



**THE UNIVERSITY
OF AUCKLAND**

**FACULTY OF MEDICAL
AND HEALTH SCIENCES**

School of Medicine



nz national
eye centre



nz national eye centre

The continuing evolution of corneal transplant surgery and what to anticipate in your patients

Professor Charles NJ McGhee

MB, PhD, FRCS, FRCOphth, FRANZCO

Maurice Paykel Professor and Chair of Ophthalmology

Director, New Zealand National Eye Centre, University of Auckland



APAOSydney2011
SYDNEY AUSTRALIA
20 - 24 MARCH 2011

Asia Pacific Academy of Ophthalmology Congress



The speaker – wee geekie to McGeeski



- 1983 Graduate in Medicine, Glasgow
- 1993 Professor of Ocular Therapeutics, University of Sunderland
- 1996 Professor of Ophthalmology, University of Dundee
- 1999 Professor of Ophthalmology, University of Auckland

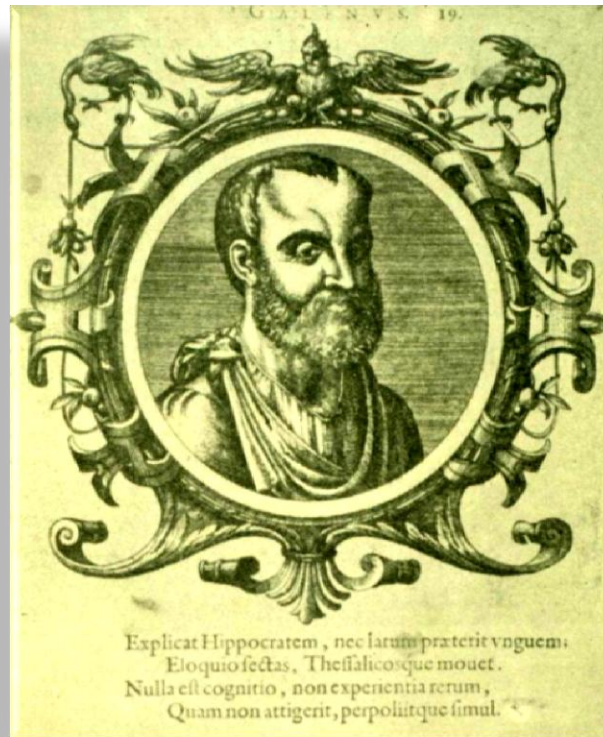




Transplantation and corneal surgery from ancient Egypt to medieval Europe



Egyptian epoch



Galen AD 130-200



St Lucy

Pre-1700: The corneal Dark Ages

Roger Frugardi (Salernitanus) 1140-95 of Salerno Medical School (9thCent)



Chirurgiae Magistri Rogerii 1180 (The Surgery of Master Rogerius)

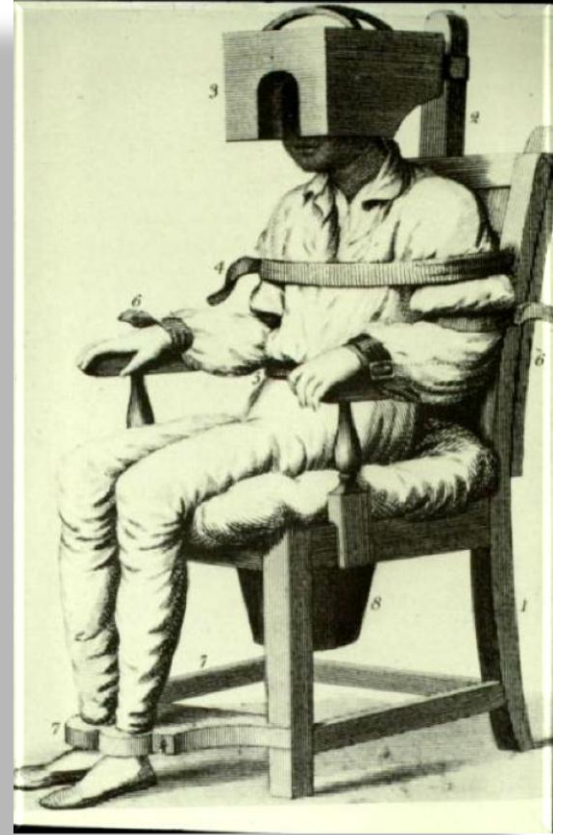
1750: Cataract surgery evolves to ECCE whilst corneal surgery remains in the dark ages



Cataract surgeons!

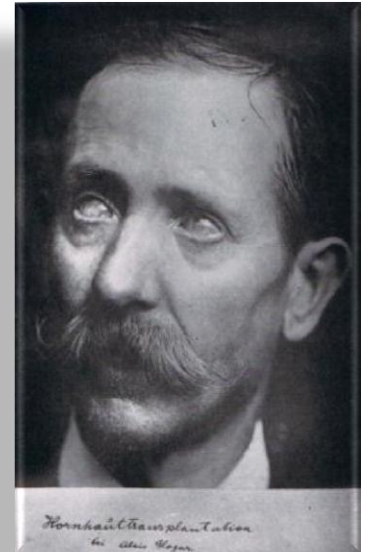


Jacques Daviel



Corneal surgeons?

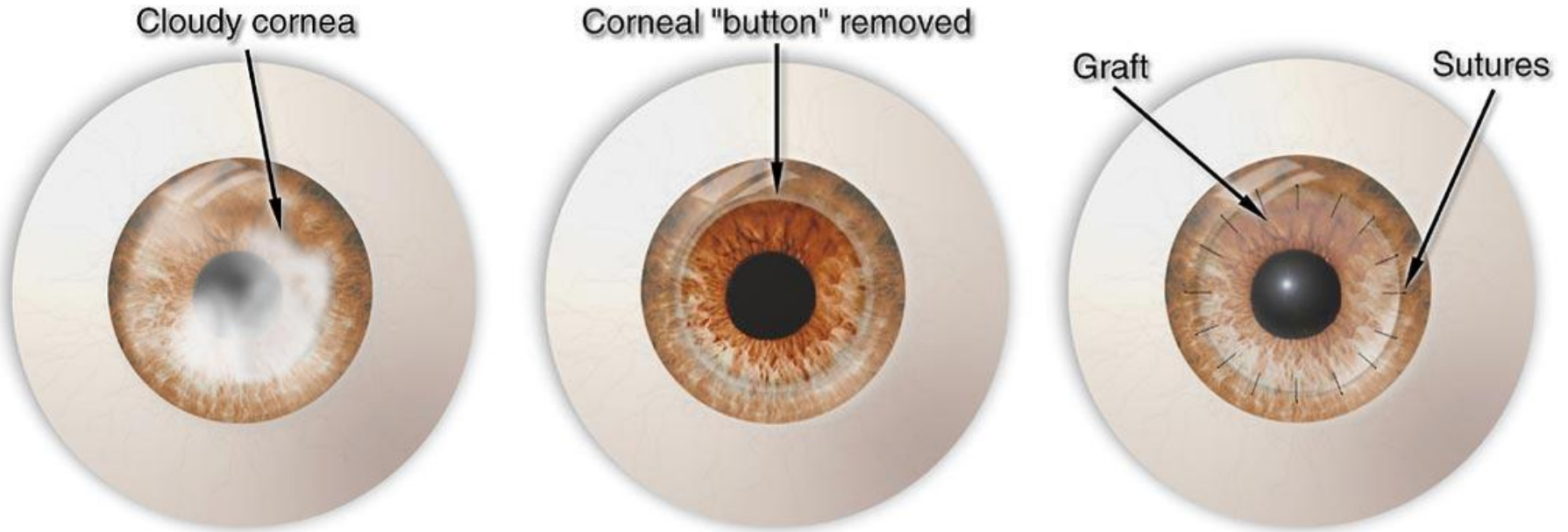
Dec 5th 1905: 1st successful corneal transplant



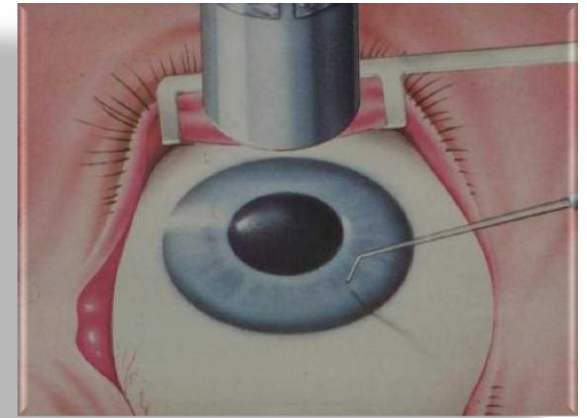
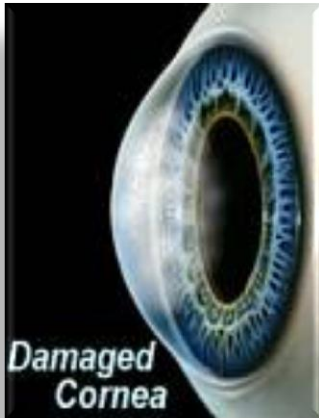
Dr Eduard Zirm operated on Alois Goggar at Olmutz,
11 year old donor and patient had bilateral lime burns with pre-op HM vision
At one year VAL 6/36 and J4 and patient lived another three years.

1905-1946: Success and early advances

"Simple" penetrating keratoplasty

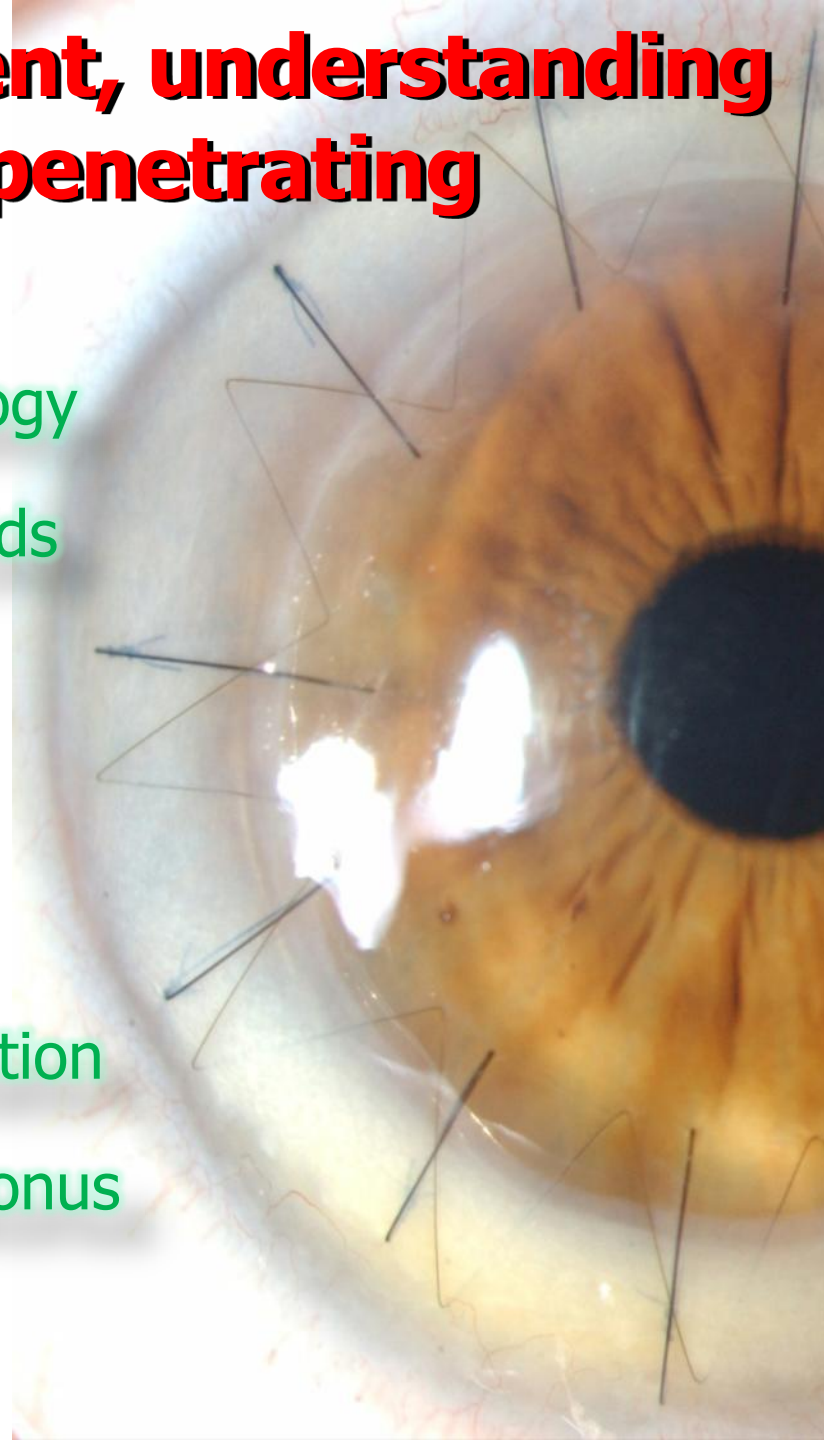


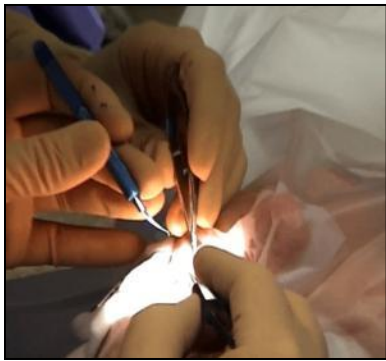
Transplantation in NZ



1950 - 2000: Refinement, understanding and the golden age of penetrating keratoplasty

- Better understanding of immunology
- Topical and systemic corticosteroids
- Topical antibiotics
- Surgical microscopes
- Emergence of eye banks
- Nylon sutures & finer instrumentation
- 95% ten-year success in keratoconus

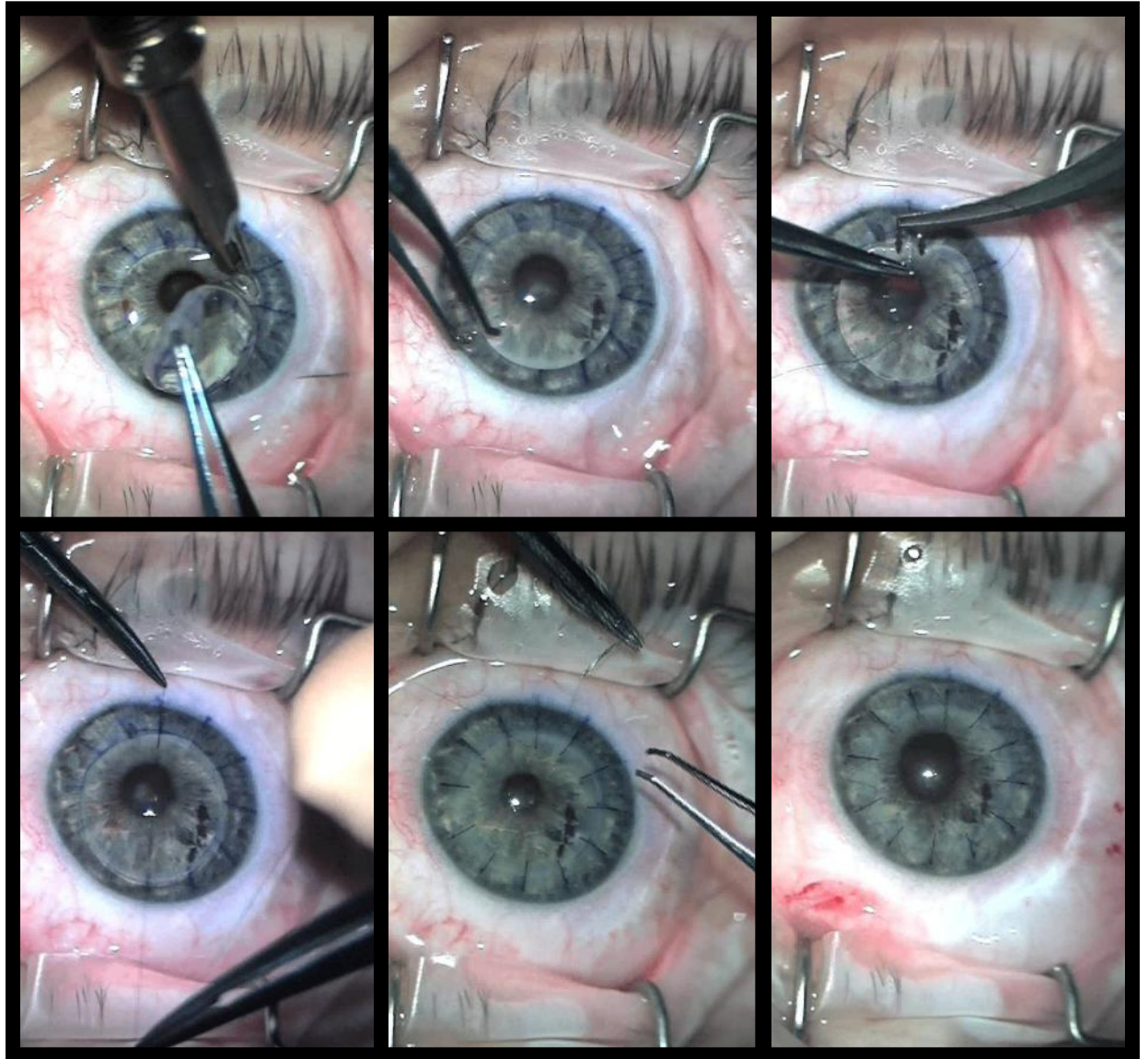




P

K

P



Penetrating keratoplasty (PKP)

Standard post op management

- Regular ophthalmic reviews
- G Antibiotic for 3-4 weeks
- G Predforte for 6-12 months

Complications

- Risk of steroid elevated IOP
- Typically 1-2 sutures will loosen
- All sutures removed at 15-18 months
- Corneal graft rejection

Acute rejection

Red eye

Photophobia

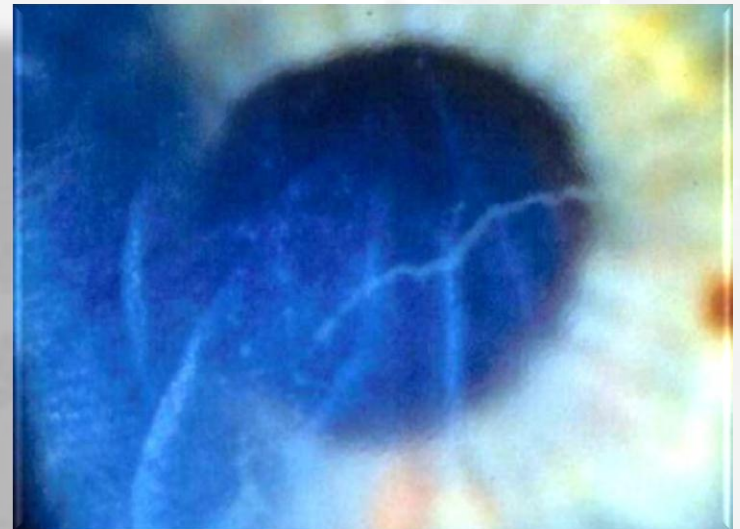
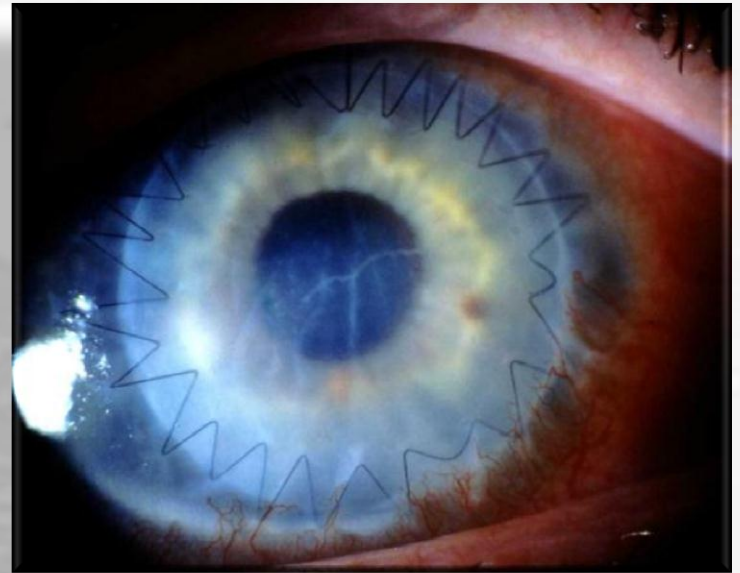
Decreased vision

**A “standard”
rejection strategy**

Intensive hourly g Predforte 1%
and/or

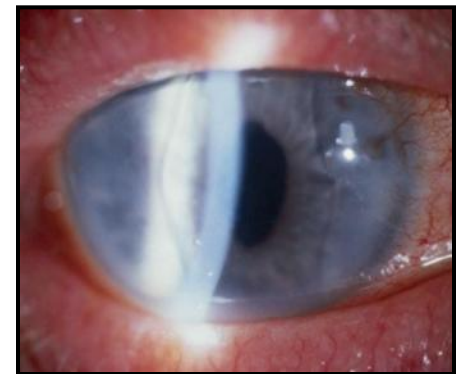
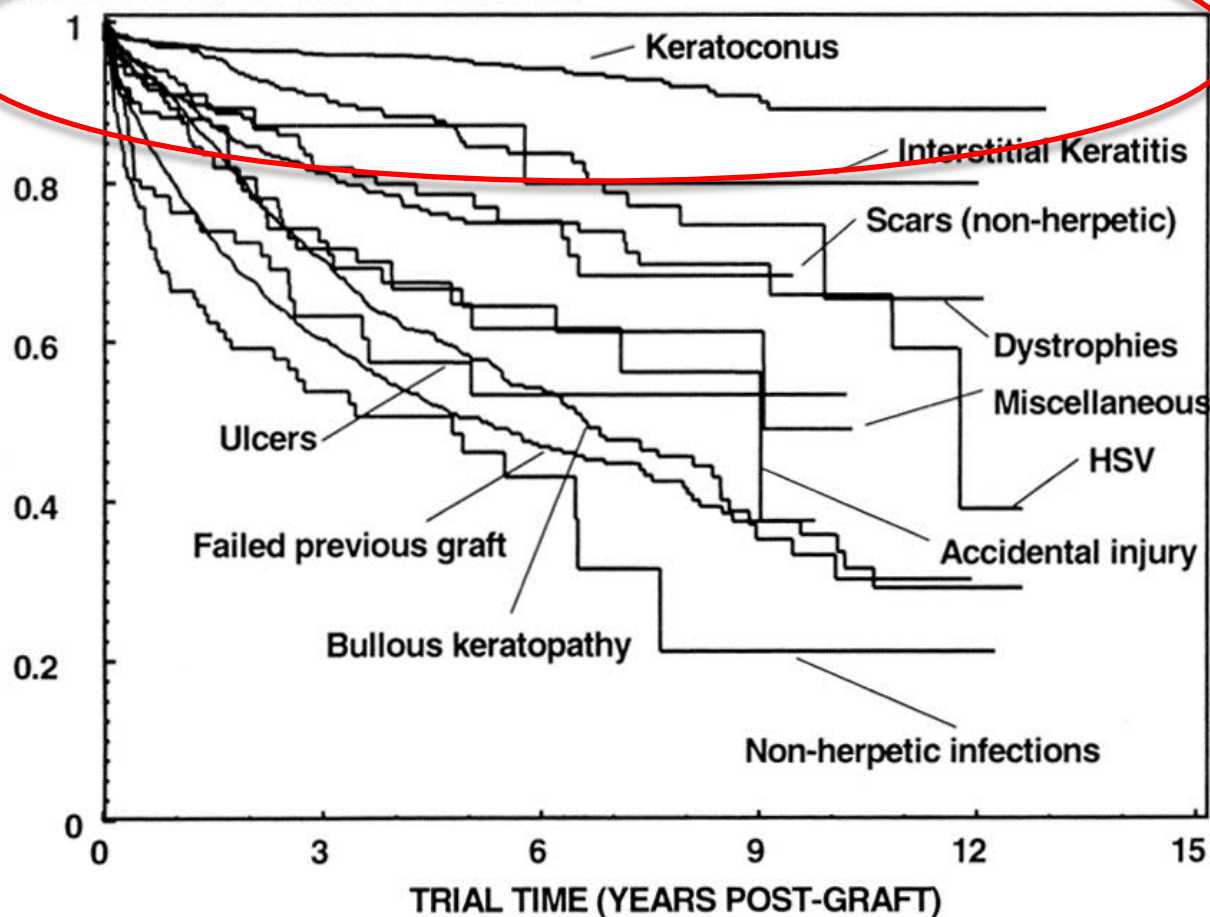
IV Methyl-prednisolone: 3-5mg/Kg

Oral Prednisolone : 1-1.5mg/Kg



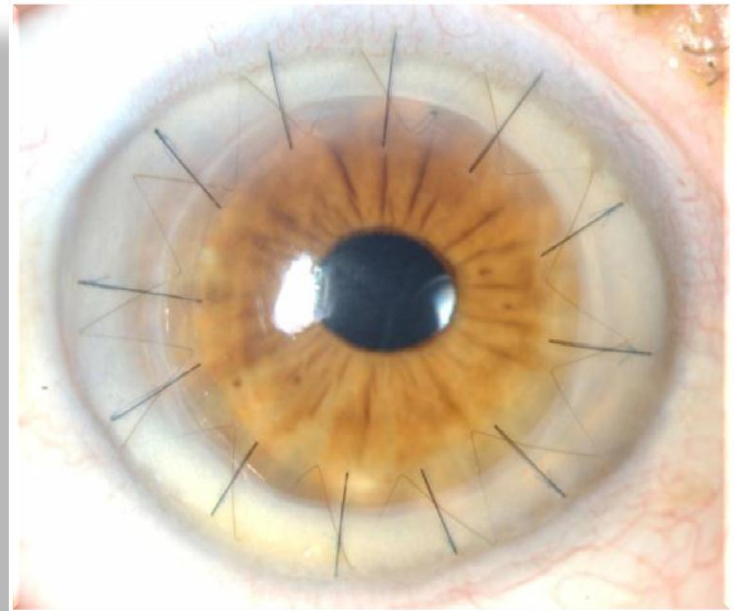
Australian Corneal Graft Register: Probability of Graft Survival

PROBABILITY OF GRAFT SURVIVAL



Global Changes in pattern of corneal transplantation

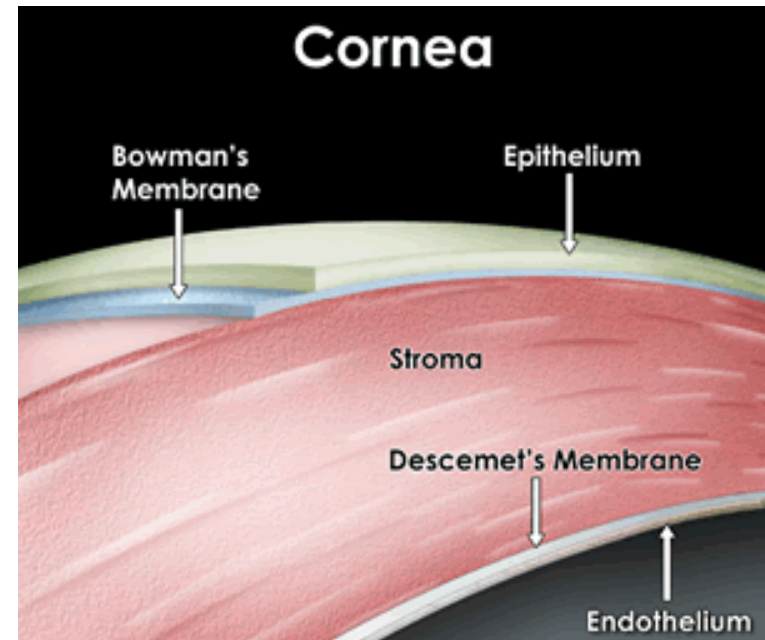
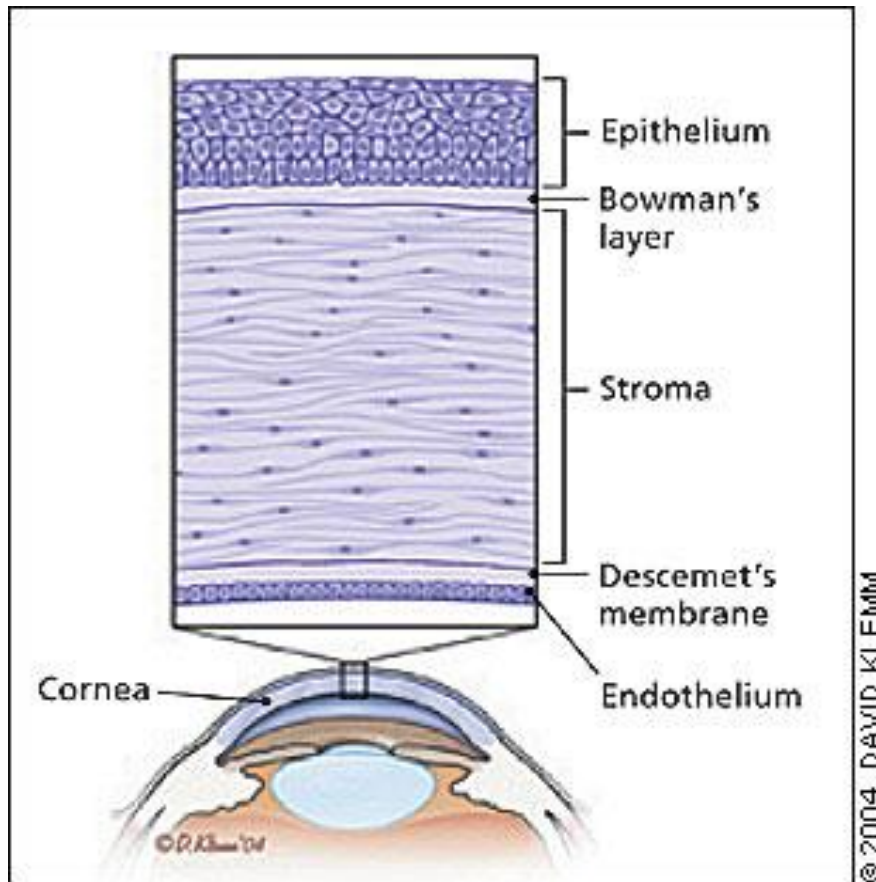
- **Established technique – PKP**
95% success in keratoconus
- **Alternatives to PKP**
 - Anterior lamellar approaches
 - Posterior lamellar approaches
- **Laboratory approaches**
 - Cellular approaches*



Anterior Lamellar Corneal Transplantation Techniques in 2012



Cornea Anatomy 101



Anterior (60%) lamellar keratoplasty: avoiding endothelial rejection

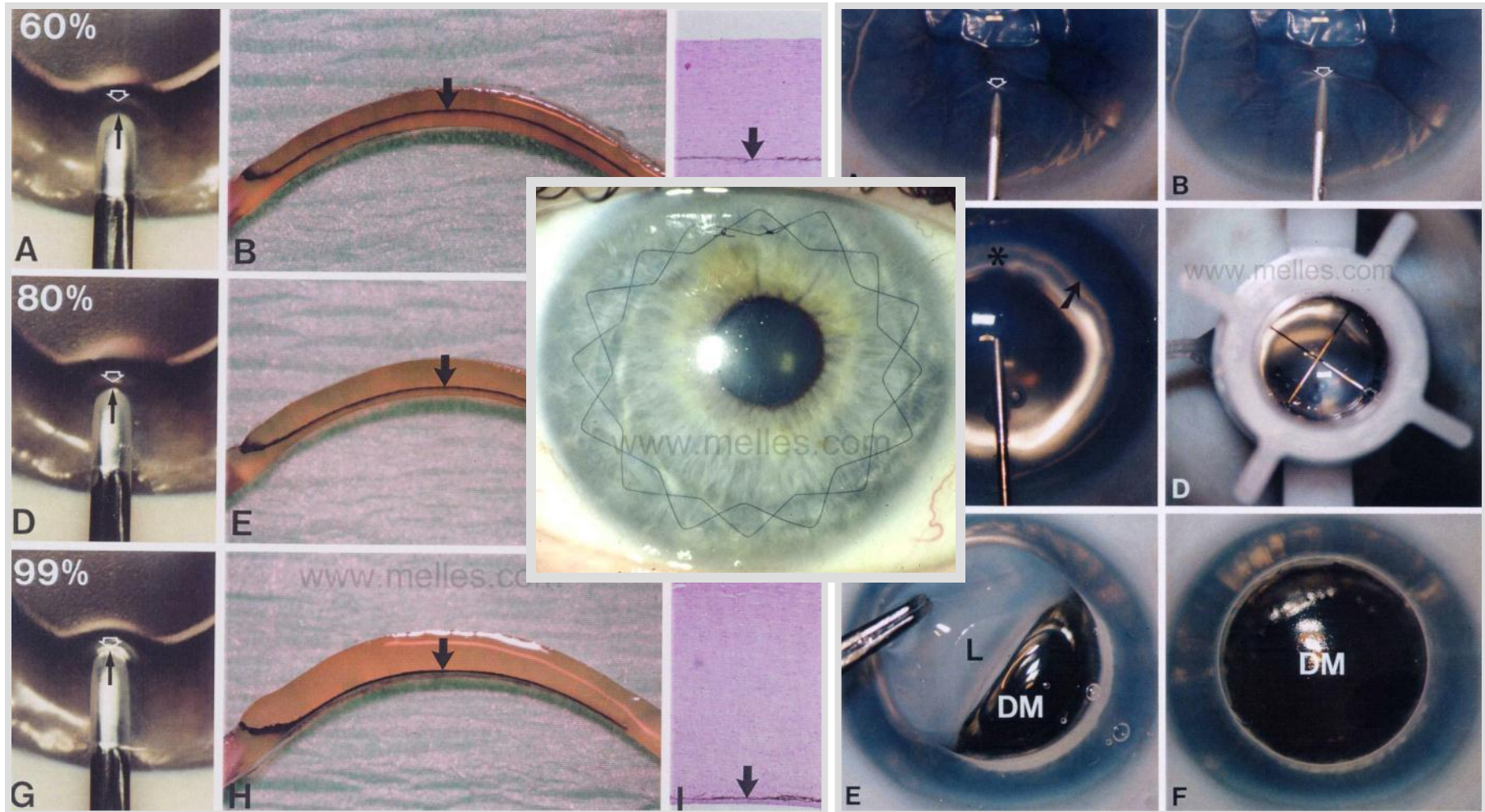


Pre-op irregular HSV scarring 6/36



Lamellar keratoplasty 6/9 BSCVA

DALK: www.melles.com



Anterior and deep anterior lamellar keratoplasty (ALK/DALK)

Traditional Lamellar keratoplasty

Plane typically 50-70% depth
Manual dissection

Deep Anterior Lamellar Keratoplasty

Aims for 90% of stromal depth
Melles direct visualisation technique
Big bubble technique
Hydro/visco dissection techniques



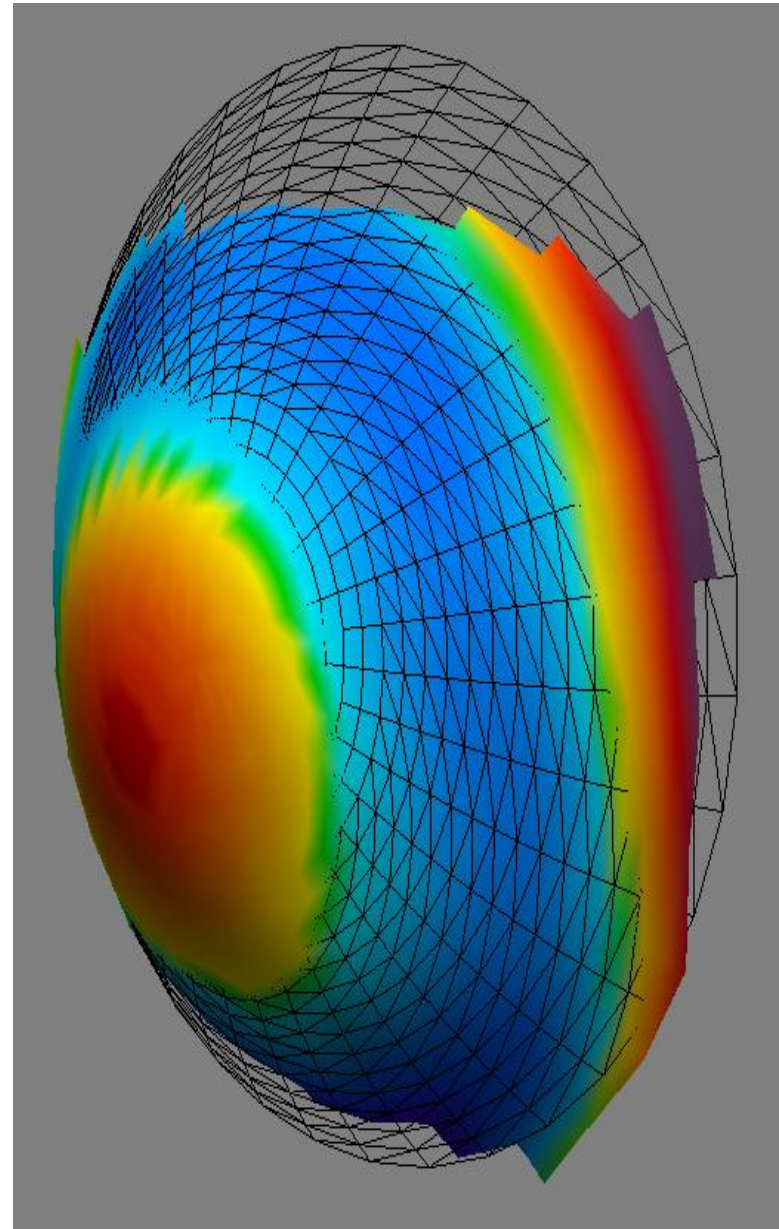
DALK: Indications

Predominantly Anterior Disease

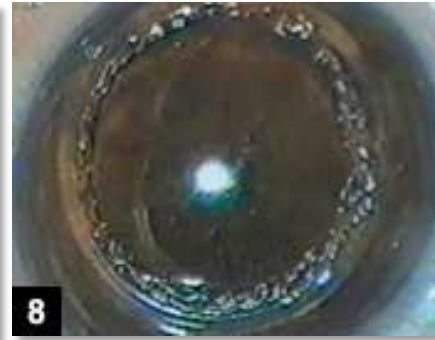
- Scars
- Anterior Stromal Dystrophies
- Stromal Dystrophies

Corneal ectasia

- Keratoconus

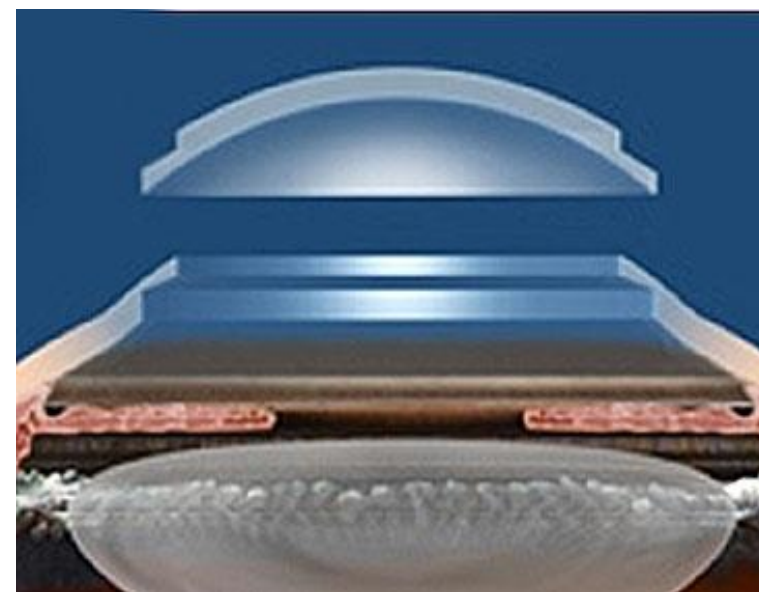
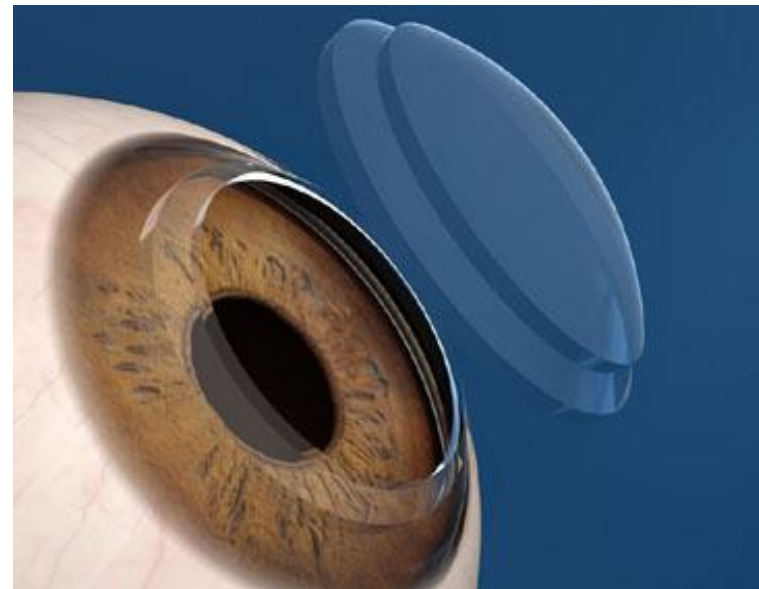
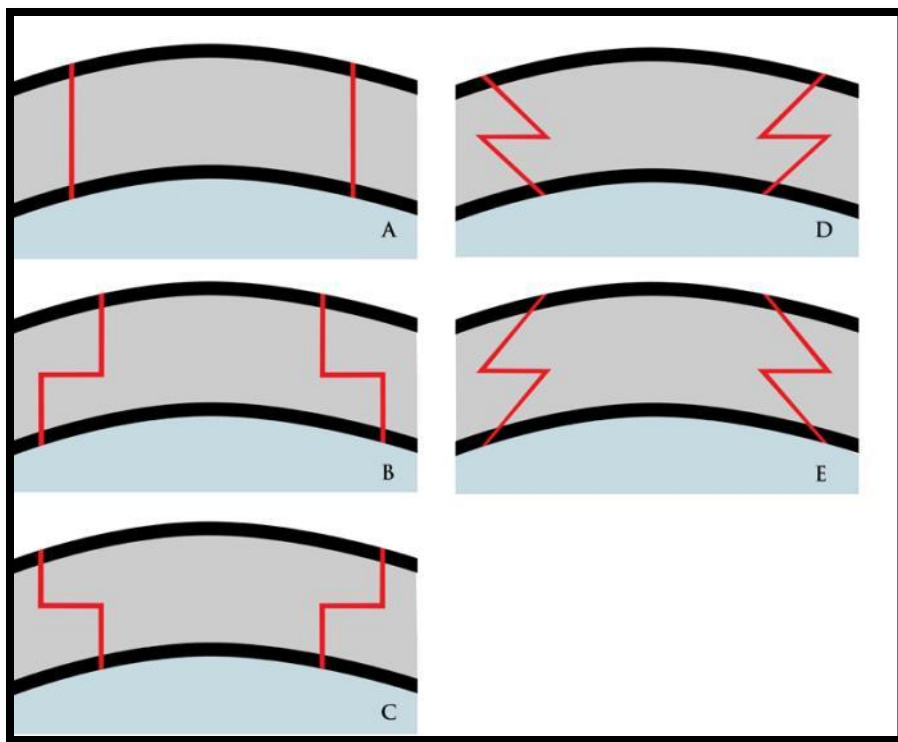


DALK: Big bubble technique



courtesy Dr J Thomas MD

“New Kid on the block” Femtosecond laser techniques



DALK: Femtosecond laser technique

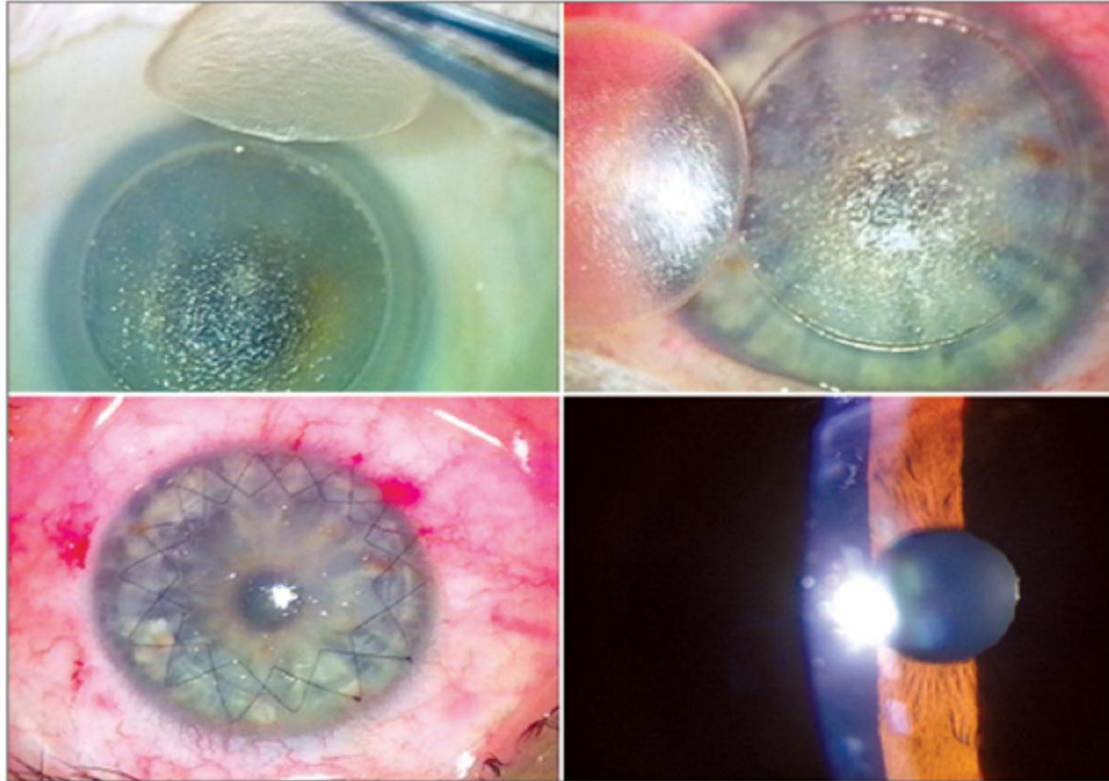
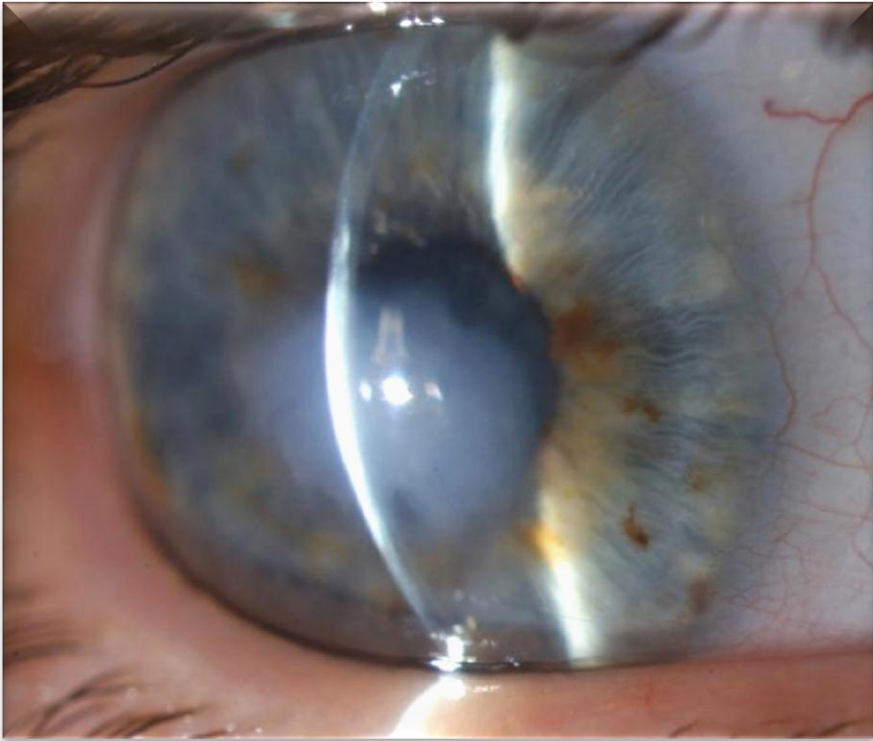


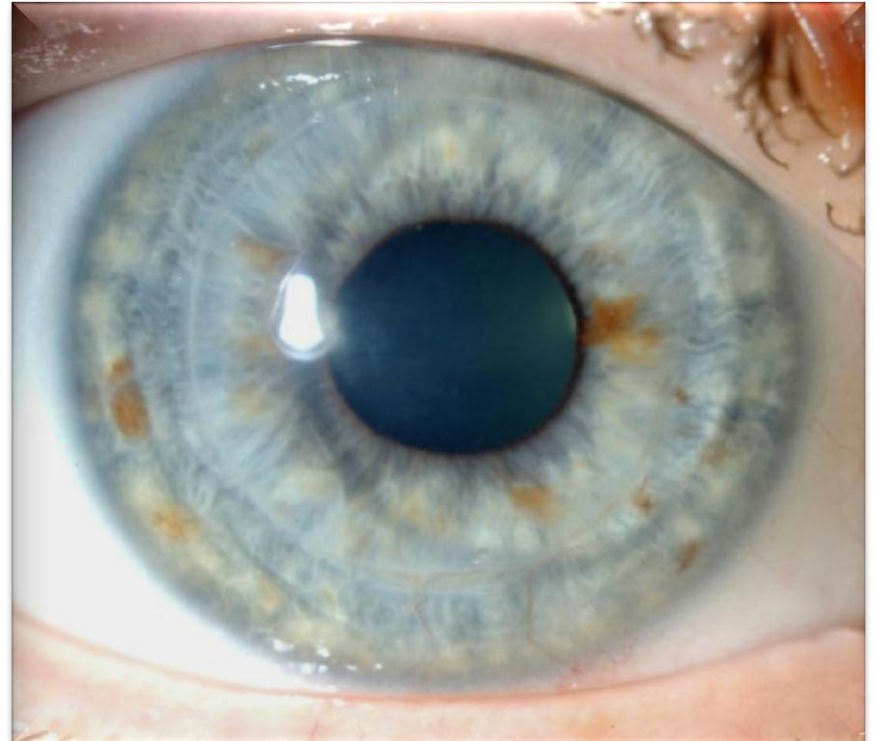
Figure 2 - Femtosecond-assisted anterior LKP. Top left. Anterior corneal cap removed from donor whole globe, showing smooth stromal surface. Top right. Anterior corneal cap excised from host eye, showing smoothness of deep lamellar bed. Bottom left. Donor graft secured to recipient bed with double-running sutures. Bottom right. Postoperative slit-lamp biomicroscopic appearance of anterior LKP at 3 months.

[illegible]

A DECADE OF Deep Anterior Lamellar keratoplasty (DALK): contact lens related pseudomonas keratitis



Pre-op irregular dense scar 3/60



18 months post DALK 6/6 BSCVA

Deep Anterior Lamellar Keratoplasty

- A useful alternative to PKP
- Particularly for keratoconus
- Technically demanding/evolving
 - Melles / big bubble / femtosecond

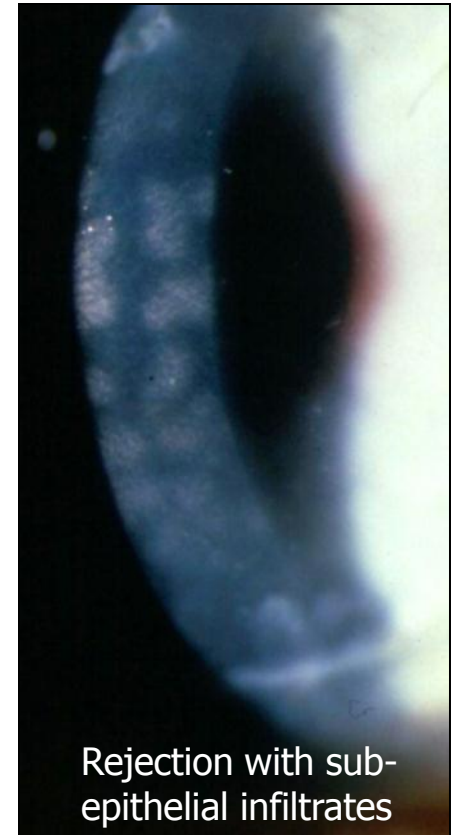
- **Major advantages**

Easier/shorter follow-up

Shorter steroid Rx

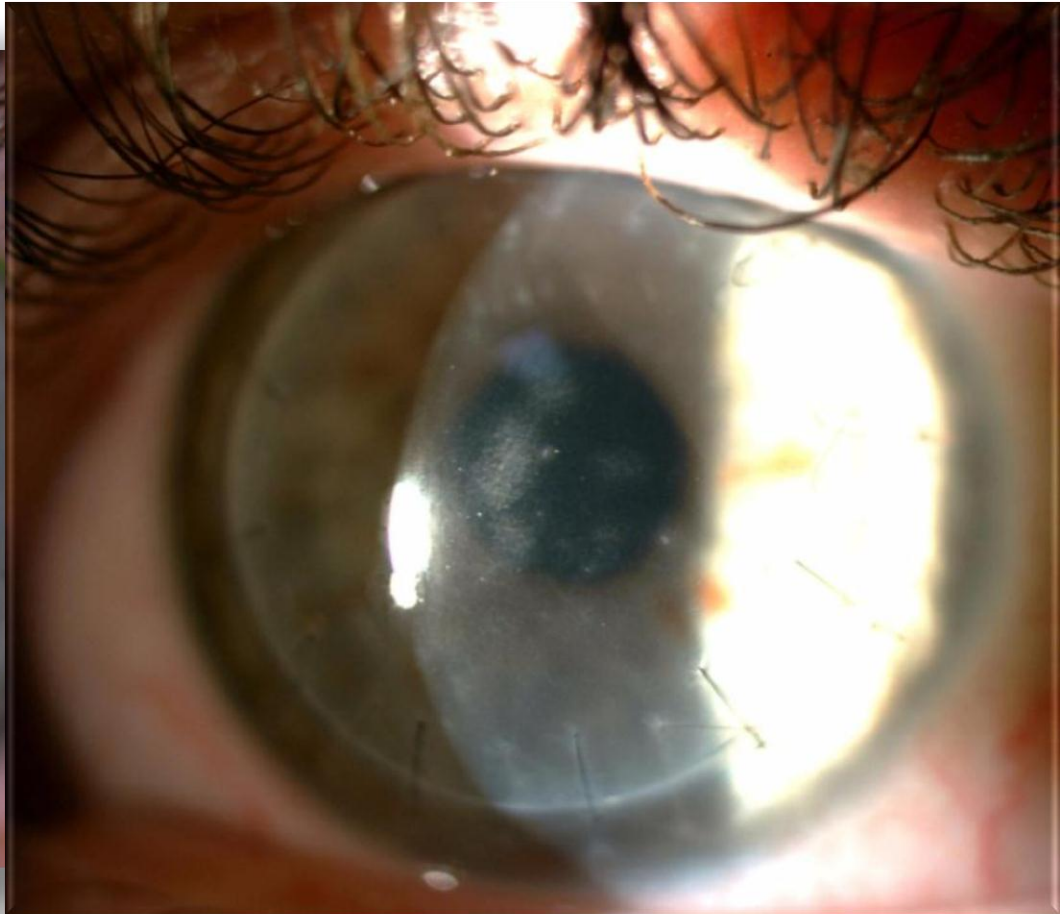
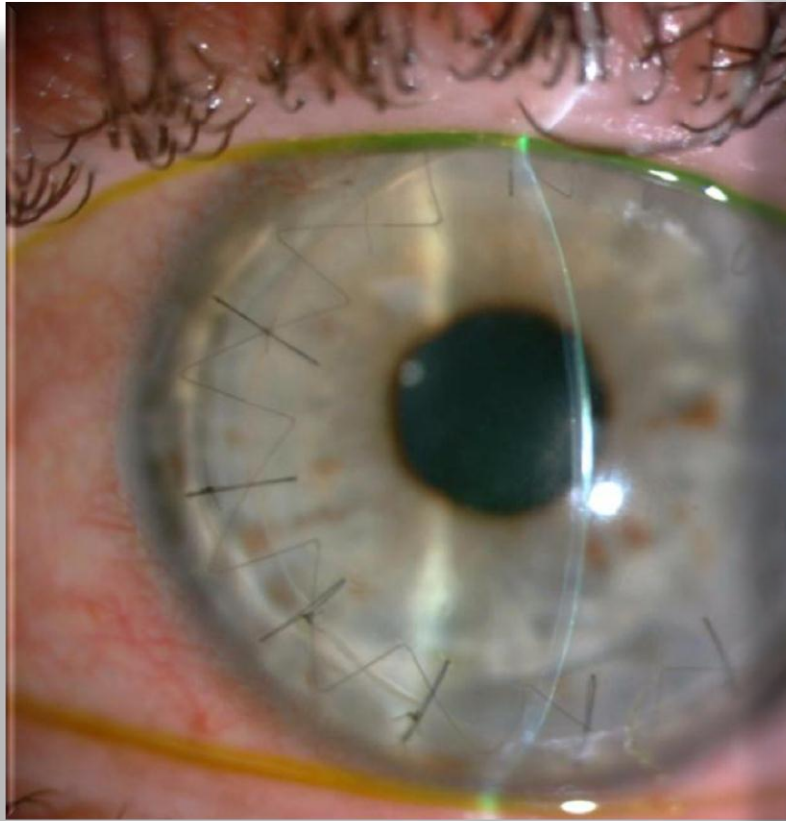
Endothelial preservation

No endothelial rejection



Rejection with sub-epithelial infiltrates

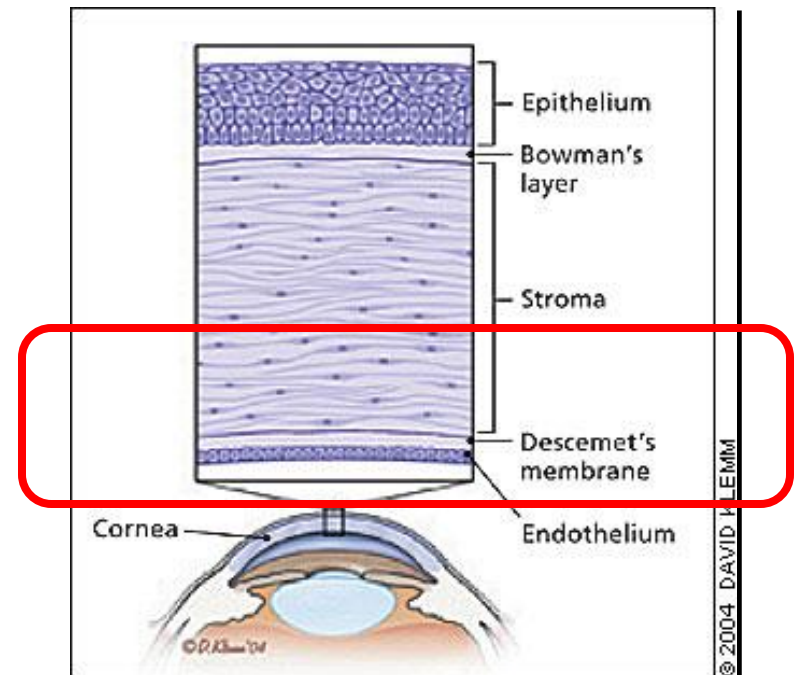
Differing presentation of acute rejection in DALK



If it looks like adenovirus restricted to the graft think rejection



EVOLUTION from penetrating to Endothelial corneal transplants:



Endothelial keratoplasty

Potential Benefits

More rapid recovery

Structural integrity

No suture related problems

Minimal astigmatism

Minor refractive shifts



The newest kid on the block

Endothelial keratoplasty

DSEK: Descemet's Stripping Endothelial Keratoplasty

DSAEK: Descemet's Automated Stripping Endothelial Keratoplasty

DMEK: Descemet's Membrane Endothelial Keratoplasty

EK/EG: *Endothelial Keratoplasty/Graft*

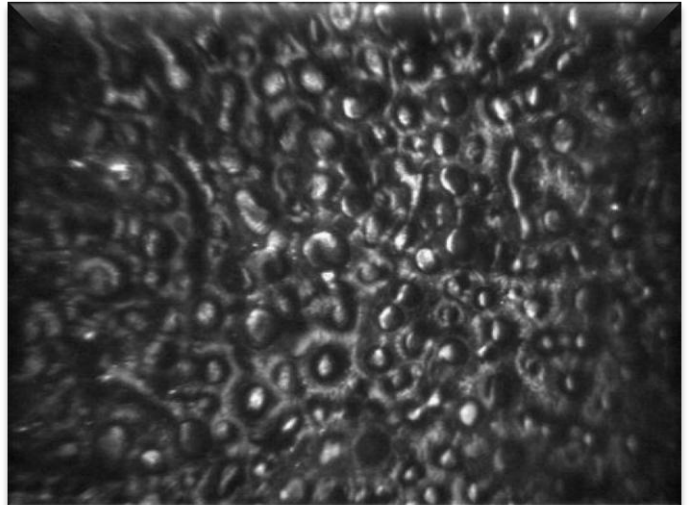
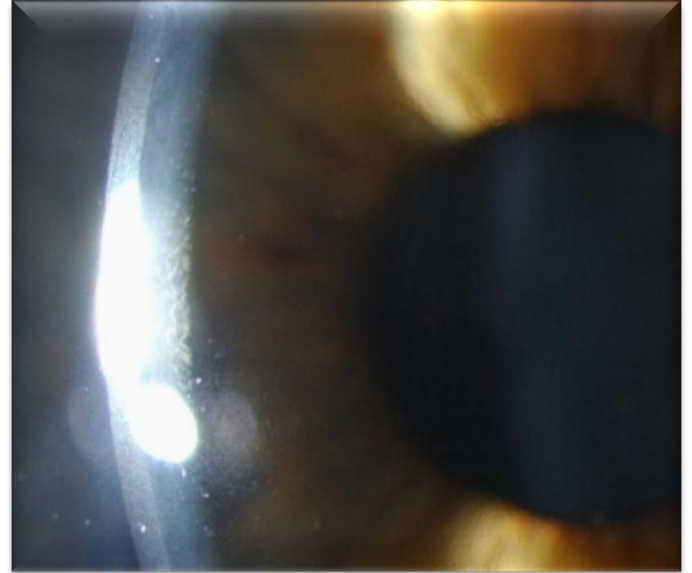
Endothelial keratoplasty: indications

Primary and secondary endothelial failure

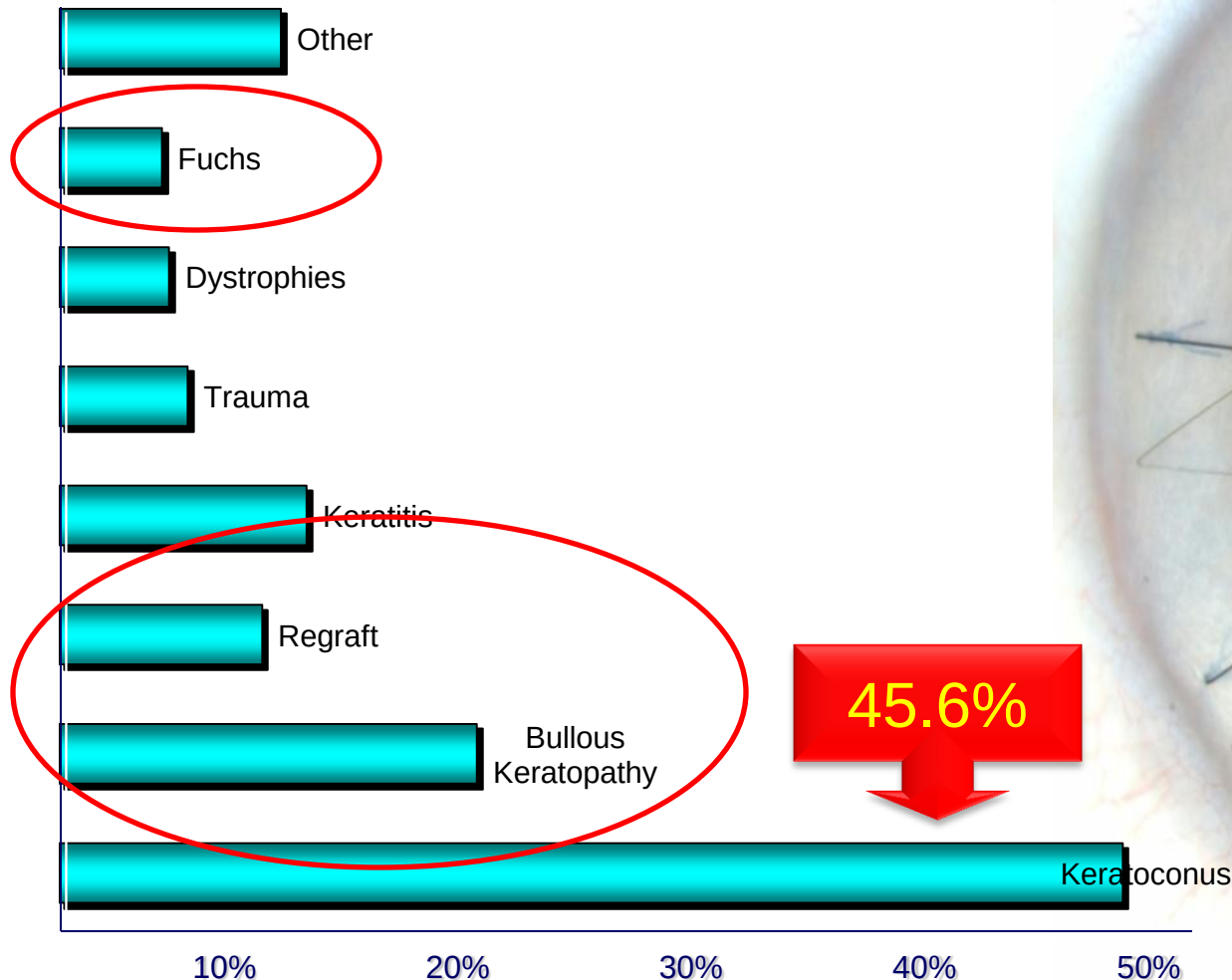
Fuchs endothelial corneal dystrophy

Pseudophakic Bullous Keratopathy

Repeat corneal graft for endothelial failure

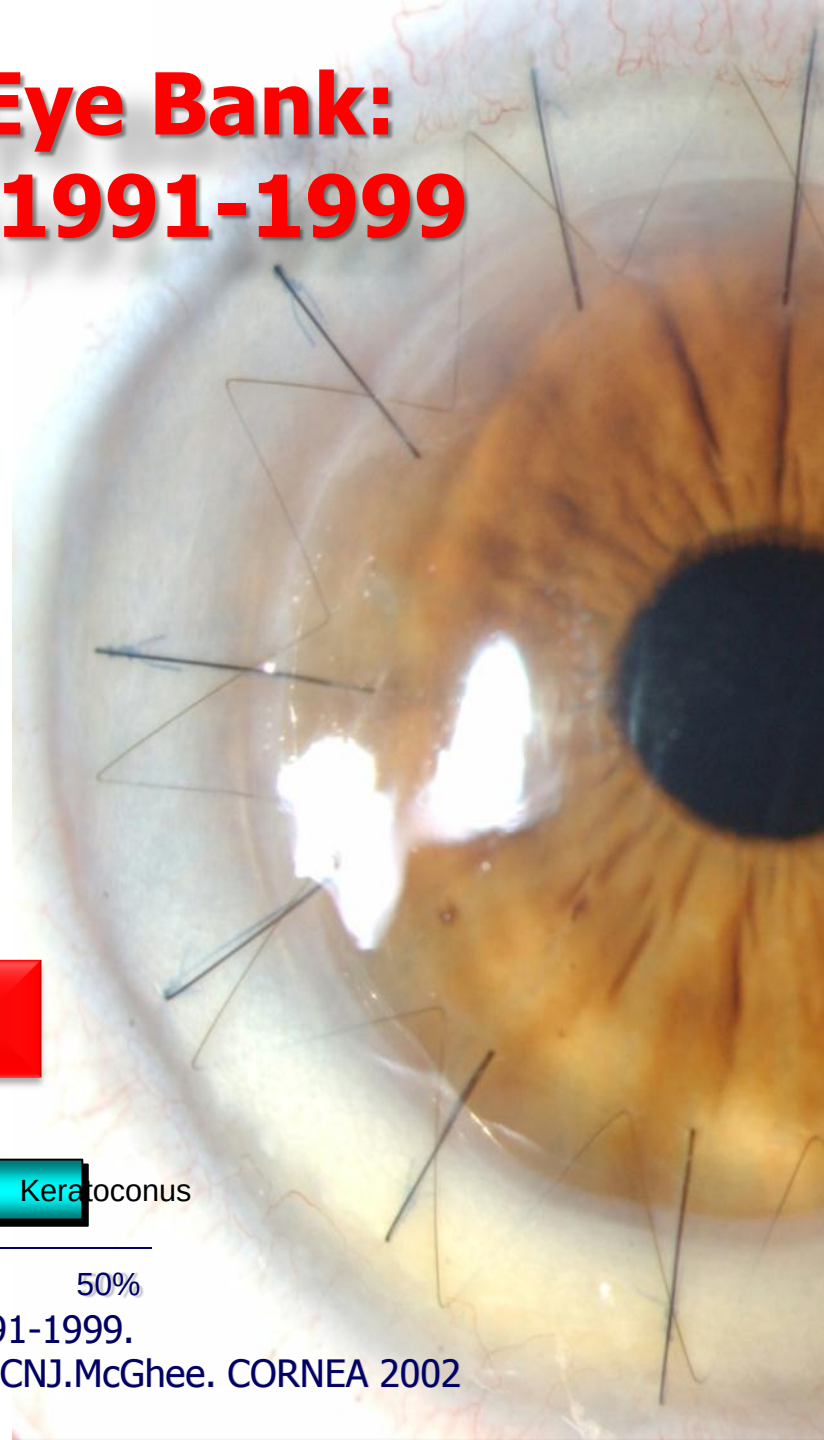


New Zealand National Eye Bank: Transplant Indications 1991-1999



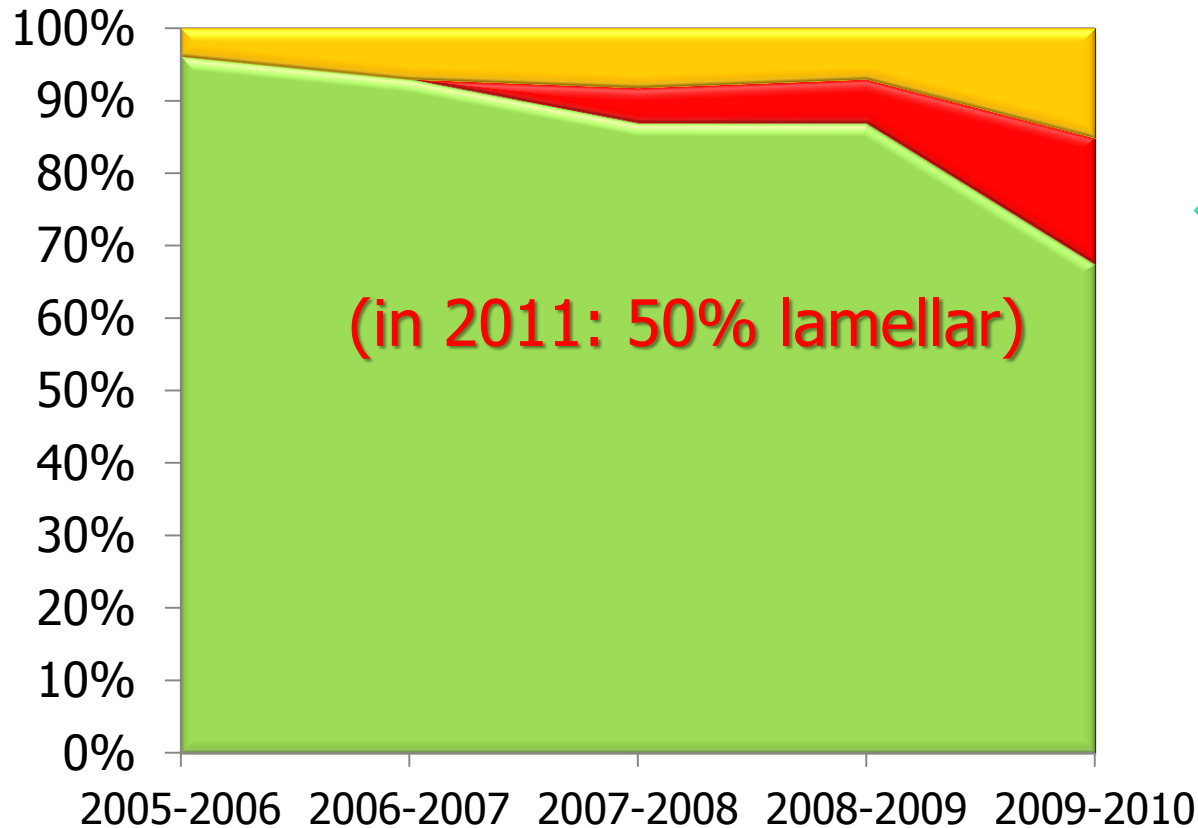
Indications for Corneal Transplantation in New Zealand: 1991-1999.

M.Edwards, GM.Clover, N Brookes, D.Pendergrast, J.Chaulk, CNJ.McGhee. CORNEA 2002



NZNEB keratoplasty type as % of total

Trends 2005-2010 (2011 = 50% lamellar)



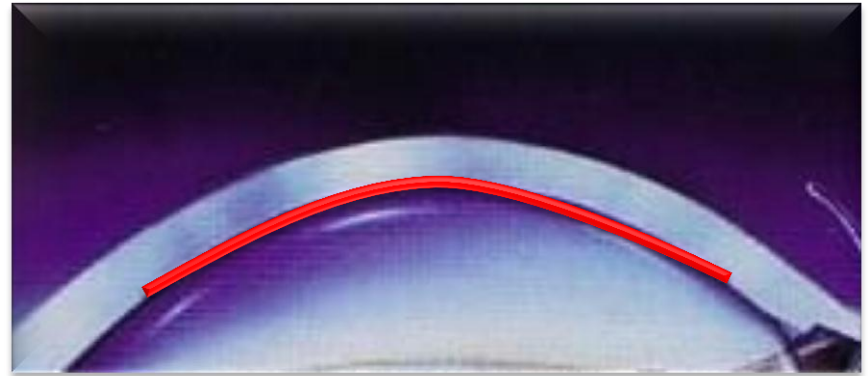
← 32%

- Procedure - LK
- Procedure - EK
- Procedure - PK

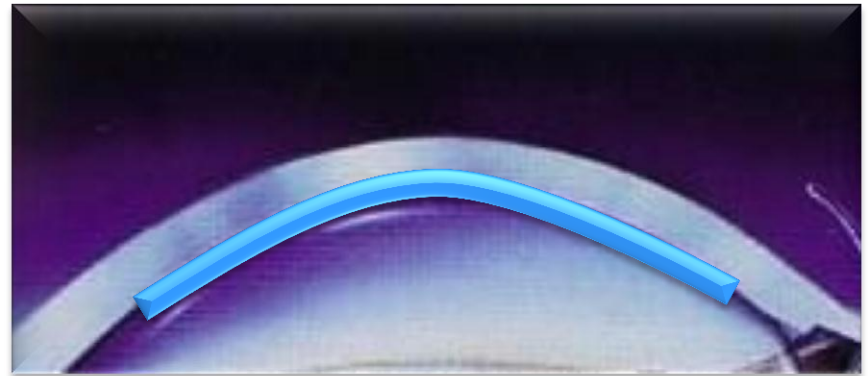
Endothelial keratoplasty

the no stitch, small incision, essentials

Removal of "sick"
Descemet's and
endothelium by
Descemetorhexis



Insertion of donor
lenticule with stroma,
Descemet's and
endothelium

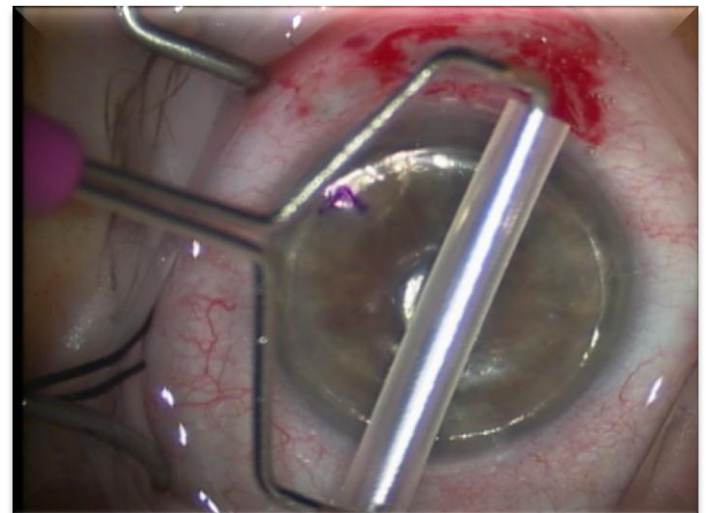
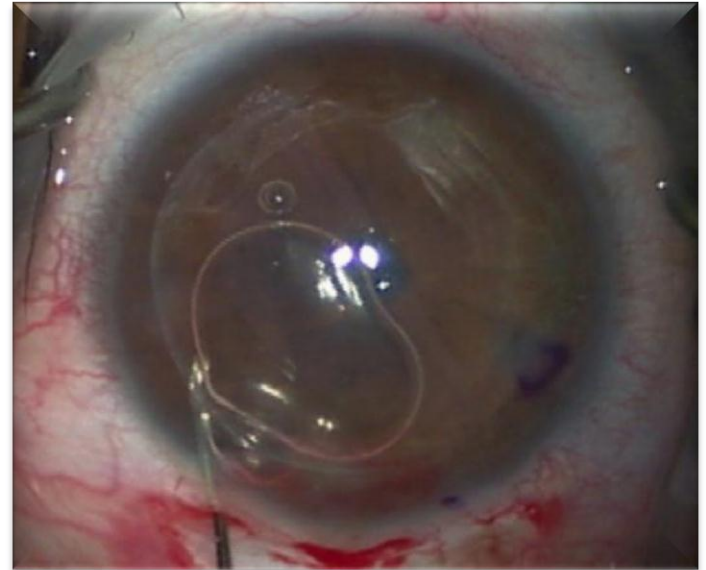


Why does the EK stick there?

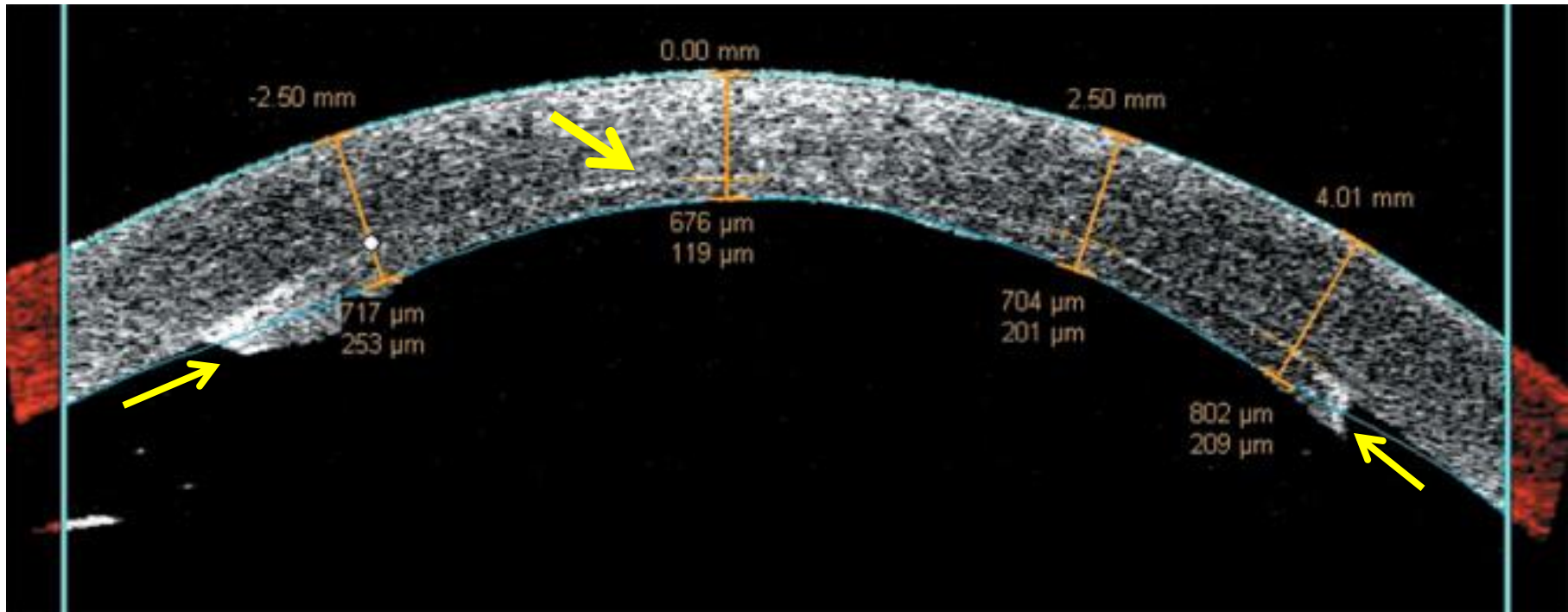
Immediate stability of graft probably due to inherent adhesiveness of bare stromal surfaces

Endothelial pump

Air/intraocular pressure

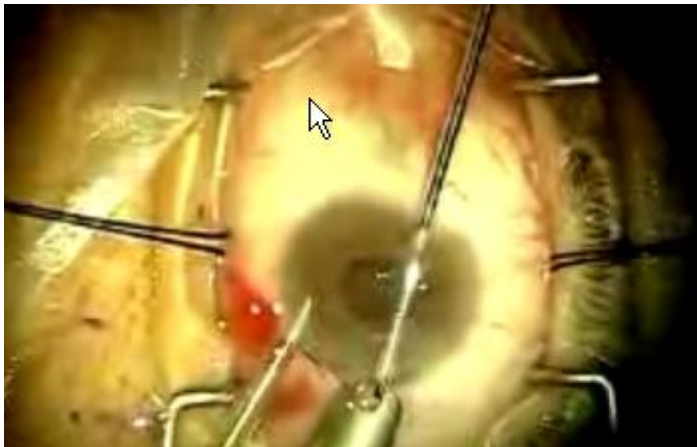


OCT of Endothelial Keratoplasty

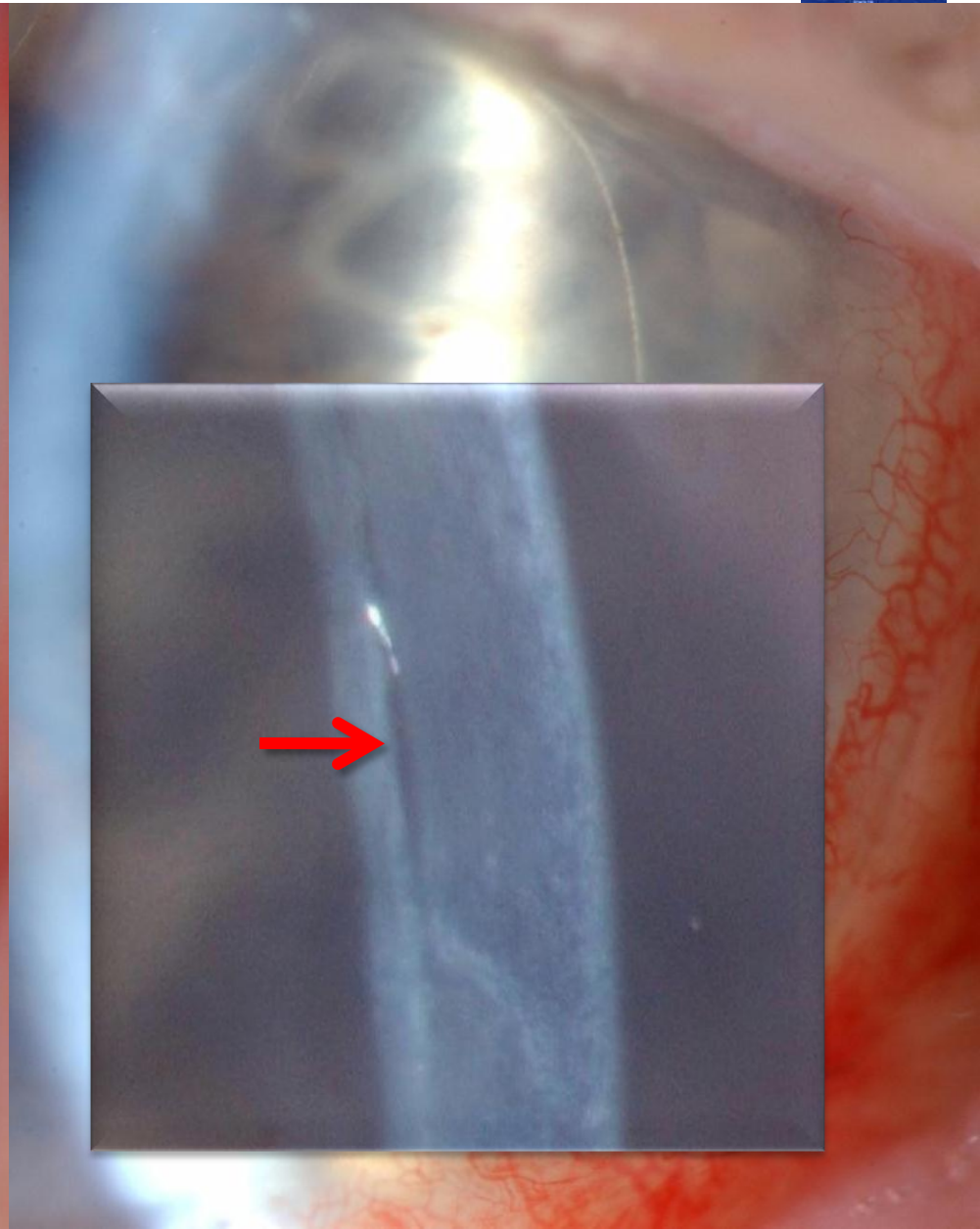
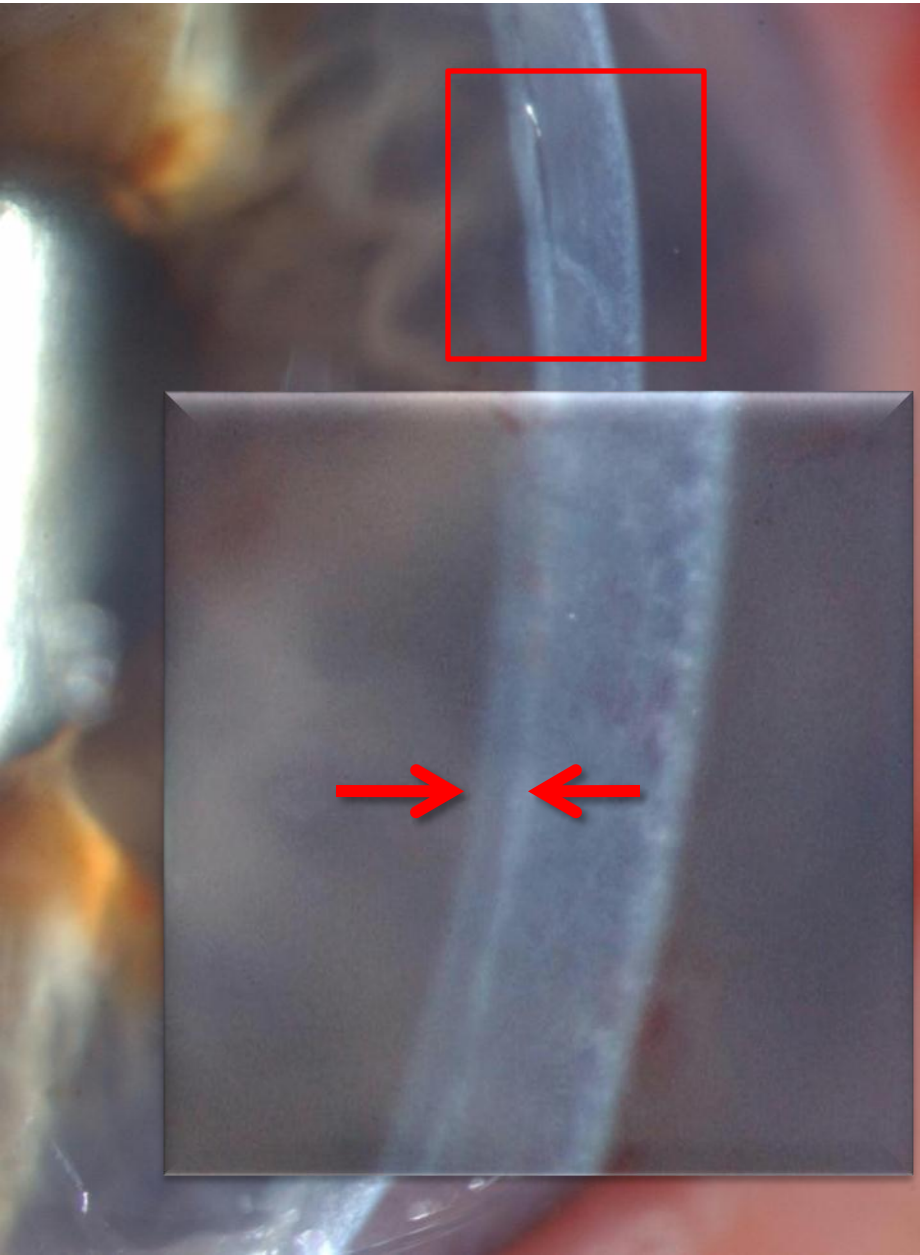


- Prepared by DSAEK method – thicker peripherally
- Overall corneal thickness 676 – 717 microns (cornea clear)
- Donor lenticule 119 μm centrally, 253 μm peripherally

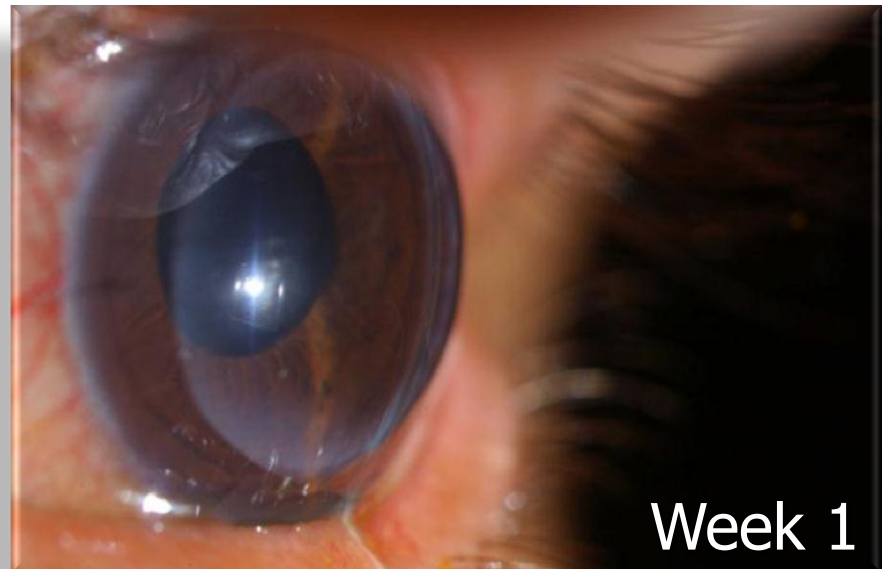
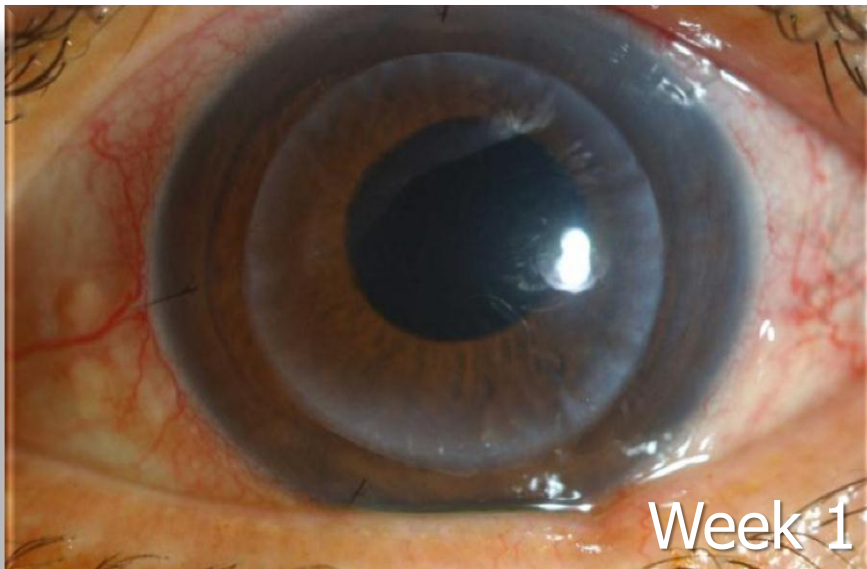
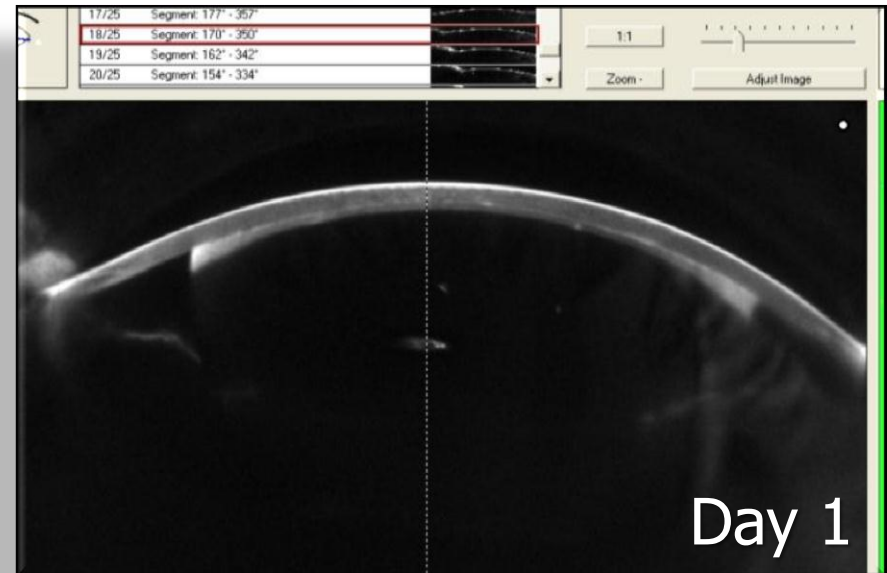
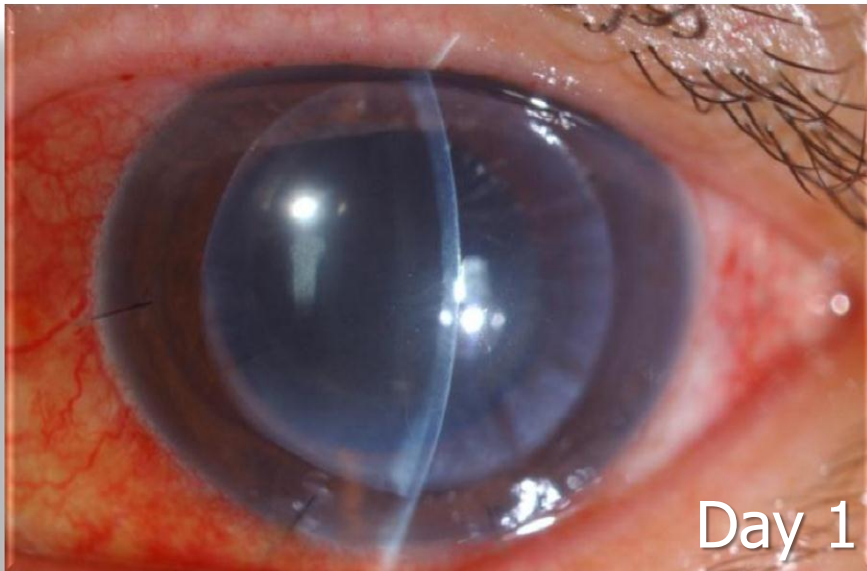
NZ EK techniques evolving



DSAEK day 1 post op

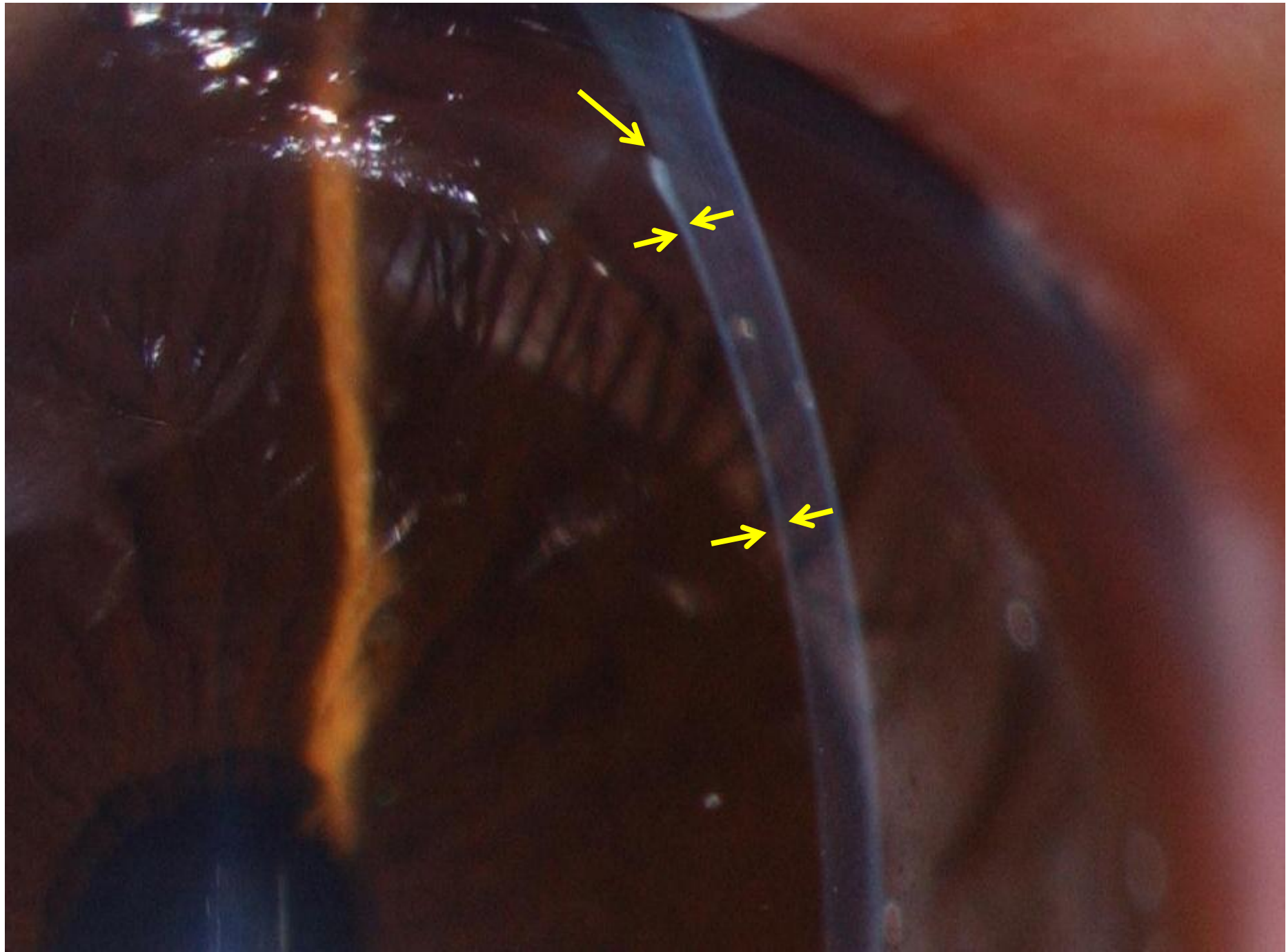


DSEK for Fuchs endothelial corneal dystrophy (OD)



DSEK @ 1 week, Fuchs Endothelial Corneal Dystrophy





Post-operative management

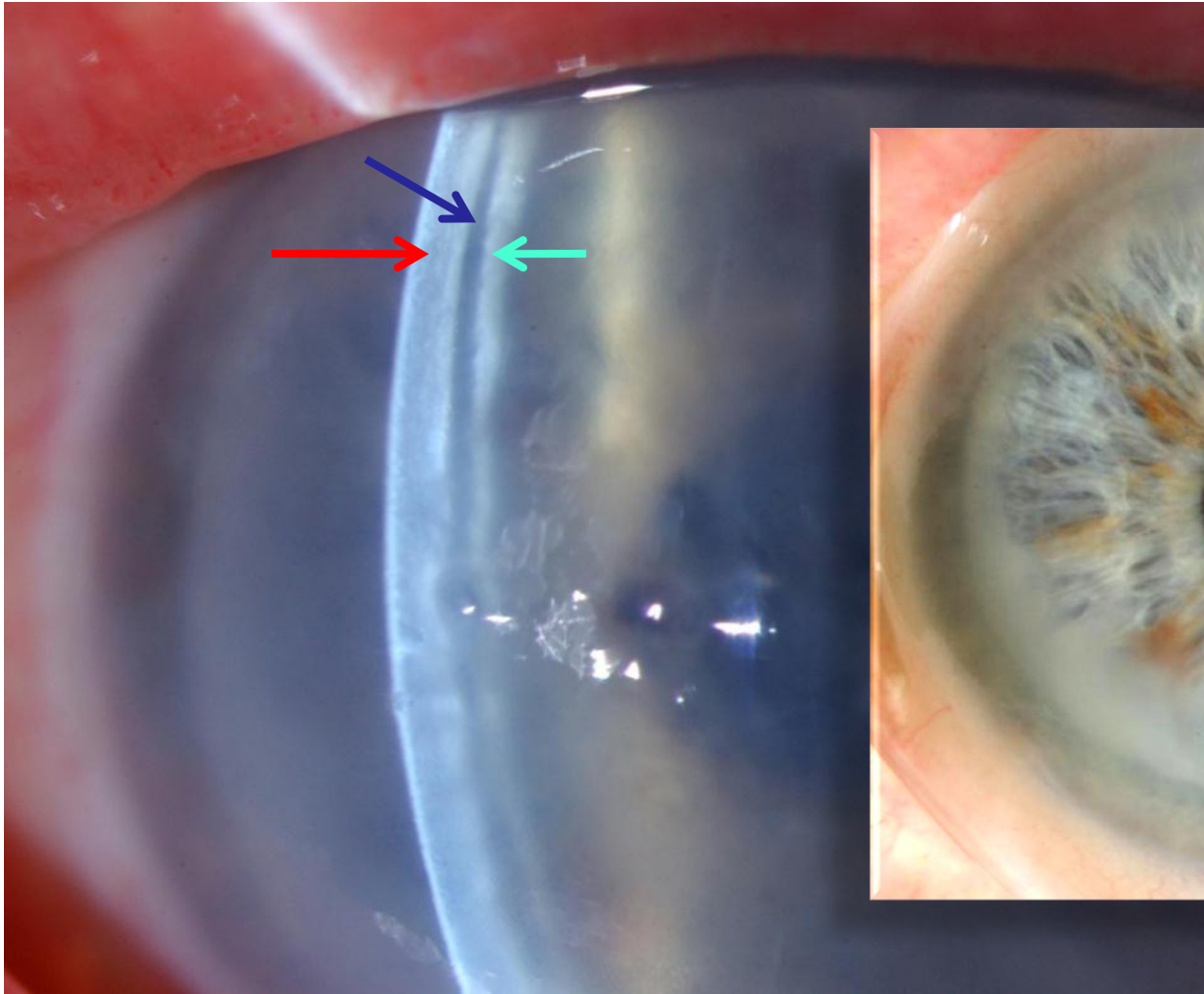
- **Antibiotic cover for 3-4 weeks**
 - G. Chloramphenicol QDS
 - G. Ciprofloxacin TDS
- **Topical corticosteroids for 6 -12 months**
 - G. Predforte QDS
 - G. Maxidex QDS

Post-operative management

Medium and longer term management issues

- Risk of graft displacement first 2 weeks
- Total duration of corticosteroid uncertain
- Possible steroid related IOP elevation
- Endothelial graft rejection
- Risk of progressive ECC loss & recurrent oedema

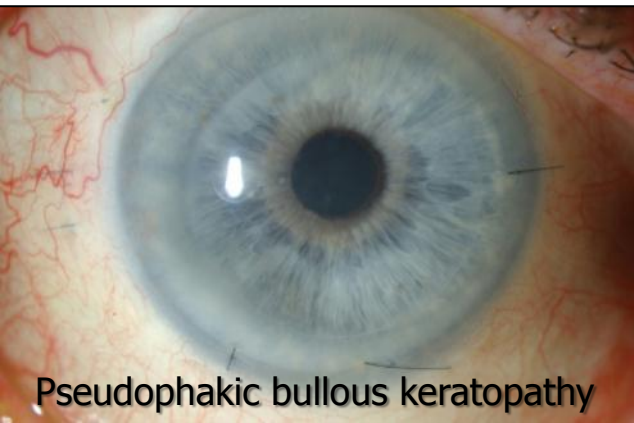
Button dislocation & rebubble



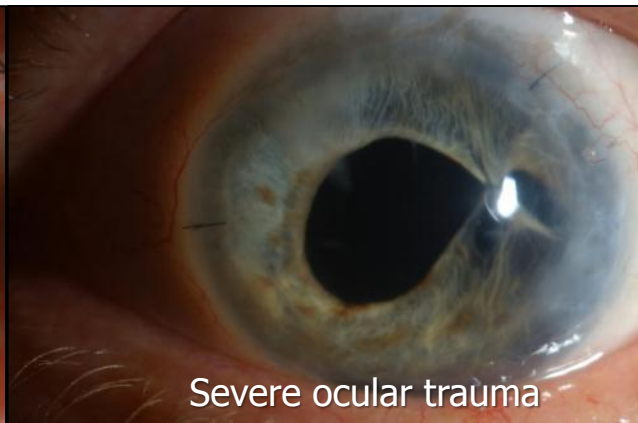
DSEK: learning curve complications 1

66 eyes of 62 patients

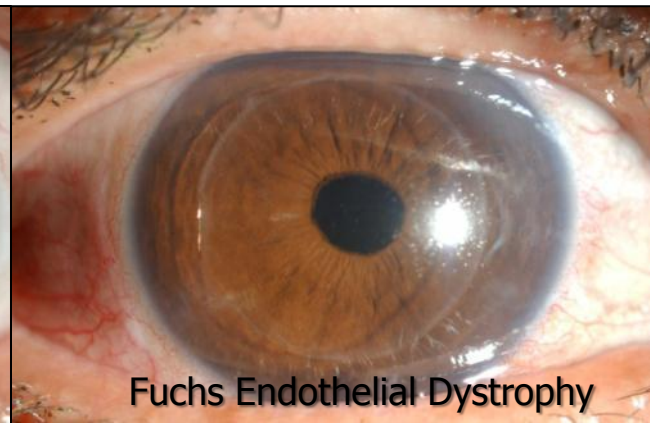
- 88% DSEKs clear at latest review (2 – 24 months)
- Of those with good potential BSCVA* >90% within 1 line
- Majority $\geq 6/12^*$, a few reached 6/6, $\sim +1.0D$ shift
- 2 raised IOP, 1 rejection, 1 mod. Uveitis, 3 post synechiae



Pseudophakic bullous keratopathy



Severe ocular trauma



Fuchs Endothelial Dystrophy

DSEK: learning curve complications 2

Displaced or intralamellar fluid 11%

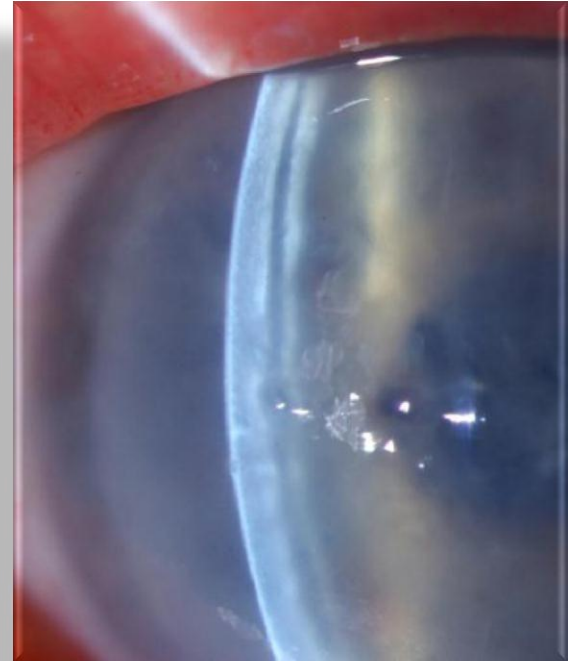
4 displaced buttons – re-bubbled*

3 persisting retained fluid - re-bubbled

Overall DSEK failure rate 9%

2 primary failures and PKP

4 repeat DSEK at 9 - 18 months



DSEK: 5 year outcomes

- DSEK or DSAEK – 165 eyes of 149 subjects
- Median age 71 (22-90), 147 Fuchs eyes
- **Survival of transplant**
 - Fuchs 95%
 - PBK/ABK 76%
 - Trab/shunt 40%
- Endothelial cell loss – mean 53%

Indications PKP, DALK or DSAEK?

Penetrating Keratoplasty

Keratoconus, trauma, full thickness scars

DALK

Keratoconus, anterior corneal scars

DSAEK

Endothelial failure, Fuchs, pseudophakic bullous keratopathy, repeat grafts



CORNEAL DONOR CRITERIA

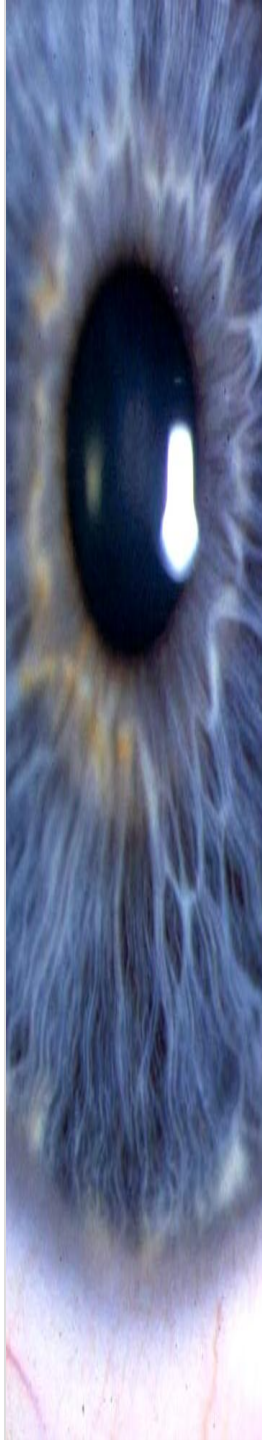
Age: 10 - 85 years, storage within 24 hours

Generally suitable:

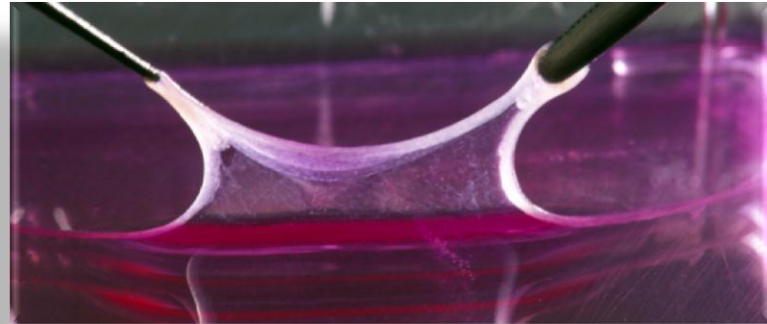
- Cancers
- Heart disease, respiratory disease
- Diabetes, arthritis
- Vision problems (glasses, contacts) & intraocular surgery

Medical contraindications:

- Death of unknown cause
- Infectious disease: - Hepatitis B,C, HIV, meningitis
- Systemic viral or fungal infection (bacterial ok)
- CNS diseases, progressive dementia
- Leukaemia, lymphoma
- Previous corneal surgery, laser vision correction
- Various congenital disorders



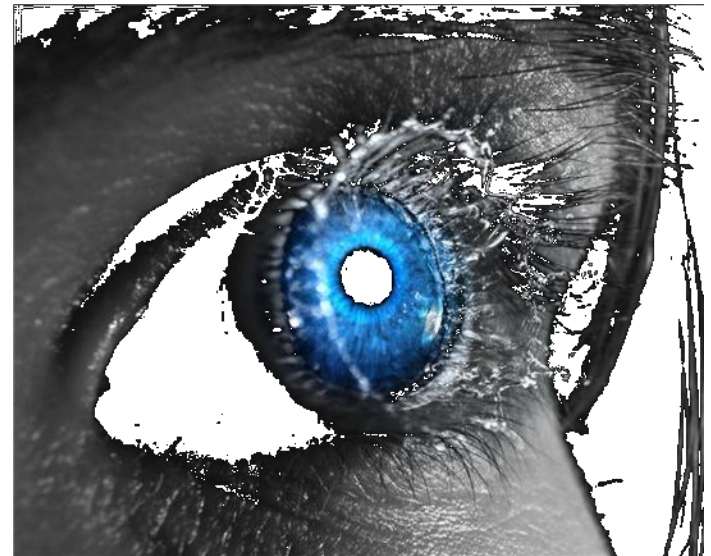
A VINTNER'S TALE: STEM CELLS AND PROLONGED REHABILITATION OF THE EXTERNAL EYE AFTER SEVERE CHEMICAL BURN



INITIAL PRESENTATION (2008)



- ◉ 42 year old male
- ◉ Vineyard worker in Australia
- ◉ Cleaning wine barrels.
Sodium hydroxide OU



LIMITED PROGRESS on standard Rx

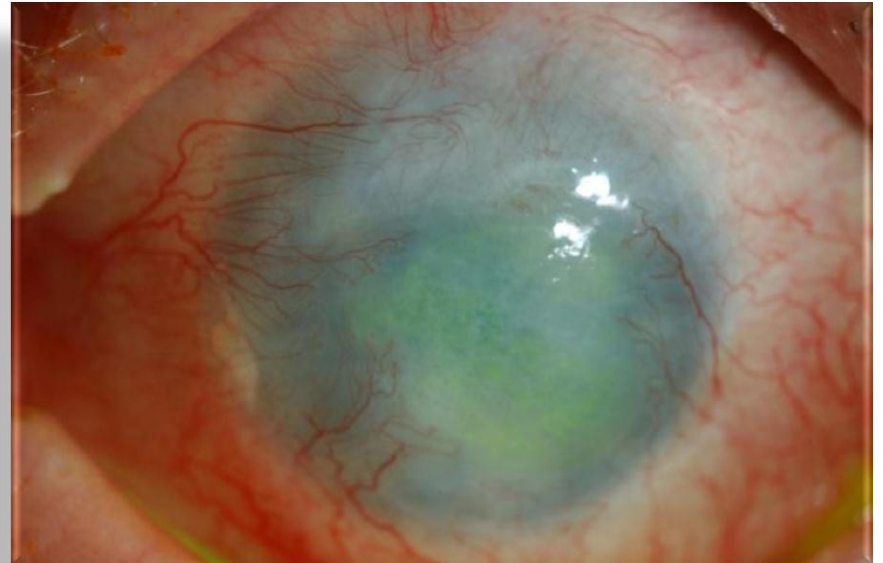
Transferred from
NSW to Auckland
on day 23

Slow recovery -
remained as an
inpatient at GLCC
corneal opaque and
heavily scarred at
day 55!



PROGRESS day 264 – a blind eye!

- Relative stability! No change in vision – only counting fingers
- Epithelium irregular with conjunctival overgrowth
- Considerable neovascularisation

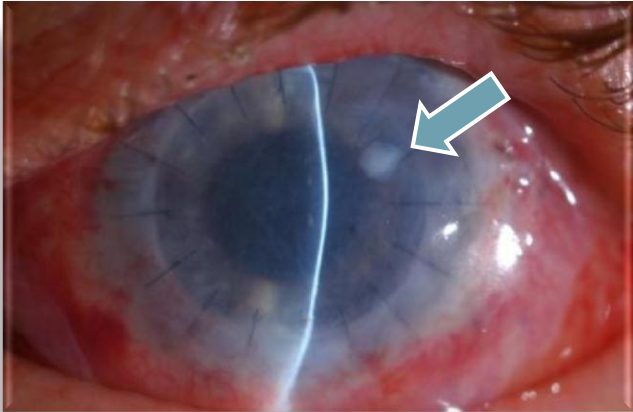


In vitro expansion of limbal stem cells

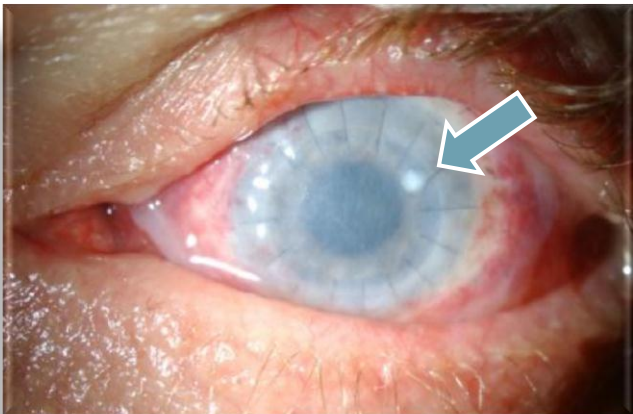
- Cell culture conducted in NZNEC labs by Jane McGhee & Trevor Sherwin
- Patient blood collected and centrifuged to separate cells & serum
- Limbal explant cultured on amnion in sterile conditions in 10% patient serum @ 37degC with 5% CO₂



STEM CELL TRANSPLANT WITH PKP



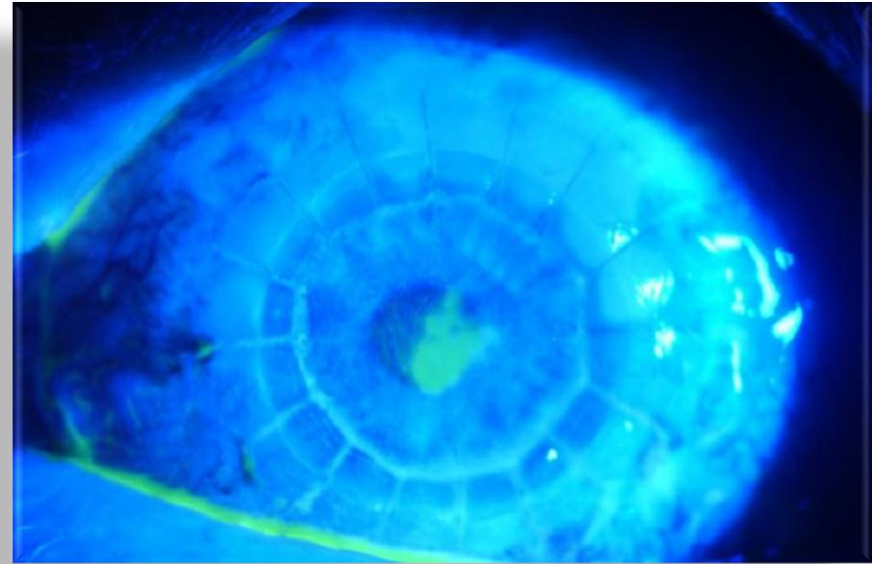
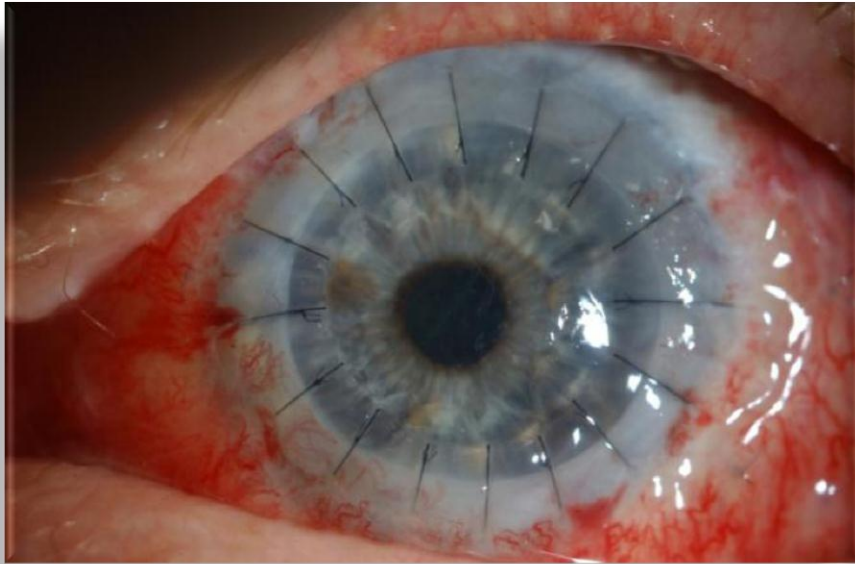
- ⦿ Day 819:
- ⦿ PKP and AMT & expanded stem cell transplant



- ⦿ Explant visible under AMT

PROGRESS

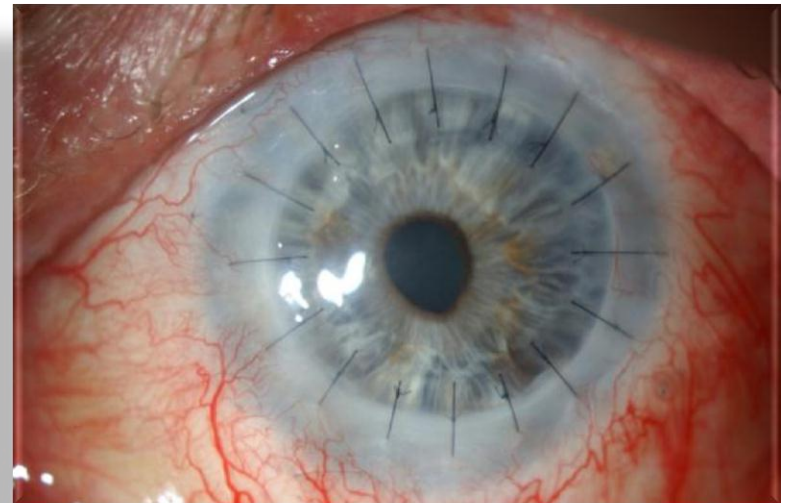
- Amnion *in situ* for 6 days, VAL 6/60 UA



- Amnion breaks up to reveal clear graft, small residual epithelial defect, and VAL 6/36!

PROGRESS: Day 1228

⦿ Visual acuity 6/12



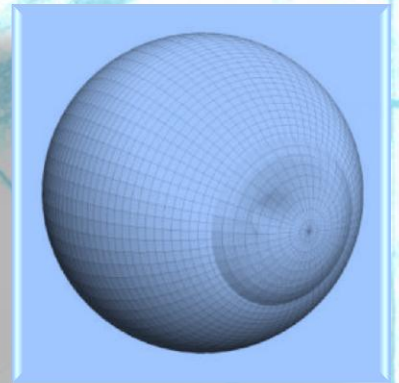
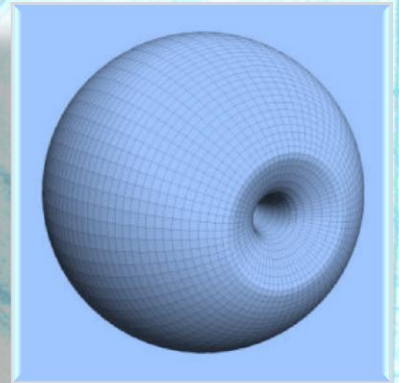
The future: the engineered cornea

Lamellar surgery refined

Genetic manipulation of transplants

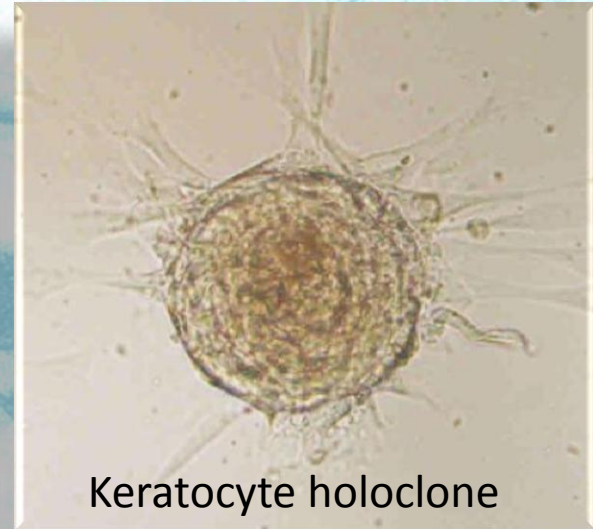
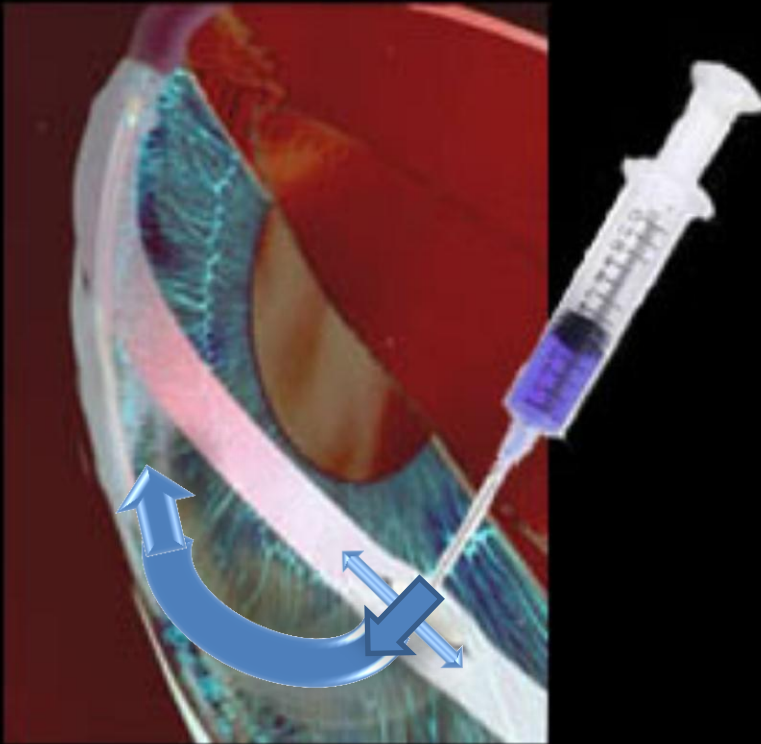
Progenitor/stem cell based transplants

Synthetic biological corneas constructed



Keratocyte transplantation in early keratoconus and stromal dystrophies

Keratocyte progenitor cells injected into a series of corneal channels



Keratocyte holoclone

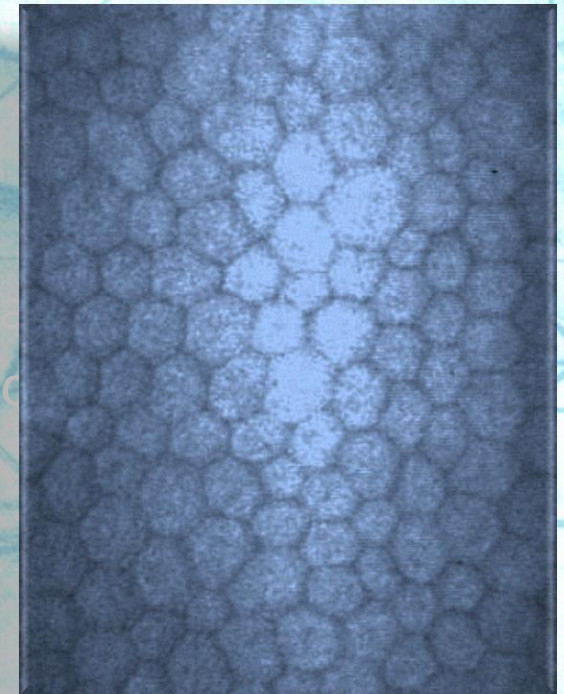


Keratocyte holoclones



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Injectable endothelial precursor cells?

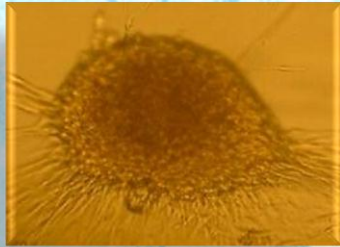


Mimura T, Yokoo S, Araie M, Amano S, Yamagami S. Treatment of rabbit bullous keratopathy with precursors derived from cultured human corneal endothelium. Invest Ophthalmol Vis Sci. 2005 ;46(10):3637-44.



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Reconstructing the cornea *in vitro*



Epithelial
holoclones



Keratocyte
holoclones



Endothelial
holoclones



Xu YG, Xu YS, Huang C, Feng Y, Li Y, Wang W. Development of a rabbit corneal equivalent using an acellular corneal matrix of a porcine substrate. Mol Vis. 2008;14:2180-9.

Conclusions

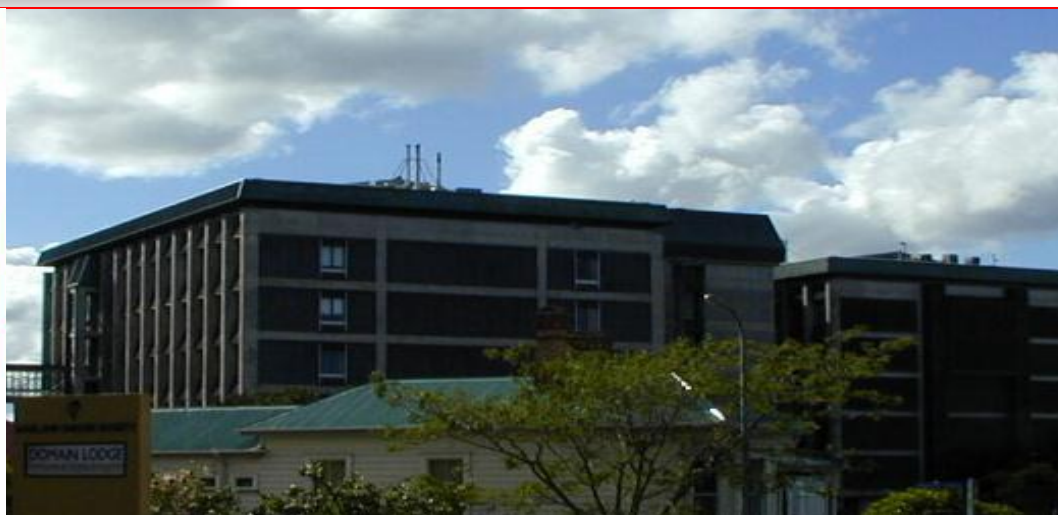
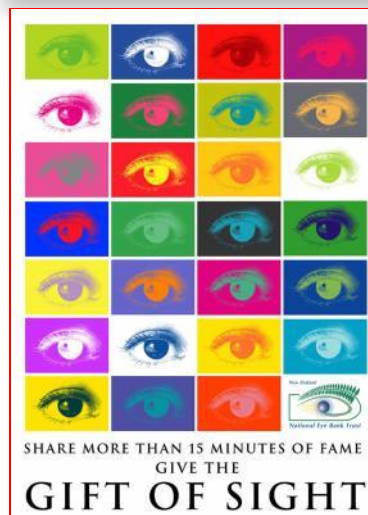
- Role for PKP for foreseeable future but more than 50% surgery now lamellar
- DALK well-established
- DSEK/DSAEK technique still maturing
- DMEK variations under study
- Cell based treatments on the horizon





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Acknowledgements



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Founder of the NZNEB

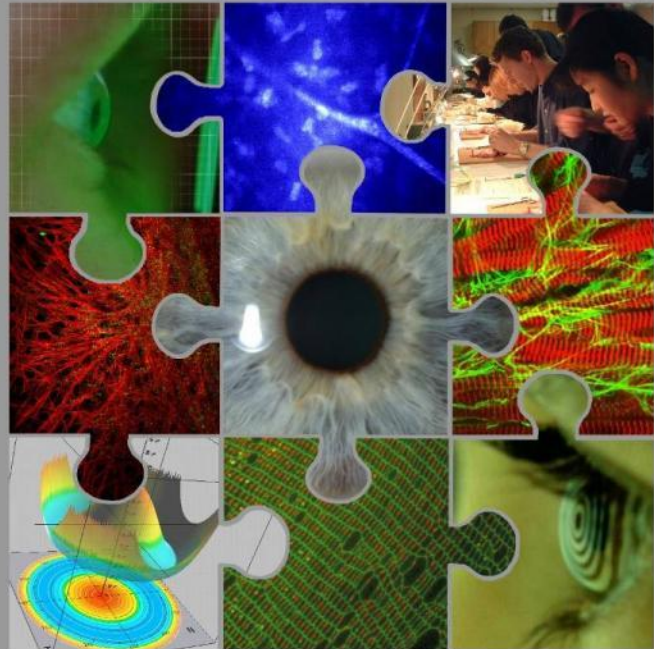
Acknowledgements : the team

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Thank you

Translational Vision Research



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Te Whare Wānanga o Tamaki Makaurau

Thank you

