

# **KERATOPROSTHESIS**

## **Beyond Corneal Graft Failure**

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Clinical Professor of Ophthalmology



# Background

- Trained with Claes Dohlman, MD, PhD in 1995 at the Mass Eye and Ear Infirmary on the Boston keratoprosthesis
- I have since performed over 60 procedures in Europe with main indications: chemical burns, OCP, SJS and some repeat graft failure.
- The short term success has been impressive
- The long term success has been limited to severe infectious complications, Glaucoma, Melts

# Blindness In Corneal Disease, World-wide

(World Health Organization 2005)

Approximately 8 million people are blind  
from corneal disease

(<20/400, best eye)

Includes 1.5 million blind children

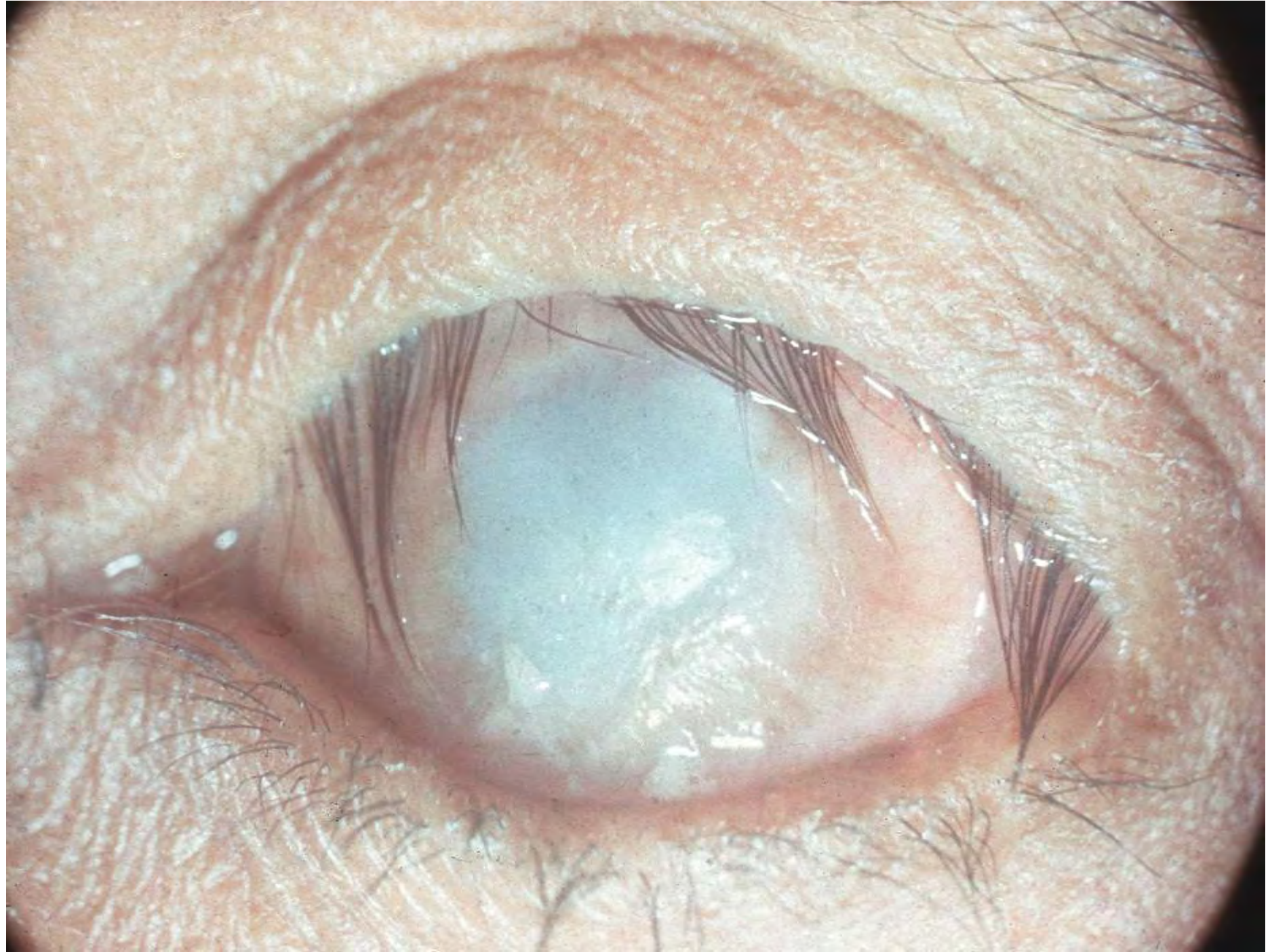
Penetrating keratoplasty has only a modest impact on corneal blindness:

**Less than 100,000 transplants are performed per year in the world - about half of them in the United States**

EBAA (Cole) 2008

**World wide outcome mediocre**

(outcome studies rarely population based)



# History Kpro

- Keratoprosthetics, replacing damaged and opaque corneae with an artificial implant, dates back more than 200 years to Pellier de Quengsy, a French ophthalmologist who proposed implanting a glass plate into an opaque cornea.
- The first surgical case in a human was performed in 1855 with a quartz crystal implant developed by Nussbaum. The prosthesis remained in the eye for six months. Over the next 50 years, more attempts were made to develop different keratoprostheses (KPros) and techniques (von Hippel 1877, Dimmer 1889, and Salzer 1895).
- Almost all the implants were extruded and in the early twentieth century, interest in keratoprostheses waned with the introduction of penetrating keratoplasty. The early pioneers in the field of penetrating keratoplasty included Elshnig in Prague (1914), Filatov (1924), and Tudor-Thomas, who introduced the technique to the United Kingdom (1936).
- Penetrating keratoplasty went from strength to strength with Stocker in the 1950s and was accompanied by the introduction of steroids and fine needles and sutures. Though more diseases became suitable for penetrating keratoplasty, there were still conditions where the prospect of successful grafts was hopeless and so interest was renewed in keratoprostheses. Many pioneers were involved in developing new KPros (Gyorffy, Sommer, Vodovozov, Stone and Herbert, Macpherson and Anderson, Binder and Binder, Fyodorov, Puchkovska, Krasnov, Cardona, Castroviejo, de Voe, Choyce, Lund, Dohlman, Casey, Donn, Buxton, Girard, Maroz, Pintucci, Marchi, Legeais, Lacombe, Worst, Polack, Aquavella, Waring, Bertelson, Singh, Mohan, Yakimako, Caldwell and Barraquer).



G. PELLIER DE QUENGSY, Fils, Docteur  
en médecine & chirurgien Oculiste des  
villes de toulouse et de montpellier,

# P R É C I S

O U

## COURS D'OPÉRATIONS

SUR LA CHIRURGIE DES YEUX,

*Puisé dans le sein de la pratique, & enrichi de  
Figures en Taille-douce, qui représentent les  
Instrumens qui leur sont propres, avec des  
Observations de pratique très-intéressantes.*

PAR Mr. G. PELLIER DE QUENGSY, fils, Docteur en  
Médecine, & Chirurgien-Oculiste des Villes de Toulouſe  
& de Montpellier, Bréveté du Roi, &c.

*Oculcrum vis nisi valeat & conflet, periculum minatur.*

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TOME PREMIER.

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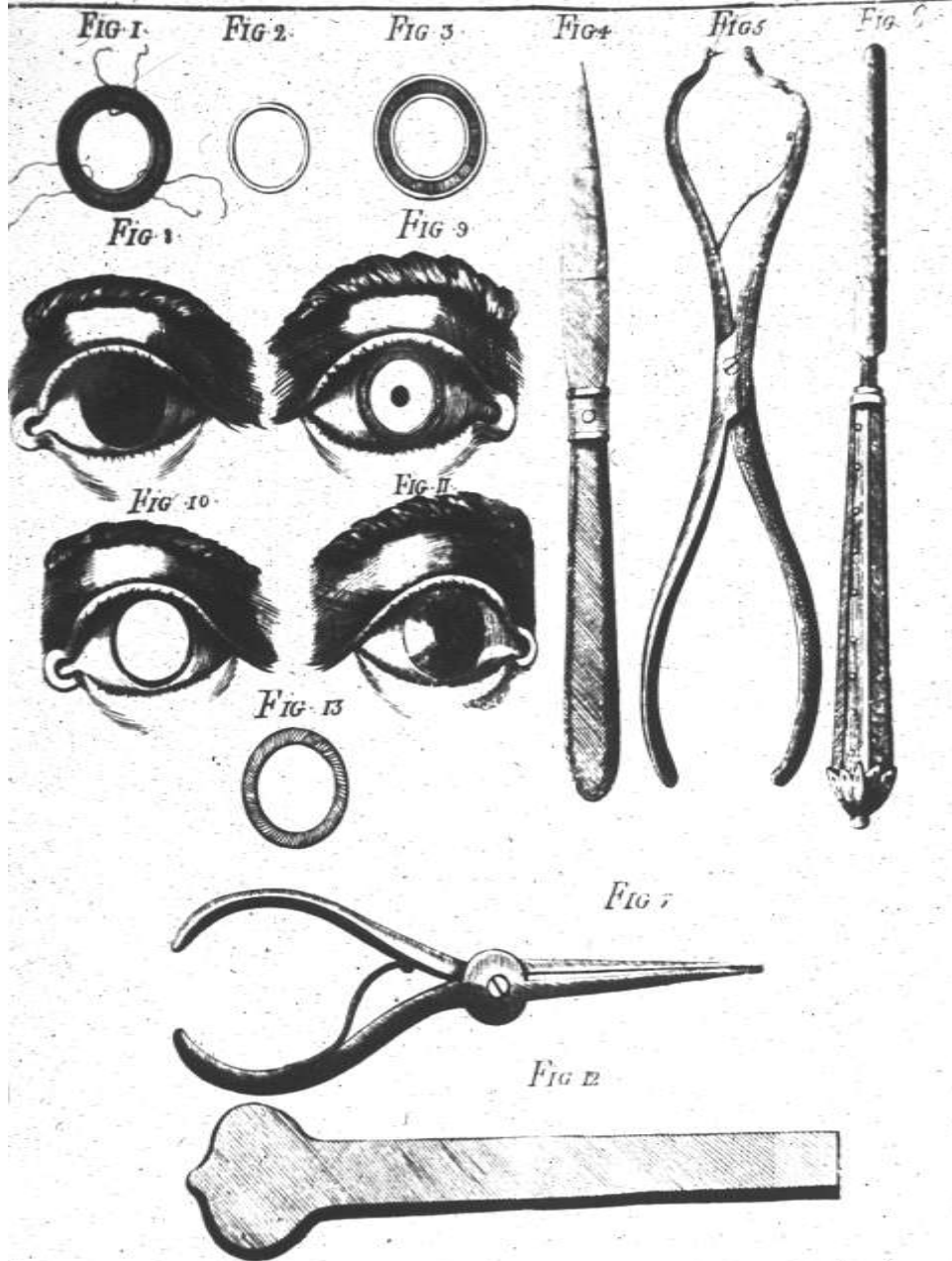


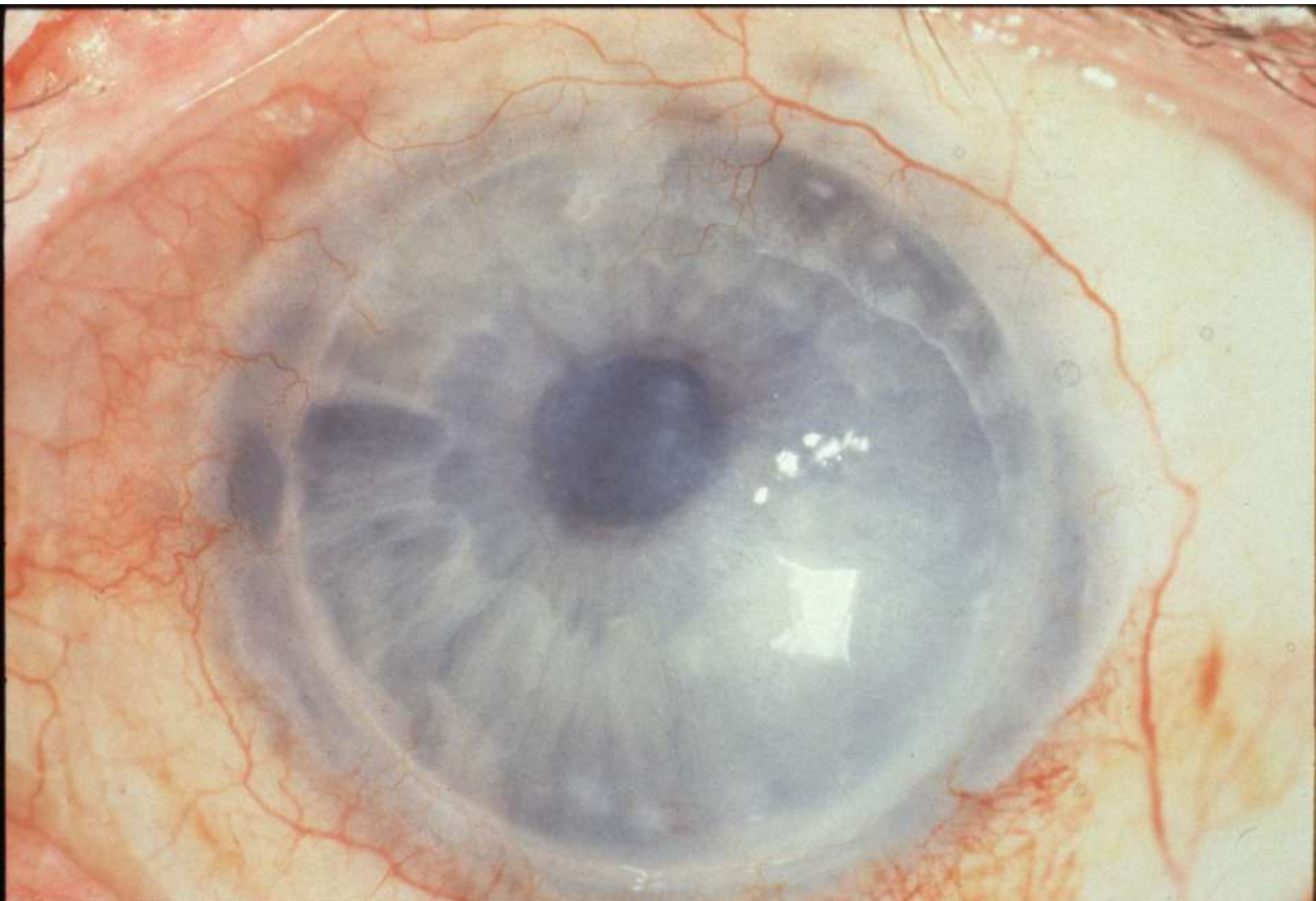
A P A R I S,

Chez { DIDOT, le jeune, Quai des Augustins.  
MEQUIGNON, Libraire, Rue des Cordeliers.

A M O N T P E L L I E R,

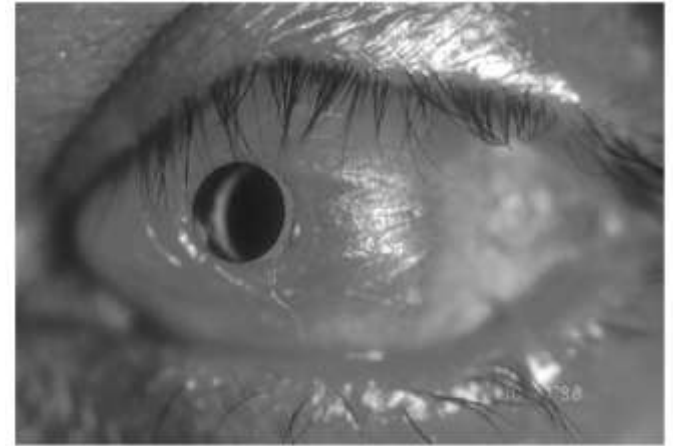
Chez { L'AUTEUR, hors la porte de Lattes, Isle des Cordeliers.  
RIGAUT, ROULLET, Libraires, & chez  
les principaux Libraires du Royaume.



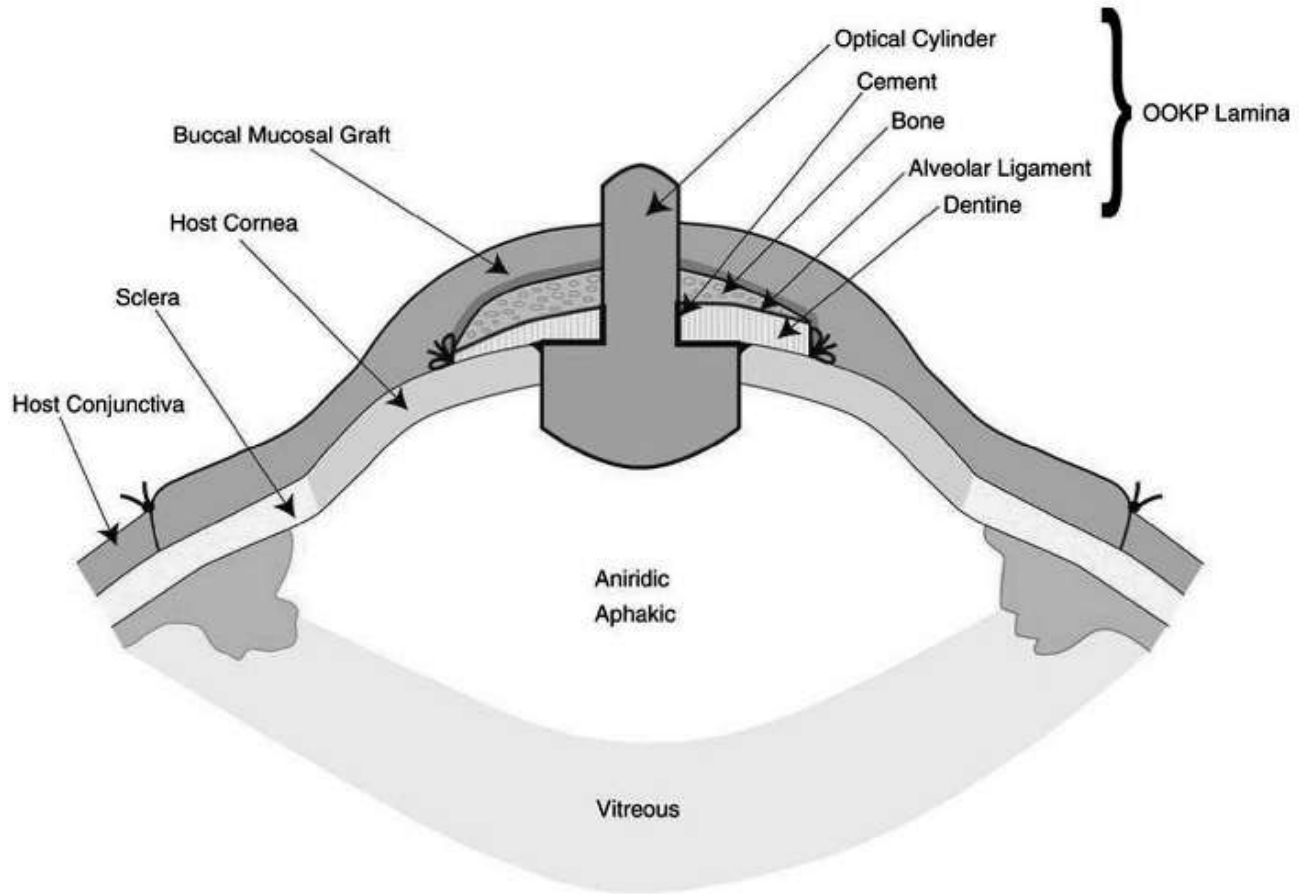


# Osteo odonto keratoprosthesis

- patient's own tooth root and alveolar bone to S ( Strampelli B. Keratoprosthesis with osteodontal tissue. Am J Oph- thalmology 1963; 89:1029–39.upport an optical cyli/Users/ajkmd/Desktop/OOKP.jpg
- nder)

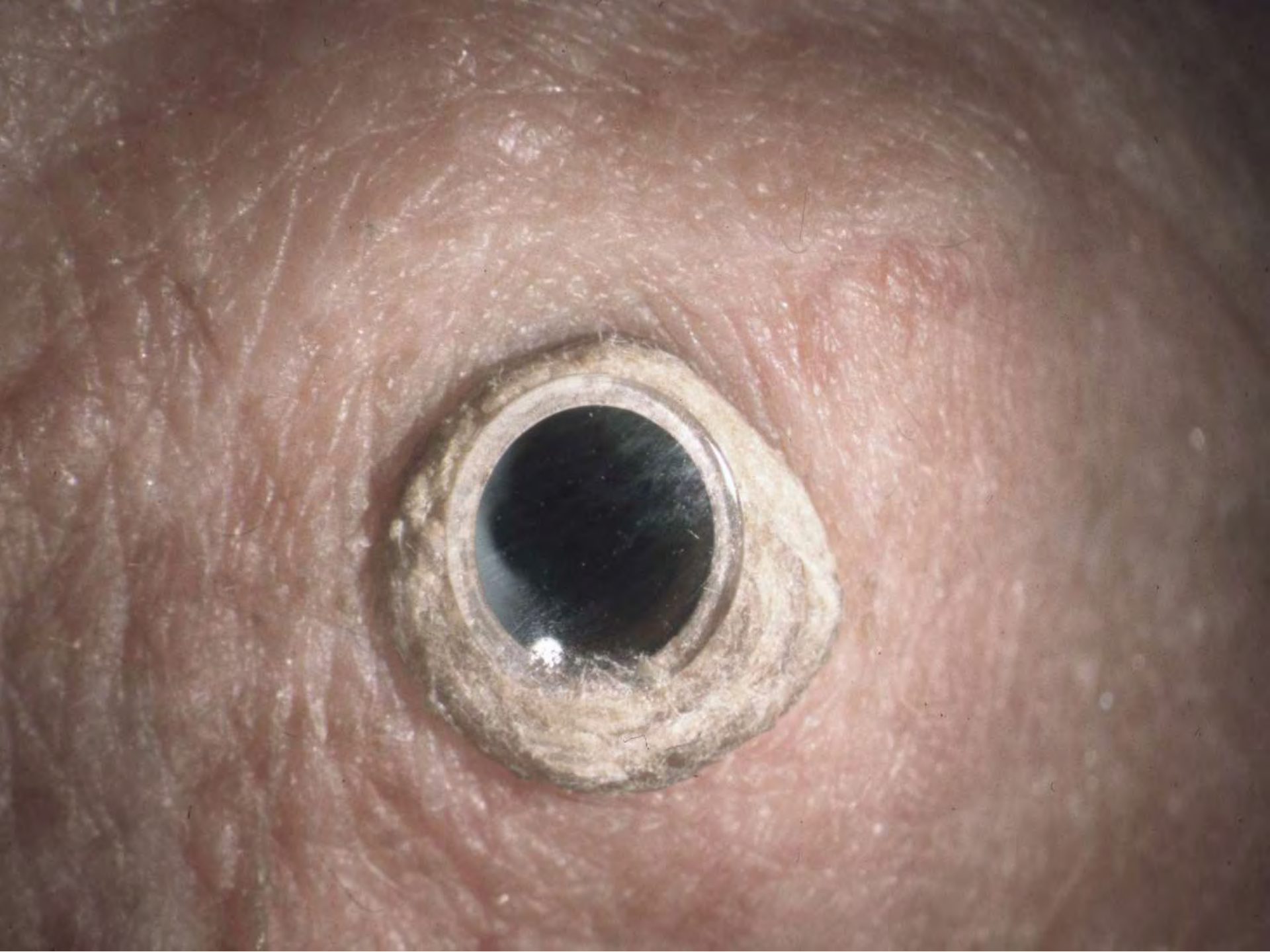


# OOKpro



# Claes Dohlman, MD, PhD

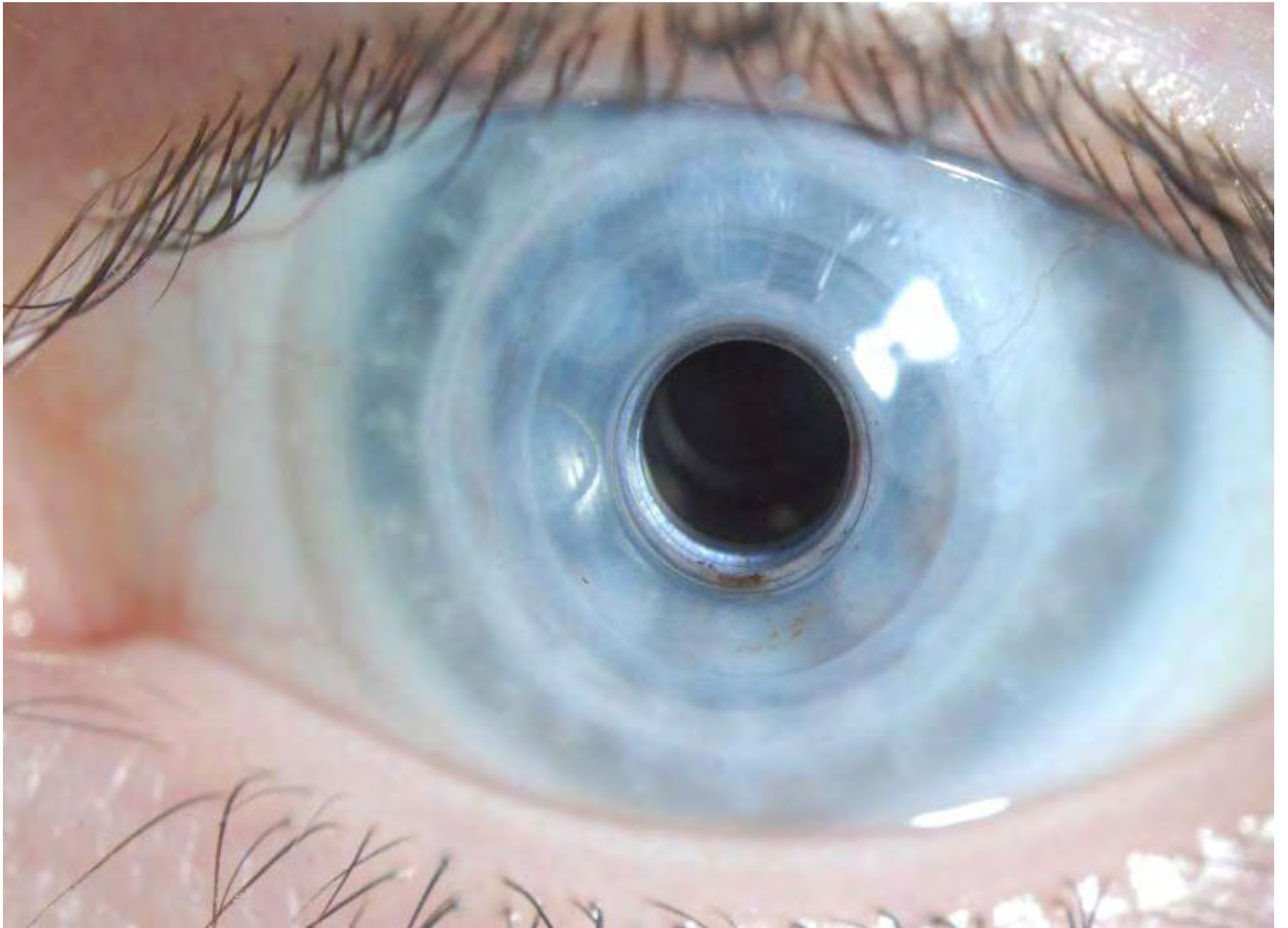




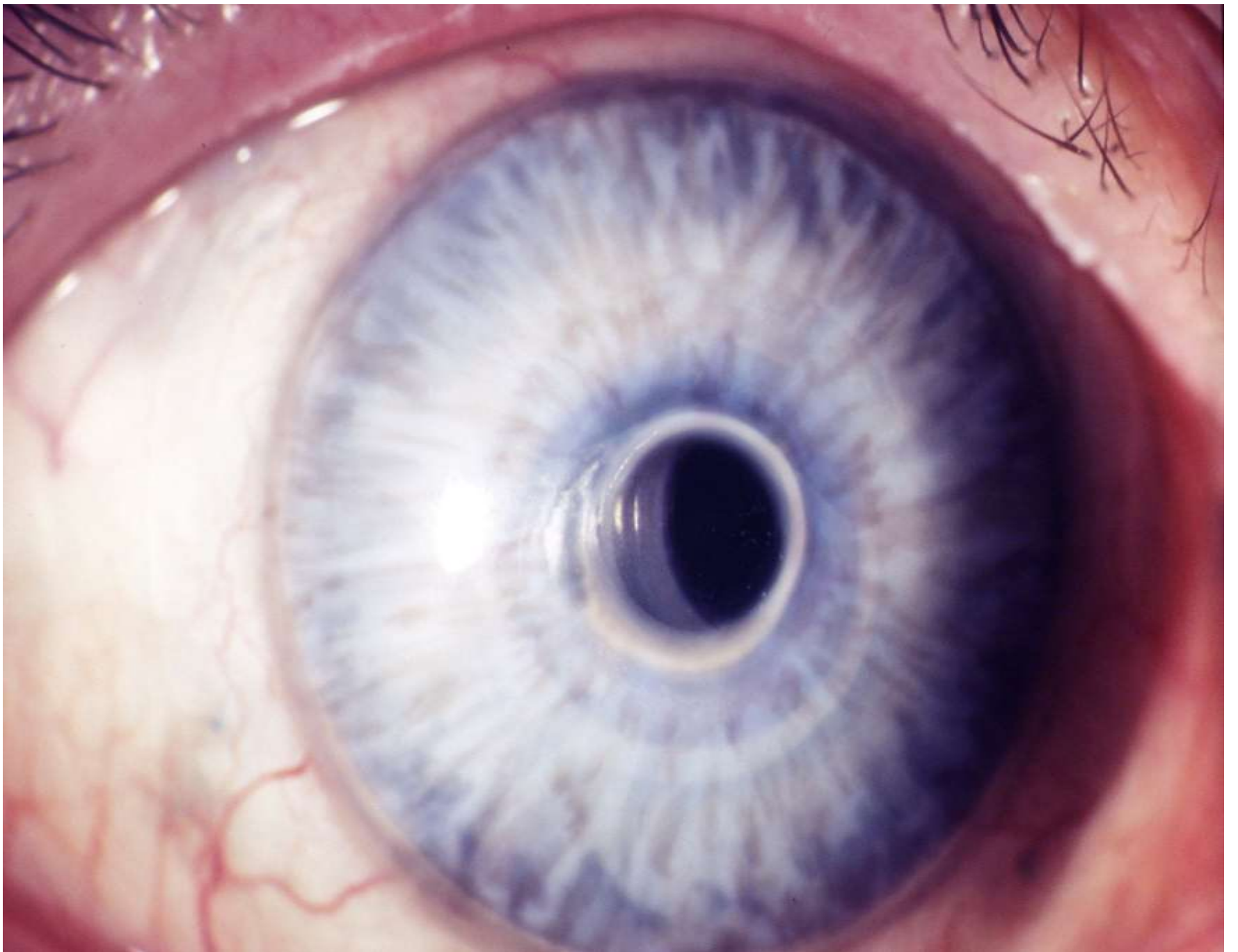












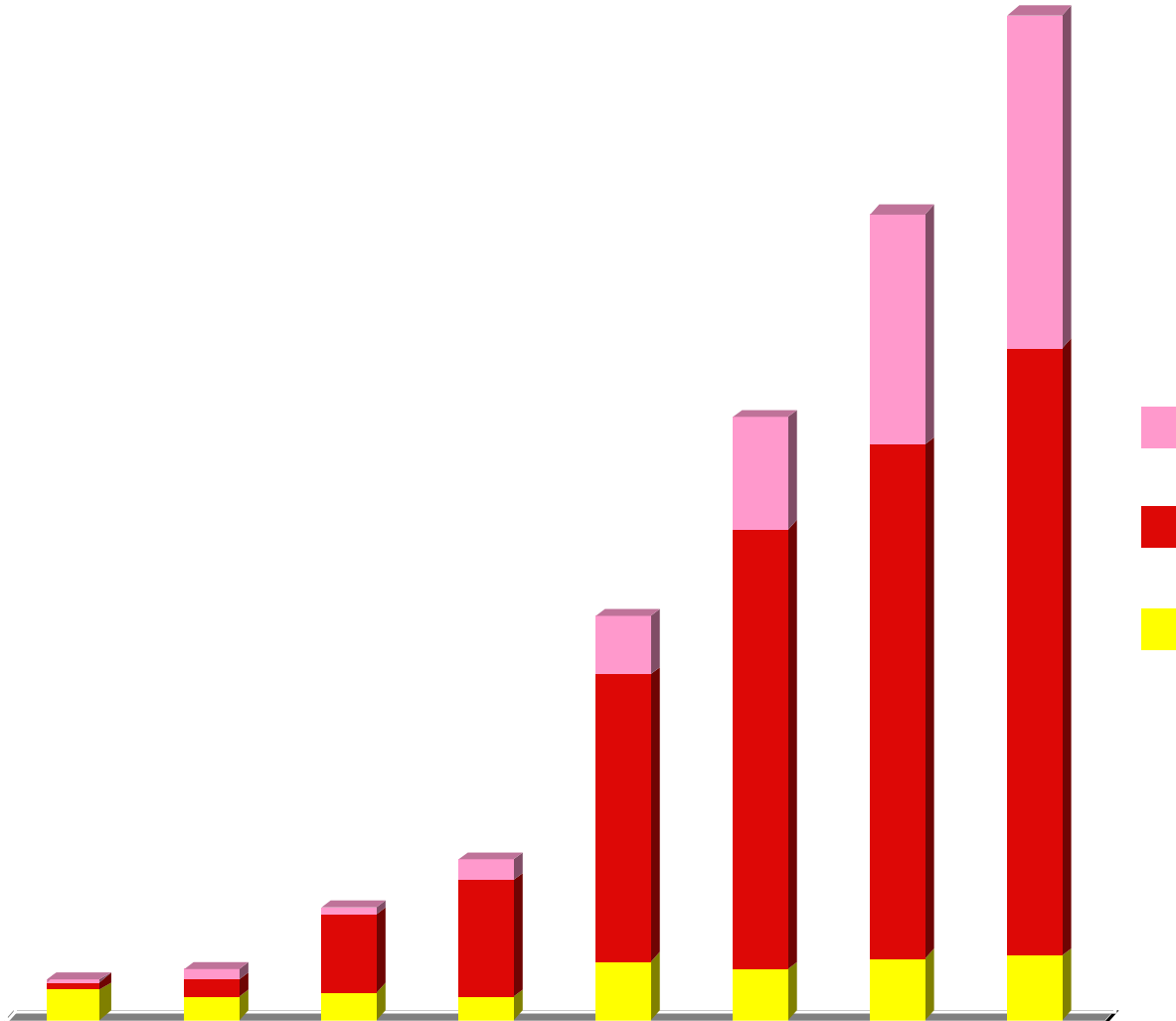


## Cost-utility of various medical interventions, adjusted to 2009 US dollars<sup>29</sup>

Intervention	Cost in \$/QALY
Initial cataract surgery <sup>30</sup>	\$2 023
Second eye cataract surgery <sup>31</sup>	\$2 727
Penetrating Keratoplasty <sup>10</sup>	\$12 194
<b>Boston keratoprosthesis (submitted paper)</b>	<b>\$15 525</b>
Photodynamic therapy for subfoveal choroidal neovascularization with ARMD <sup>32</sup>	
20/40 initial vision	\$104 158
20/200 initial vision	\$208 966
Coronary bypass surgery for occluded LAD artery <sup>33</sup>	\$44 113
Chemoprophylaxis after occupational exposure to HIV <sup>34</sup>	\$49 036
Primary pediatric heart transplant <sup>35</sup>	\$52 417
Magnetic resonance imaging for equivocal neurologic symptoms <sup>36</sup>	\$134 742
One day of chemoprophylaxis prior to receiving dental work for patients with prosthetic joints <sup>37</sup>	\$696 692

# Boston KPro Usage

1000



# Prognostic Factors

- Autoimmune diseases  
(Pemphigoid, Stevens-Johnson Syndrome, Uveitis, etc.)
- Graft failures in relatively non-inflamed eyes with intact tear and blink mechanisms  
(Following dystrophies, infections, chemical burns, etc.)







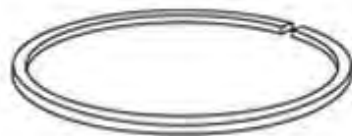
**Front Part**



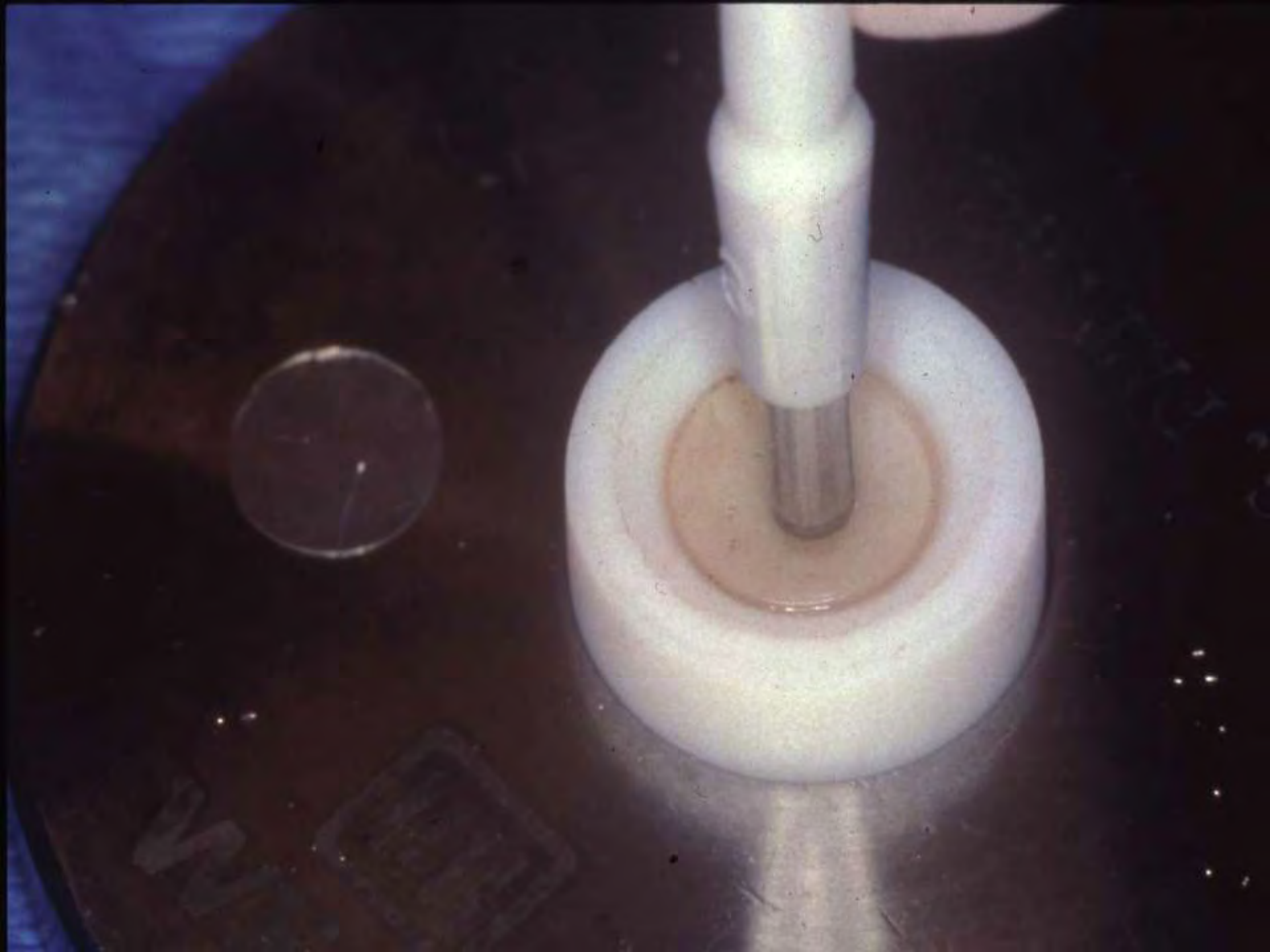
**Corneal Graft**



**Back Plate**



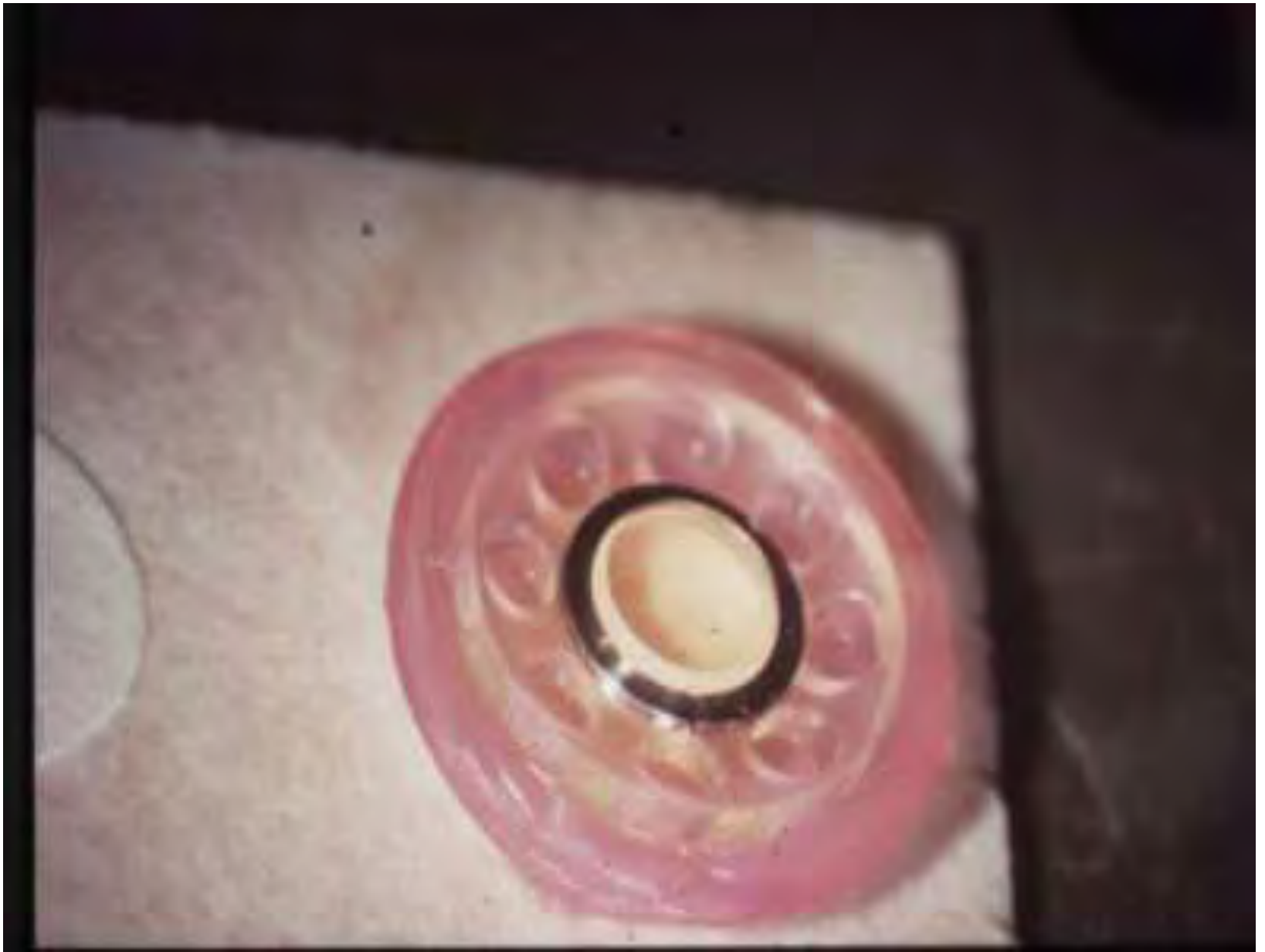
**Locking Ring**

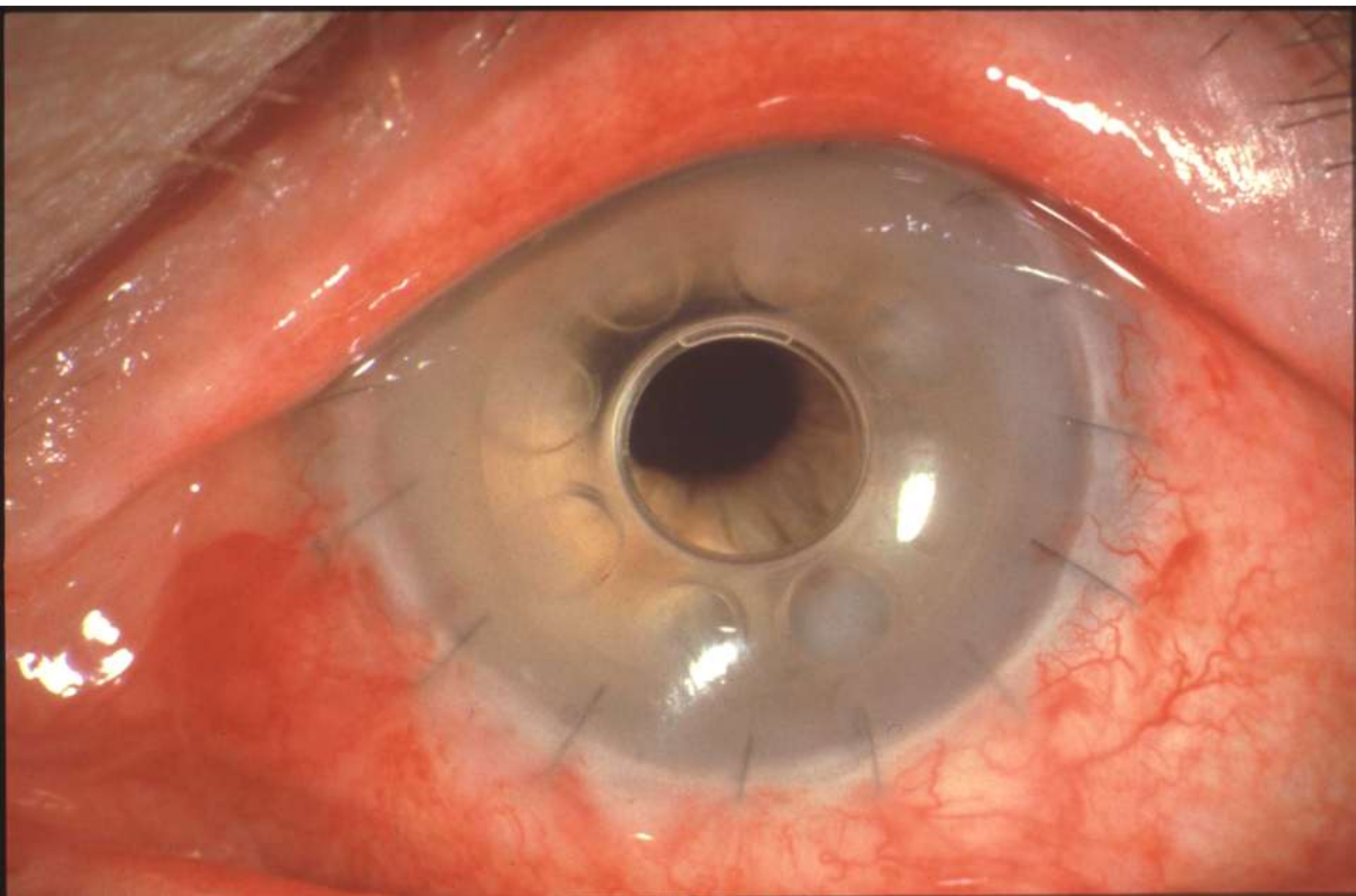


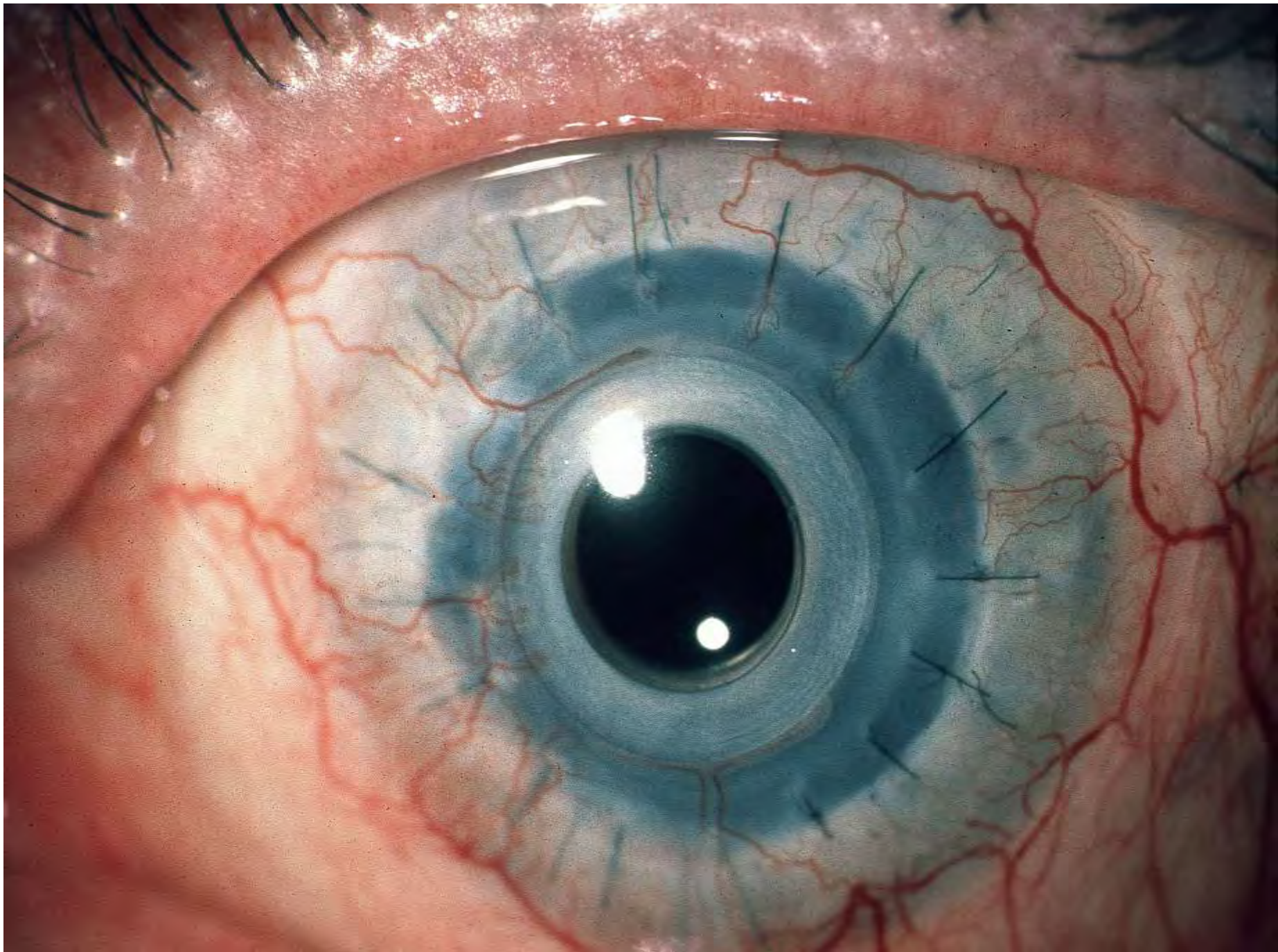






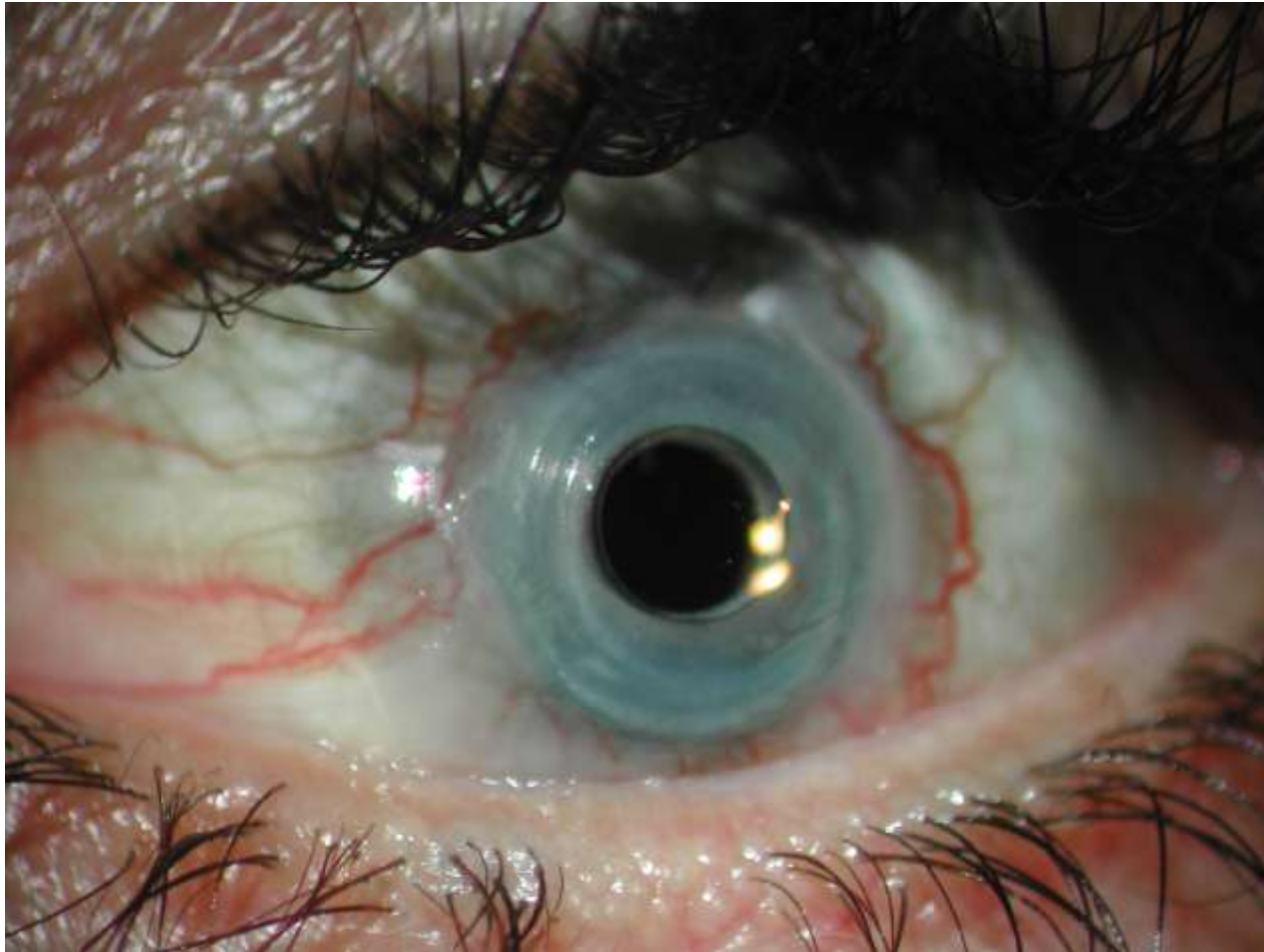




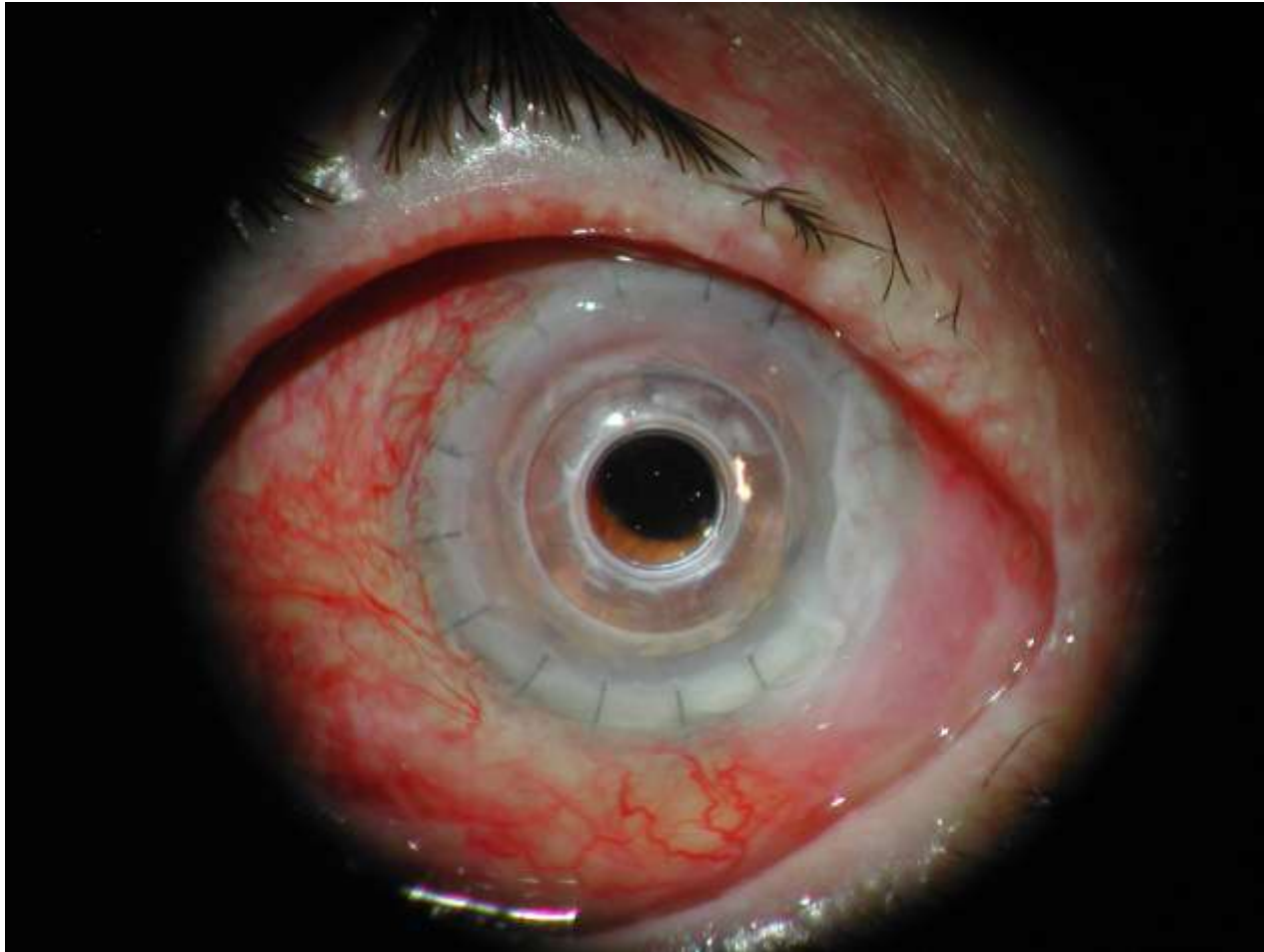




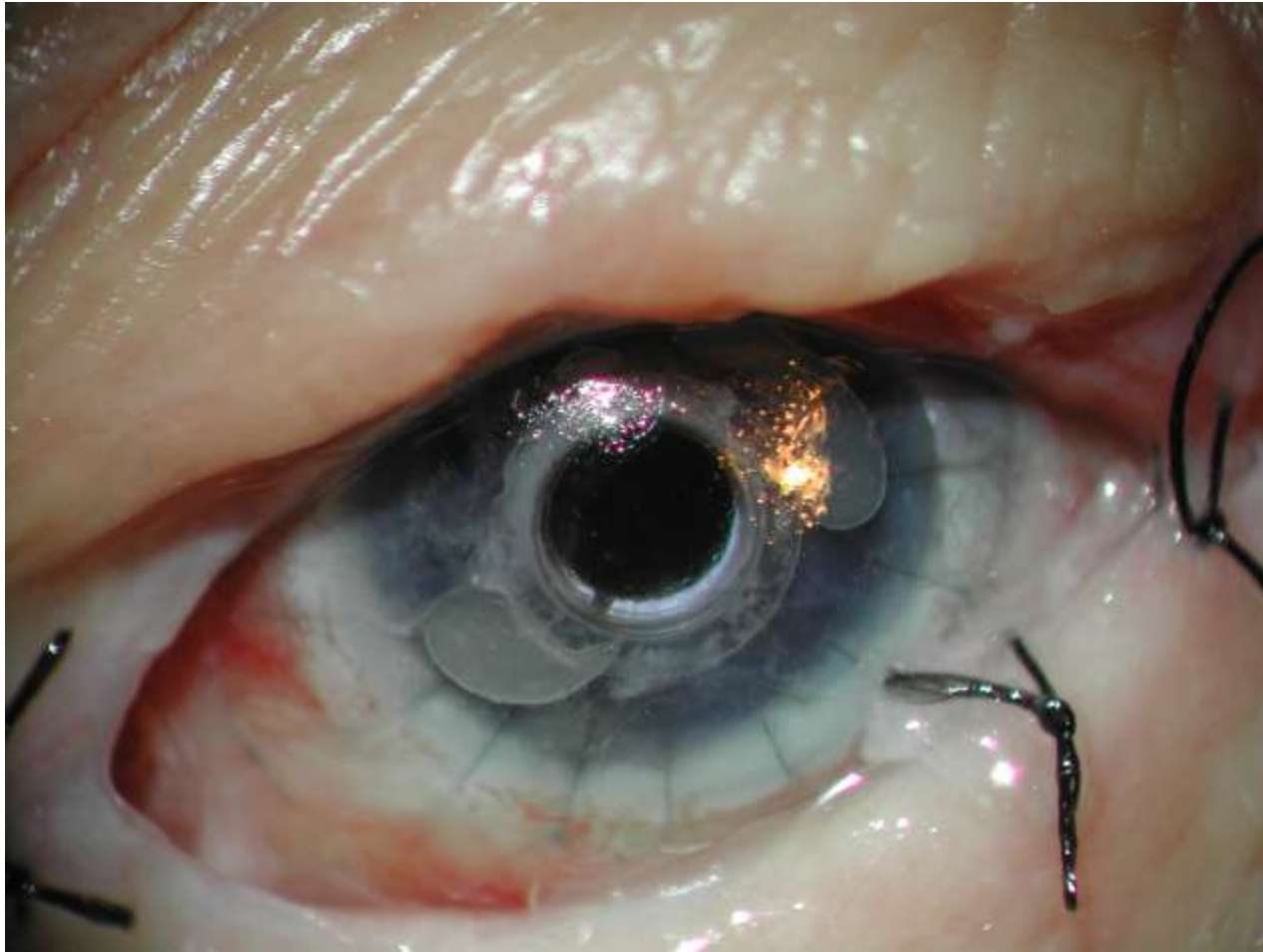
The first Boston Kpro in Europe performed in 1996, 14 years later UCVA 20/50

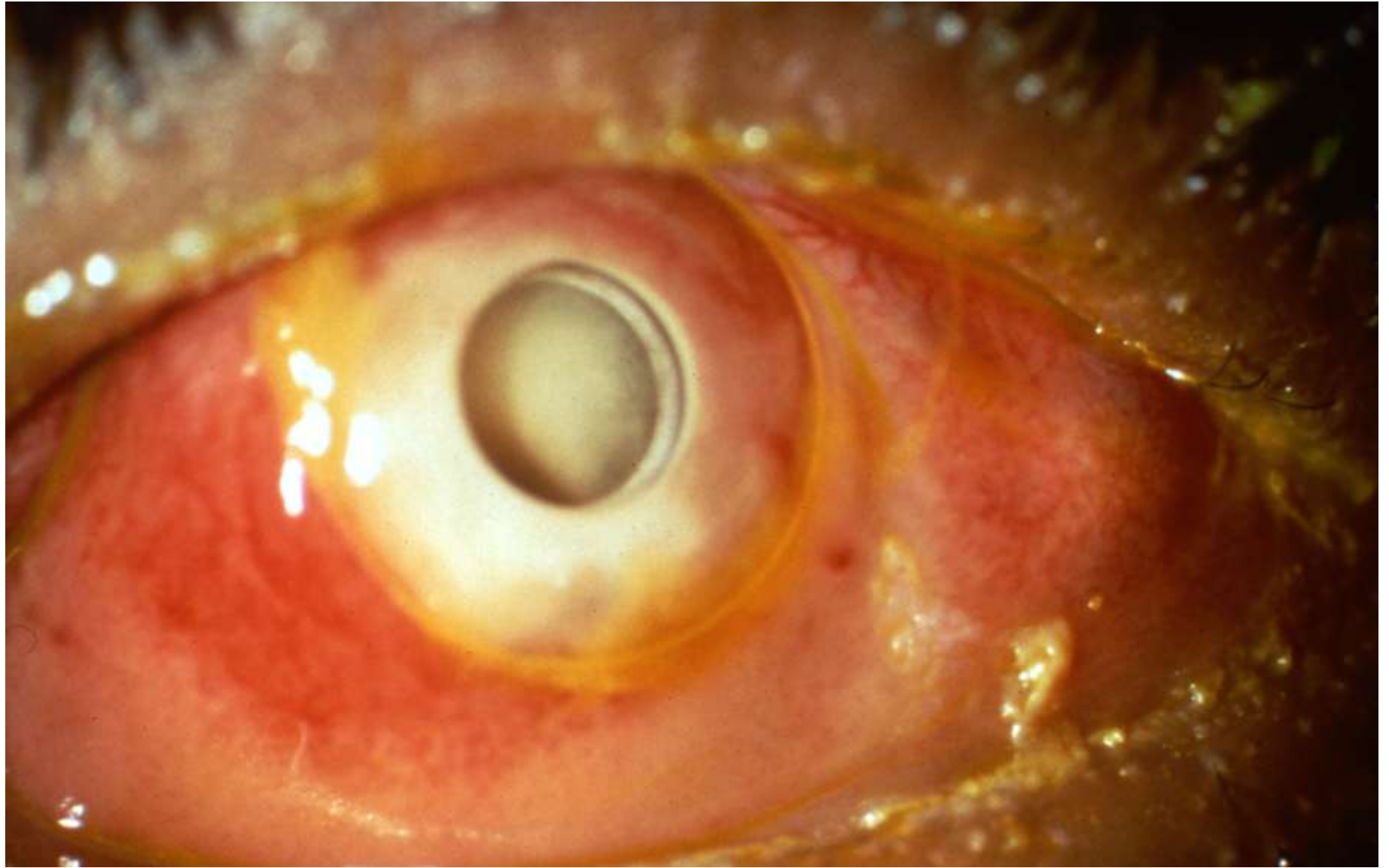


# Successful Boston Kpro 2 years out 20/40!

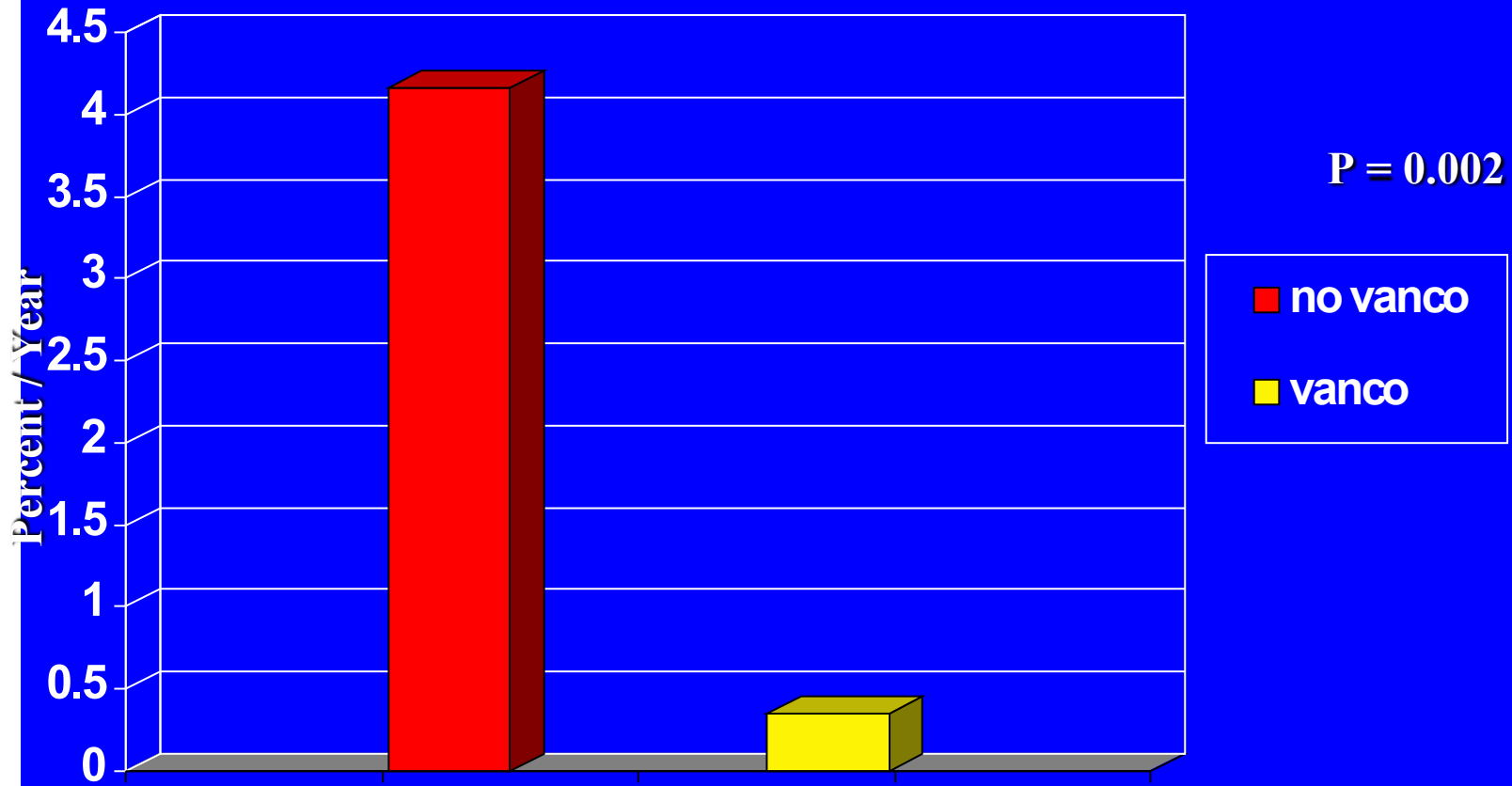


# Chemical burn pt, good early rehab





# Incidence of bacterial endophthalmitis in KPro eyes



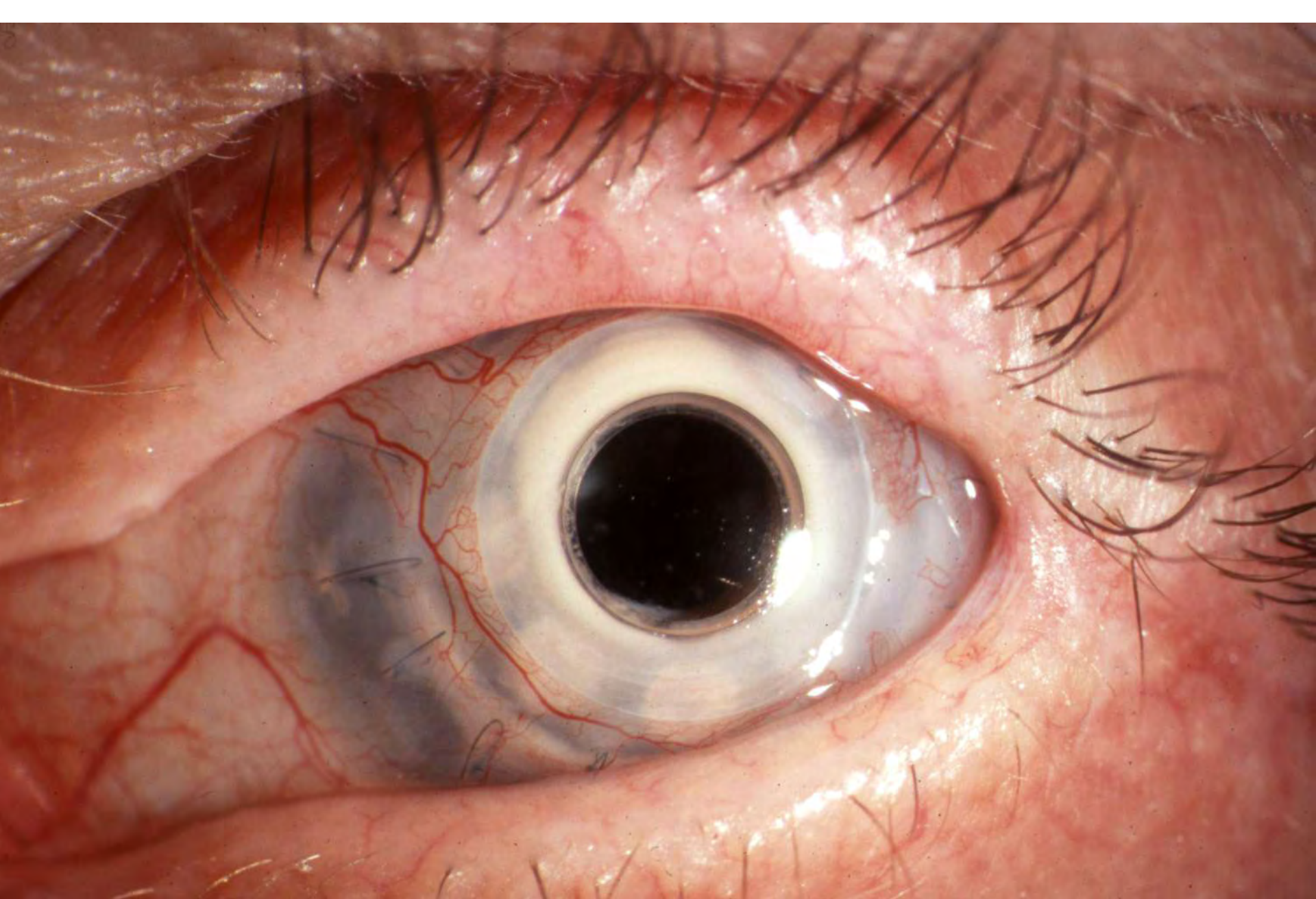
# Antibiotics Prophylaxis

- Low risk (blinks, tears, non-autoimmune):
  - Polytrim, (or fluoroquinolone, or chloramphenicol)  
once daily

# Fungal Prophylaxis in High Risk Areas

Bursts of Amphotericin B 0.15%  
twice daily for 1 week, every 3 months?

Behlau, Chodosh, Dohlman 2010



# Bioengineering efforts to block entry of bacteria

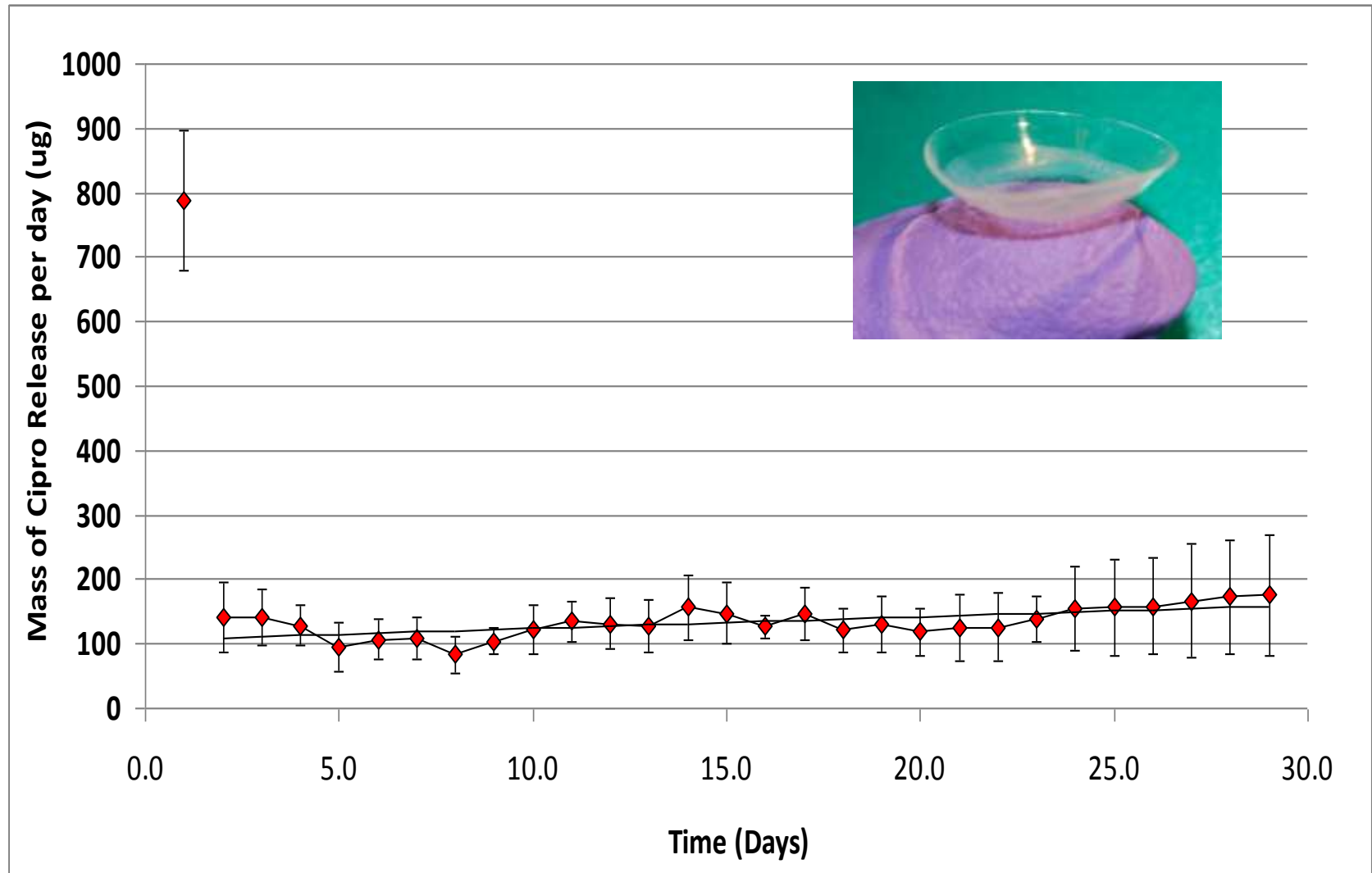
- Tightening corneal tissue around KPro stem

(Jeung, Wang, Kahone)

- Coating the KPro stem with antibacterial layer

(Behlau, Klibanoff)

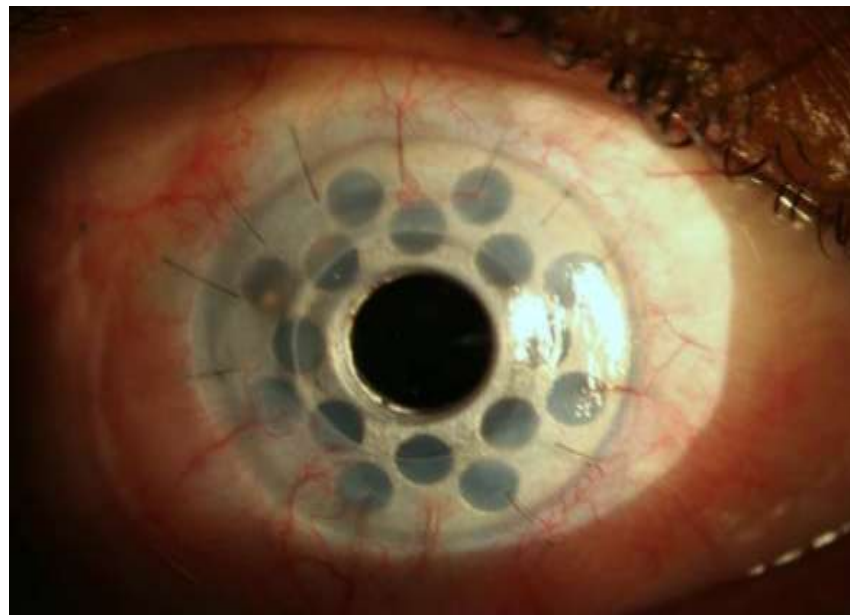
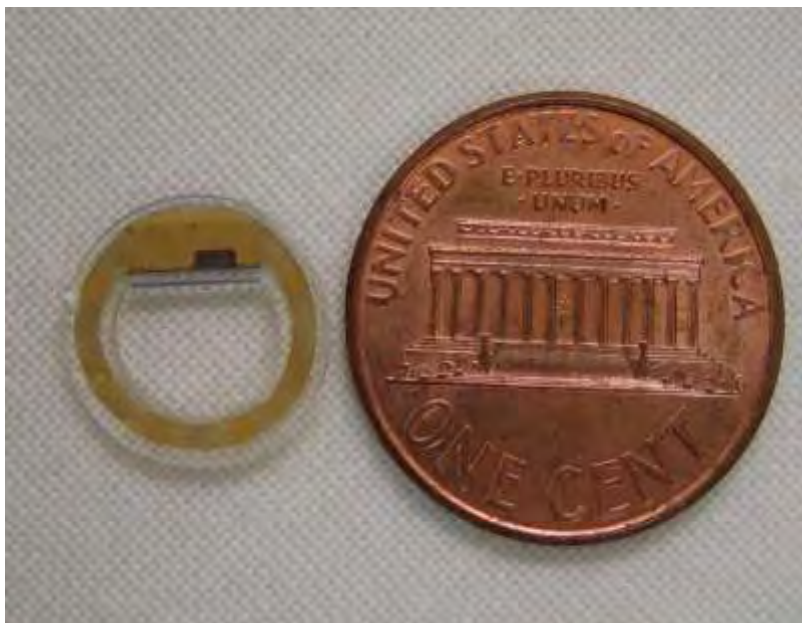
# Near Zero-Order Release of Ciprofloxacin through 4 weeks



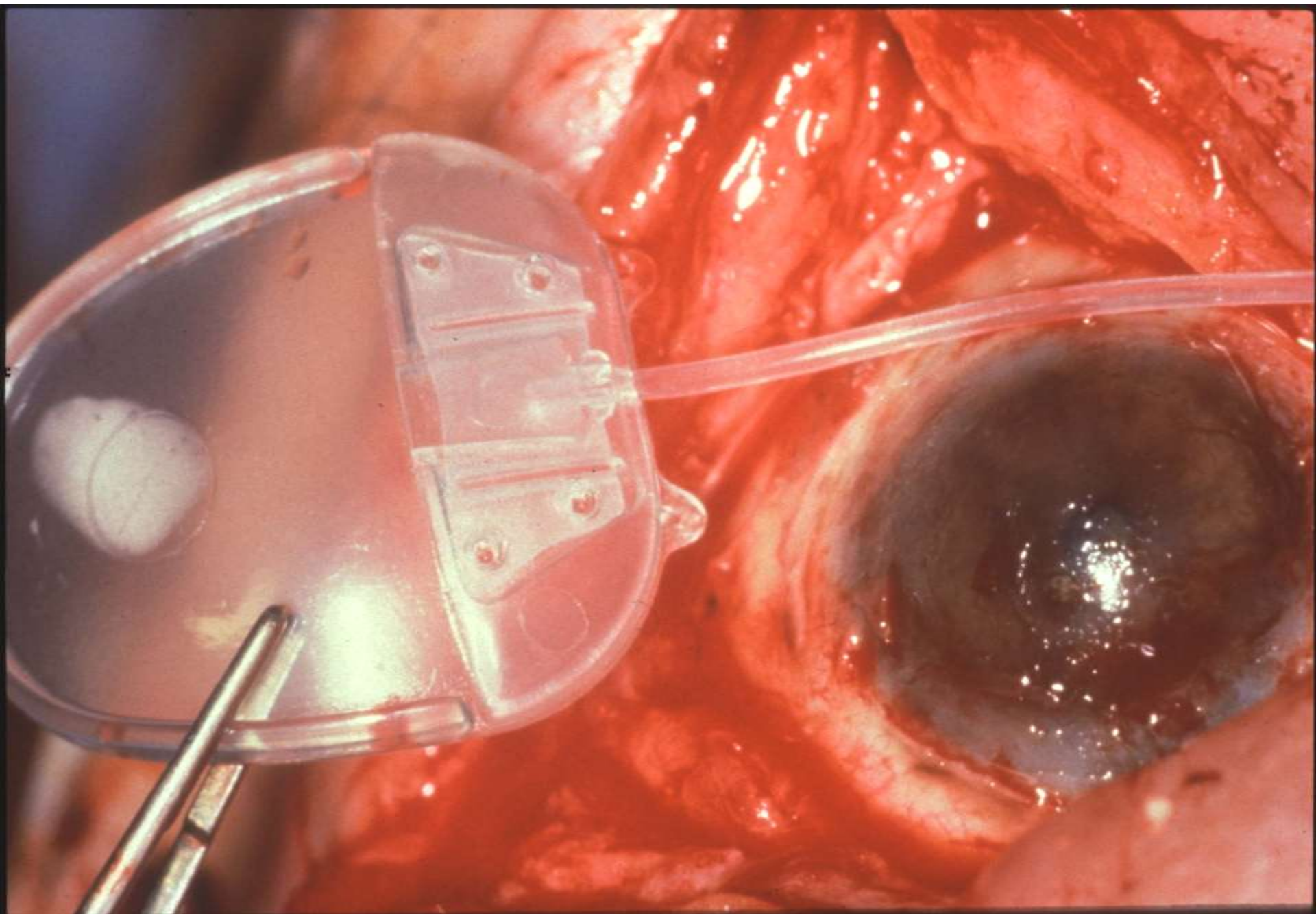
# Glaucoma in Kpro: a severe problem

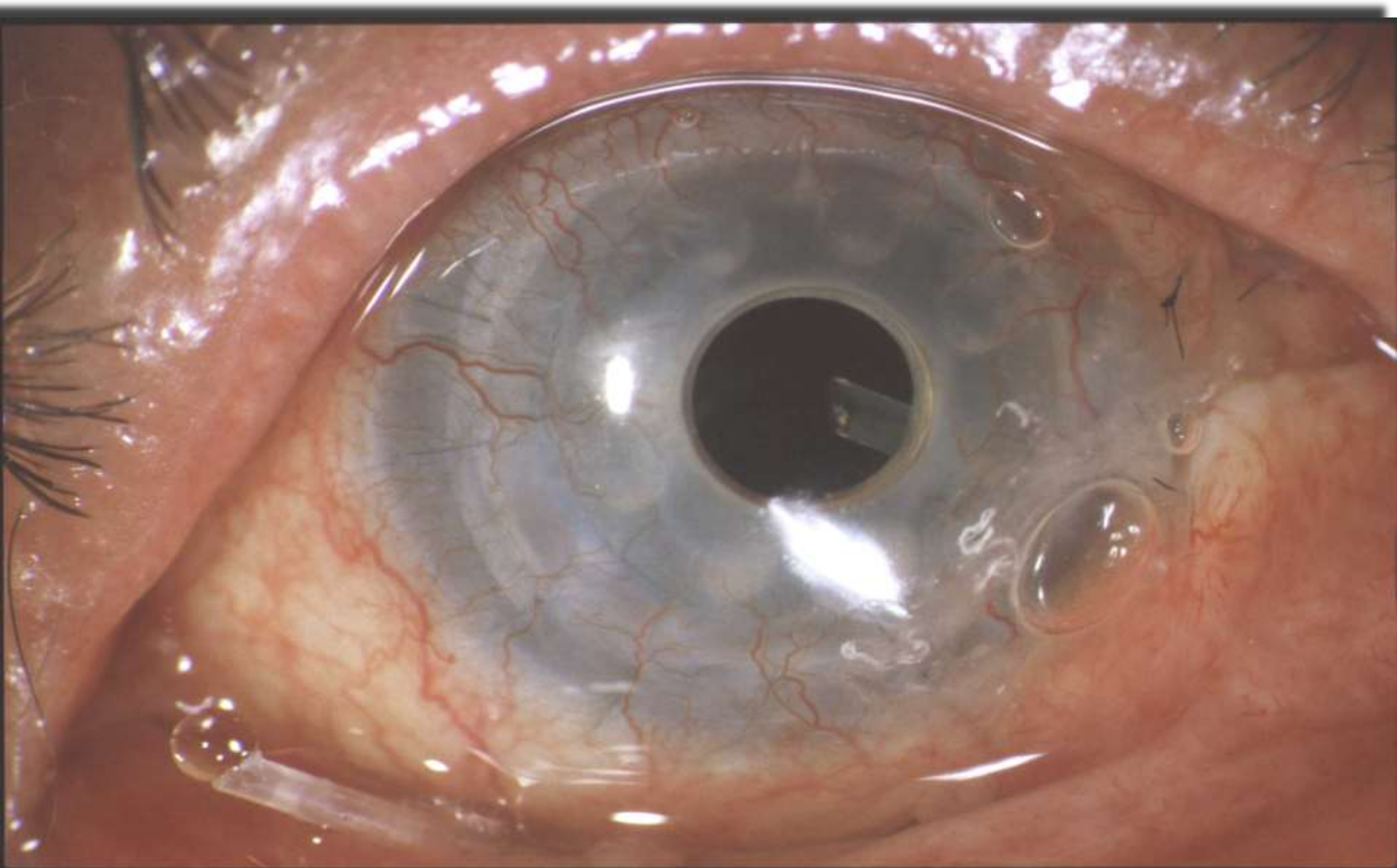
Frequent pre op

Often worsening post op



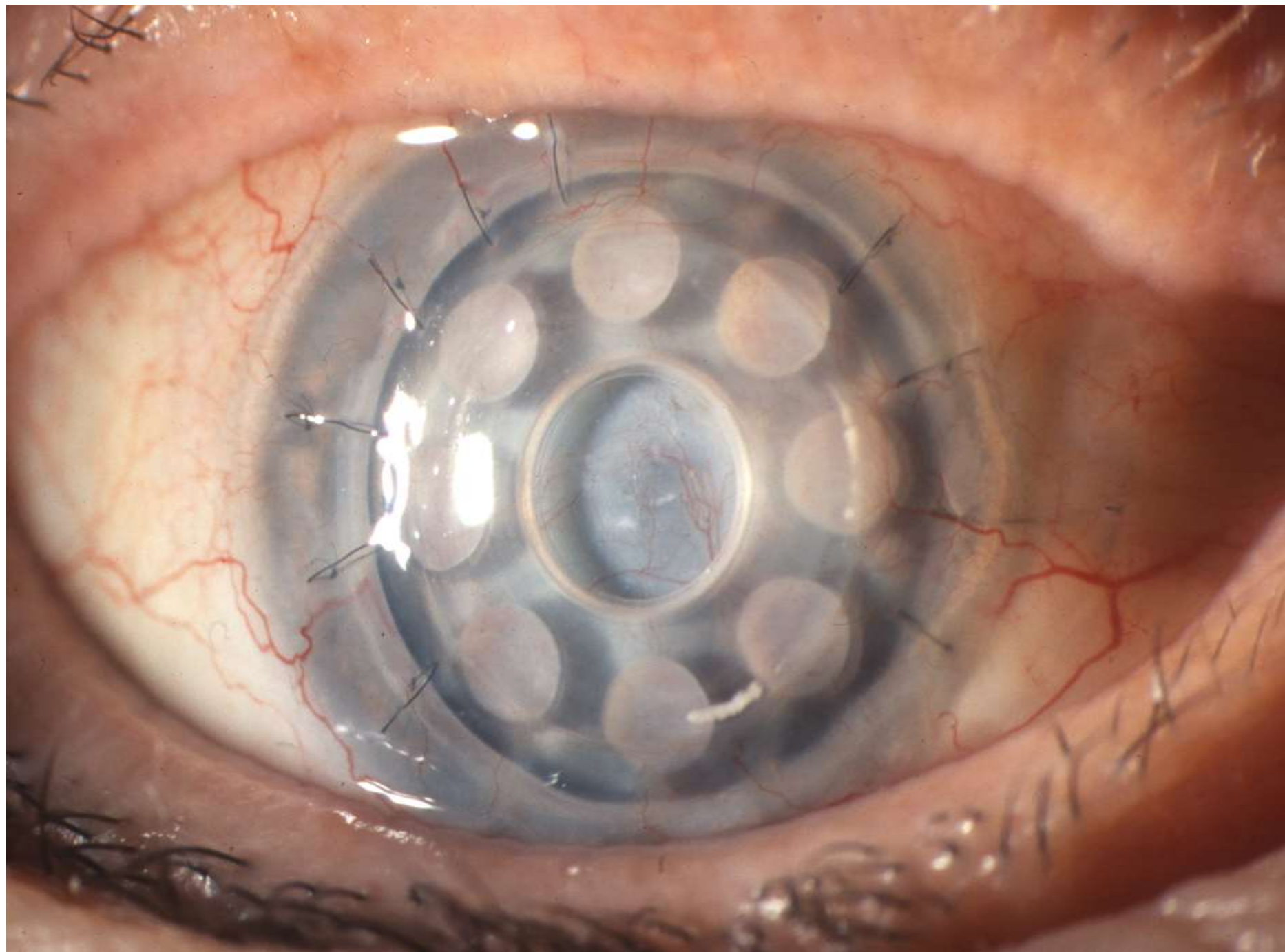
Melki S, Lopez M, Todani A, Fava M, Cade F, Cherfan D, Behlau I, Dohlman CH, 2009





# Sterile Vitritis

- Sudden massive uveitis with heavy vitreous debris but little redness, discomfort, or tenderness
- Therapy: Increased topical steroids and antibiotics. 40 mg Triamcinolone subtenon. No AC tap, inject.
- Prognosis good - clearing in a few weeks



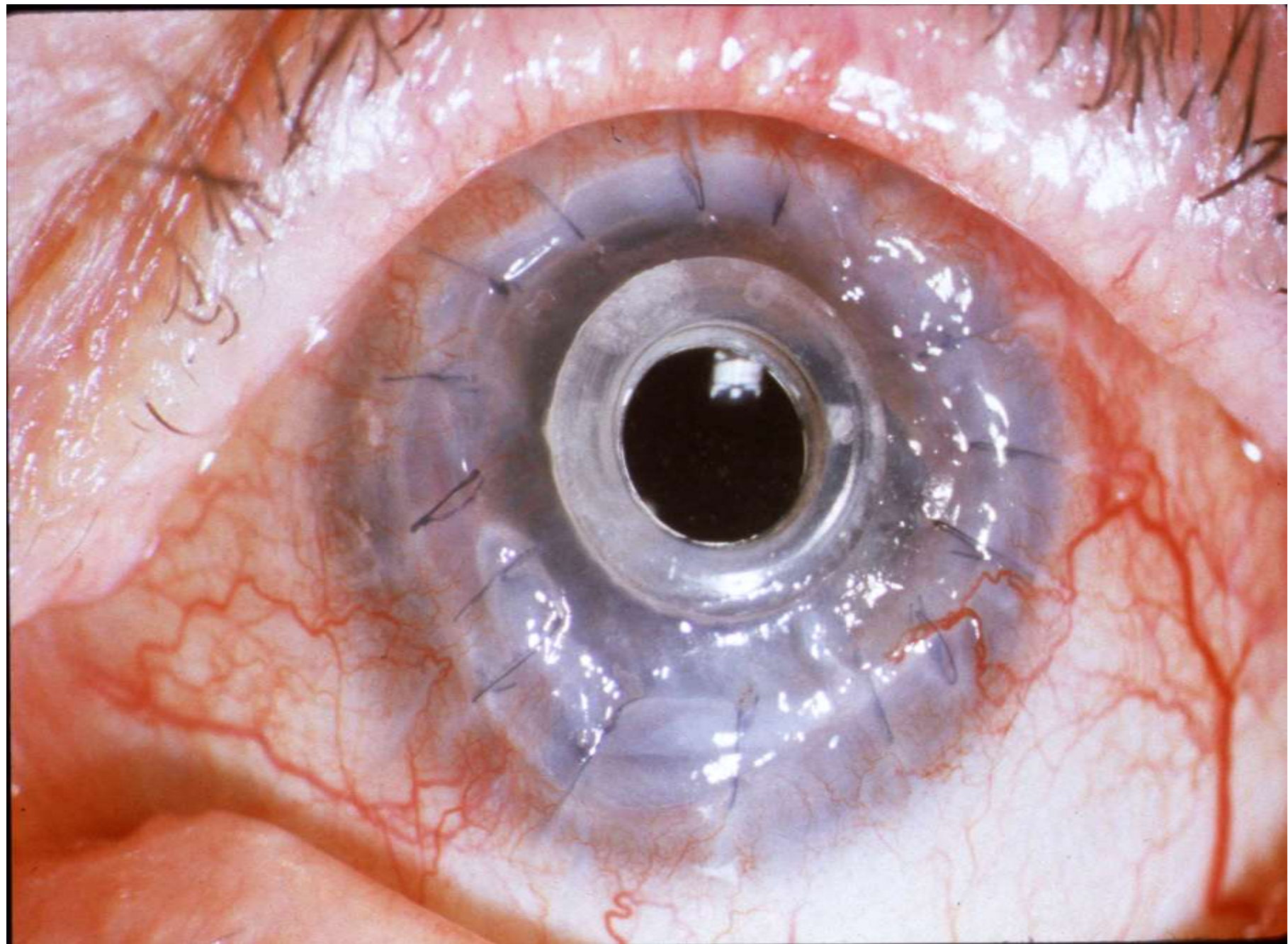
# Prognostic Factors

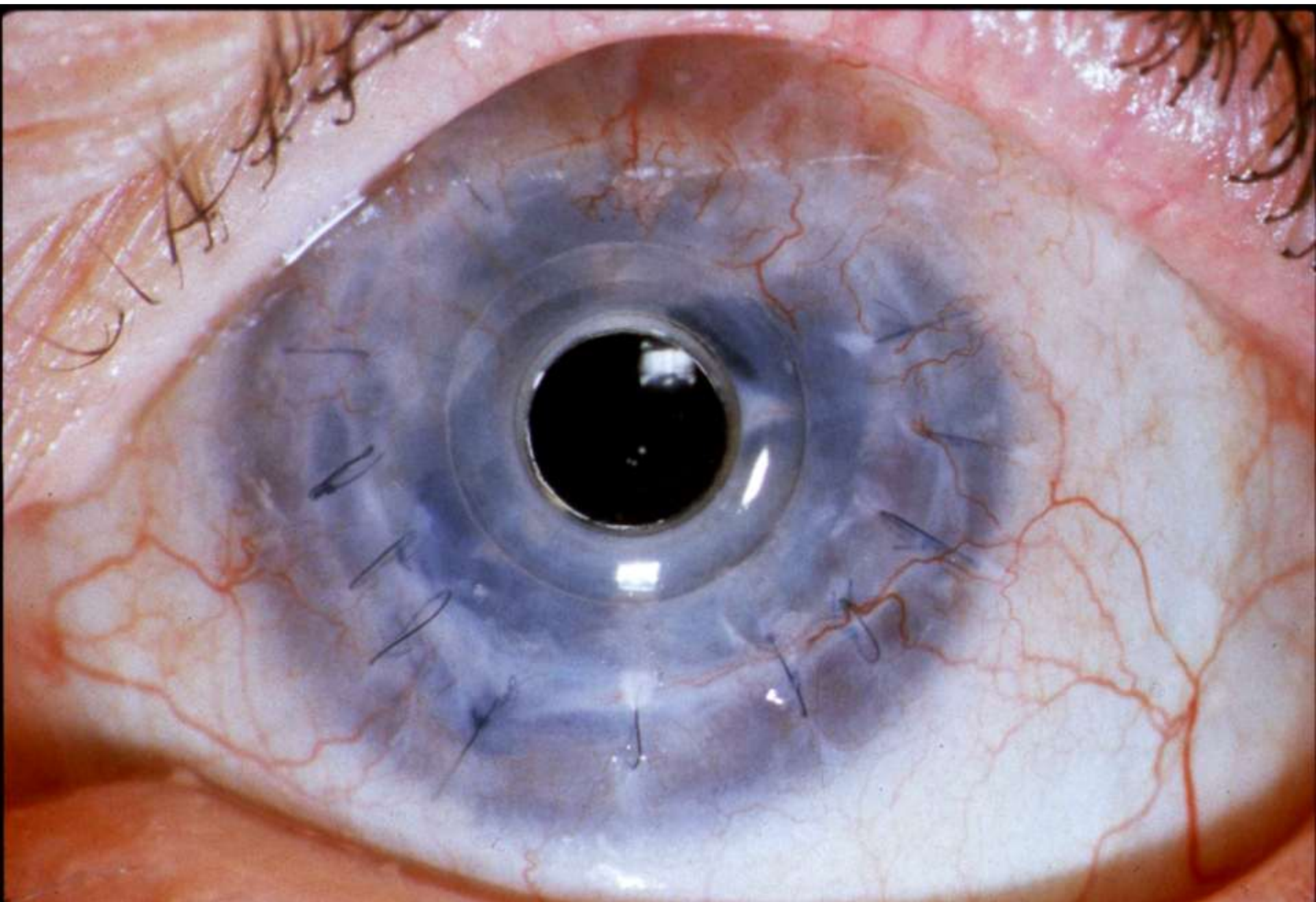
- Autoimmune diseases  
(Pemphigoid, Stevens-Johnson Syndrome, Uveitis, etc.)
- Graft failures in relatively non-inflamed eyes with intact tear and blink mechanisms  
(Following dystrophies, infections, chemical burns, etc.)

# **KPro Failures (Autoimmune cases excluded)**

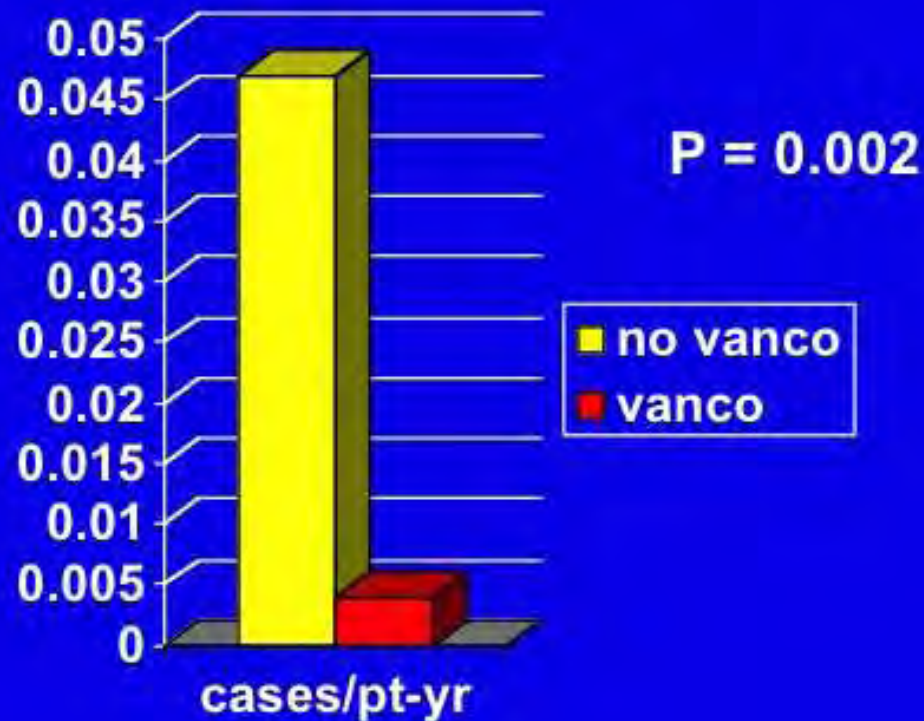
**Failures are rarely immediate but occur by long-term attrition**

- 1. Melt perforation (now very rare – fresh corneal graft as carrier, soft contact lens, back plate holes protective)**
- 2. Infection (now**

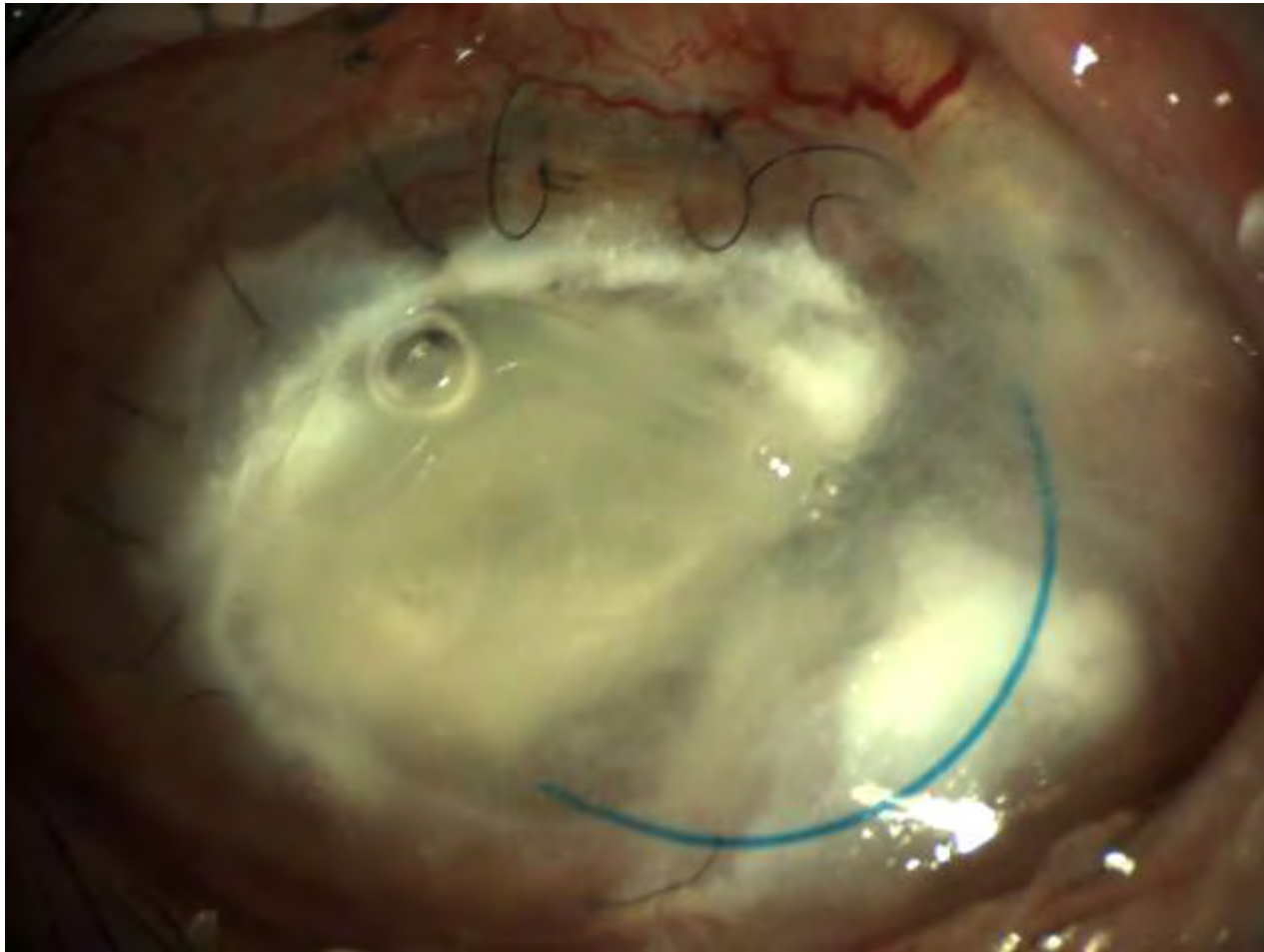




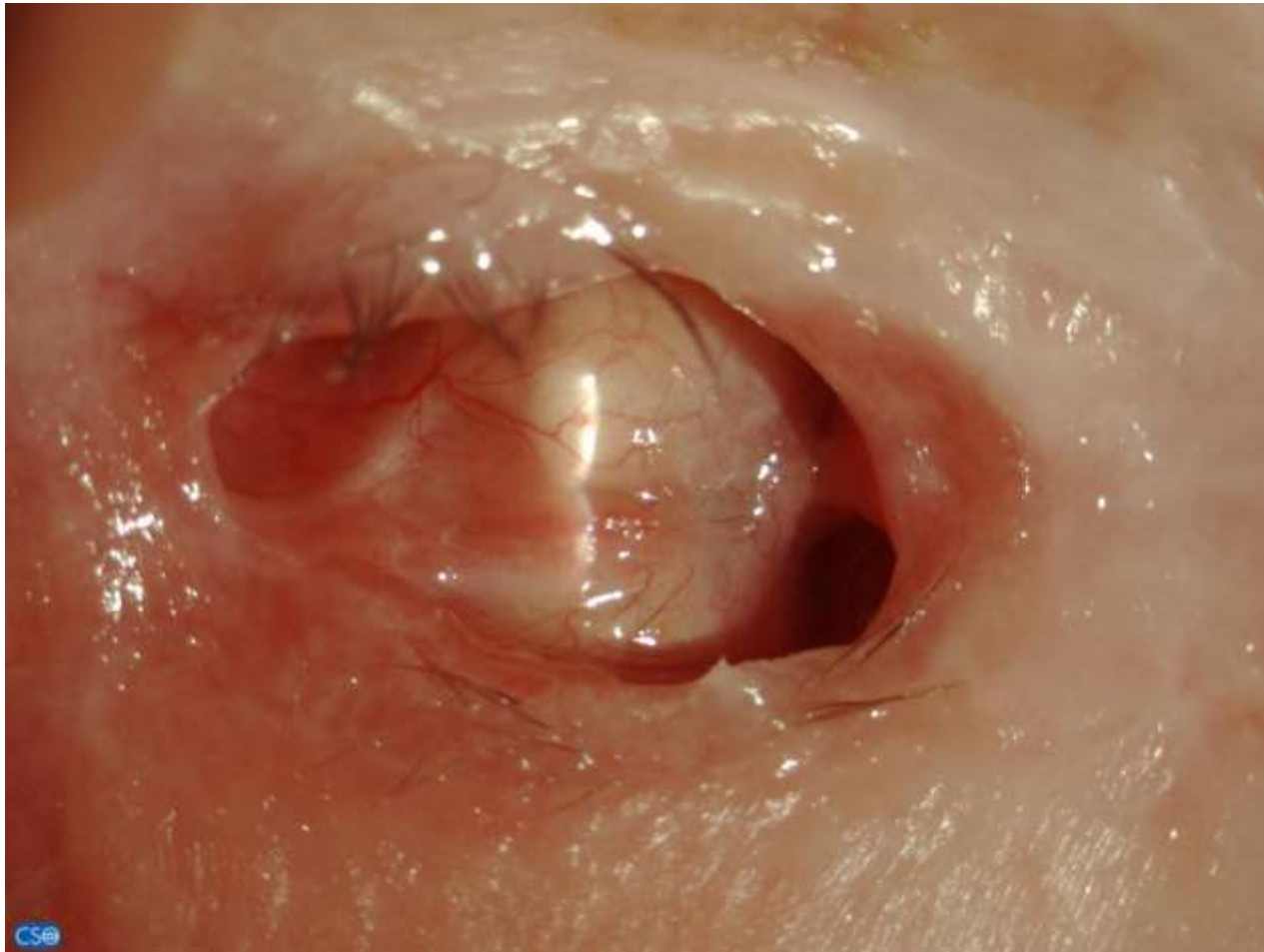
# Incidence of bacterial endophthalmitis in KPro eyes



# Complete cornea/Kpro melt...



# 2 years later



# **Prophylactic Antibiotics — for Life!**

**Vancomycin (14 mg/ml)  
with Bak**

**Fluoroquinolone**

**Both once daily**

- . Glaucoma (pressure measurements difficult – may need valve shunt)
- 4. Chronic Inflammation (from multiple previous surgeries-may result in retro

**Cumulative number of  
postoperative years with vision  
of 20/200 - 20/20  
(from LP, HM, or CF)**

**403 years**

***January, 2006***

## Antimicrobial prophylaxis for life: as important as ever

Data drawn from thousands of keratoprosthesis cases is showing that the judicious use of daily antibiotics can successfully lower postoperative infection rates. In the past, postoperative bacterial endophthalmitis frequently occurred after any type of keratoprosthesis, which contributed to the poor reputation of the procedure. Gram-positive bacteria, by far, have been

the most common culprit. Infections rarely occur during the first few months postoperatively, but may surface later, and are often related to obvious tissue melt and leak. Autoimmune diseases (Stevens-Johnson syndrome, ocular pemphigoid, graft vs. host disease, atopy, etc.) have been the most vulnerable to infection. The events have, in the most cases, resulted in rapid destruction of the eye.

However, it has become increasingly clear that very small amounts of antibiotics applied topically every day to the operated eye can be very effective in preventing bacterial infections. While this seems counterintuitive, our experience gained from thousands of KPro cases indicates that daily application of a light prophylaxis can be effective for many years without complications; it is also clear that, without any prophylactic antibiotics, the risk of infection is still very high. On the other hand, an excess of antibiotics can make the eye susceptible to fungal infections. Therefore, choosing the right antibiotic in the right concentration is very important for the long-term success of keratoprostheses. While many surgeons recommend different regimens, the procedures we follow in Boston have been very effective and are summarized here (Infectious Disease specialists Marlene Durand, MD and Irmgard Behlau, MD have been consulted):

1. For the standard patient receiving a Boston Keratoprosthesis Type I after multiple graft failures, we usually give a fourth-generation fluoroquinolone

*continues on page 3*

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*The Boston KPro  
newsletter is published  
once annually.*

### **Co-Editors:**

Rhonda Walcott-Harris  
James Chodosh, MD, MPH  
Claes Dohlman, MD, PhD

## Titanium back plates await FDA approval

Titanium is a material that has widespread application in medical bioengineering. For example, it is used in joint replacement, tooth implants, pacemakers, brain shunts, and artificial limbs; moreover, it has the reputation of being very inert and tissue friendly. Because of its versatility and strength, the Boston KPro team tested titanium as a potential material for making the back plate of the Boston KPro. As a first step, tissue culture experiments with epithelial cells showed titanium to be better tolerated than polymethyl methacrylate (PMMA).<sup>1</sup> Subsequent studies in rabbits and, since 2005, in patients have demonstrated that titanium is clearly superior in several respects: it can be machined to a very thin, yet strong and unbreakable plate; appears to cause less postoperative inflammation in the anterior chamber than PMMA; and demonstrates statistically lower rates of the frequency and severity of retroprosthetic membranes.<sup>2,3</sup> Another advantage is that titanium is non-magnetic and, thus, compatible with MRI testing.

*Titanium back plates of various dimensions and designs. Upper row:  
7.0 mm, 8.5 mm and 9.5 mm diameter.*

Since the titanium back plate is a new material, FDA approval is required before we can market and distribute this type of KPro in the United States. Several stringent FDA measures must be met before approval is granted. For example, the FDA has deemed the ethylene oxide sterilizers in local Boston area hospitals insufficient for “industrial” use; this requires that we send all packaged KPros to a South Carolina facility where long-term feasibility testing is underway. We anticipate that these measures, coupled with the FDA processing cycle, will result in a six to 12 month timeframe before we receive FDA marketing approval. Clearly, our KPro manufacturing has entered a new, more complex phase.

1. Ament JD, Spurr-Michaud S, Dohlman CH, Gipson IK. The Boston Keratoprosthesis: comparing corneal cell compatibility with titanium and PMMA back plates. *Cornea* 2009; 28:808-811.
2. Dohlman CH, Todani A, Ament JD, Chodosh J, Ciolino JB, Colby KA, Pineda R, Belin MW, Aquavella JV, Graney J. Titanium vs. PMMA back plates for Boston Keratoprosthesis: Incidence of retroprosthetic membrane. *Invest Ophthalmol Vis Sci*, 2009; ARVO poster # 1505.
3. Todani A, Ciolino JB, Ament JD, Colby KA, Pineda R, Belin MW, Aquavella JV, Chodosh J, Dohlman CH. Titanium back plate for a PMMA keratoprosthesis: clinical outcomes. *Graefes Arch Clin Exp Ophthalmol* 2011; in press.

# MMP Inhibitors

## Inhibitors Identified and/or Used in Treatment Studies

**EDTA-Ca**

**Cysteine**

**Acetylcysteine**

**Penicillamine**

**Medroxyprogesterone**

**Tetracyclines (Doxy, etc.)**

**TIMP- 1, 2, 3, 4**

**rTIMP-1, 2 (recombinant)**

**SIMP (synthetic)**

**TAPI-0**

**GM 6001**

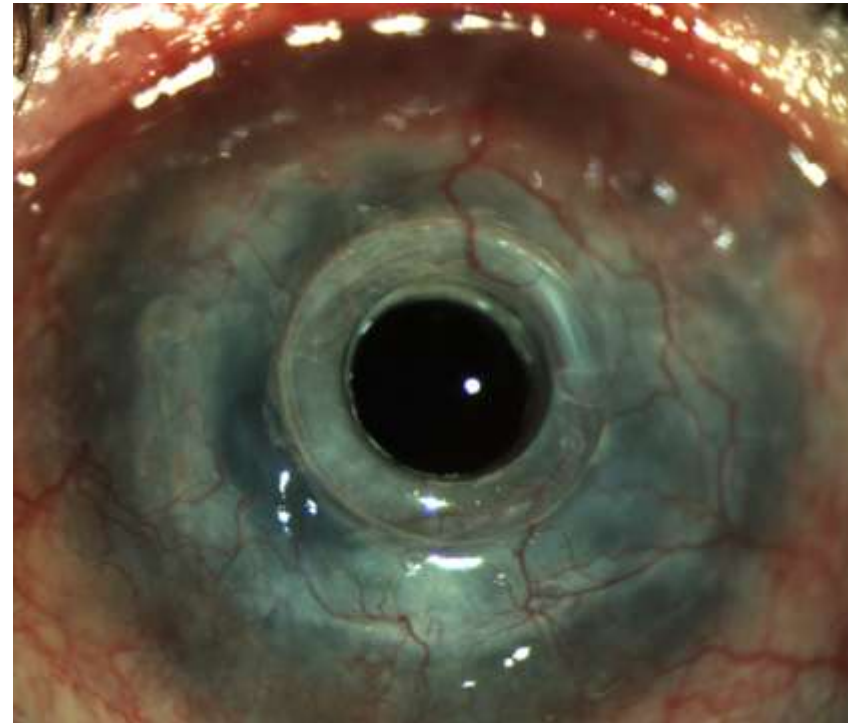
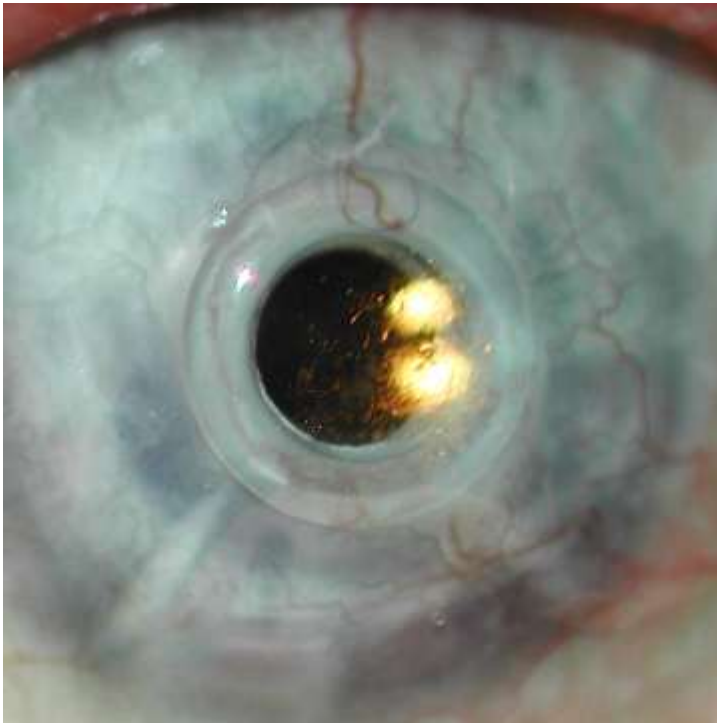
**anti-trypsin**

**-macroglobulin**

1-

2

# Dohlman's case from Boston

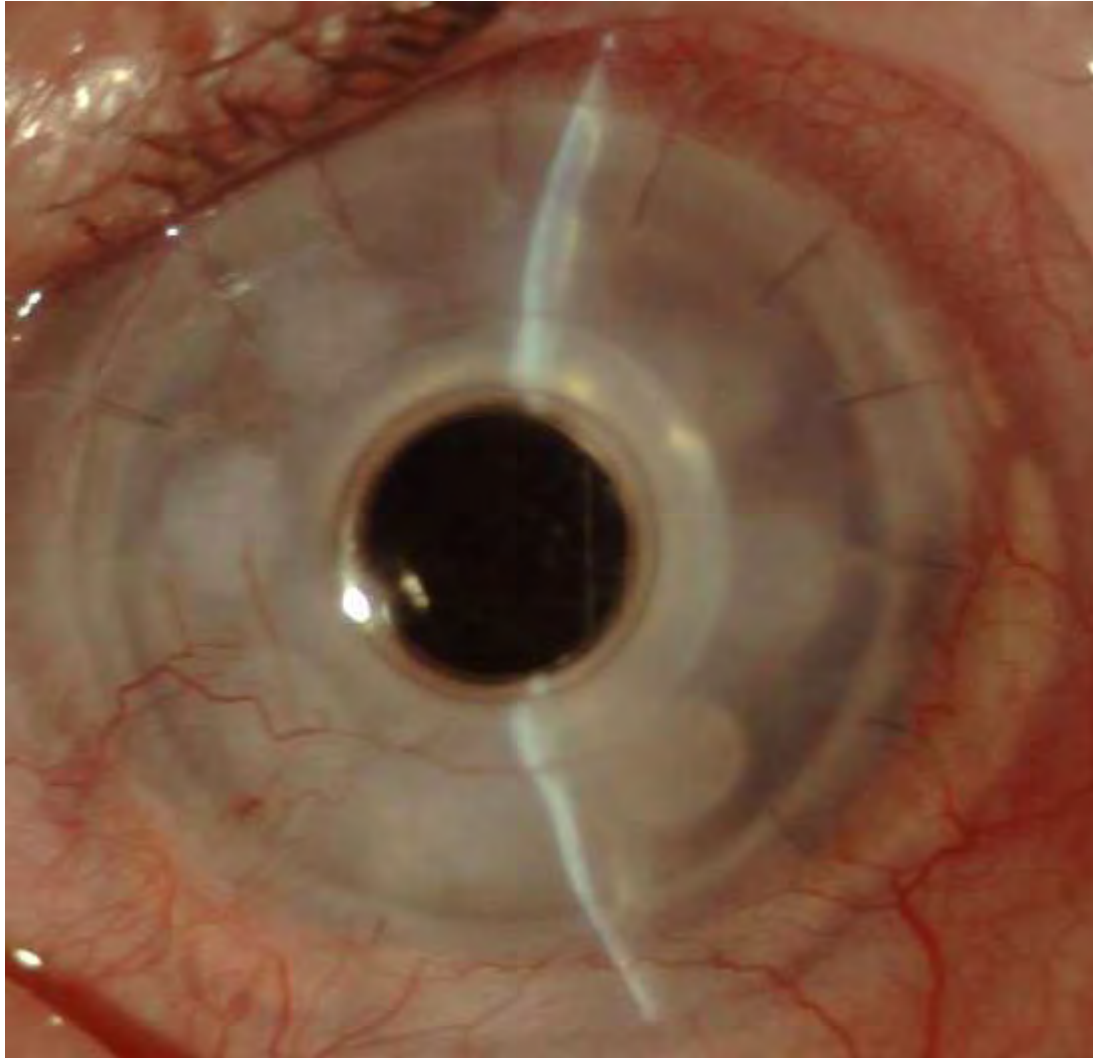




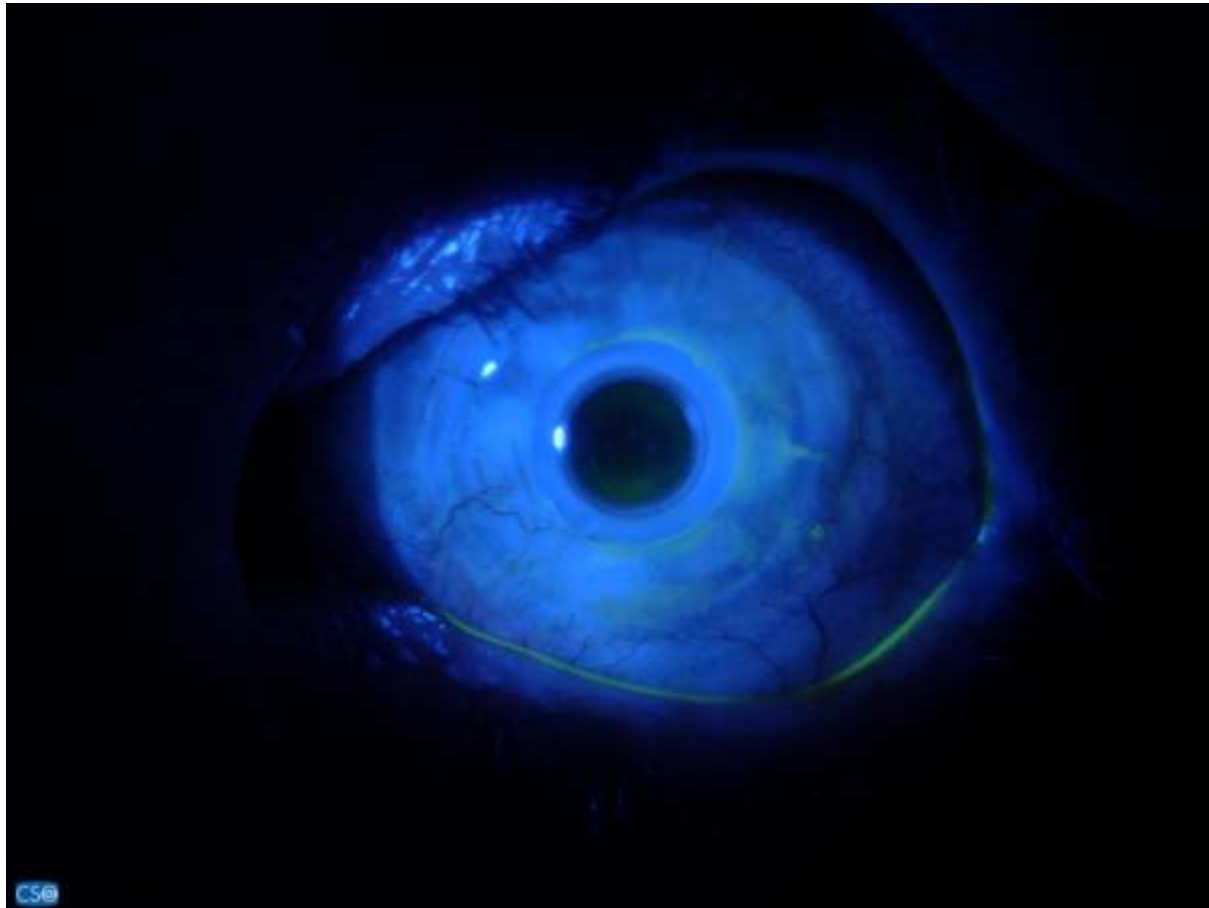
# Severe chemical burn



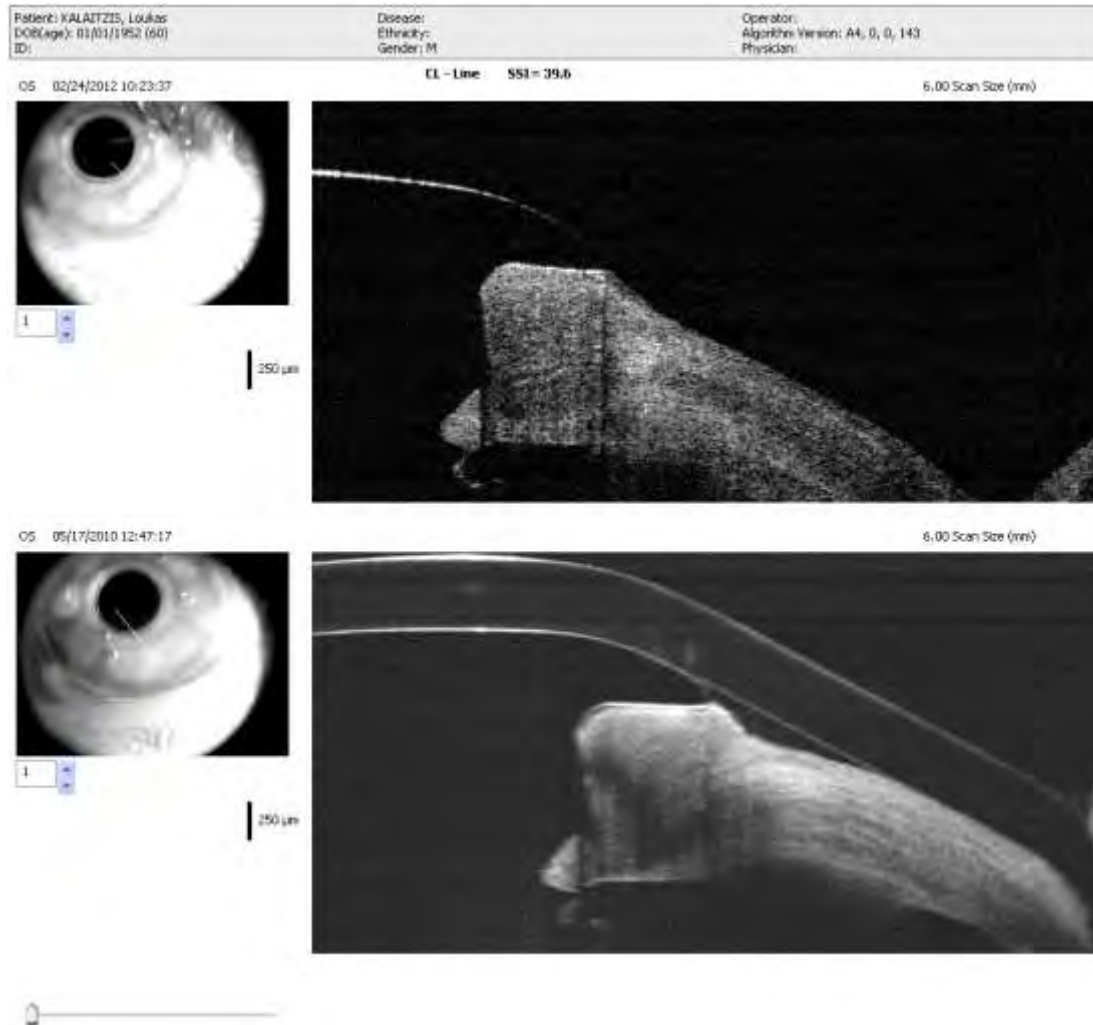
# Infero-temporal melt



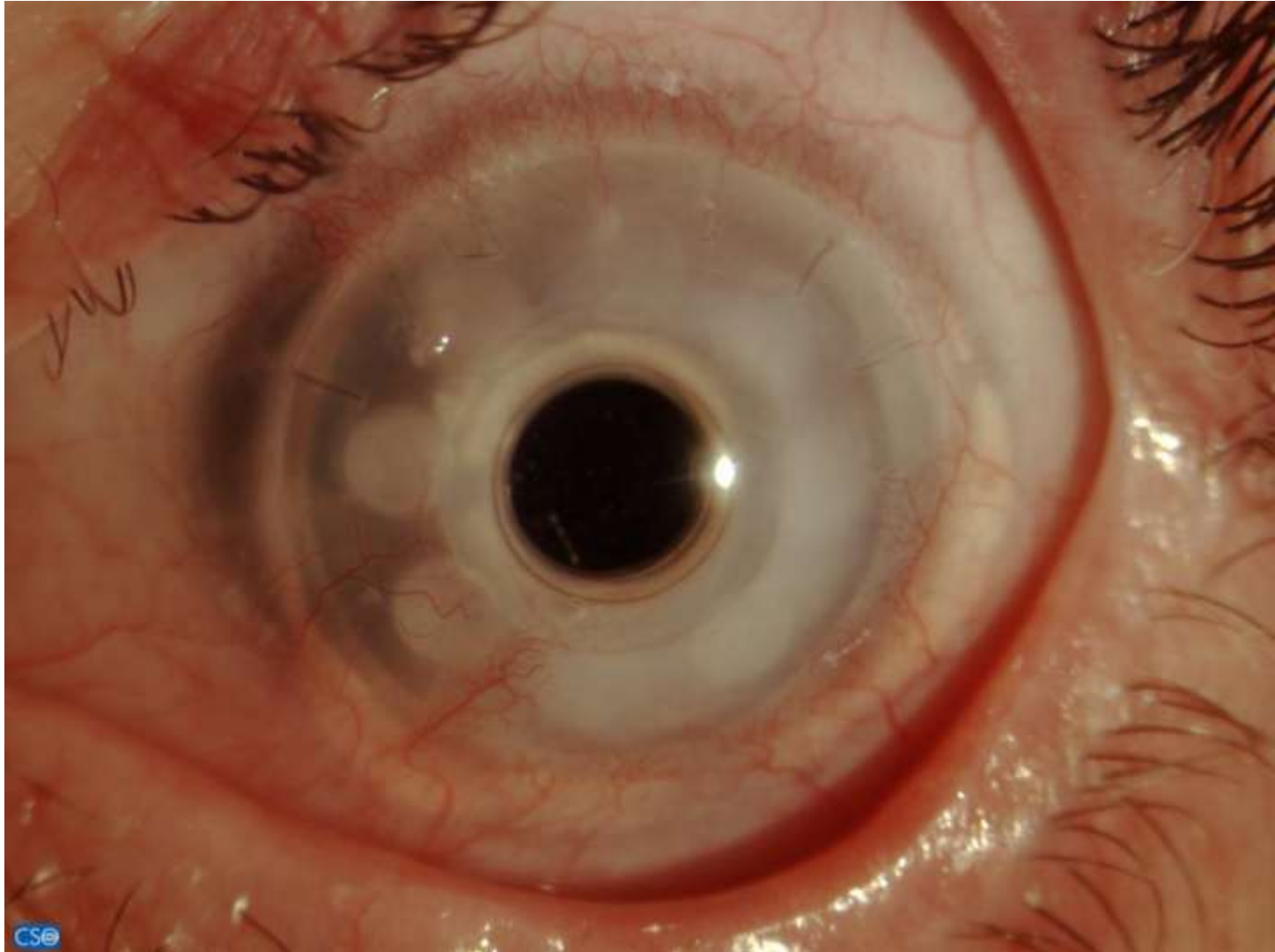
# Infero-temporal melt



# Build-up of stromal tissue: Thin below, thicker above



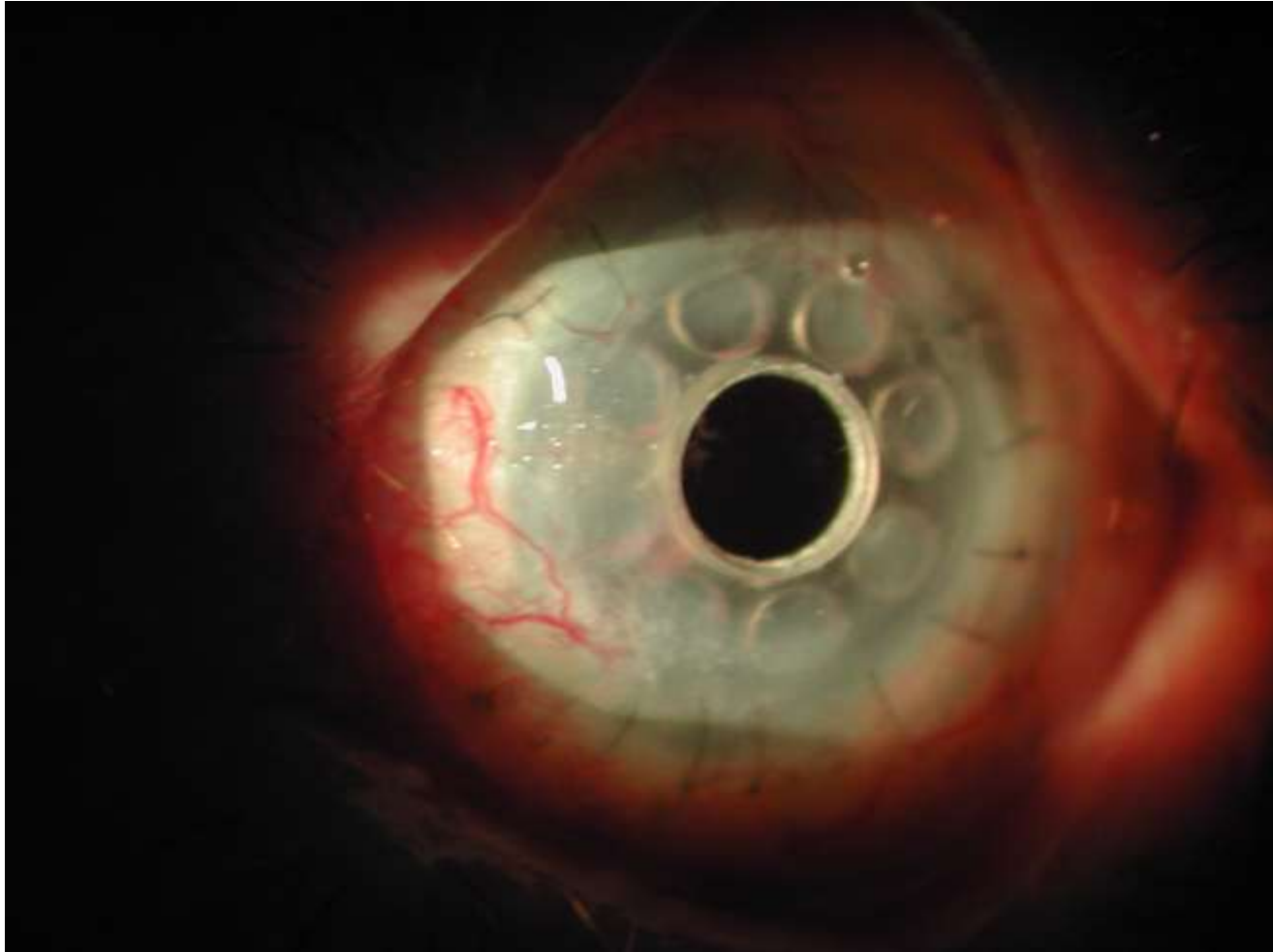
Last week minocin+Natacyn q W



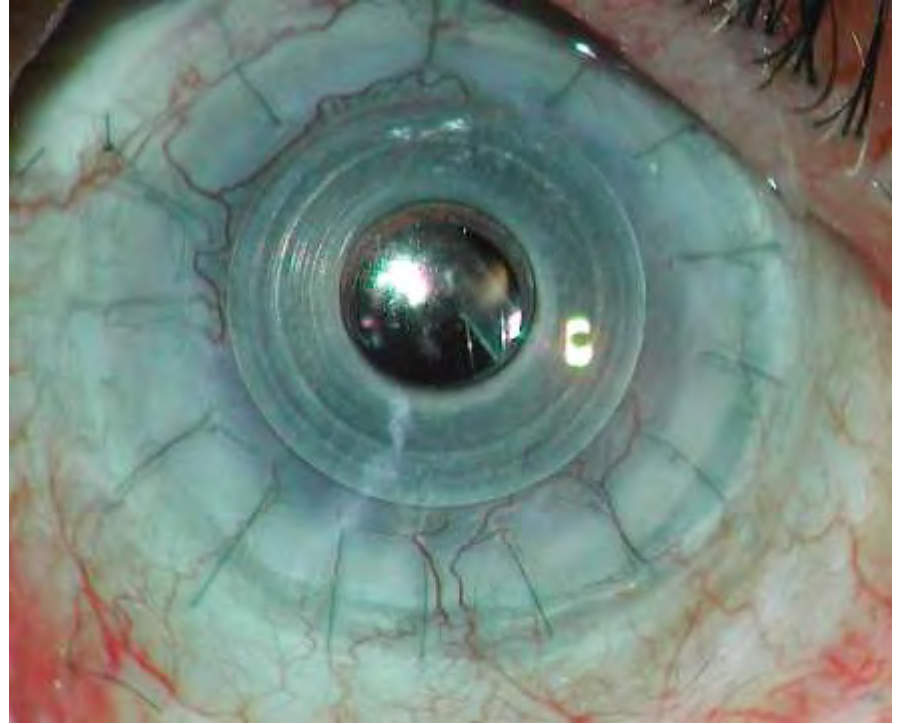
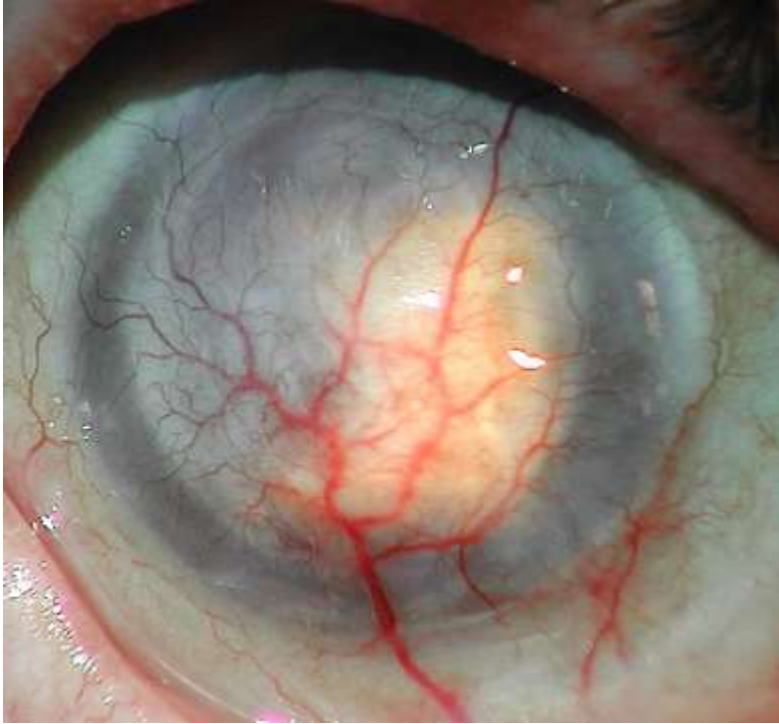
# Good optic nerve



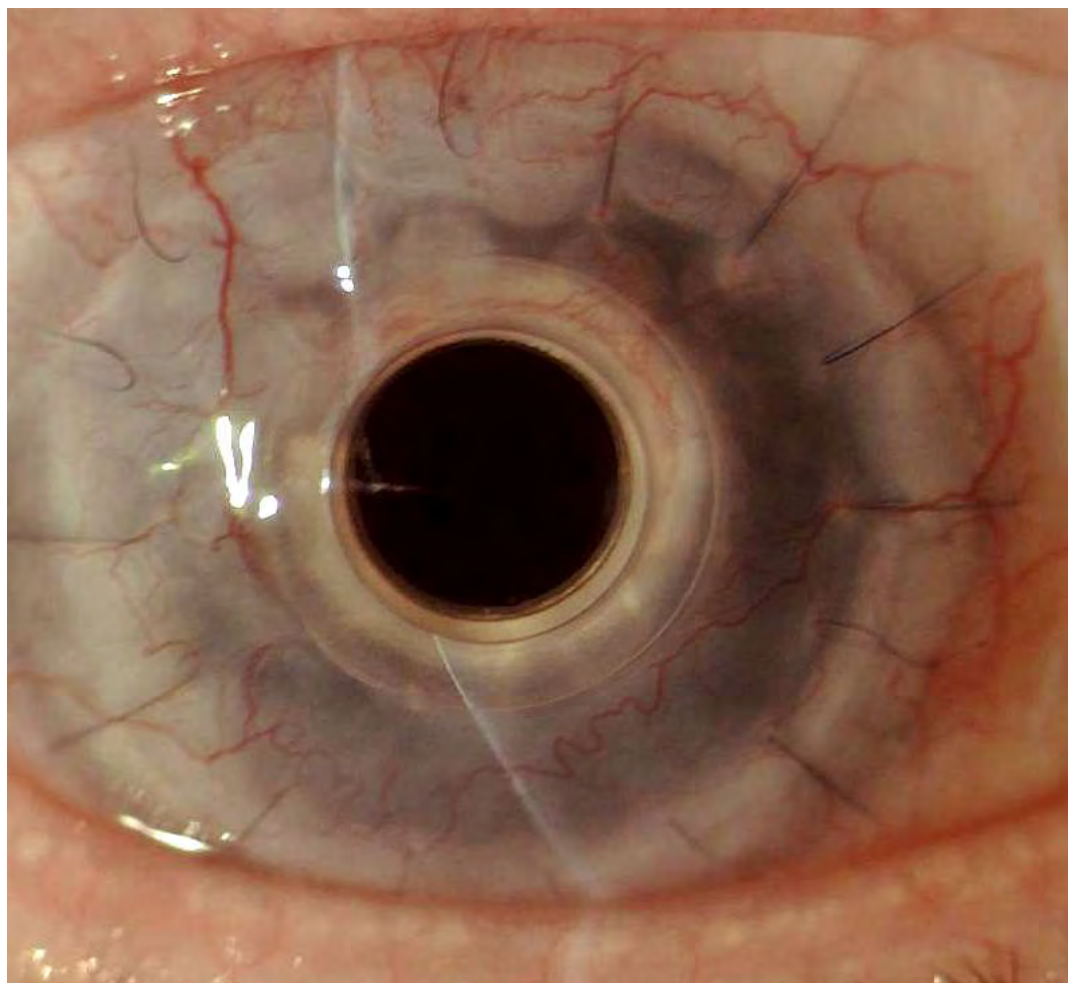
1997: first Kpro in Greece, here in  
2006



7 years 20/40!



# SN thinning



# Use of a foldable artificial cornea for Tx of blindness due to severe ocular surface disease

Vasilis Skouteris, MD

A. John Kanellopoulos, MD

Laservision.gr Institute, Athens, Greece

Professor of Ophthalmology, NYU Med  
School, NY

No financial Interests

KeraKlear: Has European CE Mark



This device has European CE Mark Approval  
This device has not received FDA Clearance

I have no financial interest in this presentation

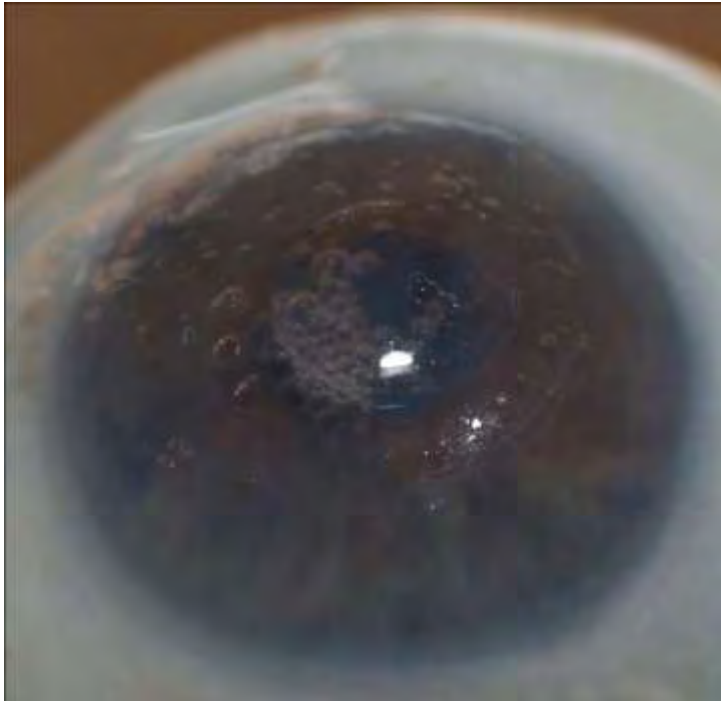


The KeraKlear does not have FDA clearance for Use in the U.S.

# KeraKlear: Has European CE Mark

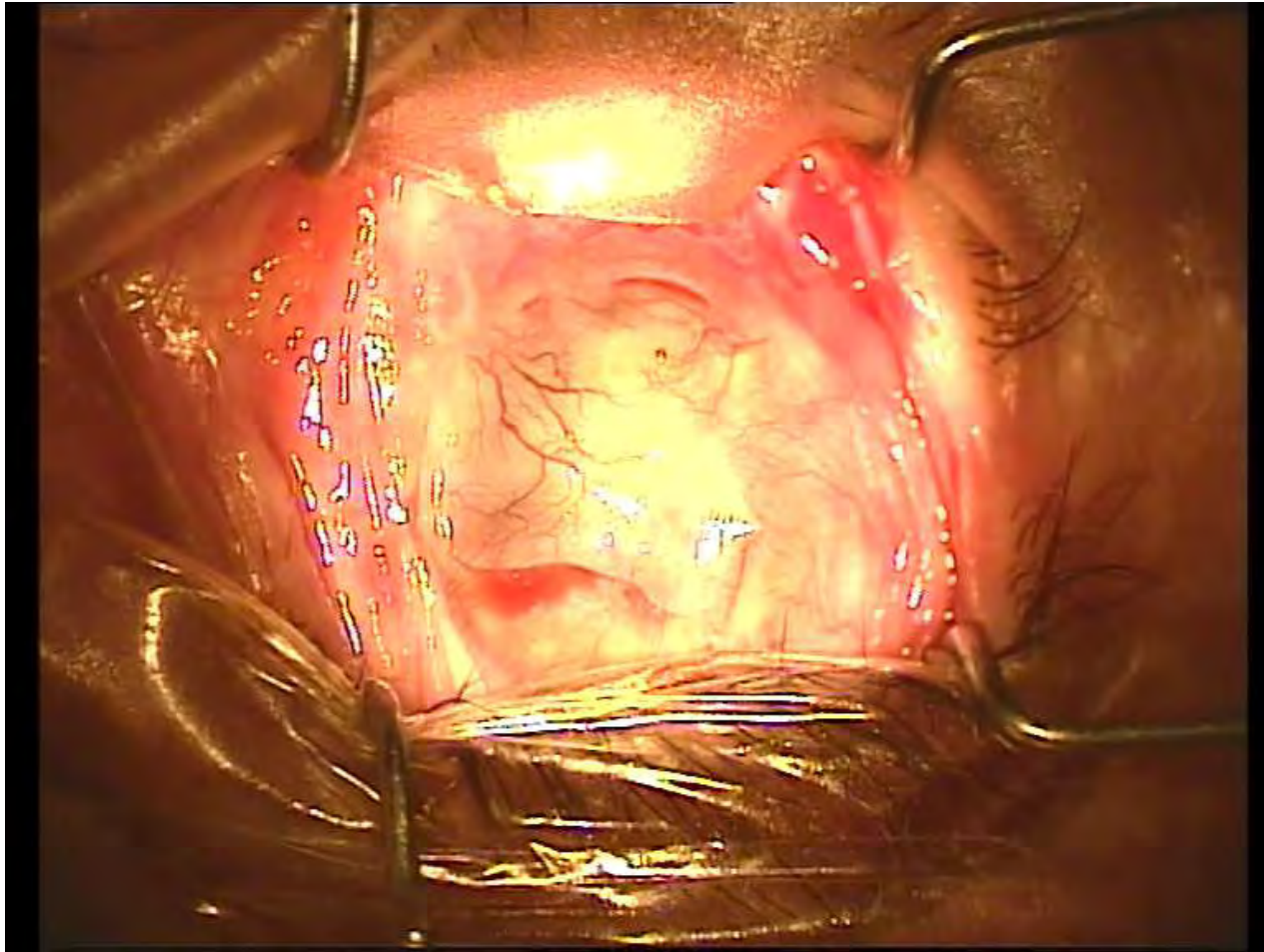
This device has European CE Mark Approval  
This device has not received FDA Clearance

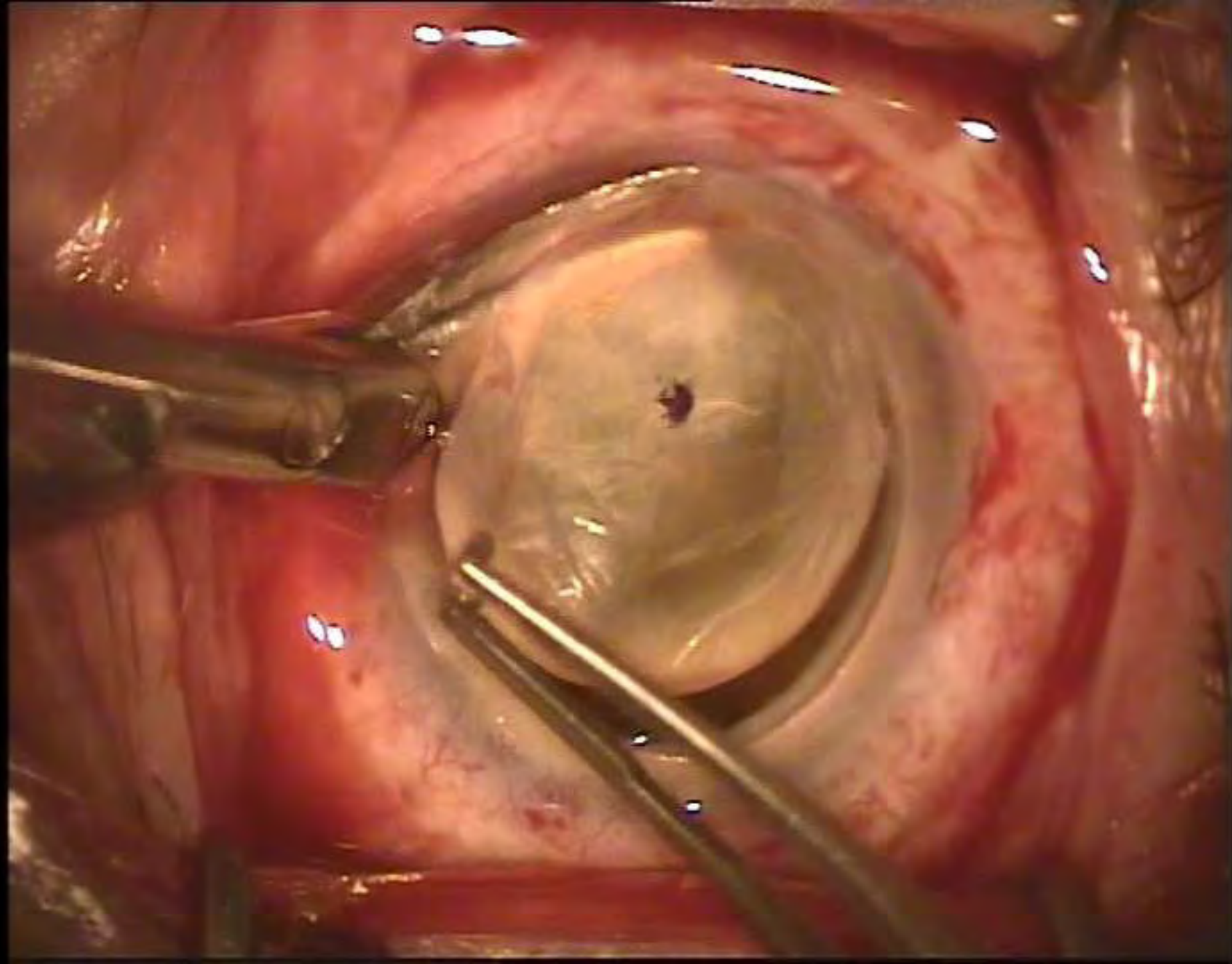
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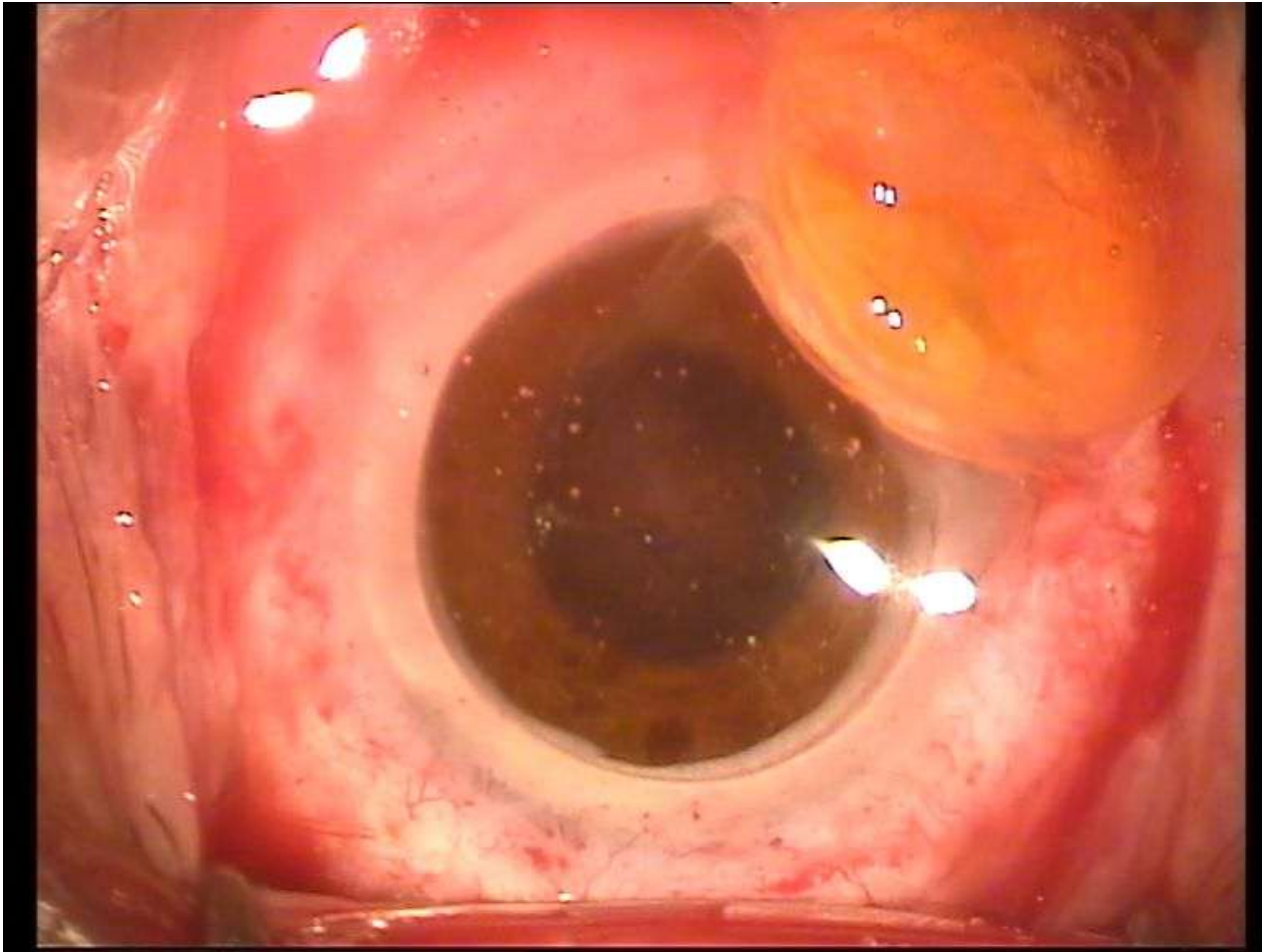


# Pre-op: BLP

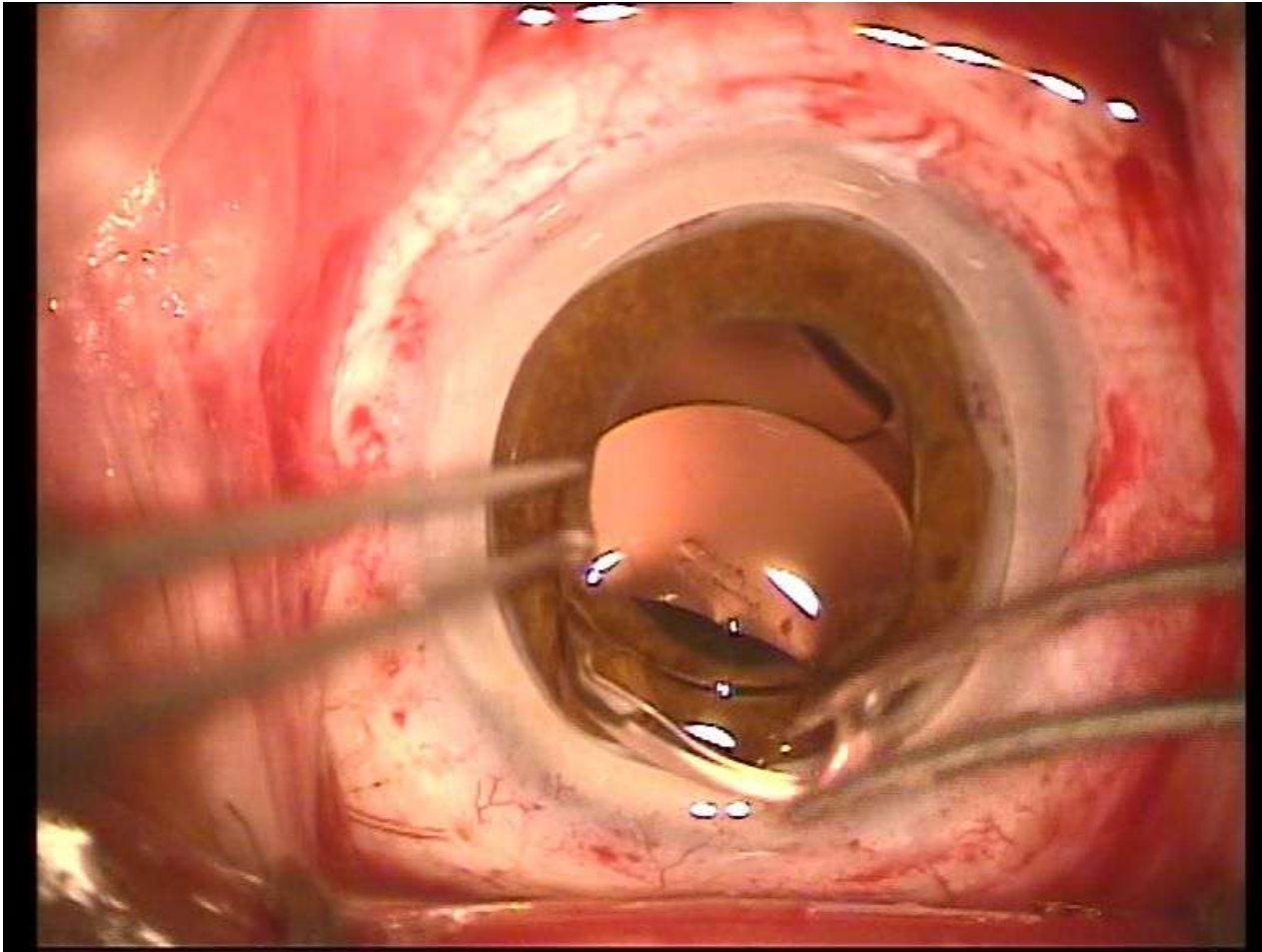




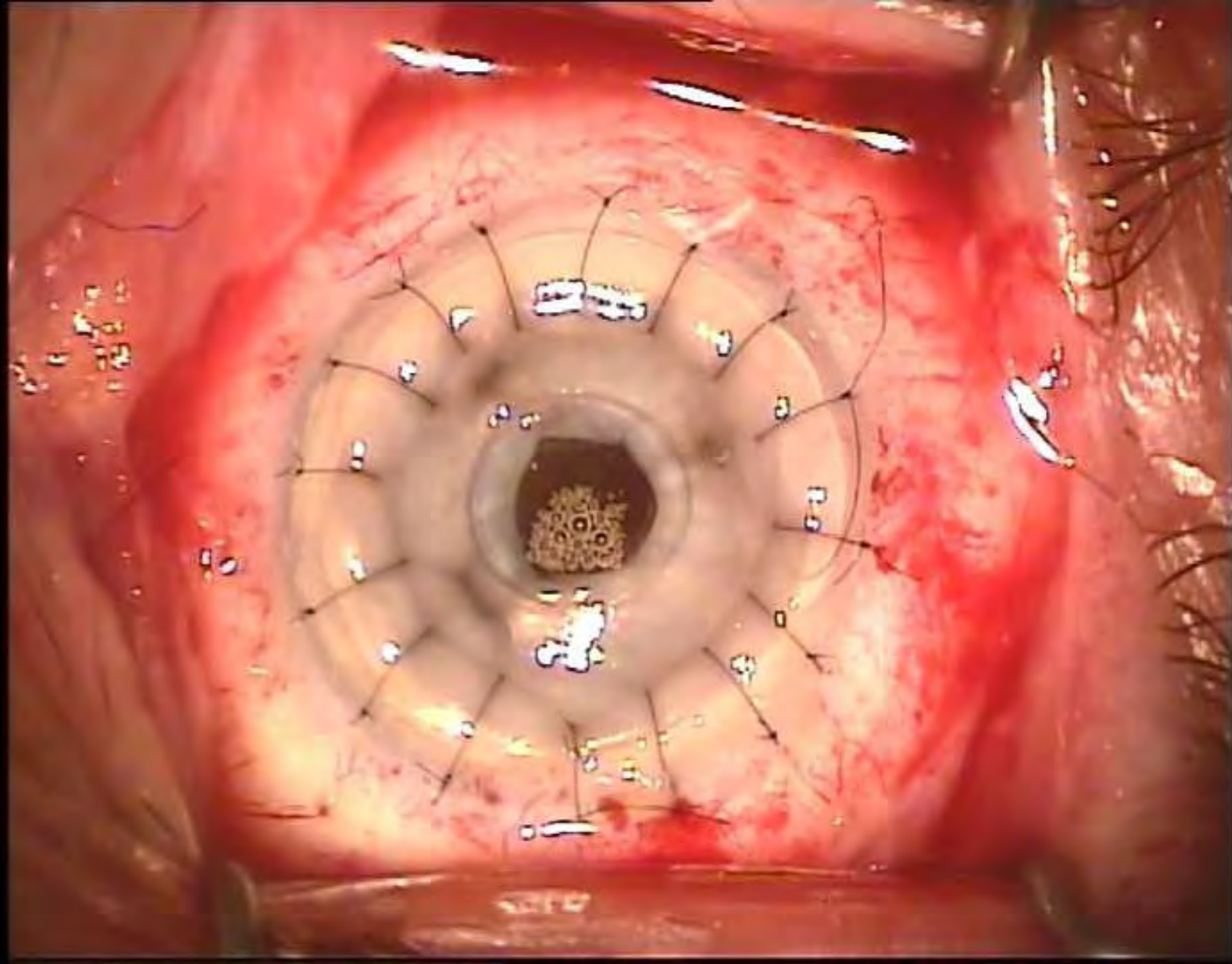
# ECCE



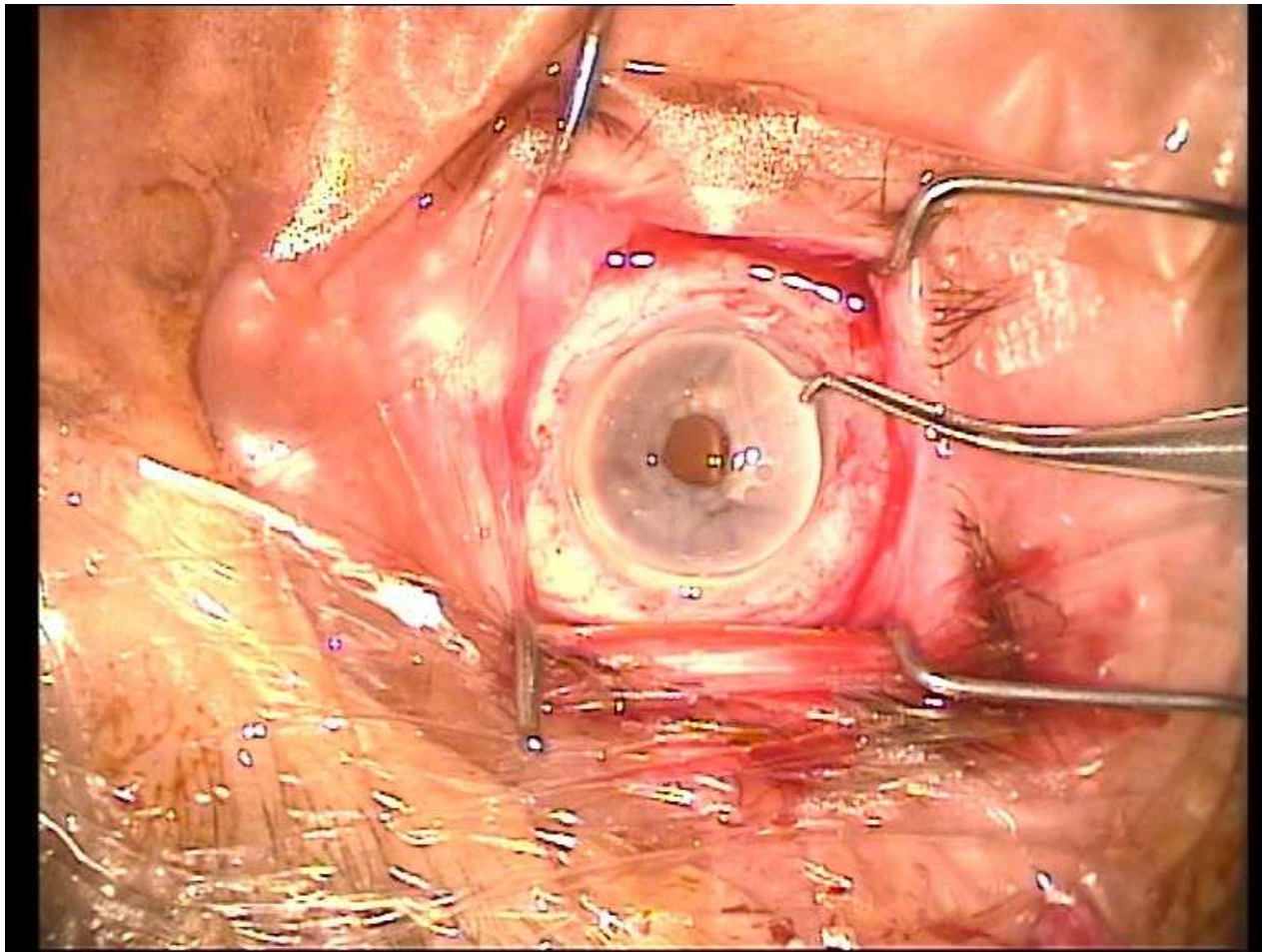
# IOL








# KeraKlear on CXLed conrea



# KeraKlear with graft 20/100



OB

CL - Line SSI= 37.8 6.00mm Scan Length

250  $\mu$ m

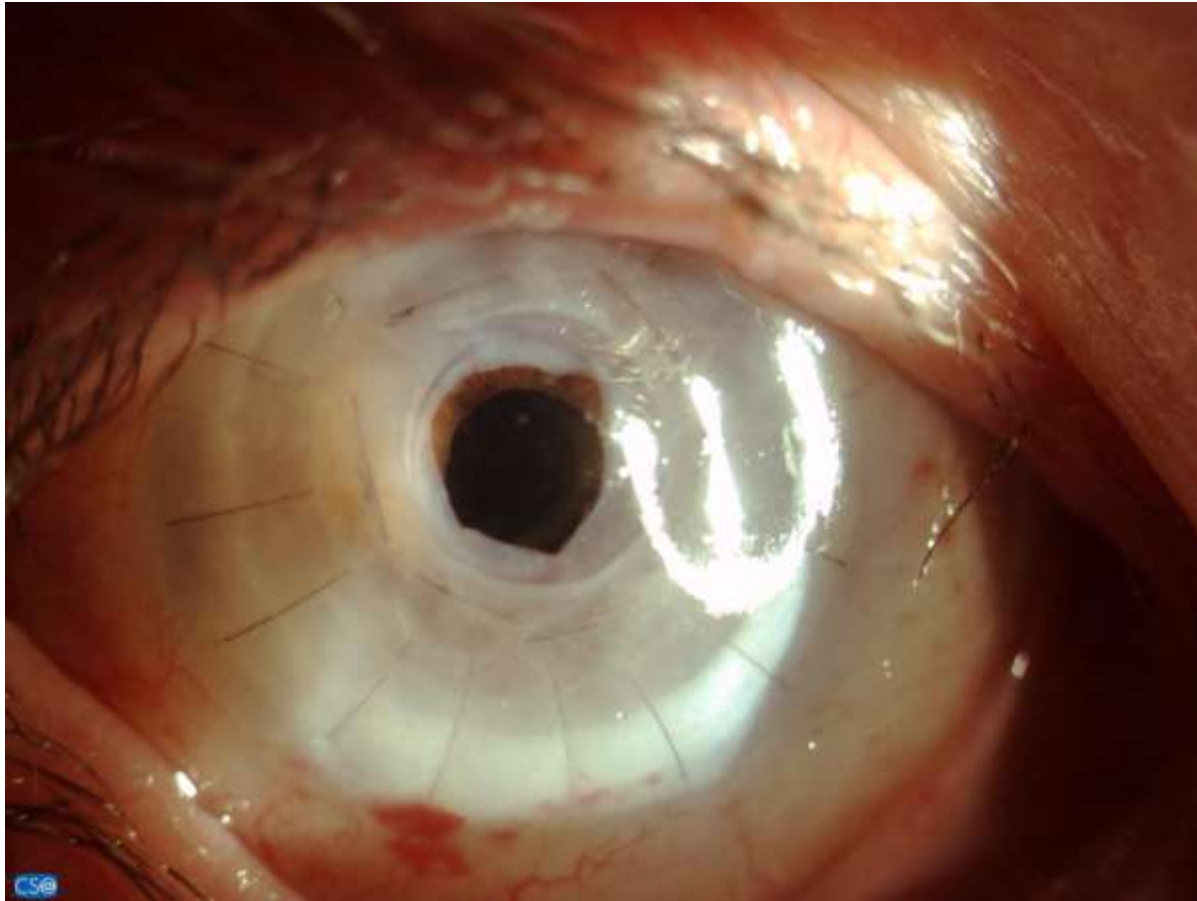
# of Averages: 1

Diagnosis:

Report Date: Wednesday May 26 20:09:57 2010

The image displays a clinical photograph of a patient's eye wearing a KeraKlear contact lens with a graft. To the right of the photograph is a topographic scan of the eye. The scan shows the corneal topography with a central area of high elevation, likely corresponding to the graft. The scan parameters include a CL - Line SSI of 37.8 and a 6.00mm scan length. A vertical scale bar indicates 250  $\mu$ m. Below the topographic scan is a cross-sectional view of the eye, showing the cornea and the graft. The graft is visible as a distinct area of high elevation. The interface also includes a 'Diagnosis' field and a 'Report Date' of Wednesday May 26 20:09:57 2010.

2 years out



# Ultimate goal



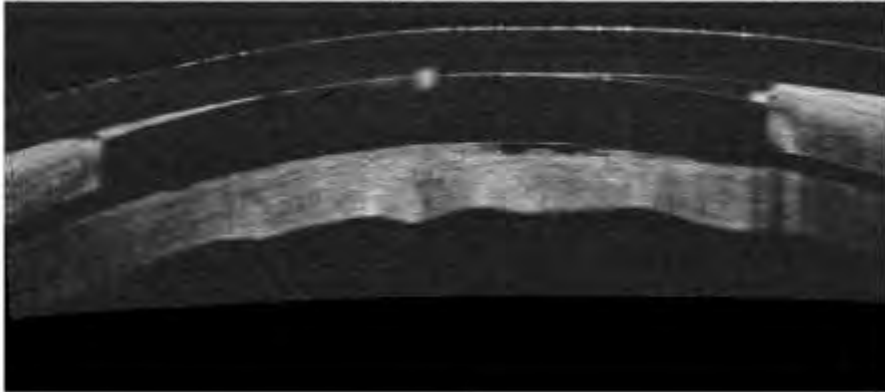




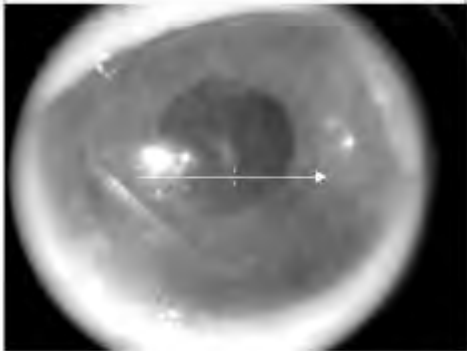
# KeraKlear OCT

Patient: Pappas KANELIPOULOU DOB (age): 03/23/1952 (58) ID:	Disease: Algorithm Version: A4, 0, 0, 143 Gender: F	Photographer: Exam Date: 11/26/2018 Physician:
---	---	--

DS      LS - Line      SSE = 38.1      A-Direct Scan Length



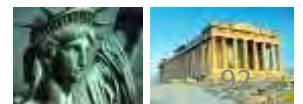
250  $\mu$ m



# of Averages:

Diagnosis:

Report Date: Thursday, December 02 09:29:43 2019



Patient: karamed keraklear  
DOB (age): 04/19/2010 (0)  
ID:

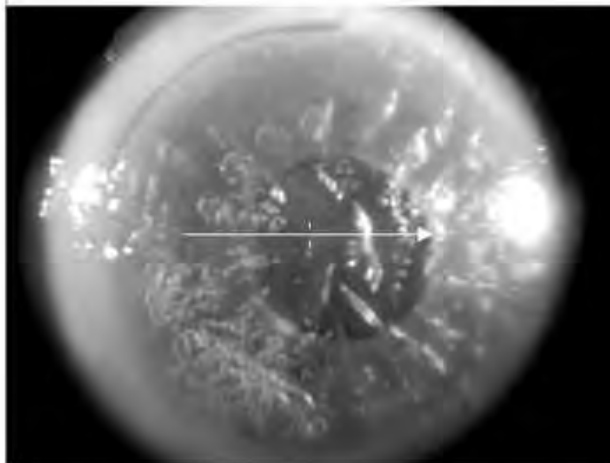
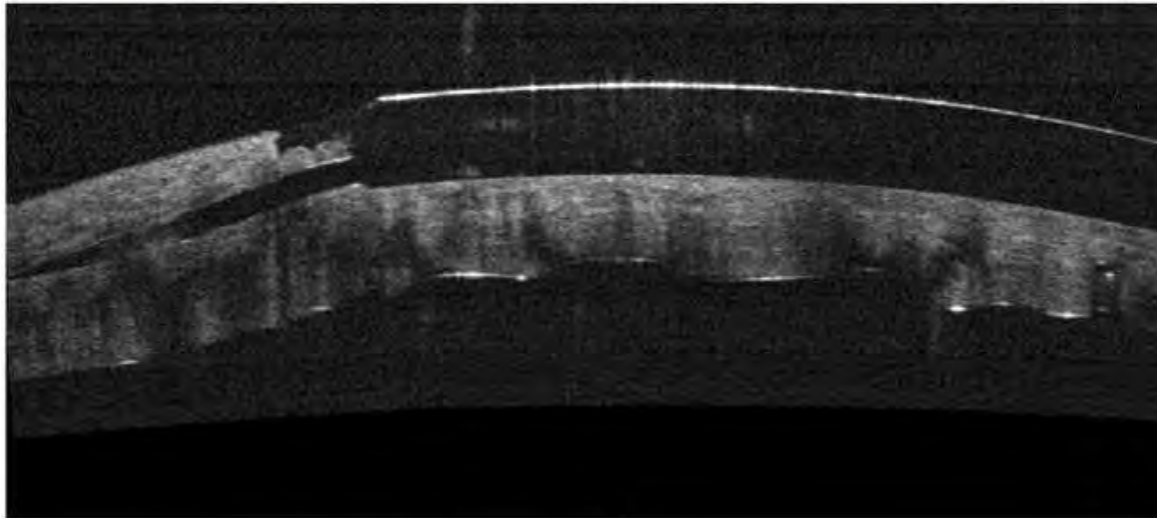
Disease:  
Algorithm Version: A4, 0, 0, 143  
Gender: M

Photographer:  
Exam Date: 04/19/2010  
Physician:

OS

CL - Line SSI = 38.1

6.00mm Scan Length



# of Averages:5

Average

No Average

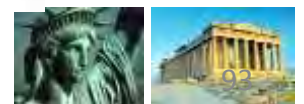
Diagnosis:

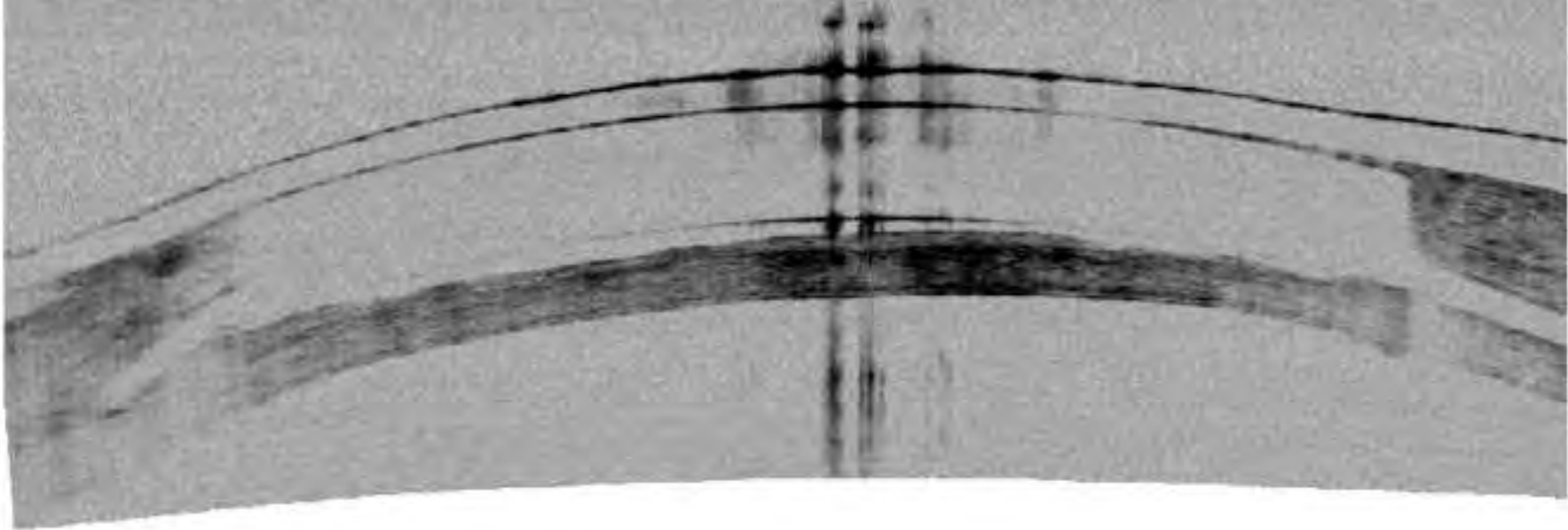
Report Date: Friday April 23 17:19:09 2010



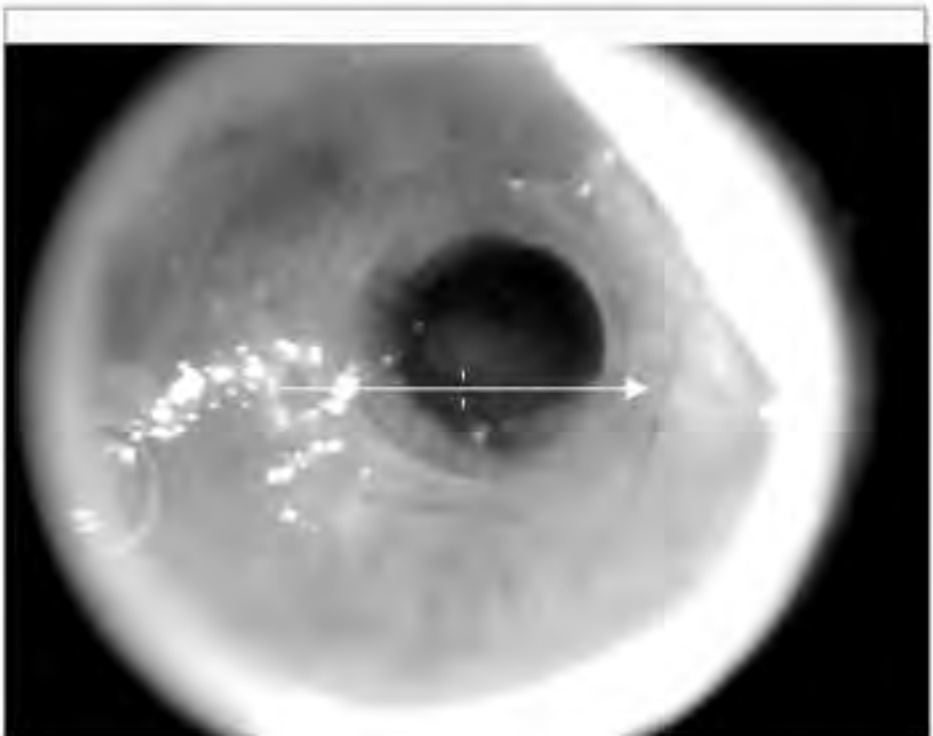
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School of Medicine

LaserVision.gr  
Institute for laser





250  $\mu\text{m}$

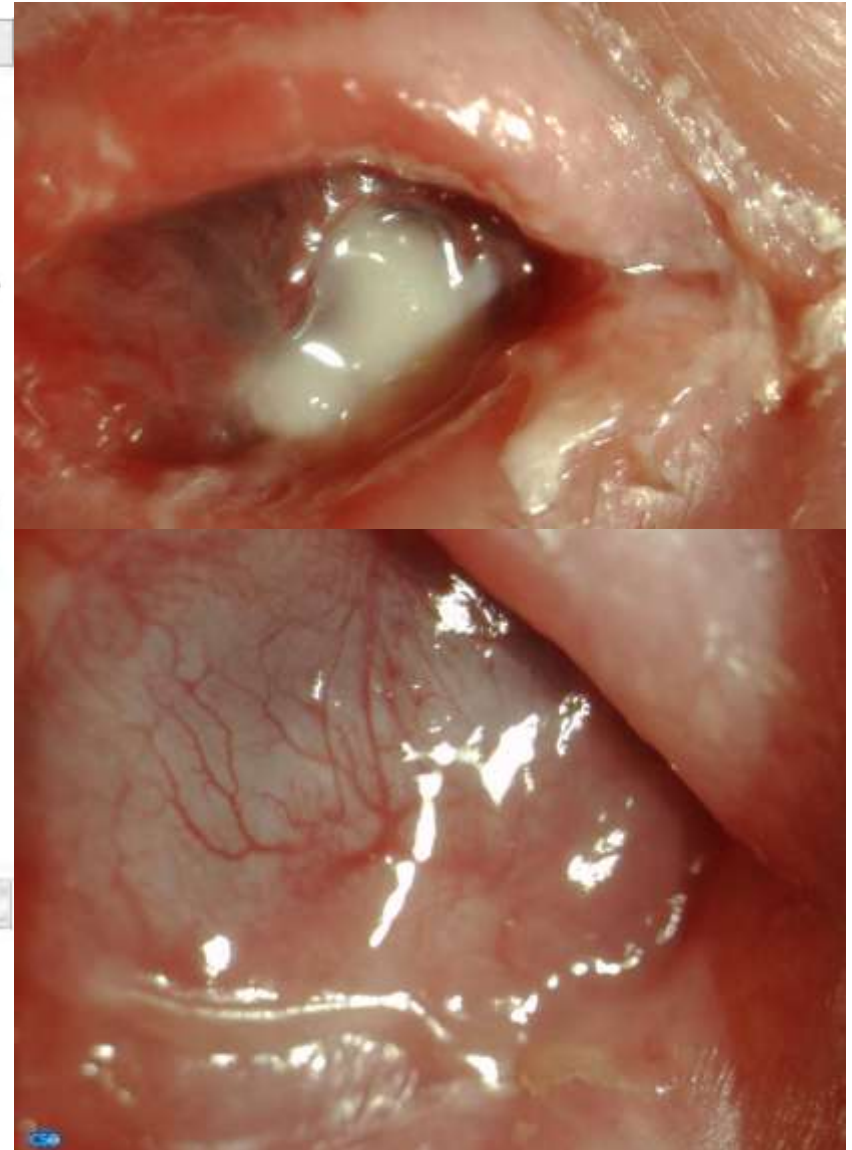


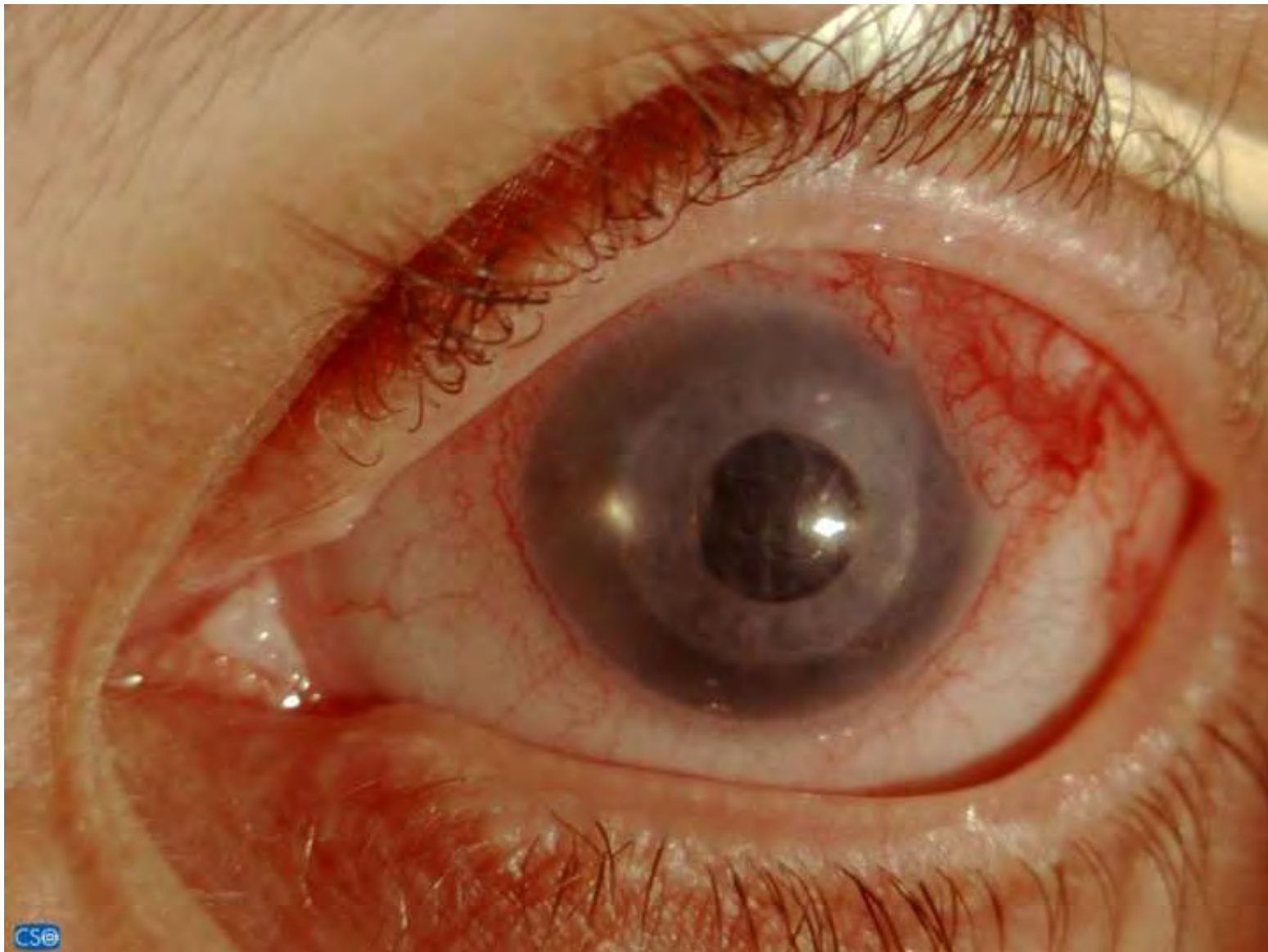
# of Averages:6

Average

No Average

# Staph infection, treated





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Institute for laser





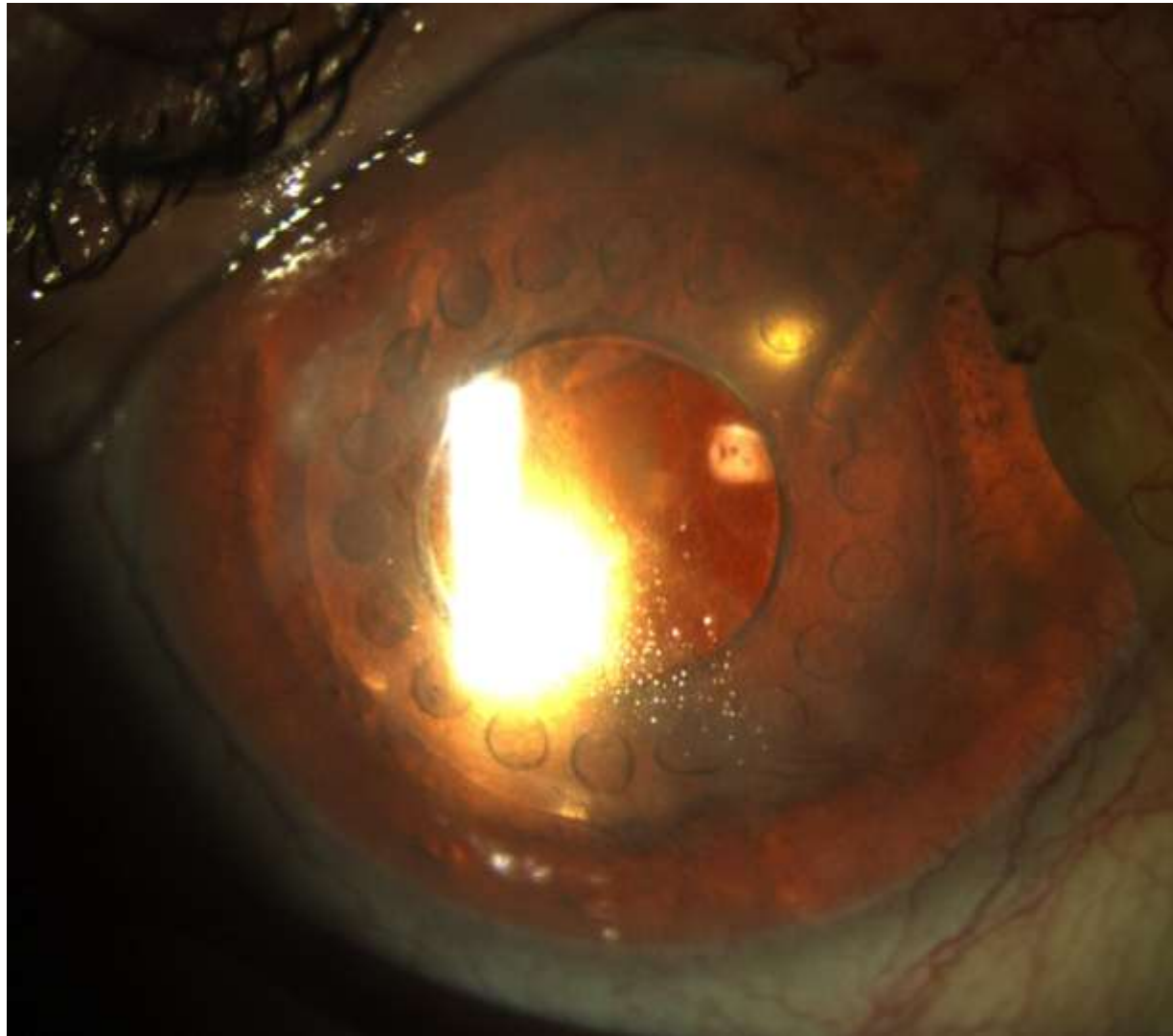
CSE



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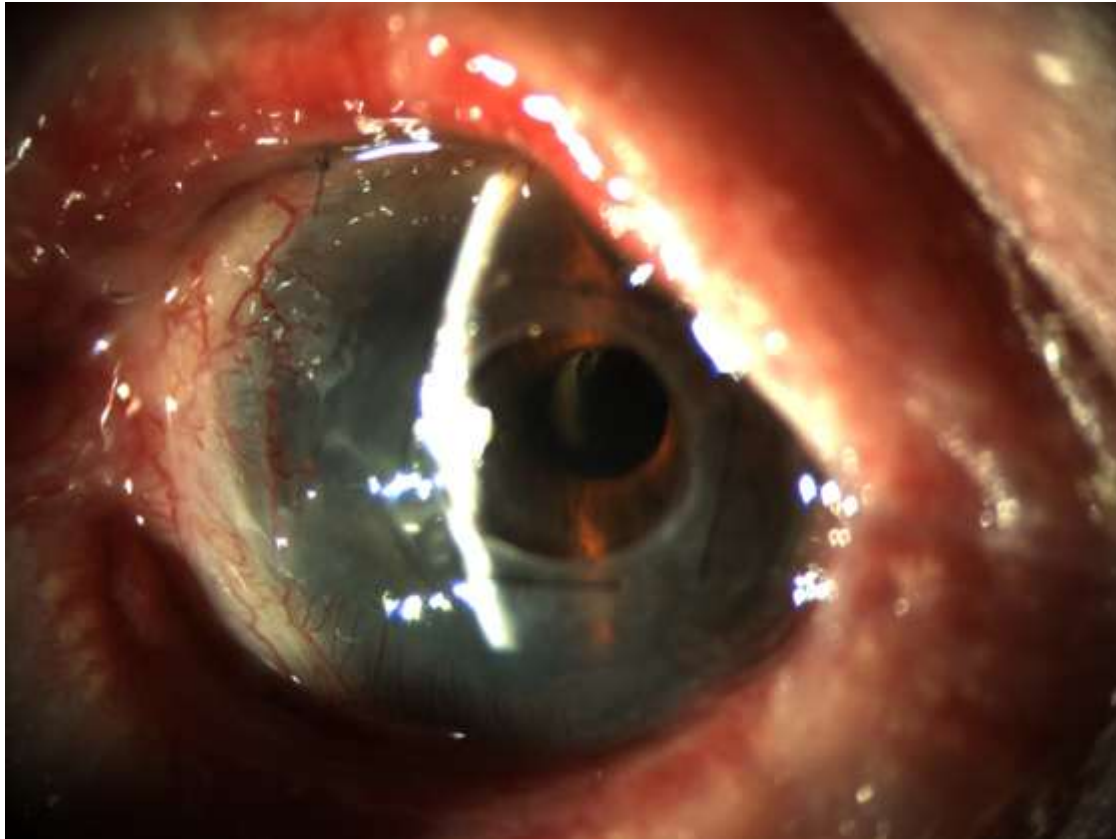


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3mos



4mos



# “haptic”

Patient: Fokos: HFERGIM5 DOB (age): 01/01/1914 (96) ID:	Disease: Algorithm Version: A4, 0, 0, 143 Gender: M	Photographer: Exam Date: 05/10/2010 Physician:
---	---	--

OD      ES - Line      SSE = 42.6      A. DDCan Scan Length



250  $\mu$ m



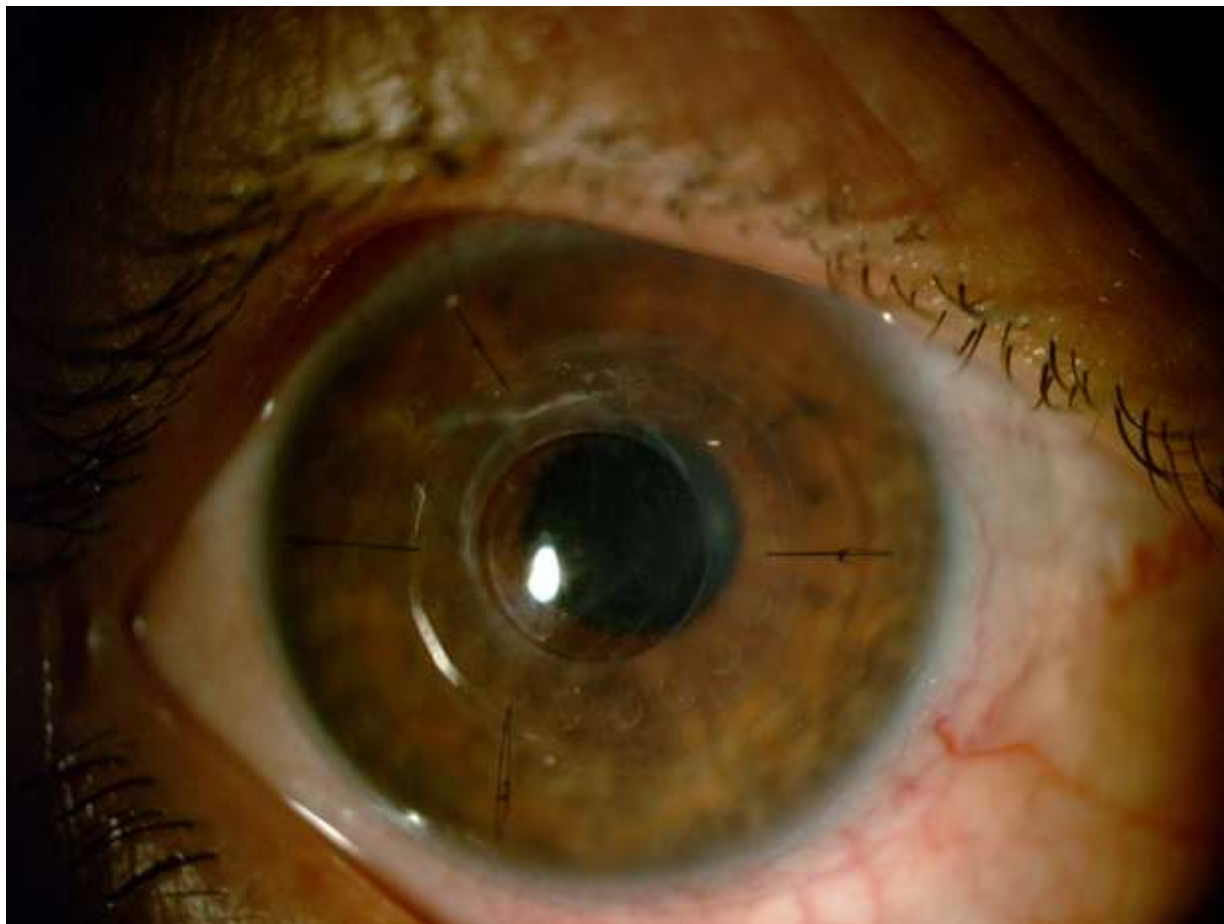
# of Averages: 15

Diagnosis:

Report Date: Wednesday May 26 20:17:03 2010

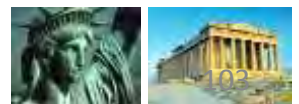
# In advanced Keratoconus!

courtesy of Dr. Vargas



# Conclusion:

- This foldable and injectable artificial cornea may be a feasible alternative to corneal transplantation in cases where there is a high risk of graft rejection or graft failure
- A significant benefit is that there is not a need for carrier donor tissue, which is unavailable in many parts of the world.
- Small external incision and simplicity of procedure may make artificial cornea surgery more accessible. .
- The implants appear to be stable over a period of two years.
- longer followup needed



# Boston Keratoprosthesis

## Prognostic categories

### 1. **Graft failures**

(after edema, infections, trauma, etc.)

### 2. Chemical burns

### 3. Autoimmune diseases

(SJS, OCP, uveitis, etc.)

# Kpro

- Extreme external disease
- Multifactorial treatment
- Poor blinking
- Rheumatology
- External disease/Melts
- IOP
- Vitritis
- INFECTION



Thank you



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