Anterior segment

Anant Sharma

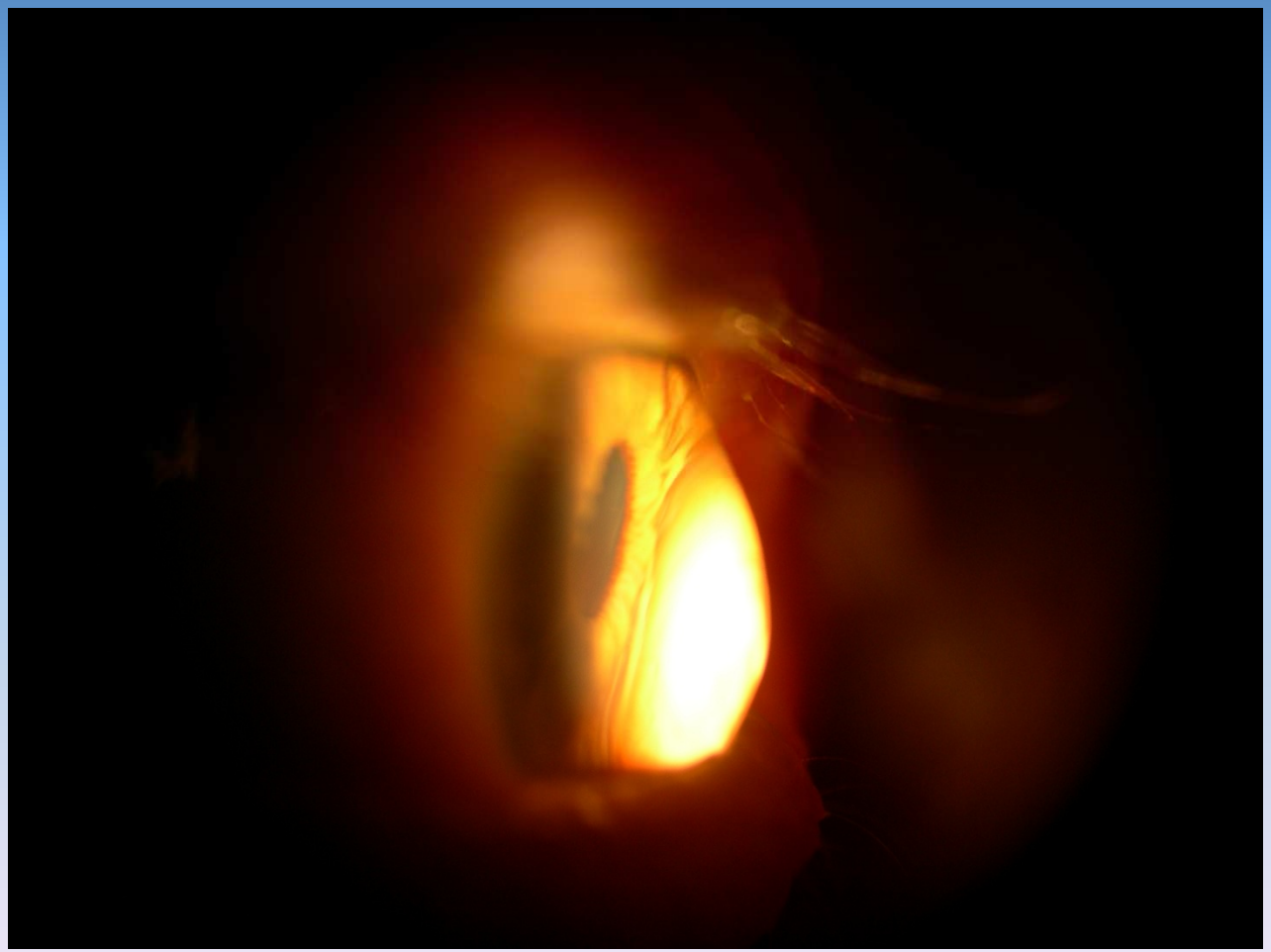
Consultant Ophthalmic Surgeon Moorfields
Bedford and Milton Keynes NHS Trust

Visiting Professor Cranfield University

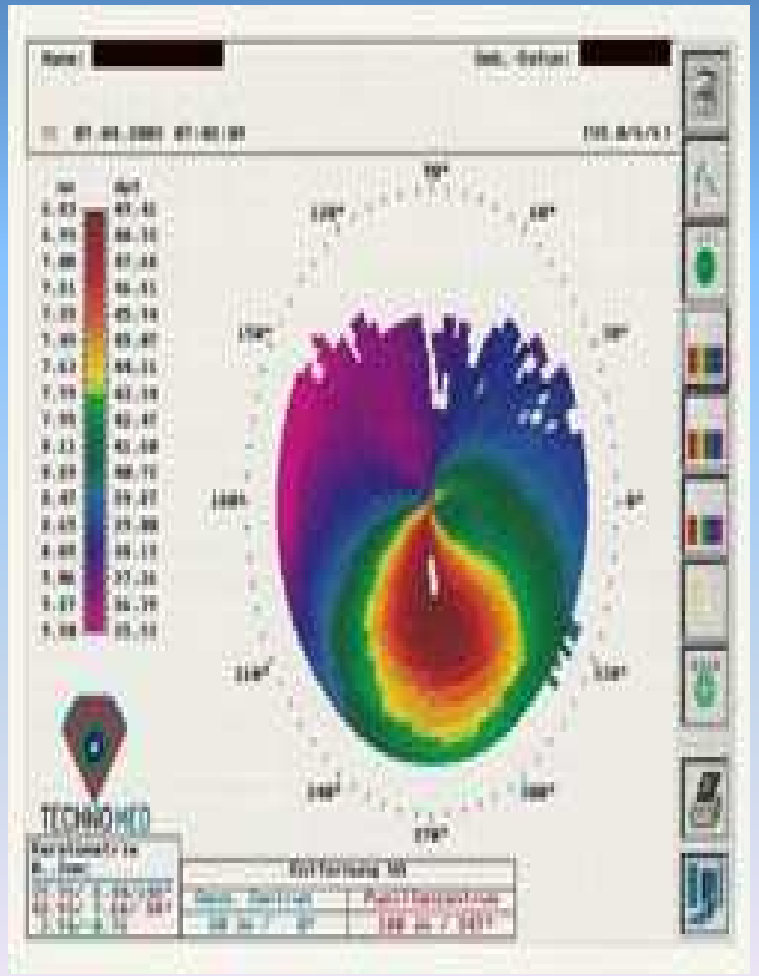
Financial disclosure

- Co inventor of Eyepeace lid massager

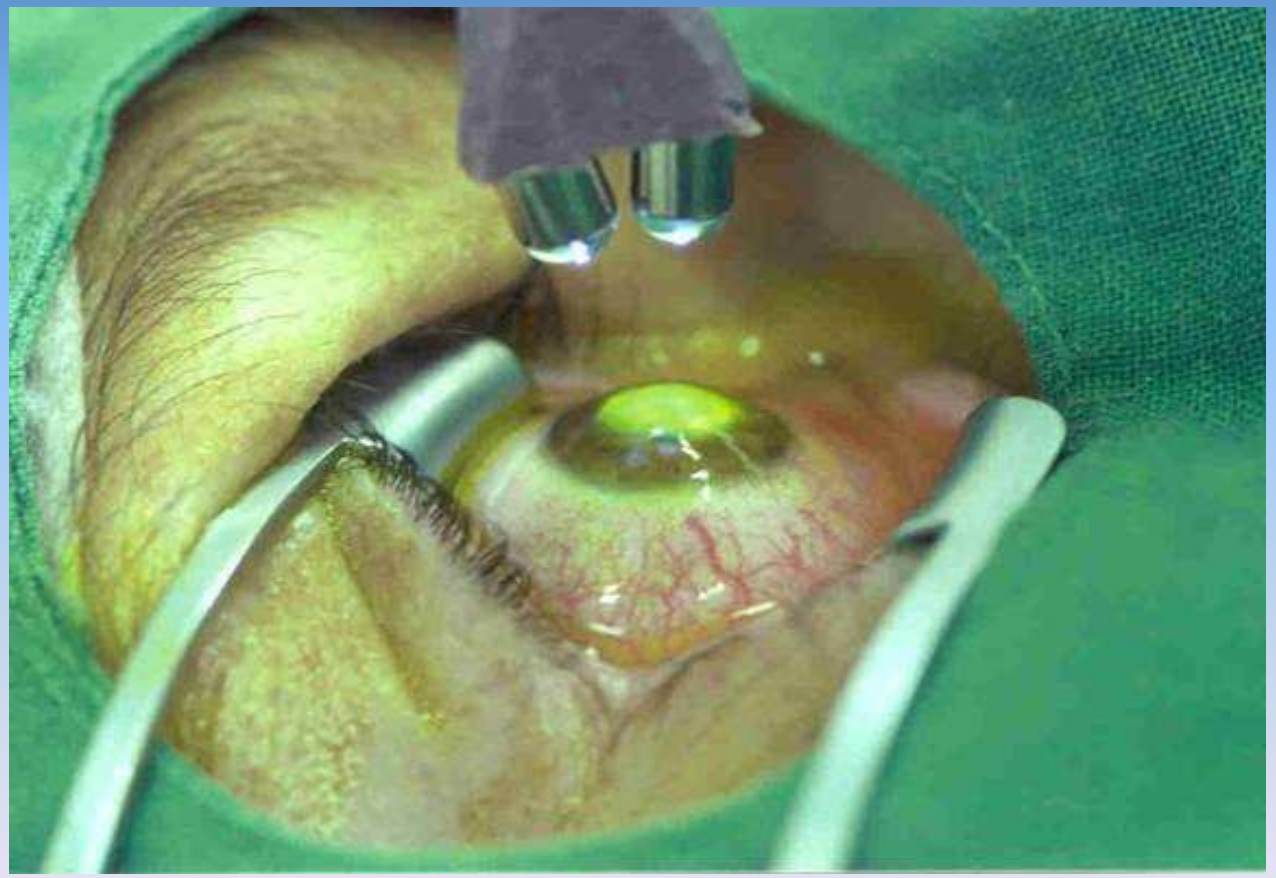
Keratoconus



Crosslinking Riboflavin and 370nm UVA

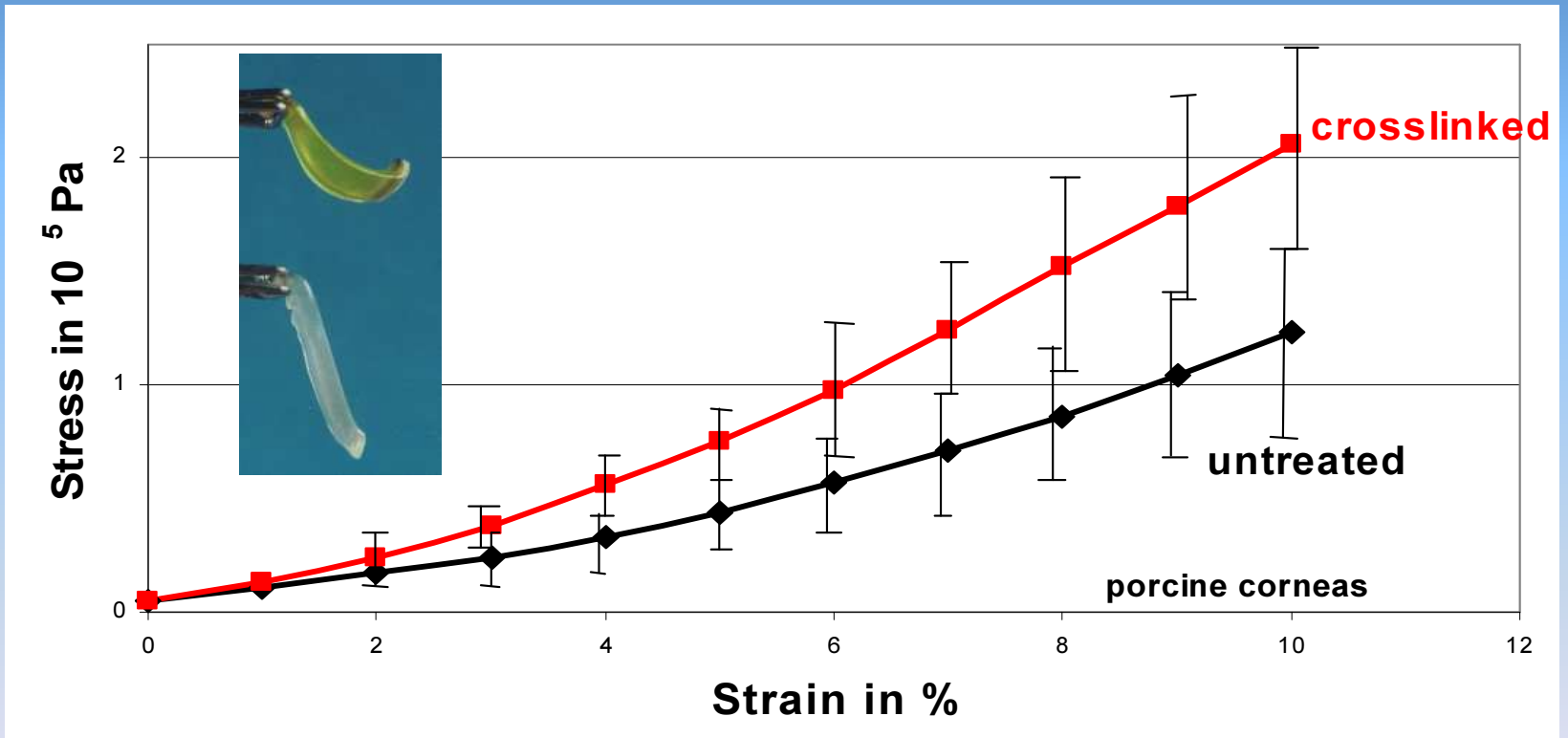


Riboflavin CXL



UVA/Riboflavin Cross-linkage
Increase in stress-strain measurements

Wollensak *JCRS 2003;29:1785*

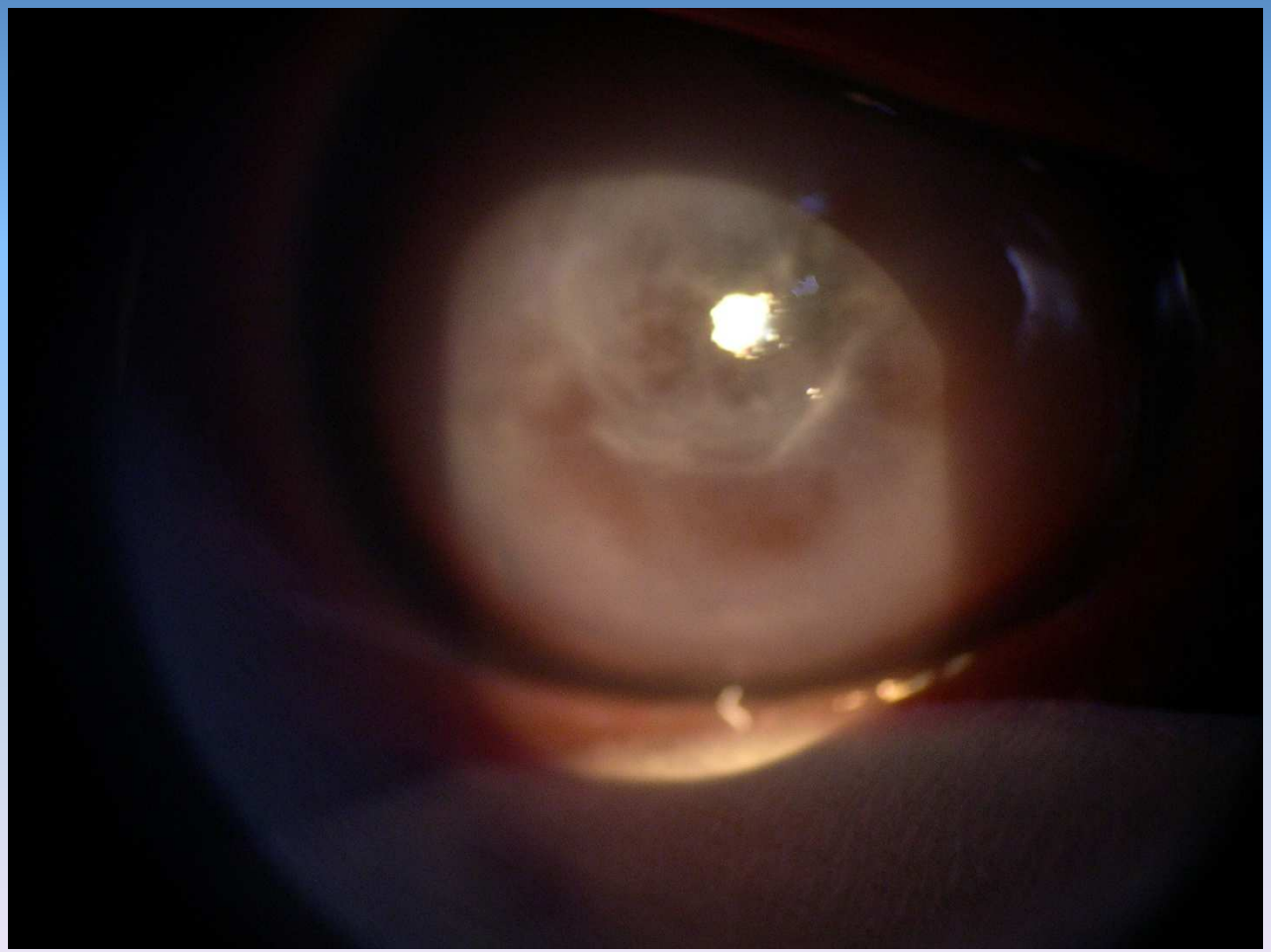


Wollensak *Acta Ophthalmologica 2009;87: 48.*

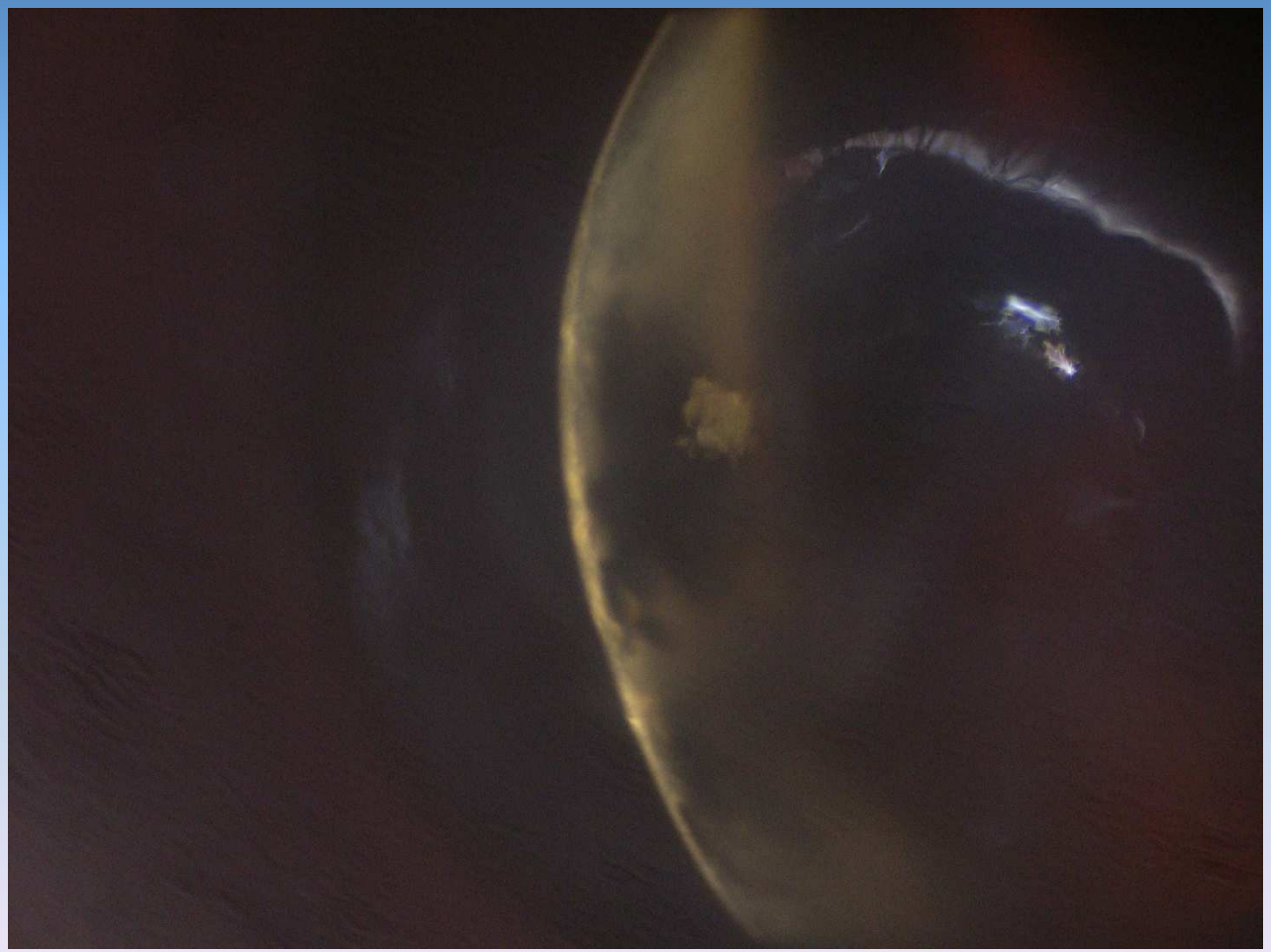
Increases in stress-strain measurements maintained in rabbit eyes 8 months after treatment

2.65 mW/cm² keratocyte loss

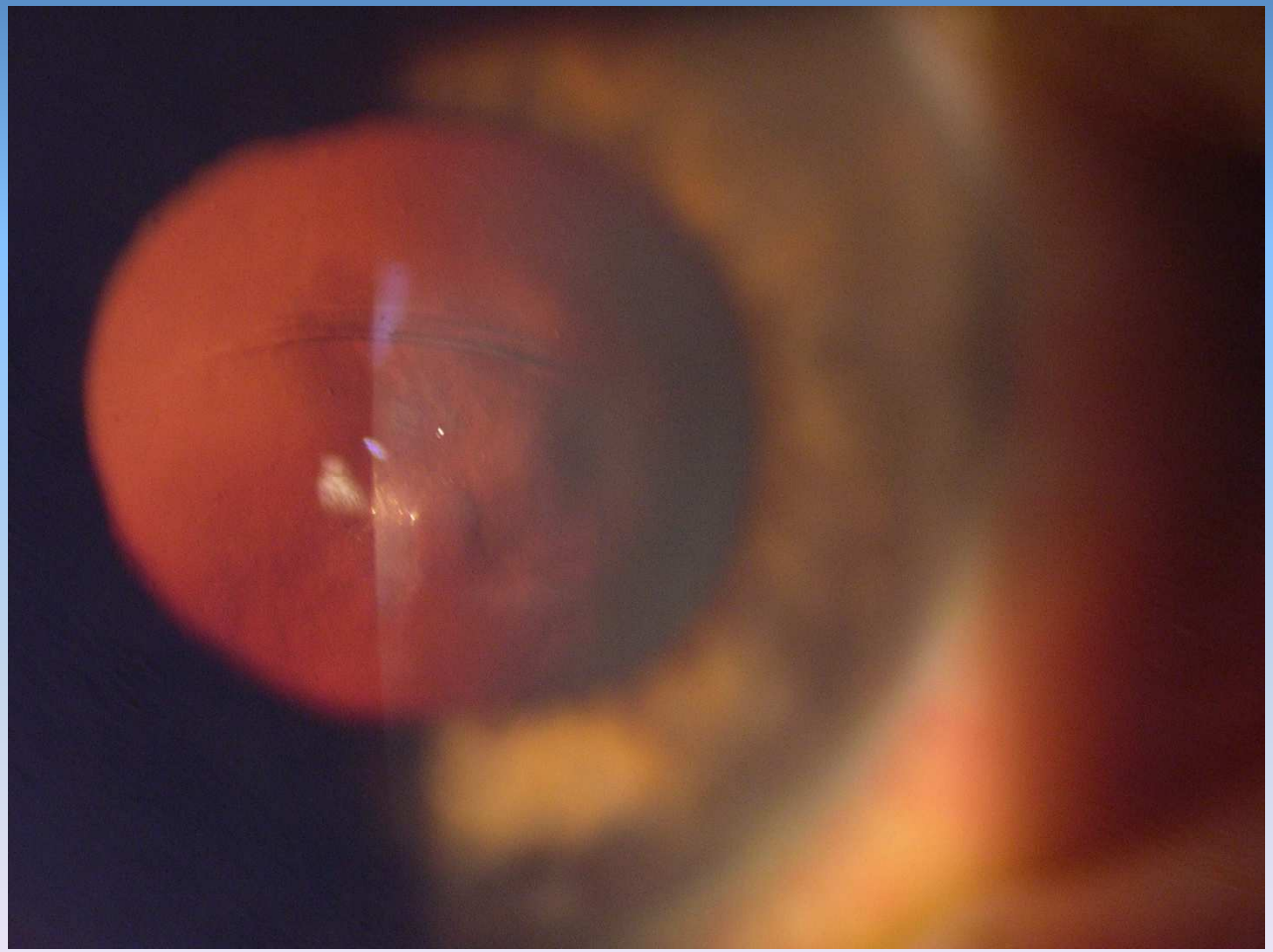
Acute Hydrops



Acute hydrops



Resolved hydrops with Descemet tear



Anterior segment advances available

- Keratoconus crosslinking
- Endothelial corneal transplantation
- Femtolaser cataract and refractive surgery (intrastromal SMILE refractive / arcute incisons)
- Meibomian gland disease / blepharitis. Imaging , measuring meniscus, hyperaemia, infrared gland imaging.Heat mask and simple / complex massaging devices
- Finger-prick autologous blood (FAB) for severe dry eyes

Keratoconus Crosslinking

- Ensure that patients have **Pentacam scans** and **refraction** with contact lenses out for a minimum of 2 weeks (RGP) and 1 week (soft).

Keratoconus (KC) inclusion criteria

Early KC (Kmax <55D)

- ≥ 1 D increase Kmax
- ≥ 1 D increase K2 or K1 front
- ≥ 0.5 D increase back K2
- ≥ 16 µm decrease minimum thickness

Moderate / Advanced KC (Kmax ≥ 55D)

- ≥ 2.5 D increase Kmax
- ≥ 2.5 D increase K2 or K1 front
- ≥ 22 µm decrease minimum thickness

Keratoconus (KC) inclusion criteria

- *High risk of progression* (1 or more)
- Age ≤ 18 years
- Age 19 – 30 years (incl.) AND Minimum thickness < 400 µm
- Age 19 – 30 years (incl.) AND Hydrops/graft fellow eye
-
- *History of progression in referral letter based on serial topography or loss of corrected vision – documentation incomplete AND age ≤ 30 years*
-
- *Previous LASIK with ectasia*

Keratoconus special situations

- *Minimum corneal thickness < 375 µm
- †Age < 16 years, or adults requiring sedation/general anaesthesia
- *Cognitive impairment
- **May be treated off pooled lists in laser suite (consultant led) or †main theatres with appropriate anaesthetic cover*

Keratoconus special situations

- *Patients who are unable to come out of contact lenses prior to Pentacam scanning (and therefore ineligible for f/u in EKC) may be offered CXL on pooled list if they are considered at risk of progression (i.e. age < 35 years) with continued f/u in Contact Lens clinic.*
- 16-18year olds as current capacity

Keratoconus Crosslinking

- **Exclusion criteria**
- Pregnancy
- Active surface disease

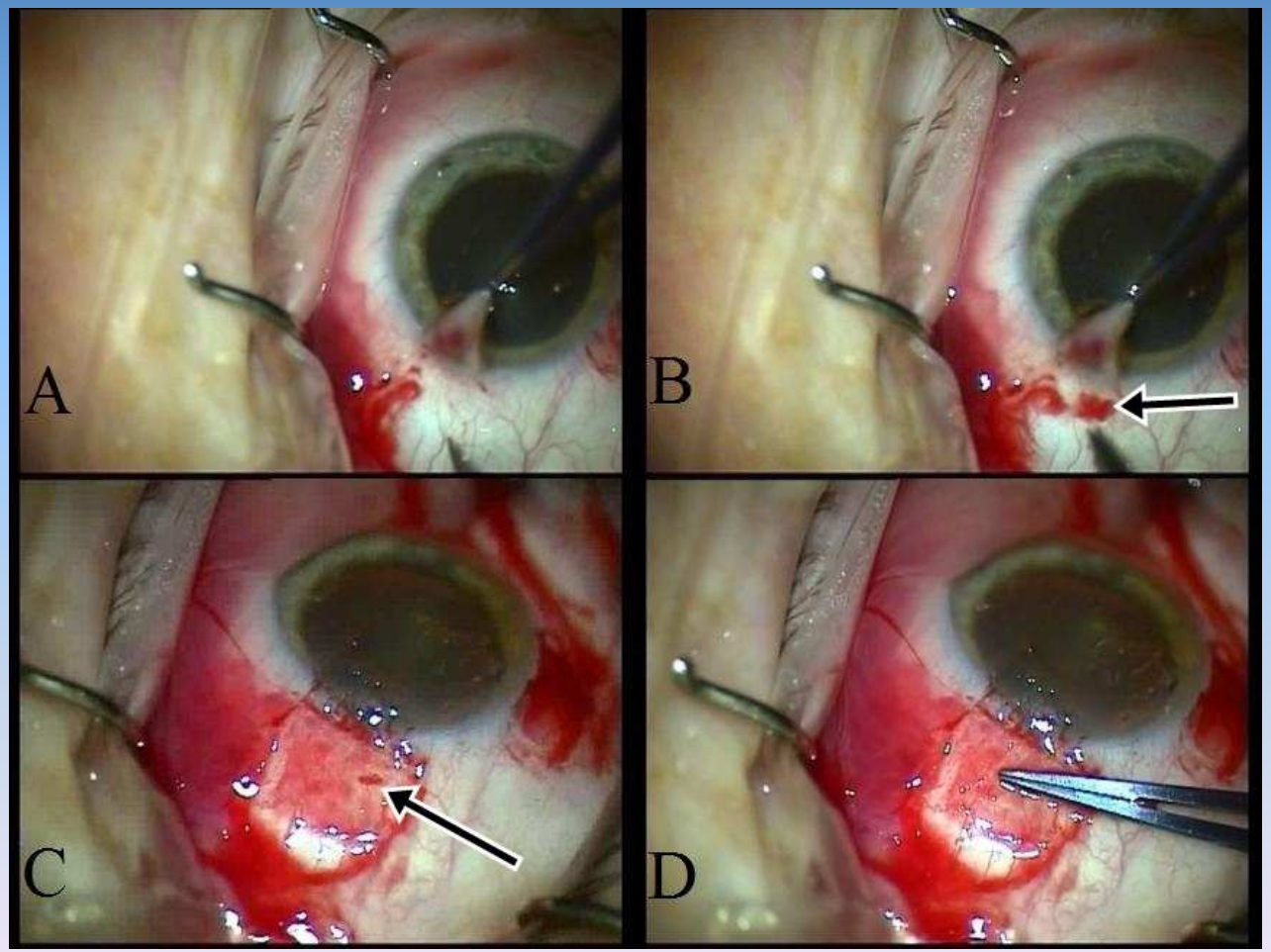
Cataracts

- **FUCHS corneal endothelial dystrophy**
- **Laser refractive surgery**
- **Pseudoexfoliation**
- **Refractive aim. Monovision.**
- **Amblyopia (upto 3% can develop post Op. Diplopia)**
- **Dry eyes. Can worsen after cataract surgery**
- Shallow anterior chamber
- Poorly dilating pupils
- Dense cataract

Intraocular lenses (IOLs)

- Monovision
- Toric IOLs to correct astigmatism
- Multifocal IOLs
- Multifocal toric IOLs
- High myopia phakic versus pseudophakic

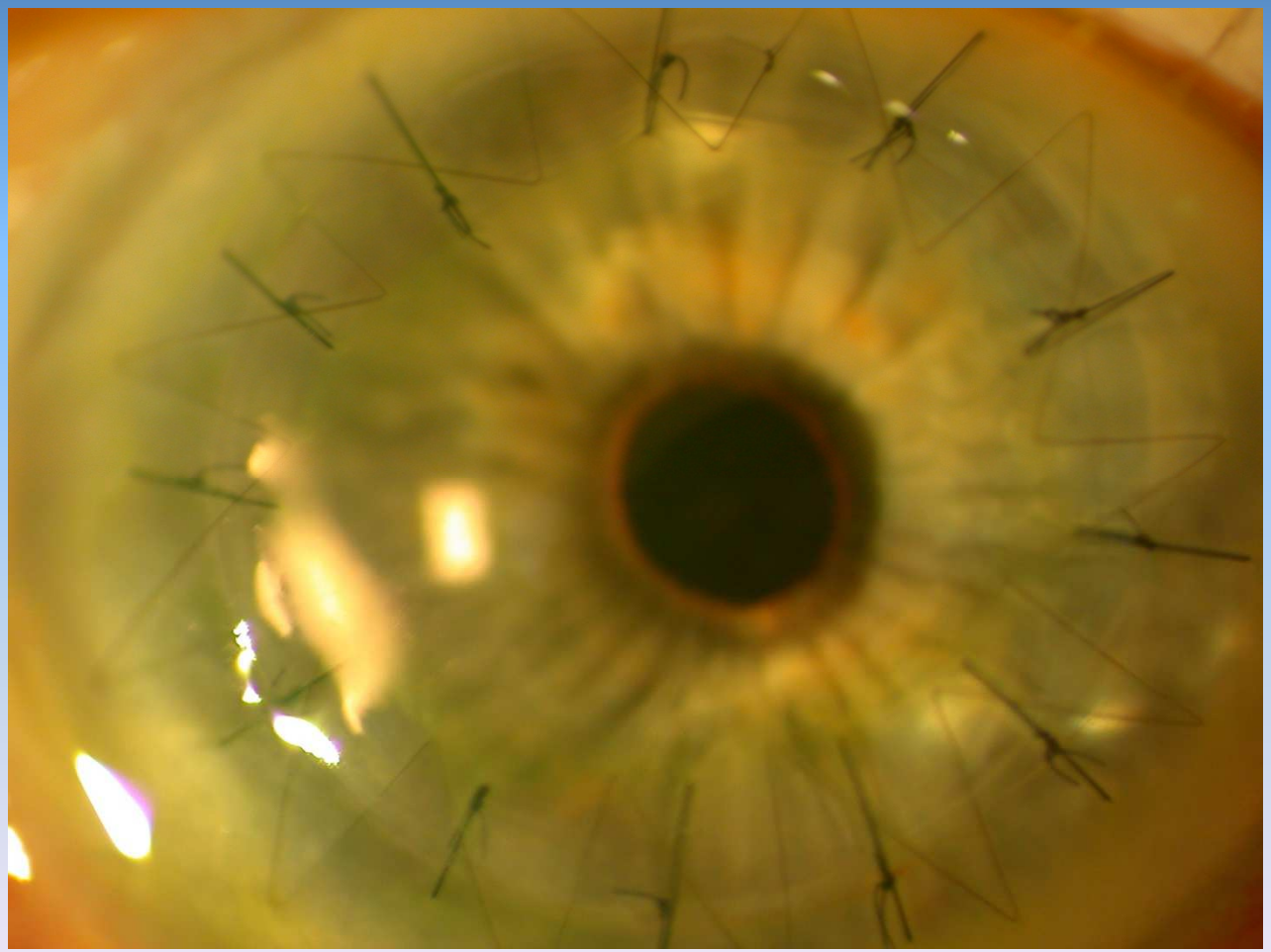
Pterygium



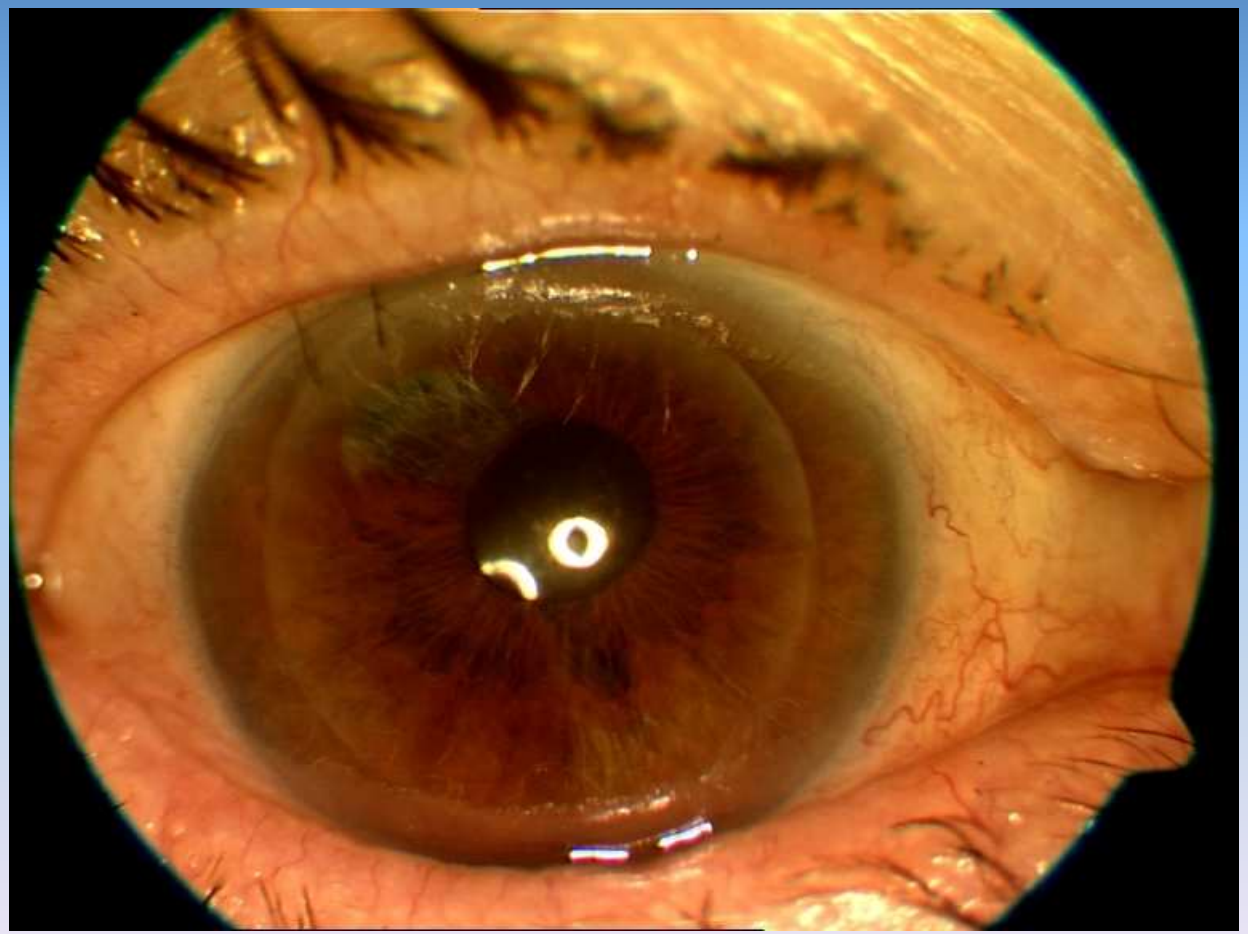
Pterygium surgery

- **Autologous fibrin glue for pterygium surgery with conjunctival autograft.** A Sharma and J Moore. CLAE. 2009 Oct;32(5) .
- **Sutureless and glue-free conjunctival autograft in pterygium surgery: a case series.** De Wit, I. Athanasiadis, A Sharma, J Moore. EYE. 2010 Sep;24(9):1474-7.

Corneal transplants



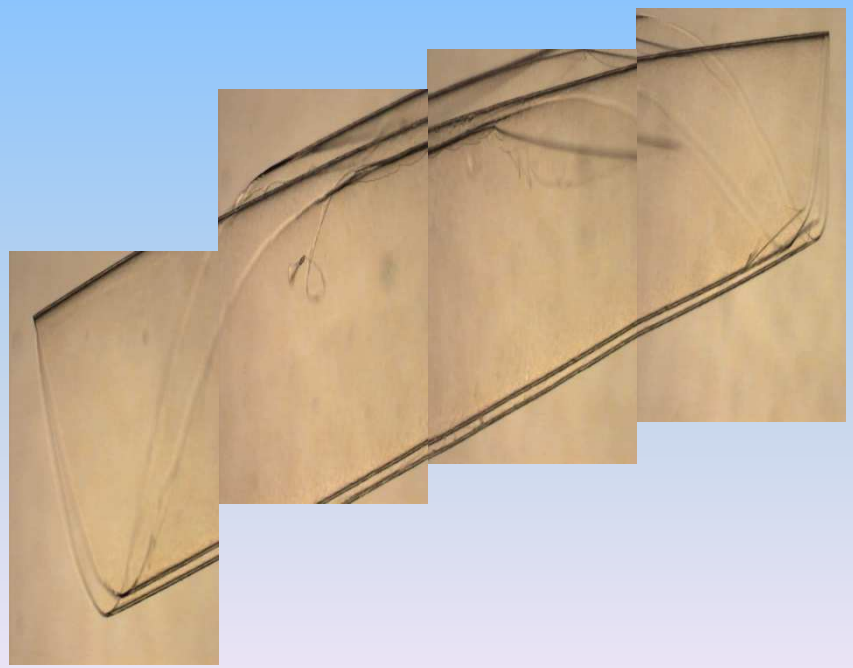
Descemet stripping automated endothelial keratoplasty (DSAEK)

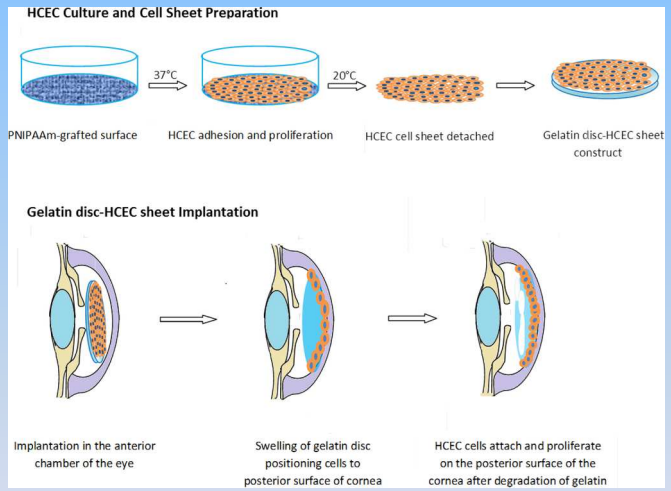


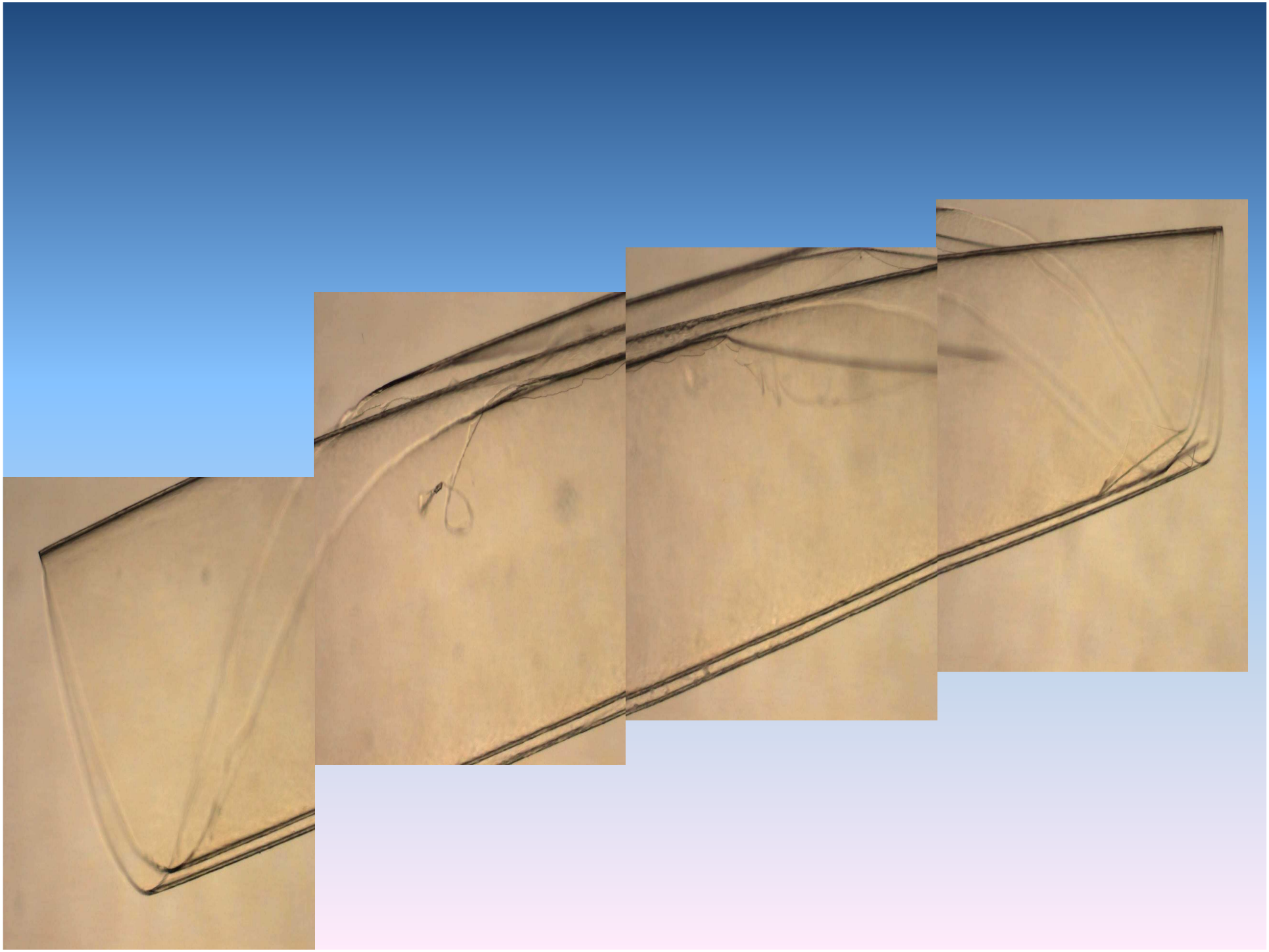
Descemet Membrane Endothelial Keratoplasy (DMEK)

Descemet Membrane Endothelial Keratoplasy (DMEK)

Endothelial cell transplantation







Dry Eye Disease - Classification

- Aqueous deficient
  - 1. Sjogrens. Primary and secondary (rheumatoid).
- Evaporative
  - 2. Anterior Blepharitis
  - 3. Meibomian Gland Dysfunction
  - Studies show prevalence of MGD in dry eye suffers to be over 80%

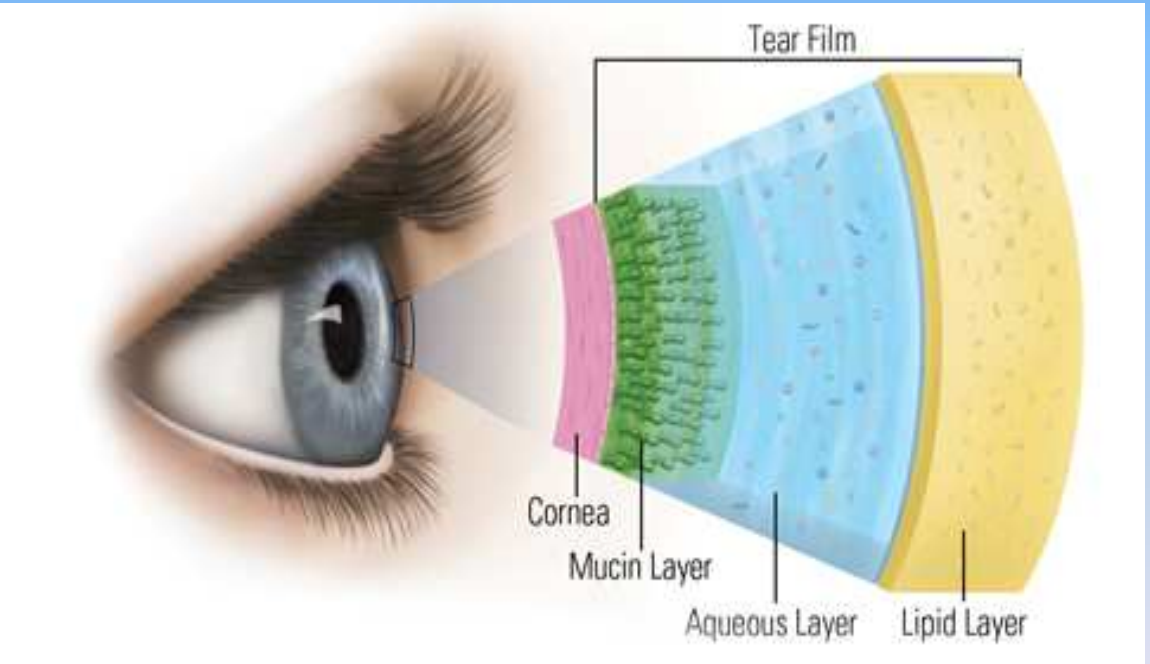
MGD / dry eye prevalence

- True prevalence of MGD is unknown but as Four million people in UK suffer from dry eyes
- Studies show prevalence of MGD in dry eye suffers to be c.60%

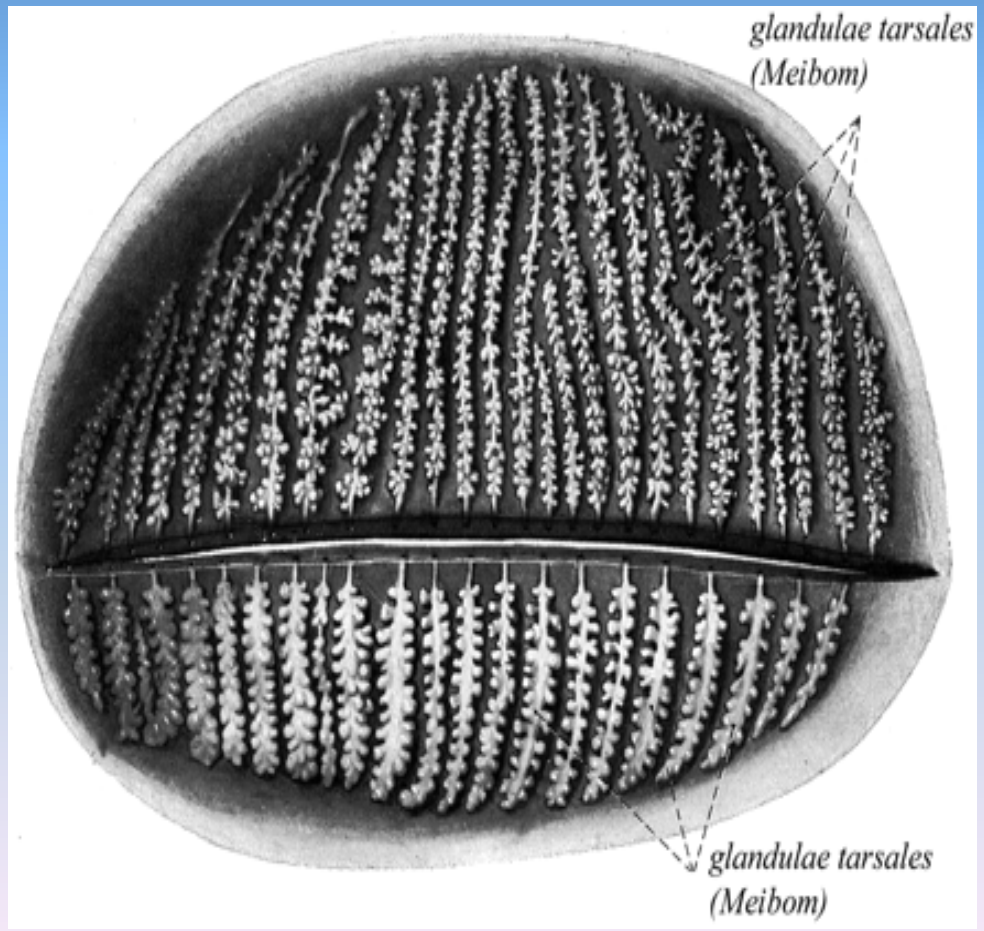
Dry eye symptoms

- Dryness, Burning, Itchiness, Stickiness, Watering, Red Eyes, Foreign body sensation
- Fluctauting vision.

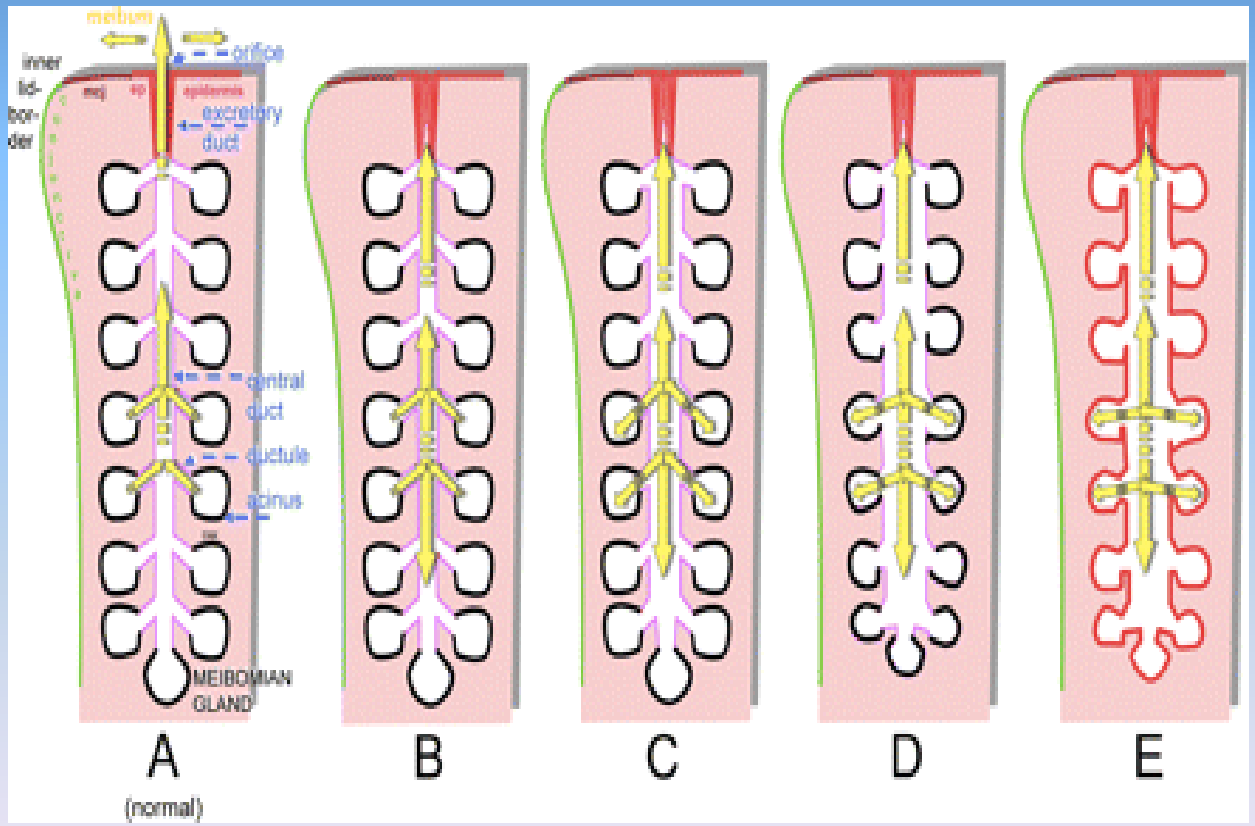
Anatomy of the Tearfilm



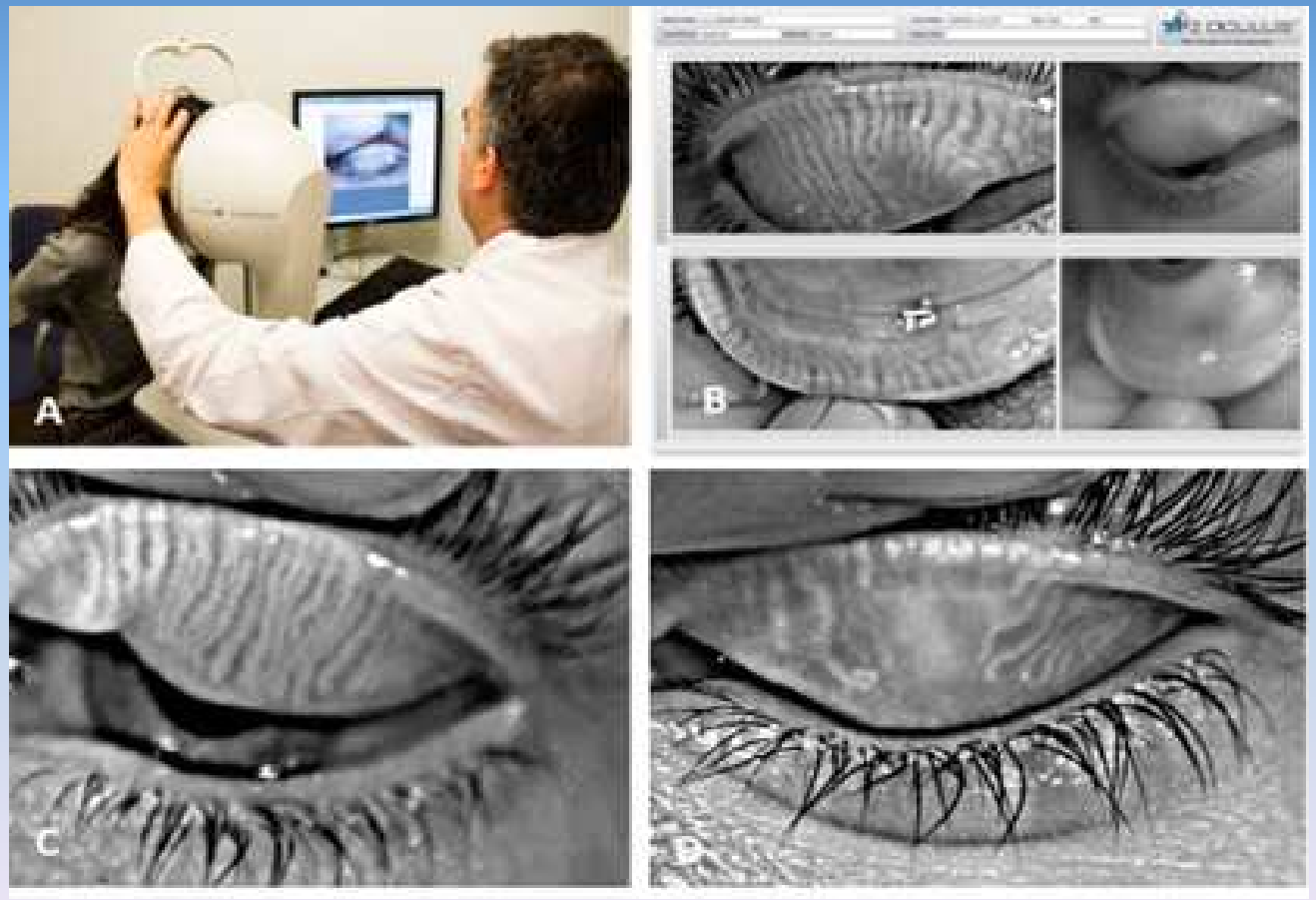
Meibomian Gland Anatomy



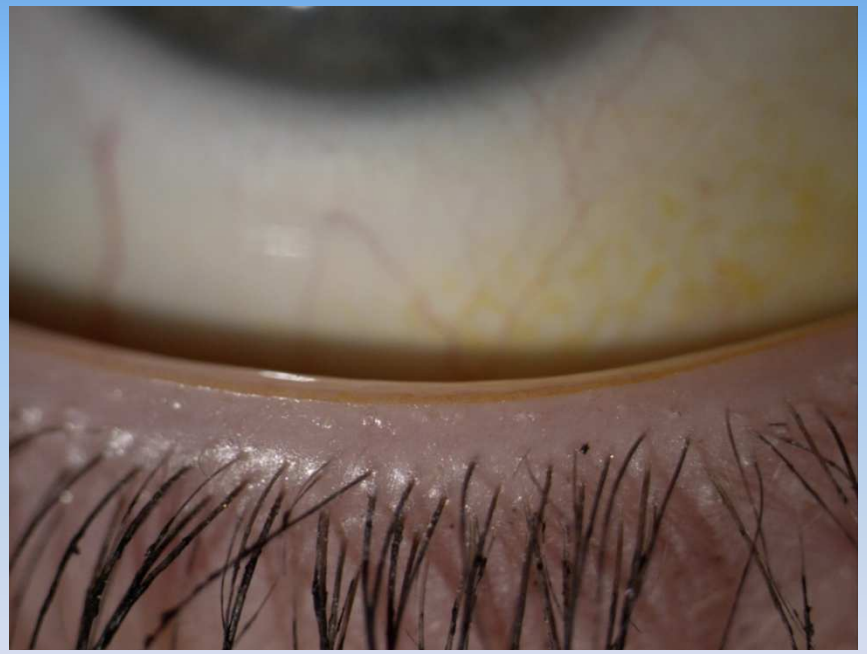
Meibomian Gland

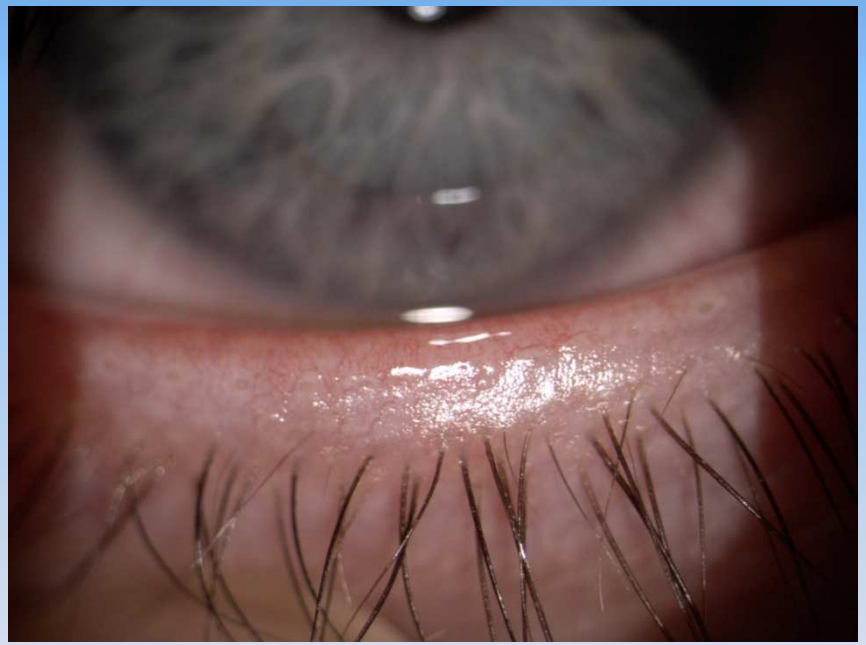


Infrared imaging of Meibomian glands

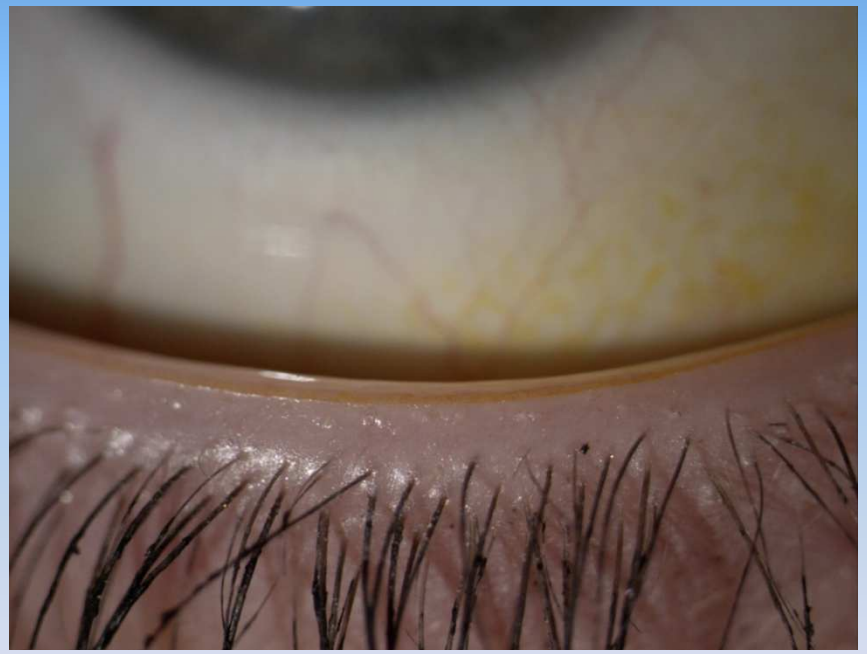


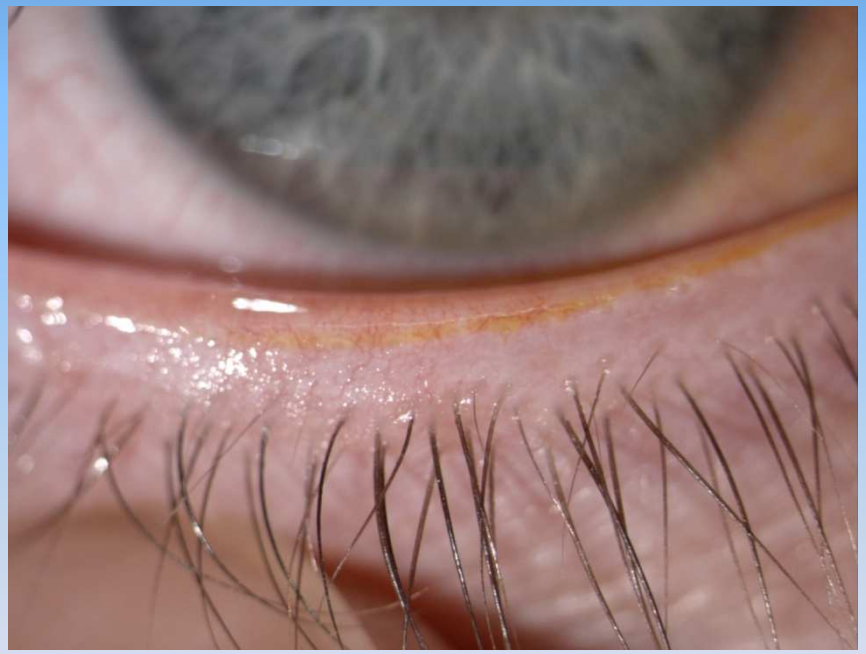
Lid margin

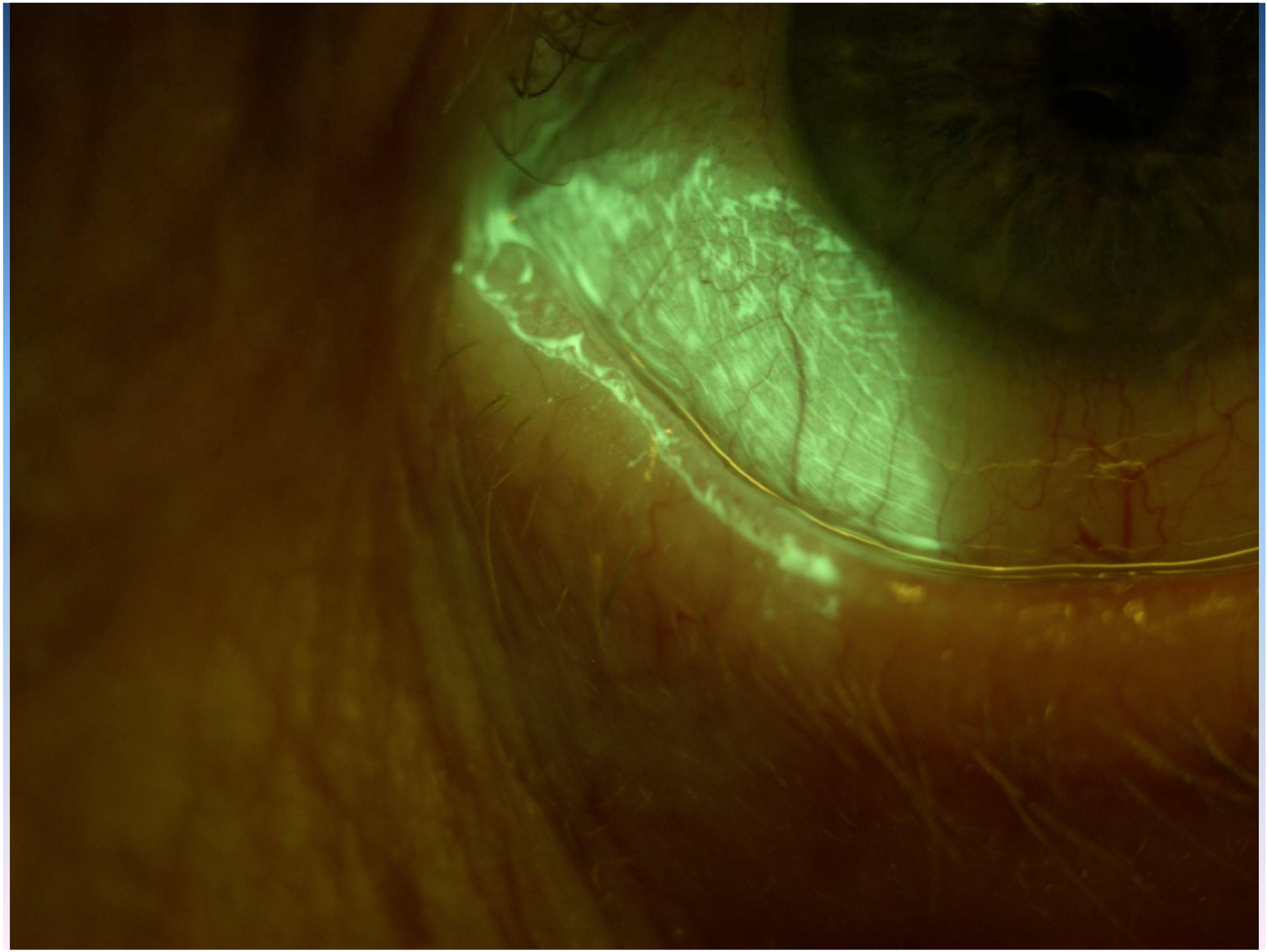




Lid margin

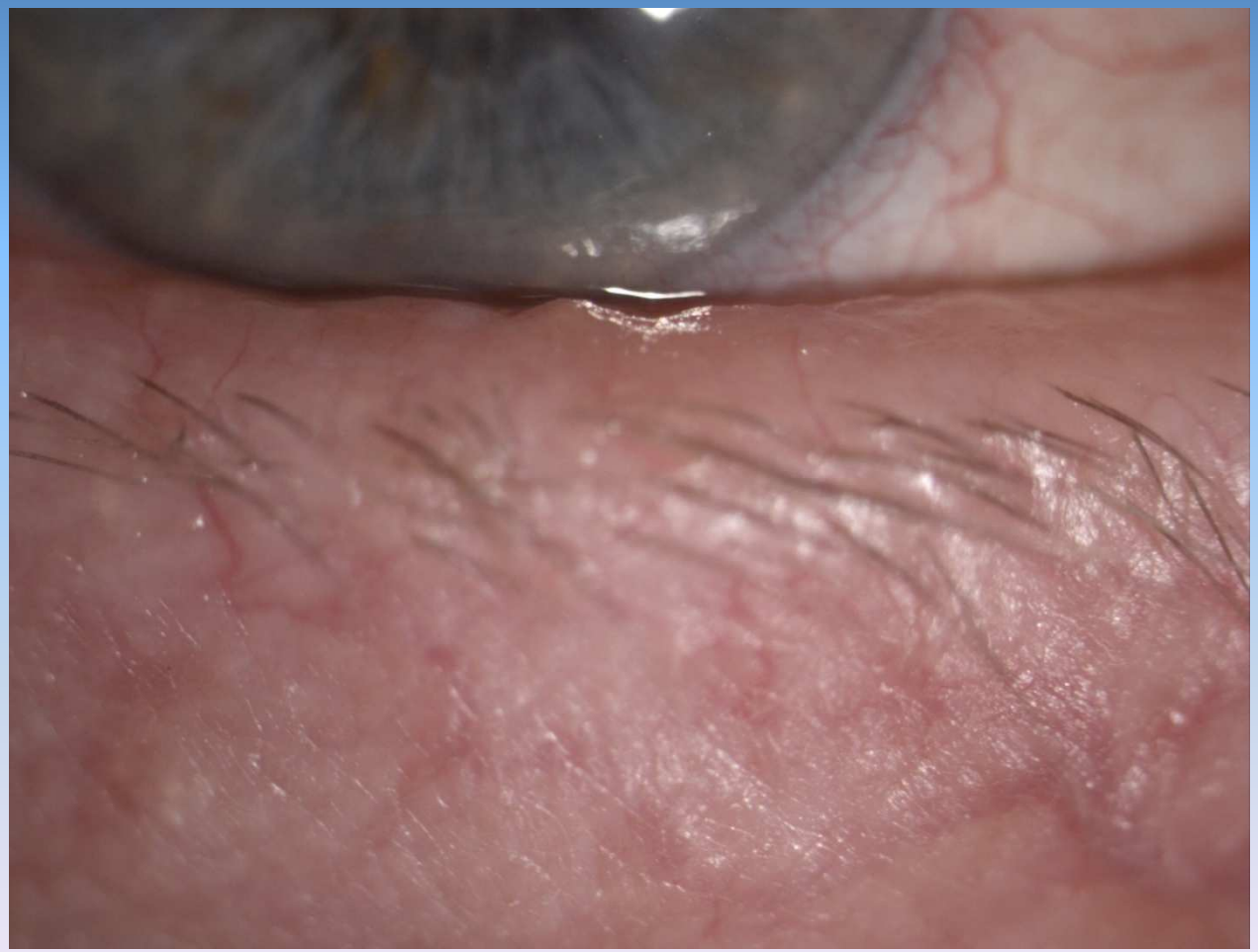




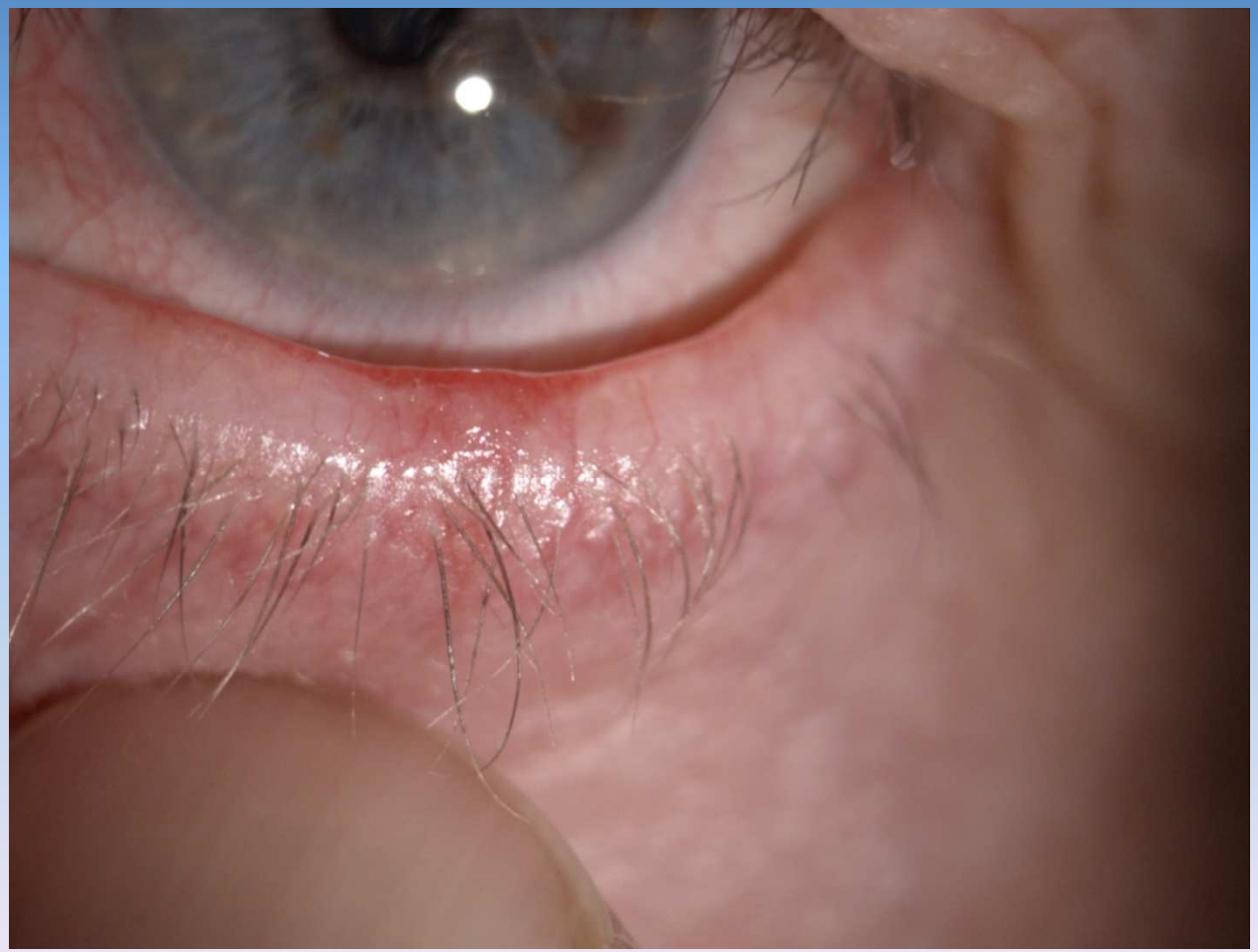


Tear break up time (TBUT)

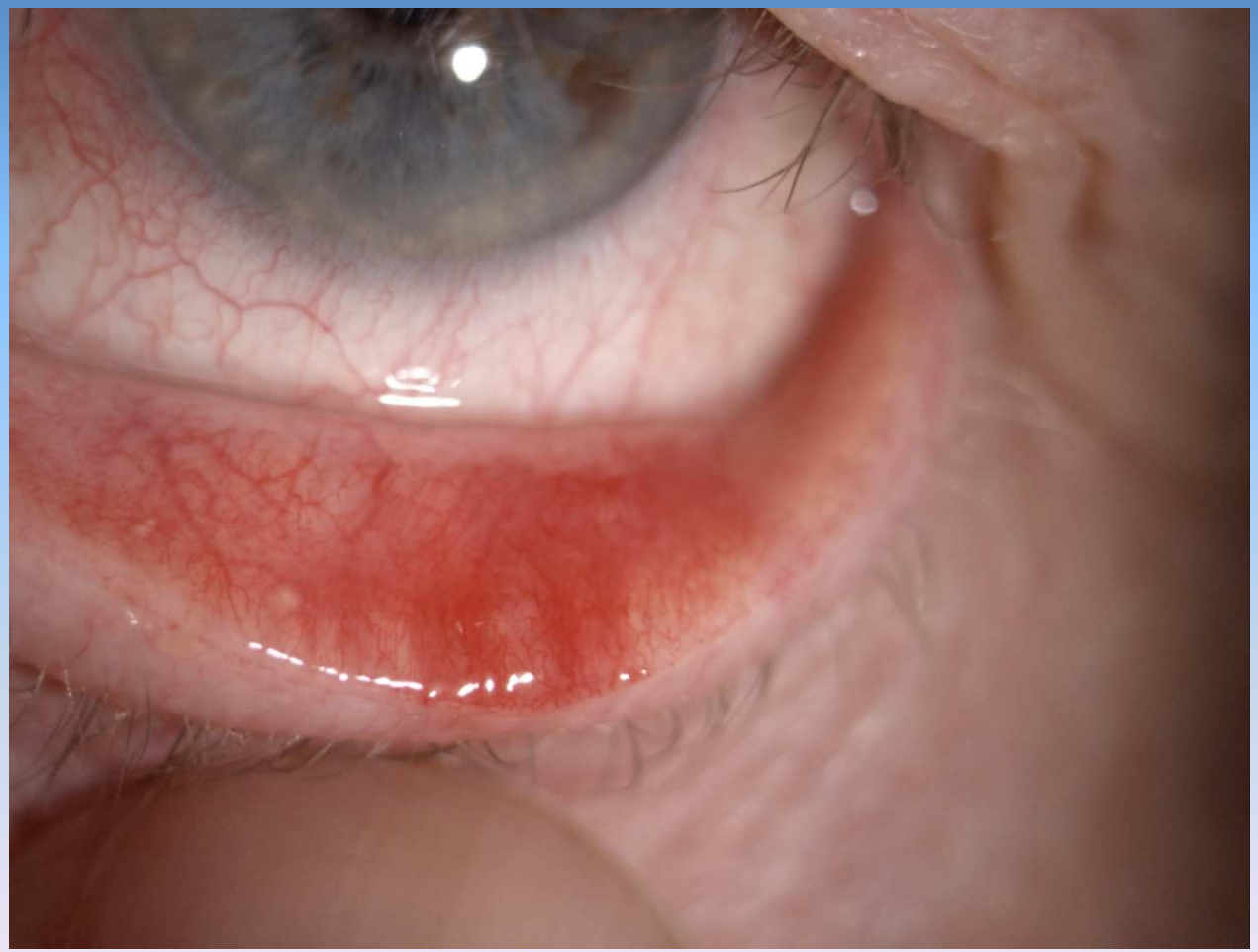
Lid Notching



Meibum accumulation and inflammation



Meibum accumulation and inflammation



Structural effect of dry eyes

- Mild dry eye disease following structural changes
- Reduced Corneal Endothelial Cell Density in Patients With Dry Eye Disease. Kheirkhah A et al. Am J Ophthalmol 2015 Jun;159(6):1022-1026
- More immune activity, less sub basal nerves.

MGD symptoms resistant to treatment

- Clinically non apparent inflammation
- In vivo detection of clinically non-apparent ocular surface inflammation in patients with meibomian gland dysfunction-associated refractory dry eye symptoms: a pilot study. Qazi Y et al. EYE (Lond). 2015 Aug;29(8):1099-110

Evaporative dry eye treatment

- Lid massage and hygiene with a heat mask
- Massage correctly in a vertical direction
- Oral omega 3 oils / diet change
- Artificial tears.
- Treat inflammation

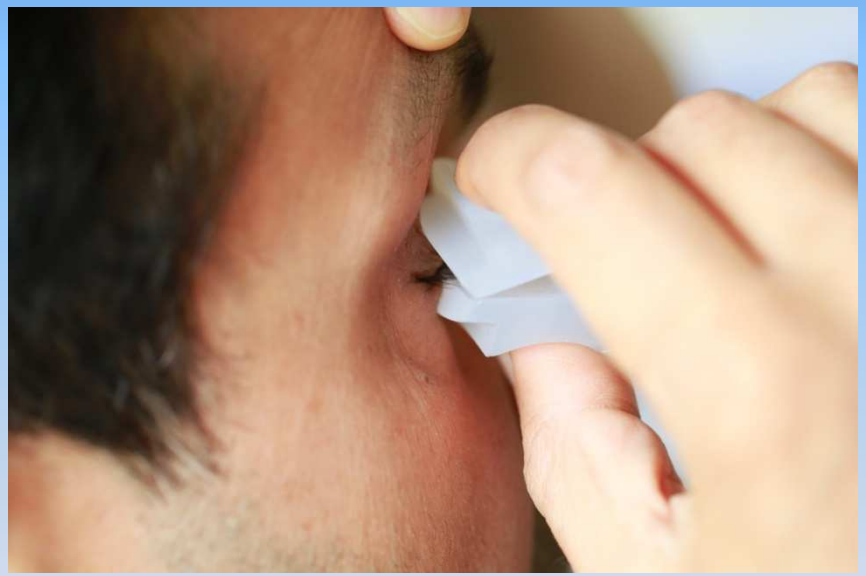
  Doxycycine, Azyter, Ciclosporin, Steroids

Correct Massage is key to MGD treatment

- Currently people suffering from MGD are instructed to use their fingers for massaging
- However, an online survey relating to eyelid massaging techniques from patients suffering from MGD showed that of the 88 people suffering from MGD
  - Only 10% of respondents massaged their eyelids vertically, the best way to express the glands
  - 32% of respondents massaged in an ineffective circular or horizontal motion
  - 43% reported no regular massaging
  - 25% reported they were not advised to massage
- The massager gives the patient confidence that they are massaging lids correctly and effectively

EYEPEACE LID MASSAGER

Eyepeace massager



Lid Massage

- Correct massage is key to MGD and evaporative dry eye.
- The Eyepeace lid massager gives the patient confidence that they are massaging lids correctly and effectively
- ESCRS 2015. J Moore et al. After 2 weeks of Eyepeace treatment, mean symptom scores improved significantly. Interferometry grading and TBUT showed marked improvement, and a significant increase in corneal temperature was shown by thermography.

Dry Eye-Tear defeciency

- Sjogrens primary or secondary (rheumatoid, other auto immune diseases)
- Dry mouth.
- Primary investigate. Serology, lip mucosa biopsy.
- Systemic disease

Treatment

- Artificial tears. Preservative free.
- Punctal plugs
- Ciclosporin / steroids / acetylcysteine for mucin
- Serum
- Fingerprick autologous blood (FAB).
- Treat lid margin disease as more common

Fingerprick autologous blood (FAB) to treat dry eyes

Collaborators

- James Wawrzynski
- Jonathan Moore
- Amit Patel
- Sunil Shah
- Bimal Kumar
- Julie Smith
- Hatch Mukherjee
- Chris Illingworth
- Derek Tole

Initial FAB trial sites

- Moorfields Eye Hospital Foundation Trust
- Bedford Hospital NHS Trust
- The Royal Victoria Hospital, Belfast
- Milton Keynes General NHS Trust
- Heart of England NHS Trust
- University Hospitals Bristol NHS Foundation Trust
- Birmingham Midland Eye Centre

Autologous serum for dry eyes and PED

Noble BA, Loh RSK, MacLennan S et al. Comparison of autologous serum eye drops with conventional therapy in a randomised controlled crossover trial for ocular surface disease Br. J. Ophthalmol. 2004;88;647-652

- Poon AC ,Geerling G, J.K. G. Dart JKG et al. Autologous serum eyedrops for dry eyes and epithelial defects: clinical and in vitro toxicity studies. Br J Ophthalmol 2001;**85**:1188-1197
- Tsubota K, Goto E, Shimmura S and Shimazaki J. Treatment of persistent corneal epithelial defects by autologous serum application Ophthalmology. 1999;106 issue 10: 1984-1989

Autologous serum for dry eyes and PED

- Fox RI, Chan R, Michelson JB, et al. Beneficial effect of artificial tears made with autologous serum in patients with keratoconjunctivitis sicca. Arthritis Rheum. 1984;27:459–461.
- Hussain M, Shtein RM, Sugar A et al. Long-term use of autologous serum 50% eye drops for the treatment of dry eye disease. Cornea 2014 Dec;33(12):1245-51

Autologous serum indications

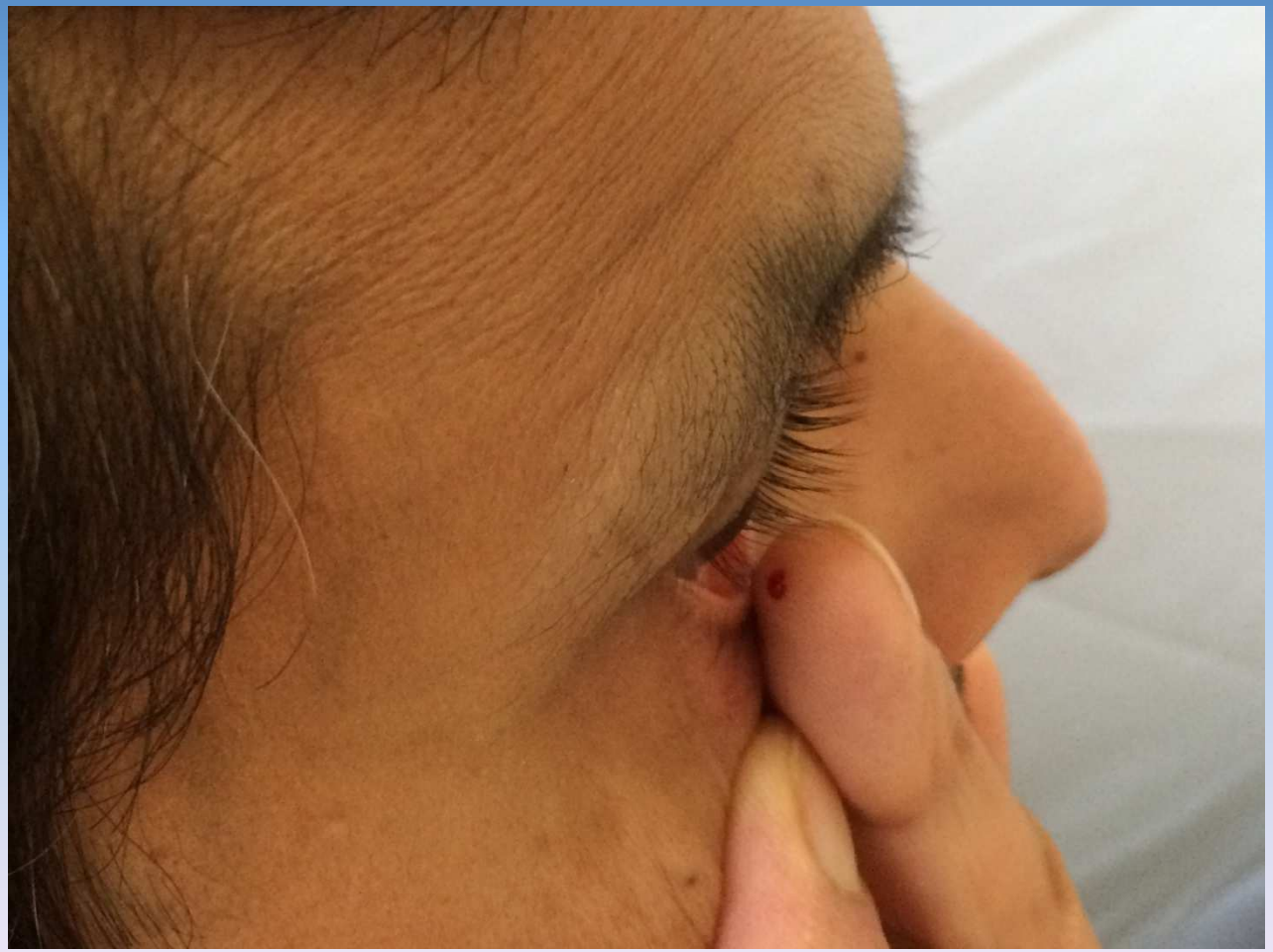
- Dry eye disease (Sjogren's and non-Sjogren's syndrome)
- Persistent corneal epithelial defect
- Neurotrophic keratopathy
- Diabetic keratopathy
- Recurrent corneal erosion syndrome
- Graft versus host disease
- Superior limbic keratoconjunctivitis
- Limbal stem cell deficiency

Autologous serum 20% cost

- **AUTOLOGOUS SERUM EYEDROPS (INITIAL VISIT ONLY) £ 1,632.39**
- **AUTOLOGOUS SERUM EYEDROPS (SUBSEQUENT VISITS) £ 1,116.79**

FAB to treat dry eyes and persistent epithelial defects

FAB to treat dry eyes and persistent epithelial defects



Patient Pamphlet

The treatment that we are investigating involves placing a drop of your own blood from your finger into your eye four times per day. ONLY USE YOUR OWN BLOOD

Preparation

You will be supplied with lancets, finger wipes and a sharps box. Please cut your nails short on the finger(s) that you wish to use.

Producing a fingertip drop of blood

Wash your hands with soap and warm water and wipe dry with a clean towel. Then use an alcohol finger wipe to wipe a finger on your non-dominant hand: Creating a drop of blood on a finger of the non dominant hand is usually easier.

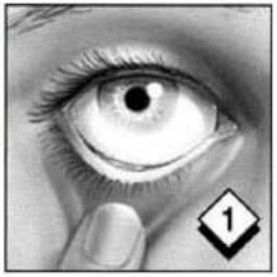
Take a new lancet and use it to prick the finger as per instructions on the lancet box. Then throw the lancet away in the sharps box. When your sharps box is full, please return it closed to the eye clinic on your next visit, where you will be provided with a new sharps box.

A small drop of blood will slowly form on your finger. You may need to squeeze your finger slightly to encourage the drop of blood to form. Pricking your finger in some places can cause much less pain than in others. It takes time to find the best place. You can use a different finger each time if you prefer.

Applying the blood drop to the eye

Looking in the mirror, pull down the lower lid of the eye to be treated with the hand that has not been pricked and touch the inside of the lower lid with the drop of blood.

Your vision may become slightly blurred or tinted red for a minute, but then returns to normal. It should not hurt or sting. If it does, report this to your doctor.



Wipe your finger again with an alcohol swab.

Helpful tips

- If treating both eyes with finger prick drops of blood, please ensure you use a different finger for each eye to avoid spreading infection from one eye to the other.
- If you develop any infection or persistent pain at your fingertips, please stop using that finger and contact your GP and the research team (contact details can be found on your patient information sheet).

FAB cost

- Per eye qds for 2 months less than <£25
- 3 sharps boxes, 240 alcohol wipes and lancets.

Blood versus serum

- Blood / plasma is not same as serum
- Plasma not as effective as serum on cell migration as fewer growth factors.
- Capillary blood (fresh) not same as venous
- Role of white blood cells and platelets
- Individual components of blood are used separtately and have been shown to be effective. Vitamins, fibronectin, EGF, platelets, WBCs, albumin , fibrin.
- Why not together as whole blood
- Is blood comparable to serum ?

Plasma versus serum

- Plasma much less effective than serum on cell culture migration as less concentration of growth factors Hartwig et al 2004

Blood

- Is a living complex solution which reacts to its enviroment to provide an effect.
- Platelets, growth factors are important but so are other higher concentration of components found in blood as fibronectin.

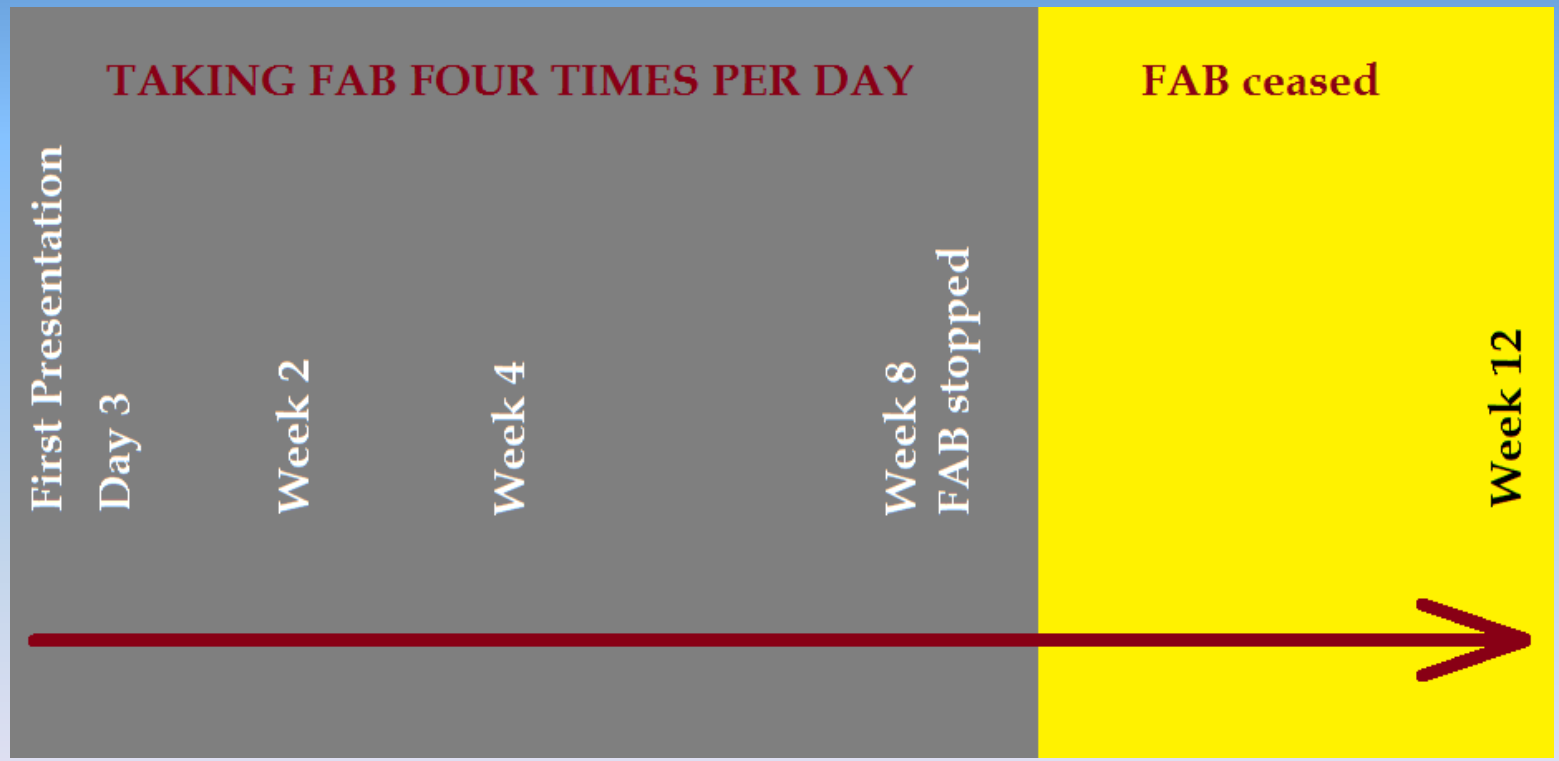
FAB: Exclusion criteria

- Fear of needles and unwillingness to carry out repeat finger pricks
- Infected finger or systemic infection or on systemic antibiotics for infection.
- Bleeding disorders does not include on warfarin or other anticoagulant therapy
- Epithelial defect was classified as a progressive corneal melt caused by an immunological process such as rheumatoid melt or Mooren's ulceration.
- Patients with active microbial infection, acute herpes simplex or herpes zoster keratitis, drug toxicity, vitamin A deficiency, or recurrent corneal erosion.
- Pregnant or breast feeding women
- Children (under 16 years old).

FAB for Dry eyes: Inclusion criteria

- Artificial tears at least qds
- Punctal plugs / refused
- Oc. Cyclosporin / refused
- In addition no anaesthetic Schirmer <5mm /stain /Ocular Comfort Index score >80%

Method -Dry eye syndrome



Patient quotes and common themes

- ‘Transformed my life’
- ‘My eyes have never felt so much better for the last 26 years’
- Coming to clinics all these years and nothing really worked until FAB.
- Getting married in 2 months could not get out of bed.

Trial design

- Primary outcome measures
  - Dry eyes: To improve signs (corneal and conjunctival staining, Schirmer's test, tear break up time) or symptoms (ocular comfort index questionnaire)
- Follow ups are 3 days, 2 weeks , 4 weeks and 2 months after commencing treatment and 1 month after stopping treatment.
- Criteria to stop treatment based on patient safety such as infection

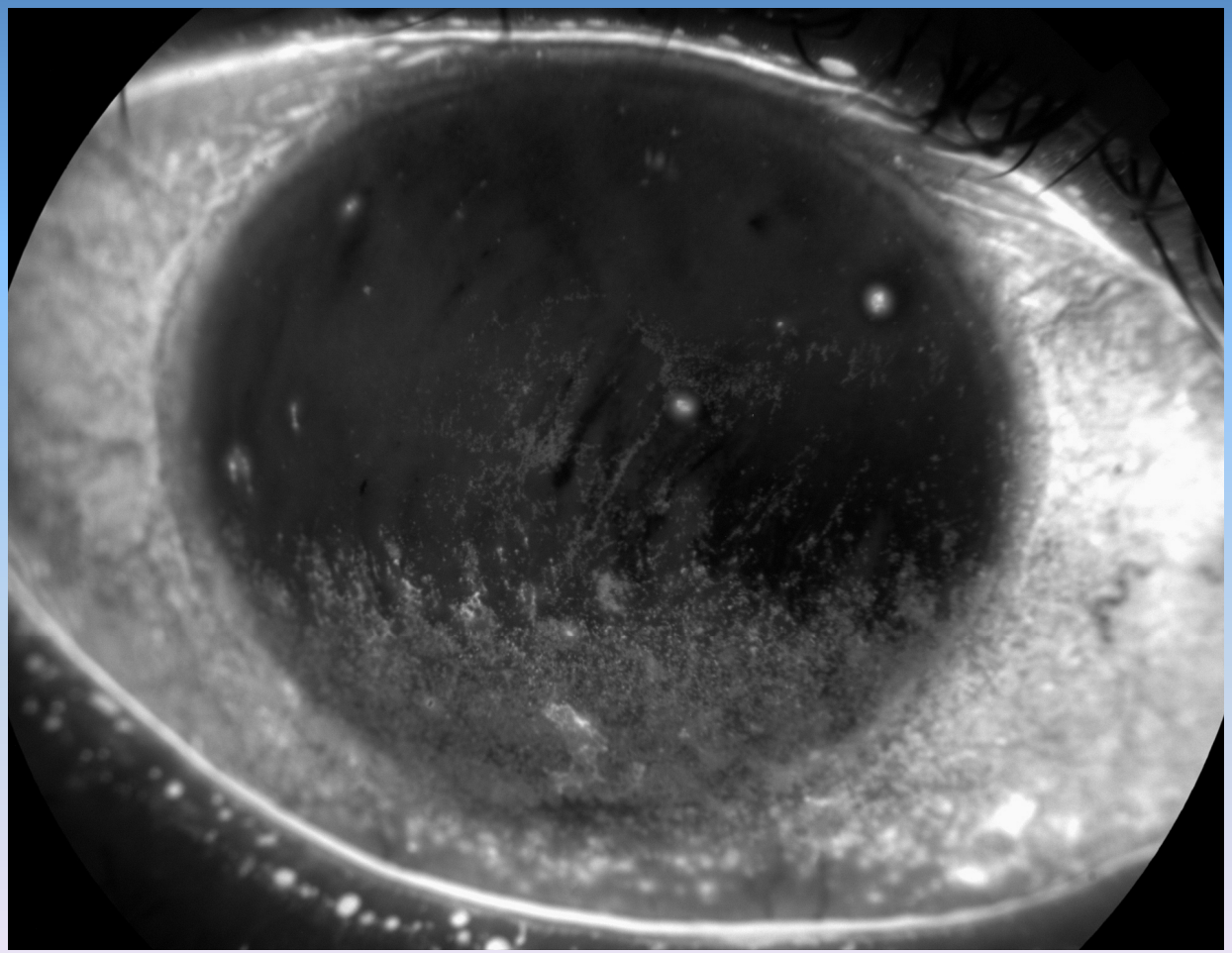
FAB for dry eyes

- 16 patients with primary or secondary Sjogren's syndrome over last 4 years.
- 6 Sjogren patients on this trial
- 1 radiotherapy dry eye
- All patients who finished trial have voluntarily continued FAB because of benefits.

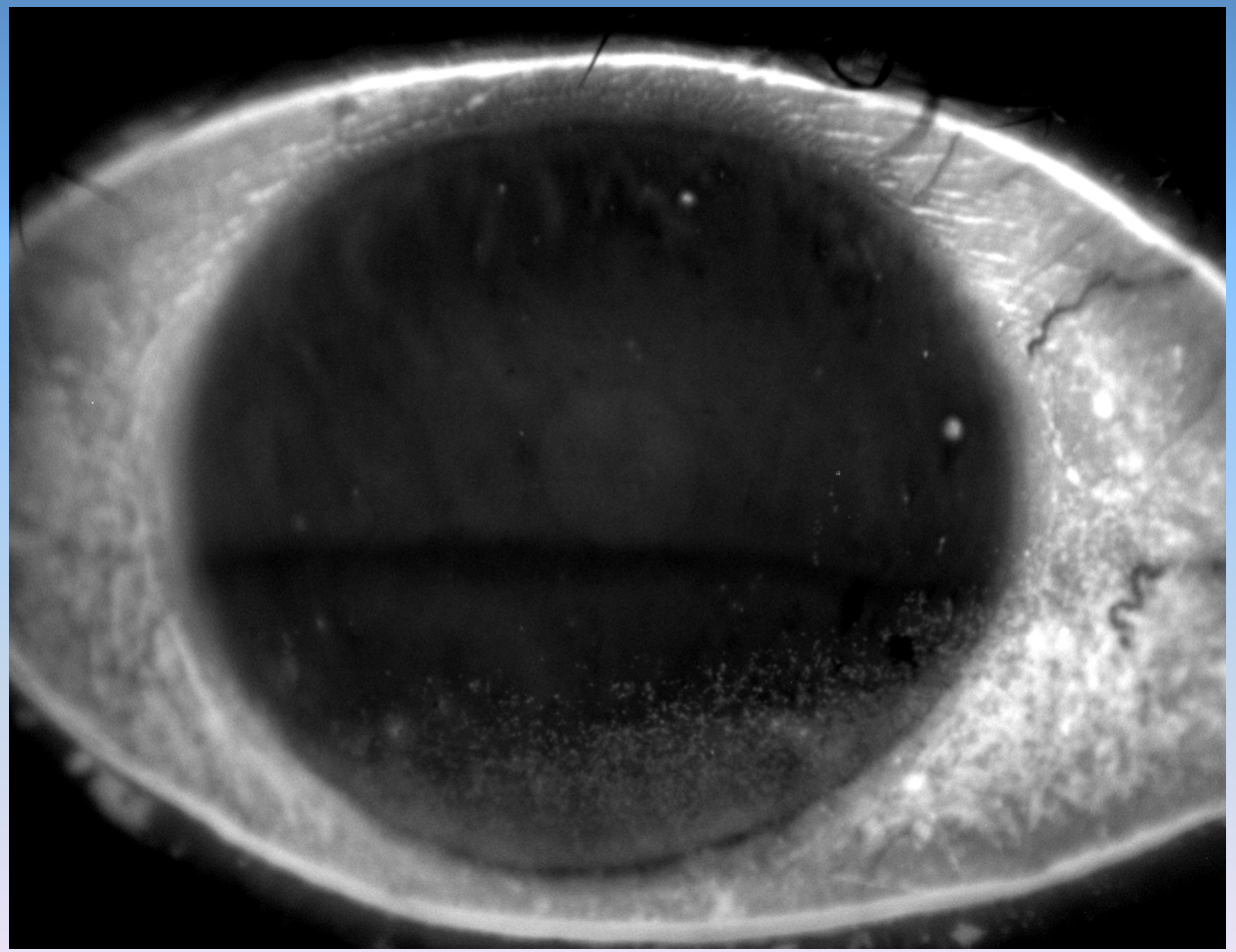
Trial Sjogren Syndrome Case histories

- 4 Primary and 2 secondary Sjogren's syndrome.
- Hourly or more frequent artificial tears, punctal plugs, tried and / or refused cyclosporin ointment.
- 5 patients had dramatic improvement in their quality of life and significant reduction in artificial tears usage
- Fifth patient had significant improvement in vision of his only eye which was the reason he was referred.

BH01AS Right pre treatment

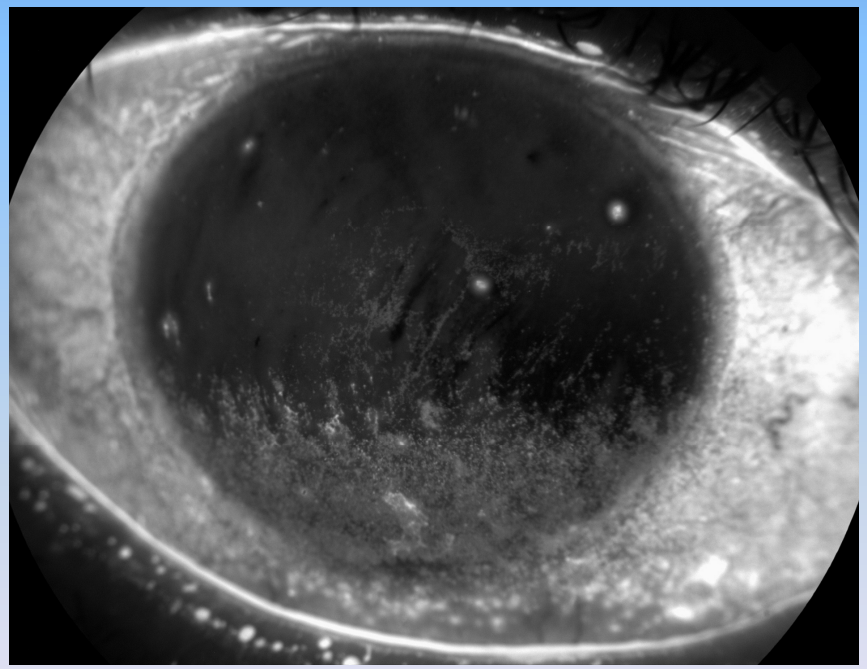


BH01AS Right post 2 months post treatment

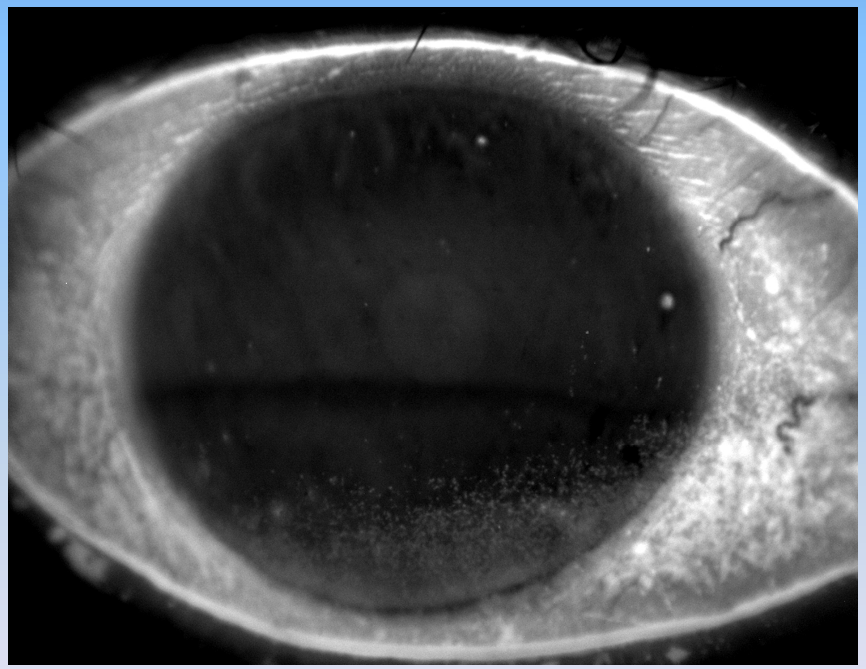


BH01AS right corneal staining

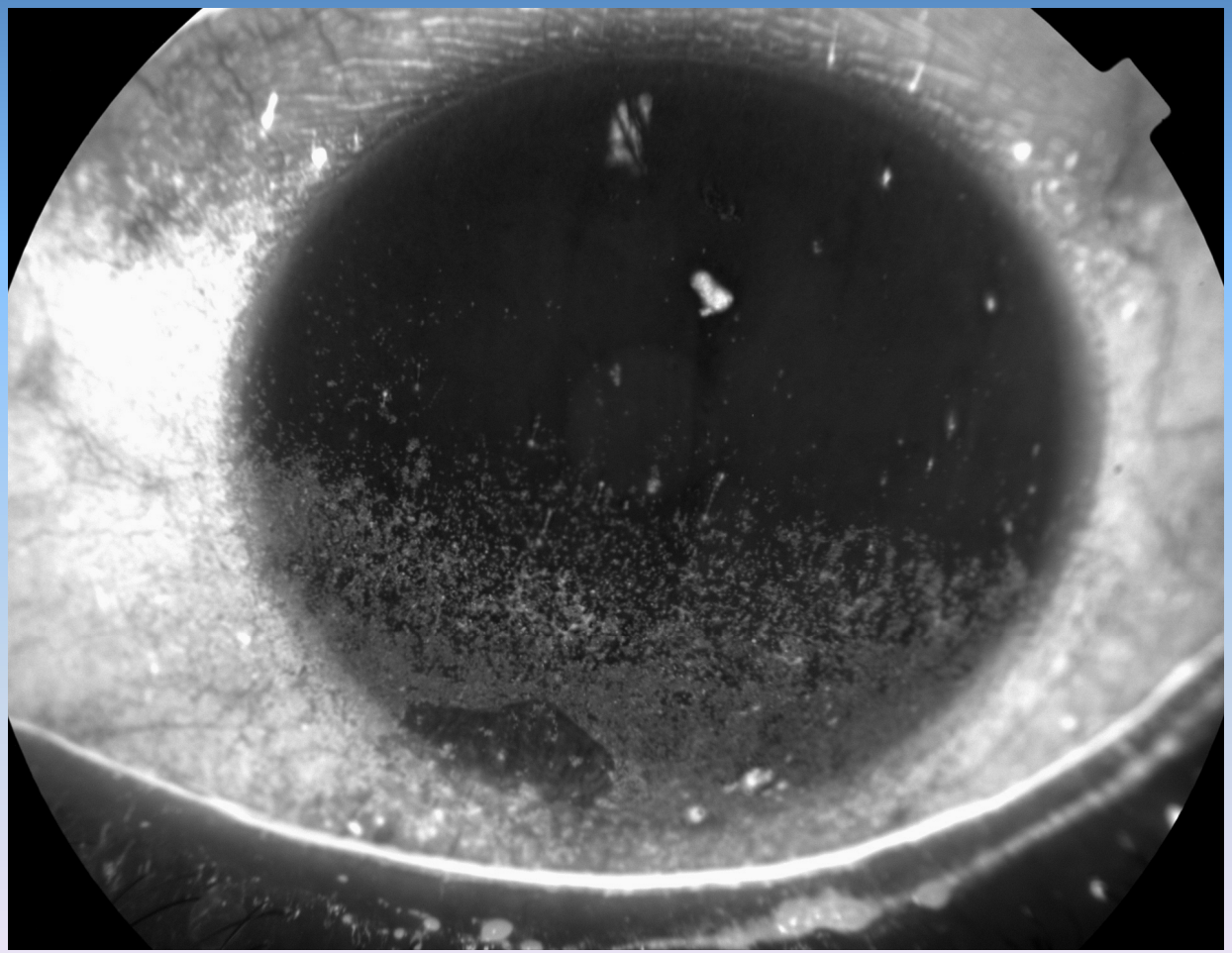
Pre treatment



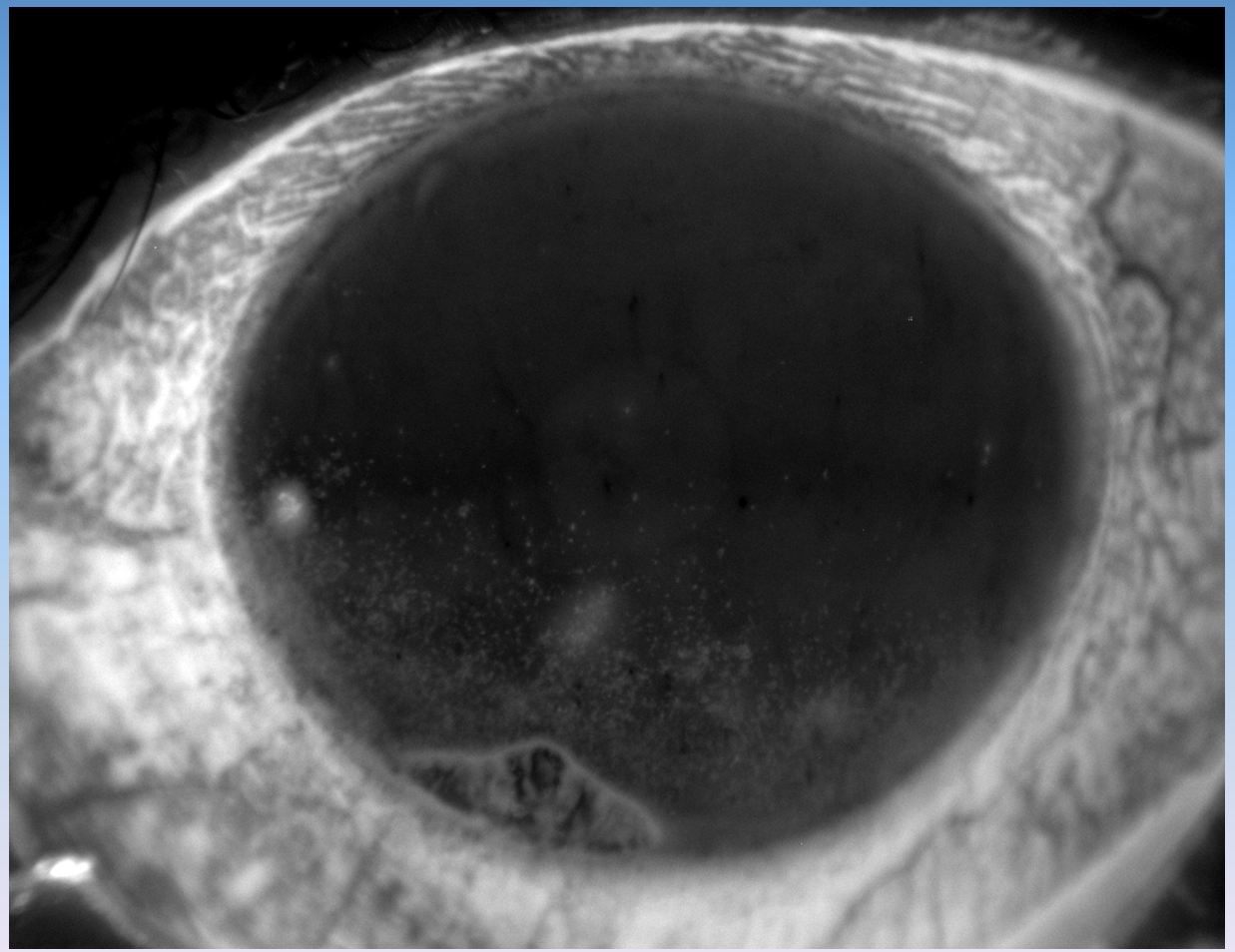
Two months post treatment



BH01AS Left pre treatment

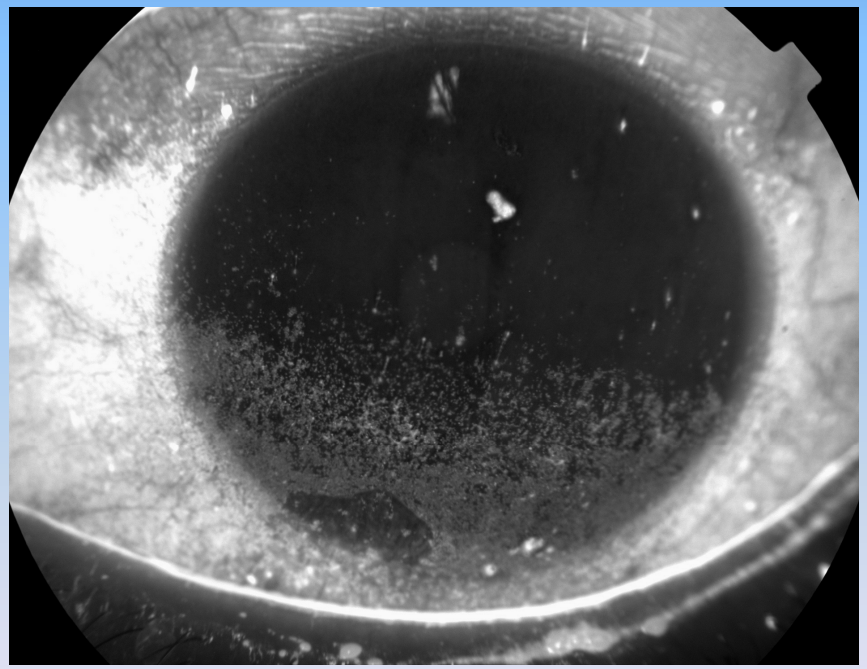


BH01AS Left 2 months post treatment

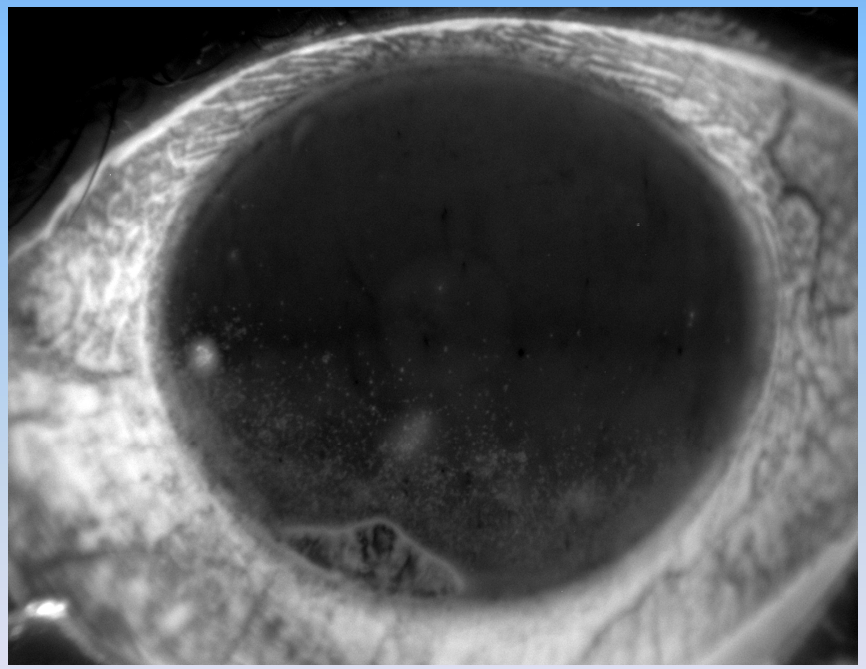


BH01AS left corneal staining

Pre treatment

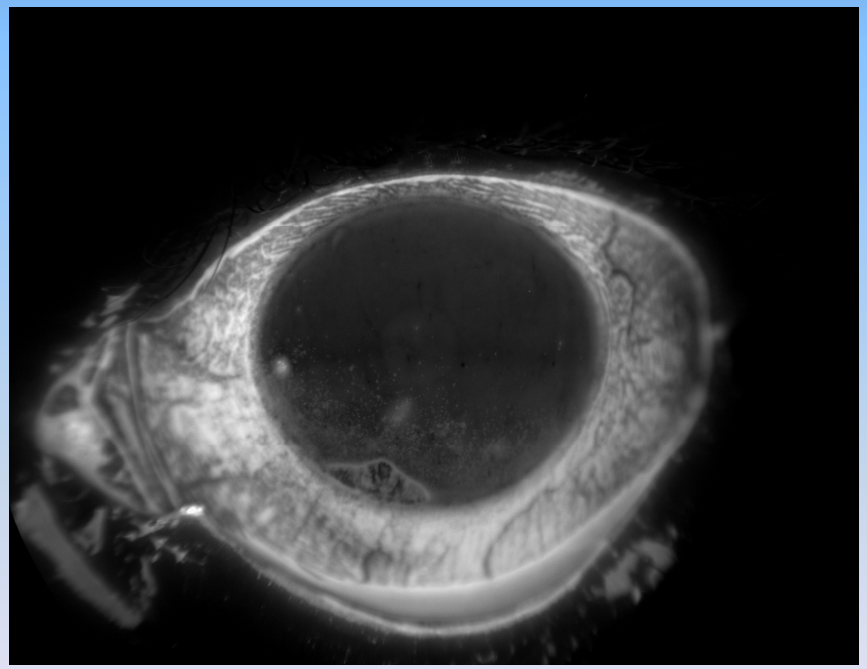


Two months post treatment

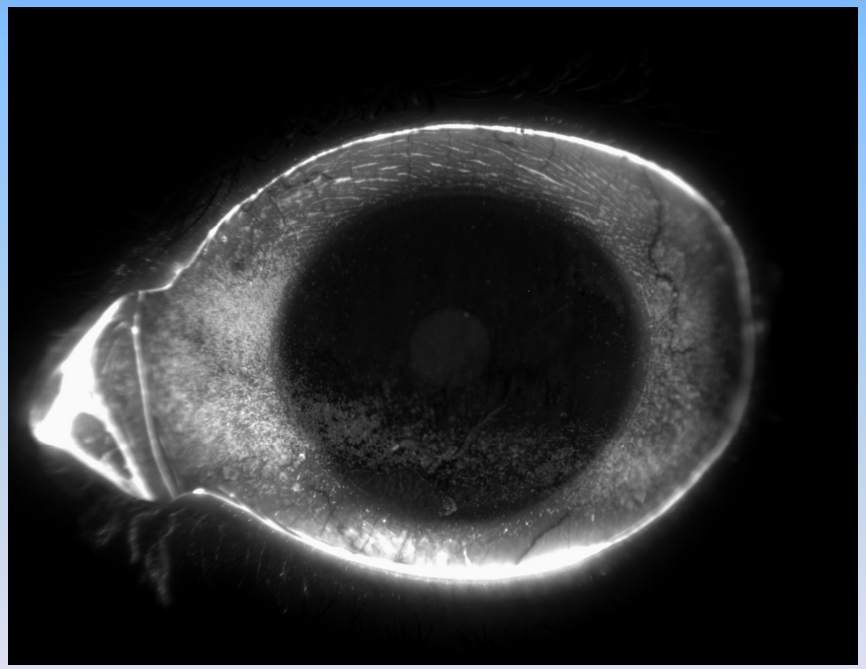


Left BH01AS

2 months Post FAB

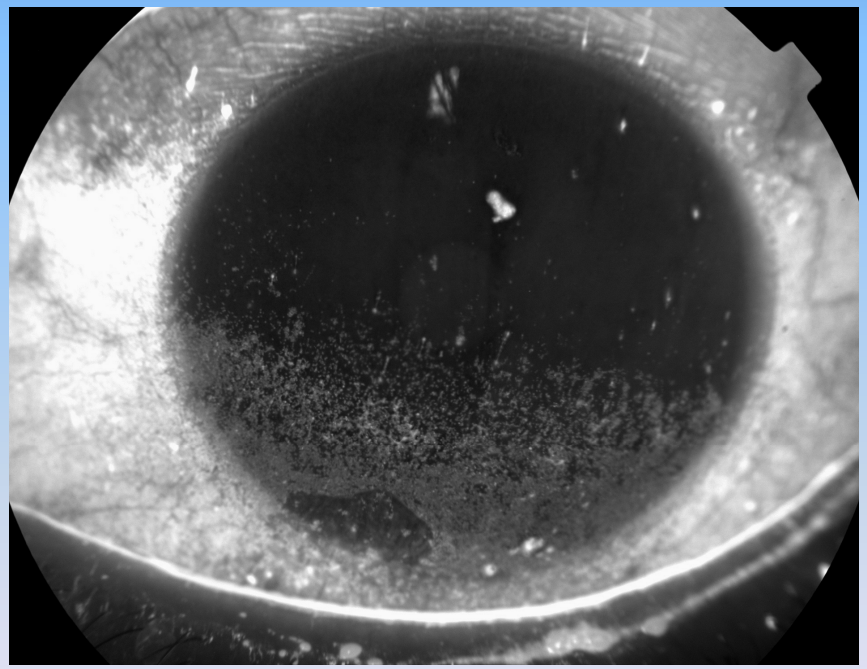


1 month off FAB

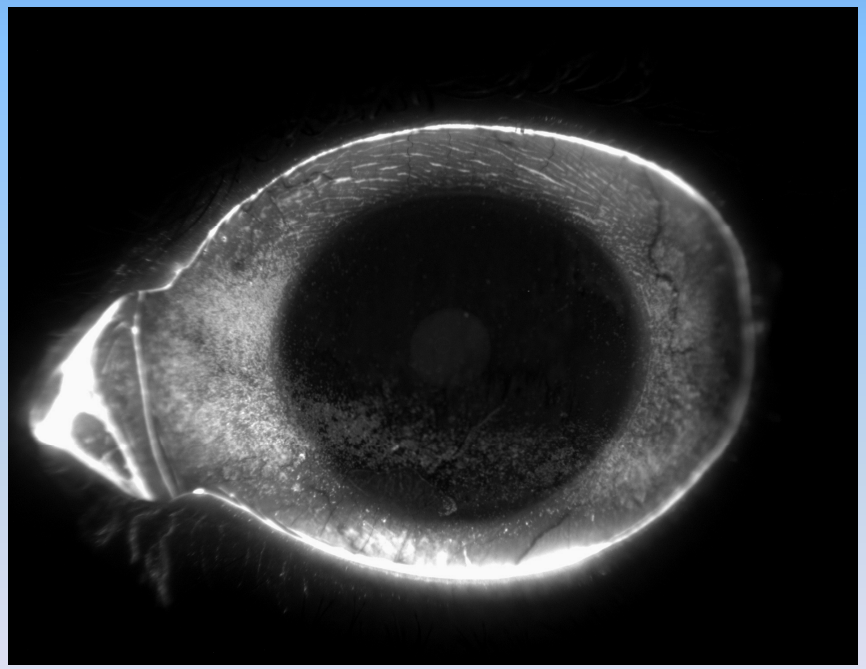


BH01AS left corneal staining

Pre treatment

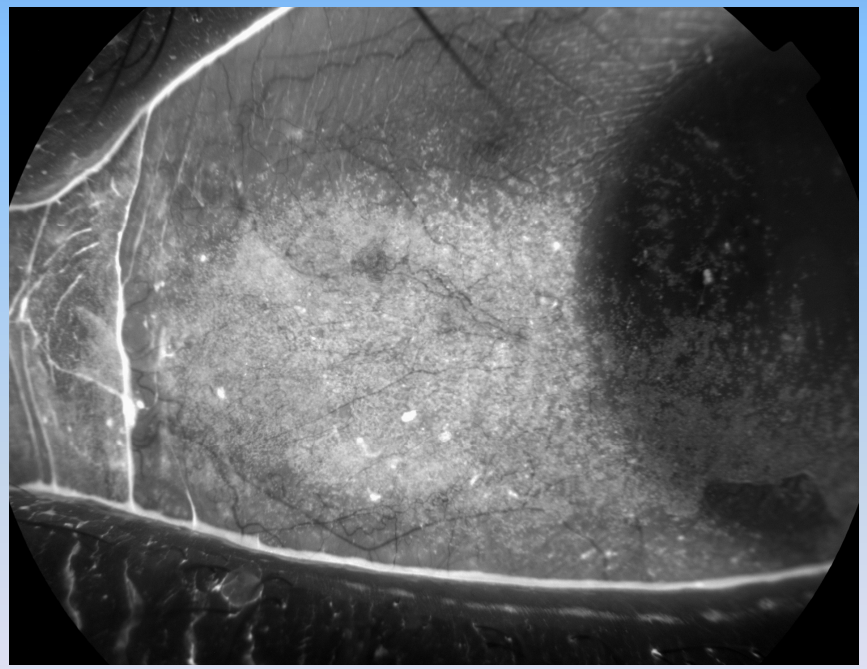


One month off treatment

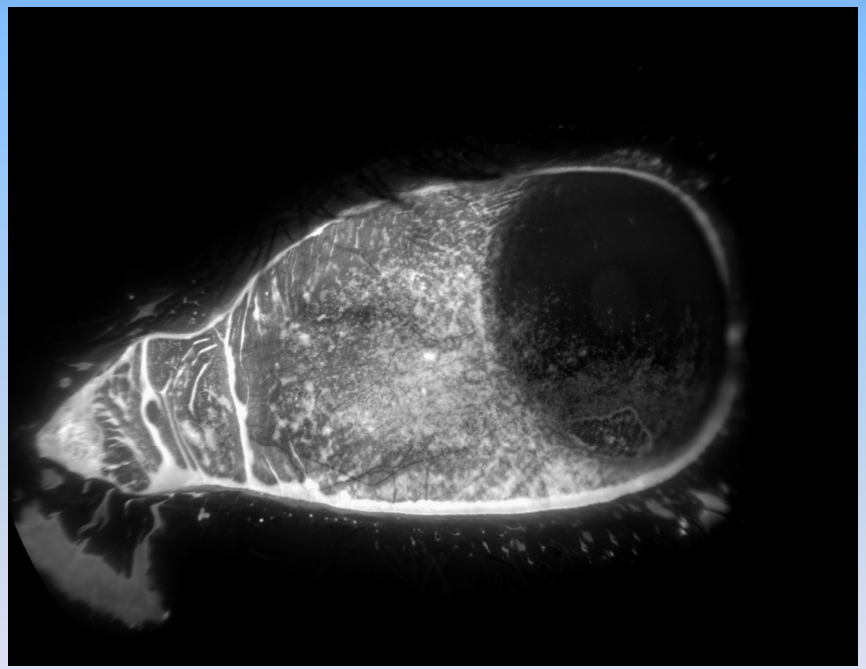


Left BH01AS

4 days on FAB

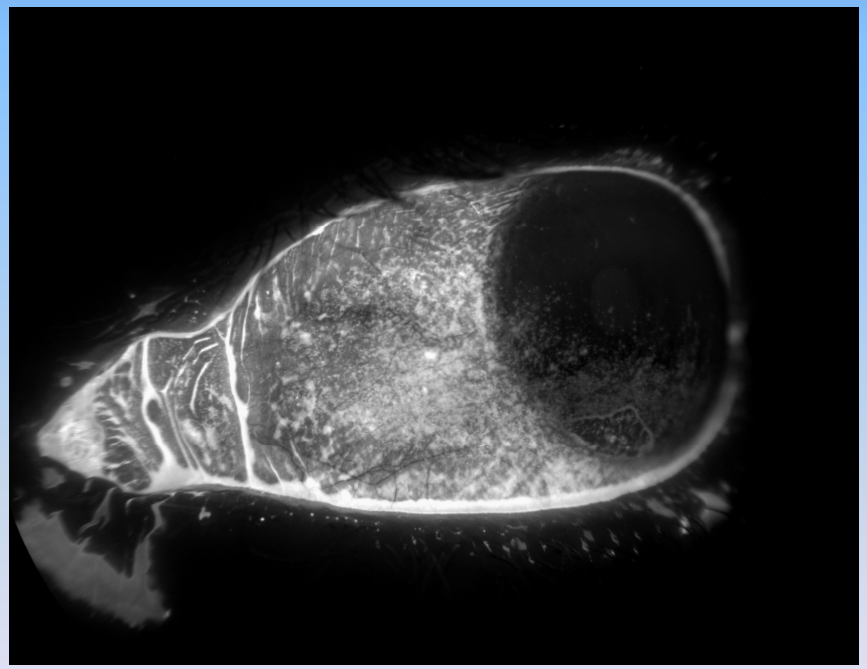


2 months on FAB

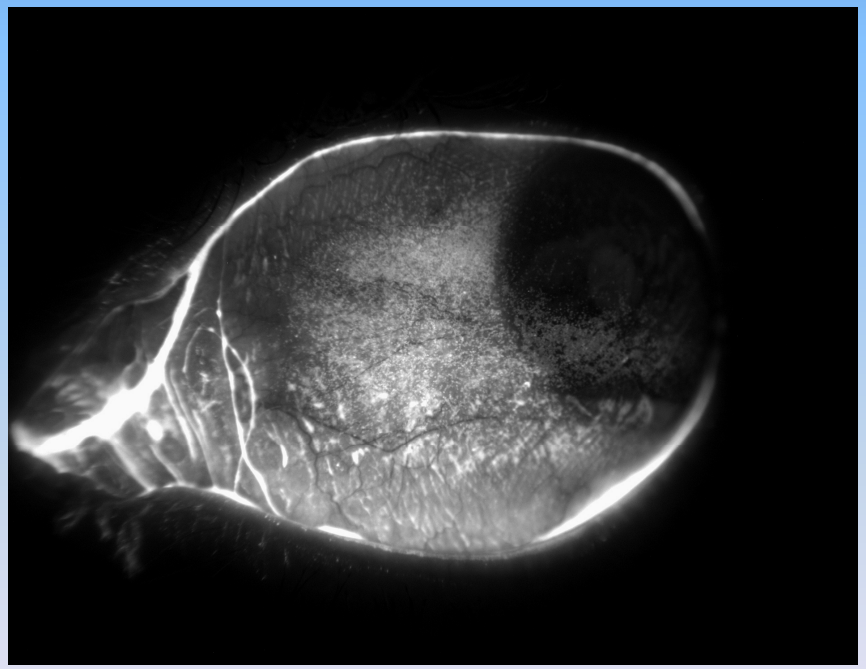


Left BH01AS

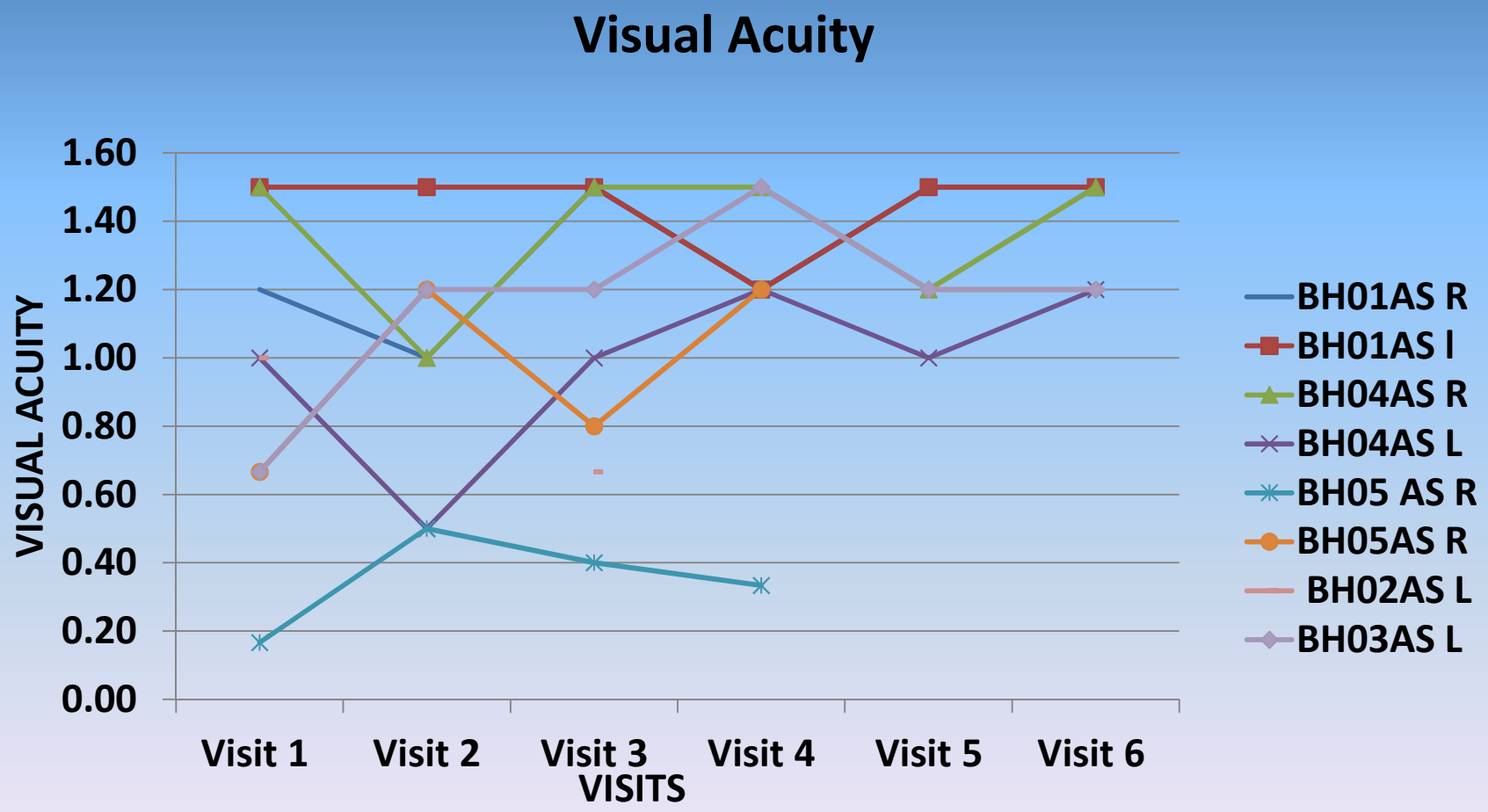
2 months on FAB



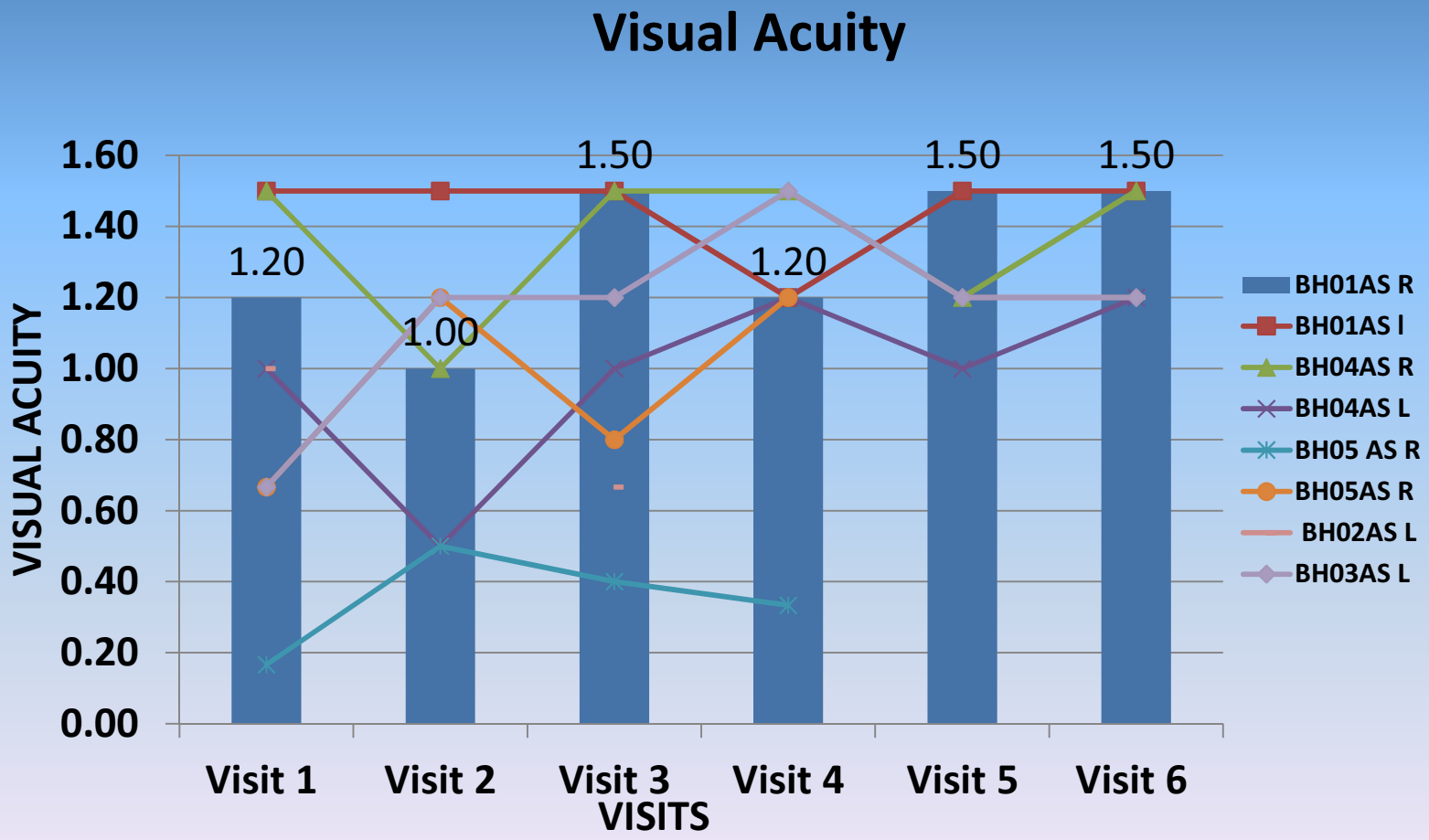
1 month off FAB



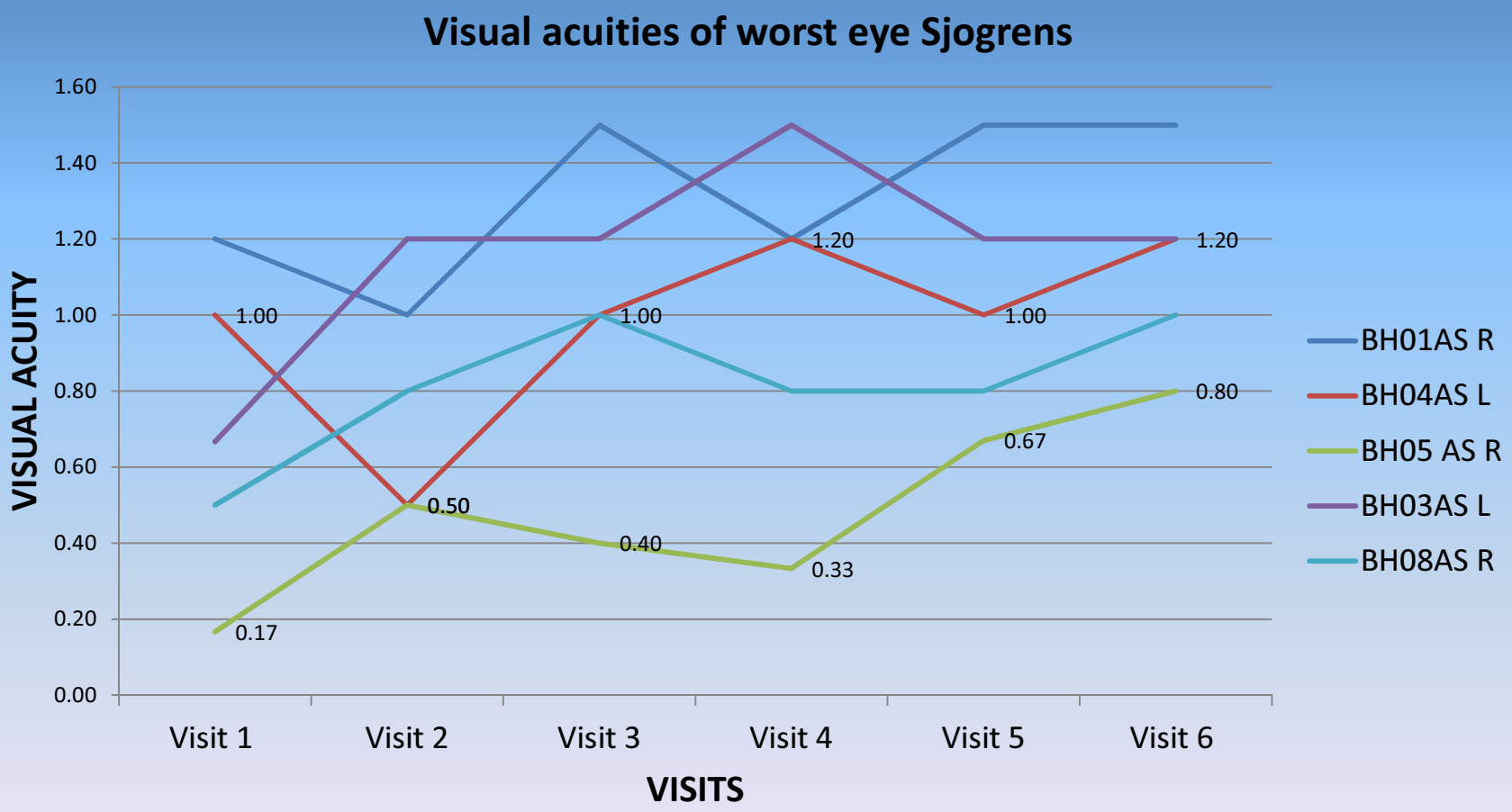
Visual acuity



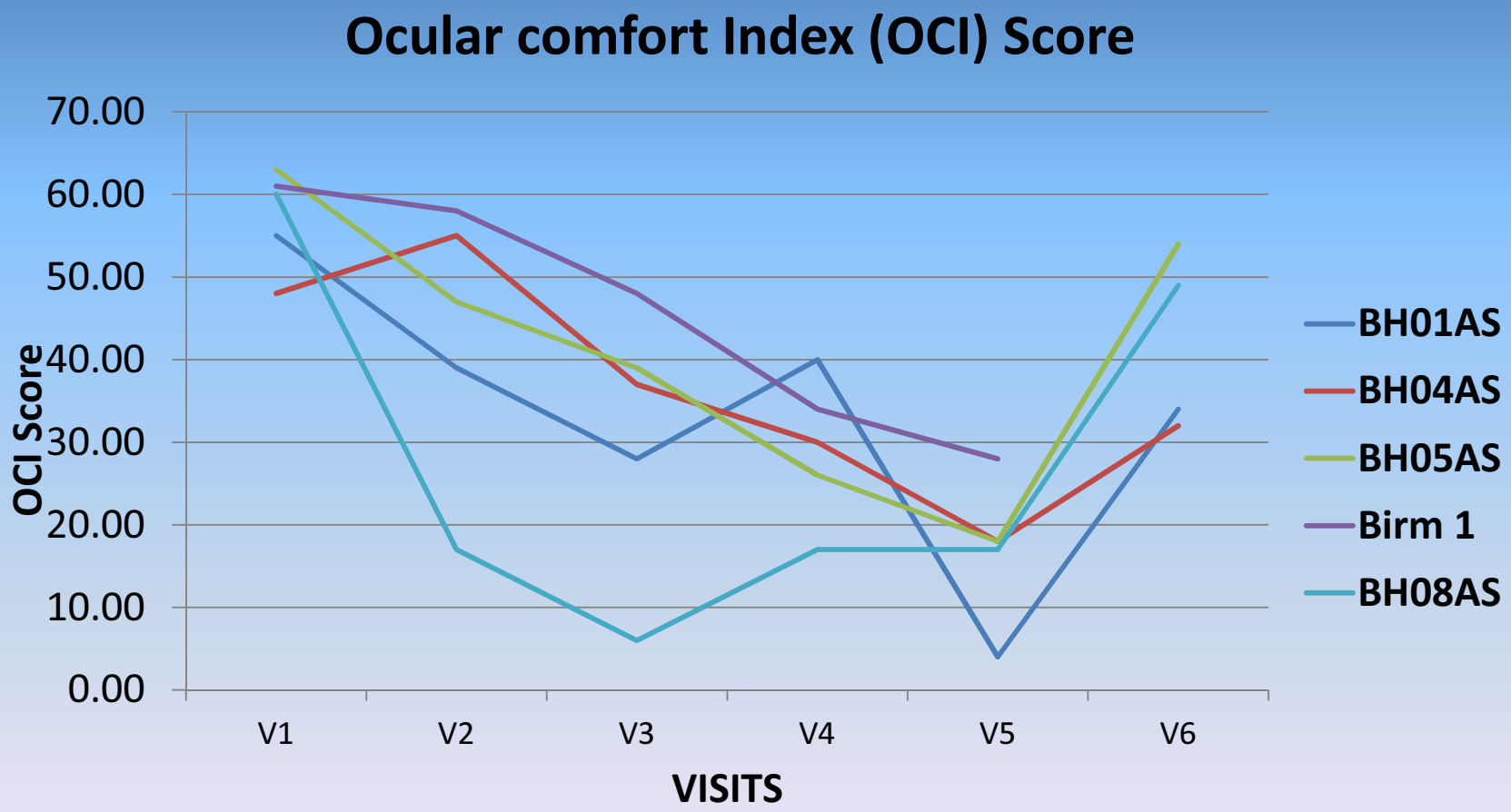
Visual Acuity



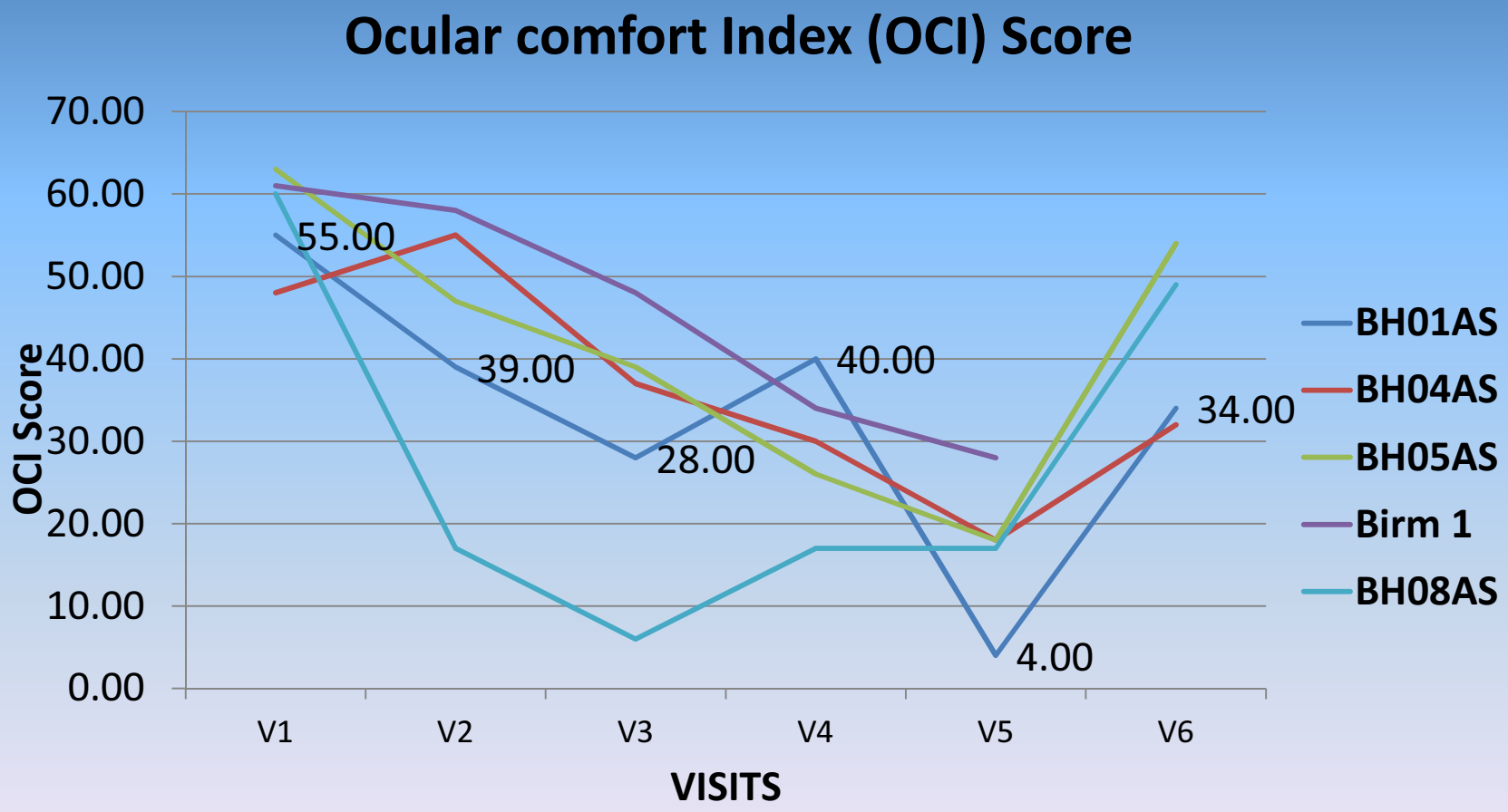
Worst Eye Visual Acuities



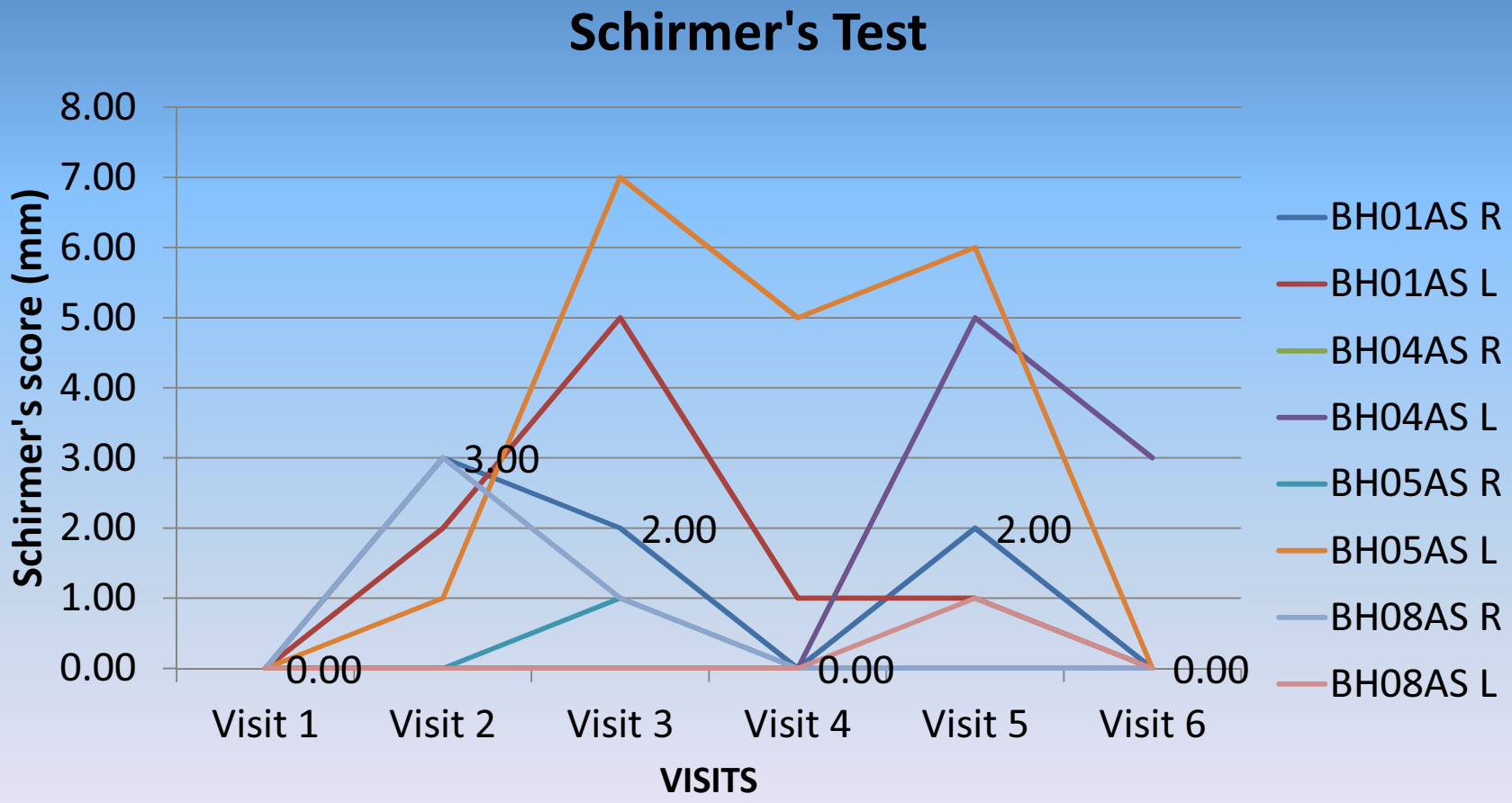
Ocular comfort Index (OCI) Score



Ocular comfort Index (OCI) Score



Schirmer’s


Schirmer's Test
Schirmer's score (mm)
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
3.00
2.00
2.00
0.00
0.00
0.00
Visit 1
Visit 2
Visit 3
Visit 4
Visit 5
Visit 6
VISITS
BH01AS R
BH01AS L
BH04AS R
BH04AS L
BH05AS R
BH05AS L
BH08AS R
BH08AS L

FAB summary

- In the limited cases appears to be effective and practical. There were no cases of infection, technique failure or significant sore fingers.
- FAB appears to show effect in the treatment of dry eyes and persistent epithelial defects.
- Consider in management while waiting for autologous serum especially for PED.

Hussain et al 2014

- Sjögren 11 patients
- Schirmers 7.3 versus 7.4
- OSCI questionnaire 39. 1 versus 48.6
- Fluorescein staining 1.5 versus 0.8

Persistent epithelial defects (PEDs)

- 3 herpes simplex keratitis persistent epithelial defects
- 1 chemical trauma
- 2 diabetic neuropathic corneas.

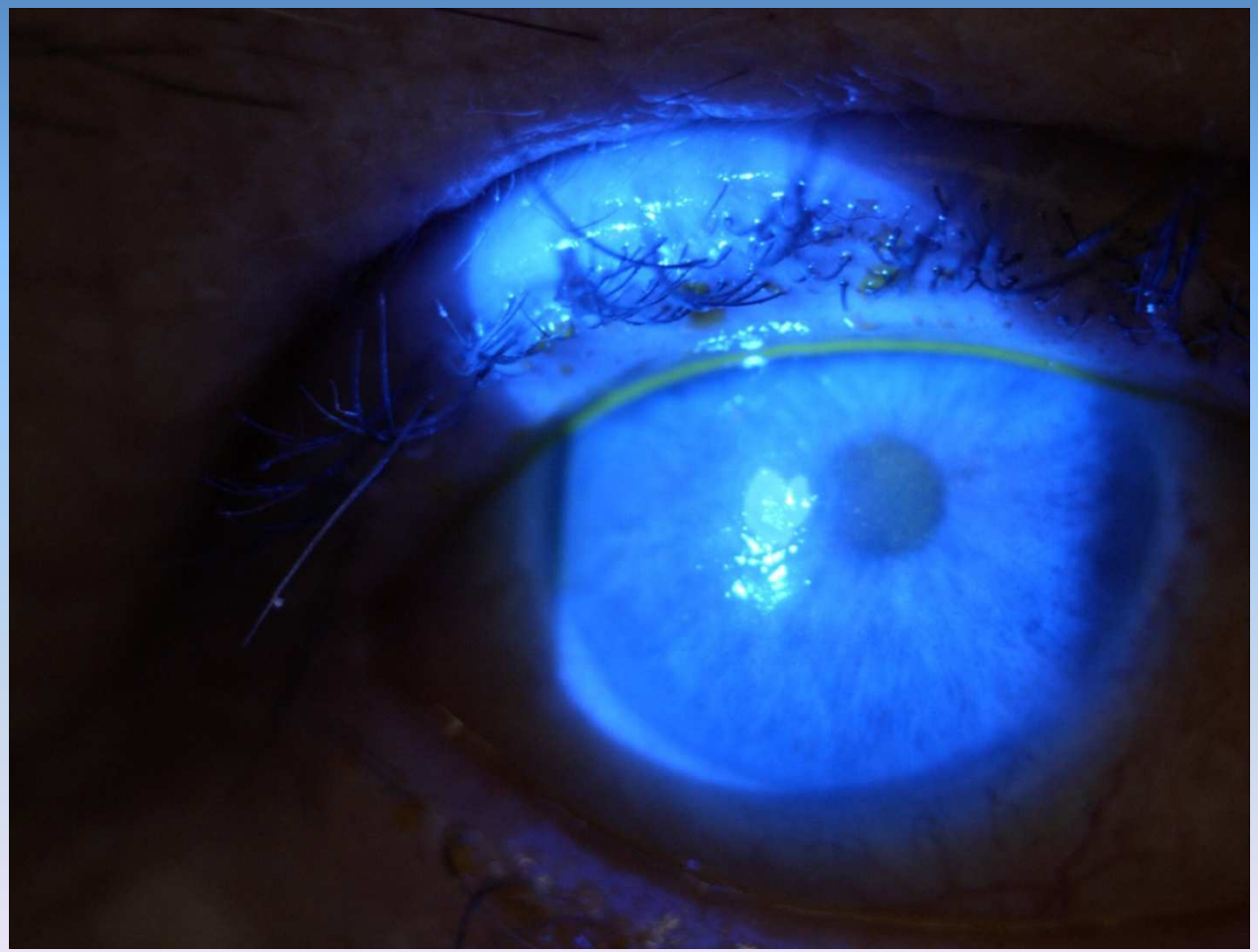
Poon et al 2001

- 6 Sjogren patients
- 2 withdrawn as side effects such as sterile infiltrate
- Remaining 4 improved subjectively and staining (symptoms within 2 days). Schirmer’s not done.

Persistent epithelial defects (PED)

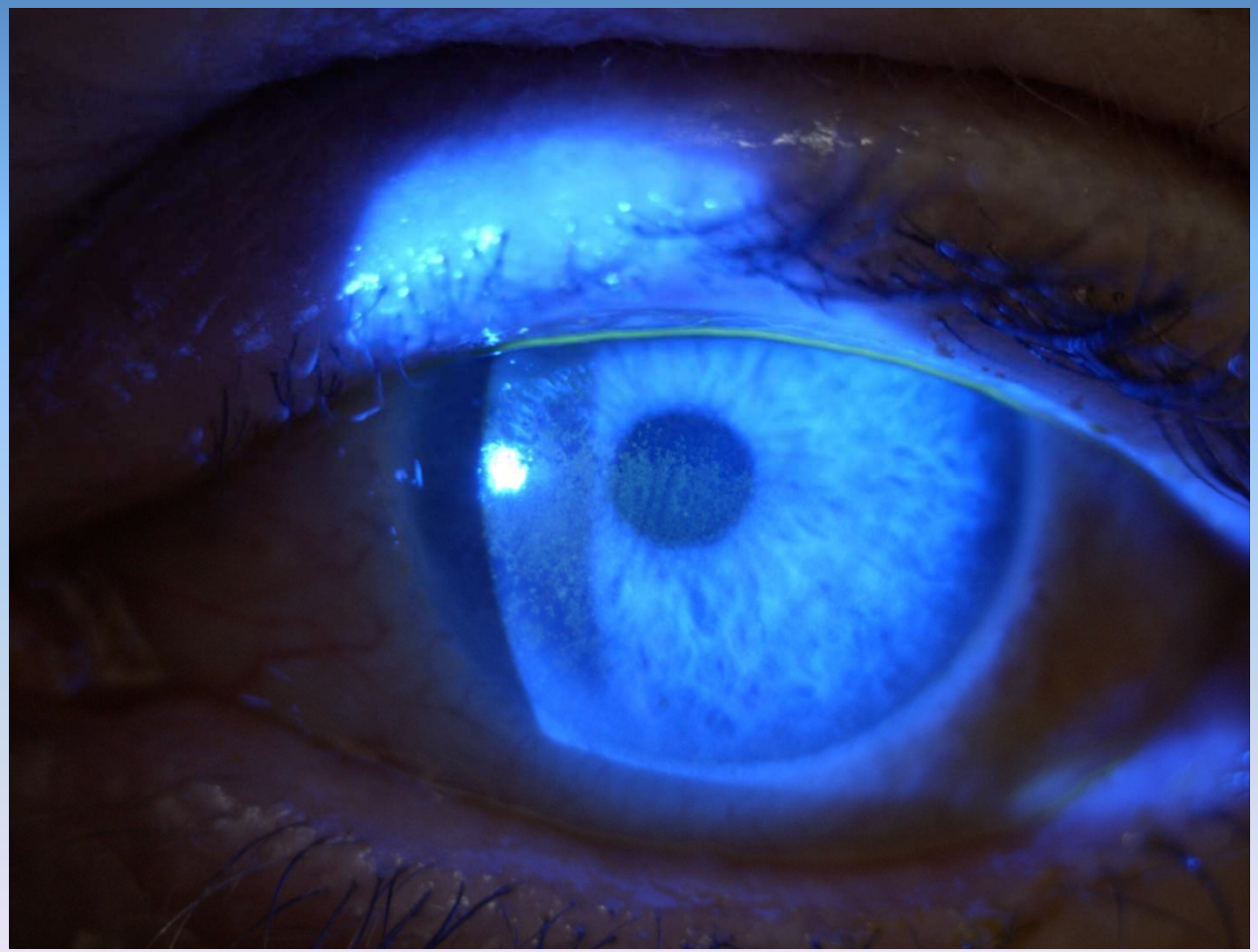
- 64 male diabetic
- Previous extensive pan retinal photocoagulation
- On regular artificial tears for 12 months
- PED right eye did not improve on 2 weeks on hourly hyaluronic acid 0.2% and soft white paraffin ointment.

Diabetic corneal ulceration
Right eye

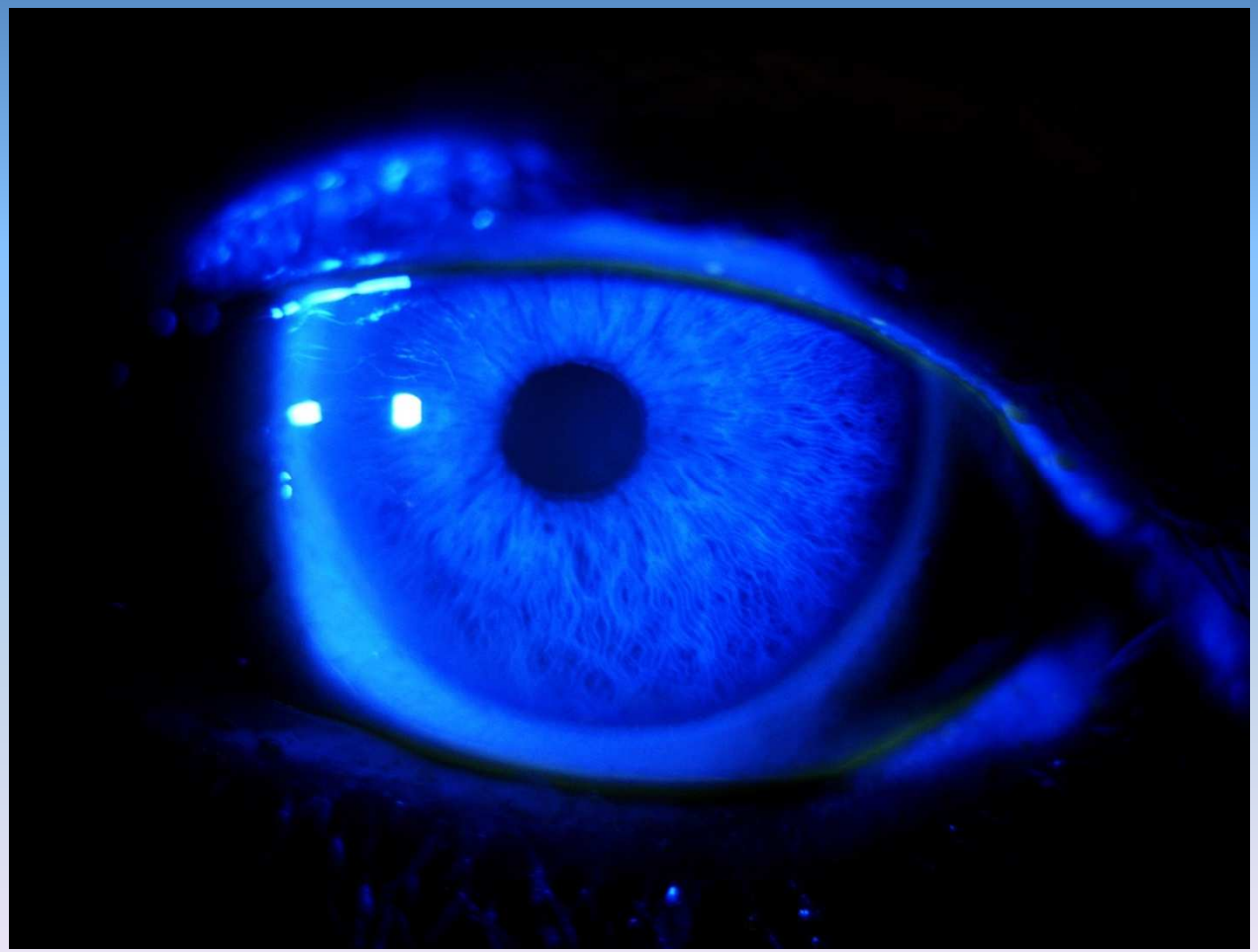


4 days post FAB

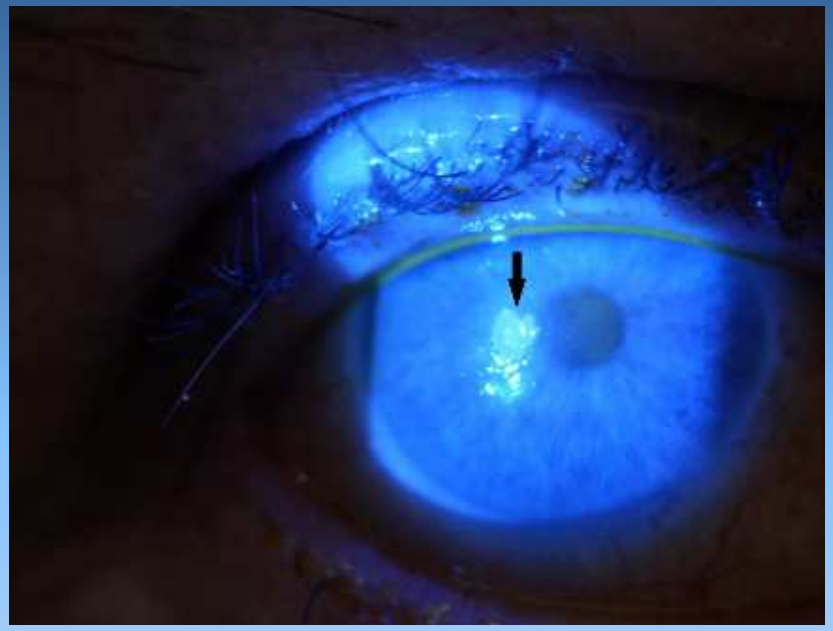
Diabetic neuropathic cornea
Left eye

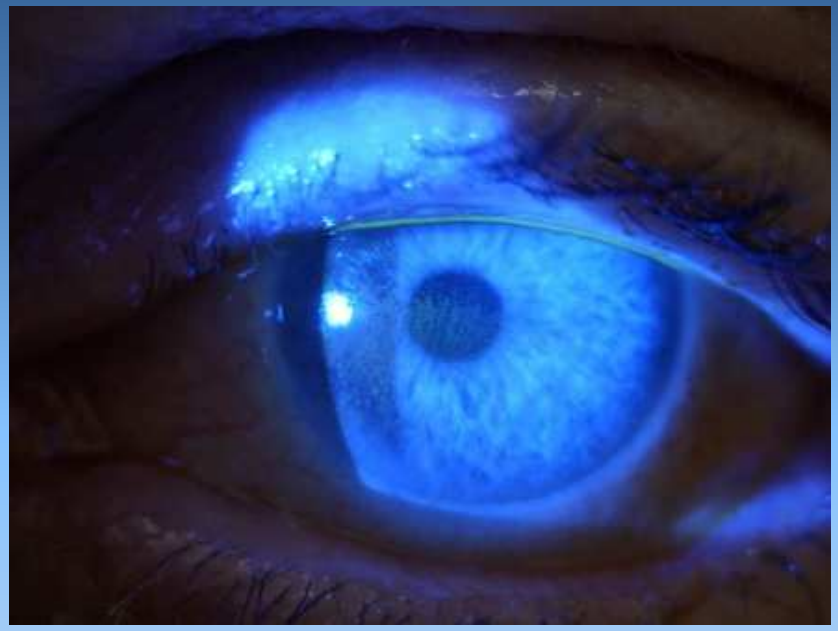


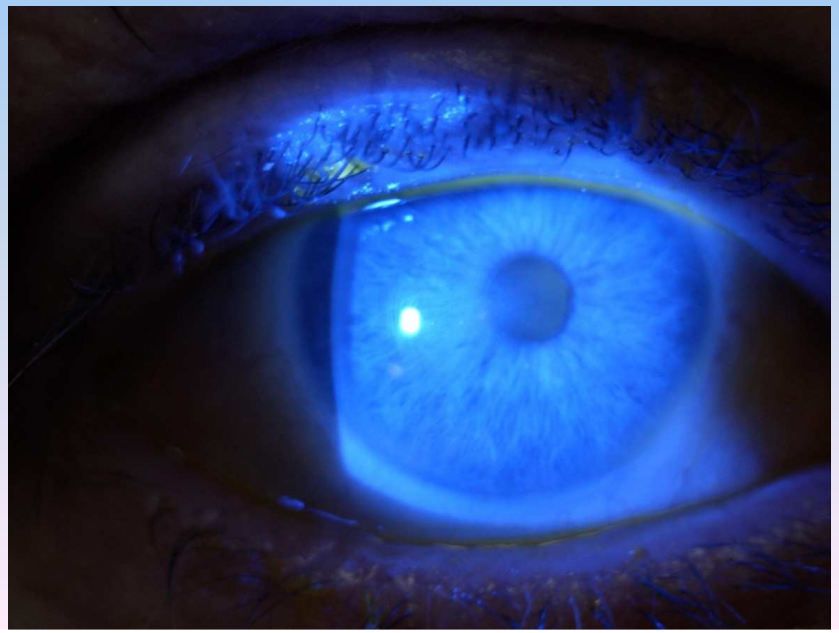
4 days post FAB treatment

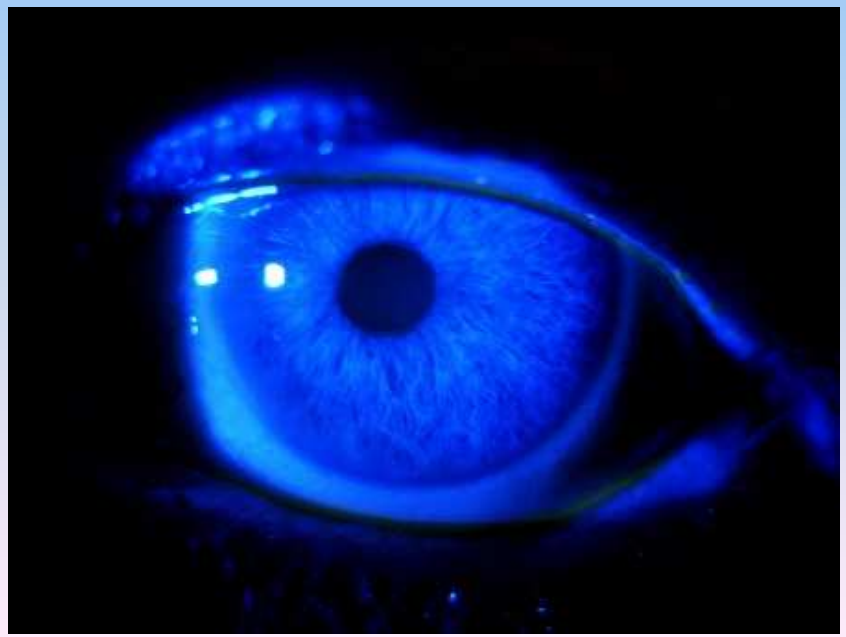


64 year old diabetic male









9 days post chemical burn persistent epithelial defect

Healed epithelial defect