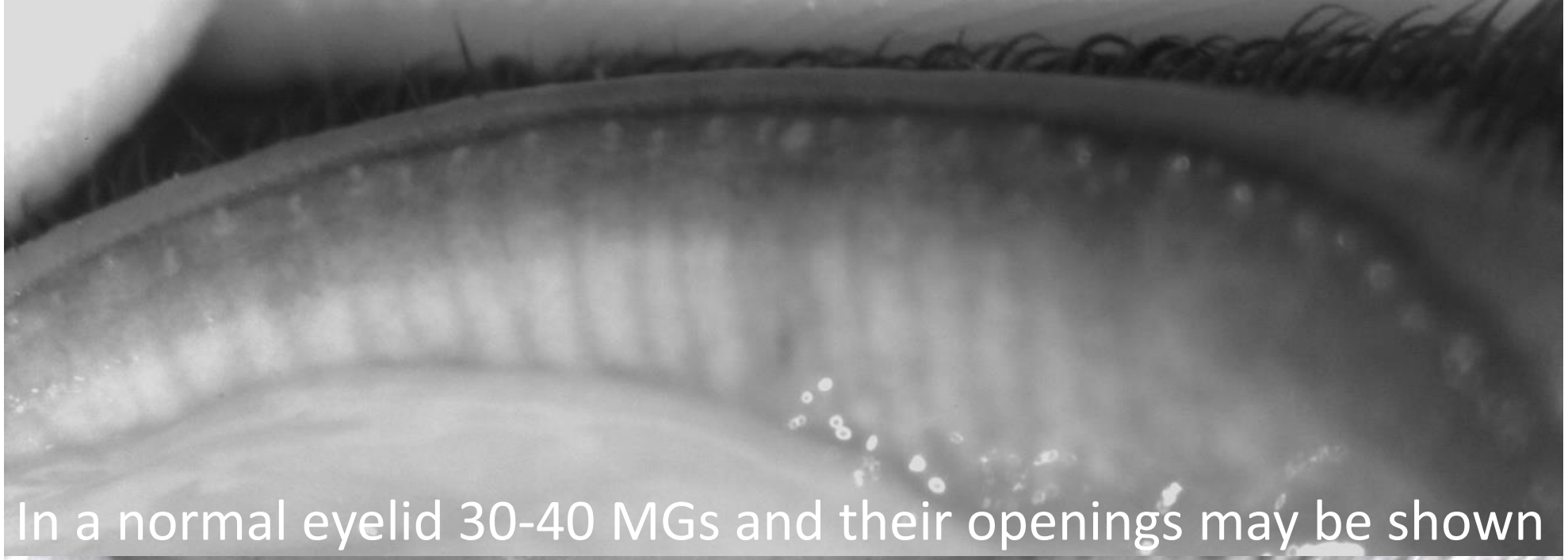
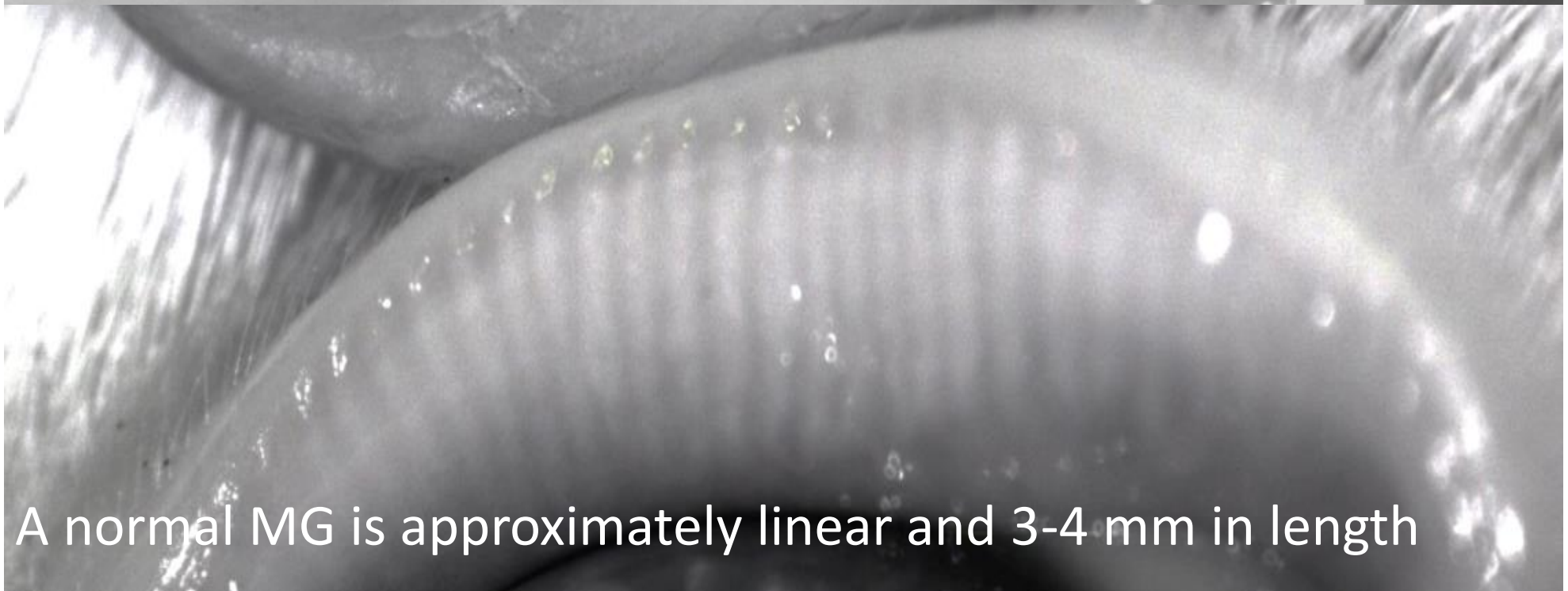


In a normal eyelid 30-40 MGs and their openings may be shown



A normal MG is approximately linear and 3-4 mm in length

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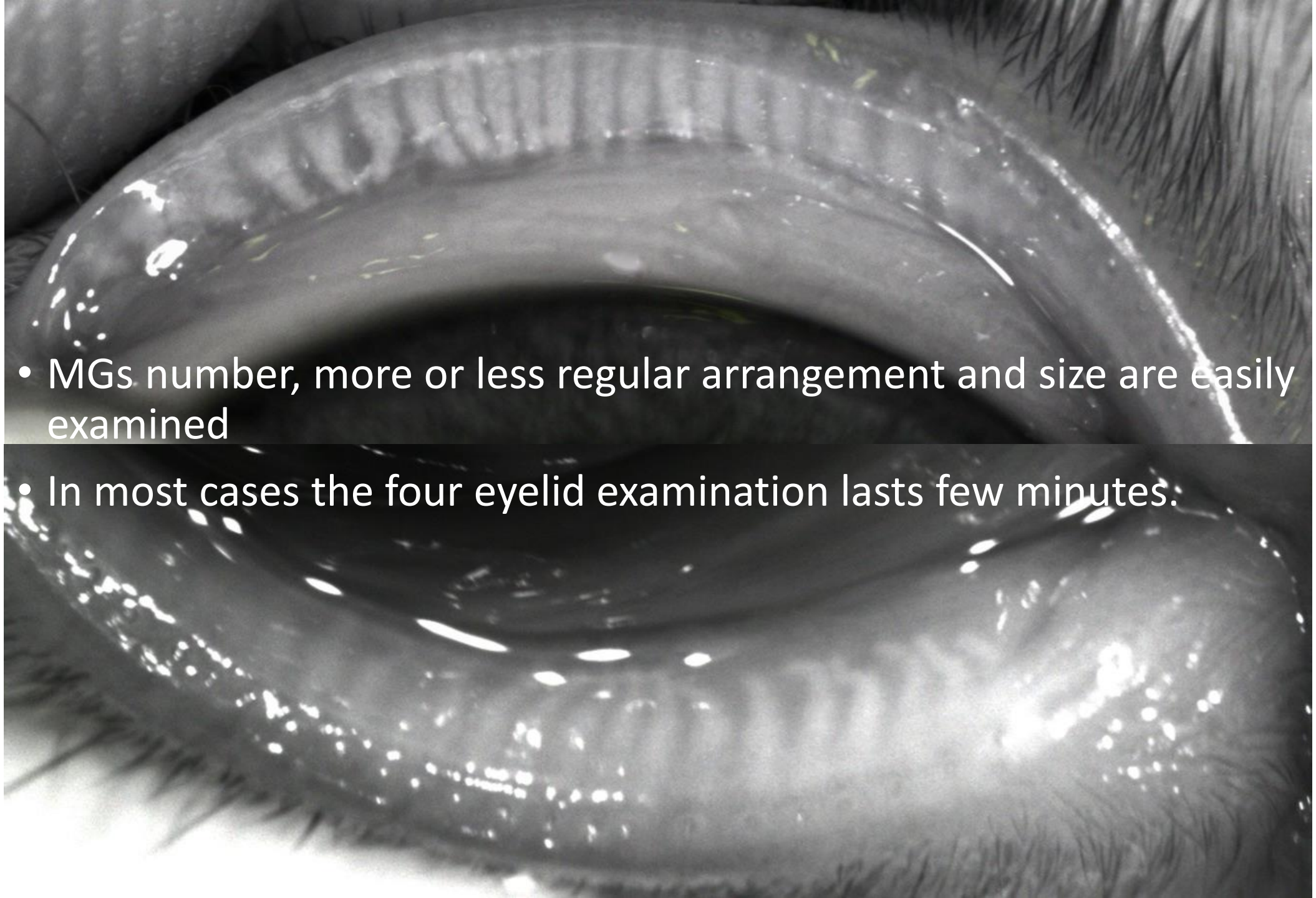
- Meibography is easily performed also in cooperative cats



C
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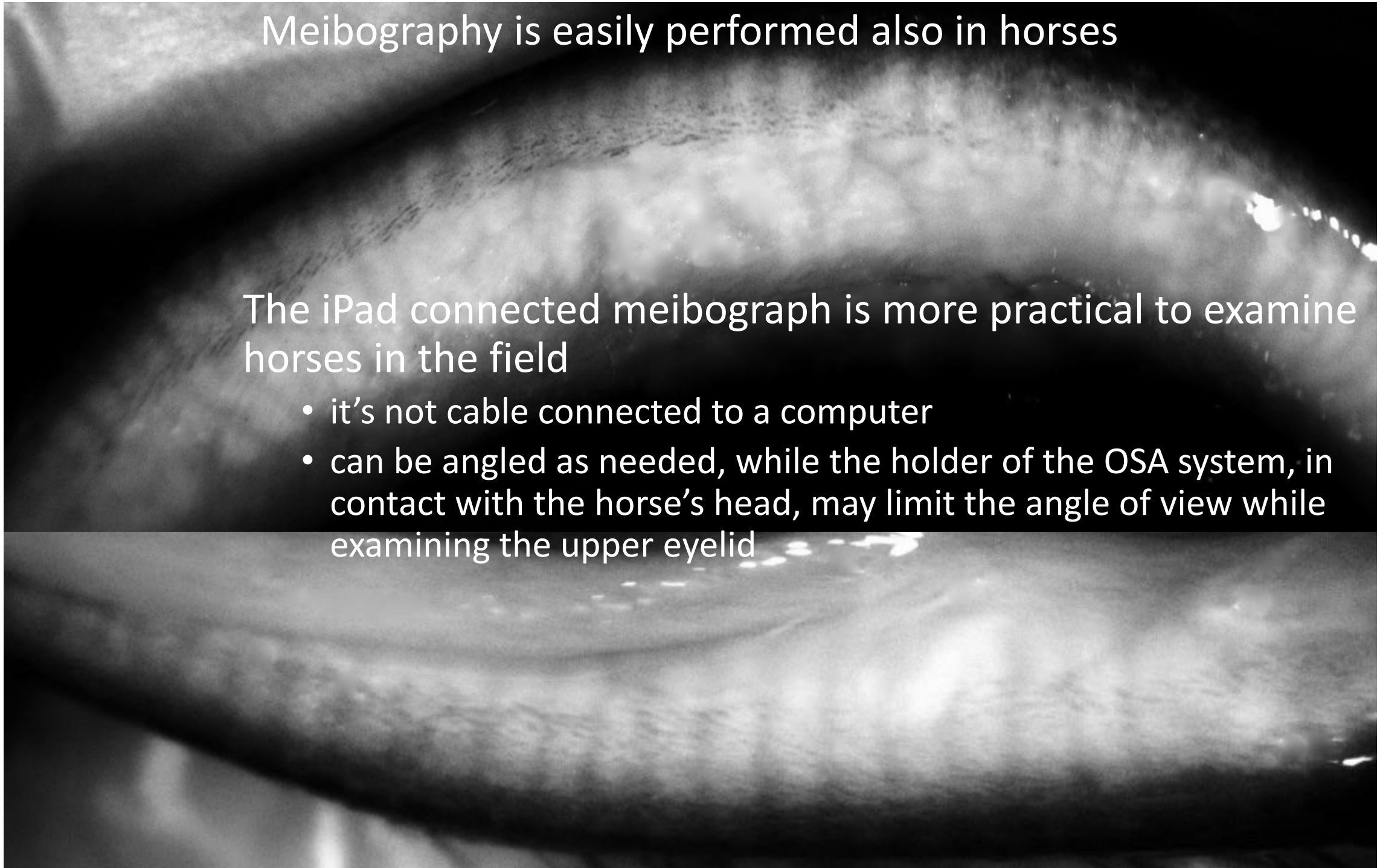
- MGs number, more or less regular arrangement and size are easily examined
- In most cases the four eyelid examination lasts few minutes.

Meibography is easily performed also in horses



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The iPad connected meibograph is more practical to examine horses in the field

- it’s not cable connected to a computer
- can be angled as needed, while the holder of the OSA system, in contact with the horse’s head, may limit the angle of view while examining the upper eyelid

H
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Since the animal is not annoyed by a visible light, it’s possible to examine a cooperative horse without sedation

- *MGs share strong similarities with the hair follicles of the cilia in embryologic development and structure*
- *If germ cells fail to differentiate completely to MGs, they become pilosebaceous units instead*

Meibomian gland dysfunction (MGD)

- *MGD is a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion*
  *This may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation, and ocular surface disease**
- Epidemiology in humans
  - Population-Based Studies: prevalence varies widely, from 3.5% to almost 70%, it's higher in reports arising from Asian populations**
  - Clinic-Based Studies: from 20% in UK to approximately 60% in Japan
  - MGD is considered a main cause of evaporative DED

* Nelson JD et al. The International workshop of Meibomian gland dysfunction: report of the definition and classification subcommittee. IOVS 52,4,1930-1937, 2011

** Knop E et al. The International workshop of Meibomian gland dysfunction: report of the subcommittee on anatomy, physiology and pathophysiology of the Meibomian gland. IOVS 52,4,1938-1978, 2011

Source: https://www.dryeyeandmgd.com

Meibomian gland dysfunction

- In dogs: Corinna Eule's study on Blepharitis and MGs. All criteria defined for MGD in humans were present in 37.5% of histopathological samples *
- In dogs: MGD studied and described by Yasunary Kitamura, Akihiko Saito and Maehara Seiya **

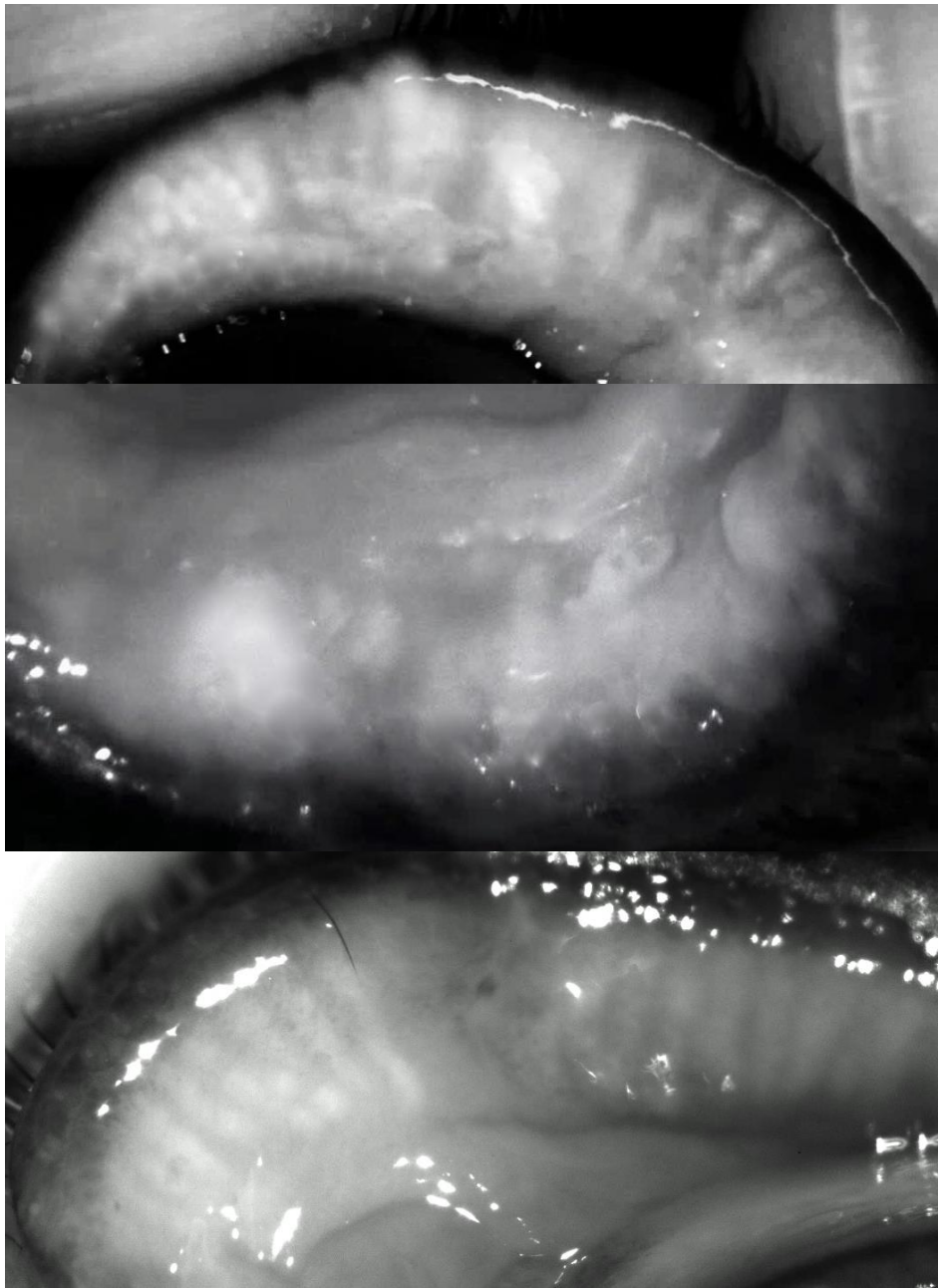
Old English Sheepdog, female, 8 years old

* Eule JC, Schleicher-Przytarski A, et al. Blepharitis and Meibomian gland dysfunction-like syndrome in dogs - Histologic evidence of a clinically neglected hot spot. ECVO Conference Proceedings, 26, Berlin, 2010

** Kitamura Y, Saito A, Maehara S. Observation of canine meibomian gland with noncontact-type meibography. Journal of Japanese Veterinary Medical Association 67: 857-861, 2014

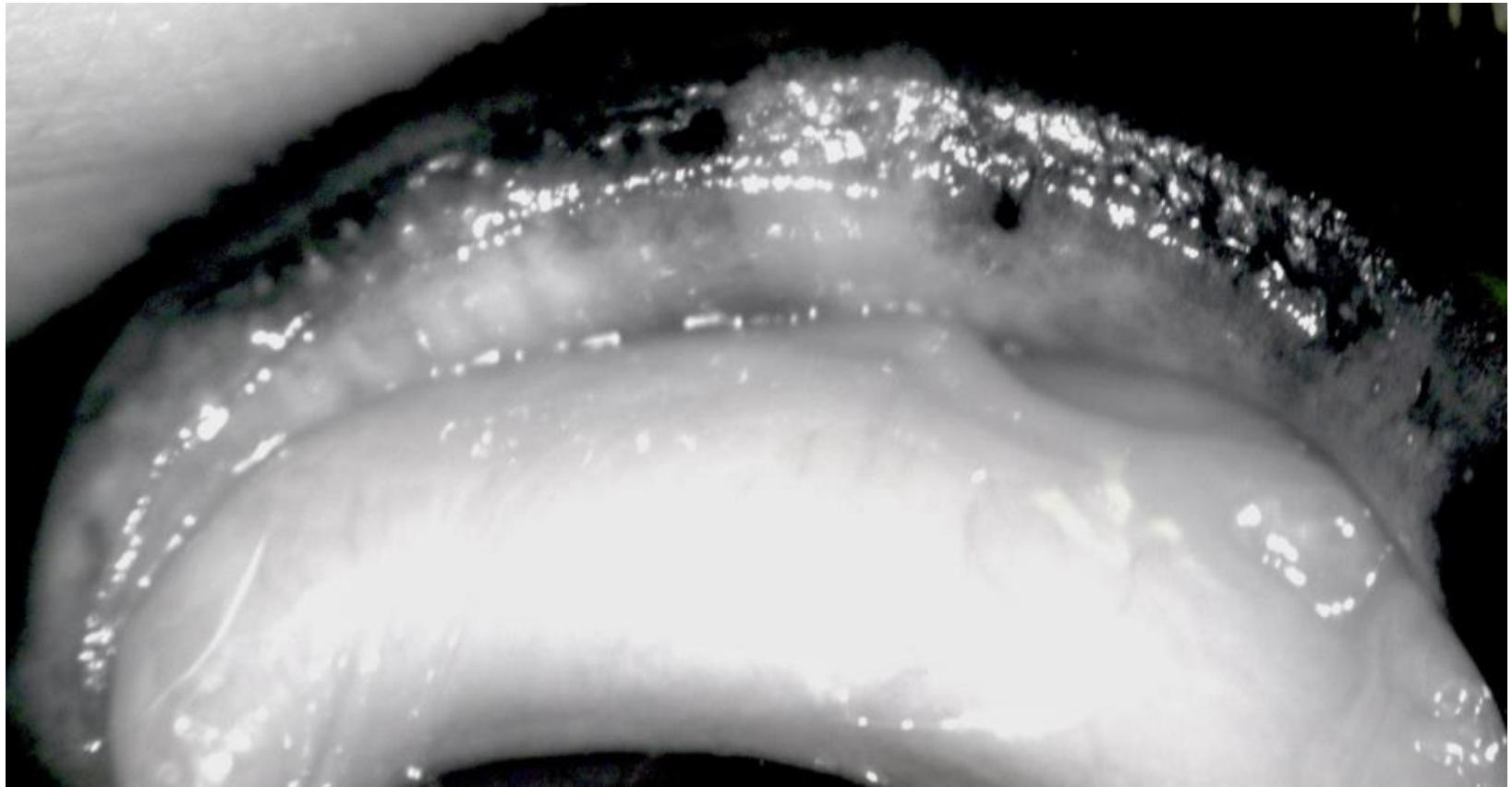
Meibomian gland dysfunction

- Anatomical changes occur in all studied species as a consequence of:
  - ageing
  - ductal opening hyperkeratinization
  - increased meibum viscosity
  - inflammatory mediators
  - bacterial lipid-degrading enzymes
  - hormonal changes
  - topical or systemic medications



Meibomian gland dysfunction

- MGD was diagnosed in 39 over 68 dogs I examined by NCIM for a history of long lasting OSD (57%)
- MGD was present in 7 over 13 KCS dogs (54%)



Palù, Crossbreed, female, 9 years old

CLINICAL SIGNS

- Continuous blinking:
  - 25 incomplete / 6 complete / min
- Red and wet eyes

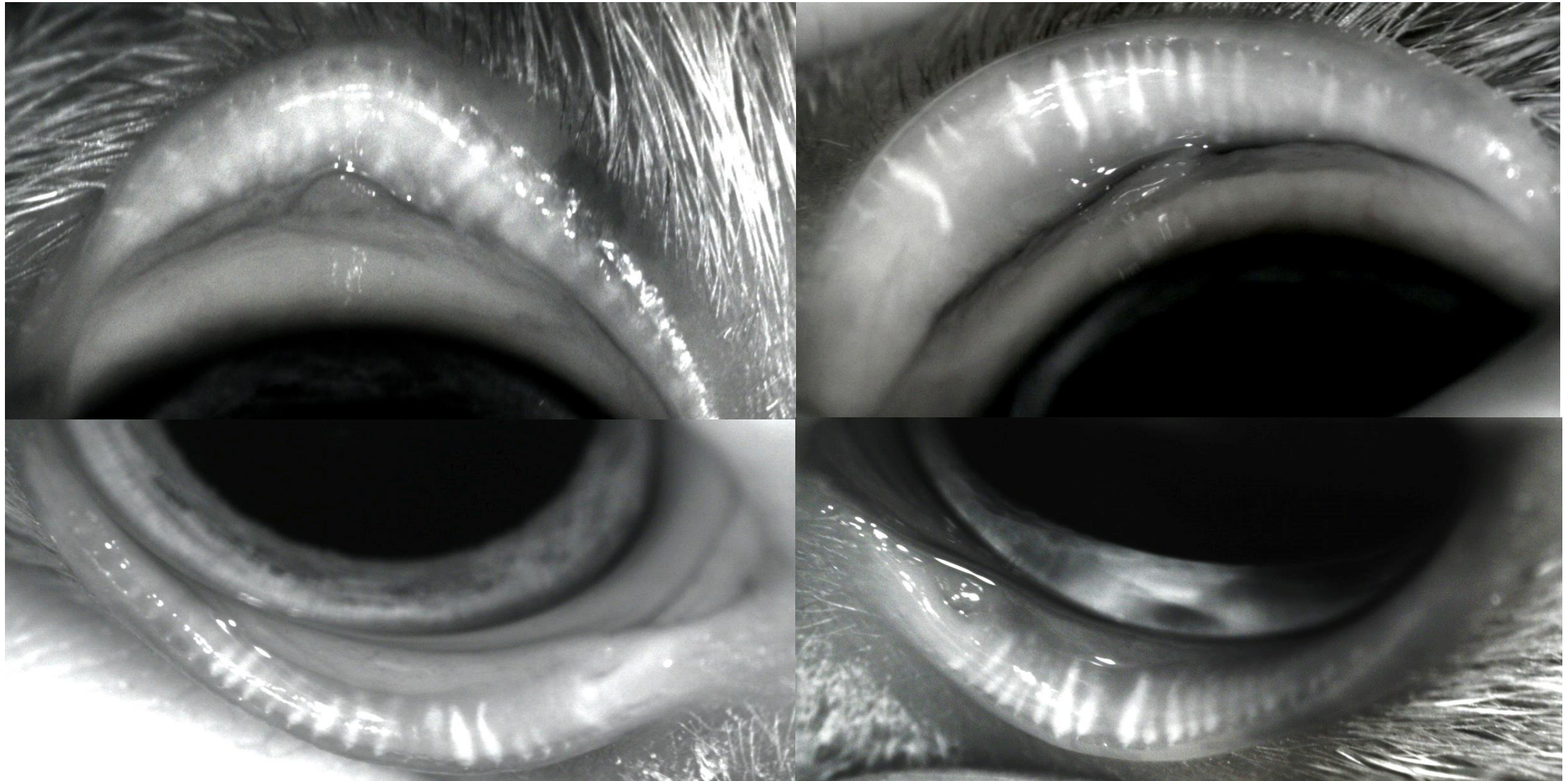
Palù

CLINICAL HISTORY

- Granulomatous sebaceous adenitis
- Uncommon skin disease found in some breeds of dogs (rarely in cats, rabbits and horses)
- Inflammatory response against the dog's sebaceous glands → destruction of the glands (probably immuno-mediated)

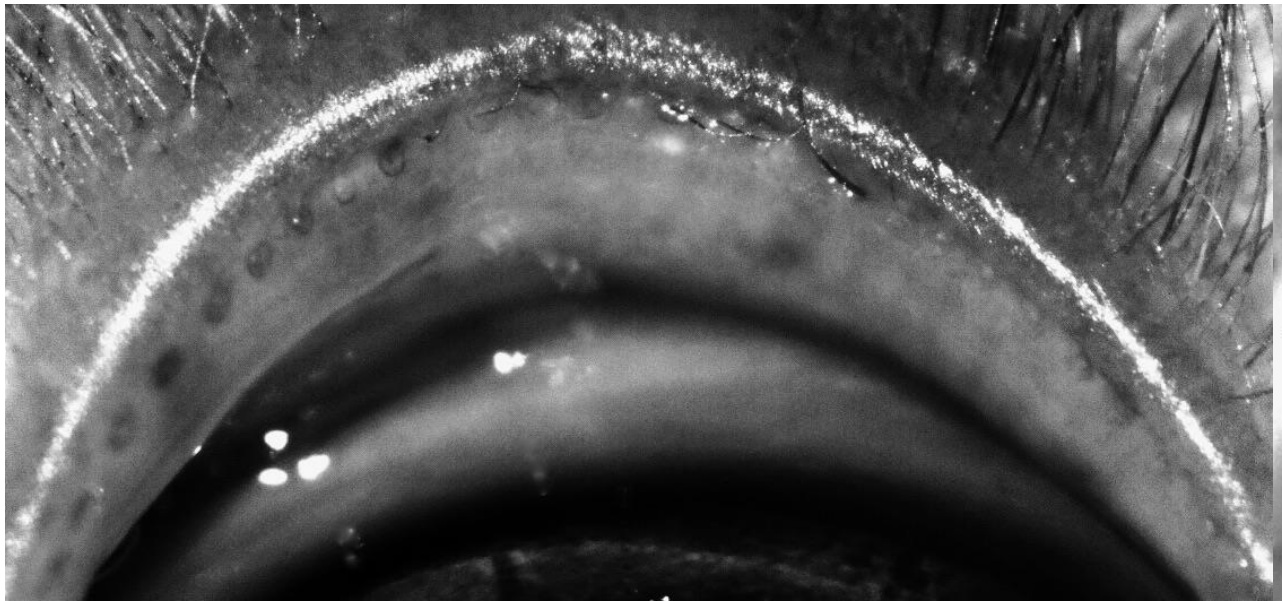
Palù: meibomian gland dysfunction

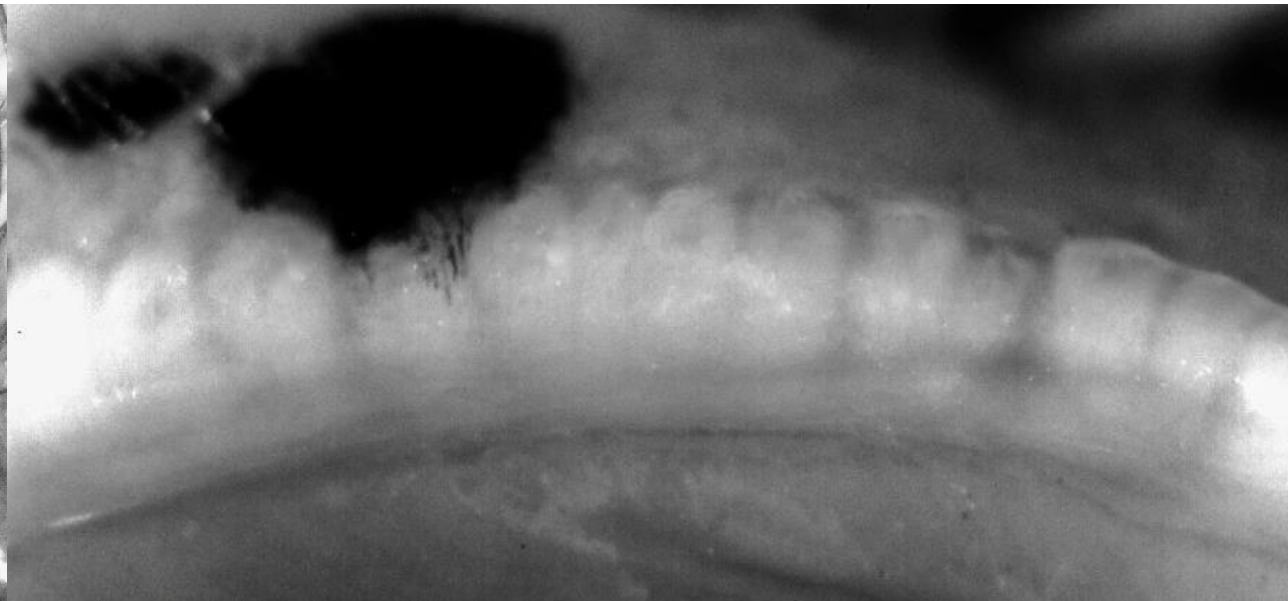
MGs atrophy, shortening, dropout



Meibomian gland dysfunction

- In some cases of MGD the eyelid mucocutaneous junction may move posteriorly with retroplacement of ductal openings
- The mucosa may also spread forward, so that the orifices appear to lie in mucosal tissue





Meibomian gland dysfunction

- MG expression can be performed as an indicator of MG function
- Expression may demonstrate the terminal ductule plugged with inspissated secretion

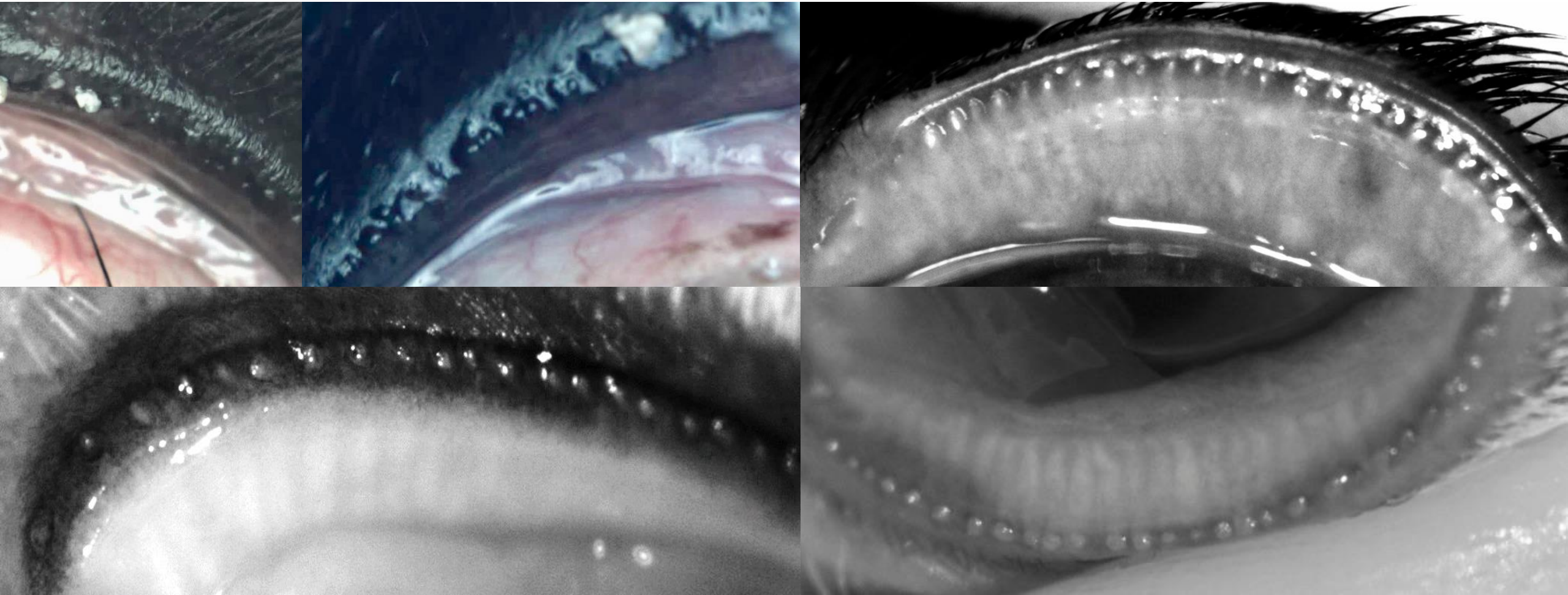
Semisolid plug of toothpastelike consistency

Normal:clear to light yellow

Abnormal: whitish-gray to yellow

Meibomian gland dysfunction

- Scattered orifices may be capped by a dome of oil with a tough surface



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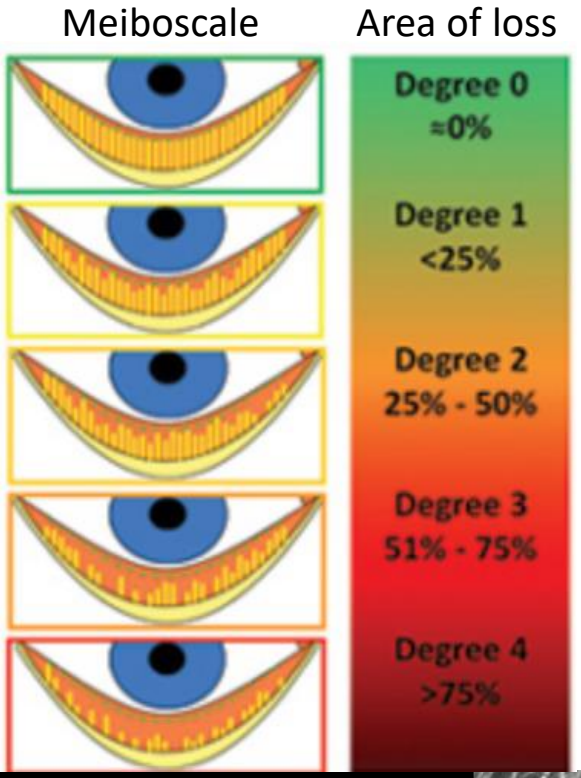
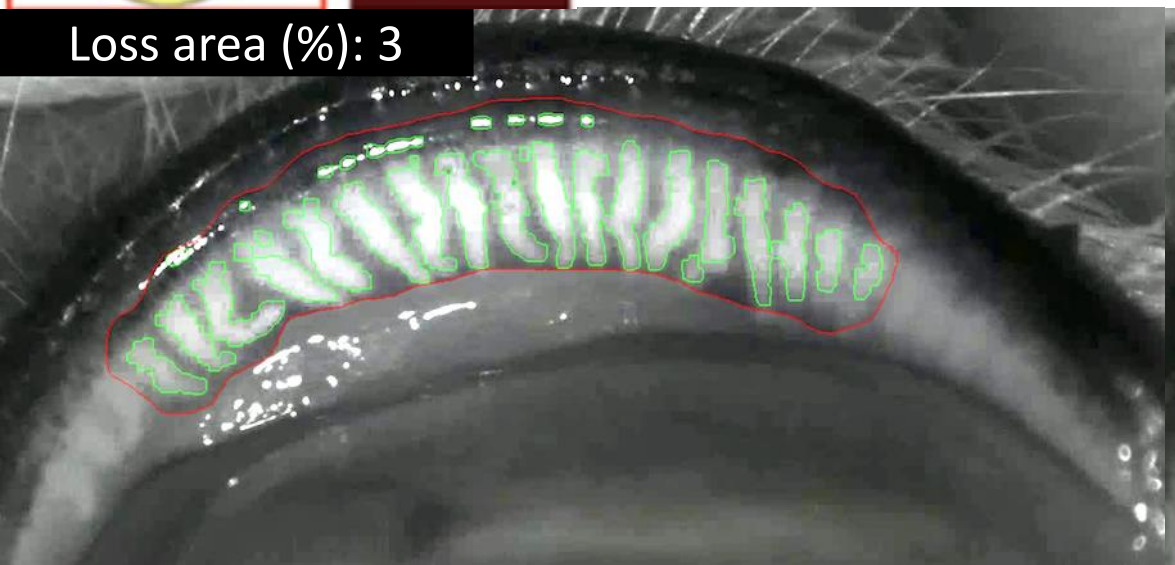
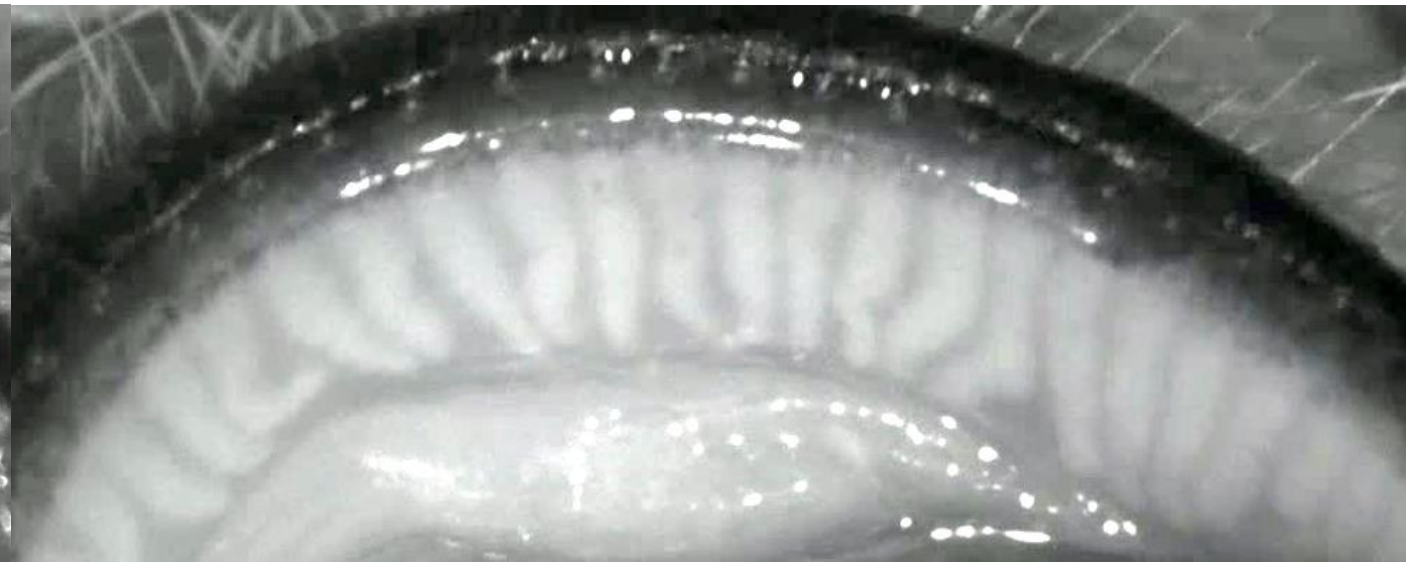
MGs scoring systems: meiboscore



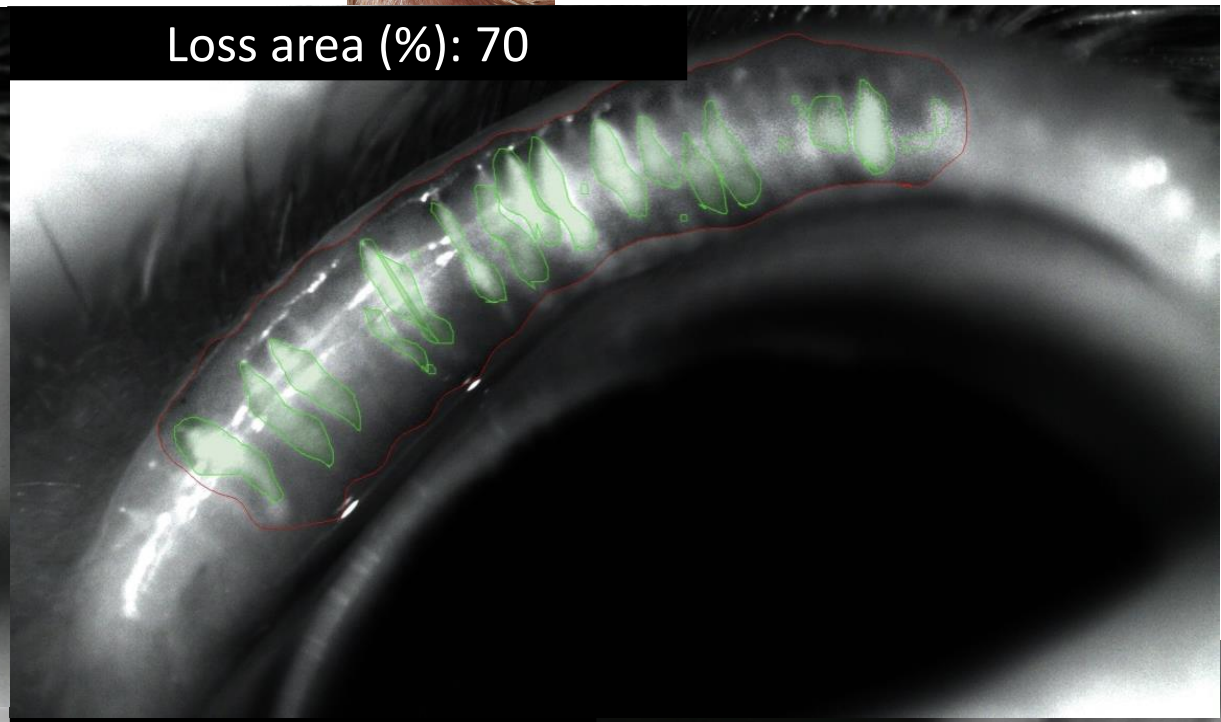
- On selected images I checked for meiboscore: ratio of meibomian gland area to total analysis area
- Meiboscore evaluates only areas of MGs dropout



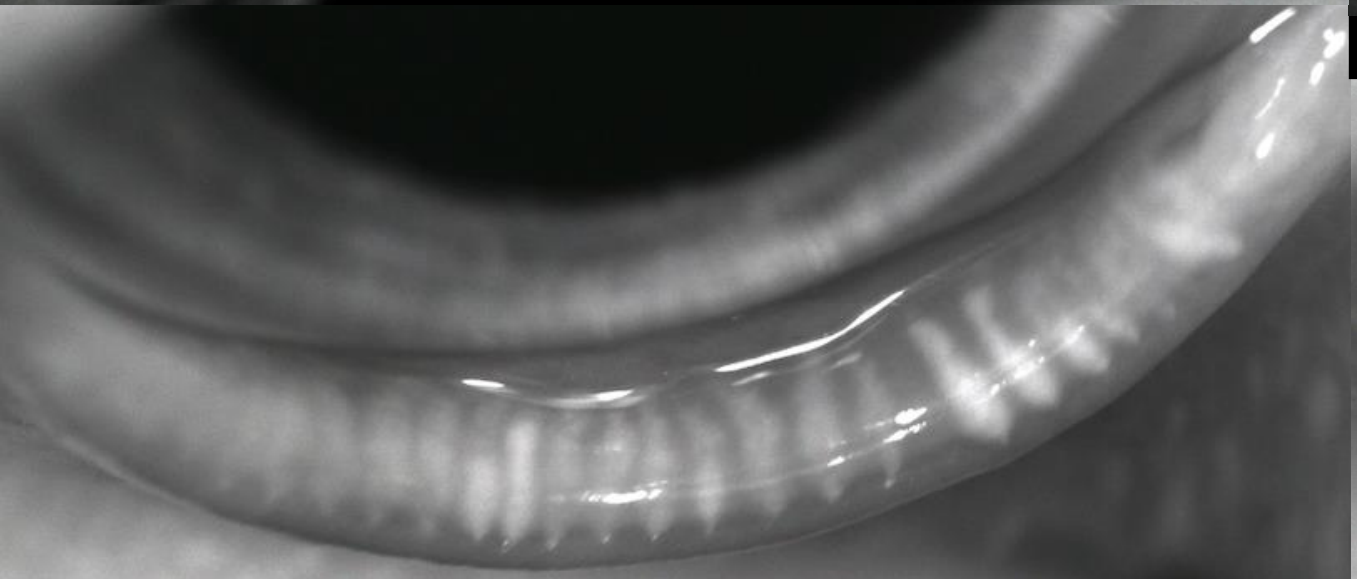


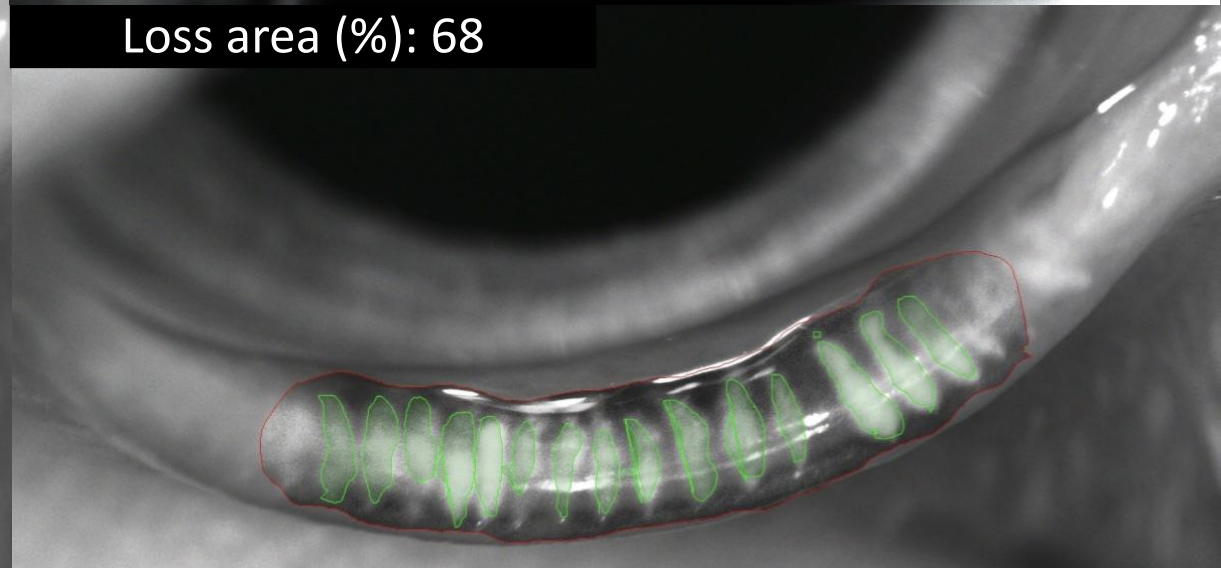
MGs scoring systems

Palù, granulomatous sebaceous adenitis and MGD



Loss area (%): 70

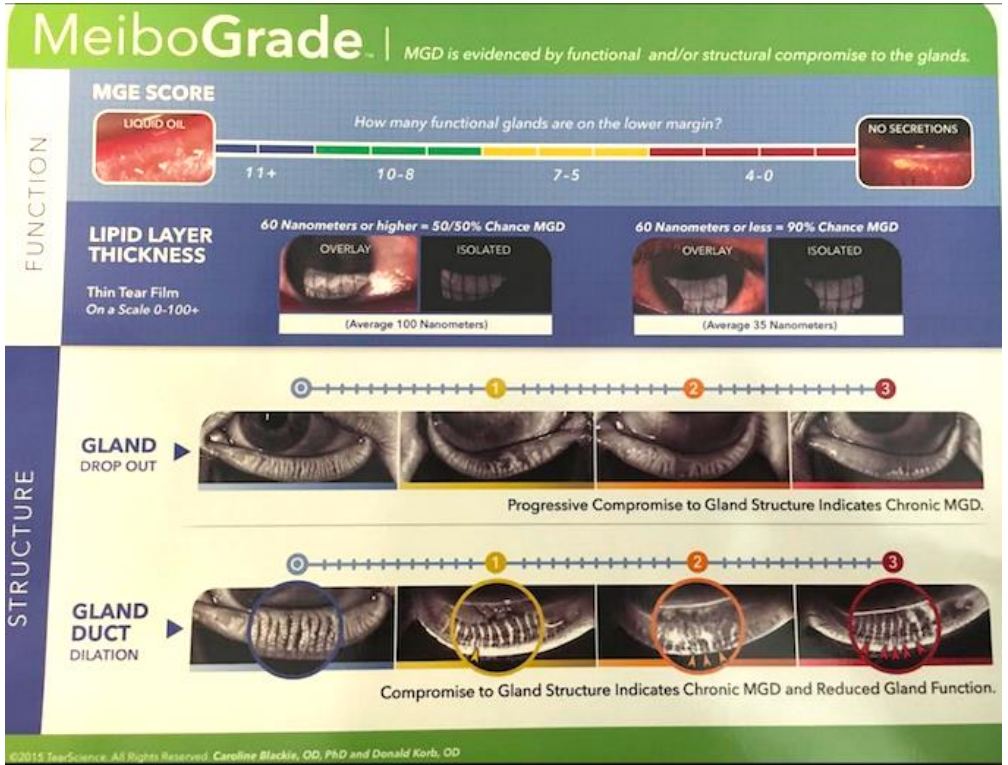




Loss area (%): 68

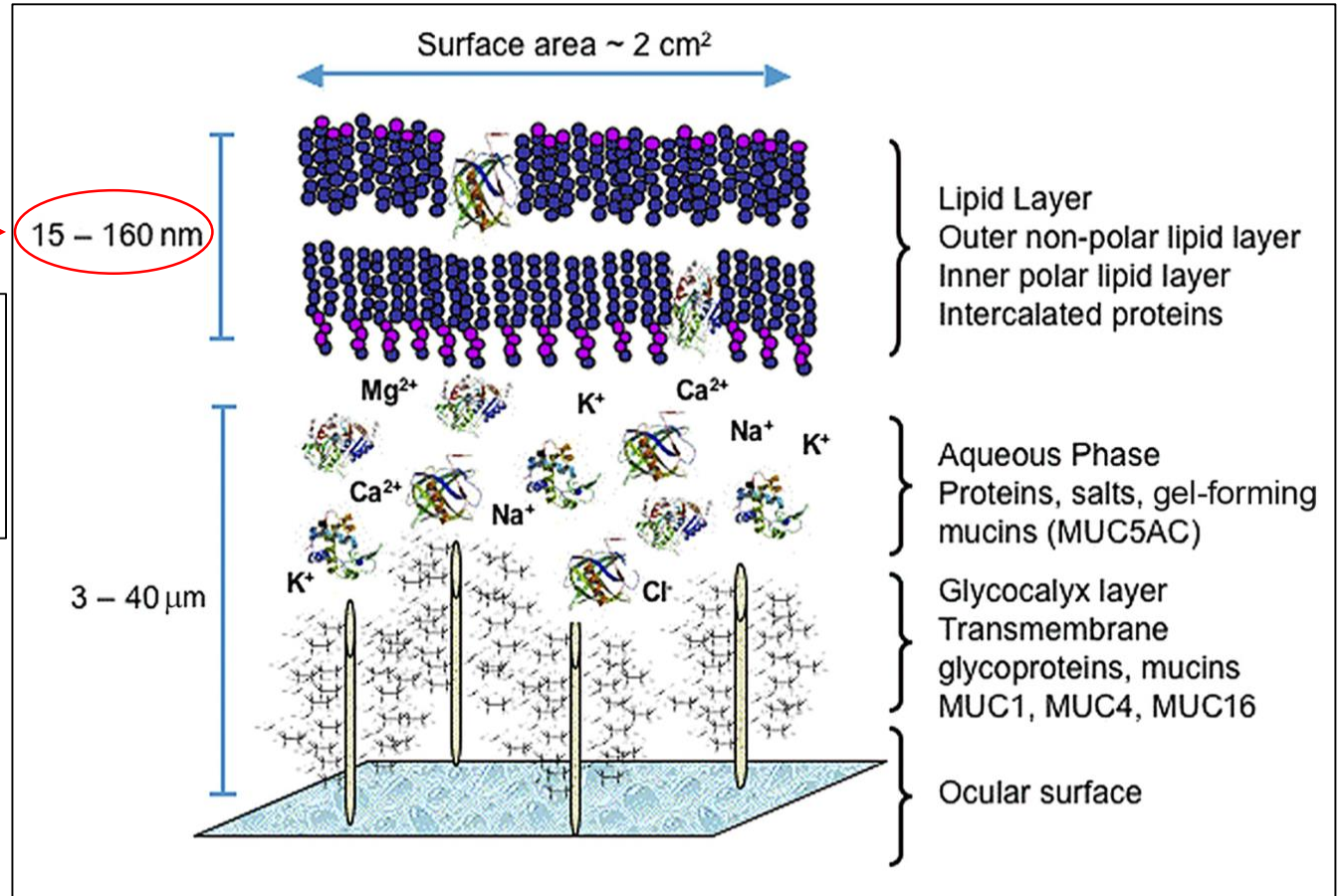
MGs scoring systems: meibograde

- Meibograde is a more accurate scoring systems based on described MGs histopathologic changes: distortion, shortening, dropout
- A score of 0 through 3 is assigned to each of the three categories
- A meibograde from 0 through 9 per eyelid is obtained by summing the scores



MGs and Tear Film Lipid Layer (TF LL)

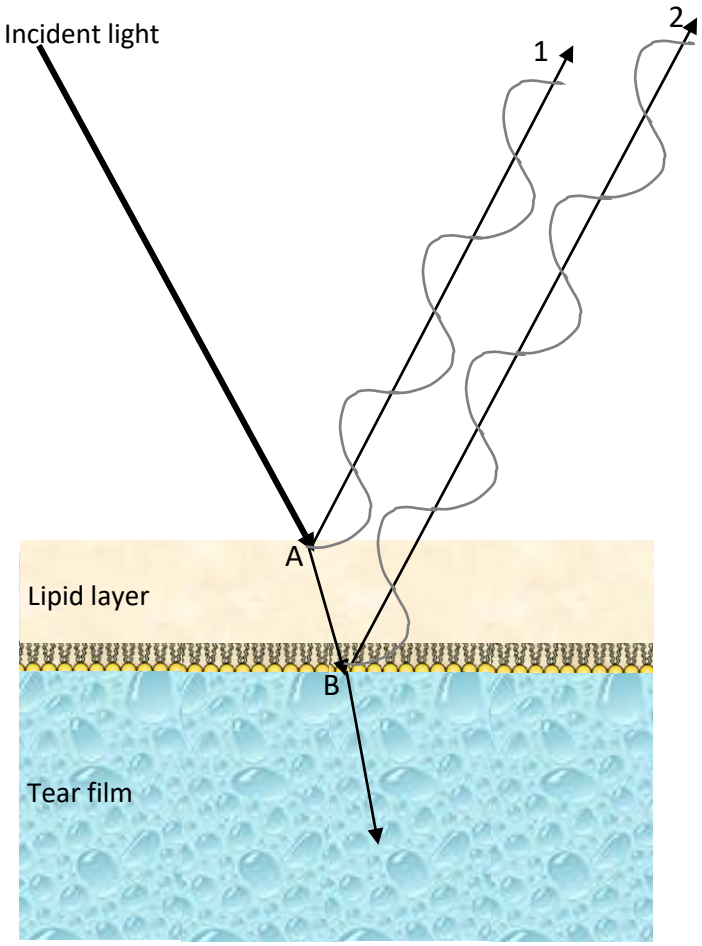
- Meibomian lipids are the main component of the superficial TF LL
- MGD alters the TF LL, increases aqueous phase evaporation and decreases TF stability
- LL composition, probably more than LL thickness, is highly correlated with TF thinning rate caused by evaporation

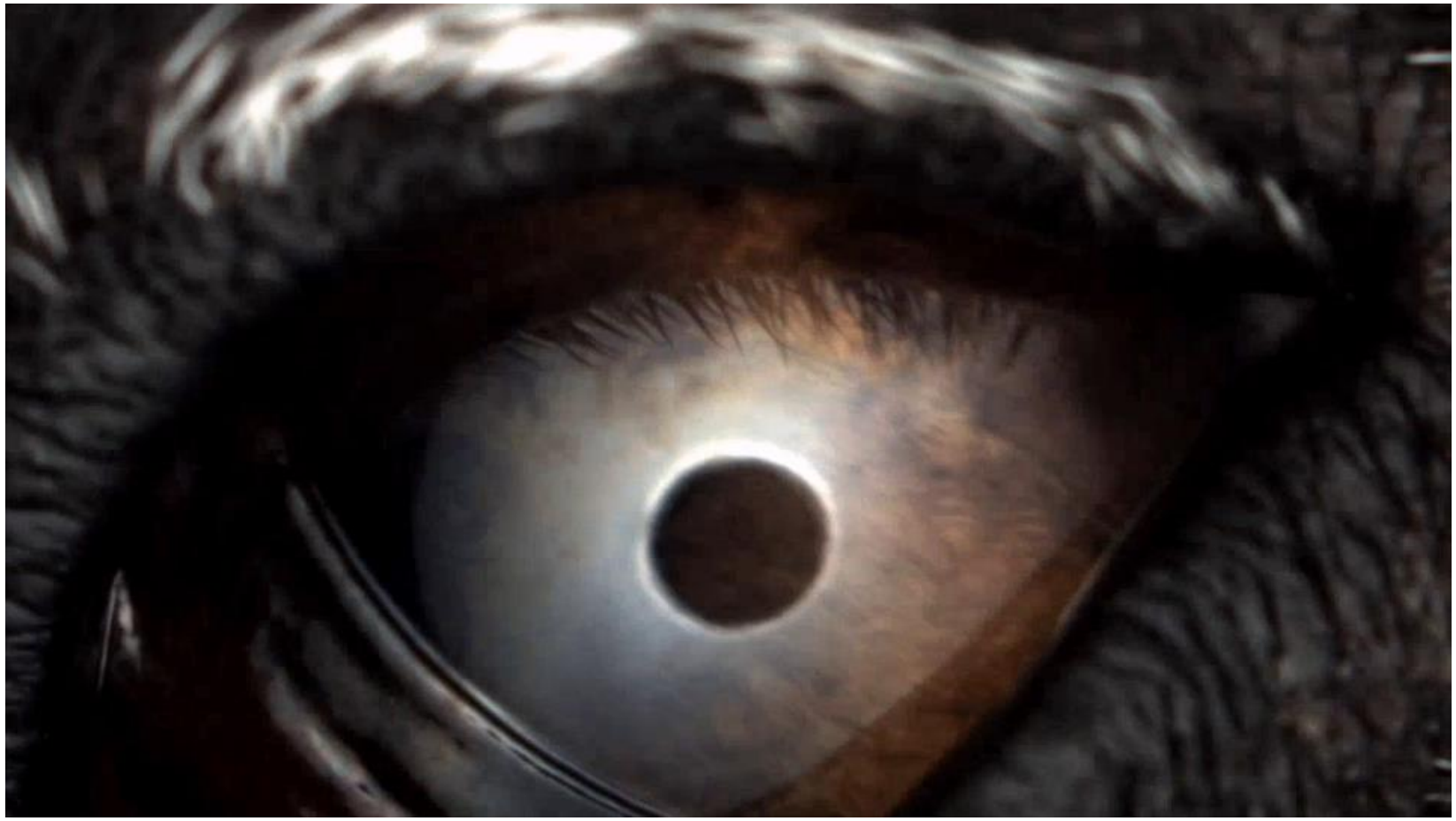


Nichols KK, Foulks GN, Bron AJ et al. The International Workshop on Meibomian Gland Dysfunction: Executive Summary. IOVS, Special Issue 2011, Vol. 52, No. 4

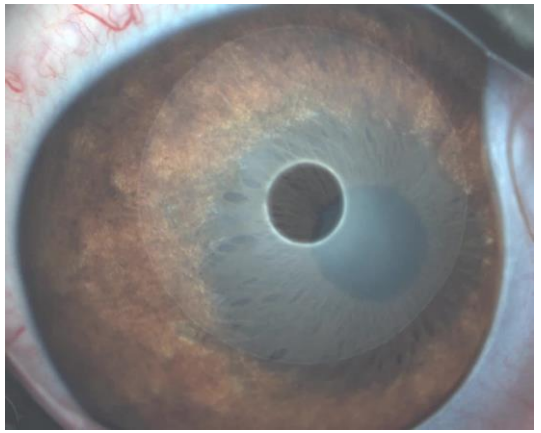
Tear Film Lipid Layer (TF LL) examination

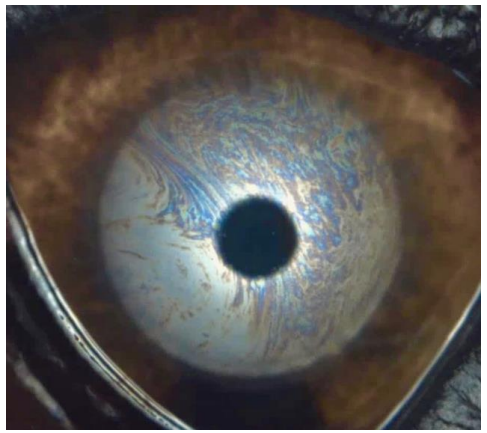
The TF LL can be visually examined by observing interference patterns generated by light reflected from its front surface (air-lipid boundary) and the lower surface (lipid-aqueous boundary)



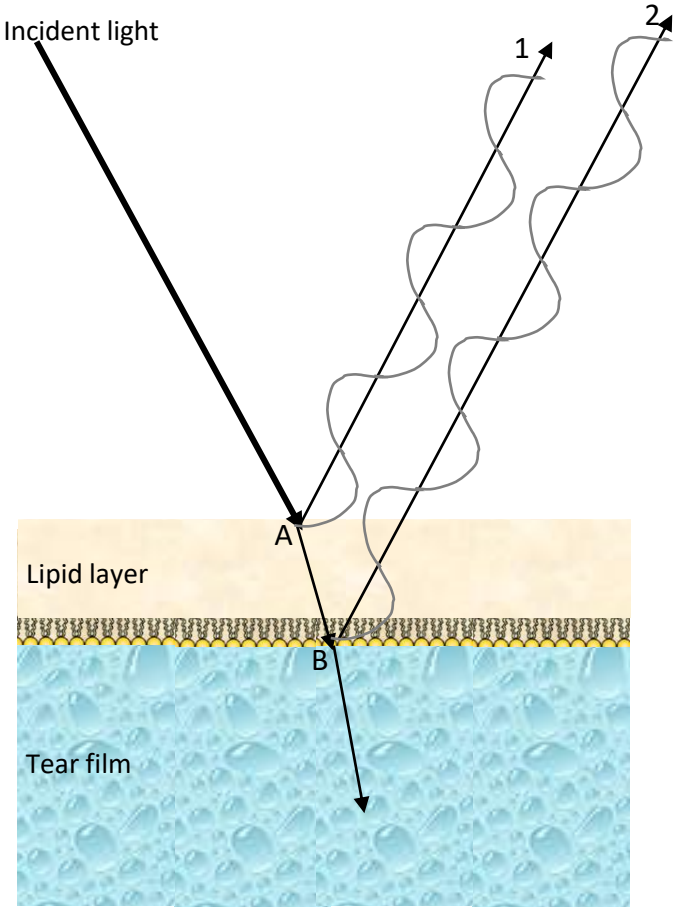


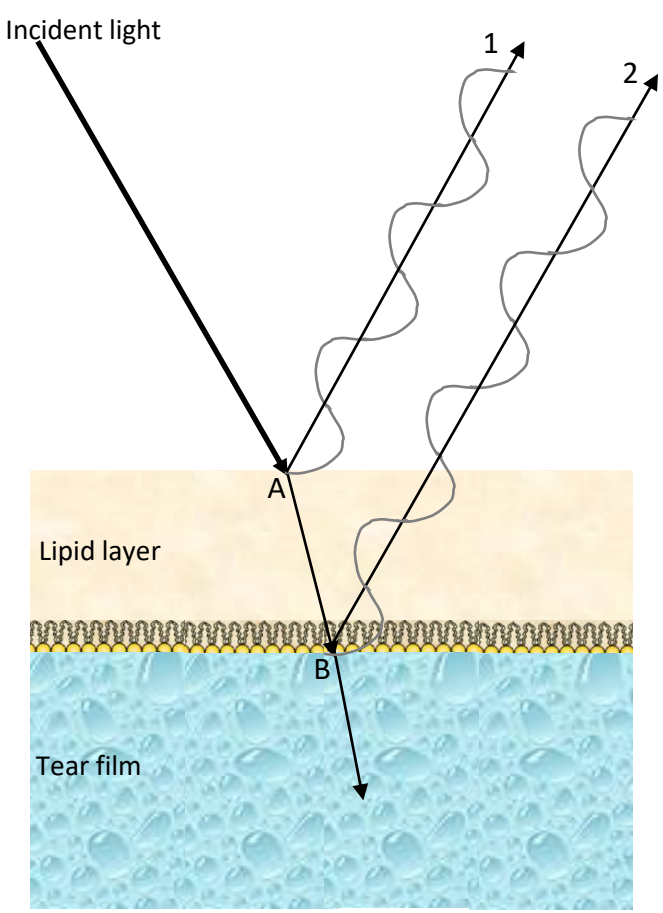
Principles of Thin Film Interferometry



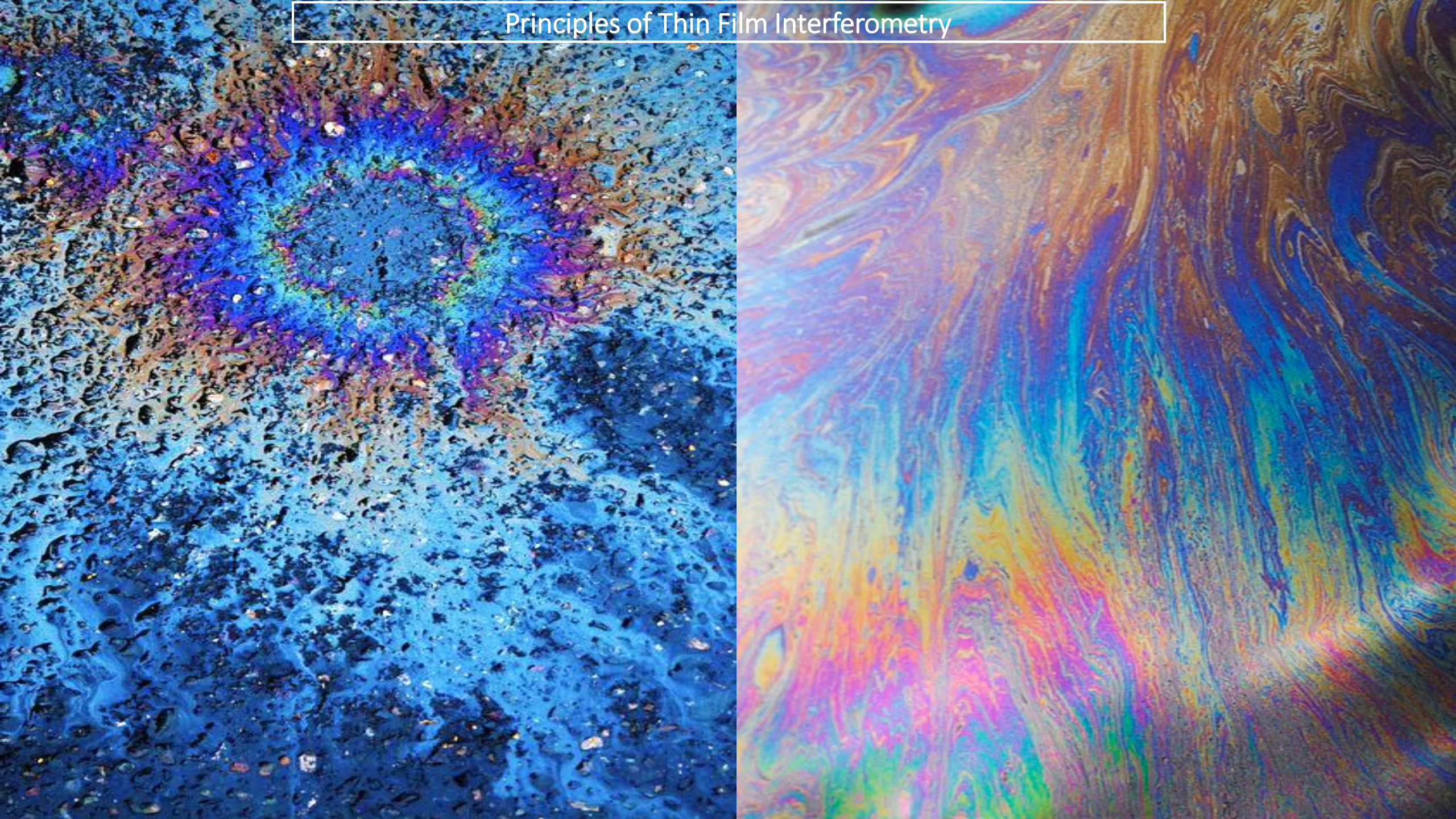


- *Light striking a thin film is partially reflected (ray 1) and partially refracted at the top surface (A)*
- *The refracted ray is partially reflected at the bottom surface (B) and emerges as ray 2*
- *The coloured interference fringes are caused by the specular reflection at A and B and the phase difference between ray 1 and 2*
- *Colour intensity and distribution vary according to the thickness of the film and the indices of refraction of the various media*





Principles of Thin Film Interferometry



TF LL interferometry

- Polarized light biomicroscopy in dogs & cats by Carrington
  - 16 different interference colours
  - 3 principal variants of surface lipid morphology (dogs) (wave, islet and granitiform)

Polarized light biomicroscopic observations on the pre-corneal tear film. 1. The normal tear film of the dog

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* Department of Pathology, Institute of Ophthalmology, 17/25, Cayton Street, London EC1V 9AT; † Royal Veterinary College Field Station, Hawkshead House, Hawkshead Lane, North Mymms, Hatfield, Herts. AL9 7TA; ‡ 24 Moreton Street, London SW1; § Contact Lens and Prosthesis Department, Moorfields Eye Hospital, City Road, London EC1V 2PD

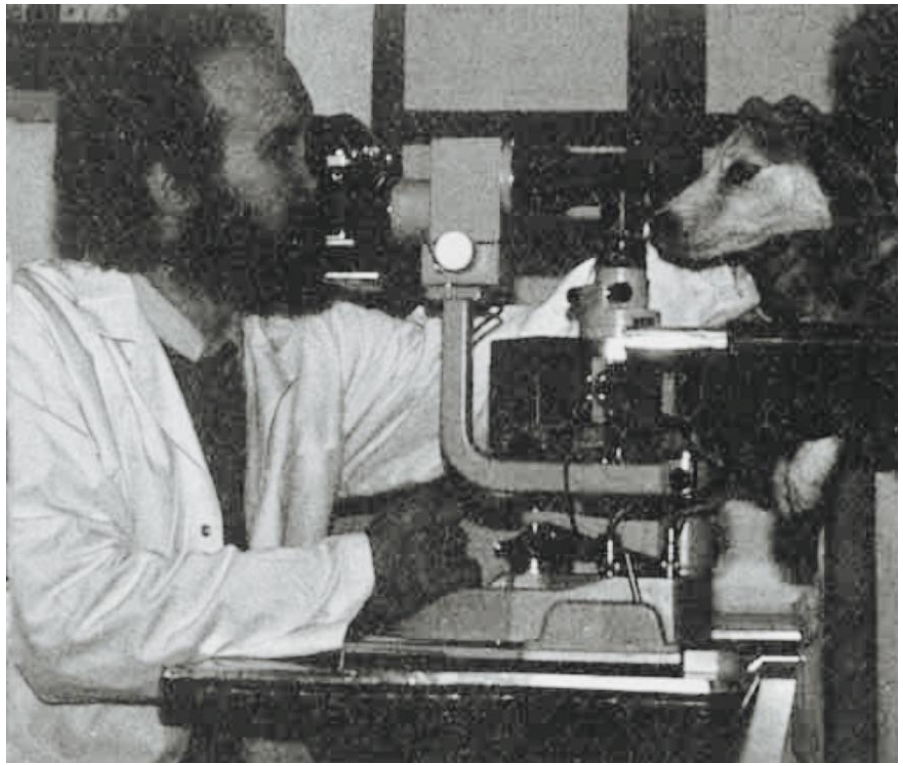
J. small Anim. Pract. (1987) **28,** 605–622

Polarized light biomicroscopic observations on the pre-corneal tear film. 2. Keratoconjunctivitis sicca in the dog

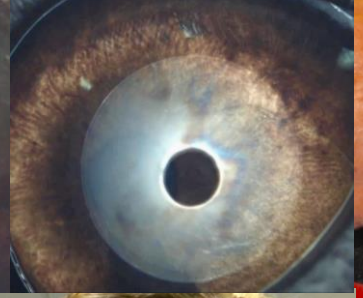
J. small Anim. Pract. (1987) **28,** 671–679.

Polarized light biomicroscopic observations on the pre-corneal tear film. 3. The normal tear film of the cat

J. small Anim. Pract. (1987) **28,** 821–826





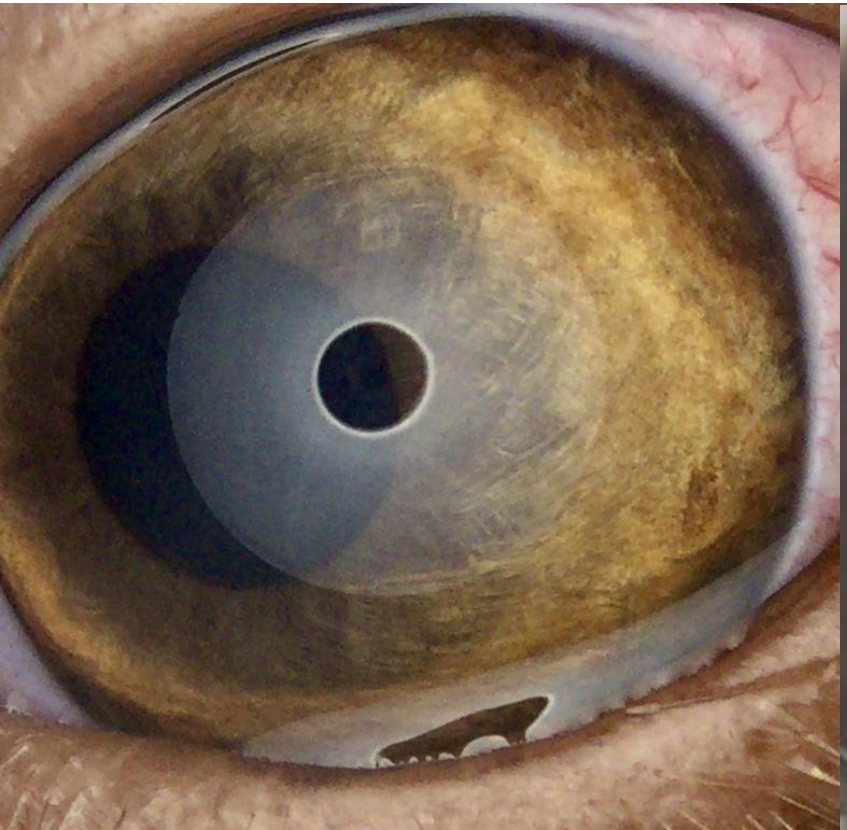



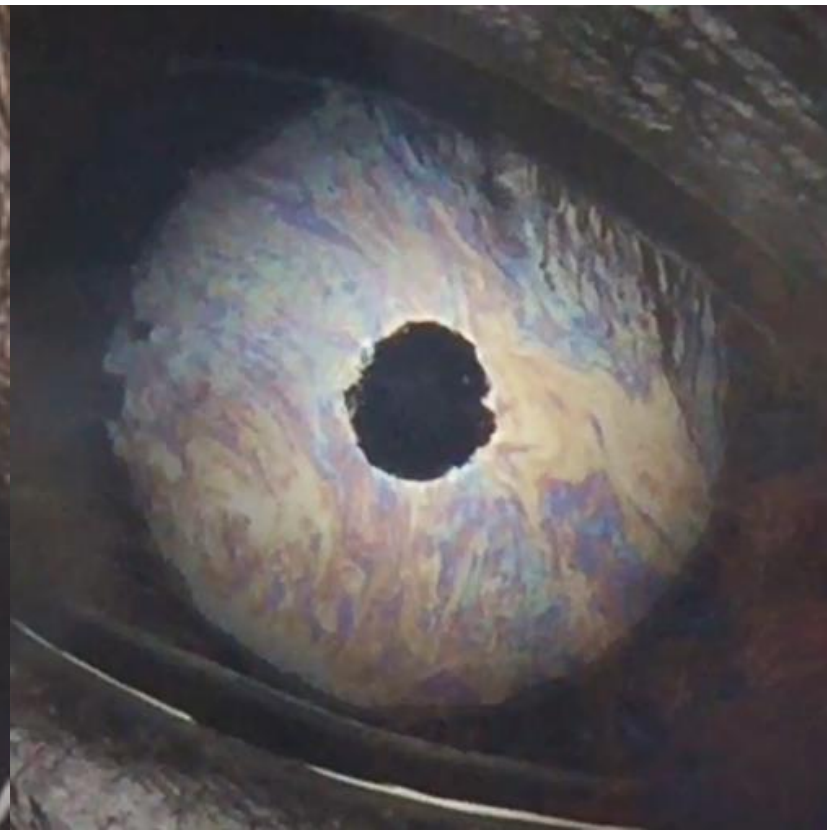


SBM


TF LL patterns

- LL thickness is evaluated by looking at LL patterns (colour & texture)
- Three main patterns:
  - faintly visible homogeneous meshwork pattern (≃15-30 nm)
  - compact meshwork pattern, grey waves (≃30-60 nm)
  - meshwork with waves and interference fringes (≃60-150 nm)

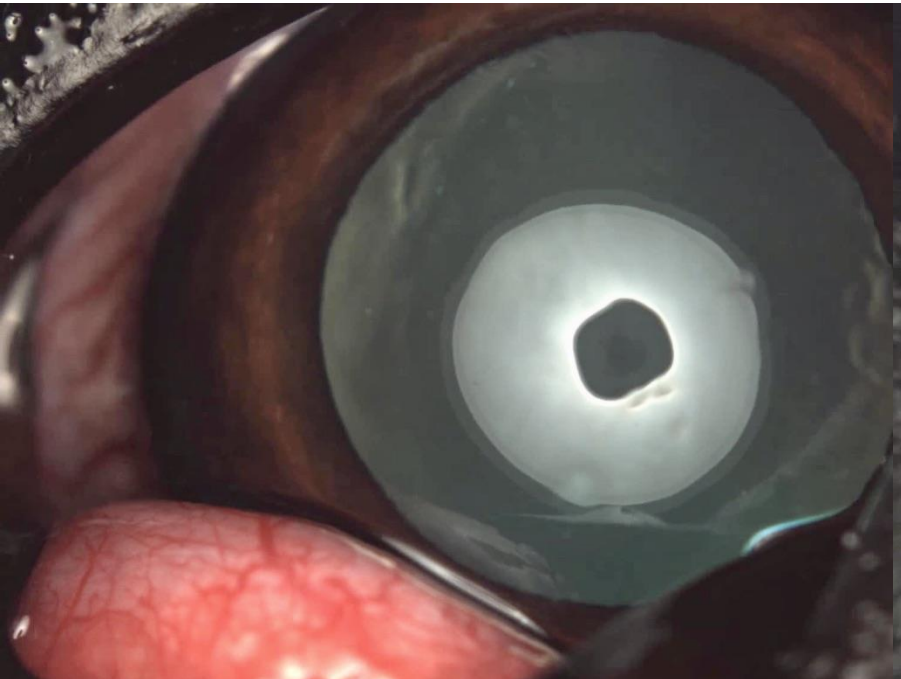


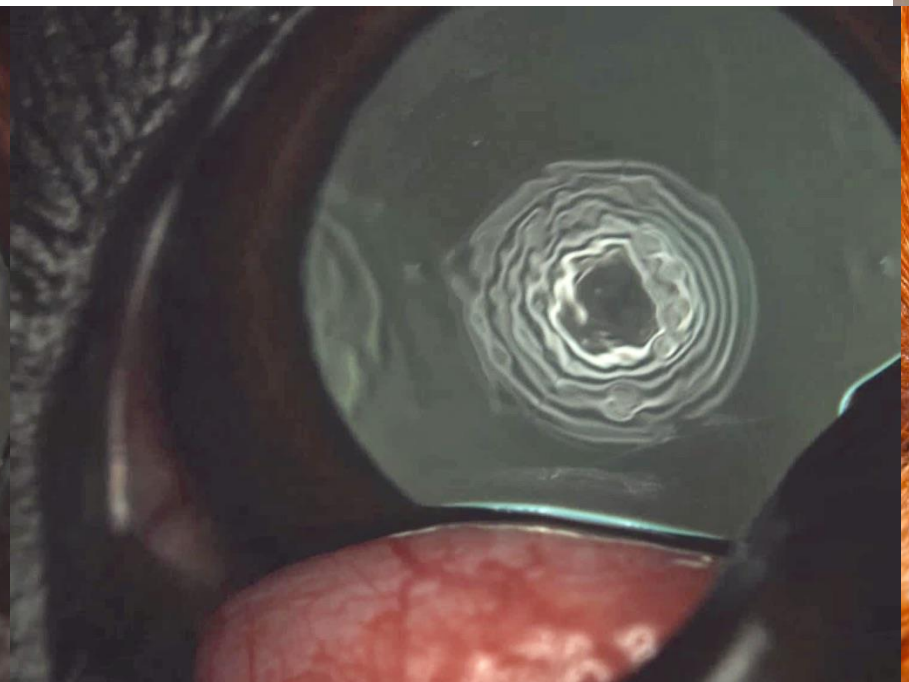


LL thickness and TF evaporation (TFE)

- TF evaporation does not necessarily correlate with thickness of the TF LL*
- LL thickness is just a parameter to be considered
- Contaminants and clumping of lipid-mucins may increase LL evaporation

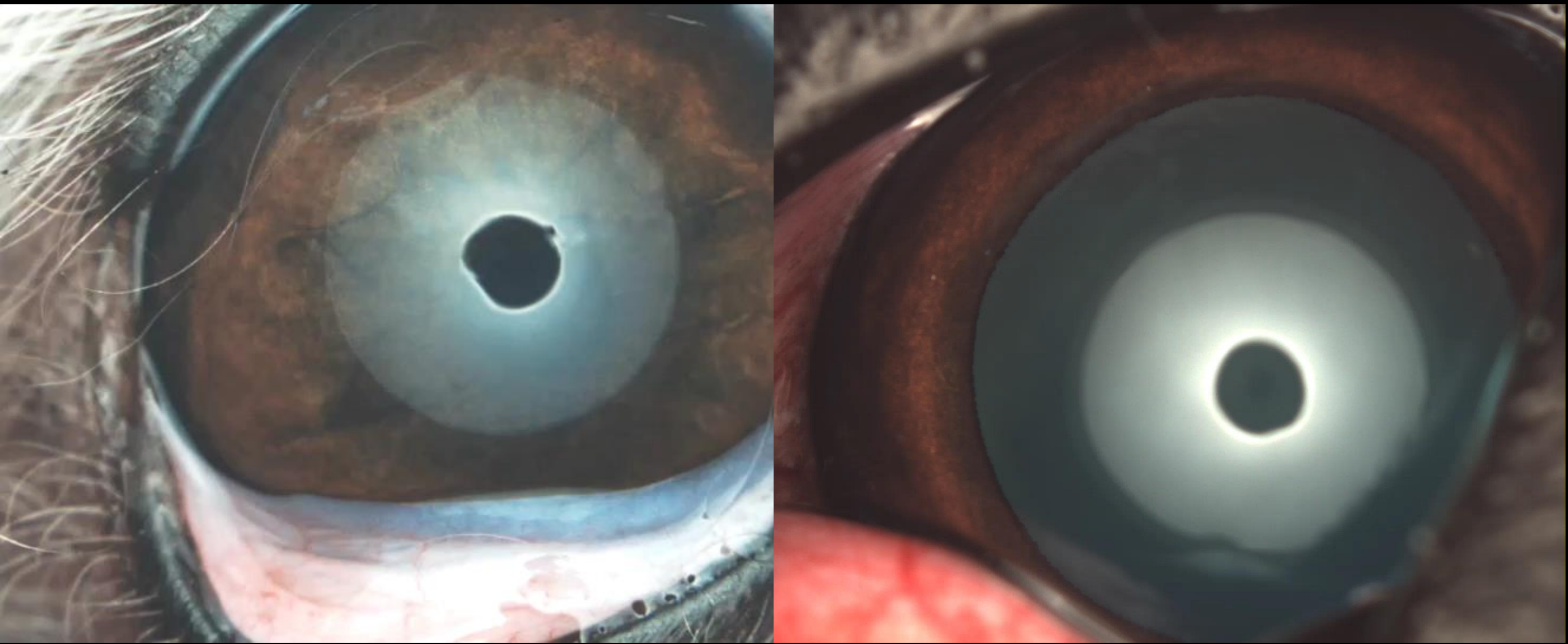
**King-Smith PE et al. Tear Film Breakup and Structure Studied by Simultaneous Video Recording of Fluorescence and Tear Film Lipid Layer Images. IOVS, July 2013, Vol. 54, No. 7, 4901*



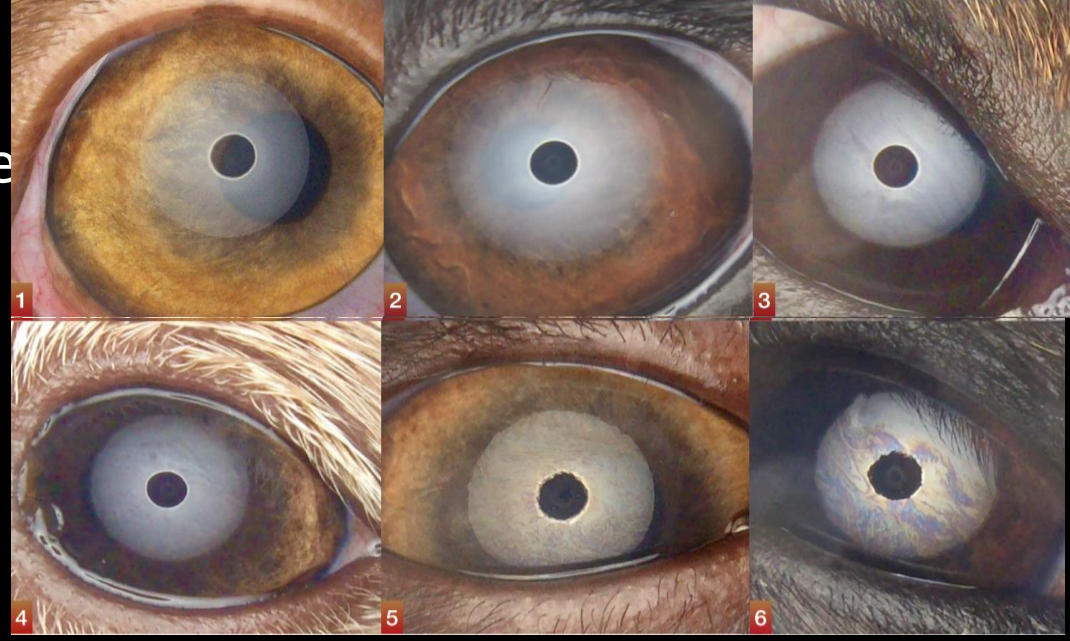


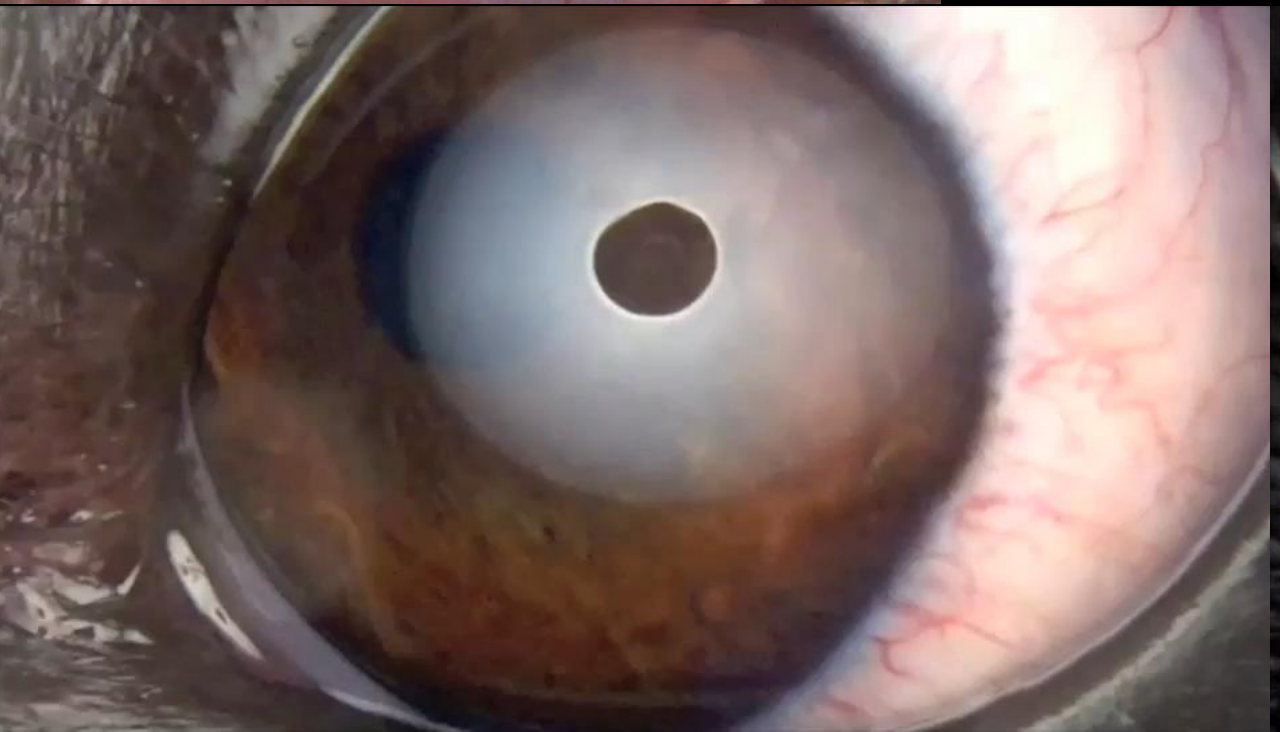
- TFE may be impacted by more than lipid layer thickness, may be a function of LL composition
- Bacterial lipases may break down esters into component acids and alcohols, causing a defective TFLL structure with increased evaporation*

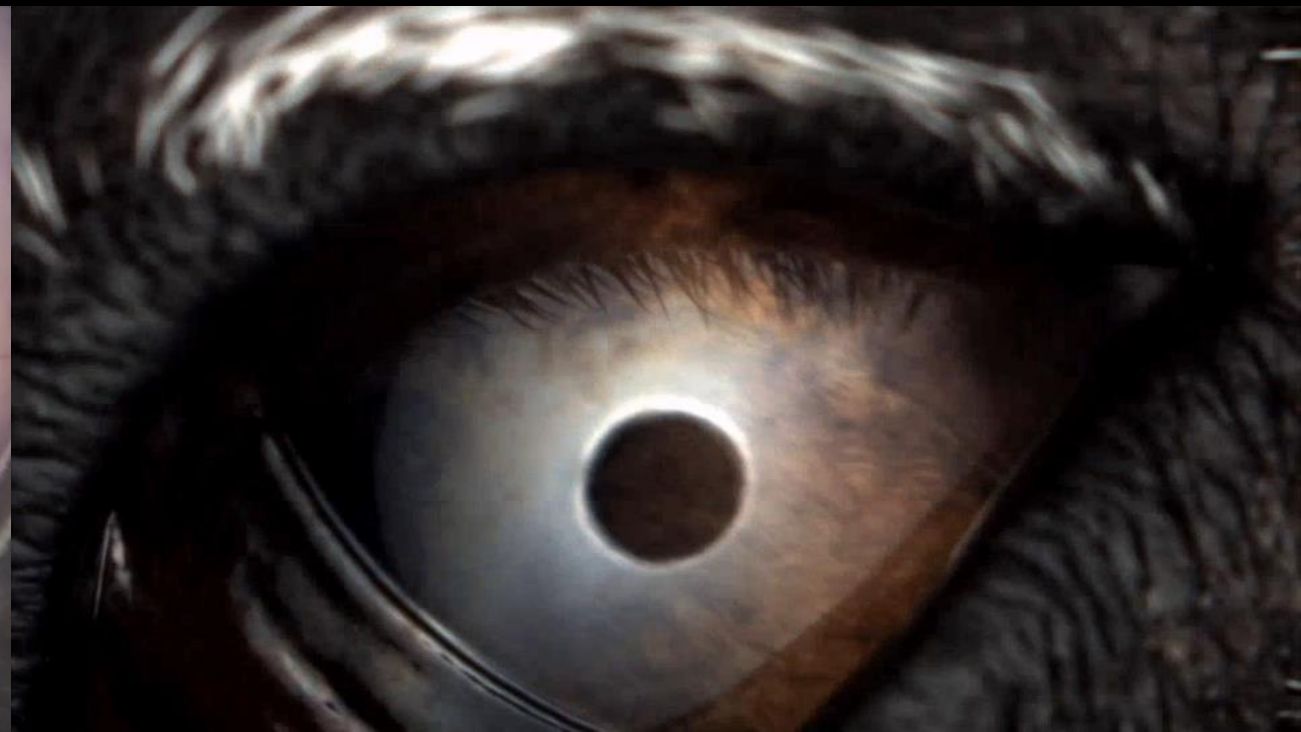
*King-Smith PE et al. Tear Film Breakup and Structure Studied by Simultaneous Video Recording of Fluorescence and Tear Film Lipid Layer Images JOVS, 54, 7, 4900-4909, July 2013



TF LL thickness
Patterns grading scale

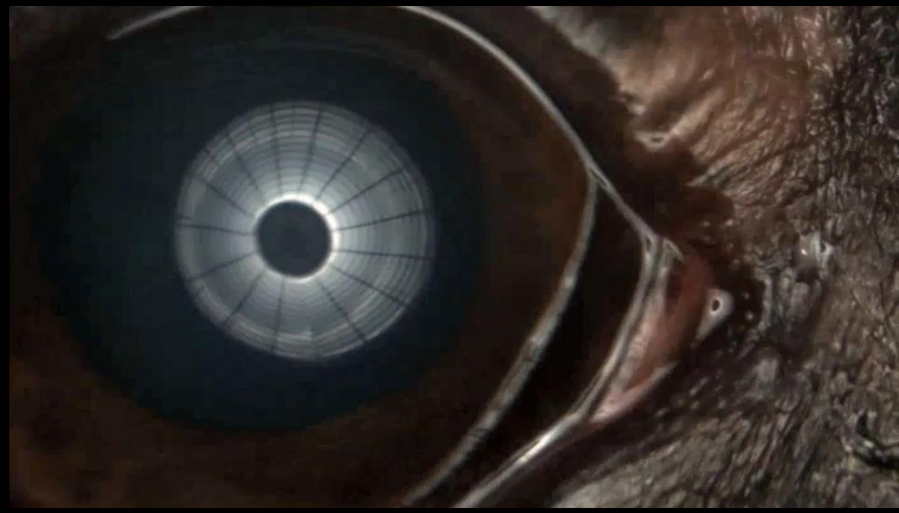


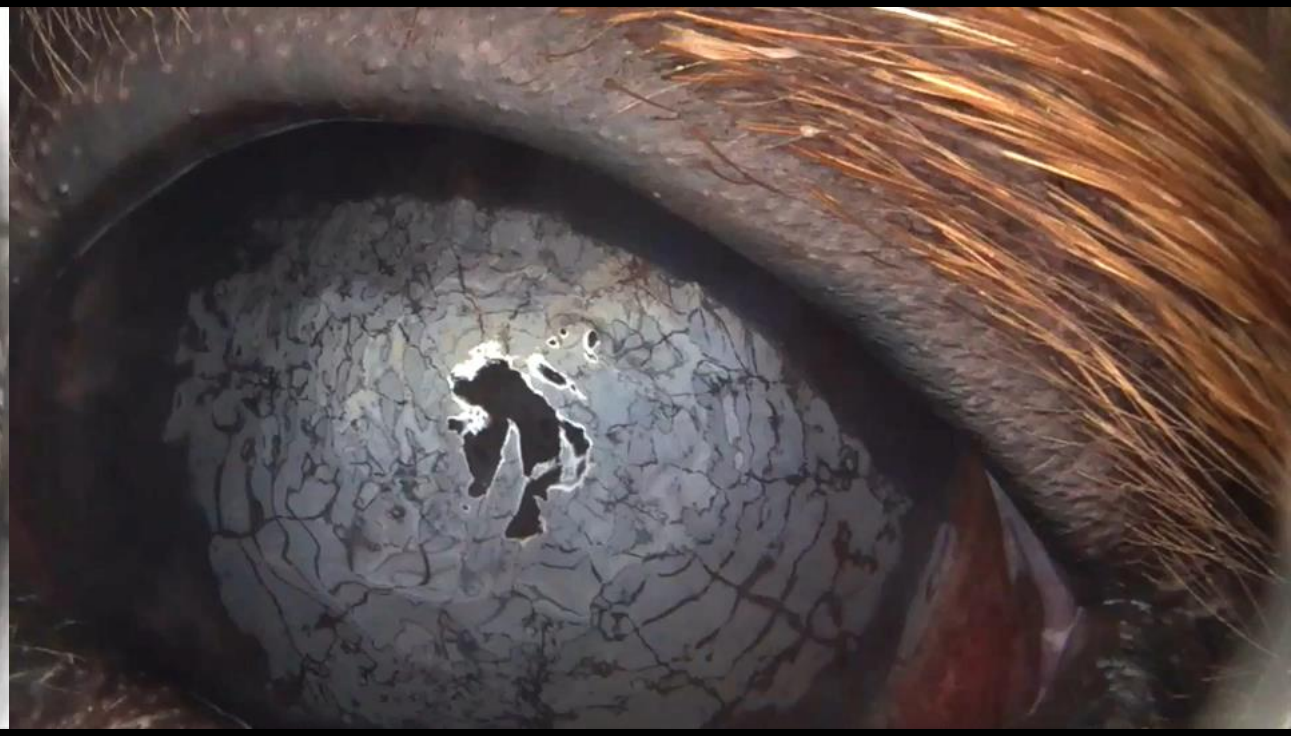




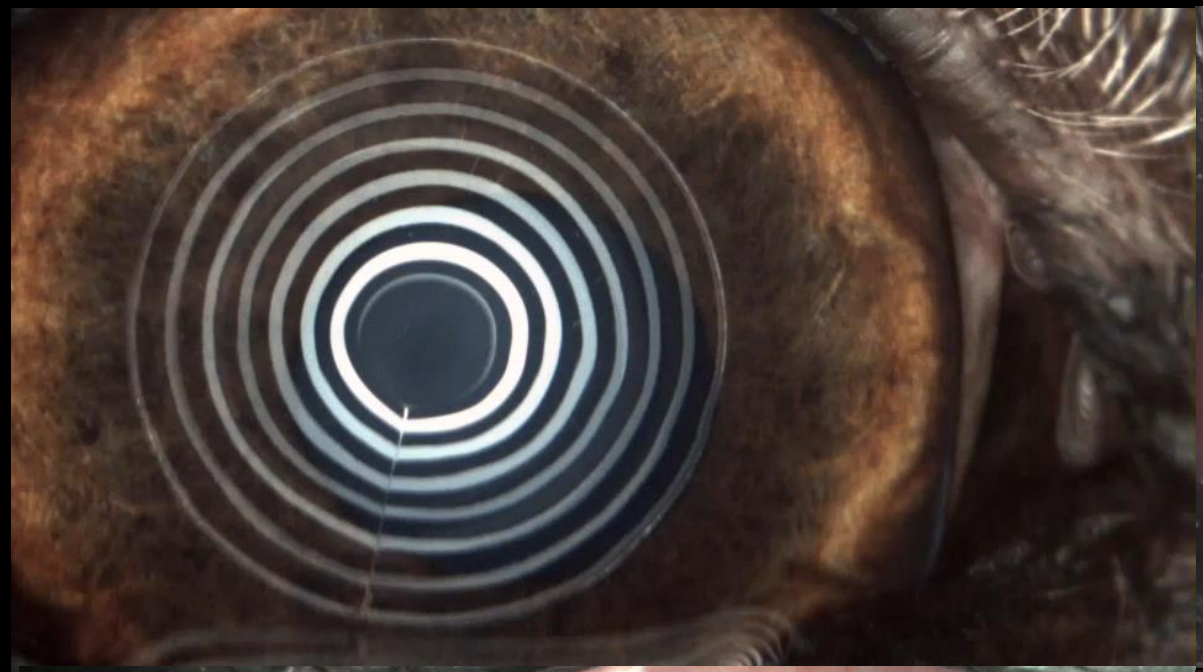
NIBUT grid

In most cases continuous eye and third eyelid movements prevent NIBUT evaluation

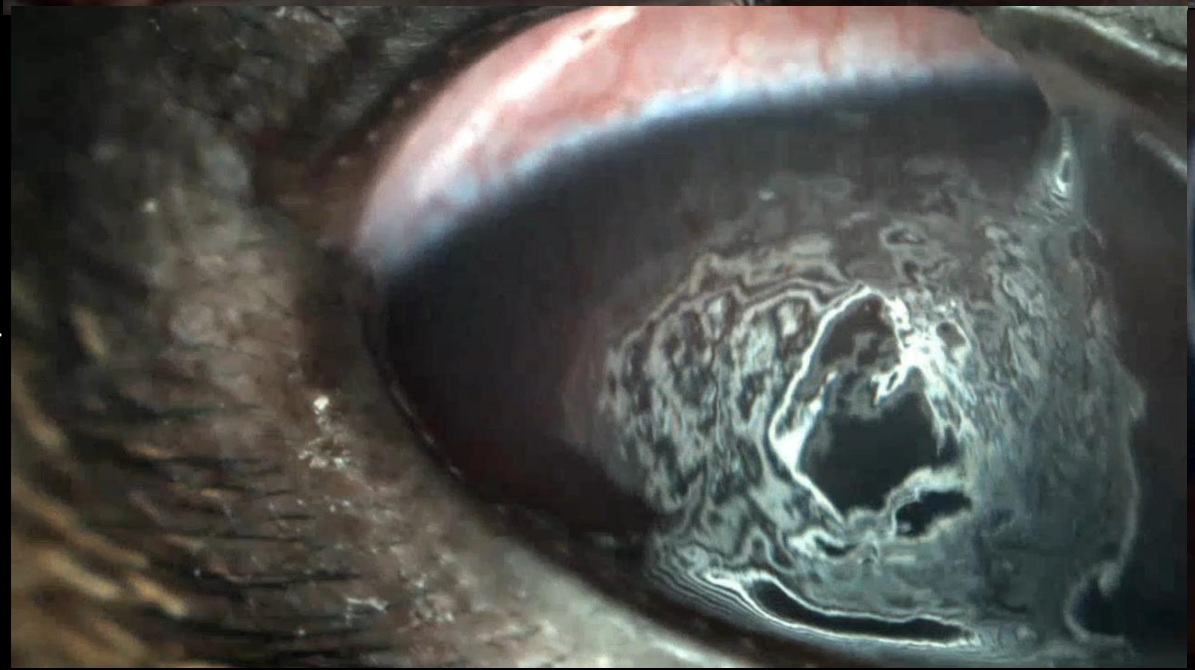




Placido disc – OS topography



BULL DOG L STT 5



JRT R STT 2

JRT L STT 5

QUESTIONS?