

# IL TRAPIANTO DI CORNEA NEL XXI SECOLO

Massimo Busin



Università  
degli Studi  
di Ferrara



# 13 luglio 1984



REPUBBLICA ITALIANA N° 2475

IN NOME DELLA LEGGE



NOI PROFESSORE DOTTOR ANTONIO ROSSI

RETTORE DELLA UNIVERSITA' DEGLI STUDI DI FERRARA

VISTO IL RISULTATO DELL'ESAME FINALE SUPERATO IL 13 LUGLIO 1984 DAL

**DOTT. MASSIMO BUSIN**

NATO A FORLÌ IL GIORNO 13 OTTOBRE 1956 GLI

CONFERIAMO IL DIPLOMA DI SPECIALIZZAZIONE IN  
OFTALMOLOGIA

CON LA VOTAZIONE DI SETTANTA SOPRA SETTANTA E LA LODE  
AFFINCHÉ POSSA VALERSENE PER OGNI EFFETTO DI LEGGE.

DATO IN QUESTA UNIVERSITÀ ADI 25 LUGLIO 1984

IL RETTORE

(Antonio Rossi)

IL DIRETTORE AMMINISTRATIVO

(Luigi Livatino)

IL PRESIDE DELLA FACOLTÀ

(Paolo Carinci)

# 14 luglio 1984



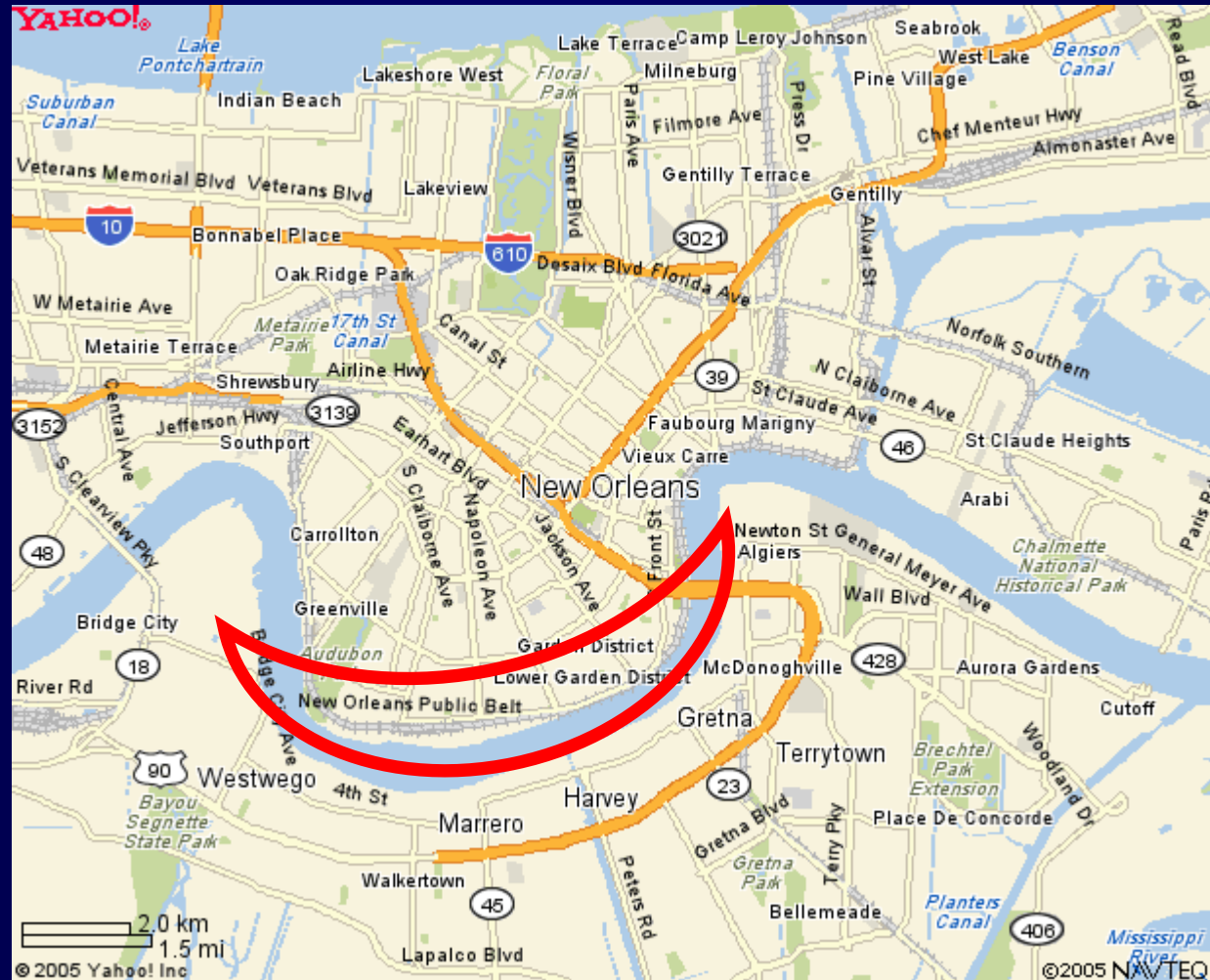
**TWA**  
**TIMETABLE**  
EFFECTIVE APRIL 1 - APRIL 25, 1981



The only widebodies  
TWA flies across the  
Atlantic and in the U.S.  
are the 747 and  
L-1011...The widebodies  
people prefer most.



# NEW ORLEANS “CRESCENT CITY”











**Louisiana State  
University  
EYE CENTER**

**HOTEL DIEU  
HOSPITAL**



# NEW ORLEANS (USA) 1984-86



**Dr. H.E. Kaufman, Dr. M.B.McDonald  
e i Cornea Fellows**

# Universitäts-Augenklinik (Venusberg)





# Privatdozent (19.12.1989) Universitätsprofessor (17.06.1991)



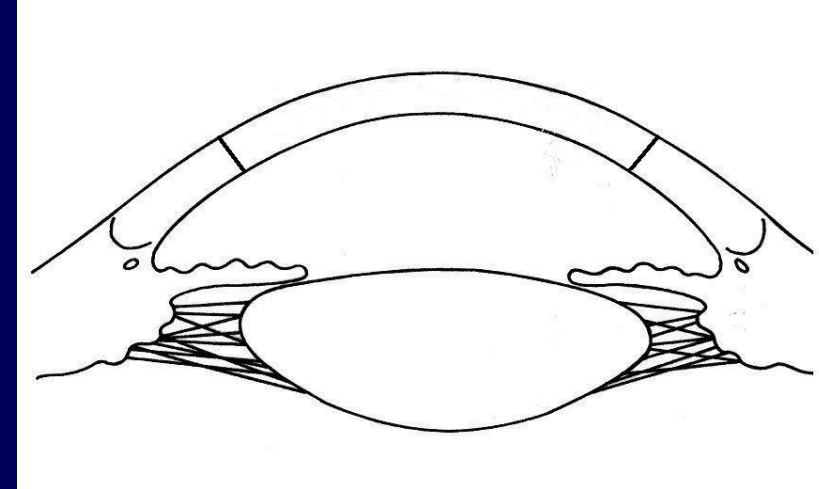
# Forlì, Gennaio 1996



# CHERATOPLASTICA NEL XX SECOLO

“Disco Perfetto in un Foro  
Perfettamente Rotondo”

- Guarigione > 1 anno
- Rimozione Suture dopo 1 anno
- Visus Limitato dalla Distorsione (delle Suture)
- Astigmatismo Finale dopo Rimozione Suture  $\geq 4$  D in  $\pm 20\%$  dei Casi

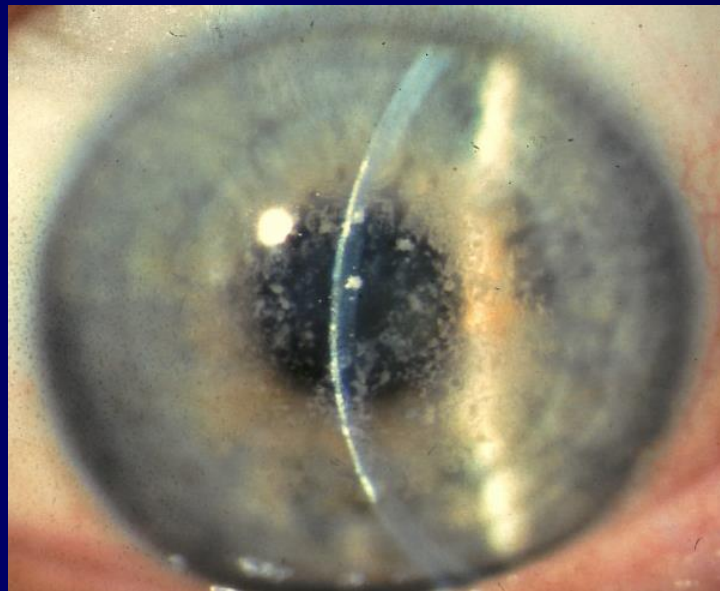
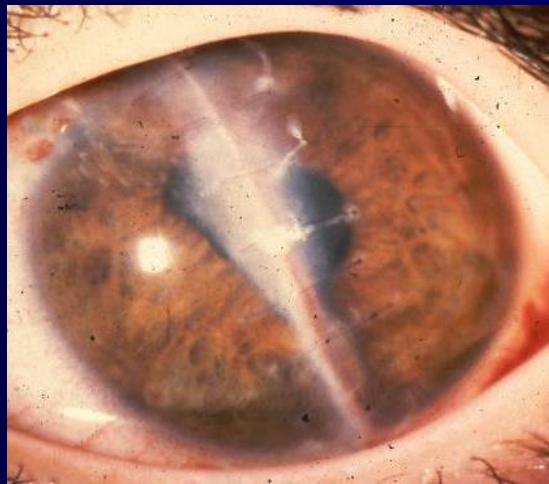




# CHERATOPLASTICA NEL XX SECOLO

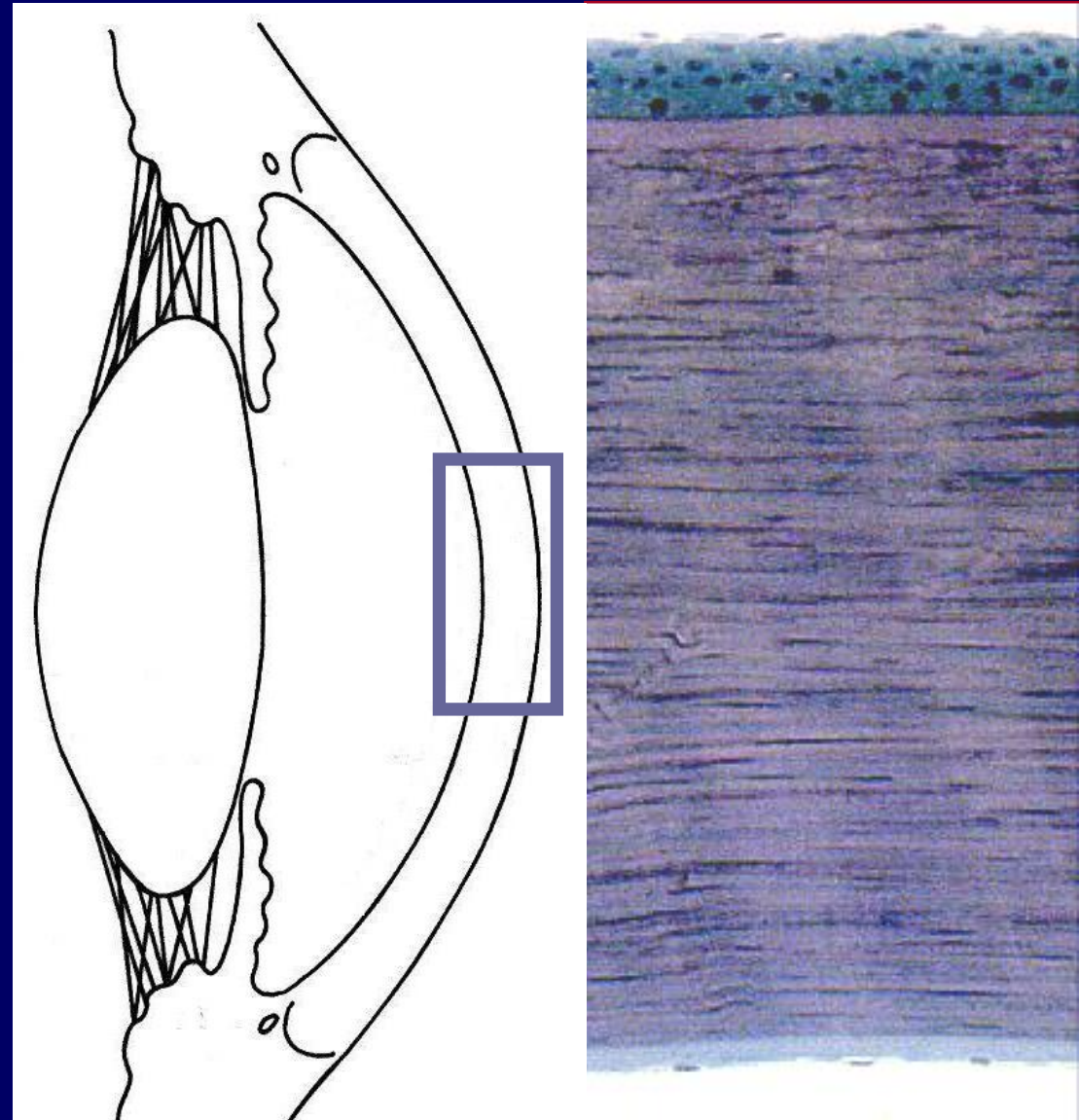
PK = Una Soluzione  
Unica per Tutti i Casi

!!!



# CORNEA

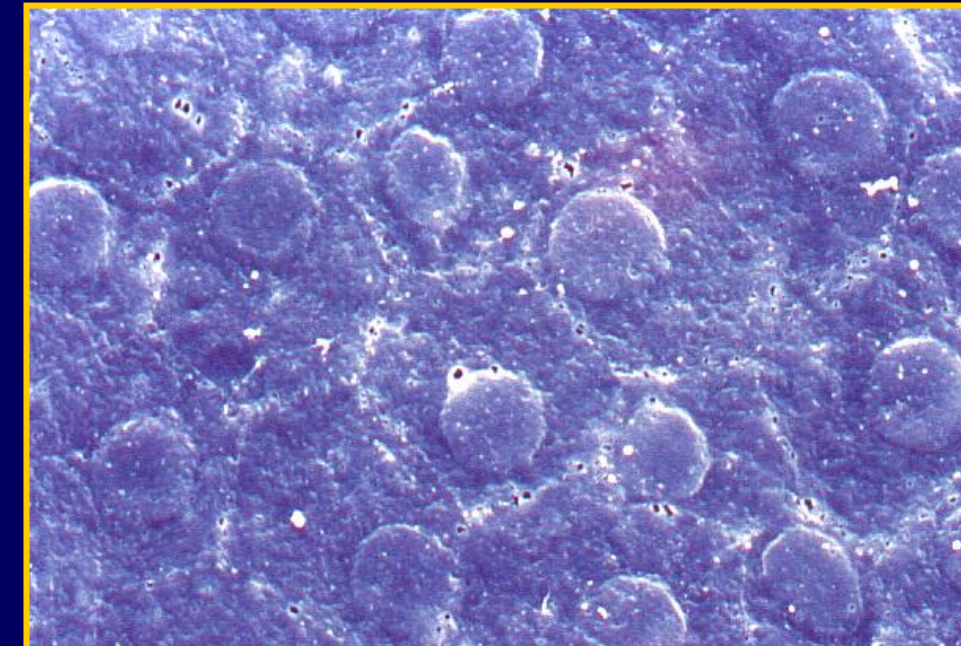
- **Epitelio**  
(Protezione)
- **Stroma**  
(Struttura)
- **Endotelio**  
(Trasparenza)





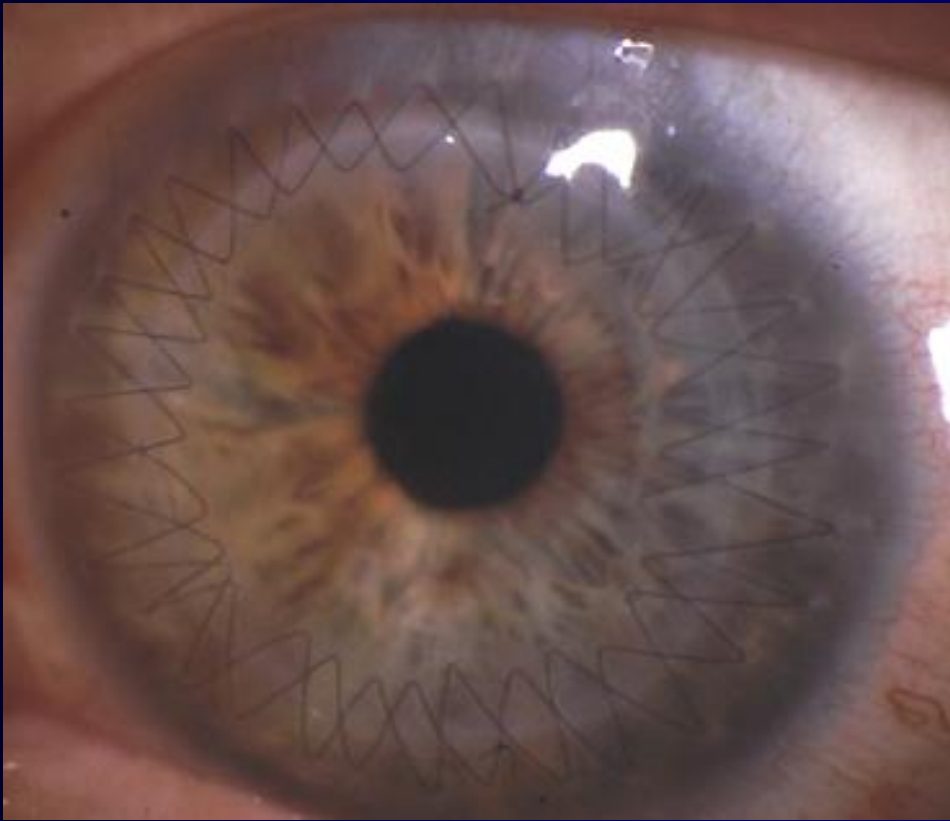
# L'ENDOTELIO CORNEALE ( $\pm 40 \mu\text{m}$ )

- Monostratificato
- Pompa  $\text{HCO}_3$
- Mantiene la Bassa Idratazione
- NON PUÓ PROLIFERARE
- Guarigione per Ingrandimento/Scivolamento

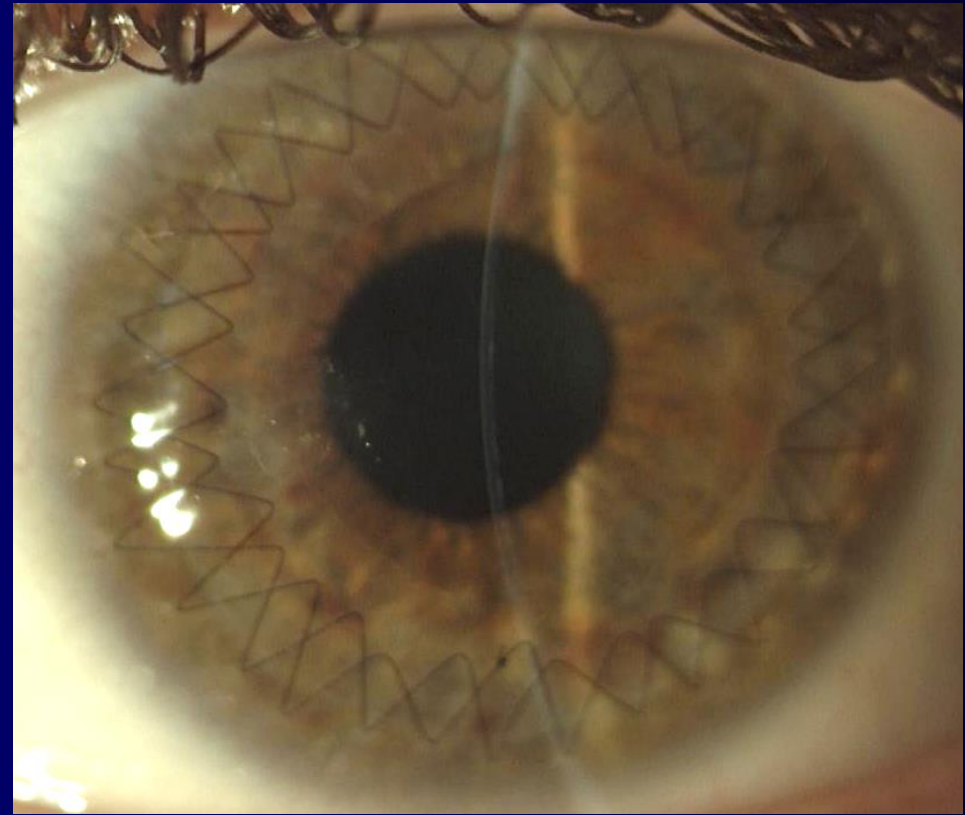




# CHERATOPLASTICA NEL XX SECOLO



**1986 Bonn  
(Germania)**

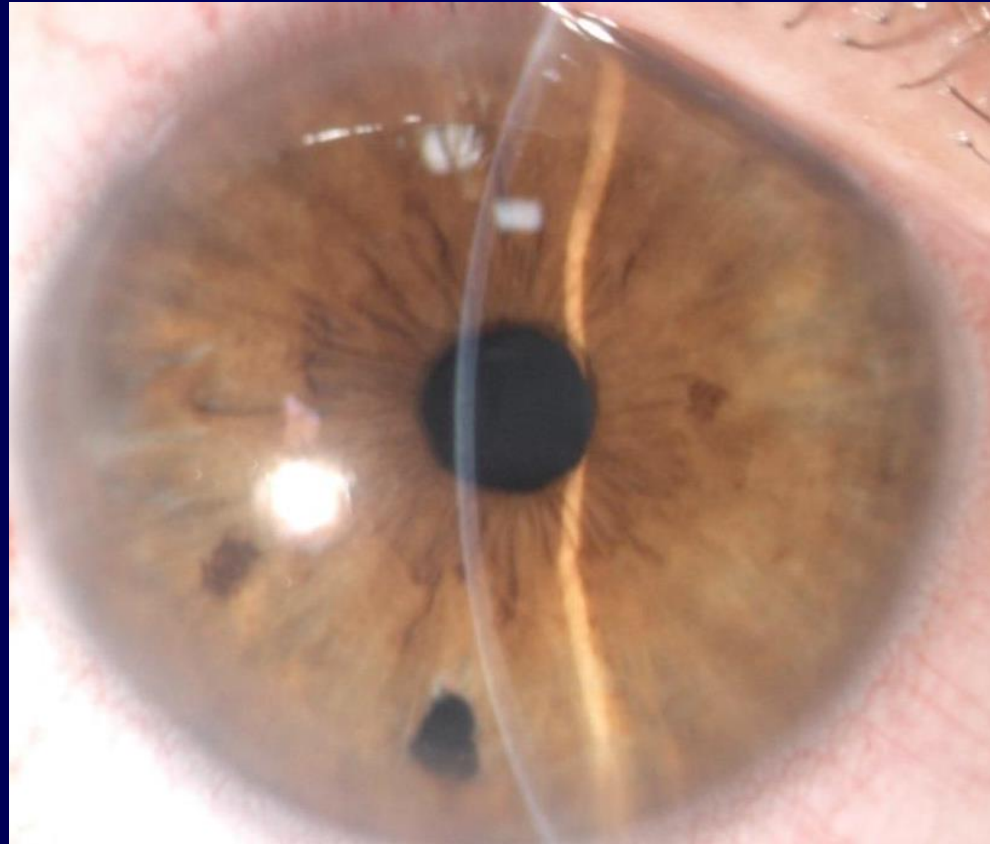


**1999 Forlì**

# CHERATOPLASTICA NEL XX SECOLO



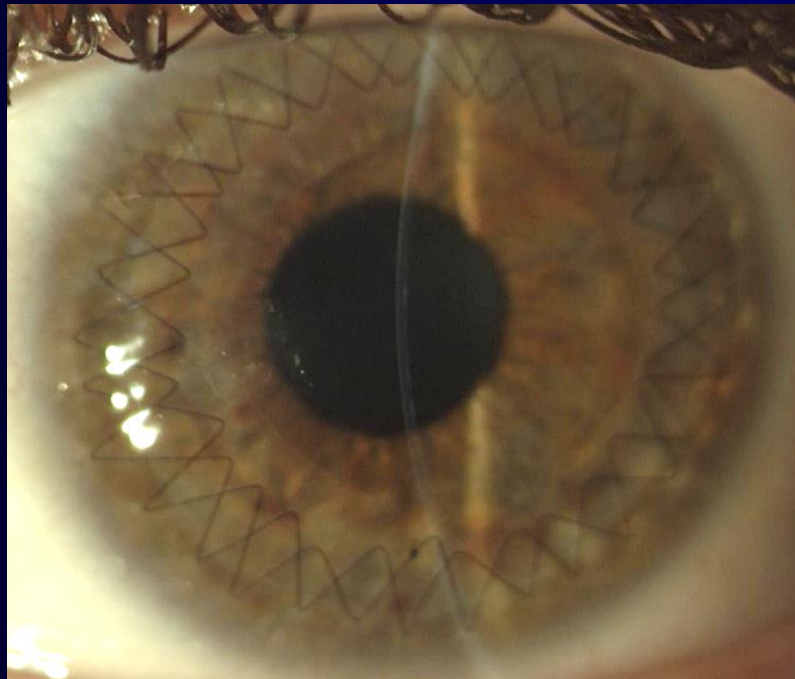
# CHERATOPLASTICA NEL XXI SECOLO



2008 Forlì

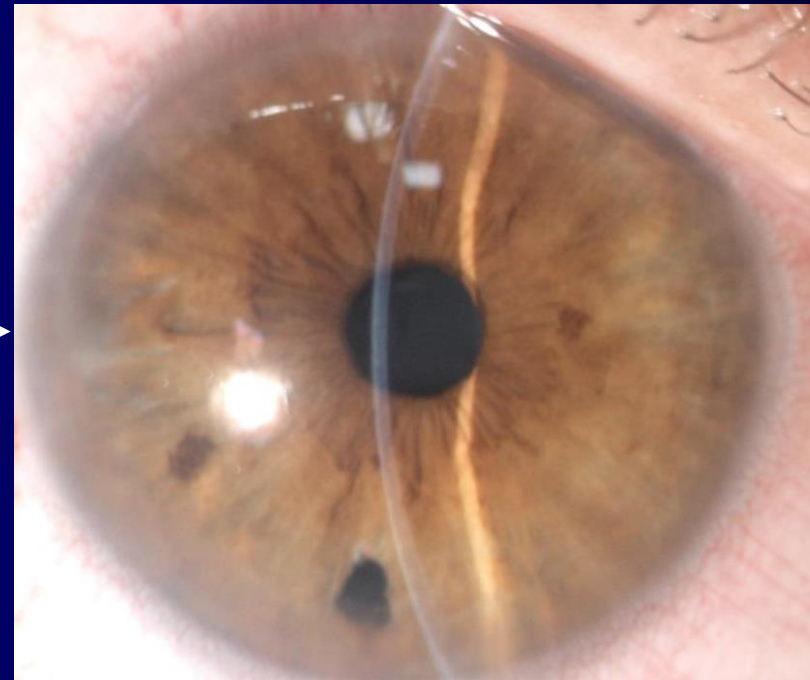


# XX vs XXI SECOLO



1999 Forlì

???



2008 Forlì

# “NUOVA” CHERATOPLASTICA

Patologie  
Corneali

Endotelio  
Sano

Endotelio  
Malato

LK Anteriore  
(PK “a fungo”)

LK Posteriore  
(PK)

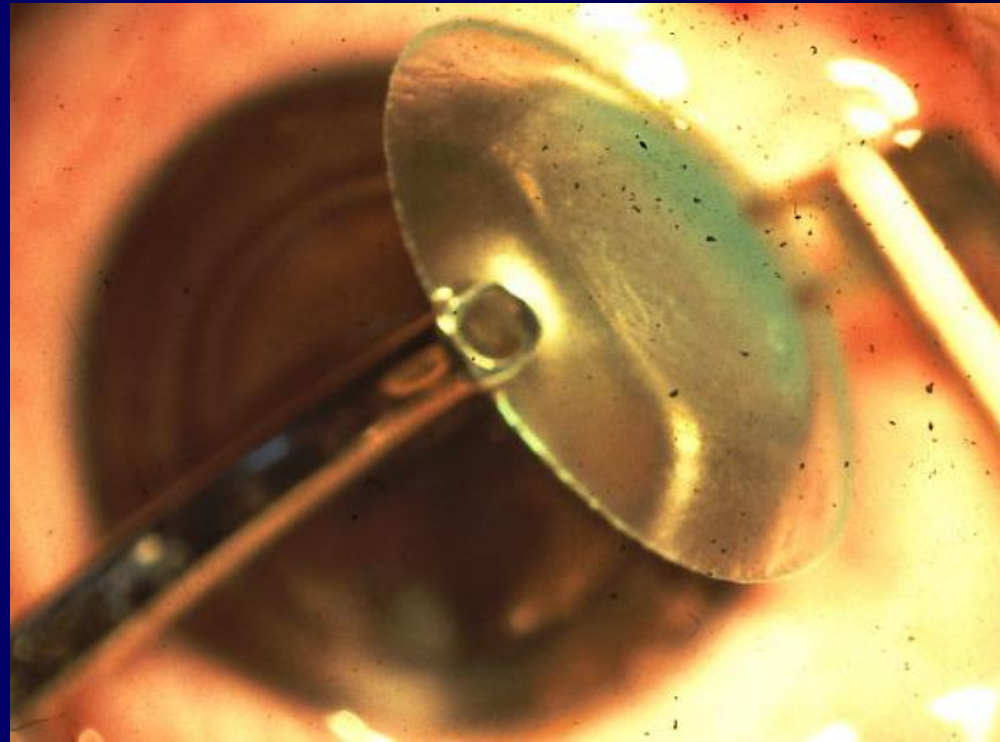
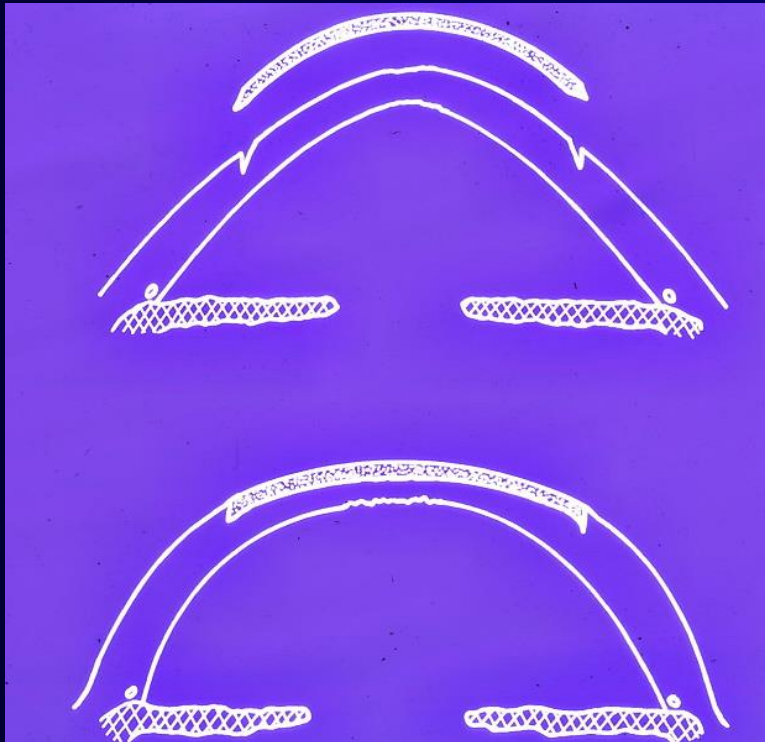
**1980**

**LK “ADDITIVA” ANTERIORE**

**Kaufman, H.E.**

**Epicheratofachia per Afachia**

**“LENTE A CONTATTO VIVENTE”**





# 1996

# LK "ADDITIVA" POSTERIORE ENDOCHERATOPLASTICA

## ENDOKERATOPLASTY: A NEW SURGICAL TECHNIQUE FOR THE REPLACEMENT OF DISEASED CORNEAL ENDOTHELIUM

Massimo Busin<sup>1</sup>, M.D., Thomas Mönks<sup>2</sup>, M.D., Robert Arffa<sup>3</sup>, M.D.

<sup>1</sup> University of Bonn, Germany, <sup>2</sup> Surgical Eye Center Viktoriahaus, Krefeld, Germany, <sup>3</sup> Allegheny General Hospital, Pittsburgh, Pennsylvania

### INTRODUCTION

To date, penetrating keratoplasty (PK) is the only available surgical treatment for endothelial decompensation. Although epithelium and stroma are not primarily affected, this procedure involves full-thickness transplantation, leading to unsatisfactory refractive results in a relatively high number of patients. A new surgical technique aimed at replacing exclusively the diseased endothelium is presented by means of a rabbit model.

### RESULTS

Despite the technical difficulty of handling very thin corneas like the rabbit ones, it was possible in all animals used in this experiment study to perform endokeratoplasty as theoretically designed. By two weeks all of the corneas with endokeratoplasty-lenticules demonstrated substantial clearing, while the scraped cornea did not. On histology only a small proportion of the endothelial cells were present on the donor lenticules.

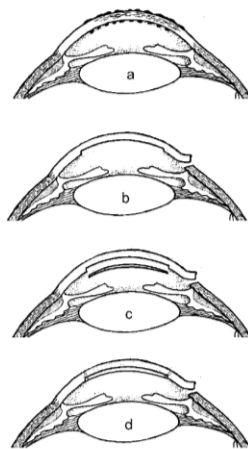


Fig. 1: Schematic representation of endokeratoplasty surgery. a) Edematous cornea; b) Removal of Endothelium from the center of the recipient cornea (arrows); c) Insertion of the endokeratoplasty-lenticule through a scleral tunnel; d) Suturing in place of the endokeratoplasty-lenticule.

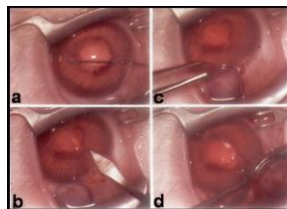


Fig. 2: Endokeratoplasty surgery in a rabbit model: A) Removal of Descemet's membrane and endothelium from the recipient central cornea; B) Enlarging the anterior chamber with a 4mm keratome; C) Preparation of a 10-0 prolene mattress suture to fixate the endokeratoplasty-lenticule; D) Mattress suture led through the recipient cornea at the 6 o'clock position.

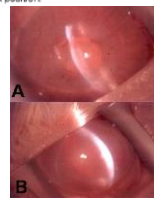


Fig. 3: Postoperative results: A) Rabbit cornea with endokeratoplasty-lenticule fixated with four 10-0 prolene mattress sutures. The slit-lamp examination reveals tight contact between donor lenticule and recipient cornea as well as only moderate corneal edema; B) Control cornea exhibiting marked edema in the central area denotes of the endothelium.

### MATERIALS AND METHODS

Donor lenticules were prepared as follows: Approximately 80% of the anterior stroma of the donor corneas was removed with a microkeratome (Storz, Heidelberg, Germany) and a 6mm button was trephined. In five eyes a 4mm limbal incision was made and the central endothelium and Descemet's membrane were removed. In four eyes a donor lenticule was then sutured to the posterior surface of the central cornea, using four to five prolene 10-0 mattress sutures. The fifth eye did not receive any lenticule and served as control. All animals were examined 1, 3, 5, 7, and 14 days after surgery and clinical pictures were taken. On the fourteenth day they were killed and the excised corneas submitted for histologic evaluation.

### CONCLUSION

Endokeratoplasty exhibits potential for endothelial transplantation and merits further study. Possible advantages of this procedure over conventional PK surgery include:

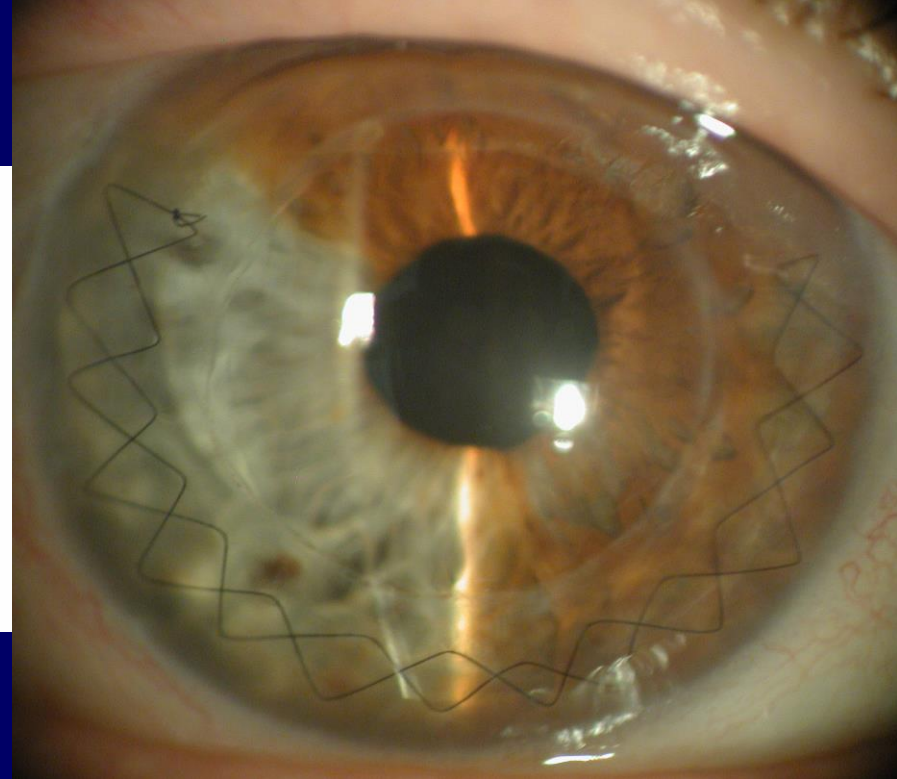
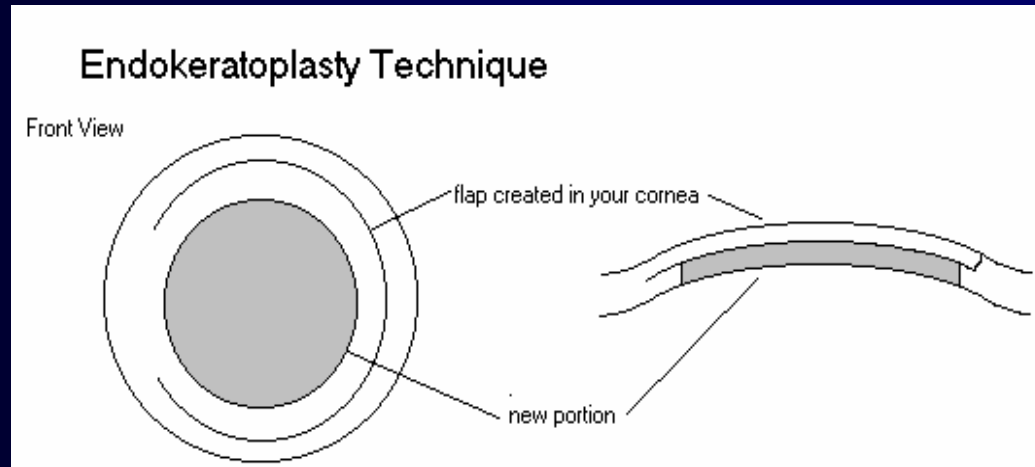
- 1) reduced postoperative corneal distortion in the absence of a full-thickness surgical wound;
- 2) increased safety secondary to the use of a short tunnel approach
- 3) reduced immunogenicity (no epithelium is transplanted).

Improved handling of the donor lenticule and use of an alternate animal model, e.g. primates, may improve endothelial cell transfer.

This study was supported in part by a grant from the Medical Eye Bank of Western Pennsylvania, Pittsburgh, Pennsylvania.

# Busin et al. OPHTHALMOLOGY, 1996 (Suppl.)

# ENDOCHERATOPLASTICA ("APPROCCIO LASIK")



Busin et al., Ophthalmology 2000

**2000**

Clinical Trial

> [Ophthalmology](#). 2000 Nov;107(11):2077-82.

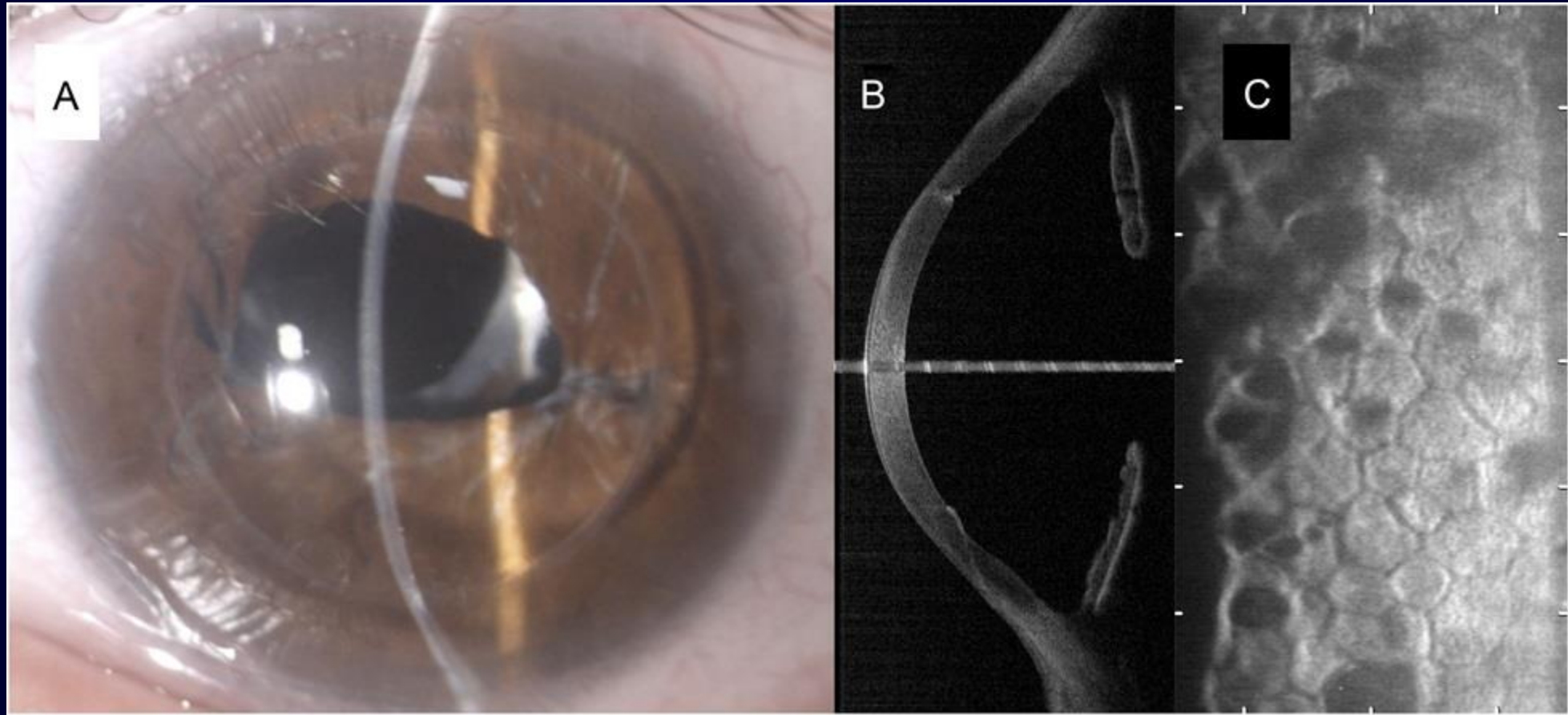
doi: [10.1016/s0161-6420\(00\)00371-7](https://doi.org/10.1016/s0161-6420(00)00371-7).

# **Endokeratoplasty as an alternative to penetrating keratoplasty for the surgical treatment of diseased endothelium: initial results**

M Busin<sup>1</sup>, R C Arffa, A Sebastiani



# 22 ANNI DOPO ENDOCHERATOPLASTICA



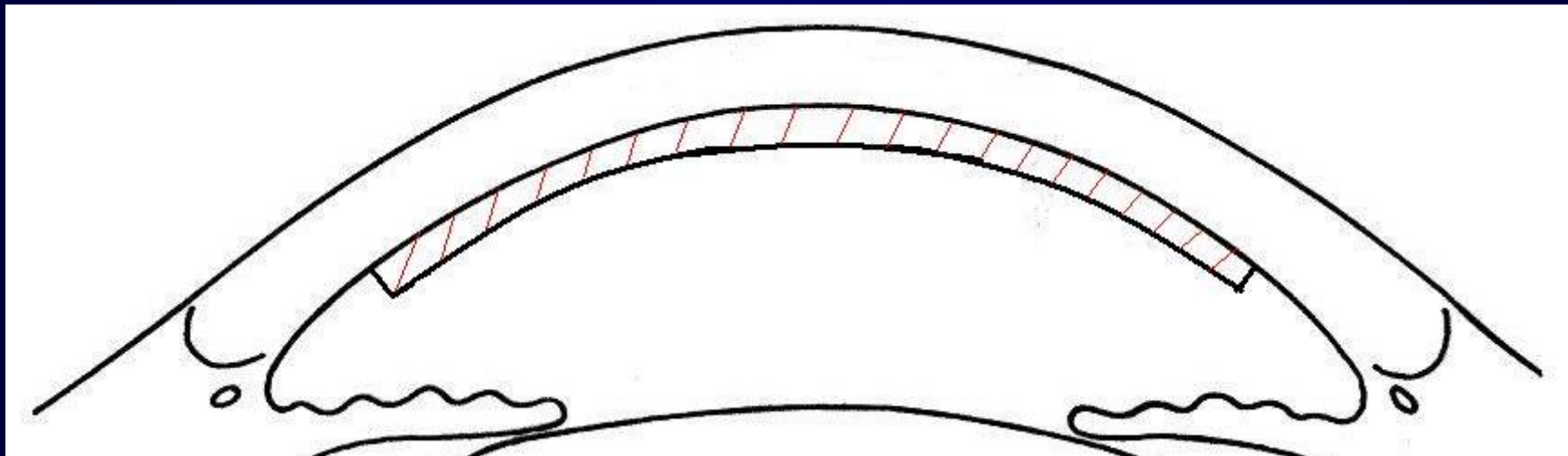
**AVcc=10/10**

**ECD=652 cell./mm<sup>2</sup>**

# LK POSTERIORE ADDITIVA

(D)escemet (S)tripping (E)ndothelial  
(K)eratoplasty

## DSEK (2002)



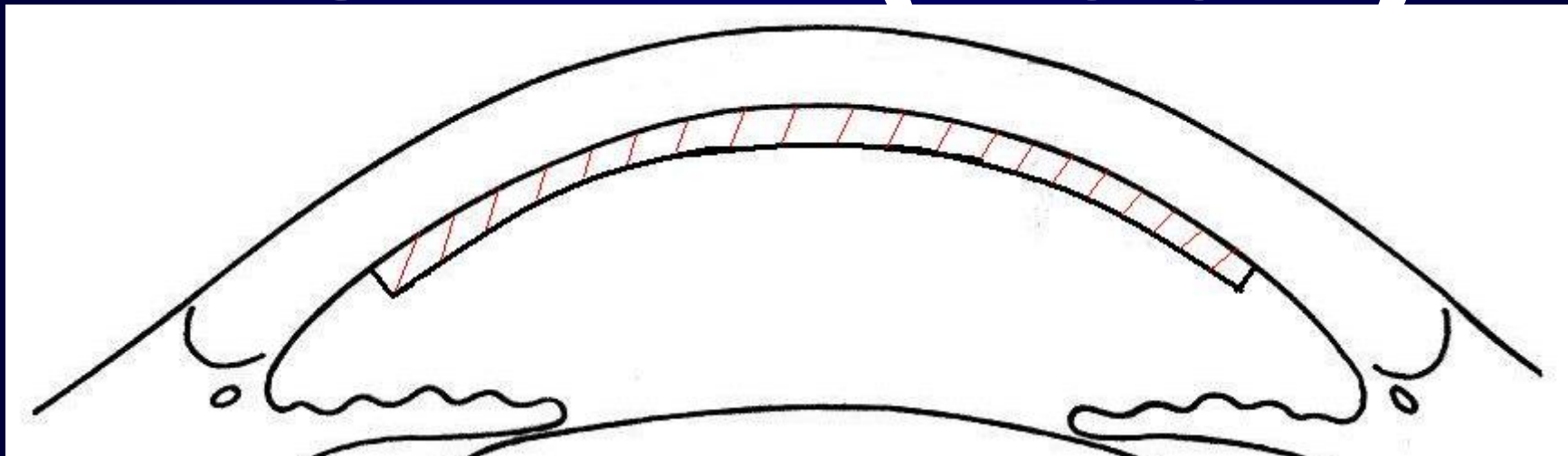
# LK POSTERIORE ADDITIVA

(D)escemet (S)tripping

(A)utomated (E)ndothelial

(K)eratoplasty

DSAEK (2004)

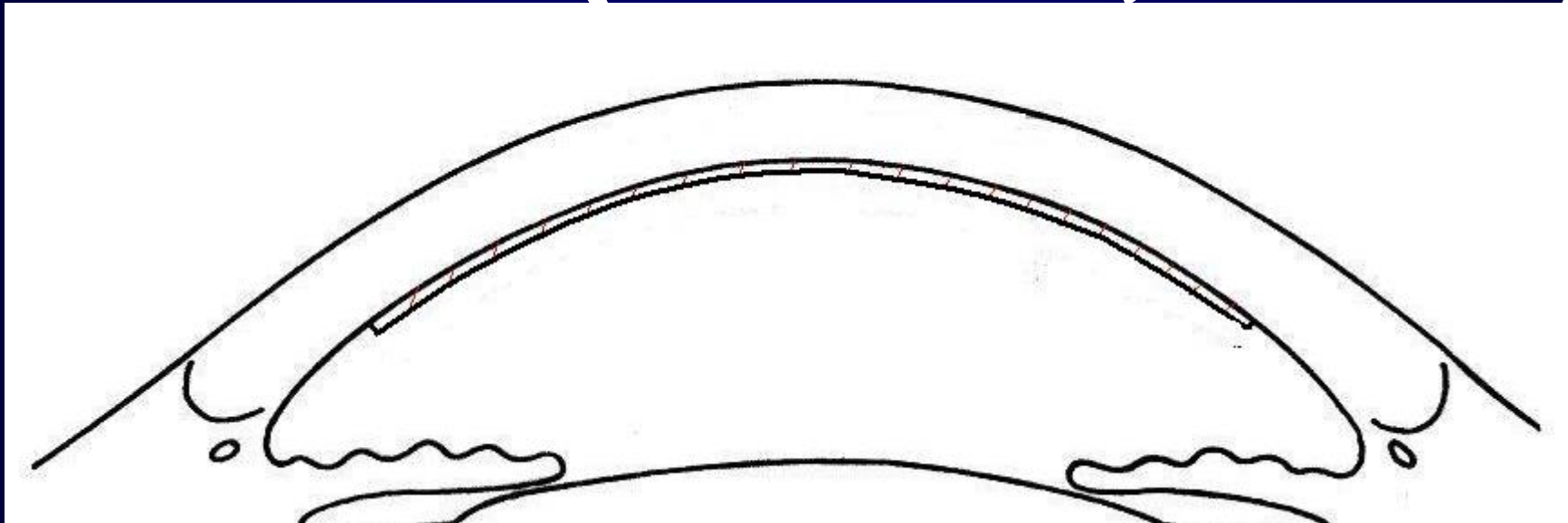




# LK POSTERIORE ADDITIVA

**U**(ltra)**T**(hin)-

**DSAEK (BUSIN, 2009)**



**2006**

**DSAEK e BUSIN GLIDE**

**2006**

# BUSIN GLIDE

- **Tecnica semplice**
- **Incisione di  $\geq 3.2$  mm**
- **Costi/ Benefici**  
**(Multi Uso)**





**2008**

# BUSIN GLIDE

> [Arch Ophthalmol.](#) 2008 Aug;126(8):1133-7. doi: 10.1001/archopht.126.8.1133.

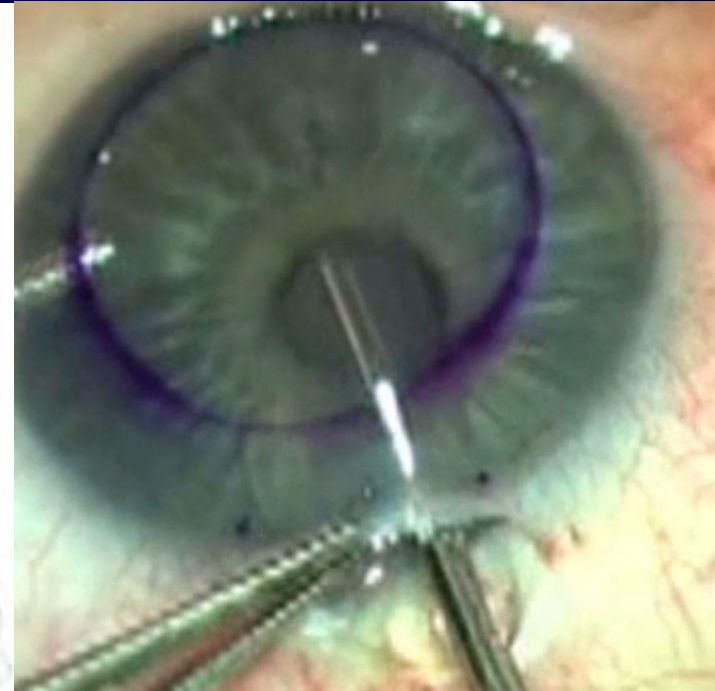
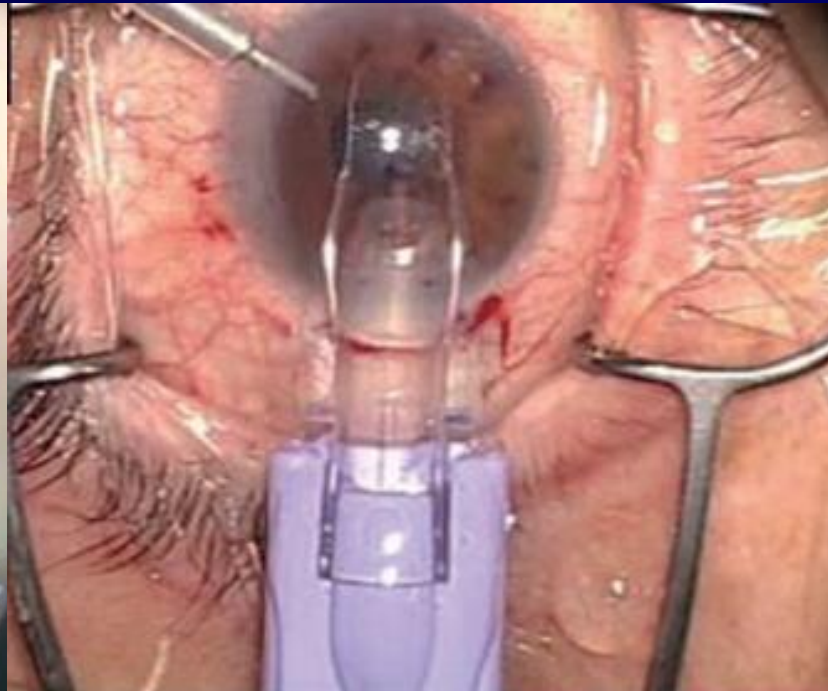
**A modified technique for descemet membrane stripping automated endothelial keratoplasty to minimize endothelial cell loss**

Massimo Busin <sup>1</sup>, Priya R Bhatt, Vincenzo Scorcia

**The Editors' Choice AAO (2008)**

**2016**

# BUSIN GLIDE



SONDAGGI USA (Eyeworld) Ott 2016

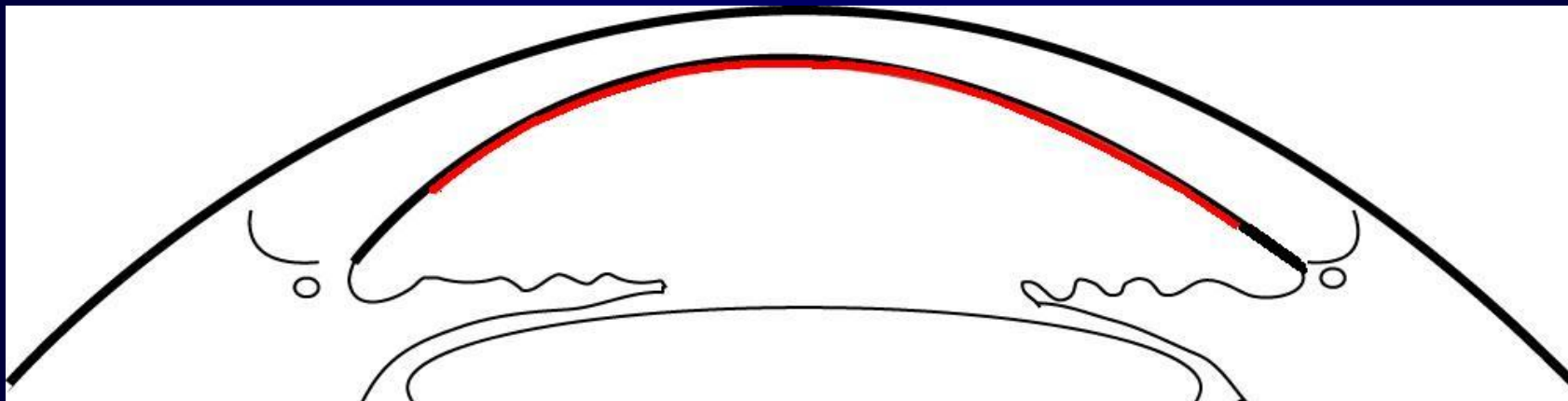
**1°** Busin Glide >30% DSAEK

# LK POSTERIORE SOSTITUTIVA

(D)escemet (M)embrane

(E)ndothelial (K)eratoplasty

DMEK (Melles, 2006)



# UT-DSAEK

2012

Comparative Study > Invest Ophthalmol Vis Sci. 2012 Jan 31;53(1):521-4.

doi: 10.1167/iovs.11-7753.

## Microkeratome-assisted preparation of ultrathin grafts for descemet stripping automated endothelial keratoplasty

Massimo Busin <sup>1</sup>, Amit K Patel, Vincenzo Scorcia, Diego Ponzin

2013

> Ophthalmology. 2013 Jun;120(6):1186-94. doi: 10.1016/j.ophtha.2012.11.030. Epub 2013 Mar 1.

## Ultrathin descemet's stripping automated endothelial keratoplasty with the microkeratome double-pass technique: two-year outcomes

Massimo Busin <sup>1</sup>, Silvana Madi, Paolo Santorum, Vincenzo Scorcia, Jacqueline Beltz

2019

> Cornea. 2019 Sep;38(9):1192-1197. doi: 10.1097/ICO.0000000000001999.

## Five-Year Outcomes of Ultrathin Descemet Stripping Automated Endothelial Keratoplasty

Silvana Madi <sup>1 2 3</sup>, Pia Leon <sup>2</sup>, Yoav Nahum <sup>4 5</sup>, Sergio D'Angelo <sup>6</sup>, Giuseppe Giannaccare <sup>7</sup>, Jacqueline Beltz <sup>2 8</sup>, Massimo Busin <sup>1 2 9</sup>



# ENDOTHELIO-IN DMEK

**2016**

> [Ophthalmology](#). 2016 Mar;123(3):476-83. doi: 10.1016/j.ophtha.2015.10.050. Epub 2015 Dec 11.

## **Contact Lens-Assisted Pull-Through Technique for Delivery of Tri-Folded (Endothelium in) DMEK Grafts Minimizes Surgical Time and Cell Loss**

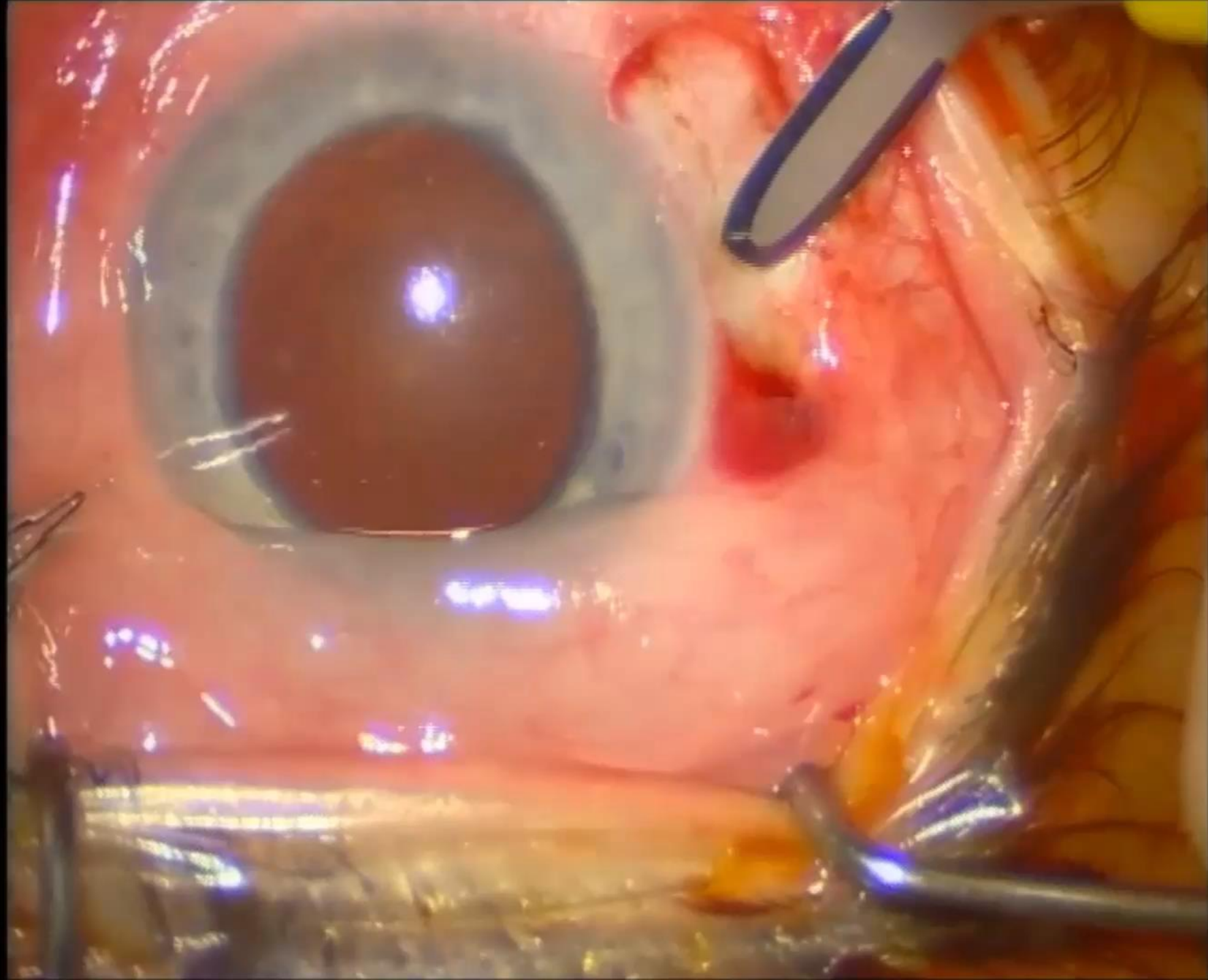
[Massimo Busin](#)<sup>1</sup>, [Pia Leon](#)<sup>2</sup>, [Vincenzo Scorcia](#)<sup>3</sup>, [Diego Ponzin](#)<sup>4</sup>

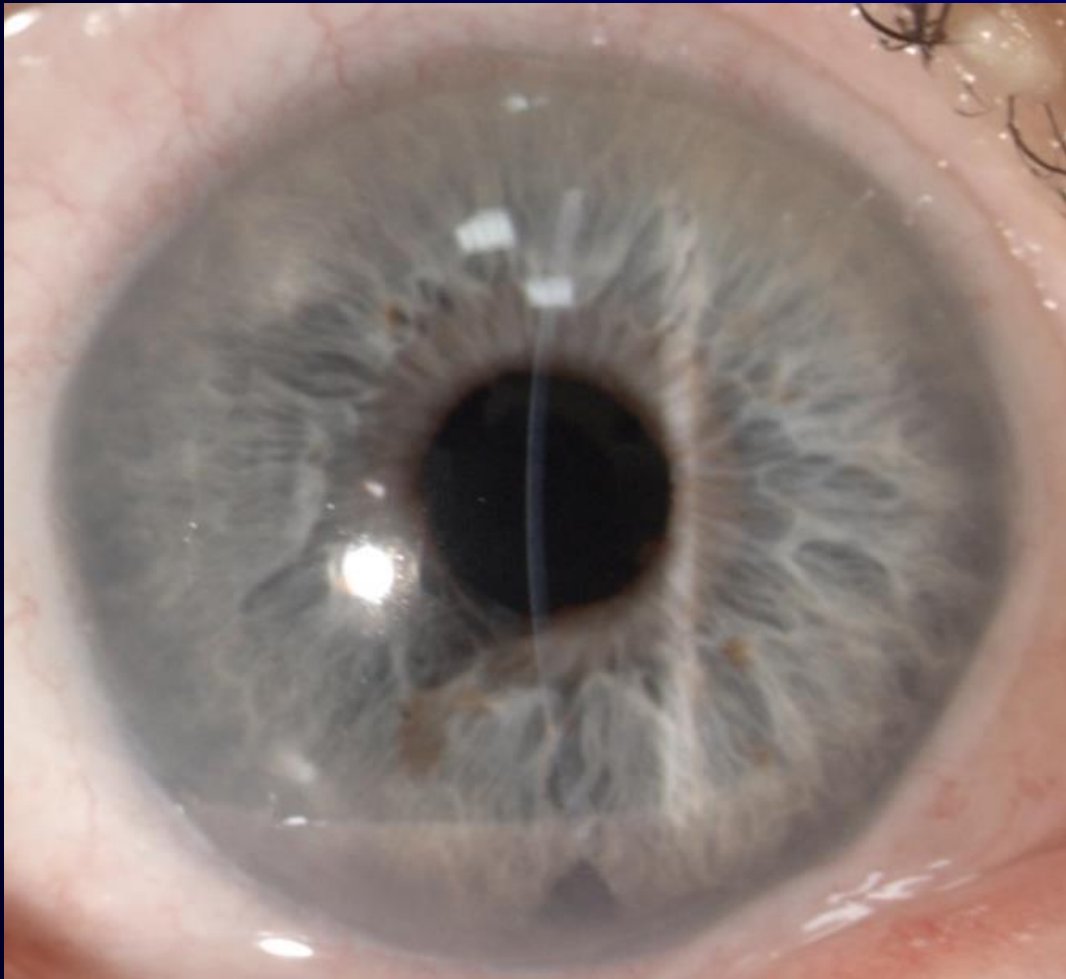
**2020**

> [Am J Ophthalmol](#). 2020 Nov;219:121-131. doi: 10.1016/j.ajo.2020.07.004. Epub 2020 Jul 11.

## **Three-Year Outcomes of Tri-Folded Endothelium-In Descemet Membrane Endothelial Keratoplasty With Pull-Through Technique**

[Angeli Christy Yu](#)<sup>1</sup>, [James Myerscough](#)<sup>2</sup>, [Rossella Spina](#)<sup>1</sup>, [Fiorella Fusco](#)<sup>3</sup>, [Sergiu Socea](#)<sup>4</sup>, [Luca Furiosi](#)<sup>1</sup>, [Luigi De Rosa](#)<sup>5</sup>, [Cristina Bovone](#)<sup>1</sup>, [Massimo Busin](#)<sup>6</sup>





**OD: 4 aa dopo DMEK**  
**AV: 10/10**



**OS: 6 aa dopo UT-DSAEK**  
**AV: 10/10**

# EK IN USA

Nel 2022:

DSAEK n = 15,544

DMEK n = 15,248



# CHERATOPLASTICA LAMELLARE NEL CHERATOCONO

Cristina Bovone



Università  
degli Studi  
di Ferrara



# “NUOVA” CHERATOPLASTICA

Patologie  
Corneali

Endotelio  
Sano

Endotelio  
Malato

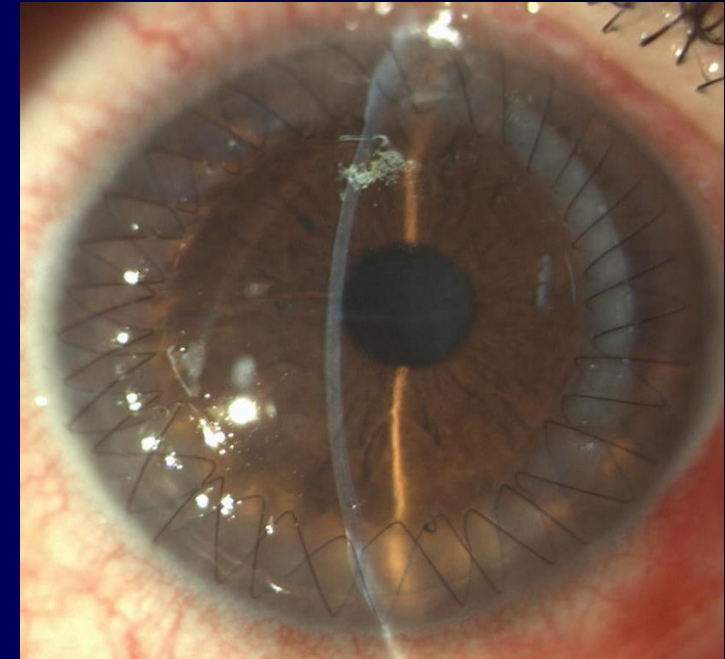
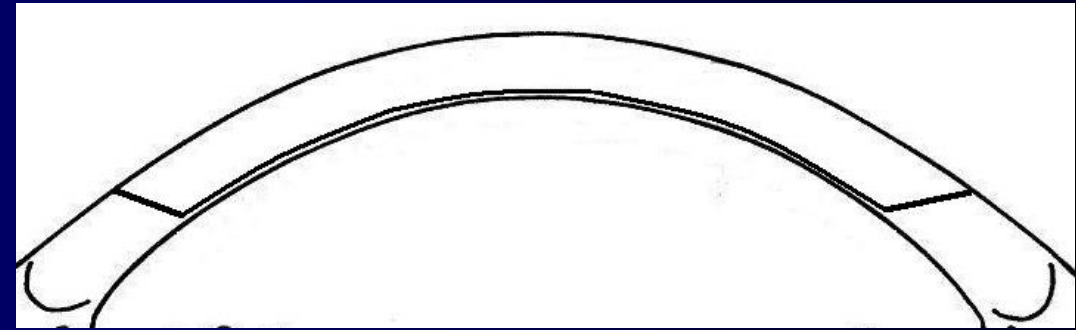
LK Anteriore  
(PK “a fungo”)

LK Posteriore  
(PK)

# LK ANTERIORE

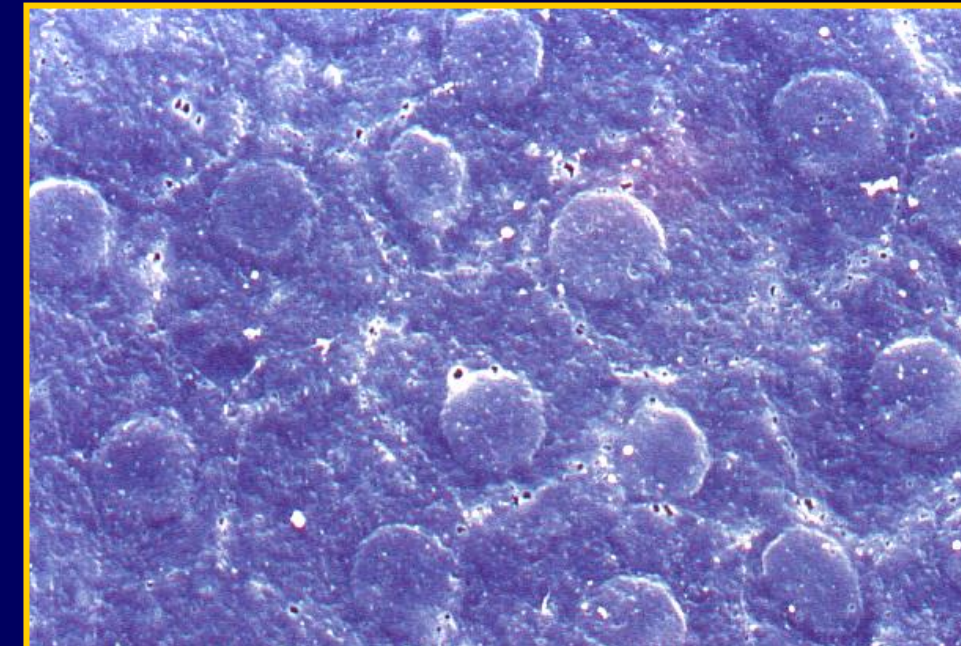
DALK → → → PK

- Suture
- Guarigione 1 Anno
- Astigmatismo  
Elevato in  $\geq 20\%$
- Endotelio Preservato



# L'ENDOTELIO CORNEALE ( $\pm 40 \mu\text{m}$ )

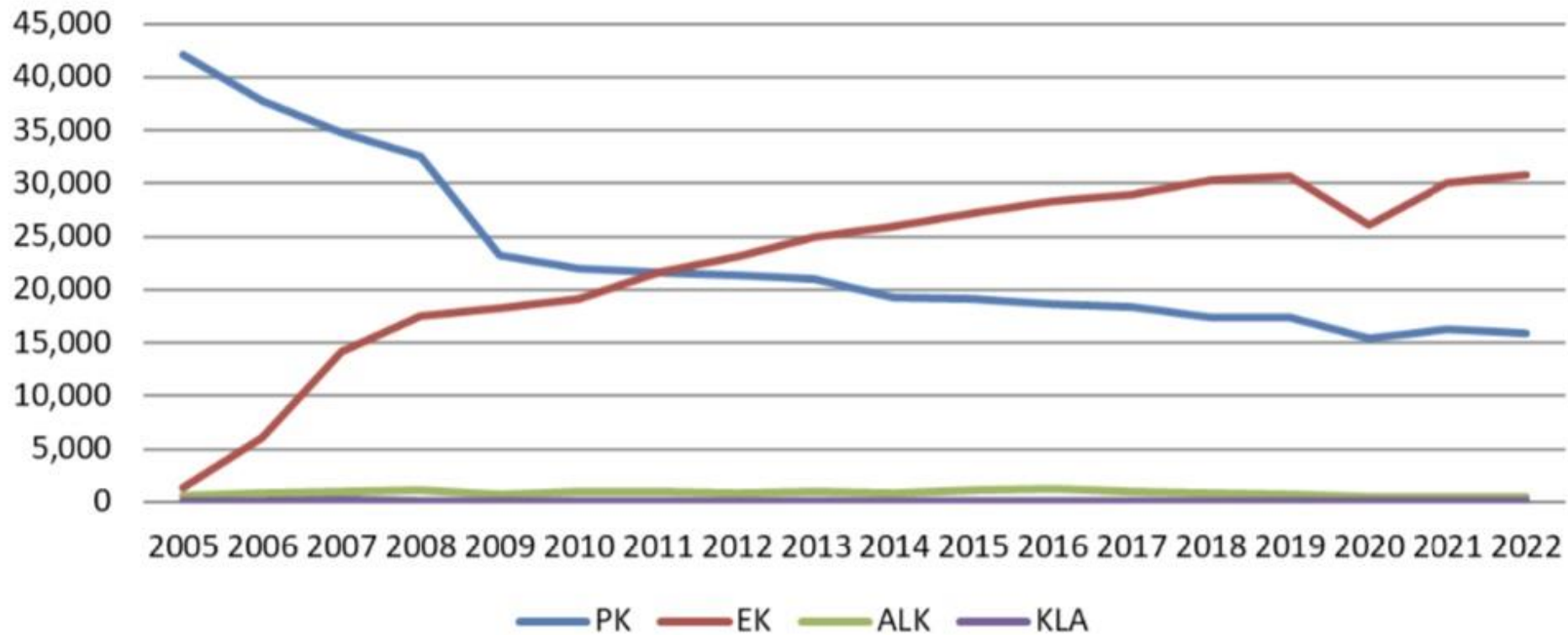
- Monostratificato
- Pompa  $\text{HCO}_3$
- Mantiene la Bassa Idratazione
- NON PUÓ PROLIFERARE
- Guarigione per Ingrandimento/Scivolamento





# KPL NEGLI USA

## Domestic Surgery Use of U.S. Supplied Intermediate-Term Preserved Tissue



# KPL NEGLI USA (2022)

TOTALE	n = 47,103
PK	n = 15,835
DSAEK	n = 15,544
DMEK	n = 15,248
<b>DALK</b>	<b>n = 476 !!!</b>

---

# DALK

1. Rare Complicanze nella PK
2. DALK non Standardizzata
3. DALK  $\approx$  PK (Visus e Refrazione)
4. **Risparmio dell'Endotelio!!!  
(ma Nessun Vantaggio a Breve Termine !!!)**

# DIMENSIONI PK (DALK)

Lembi PICCOLI



**BASSO**

Rischio Rigetto

**ELEVATO**

Errore Rifrattivo

Lembi GRANDI



**ELEVATO**

Rischio Rigetto

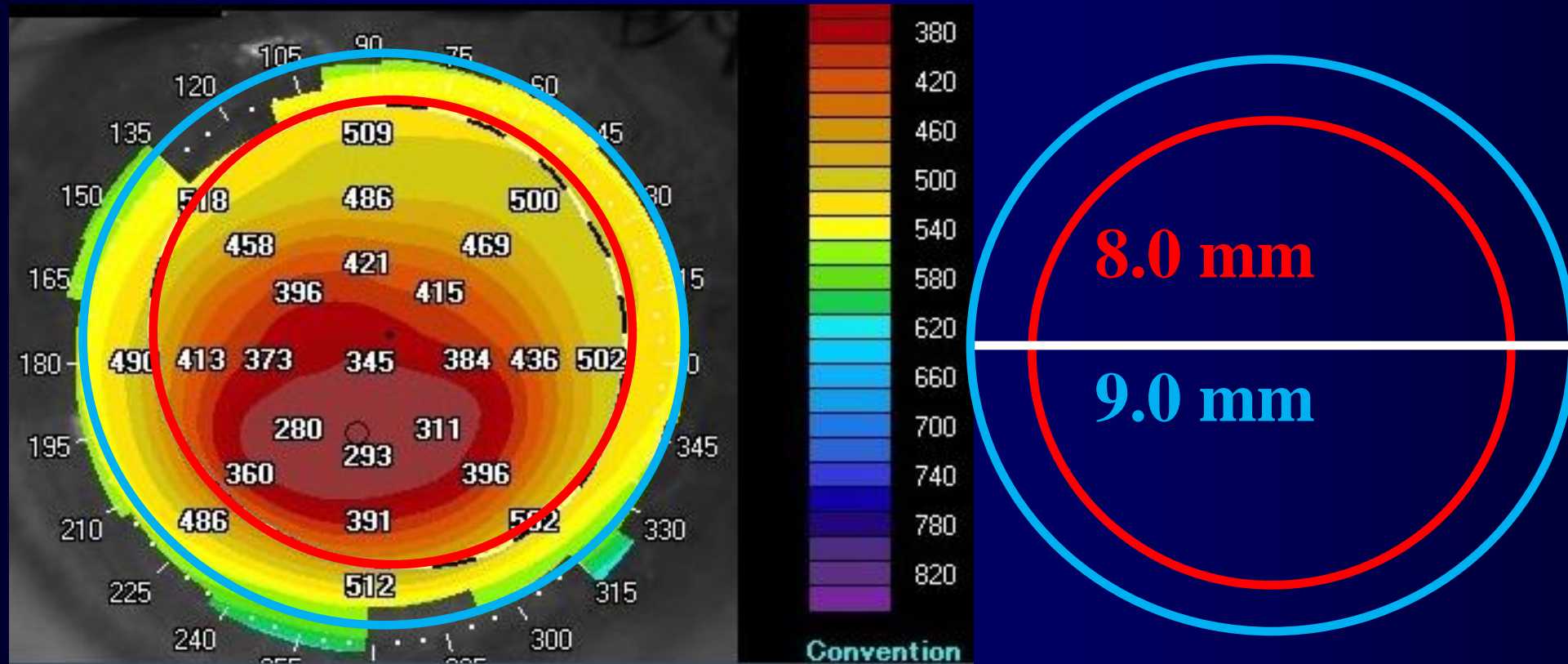
**BASSO**

Errore Rifrattivo



# DALK 9.0 mm

Lembi Grandi (9.0 vs 8.0 mm)  
INCLUDONO TUTTA L'ECTASIA



# DALK 9.0 mm

## Immunologic Stromal Rejection After Deep Anterior Lamellar Keratoplasty With Grafts of a Larger Size (9 mm) for Various Stromal Diseases

*Giuseppe Giannaccare, MD, PhD,\* Jayne S. Weiss, MD,† Laura Sapigni, MD,‡§ Cristina Bovone, MD,‡§  
Leila Mattioli, MD,‡§ Emilio C. Campos, MD,\* and Massimo Busin, MD‡§¶*

*(Cornea 2018;37:967–972)*

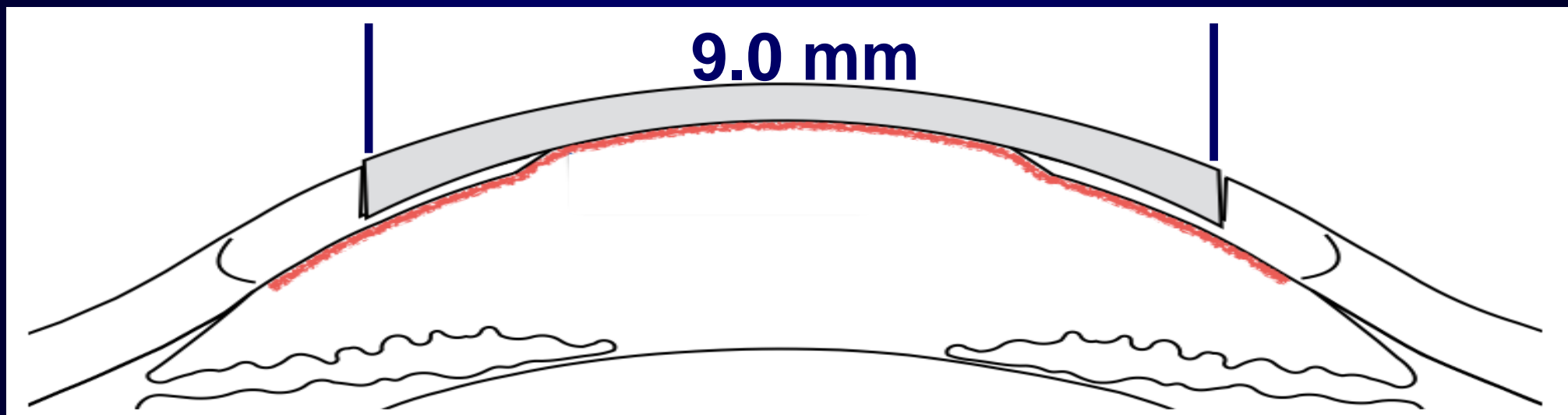
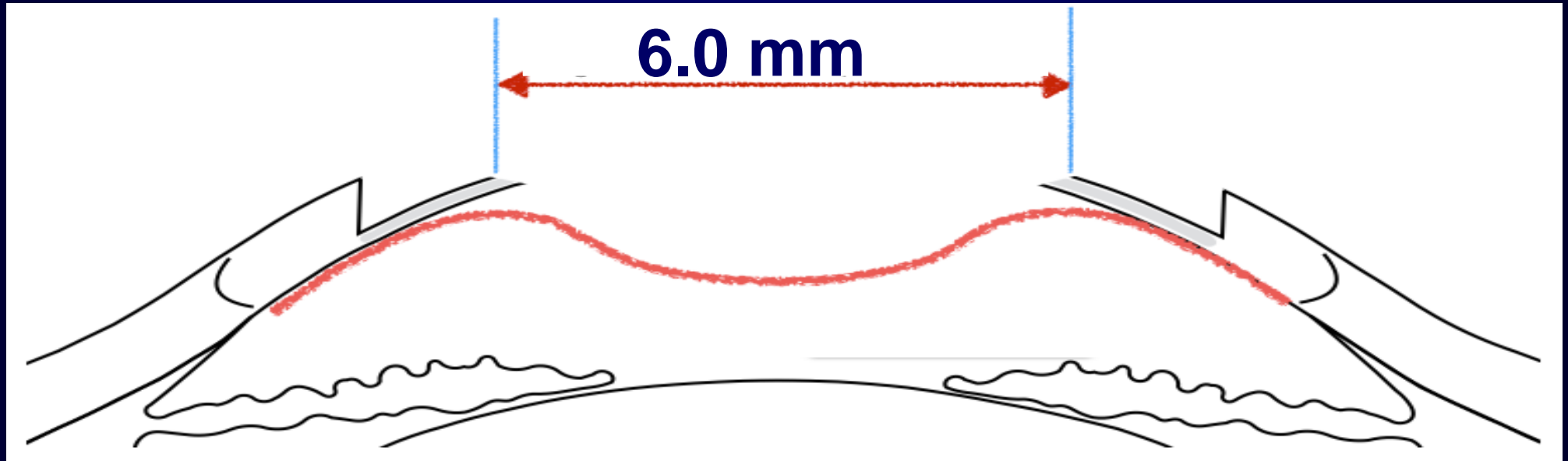
# DALK 9.0 mm

## OBIEZIONI !!!

- **La Conversione** a PK  
Richiede un lembo di **9.0 mm**
- **La Bolla** Raramente è più  
Grande di **7.5-8.0 mm**

**2014**

# DALK 9.0 mm

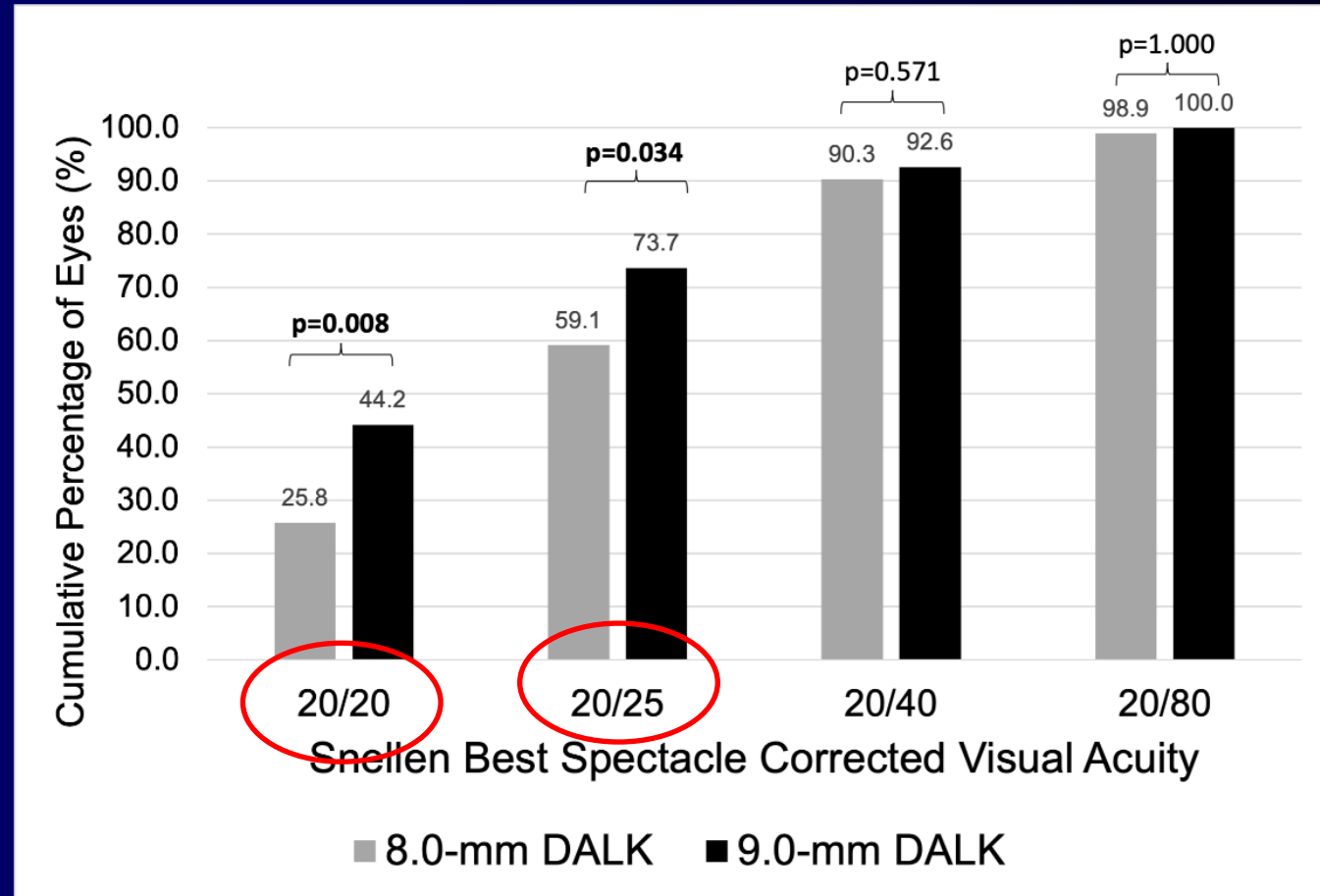




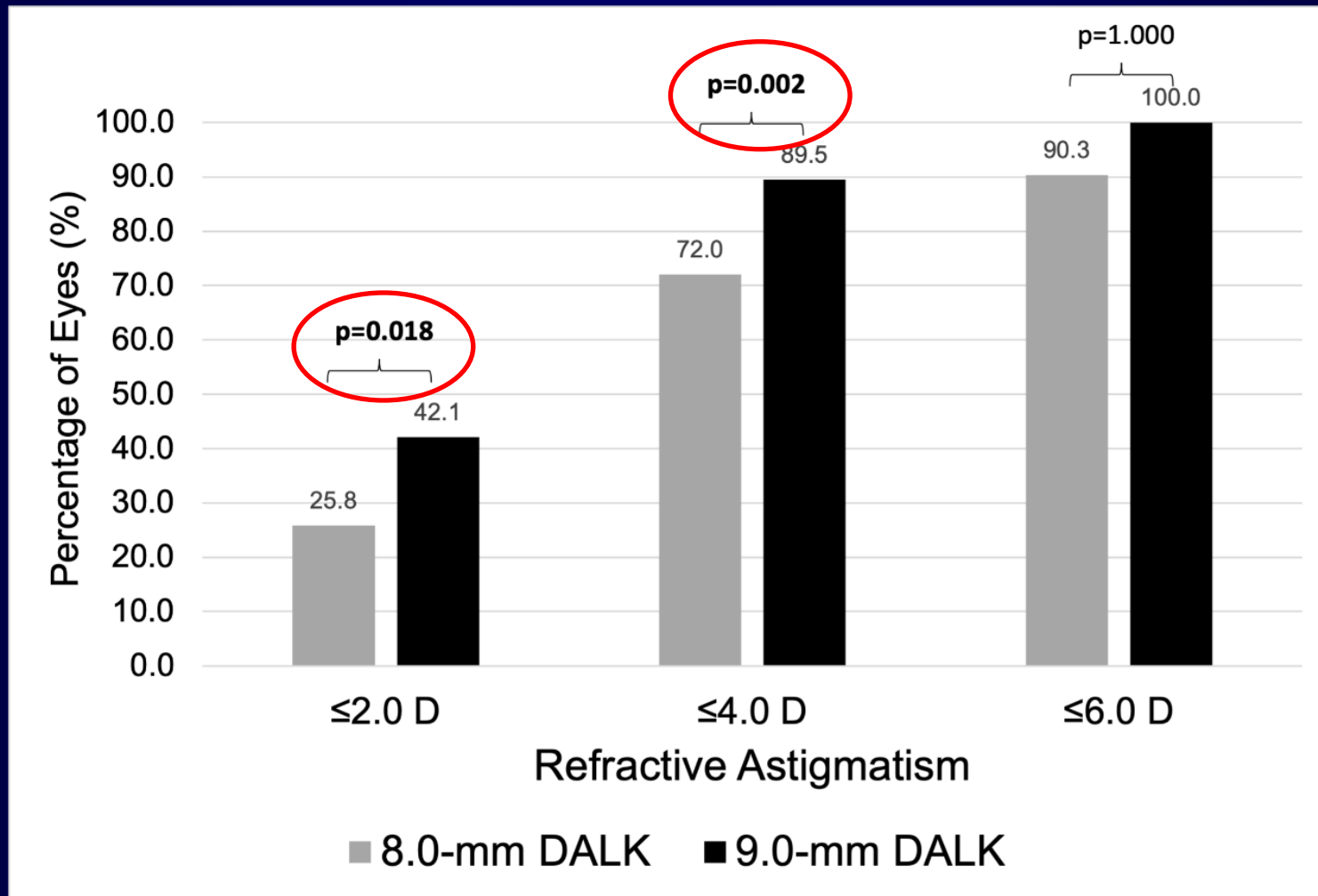
**DALK 9.0 mm**

# 9.0 mm vs. 8.0 mm DALK

Per Valori di AV  
Elevati  
9mm >> 8mm  
DALK!



# 9.0 mm vs. 8.0 mm DALK



# DALK 9.0 mm

2014

> [JAMA Ophthalmol.](#) 2014 Nov;132(11):1369-71. doi: 10.1001/jamaophthalmol.2014.2756.

## Small-bubble deep anterior lamellar keratoplasty technique

Vincenzo Scordia <sup>1</sup>, Jacqueline Beltz <sup>2</sup>, Massimo Busin <sup>3</sup>

2017

> [Ophthalmology.](#) 2017 Jul;124(7):1072-1080. doi: 10.1016/j.ophtha.2017.02.011. Epub 2017 Mar 20.

## Large (9 mm) Deep Anterior Lamellar Keratoplasty with Clearance of a 6-mm Optical Zone Optimizes Outcomes of Keratoconus Surgery

Massimo Busin <sup>1</sup>, Pia Leon <sup>2</sup>, Yoav Nahum <sup>3</sup>, Vincenzo Scordia <sup>4</sup>

2020

> [Am J Ophthalmol.](#) 2020 Dec;220:9-18. doi: 10.1016/j.ajo.2020.07.009. Epub 2020 Jul 16.

## Five-year Outcomes of Converted Mushroom Keratoplasty from Intended Deep Anterior Lamellar Keratoplasty (DALK) Mandate 9-mm Diameter DALK as the Optimal Approach to Keratoconus

James Myerscough <sup>1</sup>, Harry Roberts <sup>2</sup>, Angeli Christy Yu <sup>3</sup>, Mohamed Elkadim <sup>4</sup>, Cristina Bovone <sup>3</sup>, Massimo Busin <sup>5</sup>



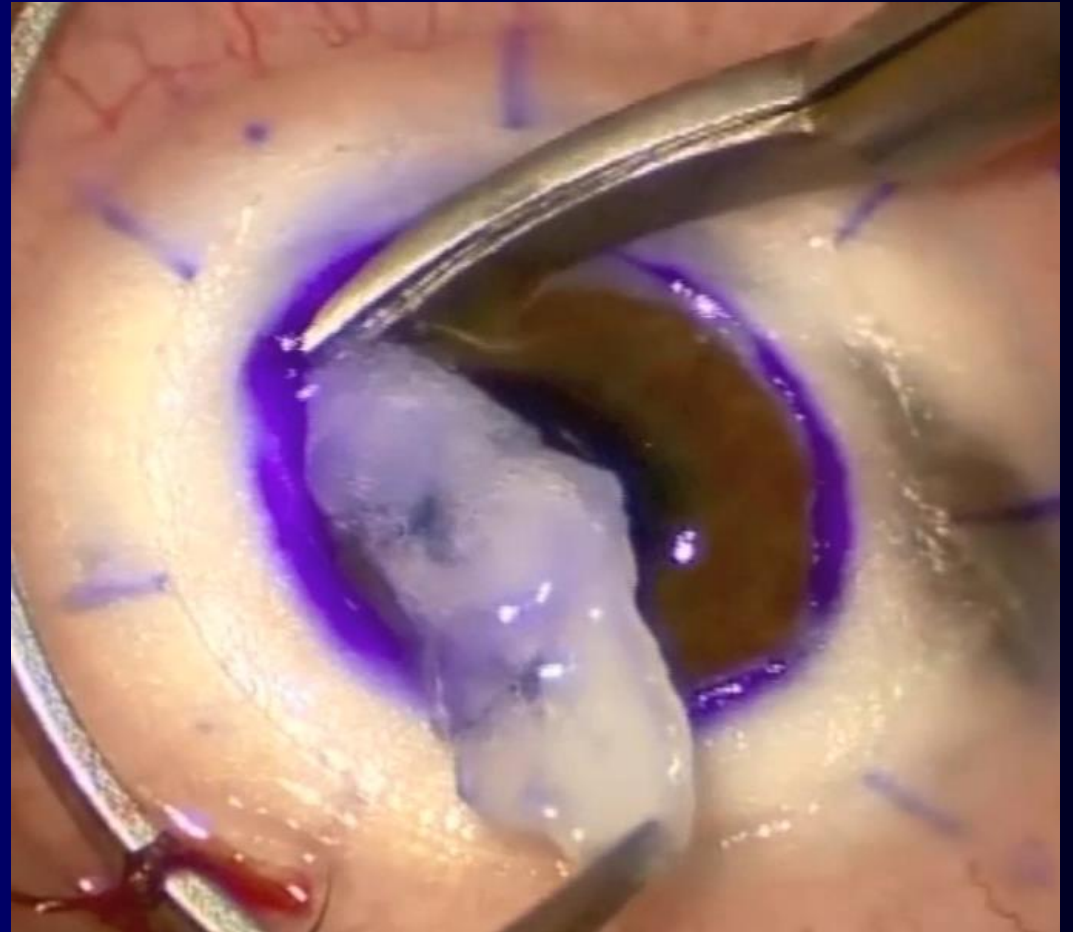
# 9.0 mm DALK

Che Sucedede...

Se E'

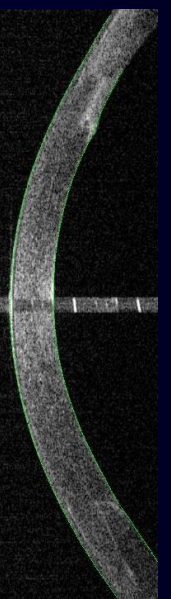
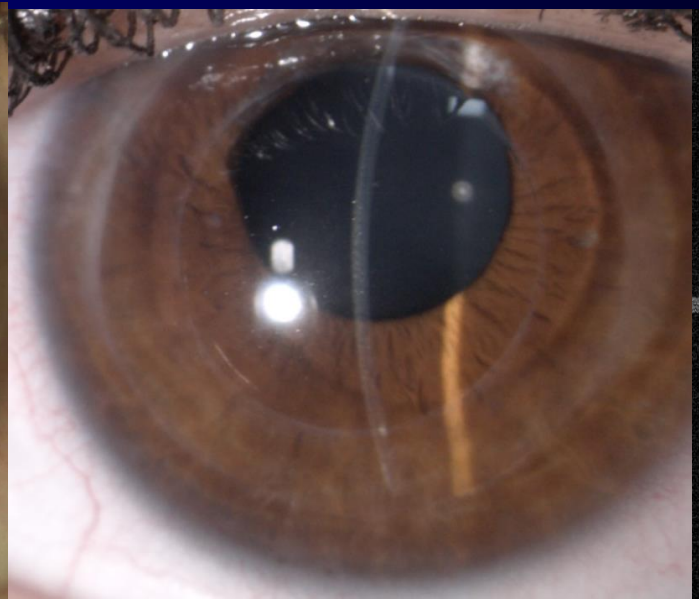
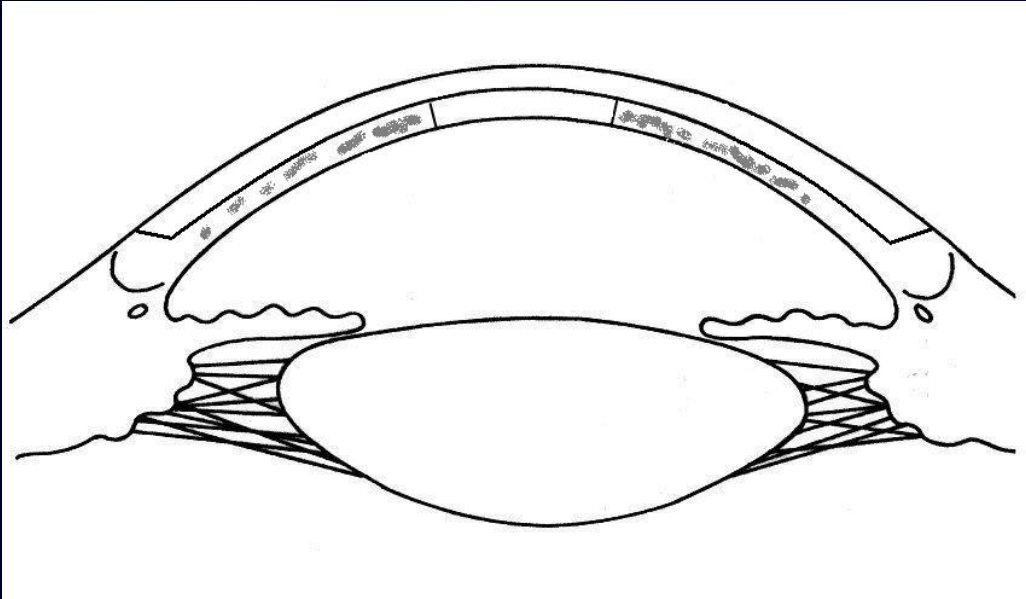
Necessario

Convertire???



**2004**

# PK “a FUNGO”



**LK ANTERIORE= “CAPPELLO”**  
(spessore =  $\pm 300 \mu\text{m}$ ; diametro = 9 mm)

**LK POSTERIORE = “STELO”**  
(spessore =  $\pm 250 \mu\text{m}$ ; diametro = 6 mm)

**2004**

# PK “a FUNGO”

CONCETTO: “RISERVA ENDOTELIALE”

AREA DI RESIDUO ENDOTELIO **SANO**

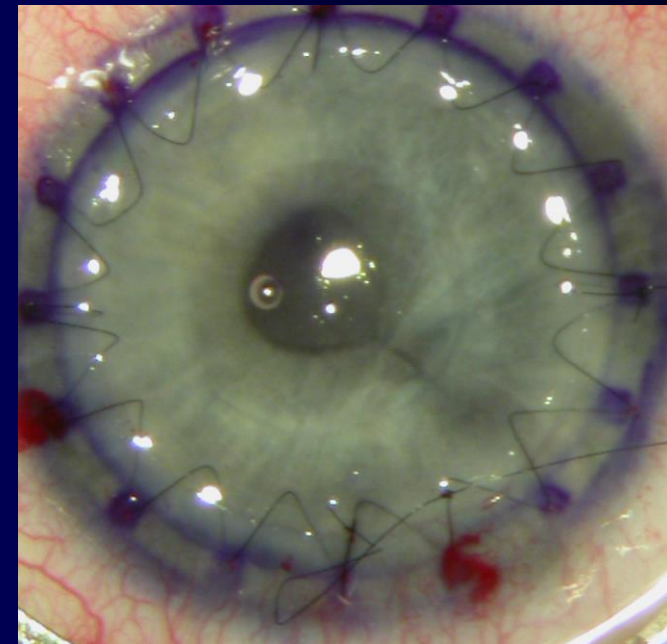
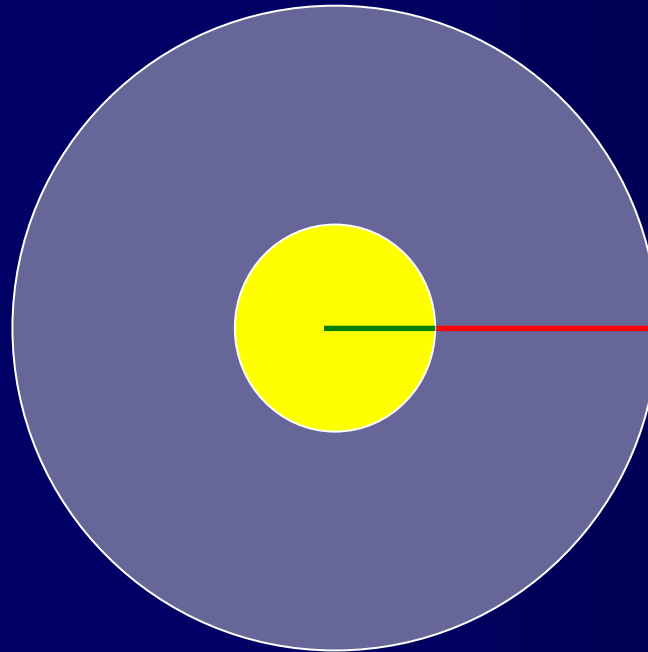
$$(6^2 \pi) - (3^2 \pi)$$



$$36 \pi - 9 \pi$$



$$27 \pi \text{ mm}^2$$



**>75% !!!**

# DALK VS. MK

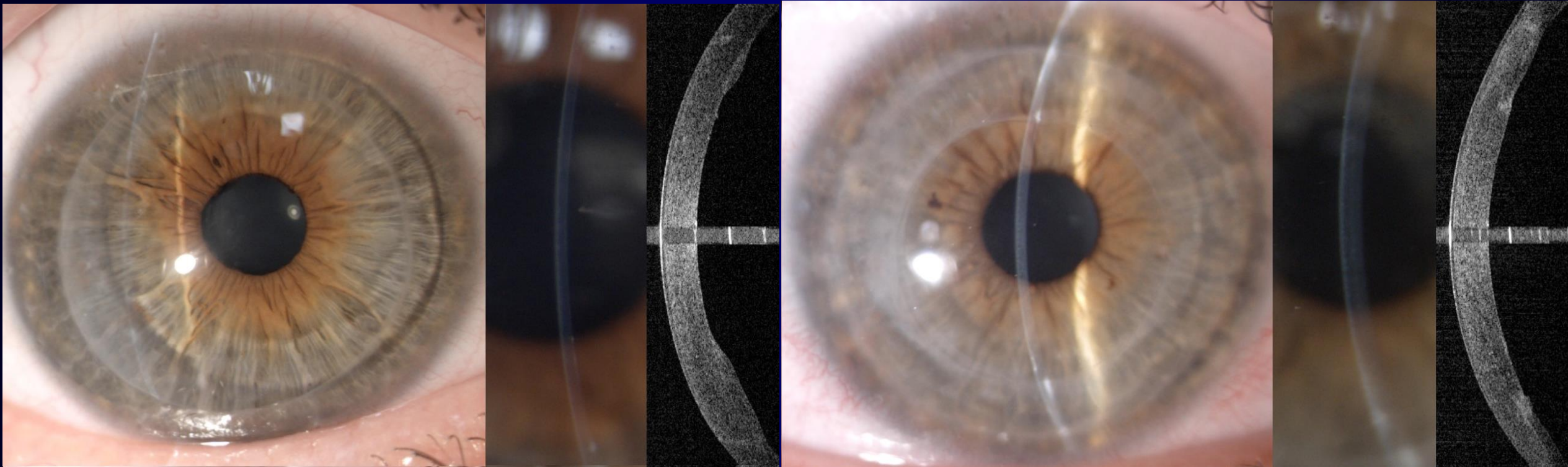
> [Am J Ophthalmol.](#) 2020 Dec;220:9-18. doi: 10.1016/j.ajo.2020.07.009. Epub 2020 Jul 16.

## **Five-year Outcomes of Converted Mushroom Keratoplasty from Intended Deep Anterior Lamellar Keratoplasty (DALK) Mandate 9-mm Diameter DALK as the Optimal Approach to Keratoconus**

James Myerscough <sup>1</sup>, Harry Roberts <sup>2</sup>, Angeli Christy Yu <sup>3</sup>, Mohamed Elkadim <sup>4</sup>,  
Cristina Bovone <sup>3</sup>, Massimo Busin <sup>5</sup>



# 5Y MK vs DALK PER KC

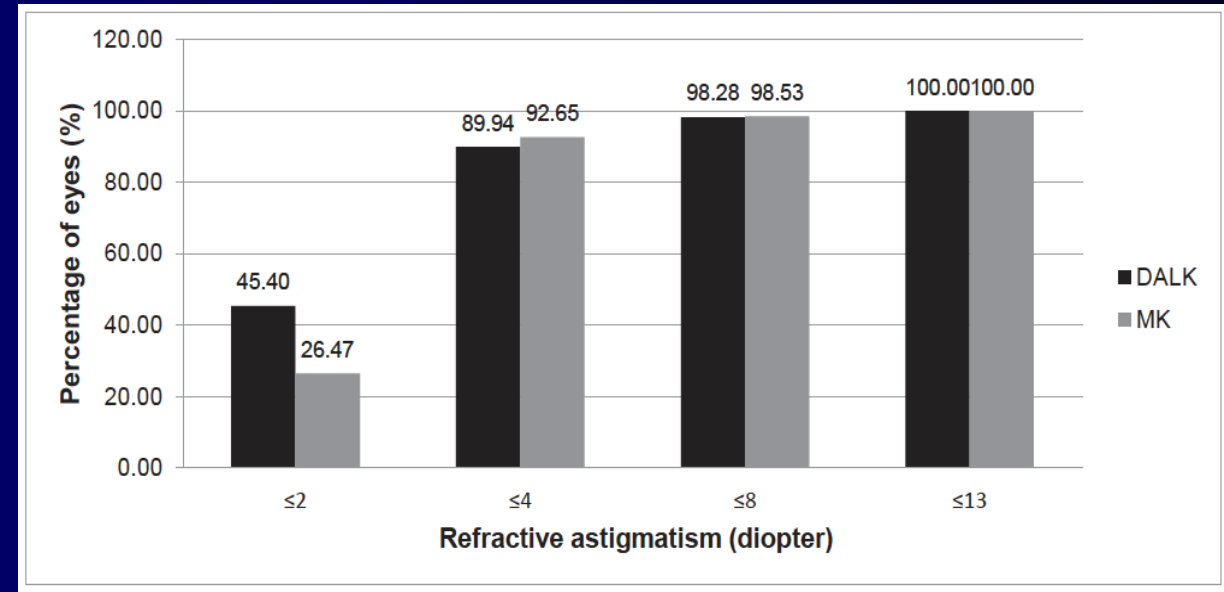
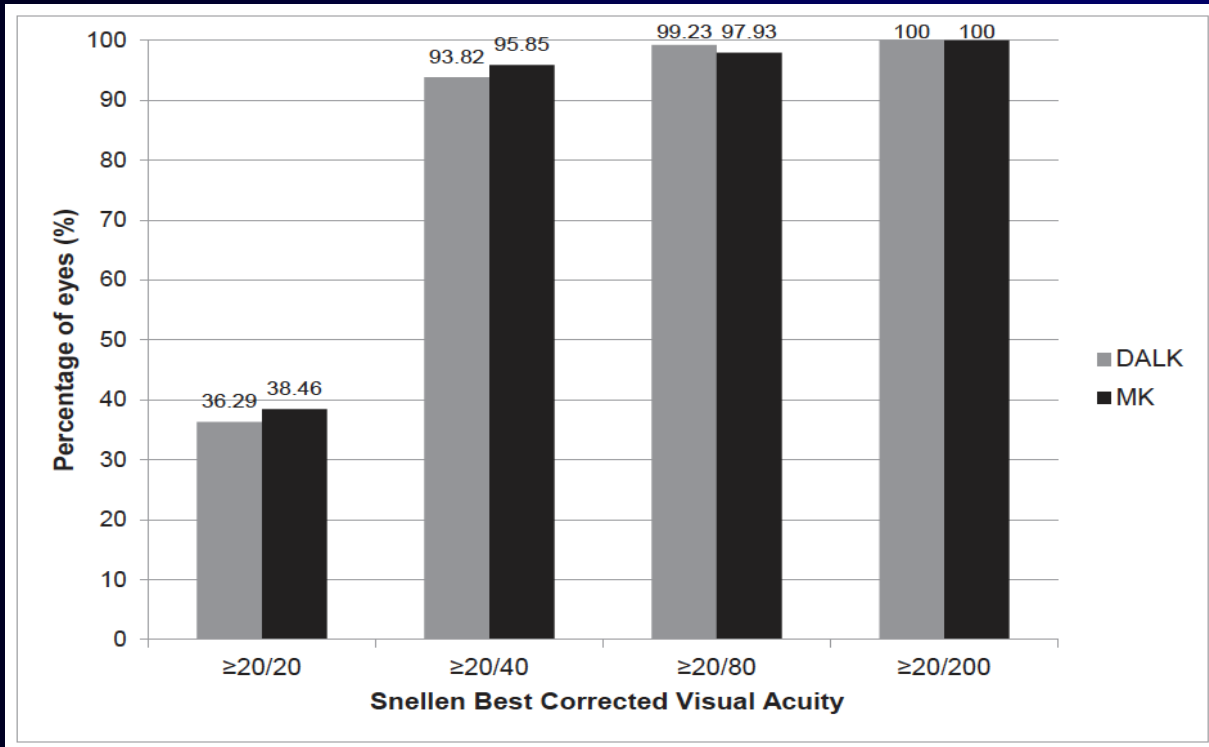


**DALK n=416**

**MK n=68**

# 5Y MK vs DALK PER KC

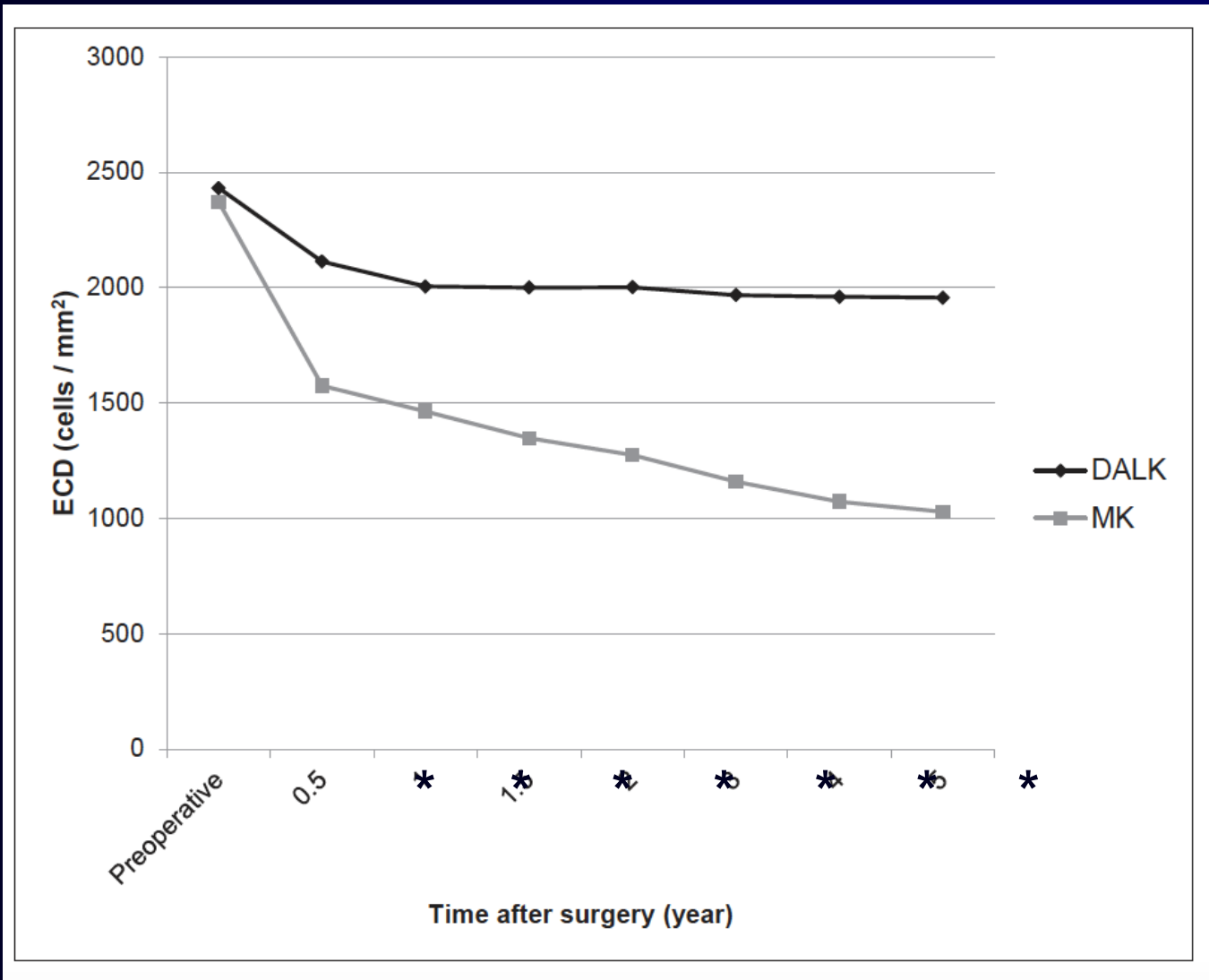
## BSCVA RA



**MK = DALK**

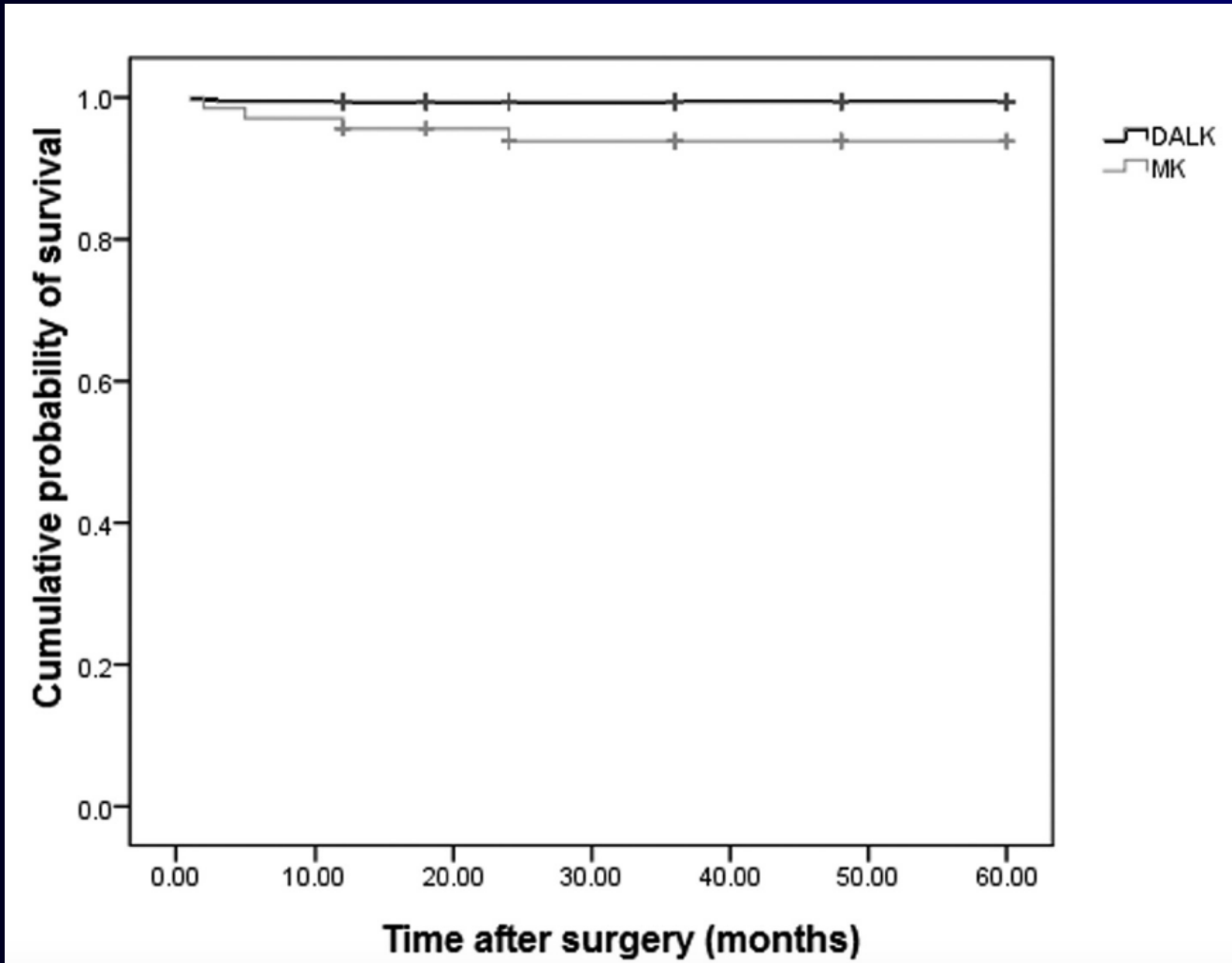
**MK = DALK**

# 5Y MK vs DALK PER KC



**\*P<0.001**

# 5Y MK vs DALK PER KC



**5 Anni  
Sopravvivenza**

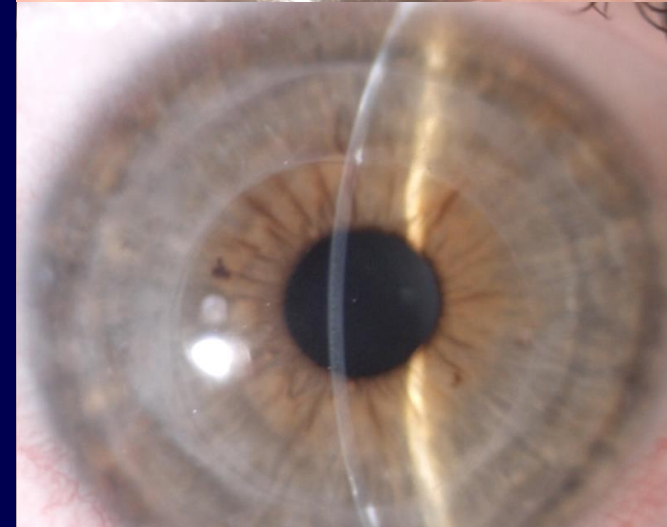
**DALK: 99%**

**MK: 94%**

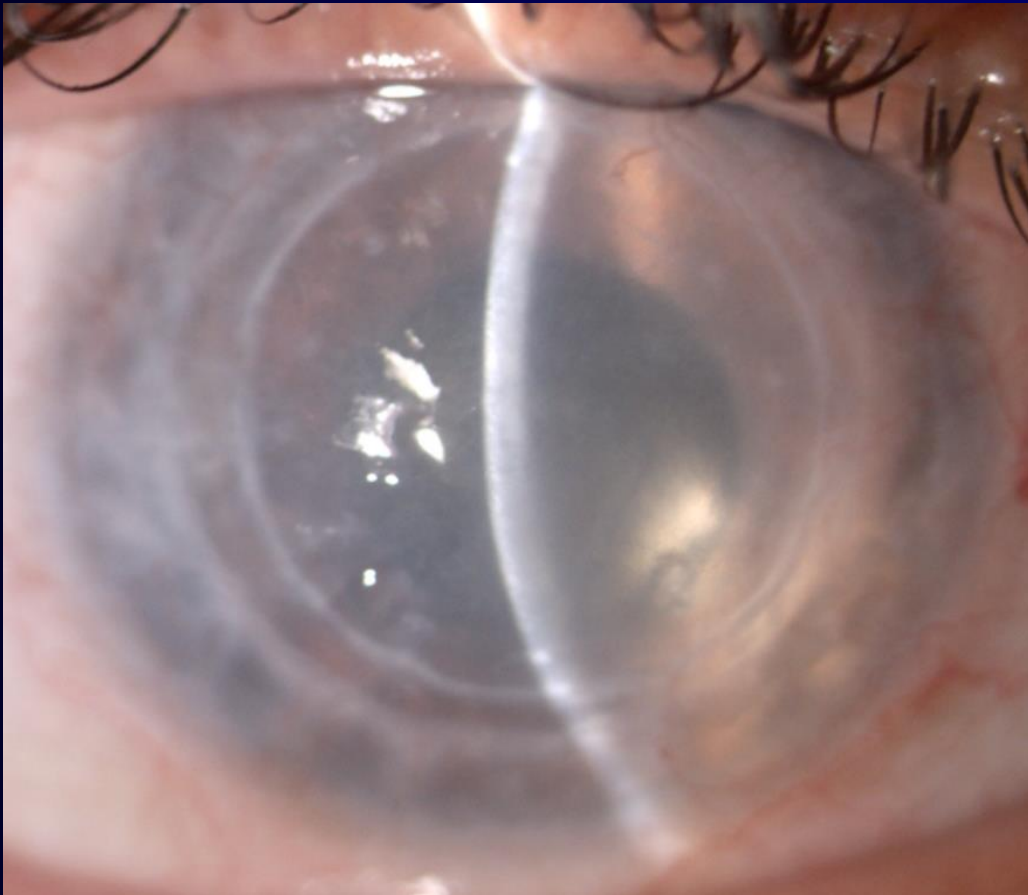


# CHERATOPLASTICA LAMELLARE A LARGO DIAMETRO (9mm)

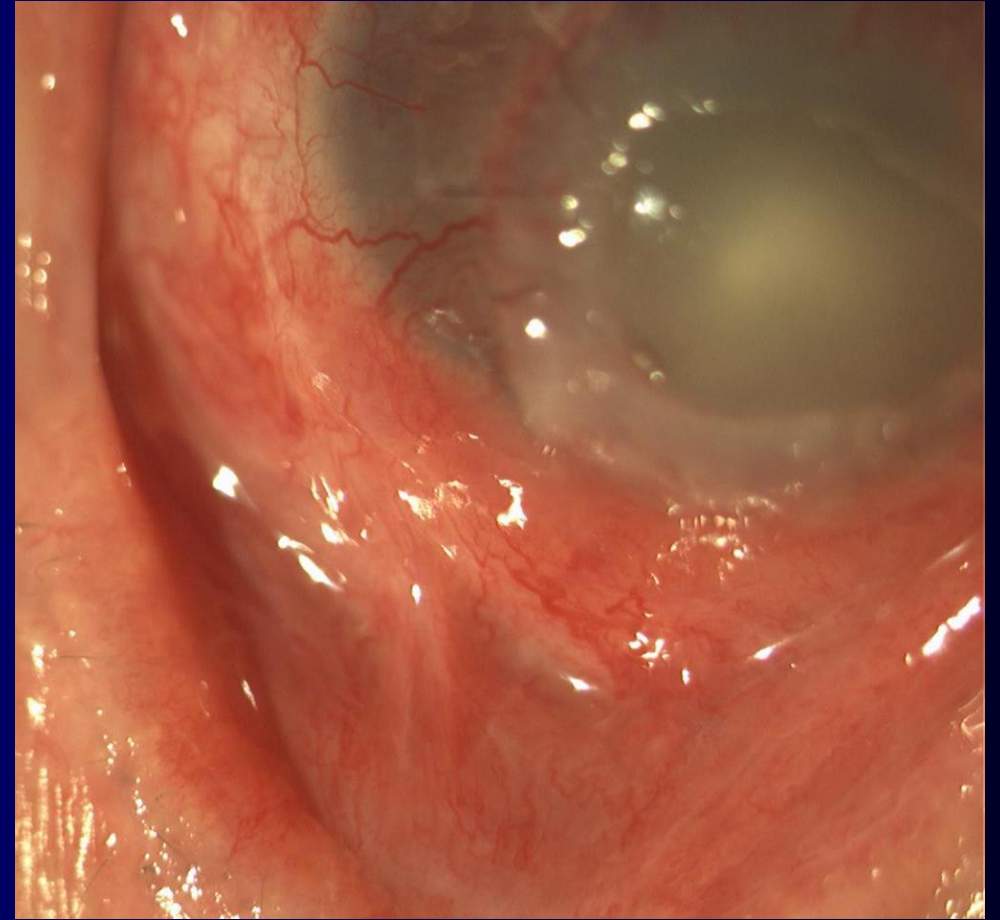
- Tentare la DALK (Big-Bubble)
- Successo della DALK > 80%
- Convertire in PK a Fungo nei Restanti Casi
- Sopravvivenza a 10 anni  
**>90% !!!**



# TUTTORA PROBLEMATICI



**SCOMPENSI MULTIPLI**

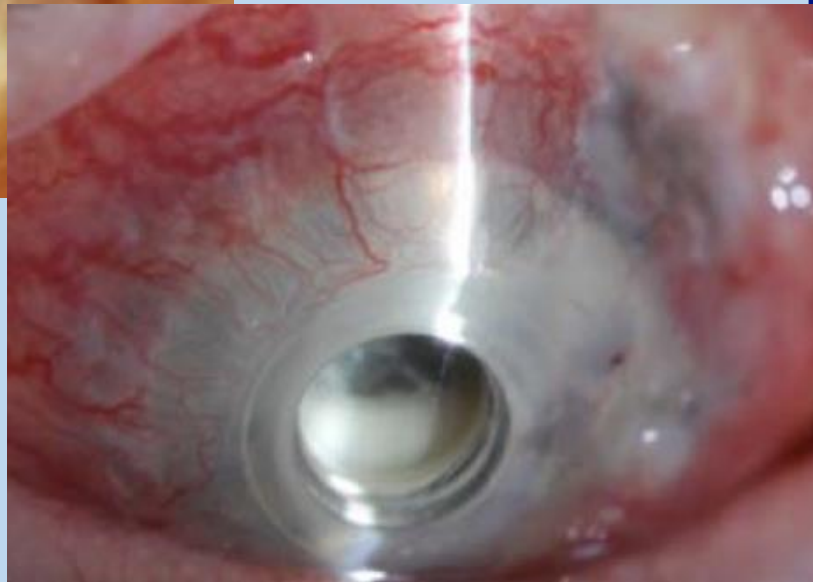
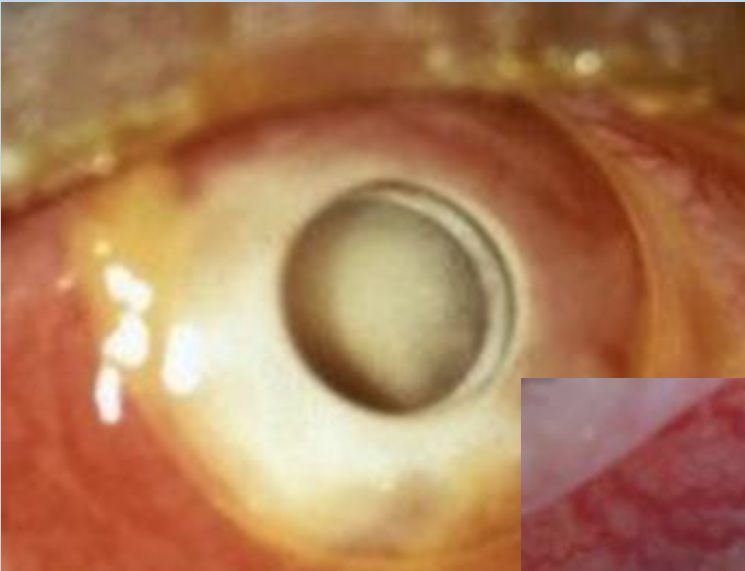


**PEMFIGOIDE**

**IL FUTURO ???**

# CORNEA ARTIFICIALE

***Plastica in Contatto con Acqueo !!!***



## COMPLICAZIONI INTRAOCULARI

**!!!**

**65% Membrane Retroprotesiche**

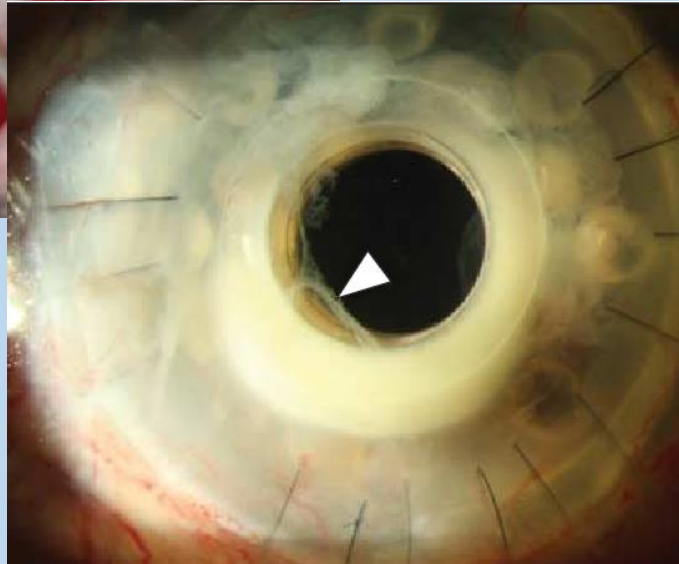
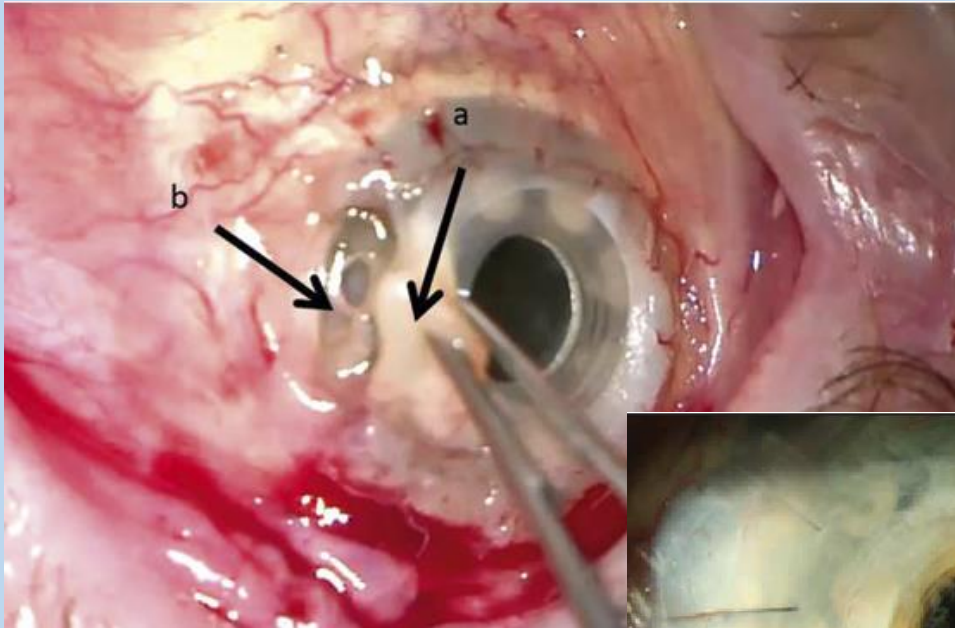
**72% Glaucoma**

**19% Distacco di Retina**

**13% Endoftalmite**

# CORNEA ARTIFICIALE

## *Esposizione Esterna*



**COMPLICANZE DI  
SUPERFICIE**

**!!!**

**Downgrowth Epiteliale  
Colliquazione Corneale  
Infezioni**



# CORNEA ARTIFICIALE

*Recupero Visivo???*

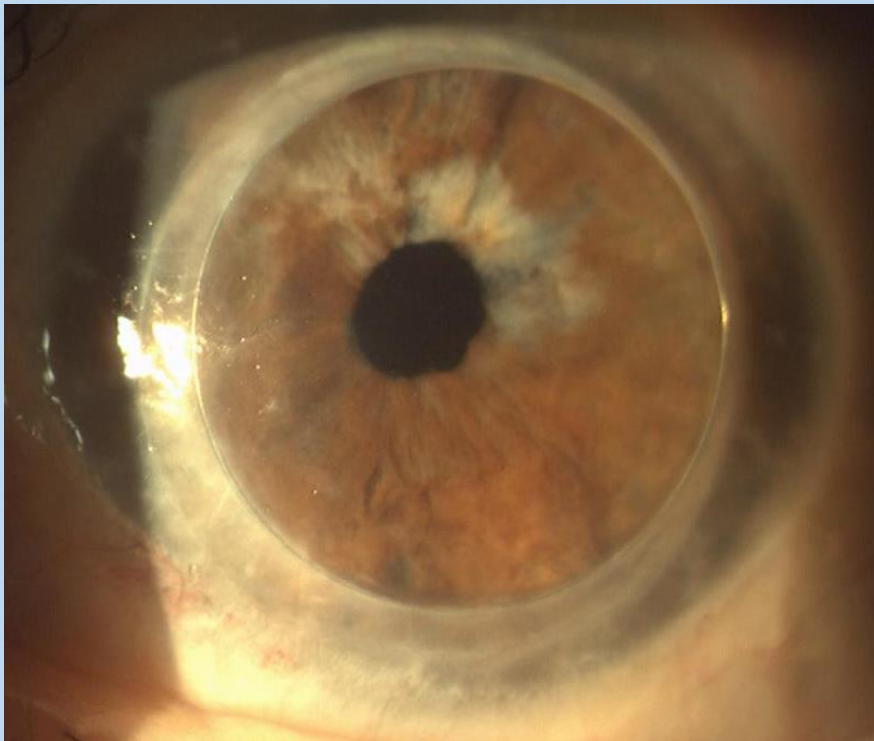
Fino al 50% dei Pazienti

**LEGALMENTE CIECHI**

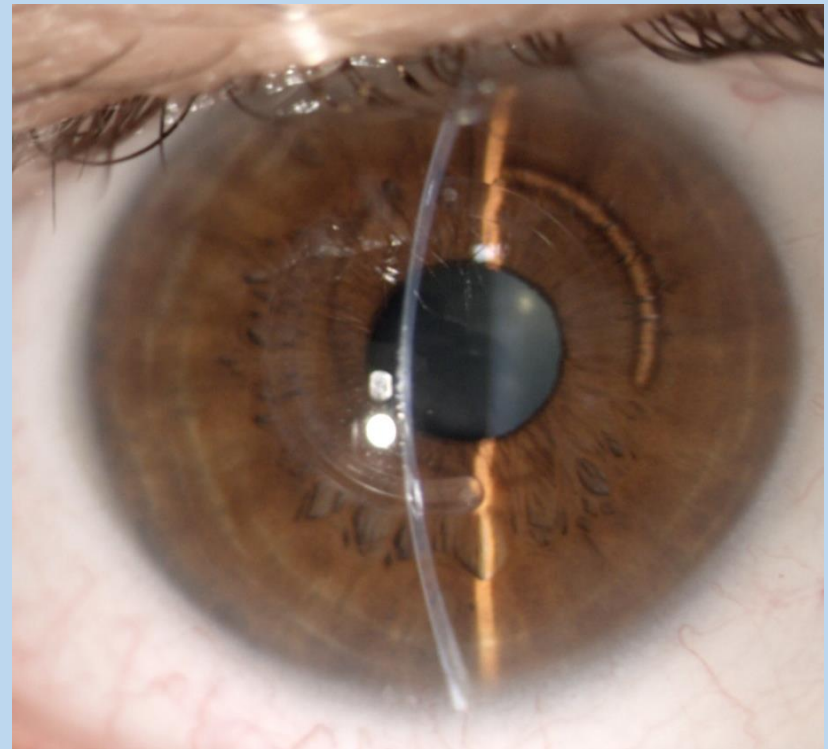
Acuità Visiva  $< 1/10 = 20/200$

entro 1 anno dall'Impianto

# **SOLUZIONE BIOCOMPATIBILE IMPIANTO INTRACORNEALE**

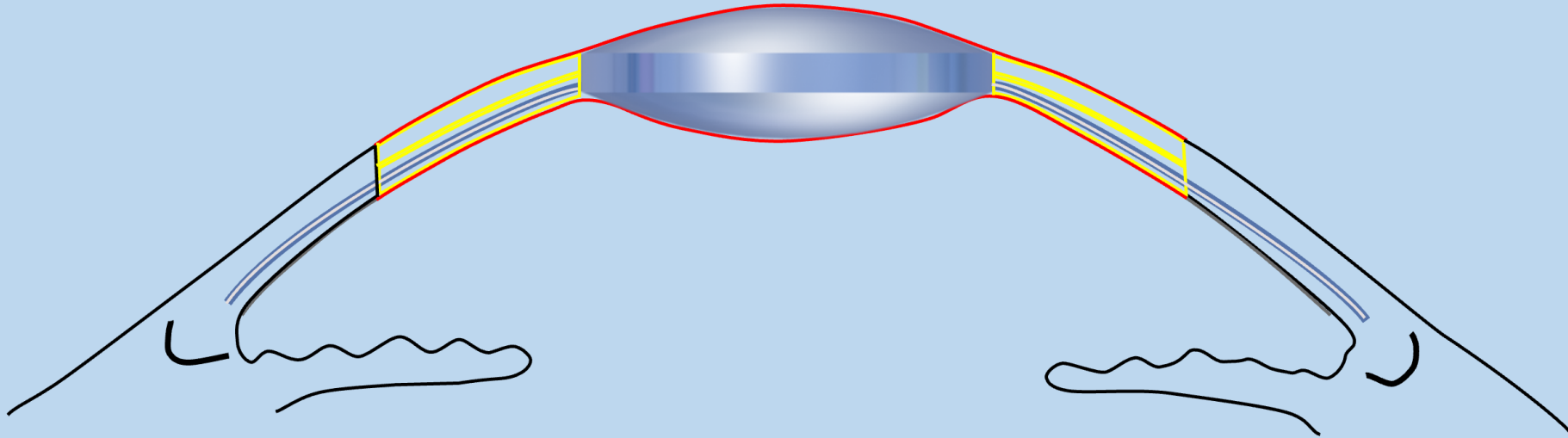


**Anello di Titanio  
(15 anni postop)**

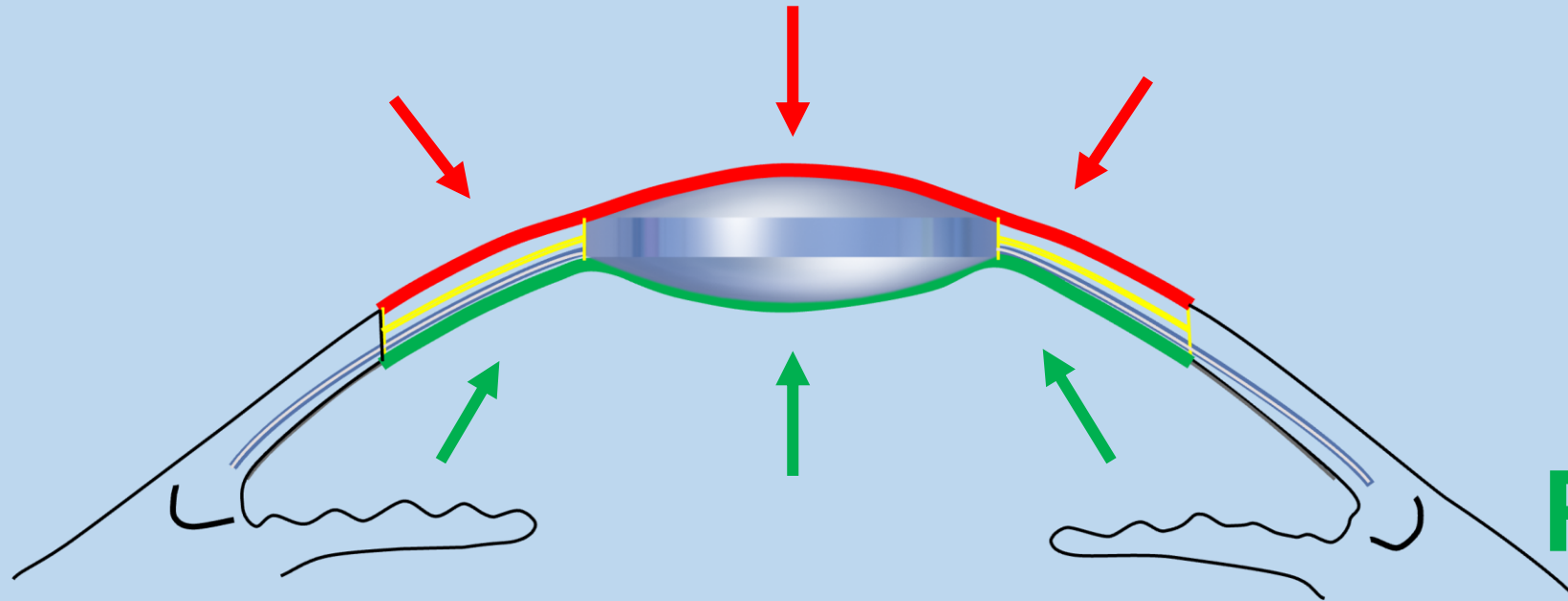


**Segmenti di Anello in PMMA  
Intracorneali (10 anni postop)**

**CORNEA IBRIDA  
BIOINGEGNERIZZATA  
SCAFFOLD DI TESSUTO CORNEALE  
+  
DEVICE INTRACORNEALE**



# CORNEA IBRIDA BIOINGEGNERIZZATA



**Anteriore**

**&**

**Posteriore**

**Involucri Biologici**

**BIOCOMPATIBILITA' !!!**

2023

# INTRA-KER





# 2023



*Ministero della Salute*

Direzione generale della ricerca e dell'innovazione in sanità

**PNRR: M6/C2\_CALL 2022 Full Proposal**



**Finanziato  
dall'Unione europea**

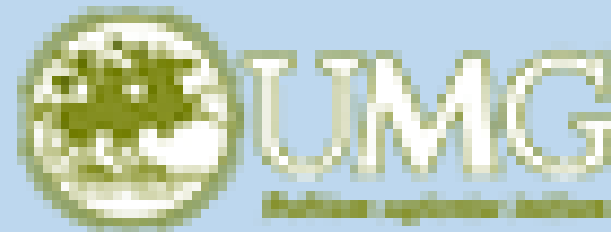
**NextGenerationEU**

**Project Code:** PNRR-POC-2022-12376494

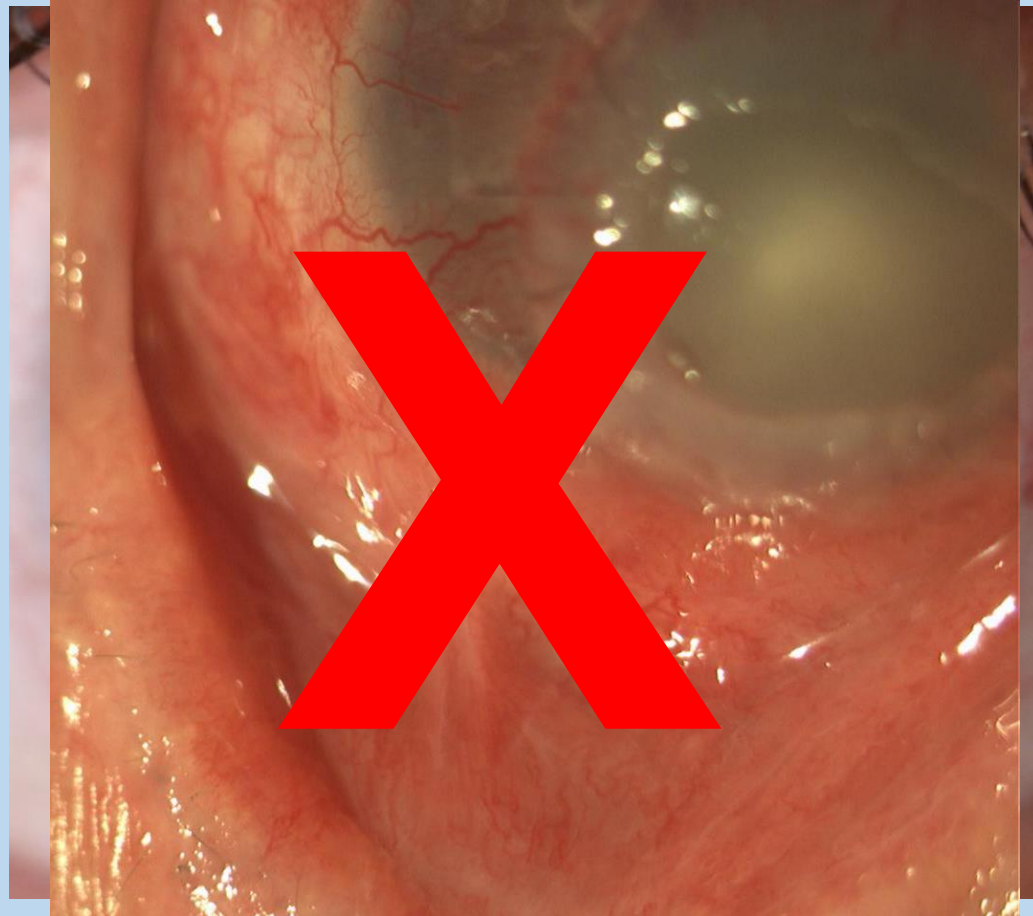
**Call section:** Proof of concept



**Università  
degli Studi  
di Ferrara**



# TUTTORA PROBLEMATICI



PEMFIGOIDE E MALATTIE  
SCOMPENSI MULTIPLE  
SUPERFICIE OCULARE

# MELTING CORNEALE



**SOLUZIONE: GUNDERSEN FLAP**

# "SMART" GLASSES???



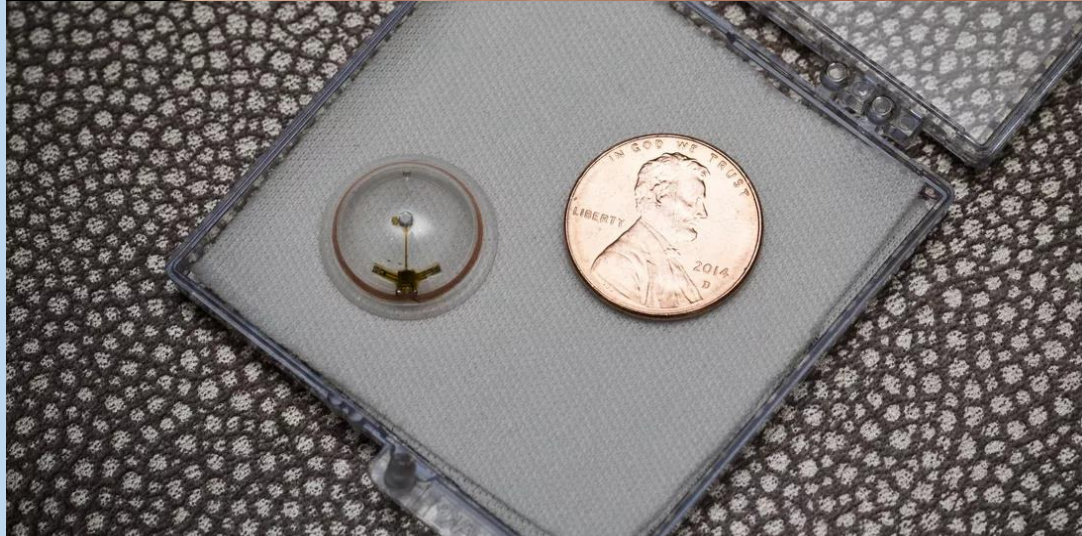
**PROJECT ARIA  
(FACEBOOK/ESSILUX)**



**GOOGLE GLASS**



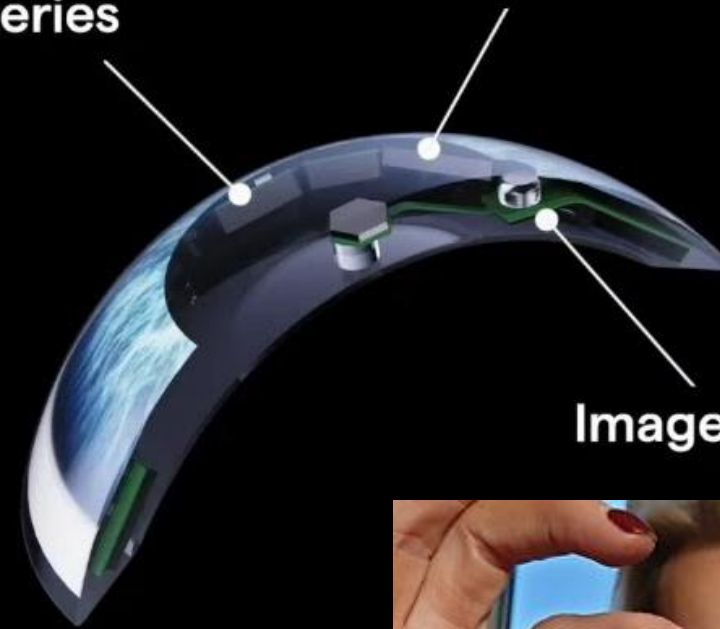
# "SMART" CONTACT LENS



Biosafe  
Batteries

Motion Sensors

Image Sensor

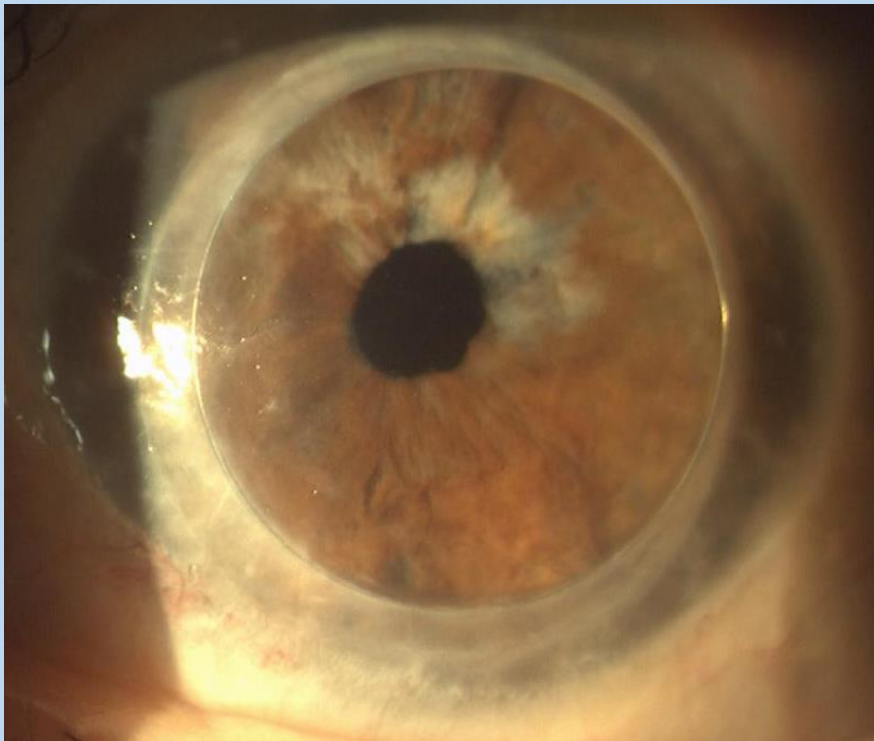


Mojo Vision

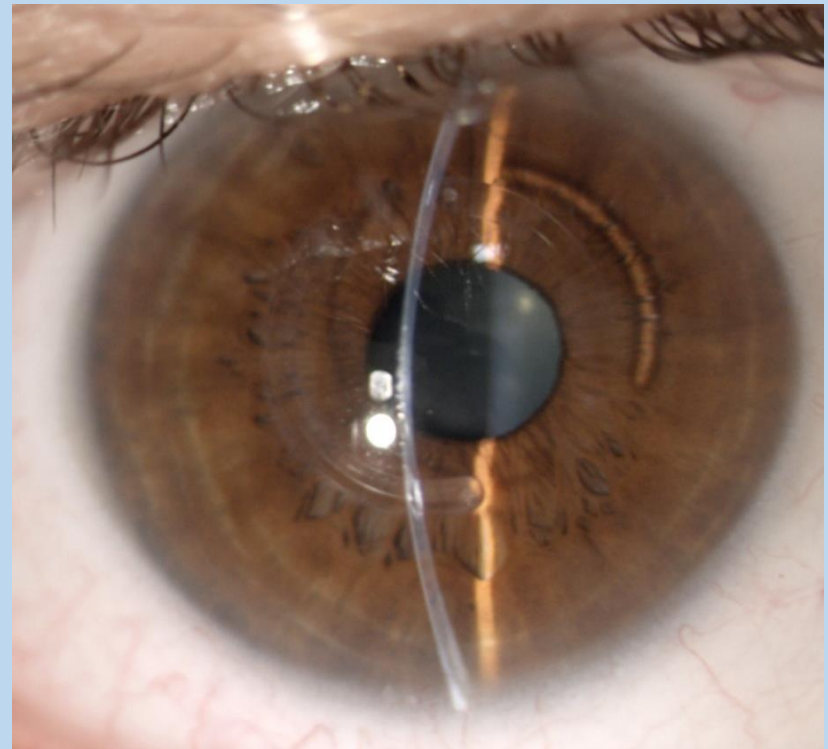




# **SOLUZIONE BIOCOMPATIBILE IMPIANTO INTRACORNEALE**

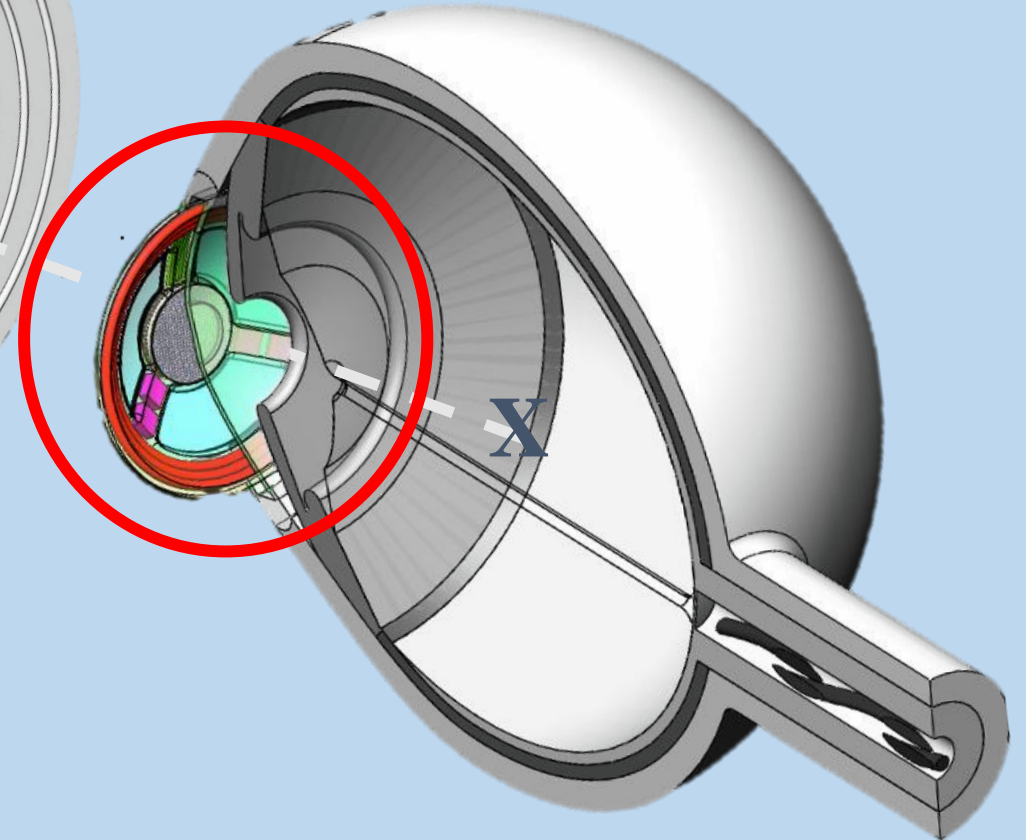
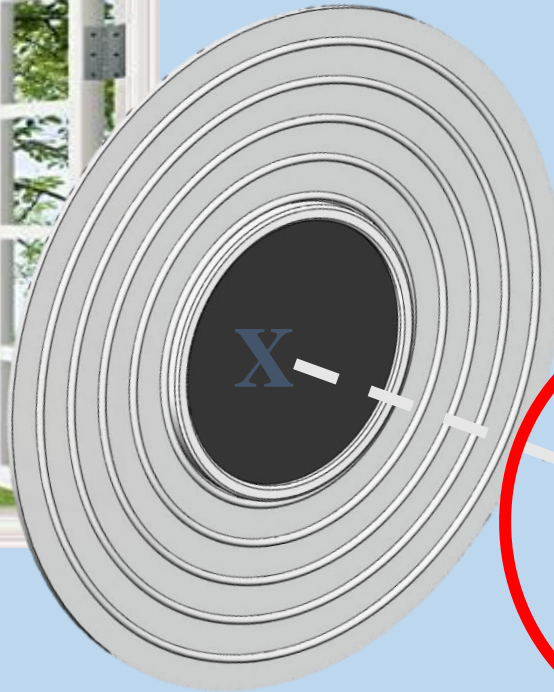


**Anello di Titanio  
(15 anni postop)**



**Segmenti di Anello in PMMA  
Intracorneali (10 anni postop)**

# "SMART" CORNEA



**INTRACORNEAL**  
**PROJECTOR !!!**



# GRAZIE

## Massimo Busin, MD



UNIVERSITÀ  
DEGLI STUDI  
DI FERRARA  
- EX LABORE FRUCTUS -



Ospedali  
Privati Forlì

