"Possibilità terapeutiche del cross-linking e delle cheratoplastiche lamellari"

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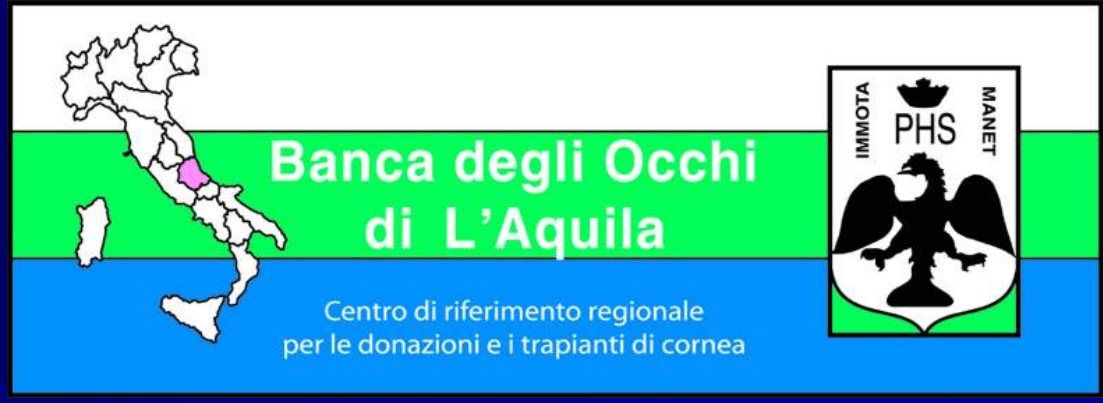
VII Corso S.I.B.O.
L'Aquila, 24 Novembre 2012

GENNAIO 2004
GIUGNO 2012



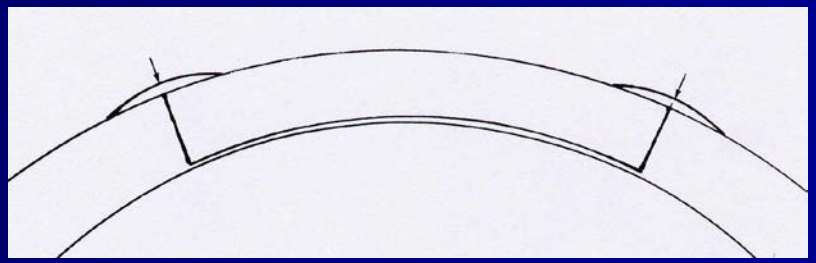
Quando la patologia corneale interessa solo alcuni strati corneali l'intervento di elezione è una

cheratoplastica lamellare

- ✓ **Anteriore**
- ✓ **Posteriore**

Cheratoplastica Lamellare (LK)

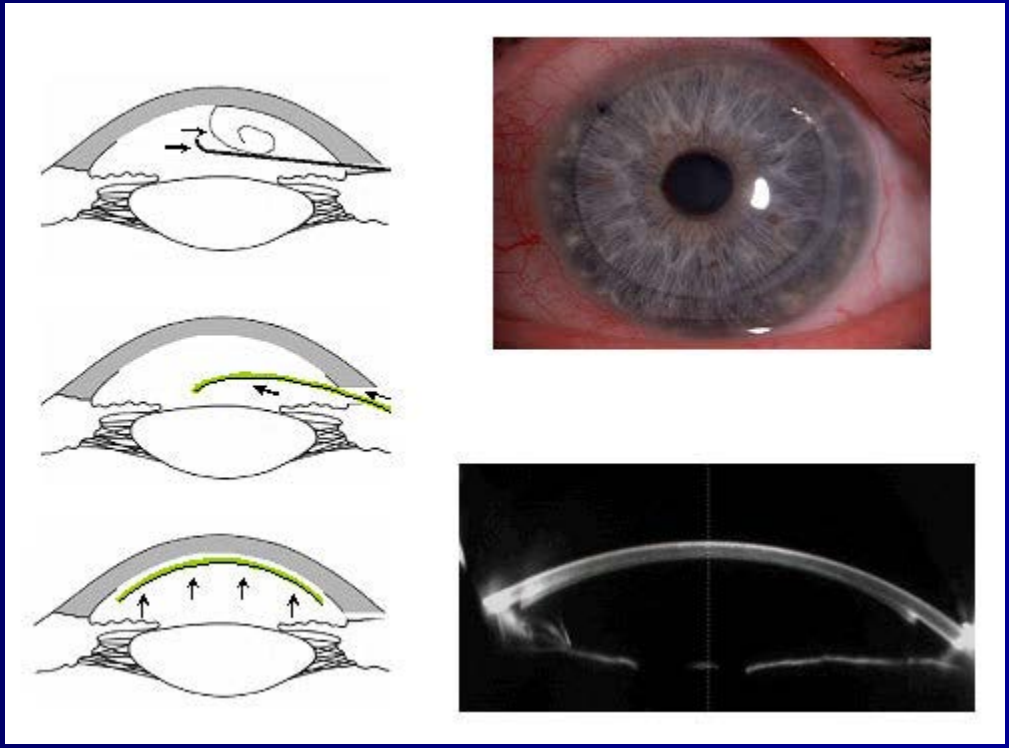
Consiste nella rimozione di alcuni strati di cornea, di spessore sufficiente per rimuovere il tessuto patologico, sostituendoli con tessuto corneale donatore



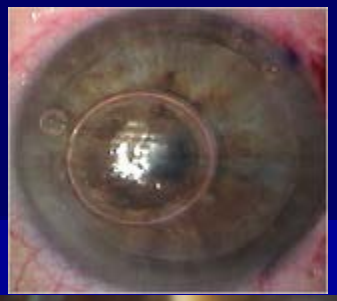
Cheratoplastica Lamellare Endoteliale (EK)

DSEK (Descemet's Stripping Endothelial Keratoplasty) - Frank Price

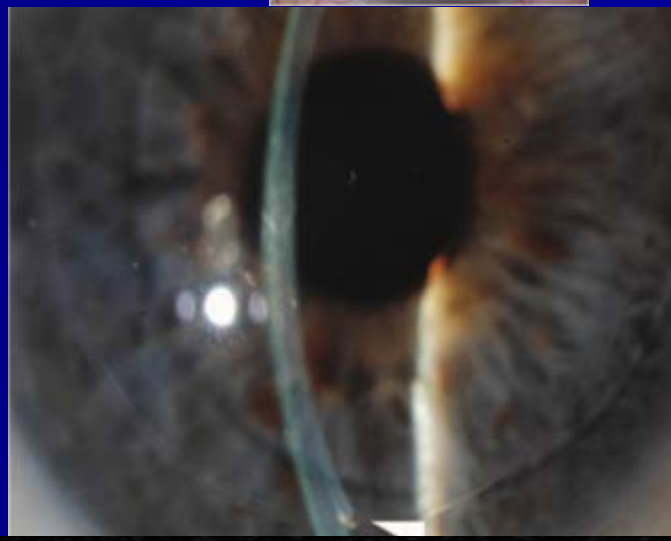
DSAEK (Descemet's Stripping Automated Endothelial Keratoplasty) - Mark Gorovoy

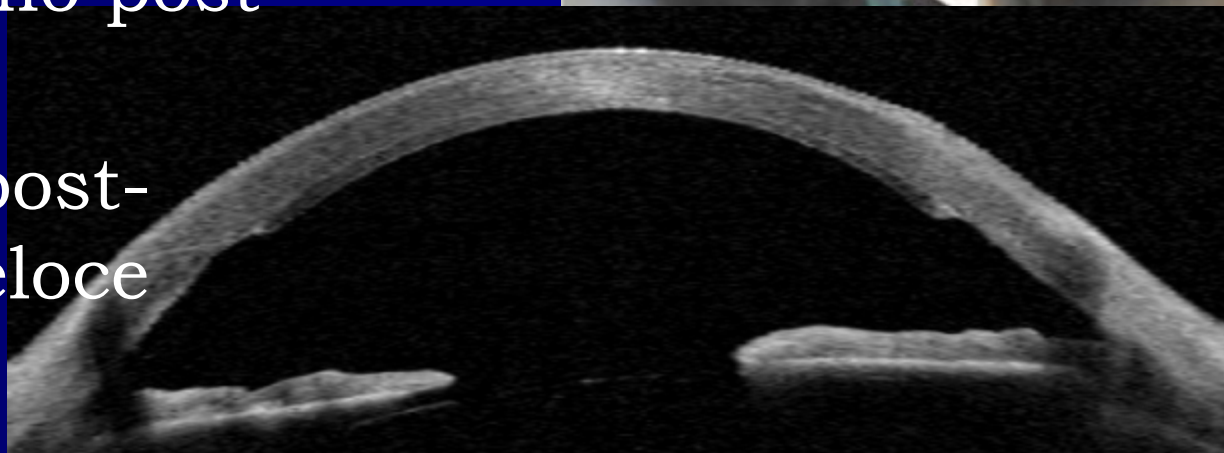


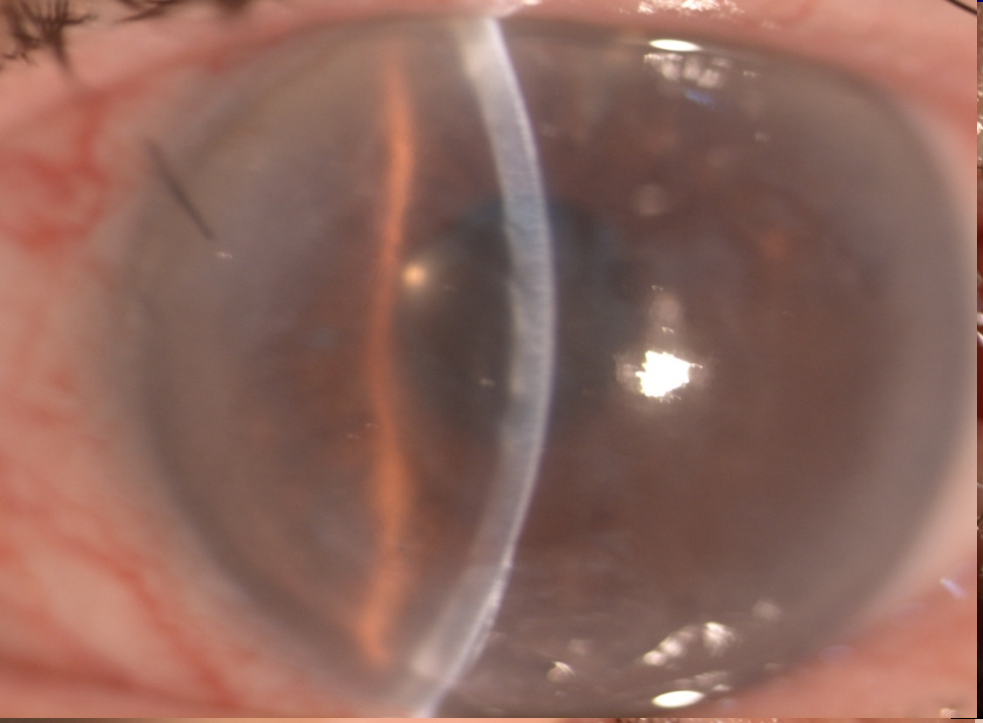
Cheratoplastica Lamellare Endoteliale (EK)

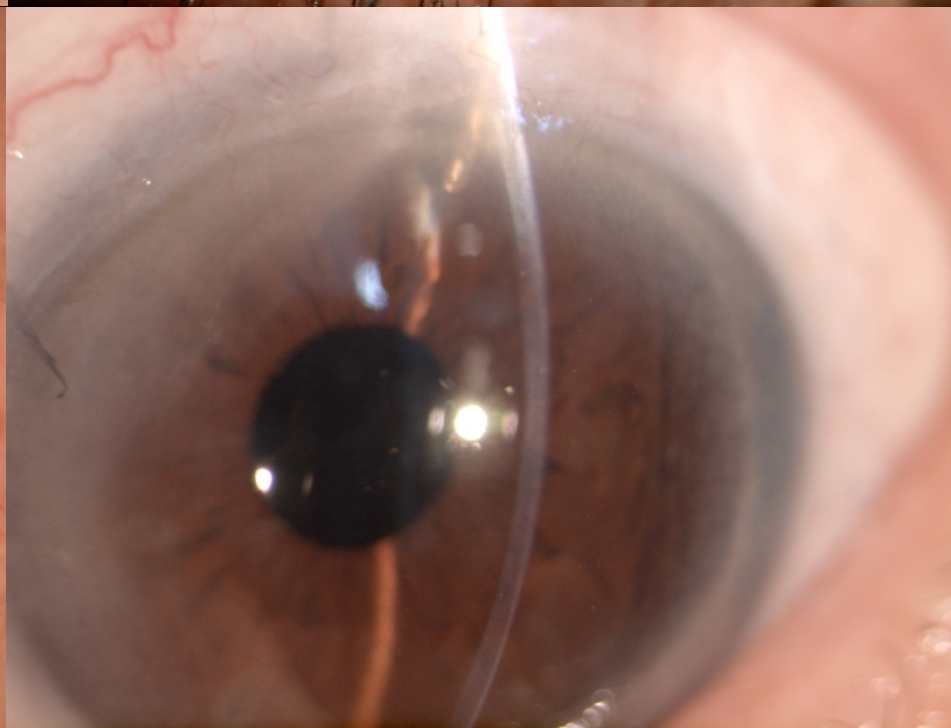


- ✓ minor rischio di infezioni post-operatorie
- ✓ minor rischio di rigetto del trapianto (7.5% nella EK contro i 13% della PK)
- ✓ miglior risultato rifrattivo con <astigmatismo post-operatorio
- ✓ recupero visivo post-intervento più veloce



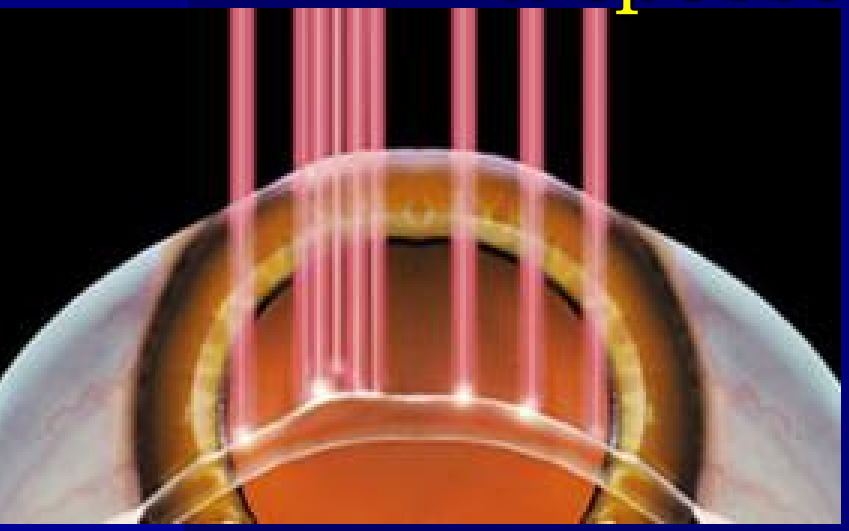




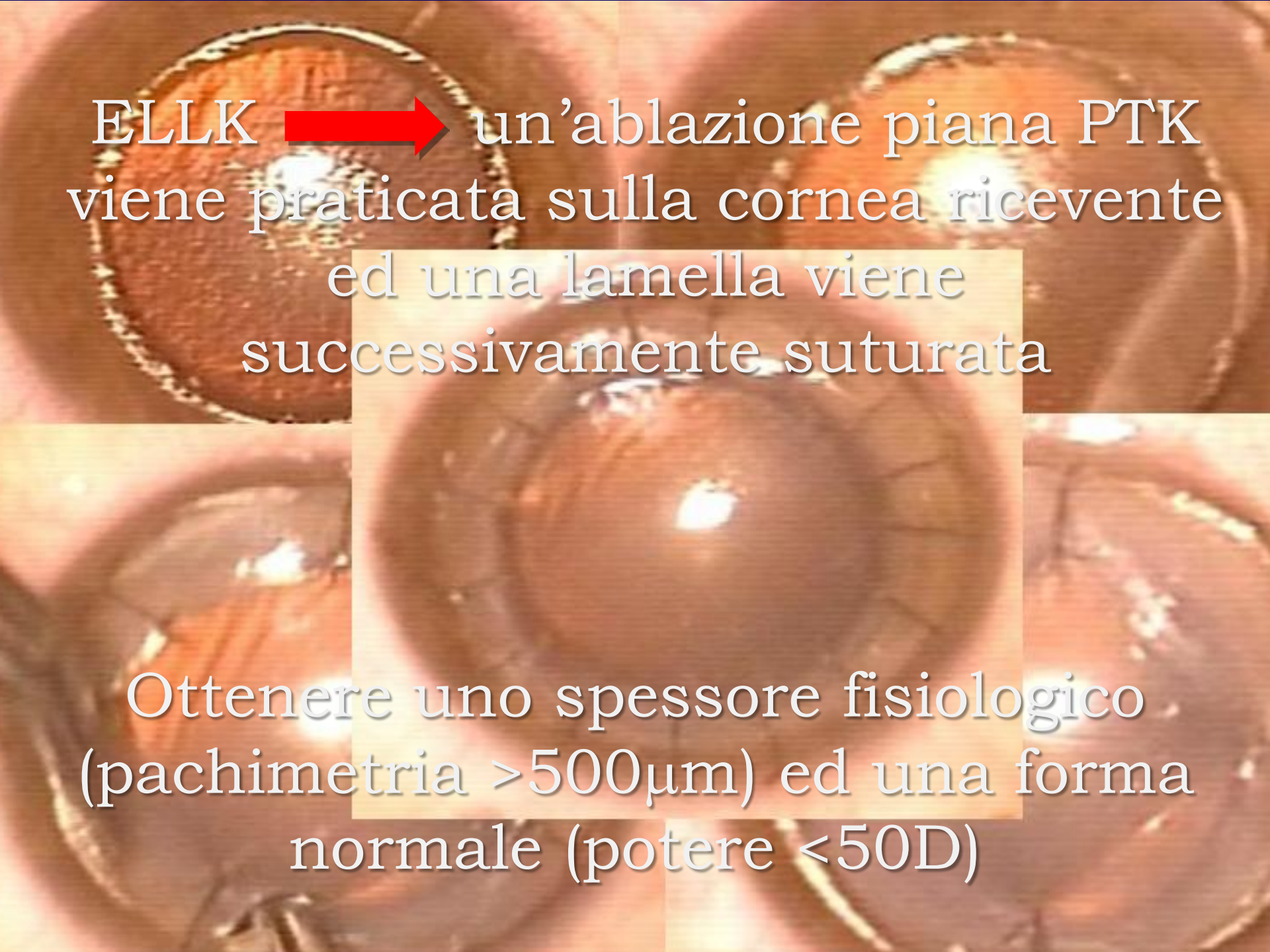



L'uso del *laser ad eccimeri* per rimodellare la cornea rappresenta la maggior innovazione nella chirurgia rifrattiva

Per migliorare i risultati anatomici e funzionali della cheratoplastica lamellare nel cheratocono è stata messa a punto la Excimer Laser Lamellar Keratoplasty (ELLK) a spessori differenziati



(Eckhardt HB 1996; Buratto L 1998; Bilgihan K 2006; Spadea L 2009)



ELLK → un'ablazione piana PTK viene praticata sulla cornea ricevente ed una lamella viene successivamente suturata

Ottenere uno spessore fisiologico (pachimetria >500µm) ed una forma normale (potere <50D)

ARTICLE

Excimer laser–assisted lamellar keratoplasty for the surgical treatment of keratoconus

Leopoldo Spadea, MD, Daniele Giammaria, MD, Arianna Fiasca, MD, Valerio Verrecchia, MD

J Cataract Refract Surg 2009; 35:105–112 © 2009 ASCRS and ESCRS

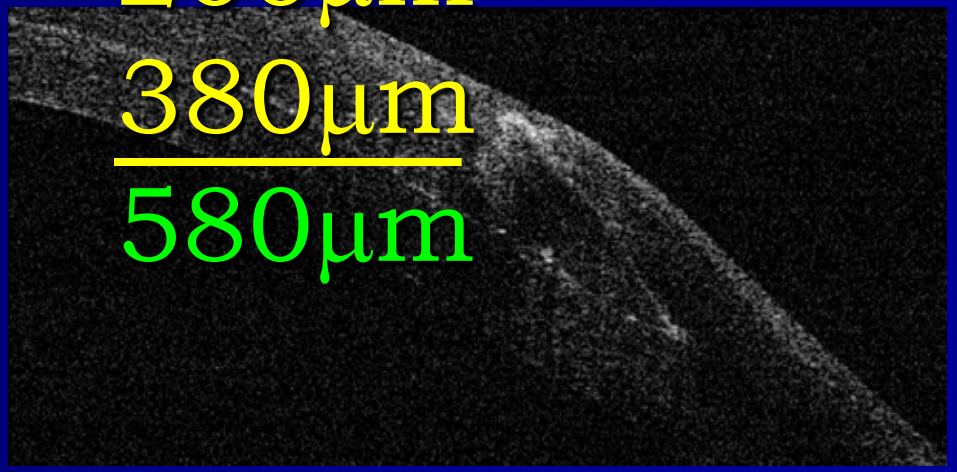
Esempio ELLK :

KC Cornea 400µm

PTK abl. 200µm

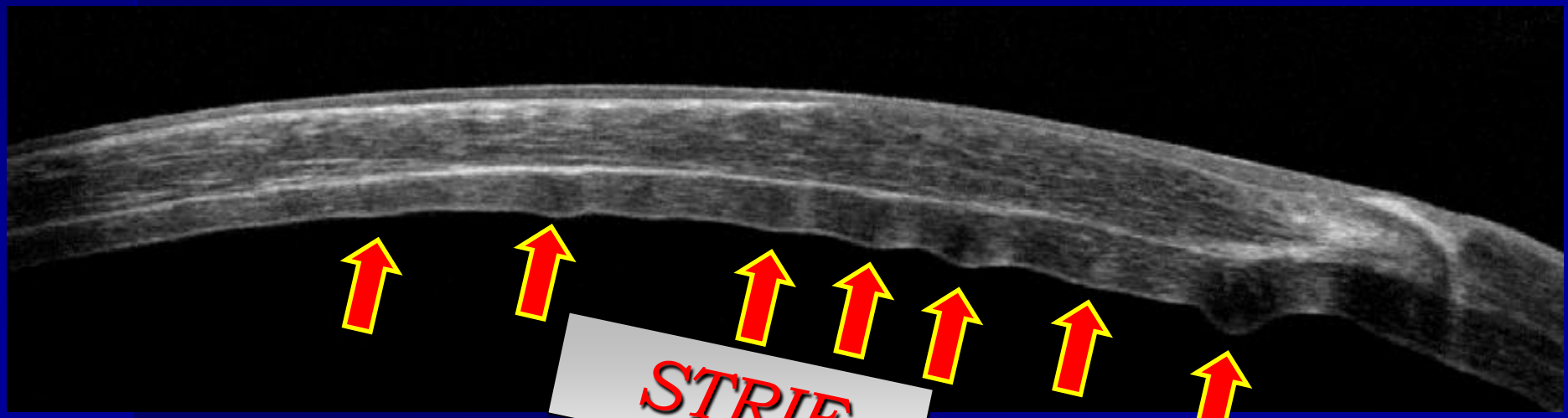
Lamella 380µm

Finale 580µm



In alcuni casi l'effetto meccanico del KC originale persiste

ELLK è limitato ai casi di cheratocono lievi e moderati



Un nuova generazione di *laser ad eccimeri* con un software dedicato ai trapianti lamellari con il laser ci consente di fare delle

ablazioni customizzzate

sia per il letto ricevente che per la lamella

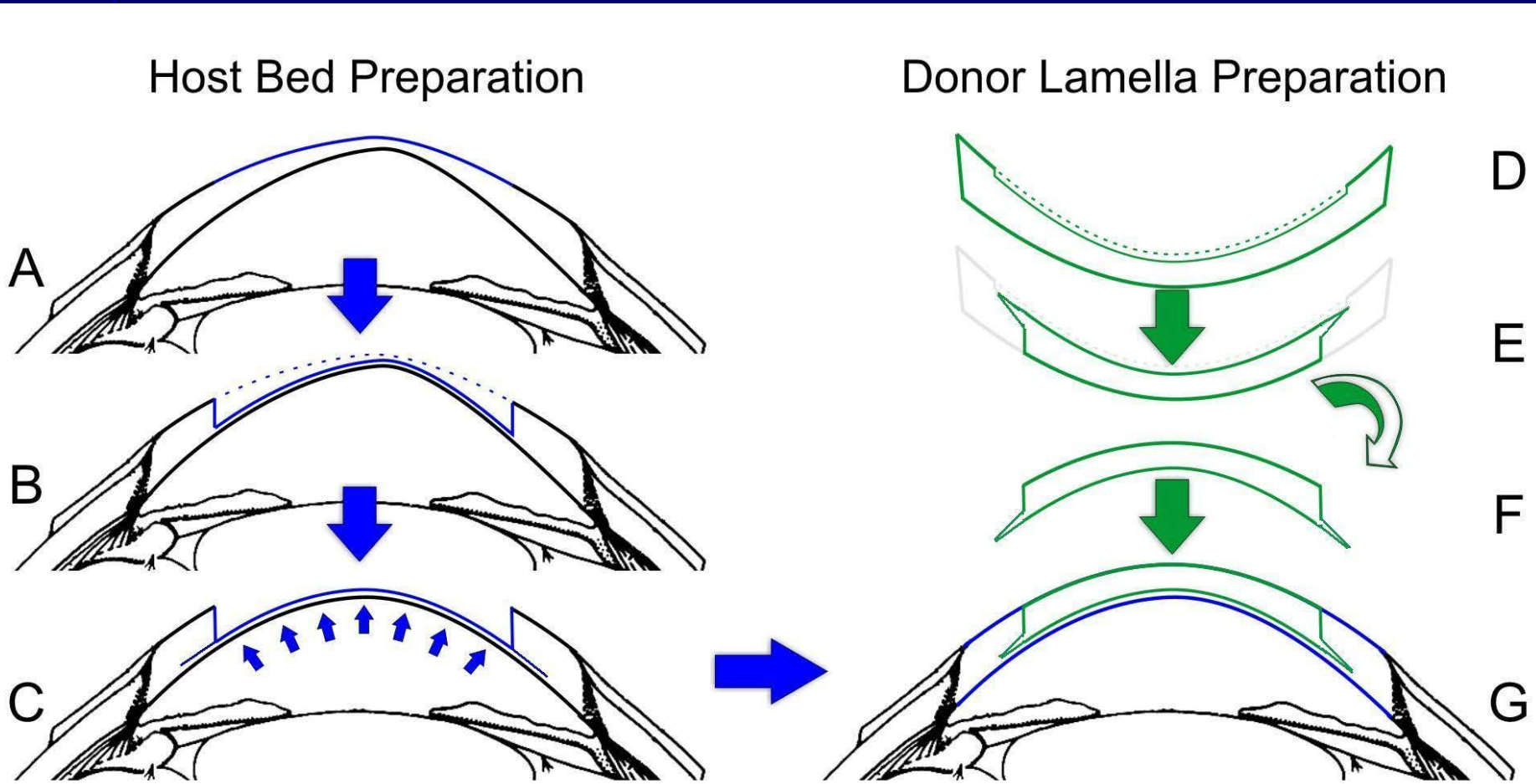
CLAT®
Corneal Lamellar Ablation for Transplantation

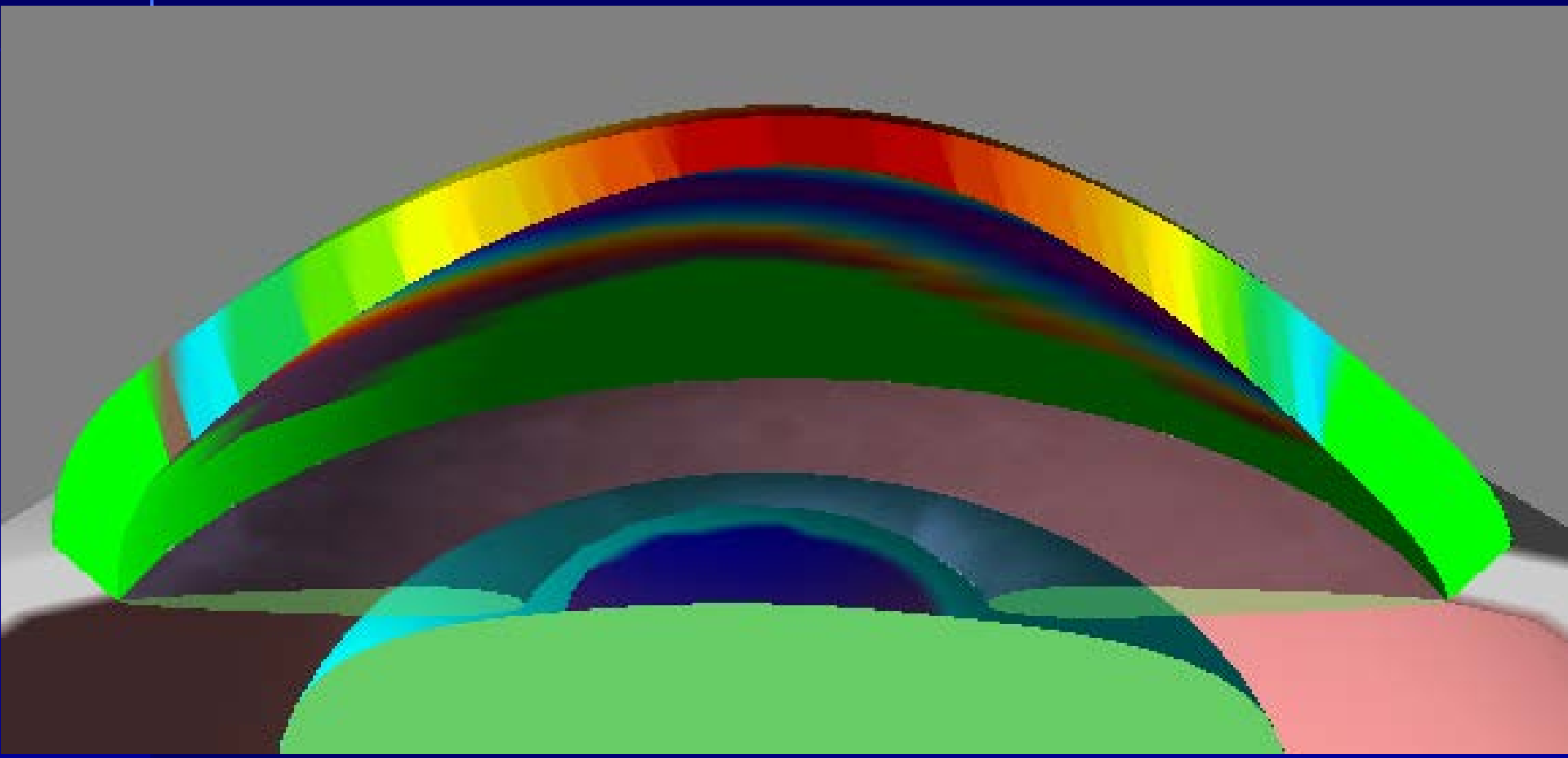
ARTICLE

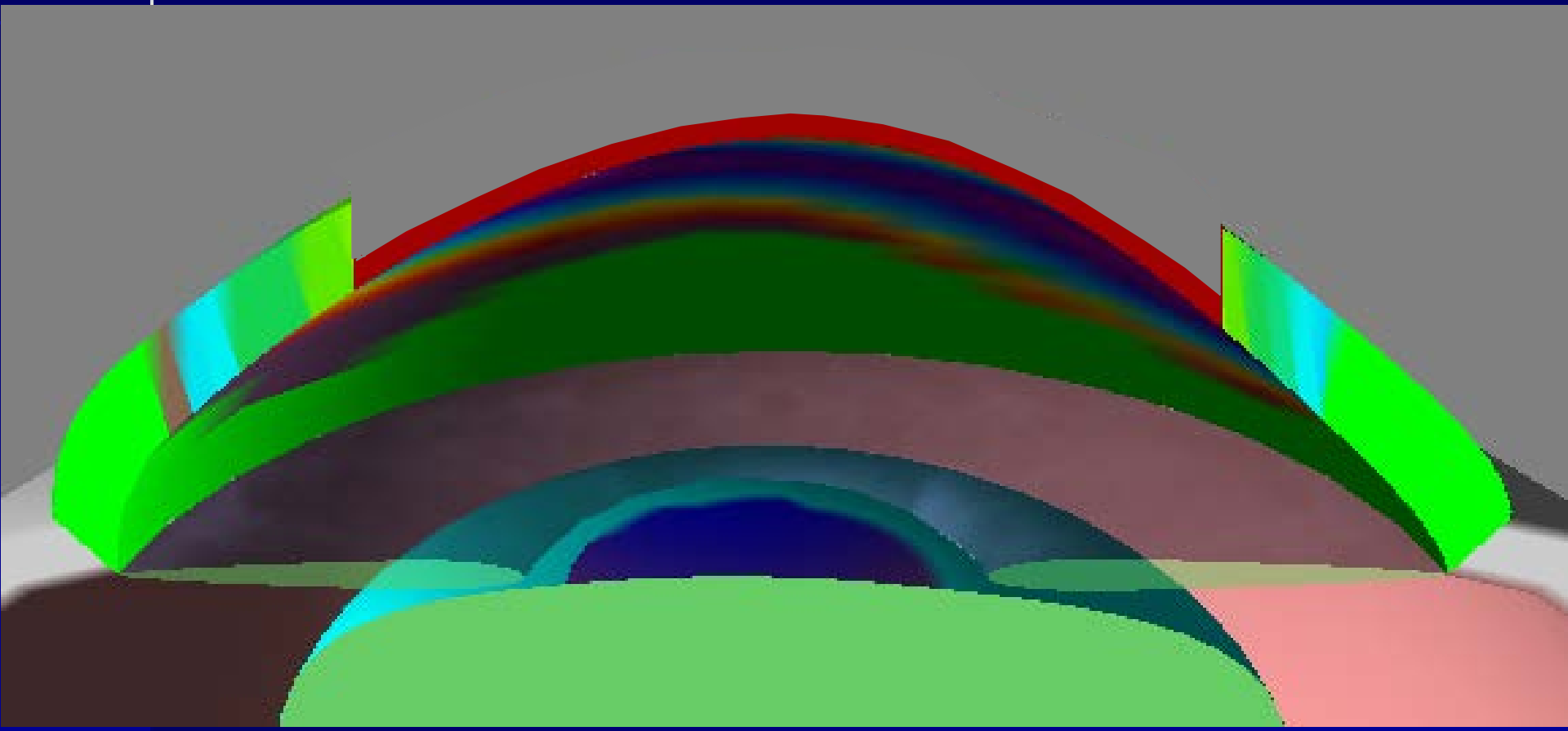
Optical pachymetry–guided custom excimer laser-assisted lamellar keratoplasty for the surgical treatment of keratoconus

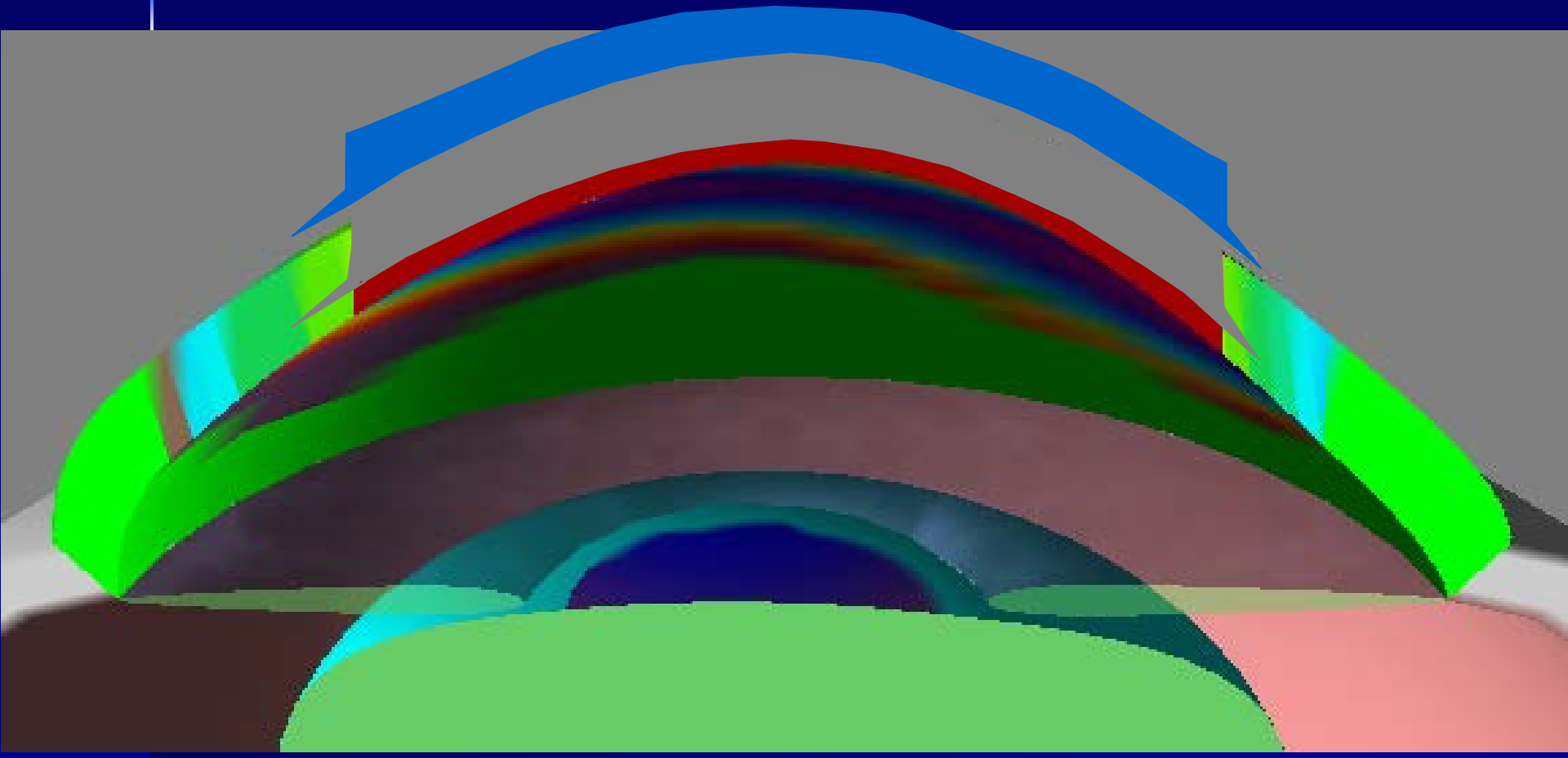
Leopoldo Spadea, MD, Riccardo Gizzi, MD, Nicole Evangelista Conocchia, MD, Sara Urbano, BS

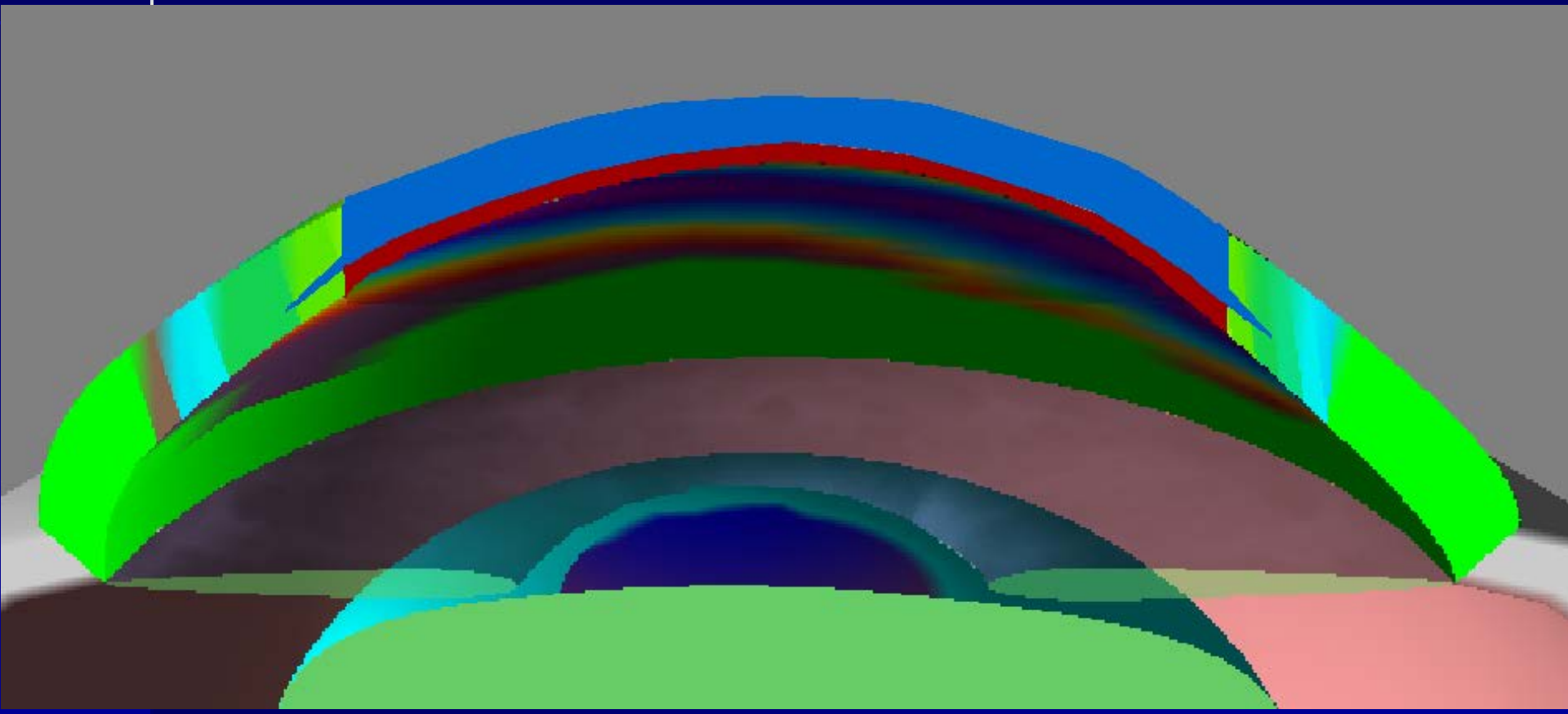
J Cataract Refract Surg 2012; 38:1559–1567

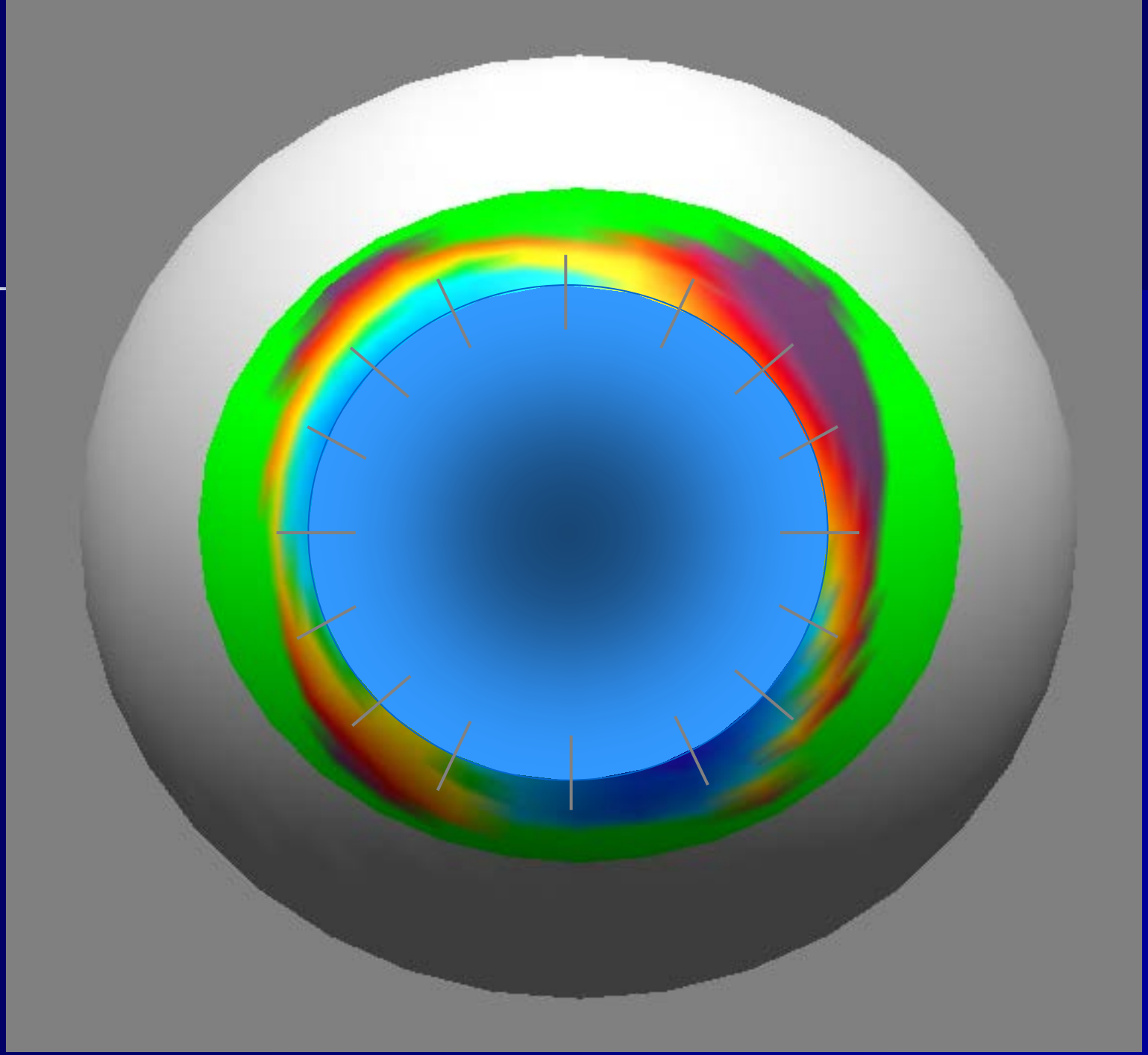

Host Bed Preparation
Donor Lamella Preparation
A
B
C
D
E
F
G

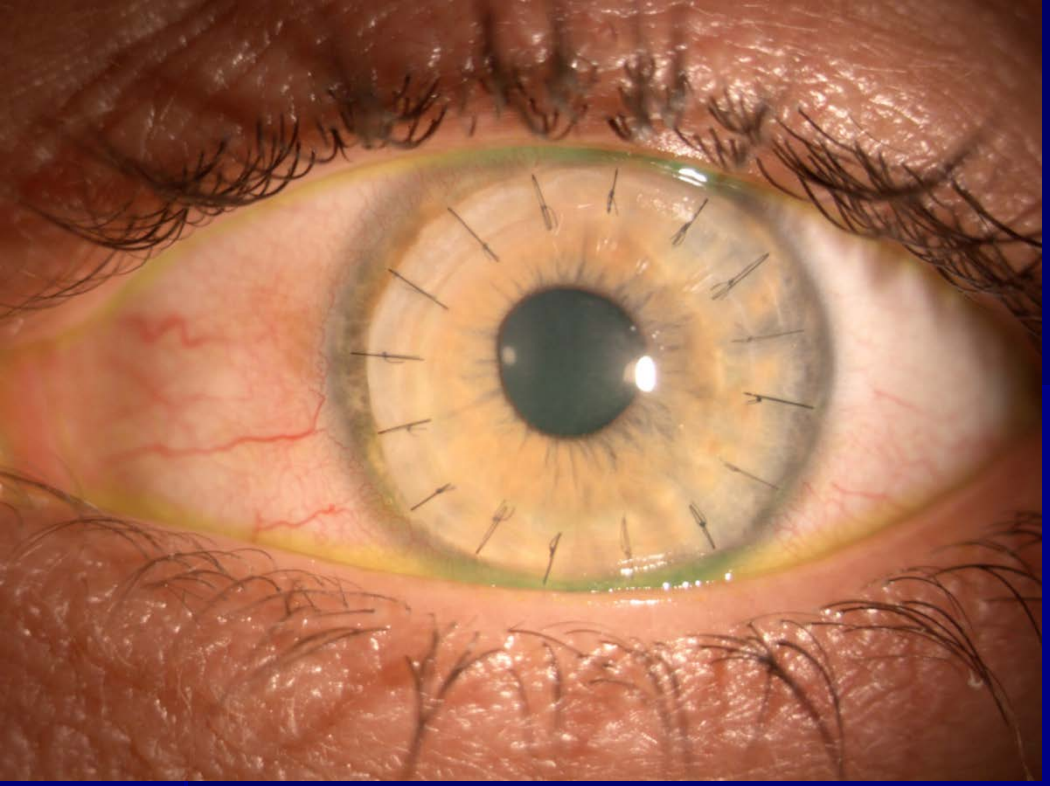




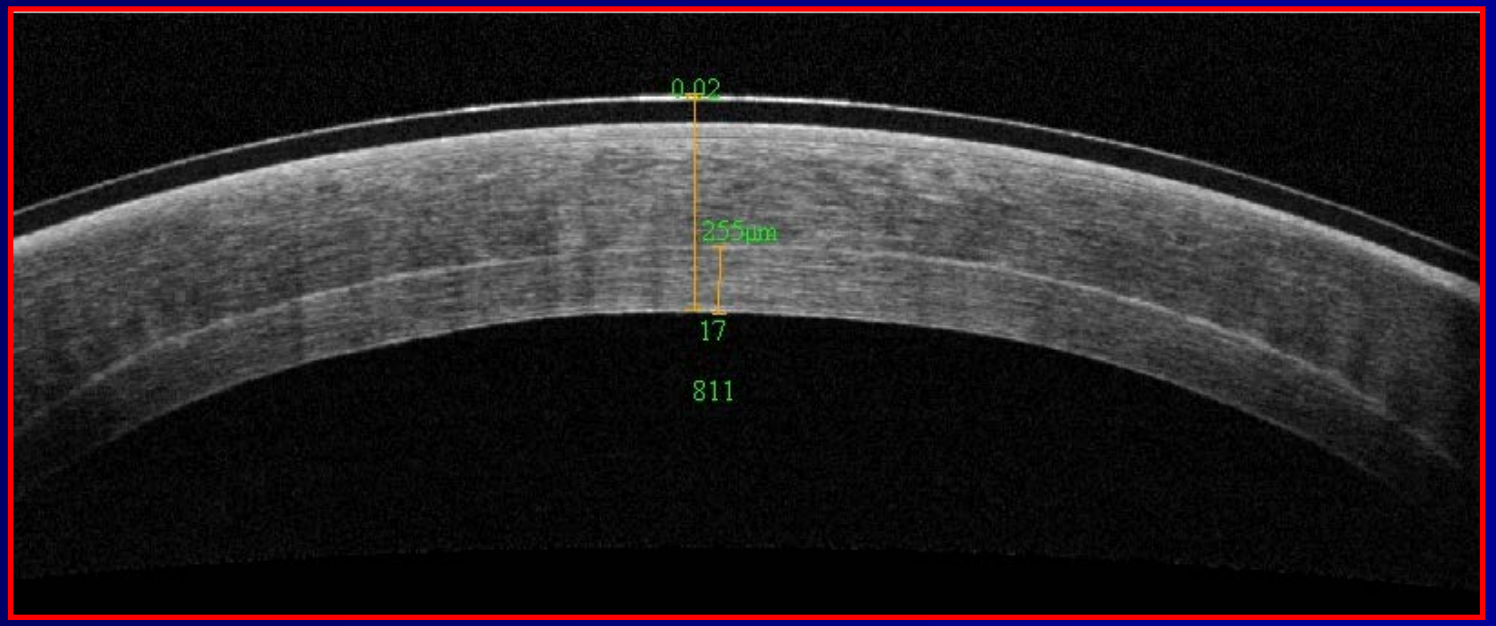




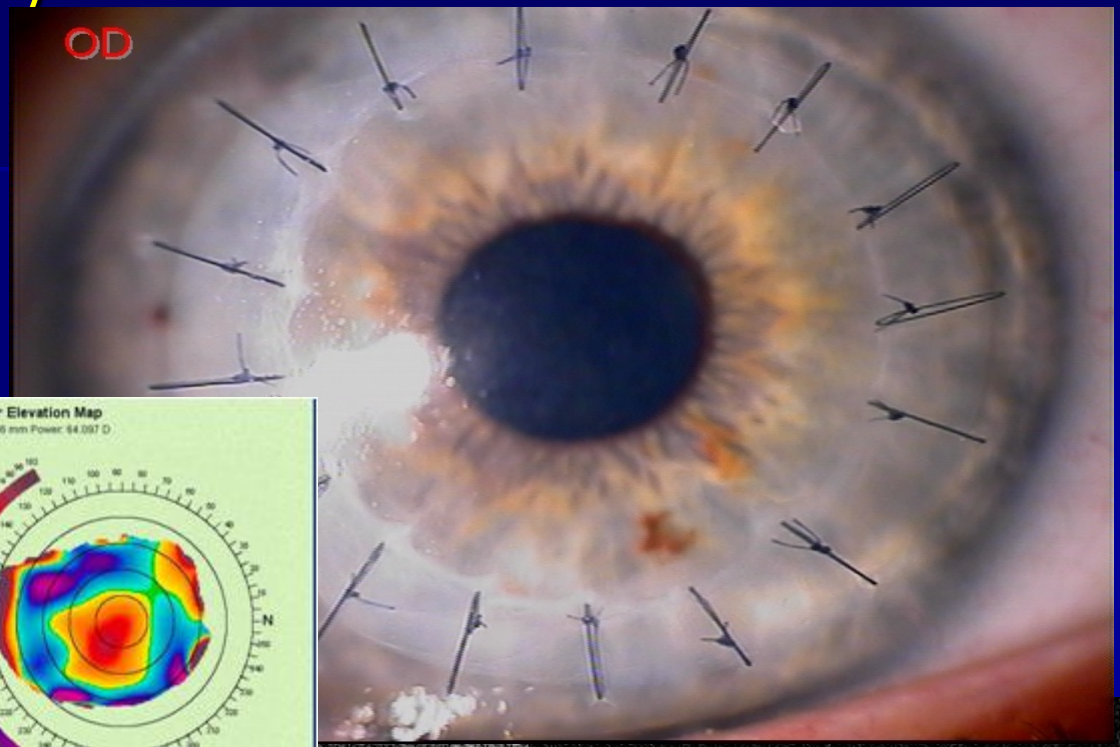


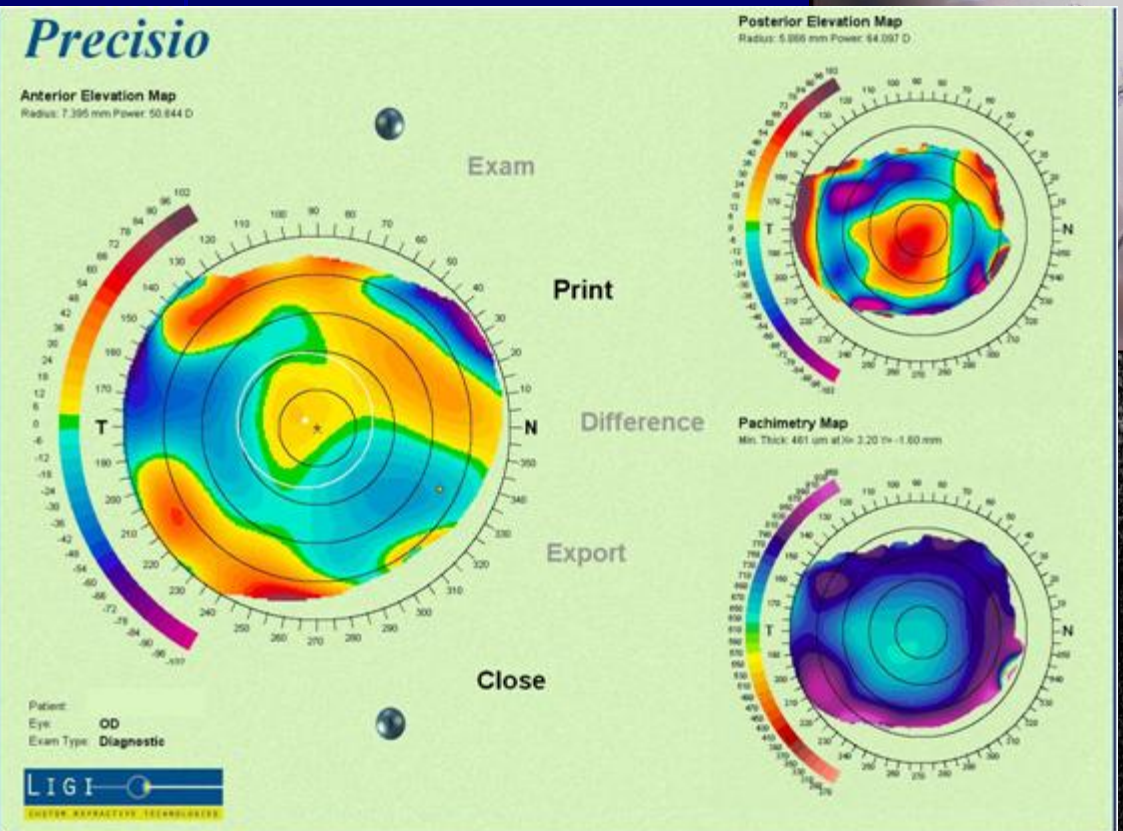


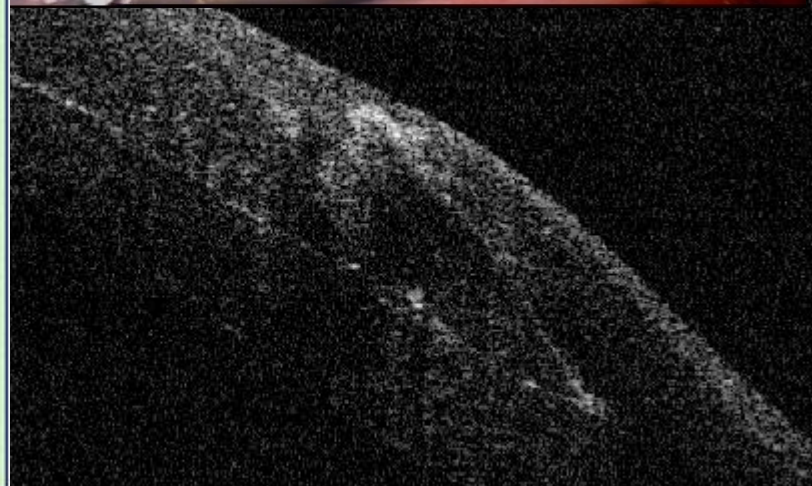
L.F. ♂ 34aa
1 sett post-CLAT
UCVA 4/10



S.P. ♀ 24aa 2m post-CLAT
UCVA 3/10 BCVA 6/10

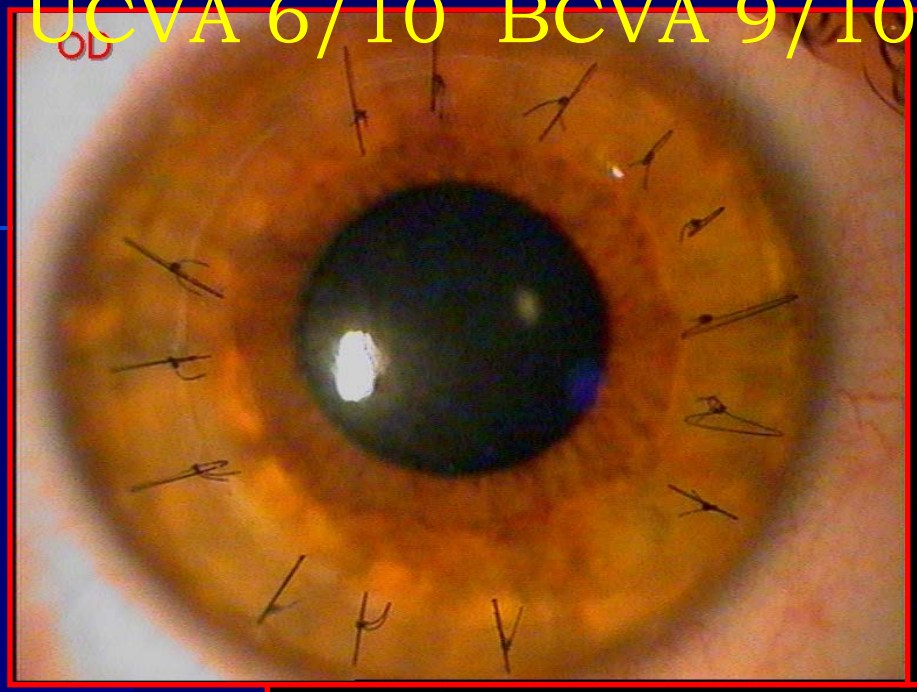


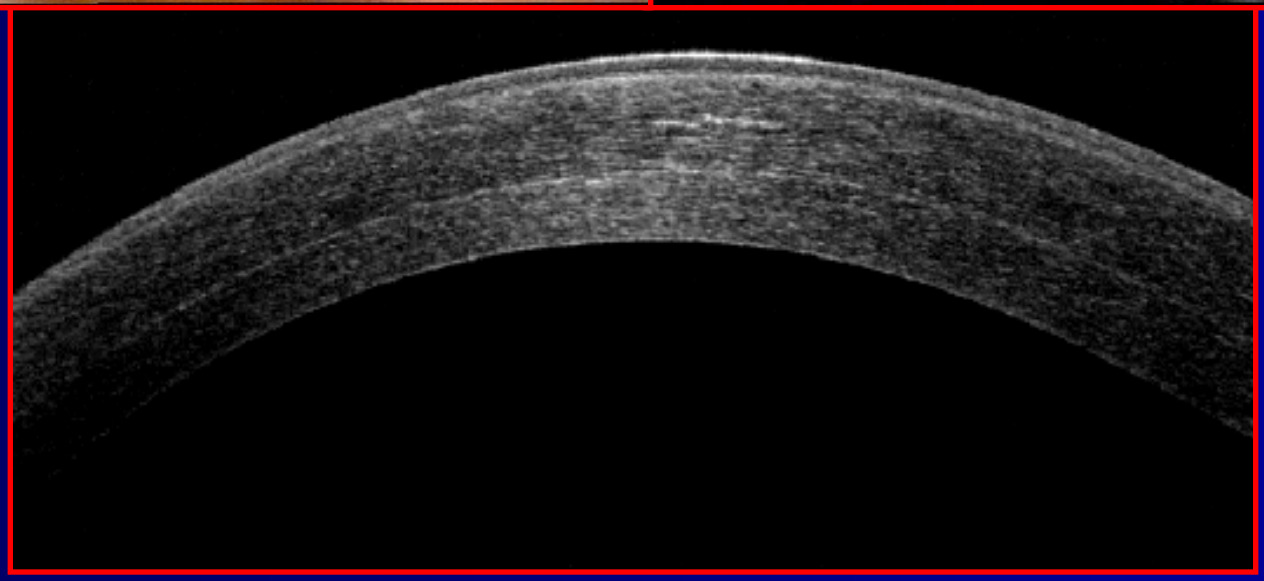




R.O. ♂ 29aa 6m post-CLAT

UCVA 6/10 BCVA 9/10

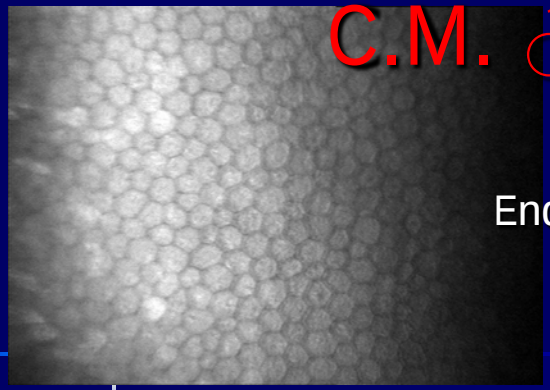




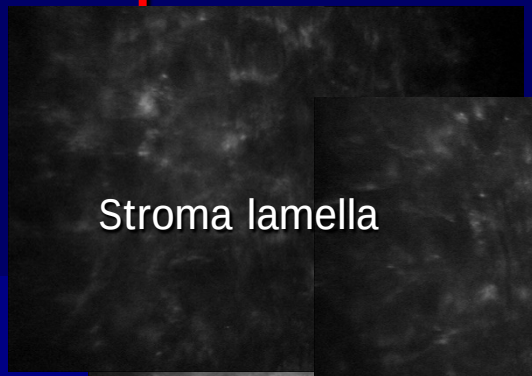
C.D. ♂ 27aa

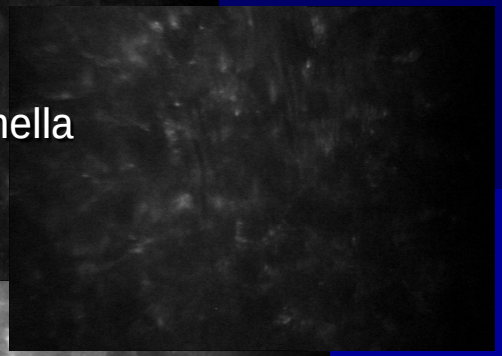
3 aa post-CLAT	
UCVA	6/10
BCVA	10/10

C.M. ♂ 39aa OD 2aa post-CLAT

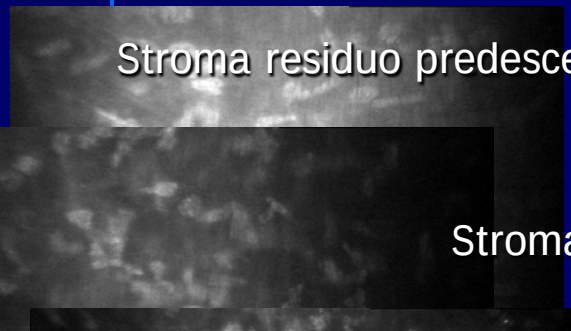


Endotelio

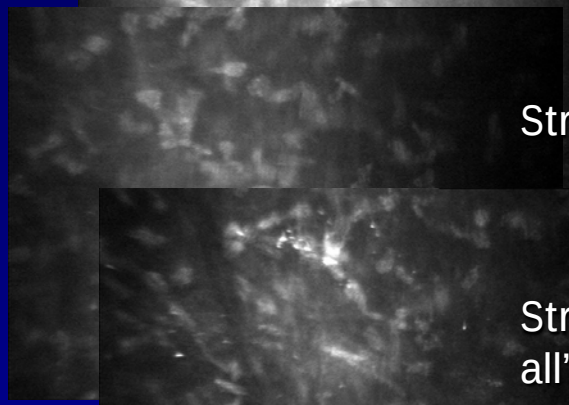




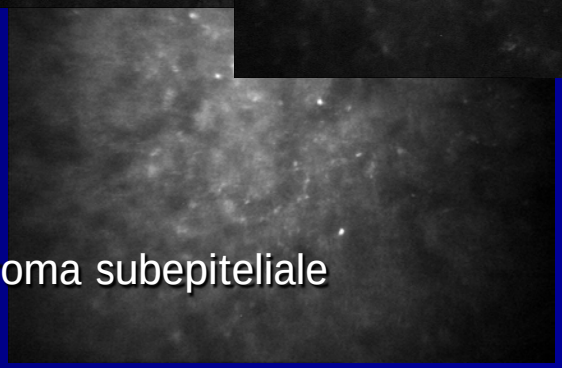
Stroma lamella



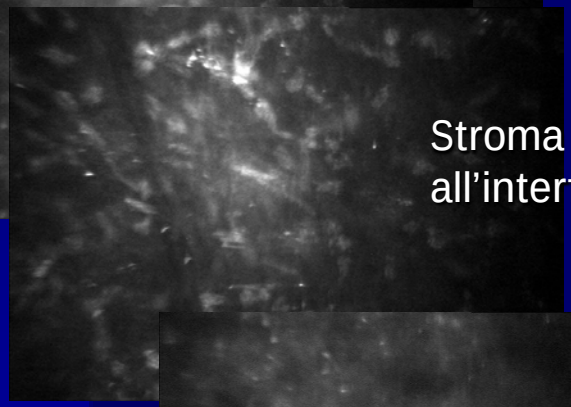
Stroma residuo predescemetico



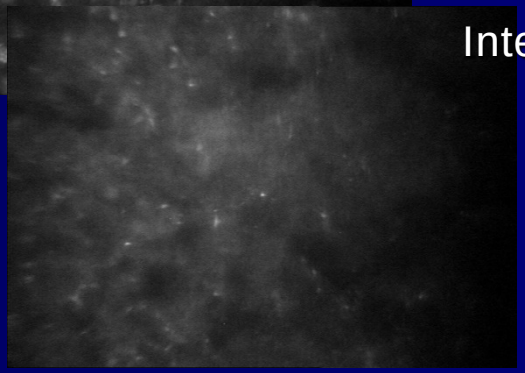
Stroma residuo



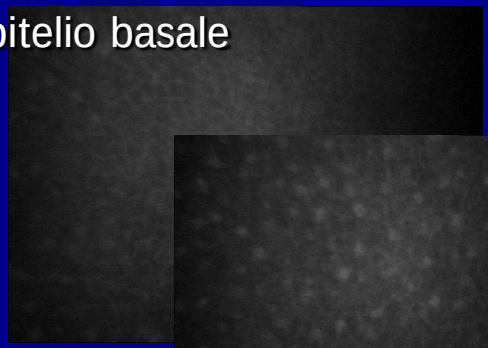
Stroma subepiteliale



Stroma residuo all'interfaccia



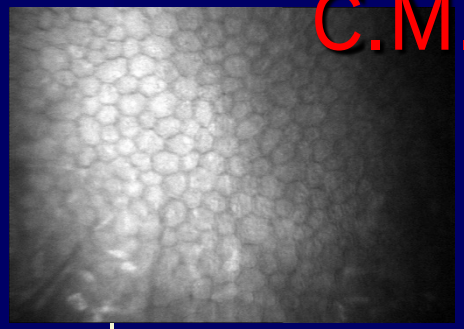
Interfaccia



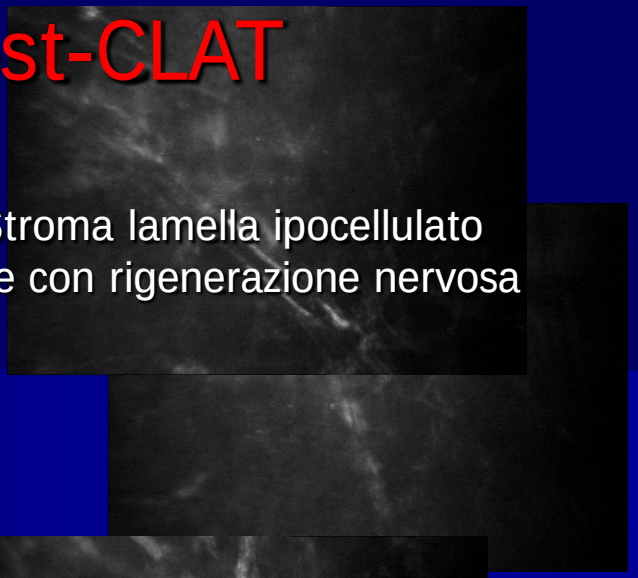
Epitelio basale

Epitelio superficiale

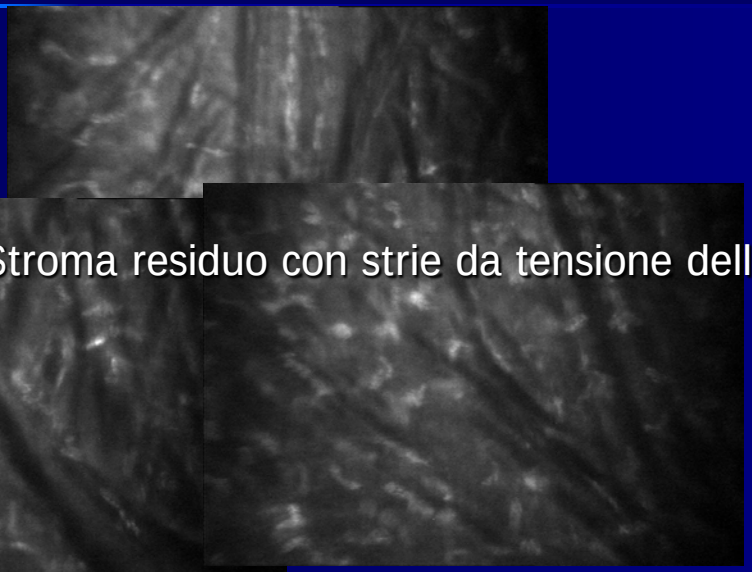
C.M. ♂ 39aa OS 2m post-CLAT



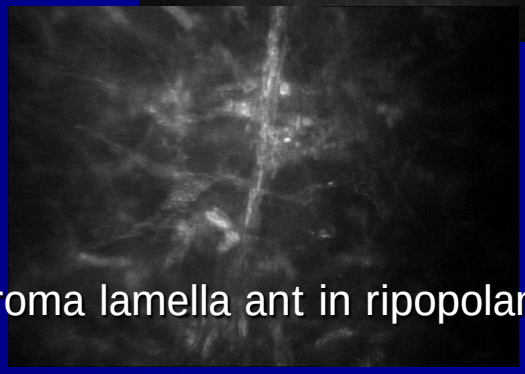
Endotelio



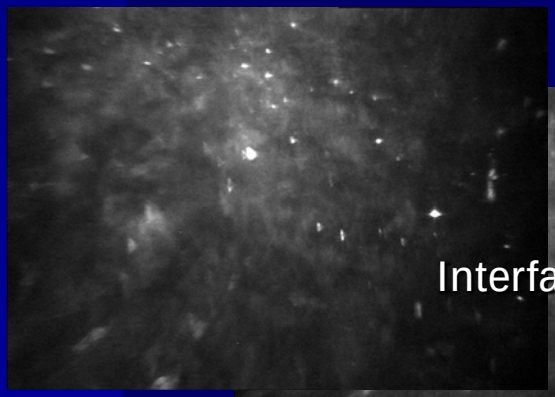
Stroma lamella ipocellulato
e con rigenerazione nervosa



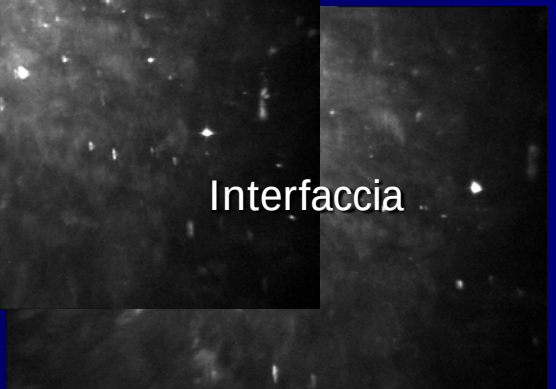
Stroma residuo con strie da tensione delle suture

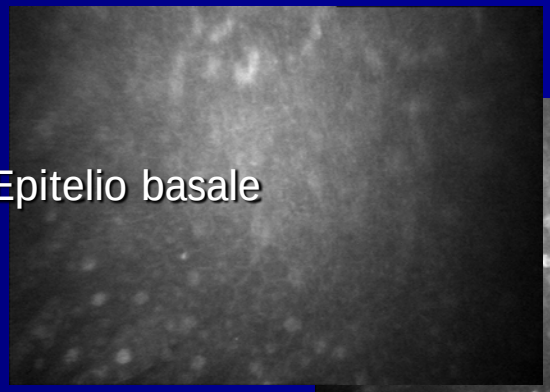


Stroma lamella ant in ripopolamento

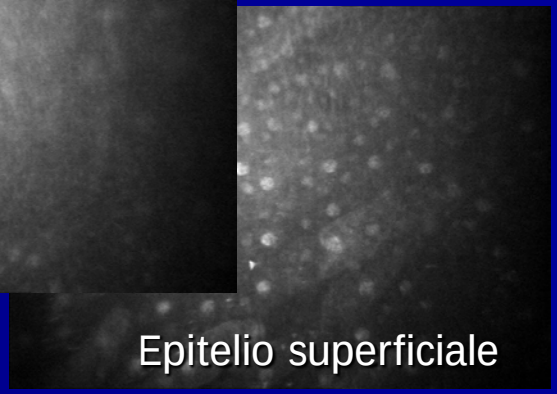


Interfaccia



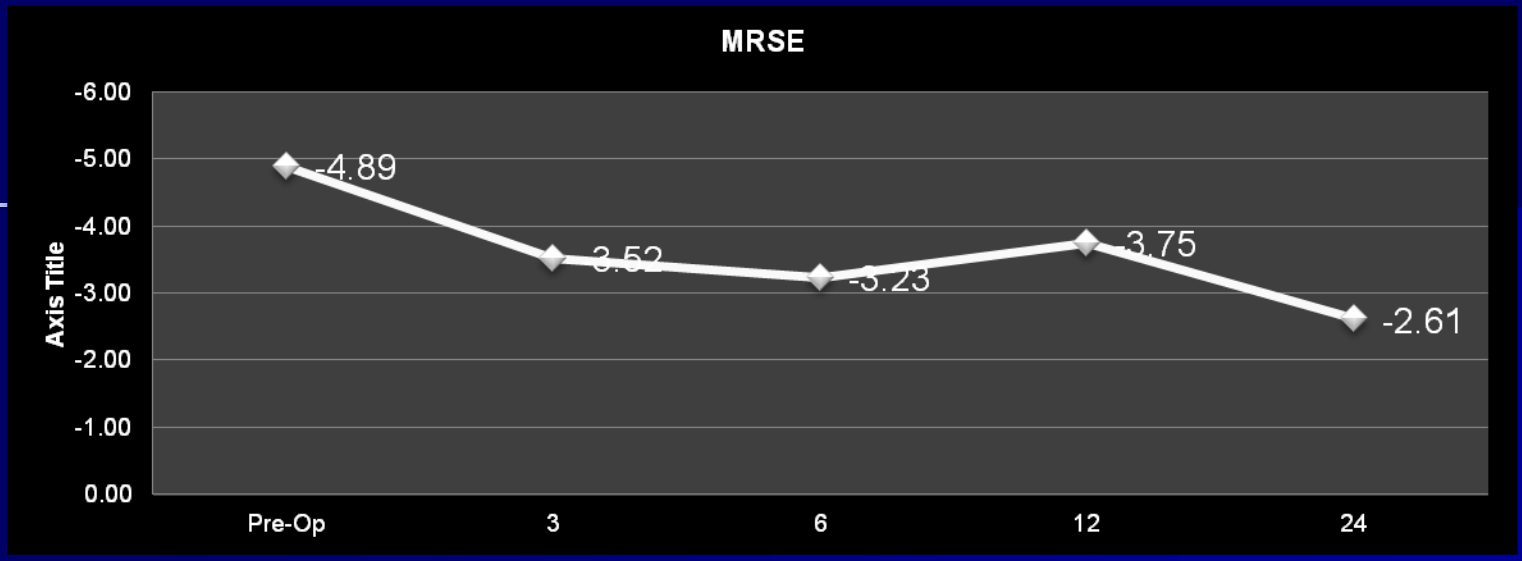


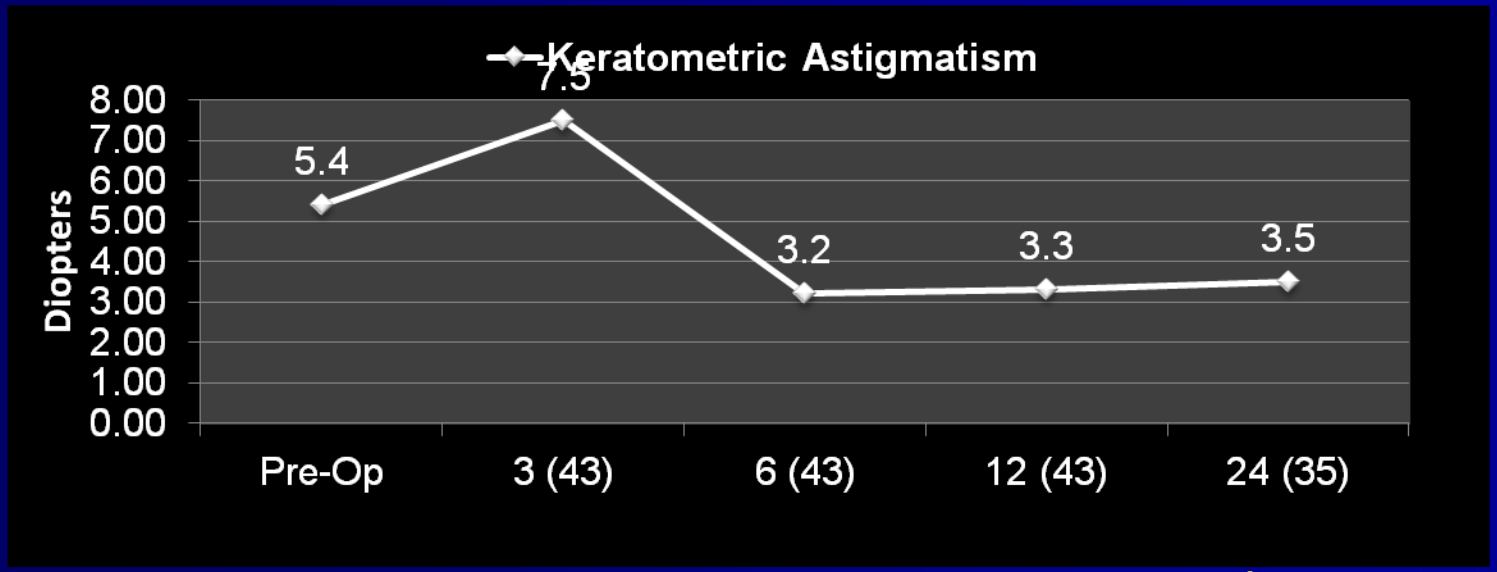
Epitelio basale



Epitelio superficiale

CLAT Risultati





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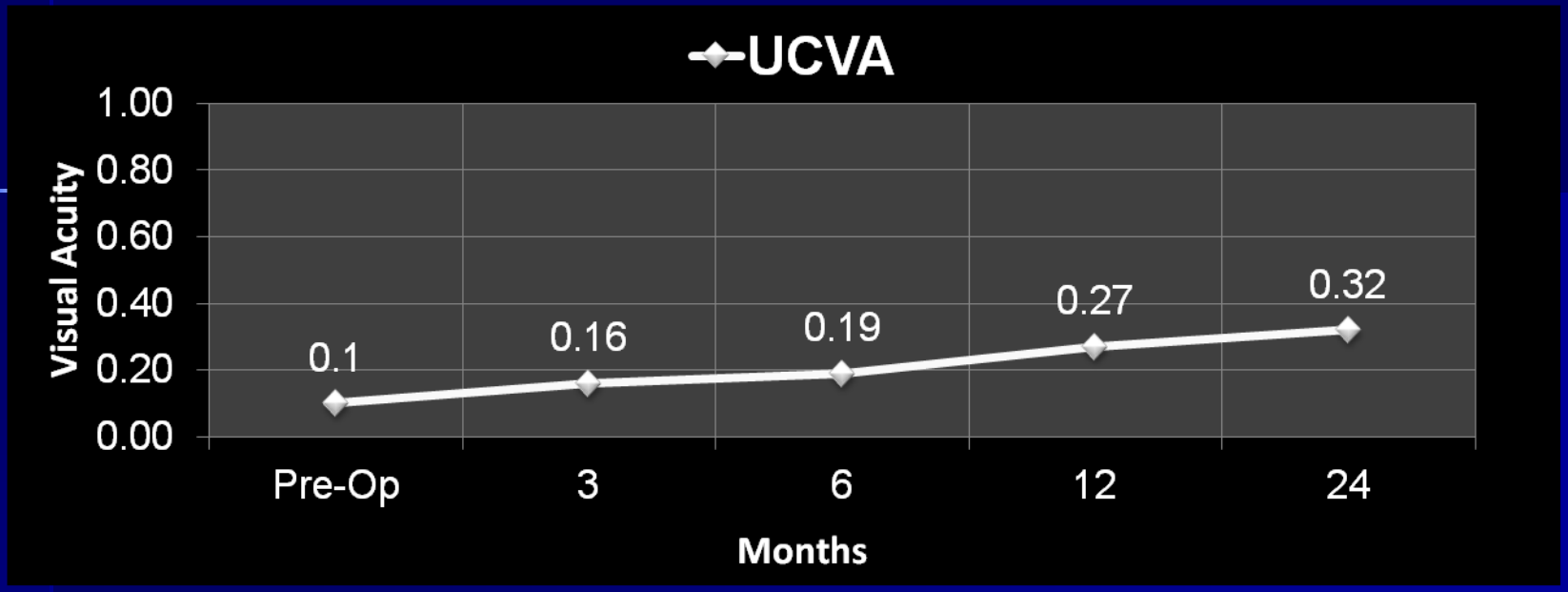
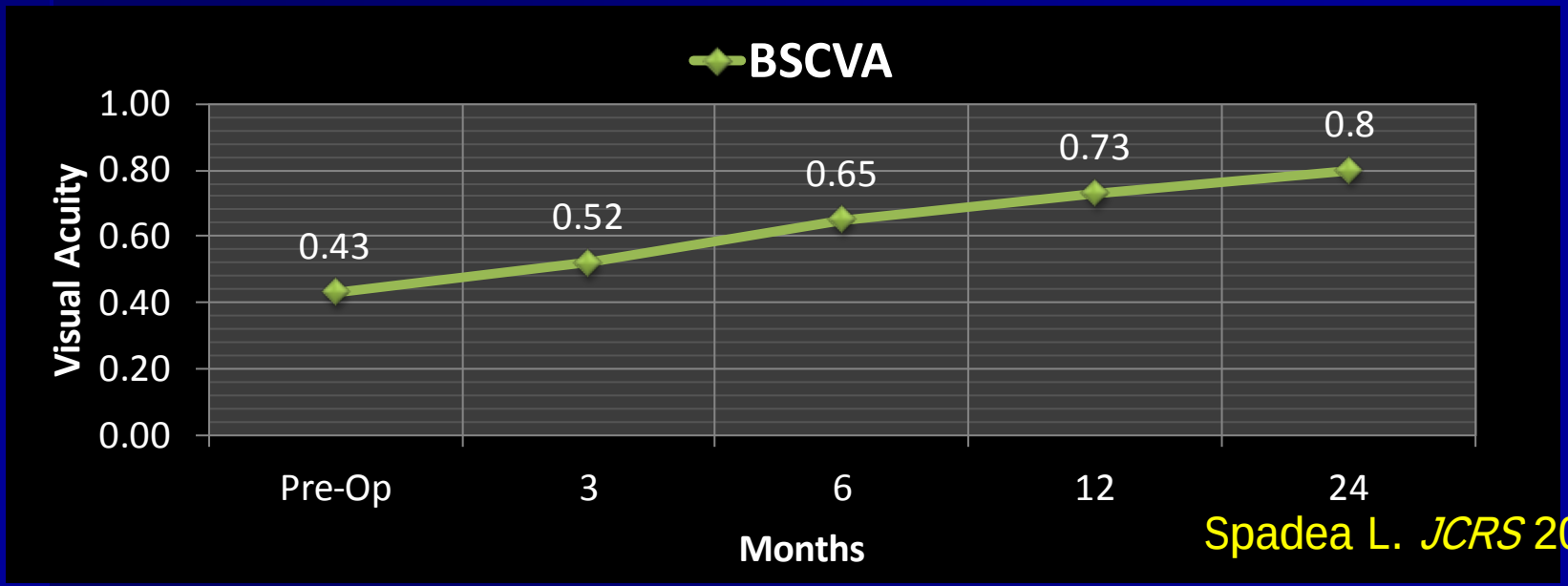
CLAT Risultati





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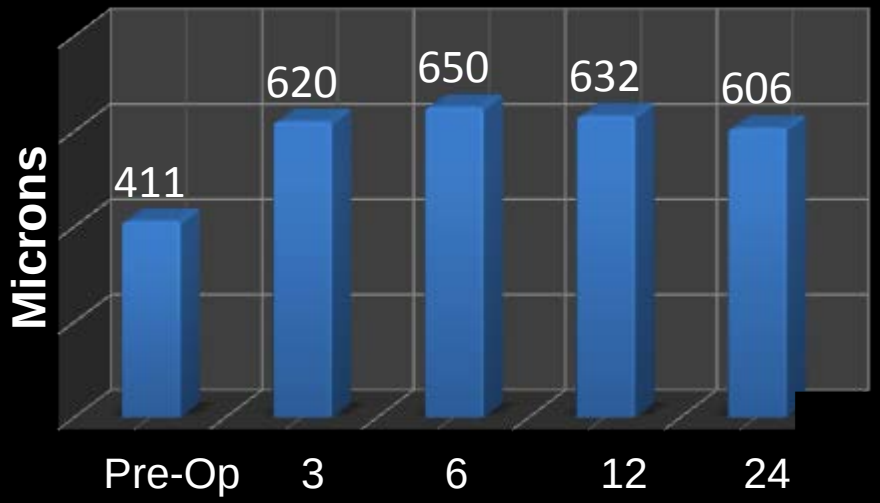
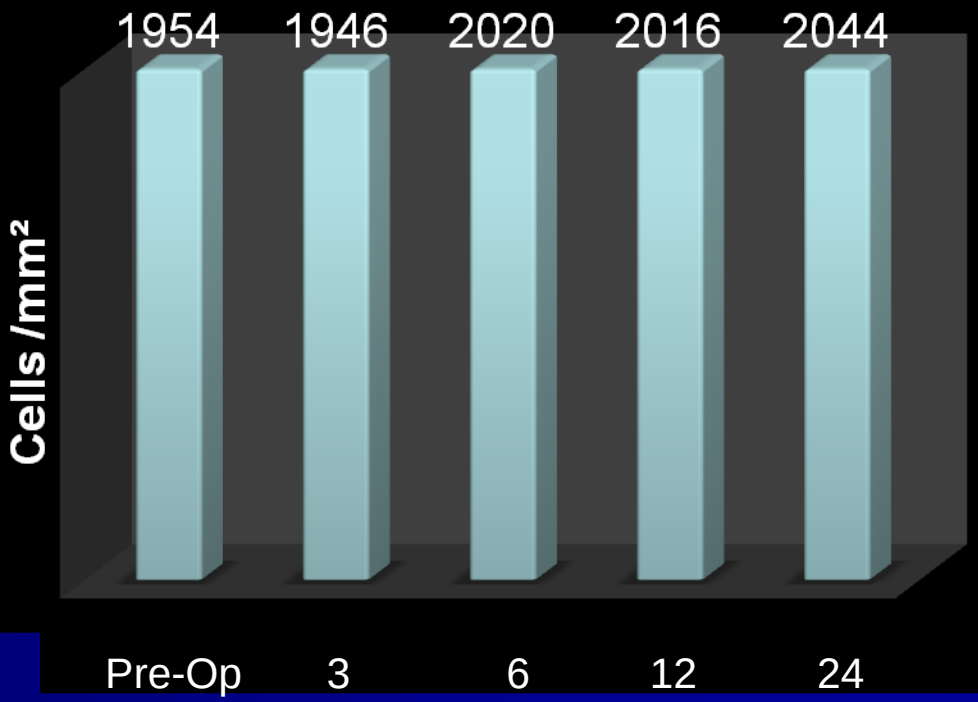
Corneal Pachimetry



Endothelial Cell Count



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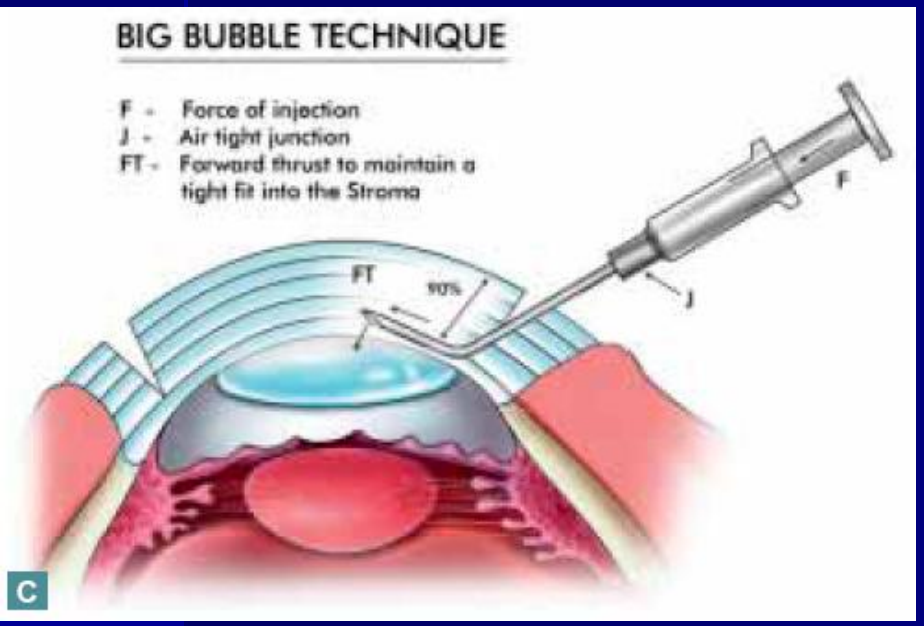
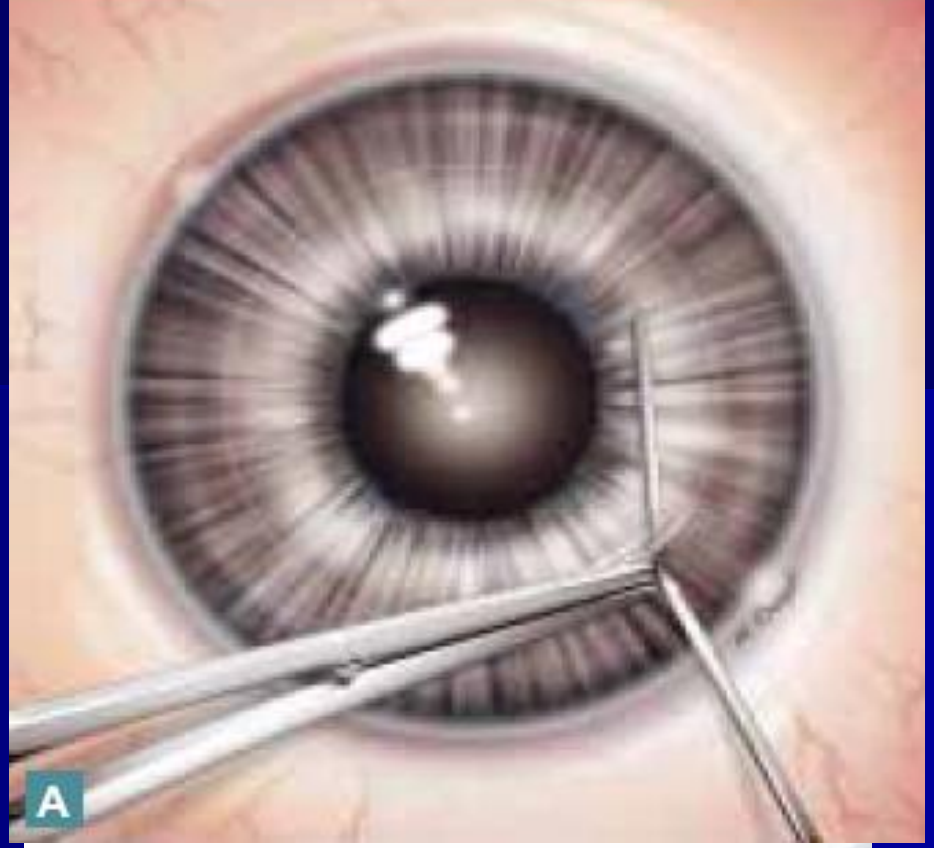
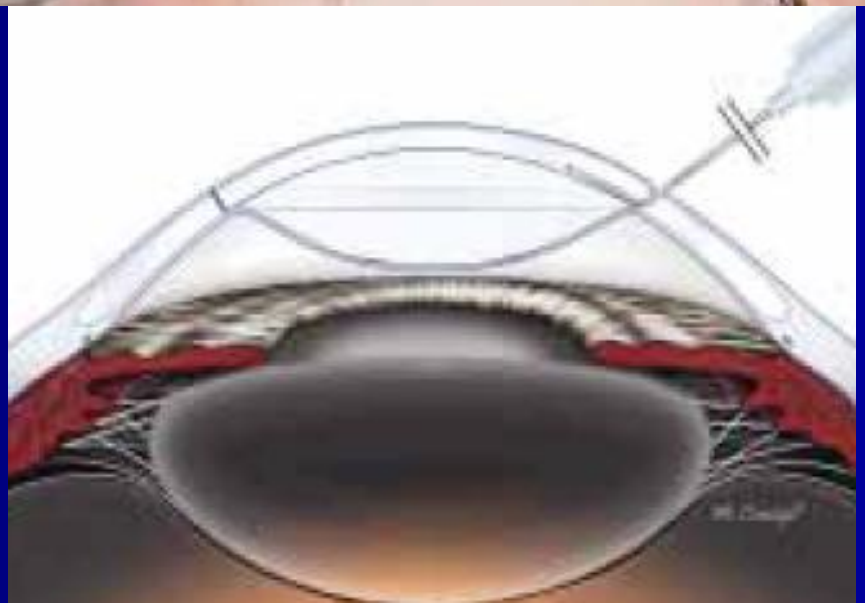
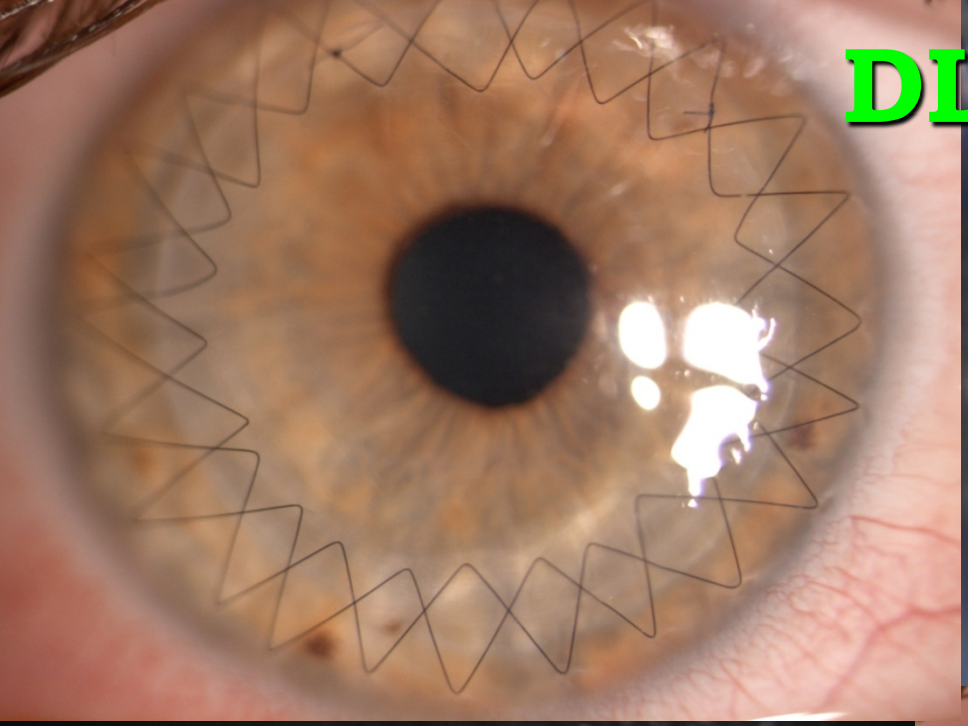
Cheratoplastica lamellare profonda (DLK) (Big-Bubble)

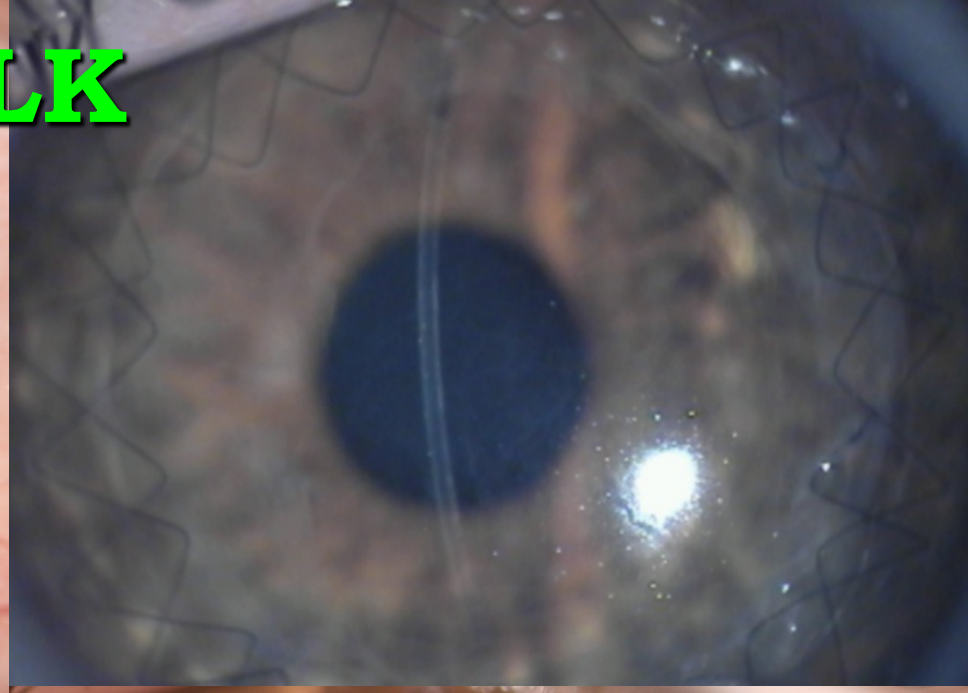


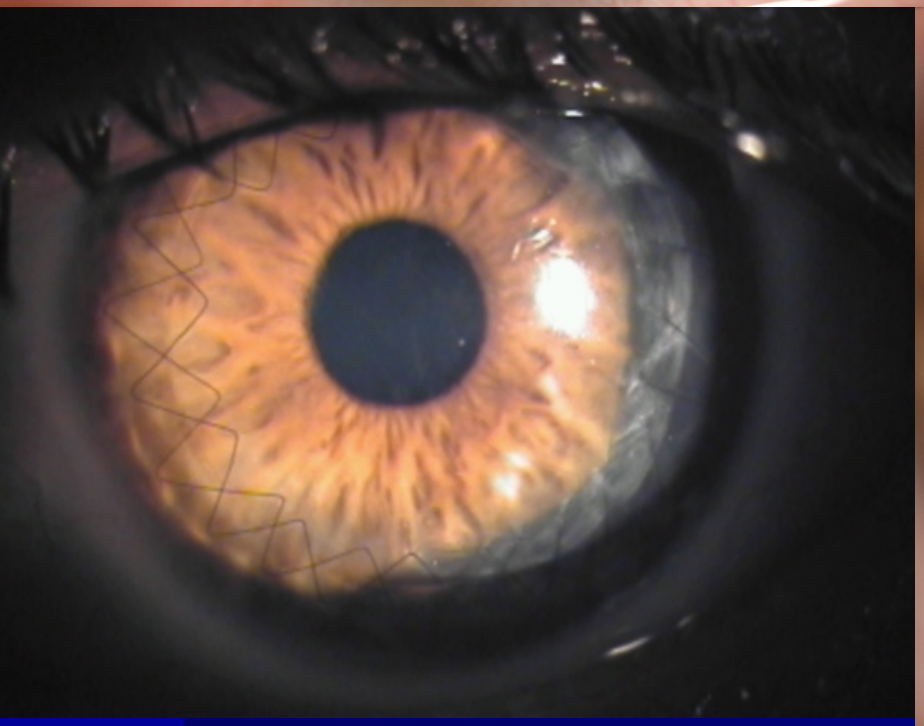


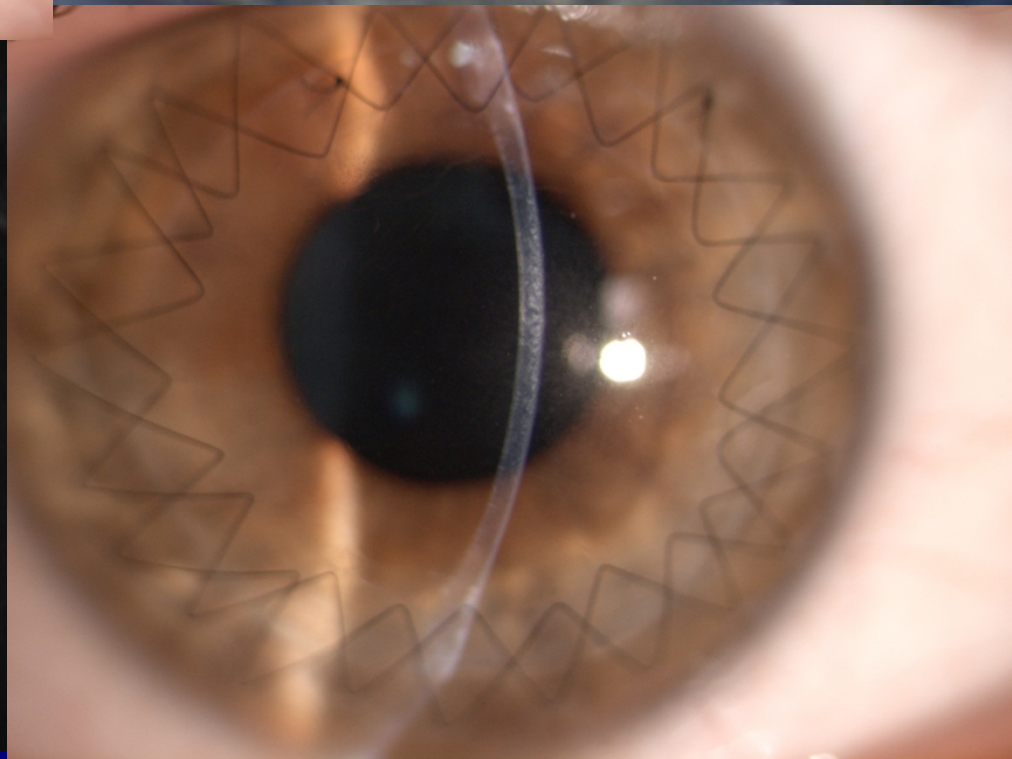


DLK





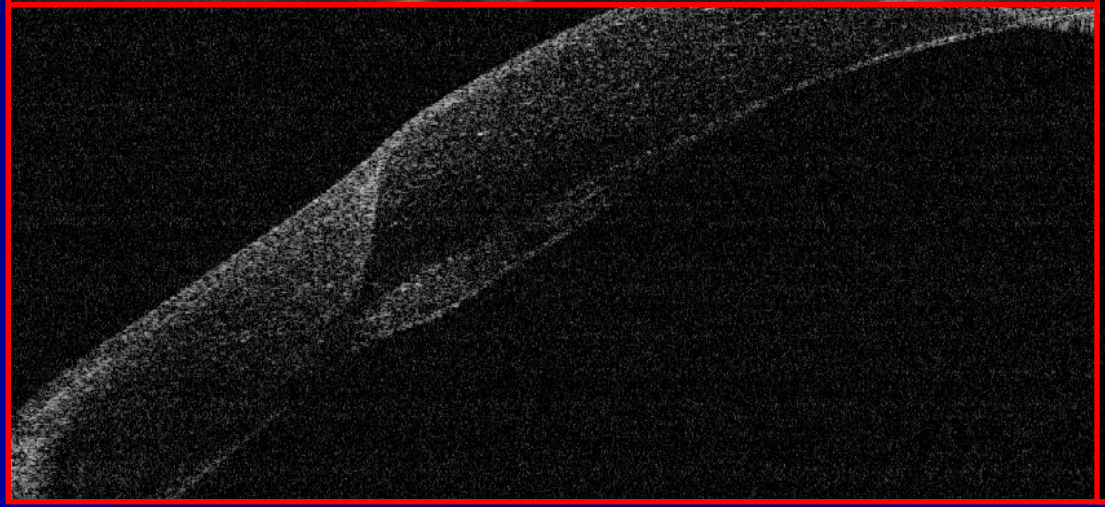


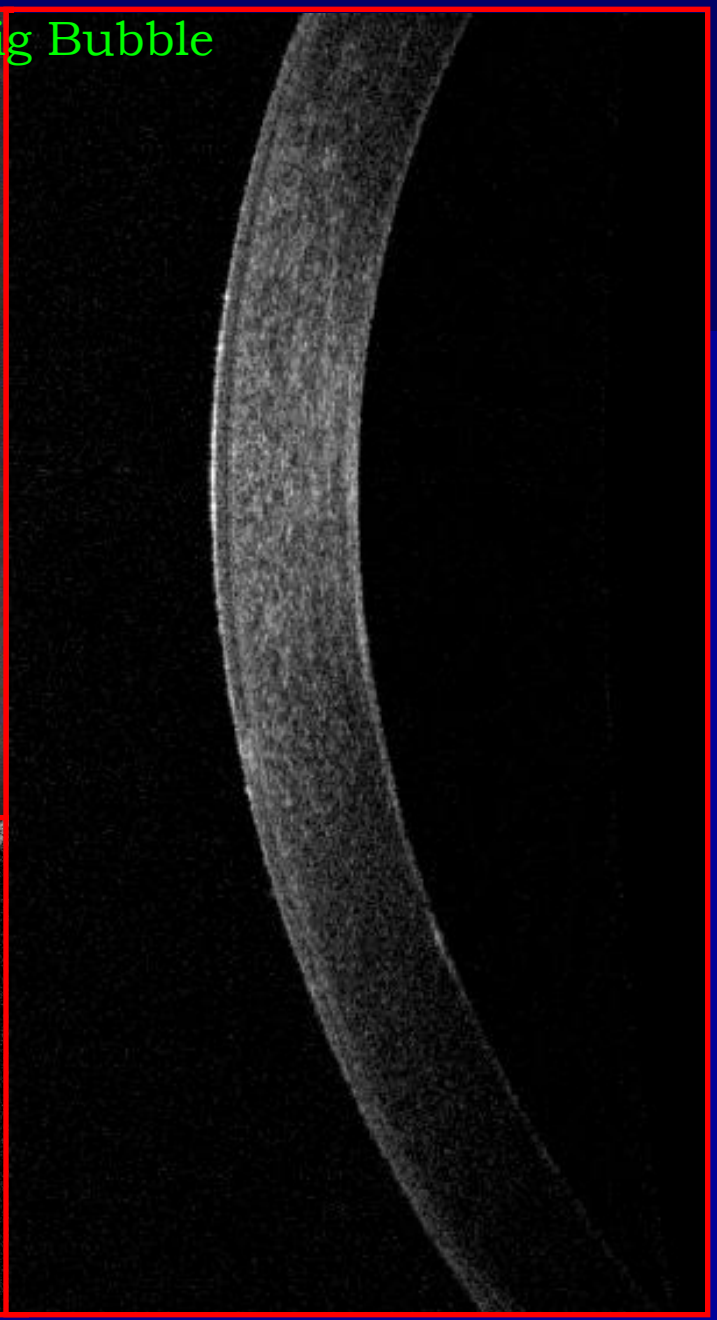


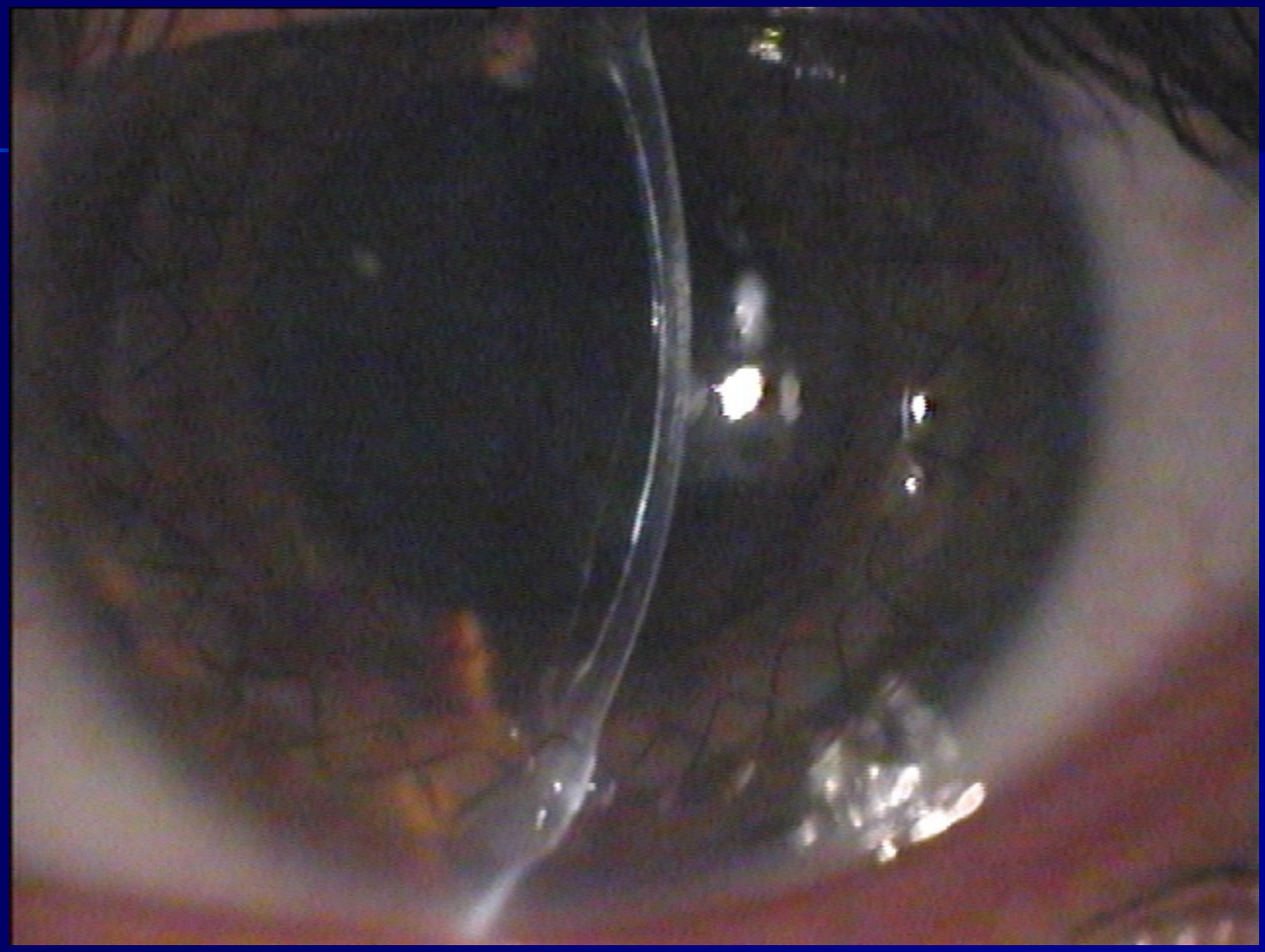
DLK

G.F.R. ♂ 45aa

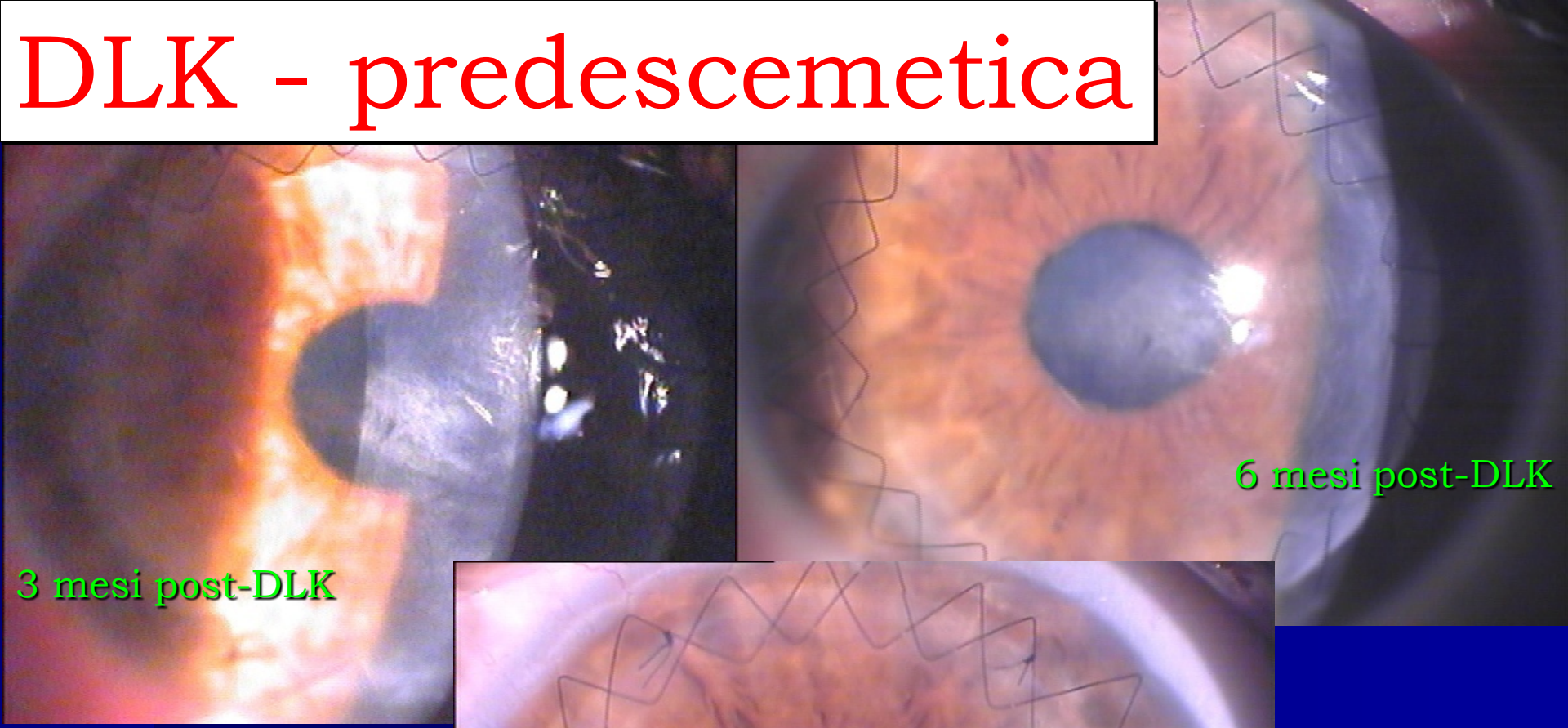
1 anno post-DLK Big Bubble





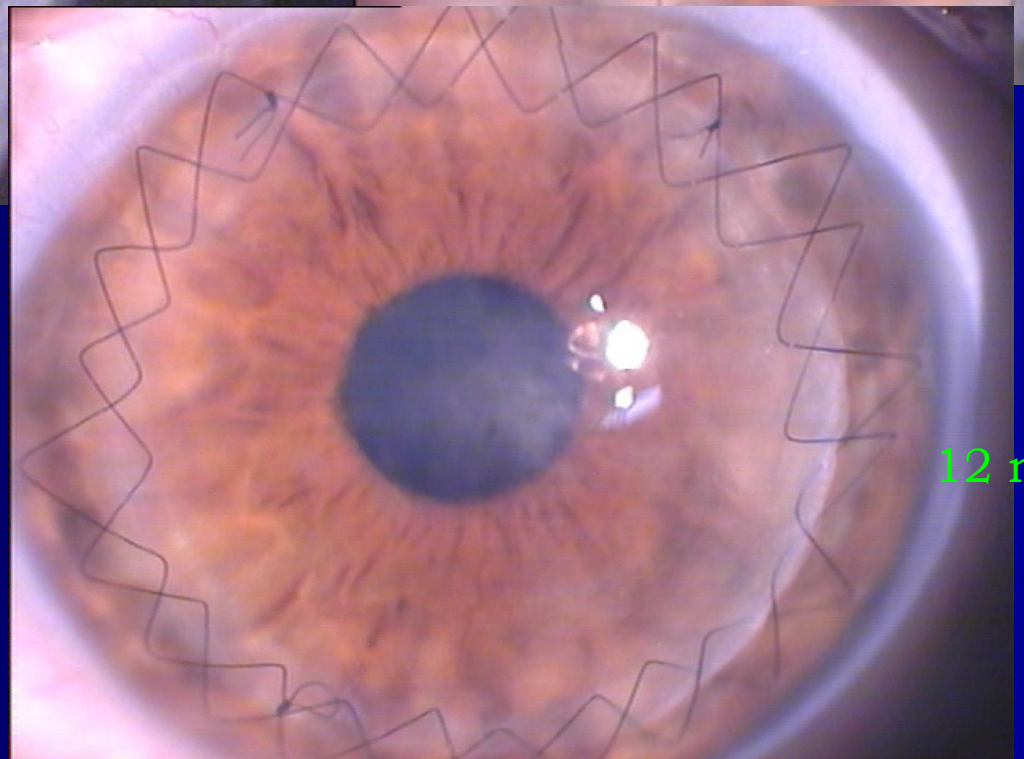


DLK - predescemetica



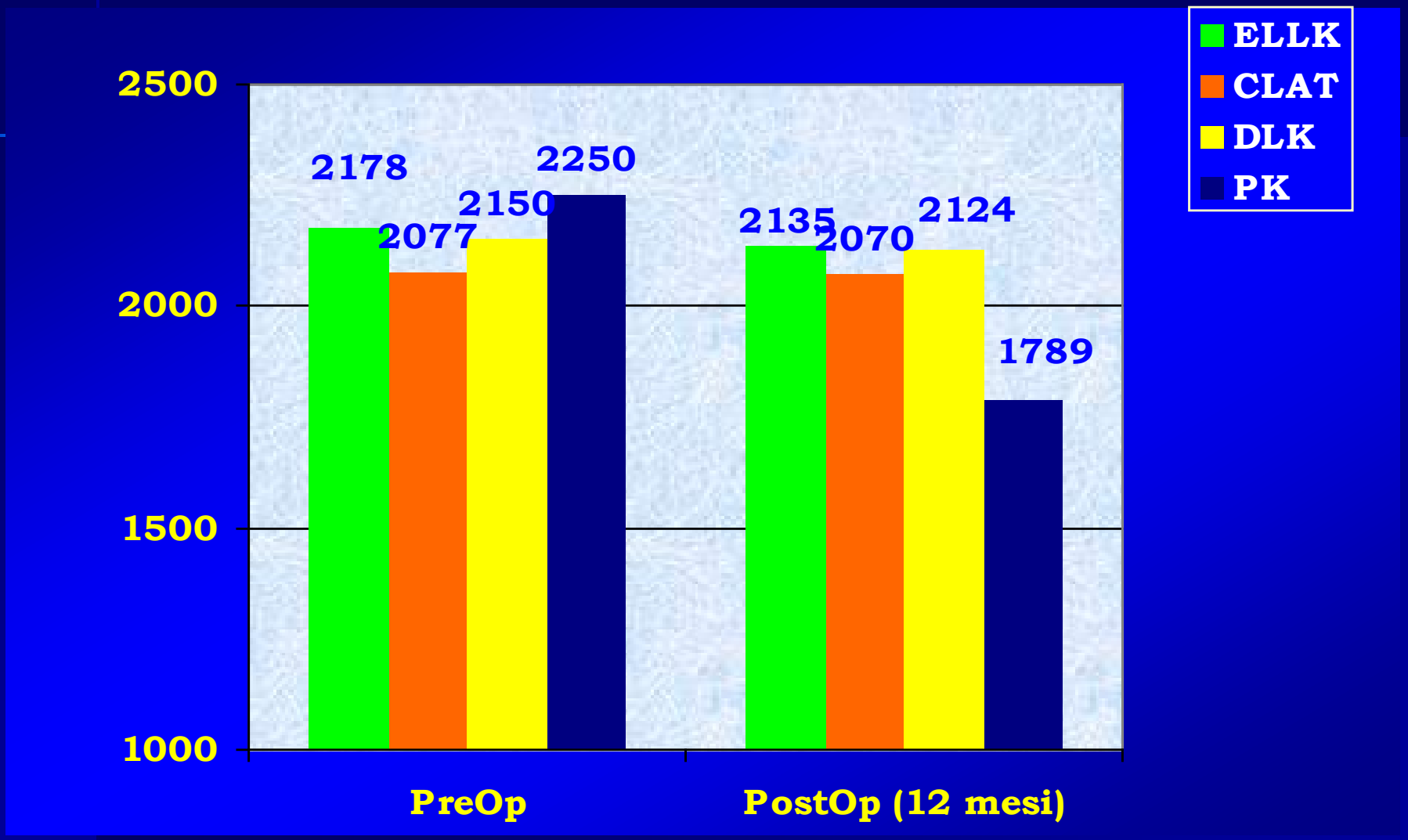
3 mesi post-DLK

6 mesi post-DLK



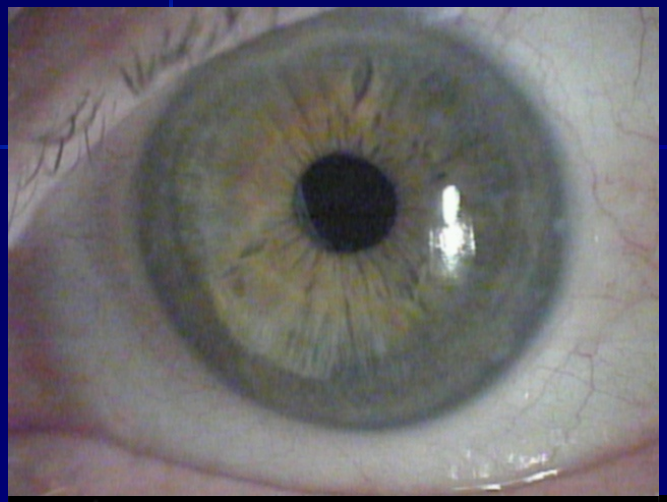
D.C.L. 41aa
12 mesi post-DLK
UCVA 4/10
BCVA 10/10

Risultati Cheratoplastiche KC

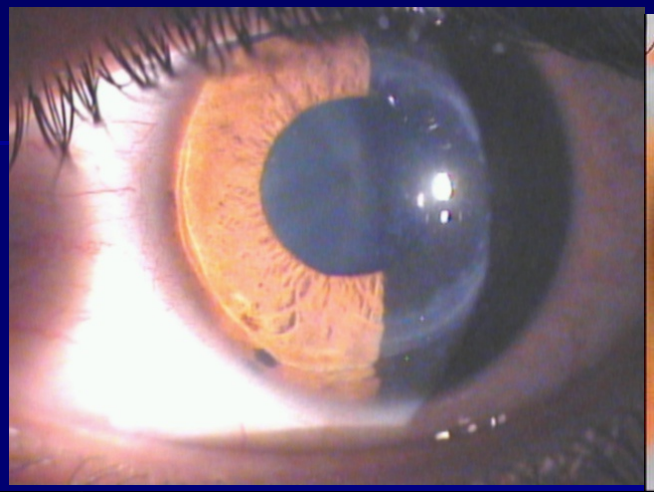


DCM endoteliale

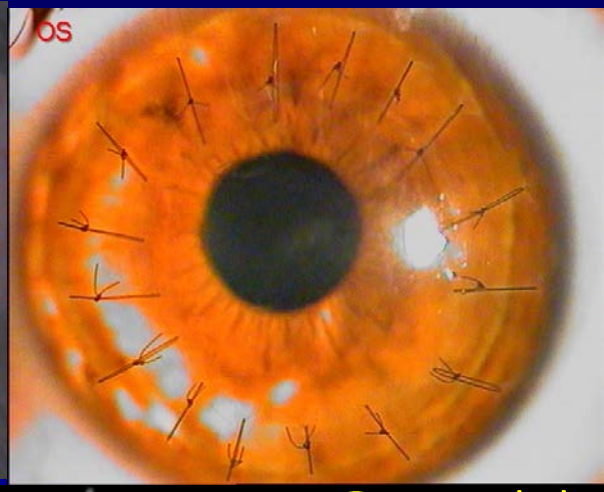
Pattern endoteliale



post PK

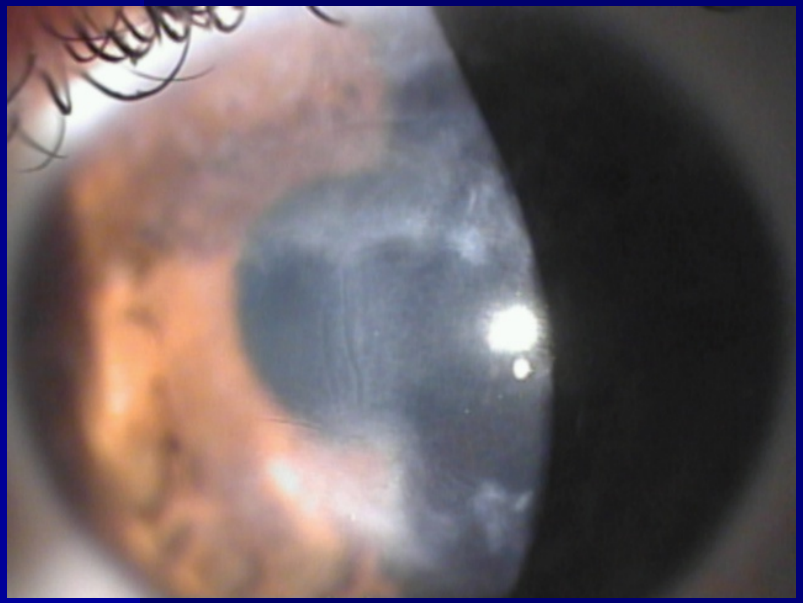


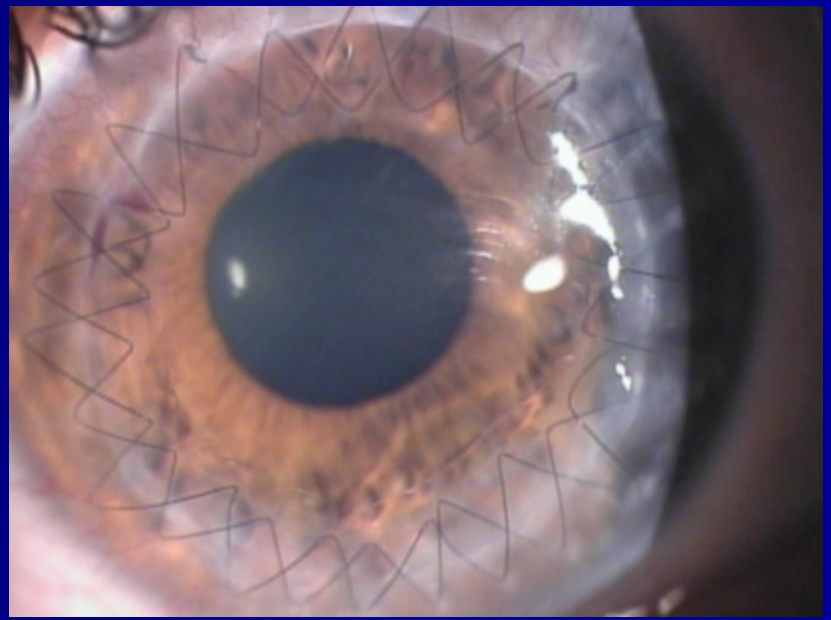
post DLK



post CLAT

L’esecuzione di una LK non pregiudica, comunque, una PK nel caso di risultati non soddisfacenti






Clinica Oculistica – Ospedale S. Salvatore
L'Aquila
13 Giugno 2006

Refractive Surgery 2012: The Era of Lasers and Lenses
ISRS Annual Meeting

Subspecialty Day - November 9 – 10

Crosslinking: Epithelium On or Off?

Leopoldo Spadea

Associate Clinical Professor of Ophthalmology

University of L'Aquila - ITALY
Department of Biotechnological and Applied Clinical Sciences

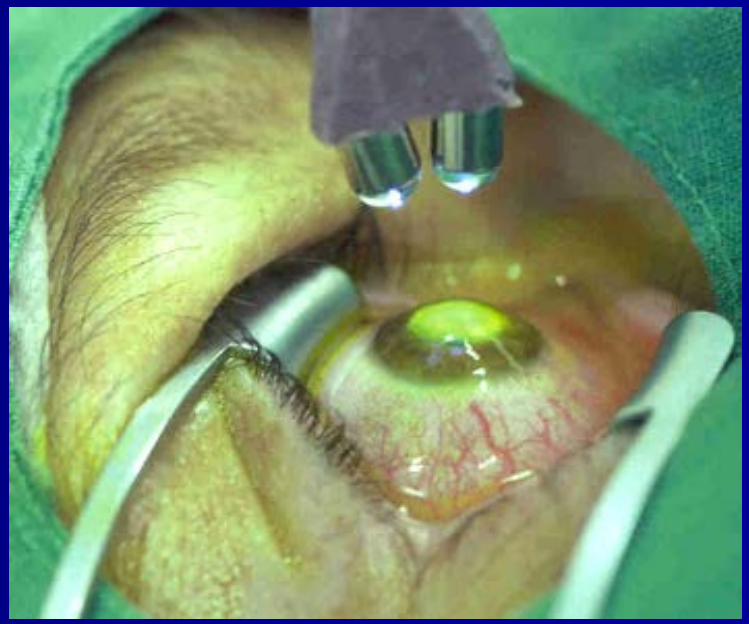
CORNEAL COLLAGEN CROSS LINKING (CXL)

Photopolymerization process of stromal fibers by combined action

- **PHOTOSENSITIZING SOLUTION**

  (Riboflavin – Vit B2)

- **UVA** from a solid state UVA 370nm source



Currently, there are 2 ways to apply the riboflavin to the cornea

The epithelium can be:

1. removed → **Epi-Off**

(Wollensak, Spoerl and Seiler, 2003)

2. left → **Epi-On**

(Boxer Wachler, 2004)

CXL Epi-Off/Epi-On

PATIENT PREPARATION

- Instillation of a miotic agent (Pilocarpine 2%) at least 30 min before surgery
- Topical anesthesia (Lydocaine 4% drops)

CXL Epi-Off

SURGICAL TIMING

- Epithelial removal (blunt spatula): 9 mm diameter
- Solution: Riboflavin 0.1% + Dextrane 20%
- Soaking time 15-20 min
- UVA Source: 370 nm
- Energy: 3 mW/cm²
- Exposition time: 30 minutes

CXL Epi-On

No epithelial removal but…
Problems:

1. Riboflavin (molecular weight 376.37 g/mol) is a hydrophilic macromolecule and cannot penetrate intact epithelium

(Spoerl E, 2007)

2. Corneal epithelium plays a role as barrier to UVA penetration *(Kolozsvari L, 2002)*

CXL Epi-On

- **intact epithelium** → barrier for riboflavin

PHYSICAL TOOLS

- Intrastromal application of riboflavin (Femto-Pockets) *(Kanellopoulos J, JRS 2009)*
- Injection of riboflavin into the stroma (micro-needles) *(Dauqimont L, J M Biol 2010)*
- Epithelial-disruptor/scratches *(Daya S, Cat Refr Surg Today Europe 2011)*
- Iontophoresis

CXL Epi-On

- Iontophoresis

Ocular iontophoresis uses movement of ions under an electric field to apply riboflavin (-) to the stroma through the epithelium

(Vinciguerra P, ESCRS 2012)

CXL Epi-On

- **intact epithelium** → barrier for riboflavin

CHEMICAL TOOLS

Pharmacologic change of epithelial tight-junctions:

- Benzalkonium chloride (BAC)
- EDTA
- Trometamol

augmented with topical anesthetics (proparacaine, tetracaine, oxybuprocaine), and with gentamicin

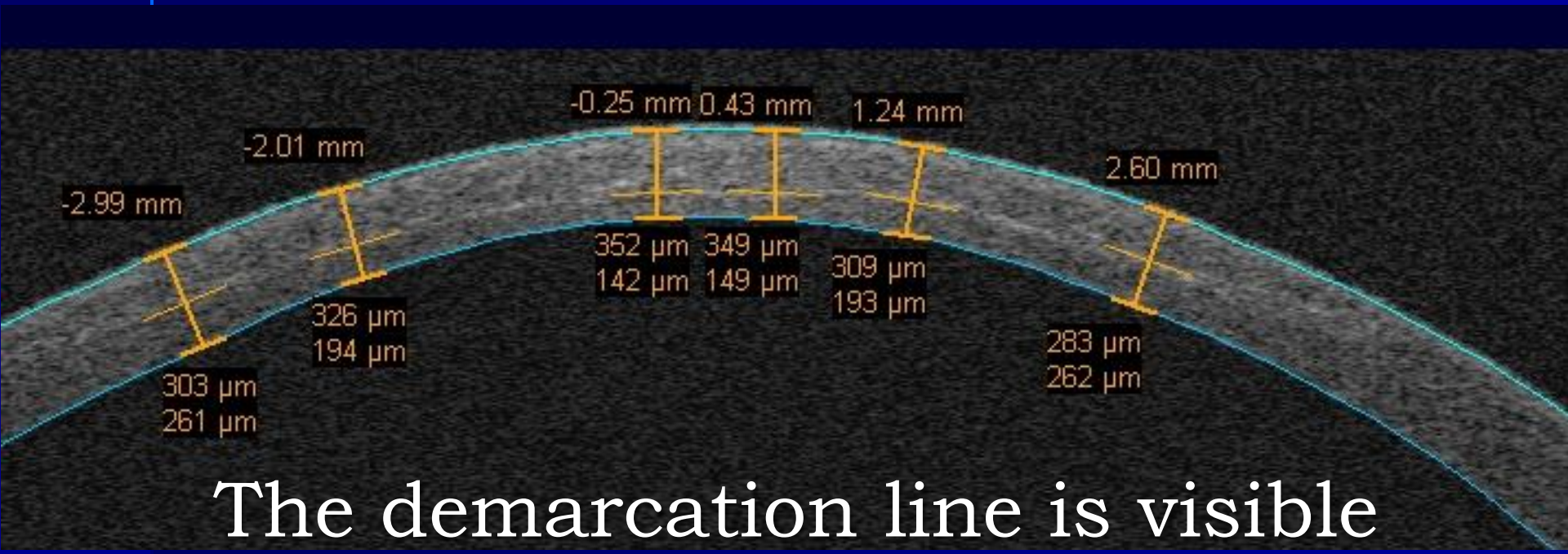
KERATOCYTES APOPTOSIS

- CXL leads to dose dependent keratocyte damage
- Epi-Off: Keratocytes damage reaches a depht of 300µm using a surface UVA dose of 3mW/cm^2

CONTROL

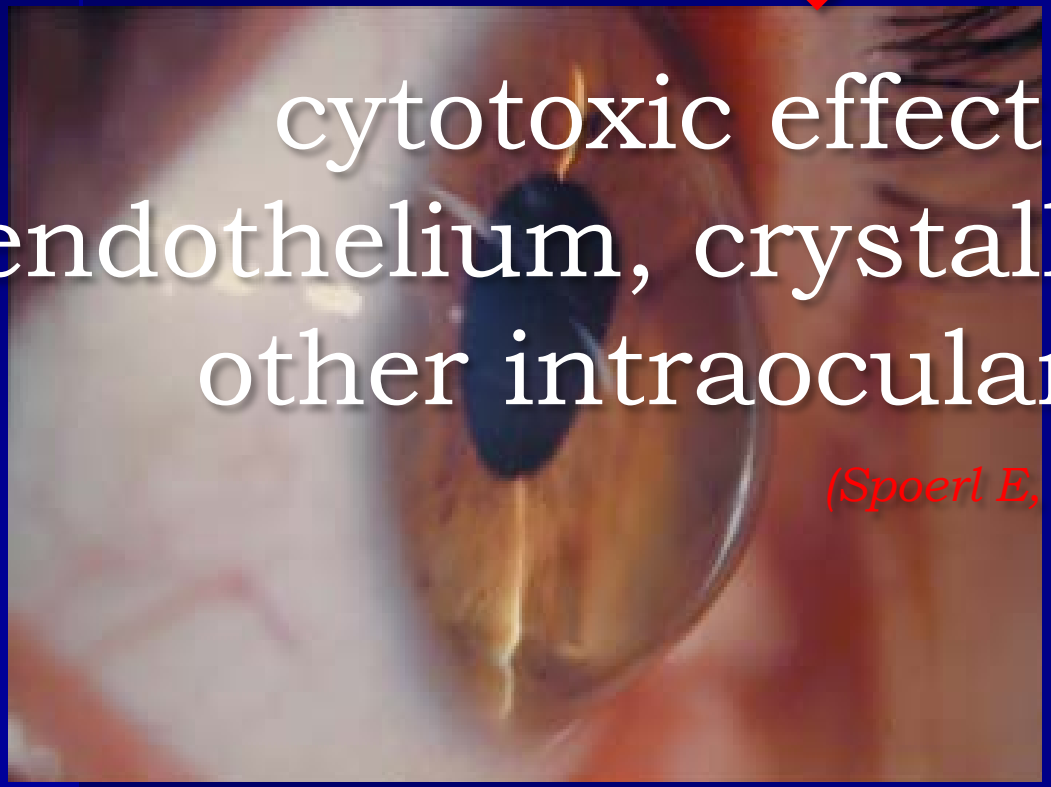
CXL Epi-Off: one month

CXL Epi-Off
AS-OCT



The demarcation line is visible at 290/350µm

CXL **Epi-Off**: Corneal thickness of at least ***400µm***



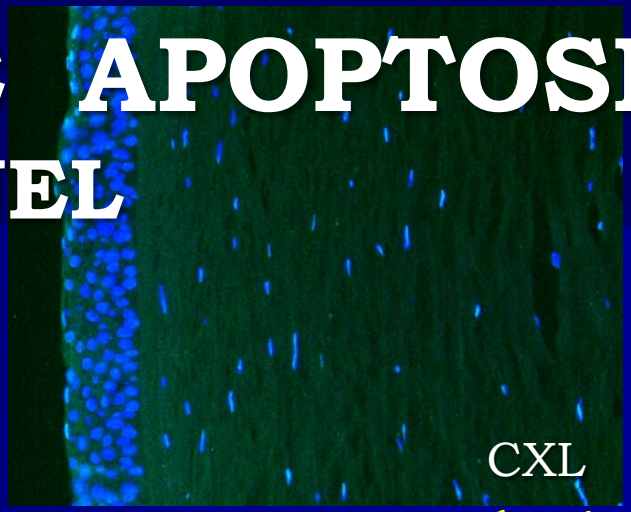
cytotoxic effect on the endothelium, crystalline lens and other intraocular tissues

(Spoerl E, 2007; Wollensak G, 2006)

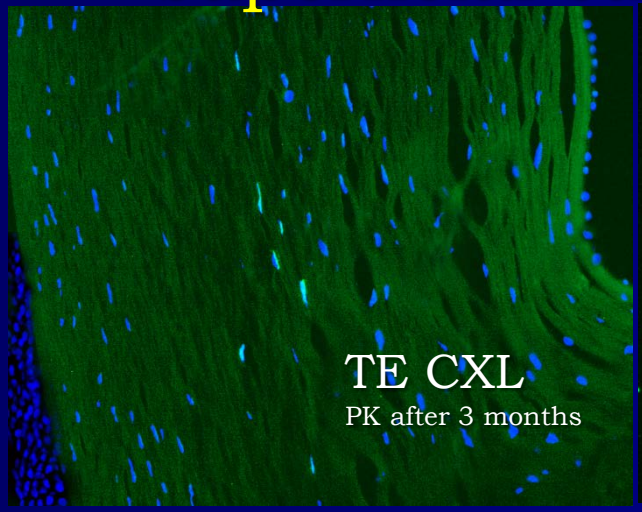
CXL Epi-On

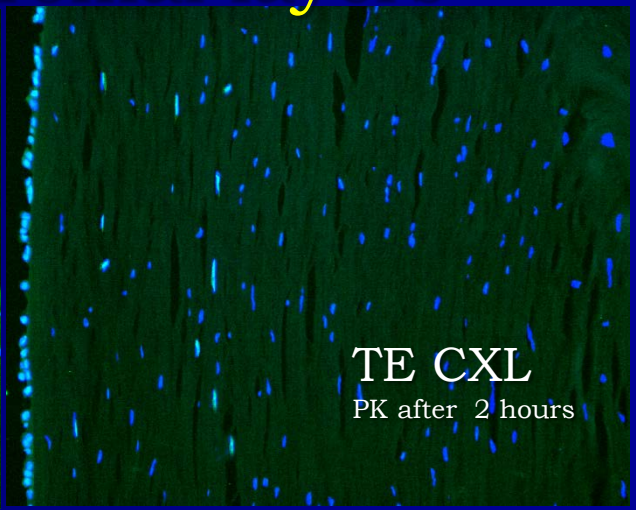
KERATOCYTE APOPTOSIS

TUNEL



Apoptotic keratocytes are present only in the superficial stromal layers

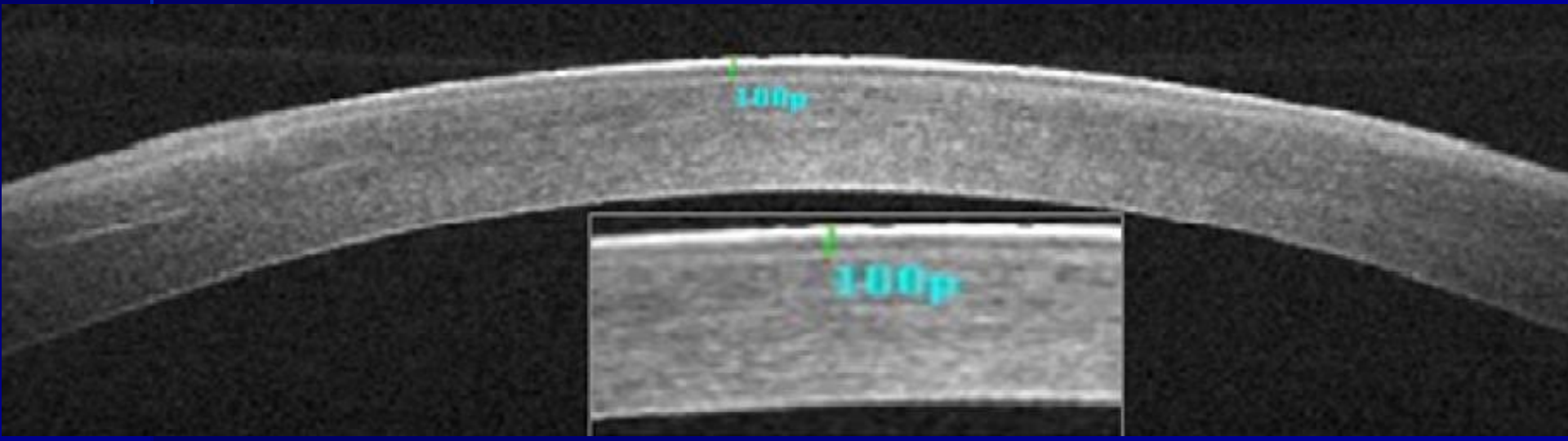




(Mencucci R, ASCRS 2012)

CXL Epi-On
AS-OCT
Transepithelial CXL

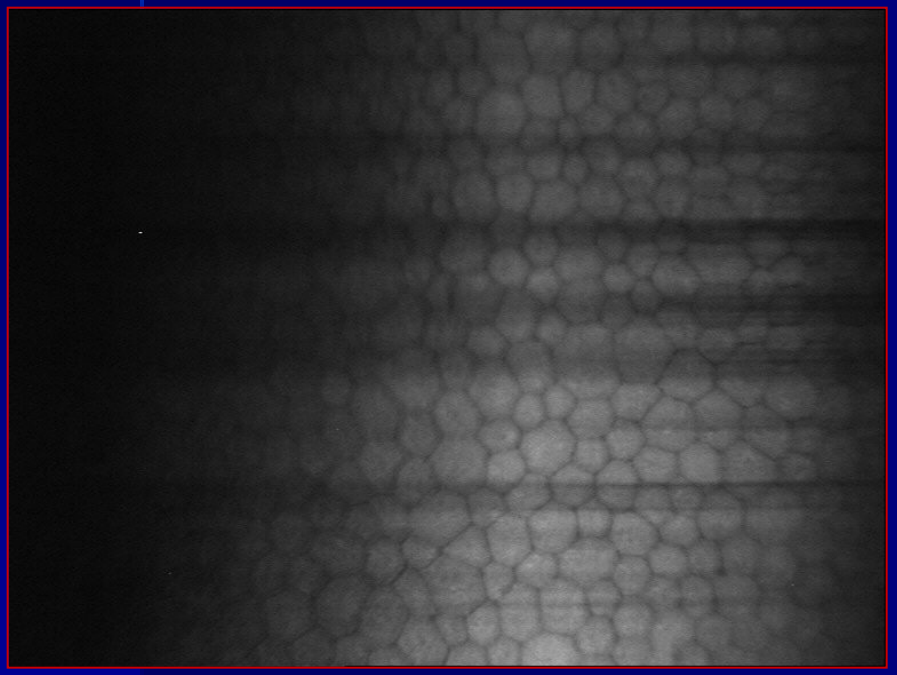
Ricrolin TE® (Sooft, Italy)



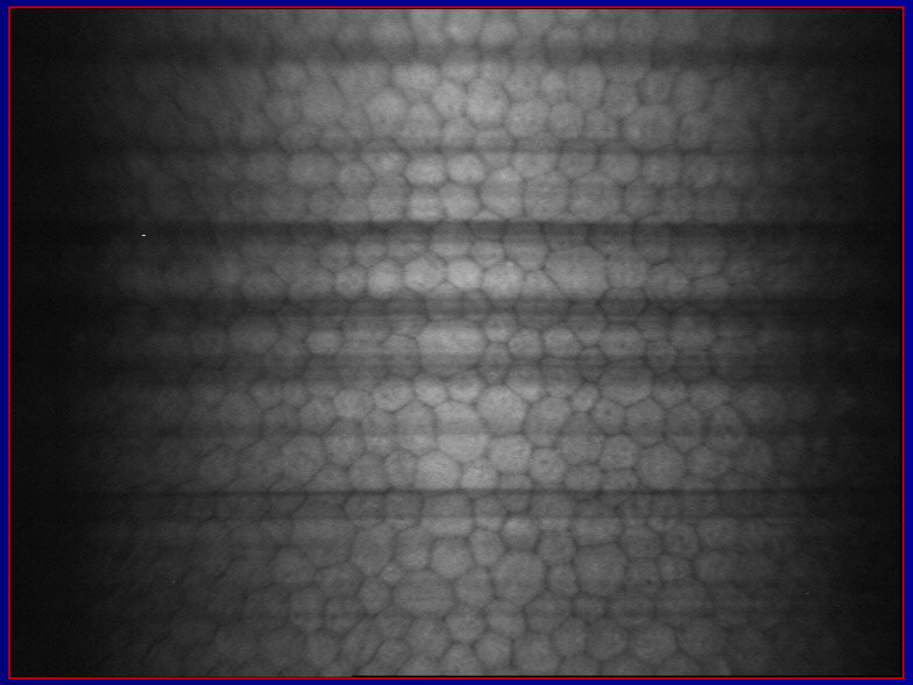
The demarcation line is visible at 100-140µm

(Filippello M, JCRS 2012; Caporossi A, Eur J Ophthal 2012)

ENDOTHELIUM
Epi-Off
no damage



untreated endothelium

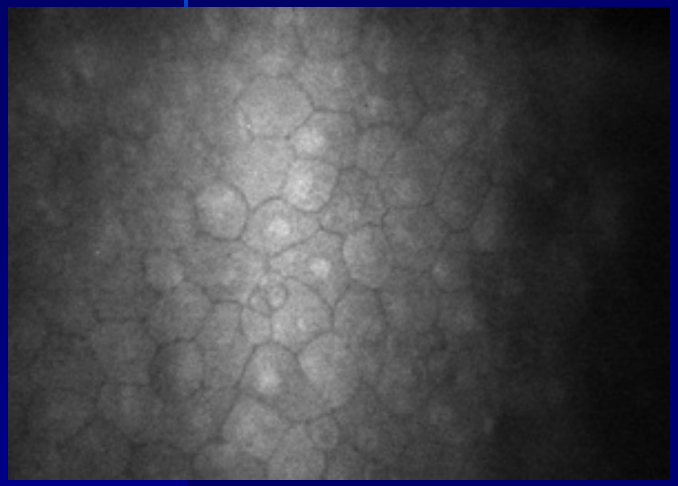
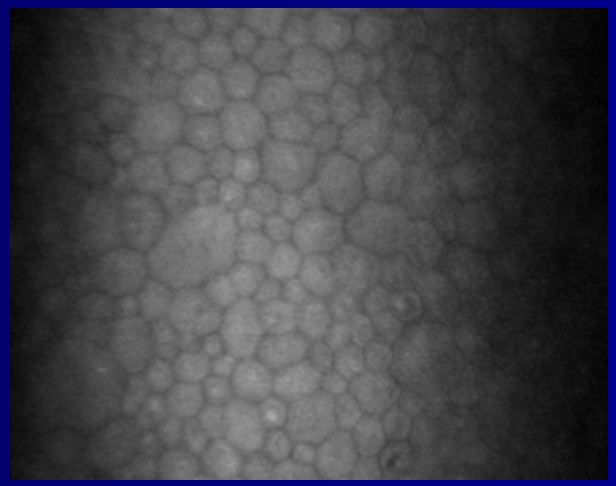
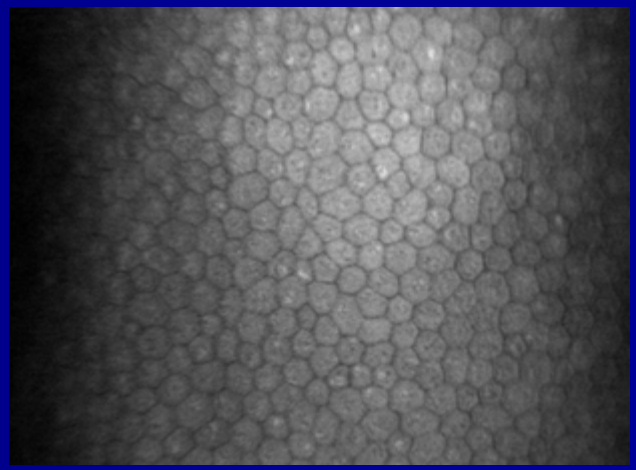


endothelium treated with CXL Epi-Off

ENDOTHELIUM

Epi-On

no damage

No significant corneal endothelial cell changes both in quality and quantity

BIOMECHANICAL EFFICACY

- In rabbits with **Epi-On** TE CXL the stiffening effect was **one fifth** that with the **Epi-Off** procedure

(Wollensak G and Iomdina E, JCRS 2009)

CXL Epi-Off Complications

- Infectious Keratitis (Case reports)
  - Bacterial
  - Acanthamoeba
  - Herpetic (UV exposure? Mechanical trauma? Corticosteroids?)
- Stromal haze
- Sterile infiltrates
- Diffuse lamellar keratitis

(Hovakiman M, J Ophthalmol 2012
Dhawan S, J Ophthalmol 2011
Koller T, JCRS 2009)

CXL Epi-On Complications

- No serious complications were described

(Spadea L, Ophthalmology 2011; Filippello M, JCRS 2012)

- Only some redness and photophobia for 24 to 48 hours

(Koppen C, JCRS 2012)

- Sporadic transient subepithelial haze

(Leccisotti A, JCRS 2010)

CXL Epi-Off
Results at least 1 yr FU

(Hundreds of peer-reviewed studies)

- Kmax: reduction approx 2D
- CDVA: improvement approx 1 Snellen line
- UDVA: variable improvement
- Refractive parameters (spherical equivalent, cylinder): variable changes, approx 2D

CXL Epi-On
Results at least 1 yr FU

*Transepithelial **Epi-On** CXL with enhancers (BAC, trometamol, EDTA, proparacaine, gentamicin) was less effective than **Epi-Off** CXL in stabilizing progressive keratoconus*

(Leccisotti A, JRS 2010; Koppen C, JCRS 2012)

CXL Epi-On
Results at least 1 yr FU
(Peer-reviewed studies)

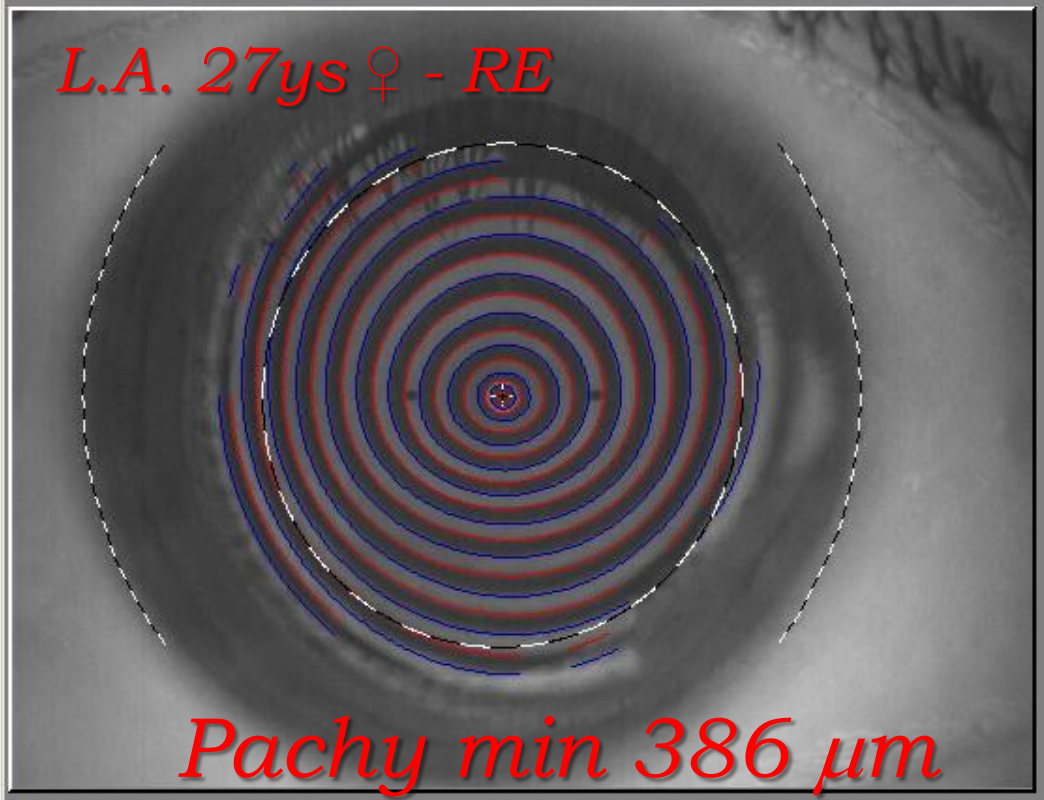
	Leccisotti, 2010	*Spadea, 2011*	*Koppen, 2012*	*Filippello, 2012*
CDVA	+32%	+12%	+8%	+31%
UDVA	NE	+5%	NE	+32%
MRSE	<0.35D	<0.20D	NE	NE
Refr cyl	NE	NE	-0.08	NE
K max	>0.51D	<2.72D	>0.65D	<1.20D
Sim K	<0.10D	<0.90D	<0.11D	NE

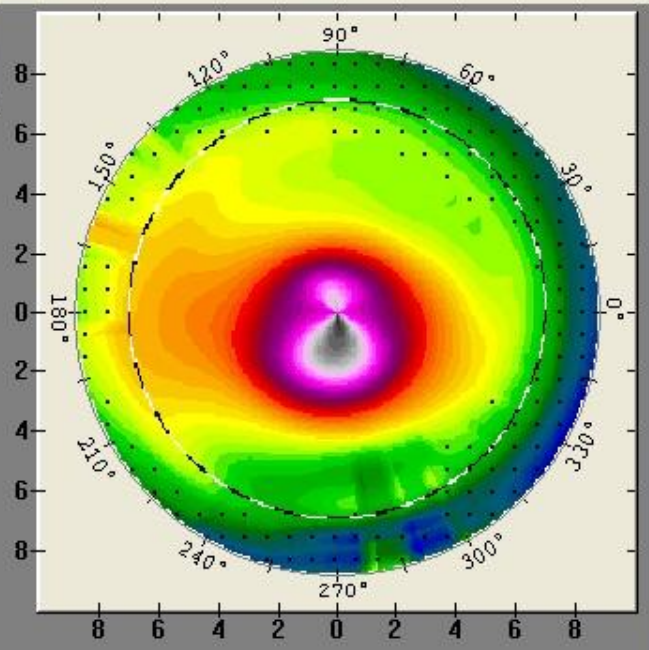
OCULUS - KERATOGRAPH

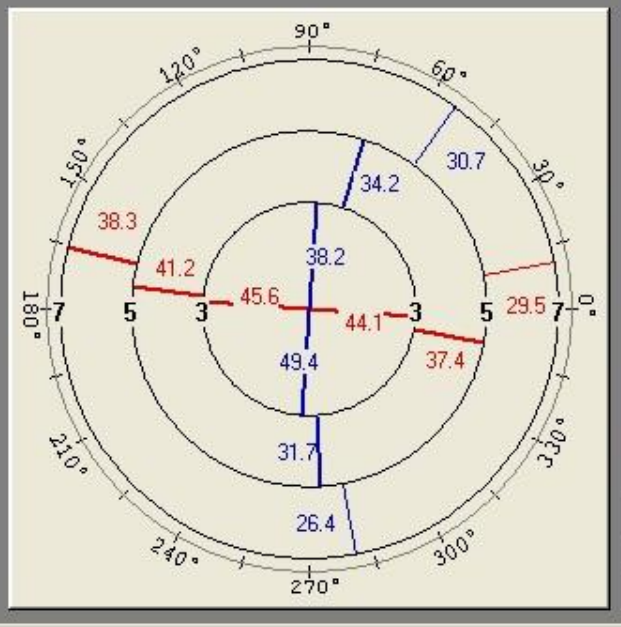
Paziente Esame Visualizza Lenti a contatto Impostazioni Varie JPG Stampa

Nome: Data es.:

Data di n.: Occhio: Data tie.:

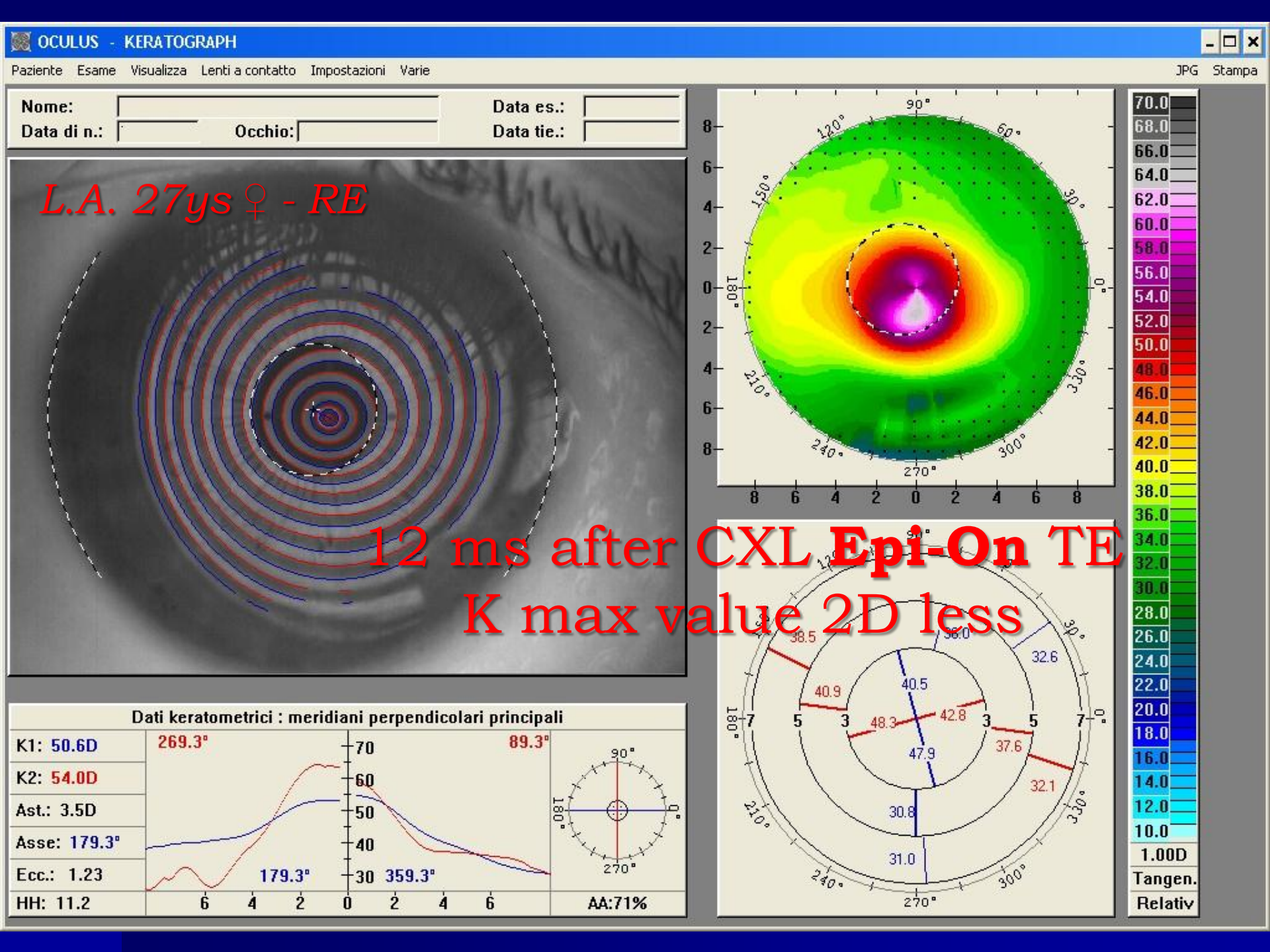






Dati keratometrici : meridiani perpendicolari principali

K1: 51.0D	91.5°	271.5°	
K2: 54.4D			
Ast.: 3.4D			
Asse: 1.5°			
Ecc.: 1.27	181.5°	1.5°	
HH: 11.4	6 4 2 0 2 4 6		AA:67%

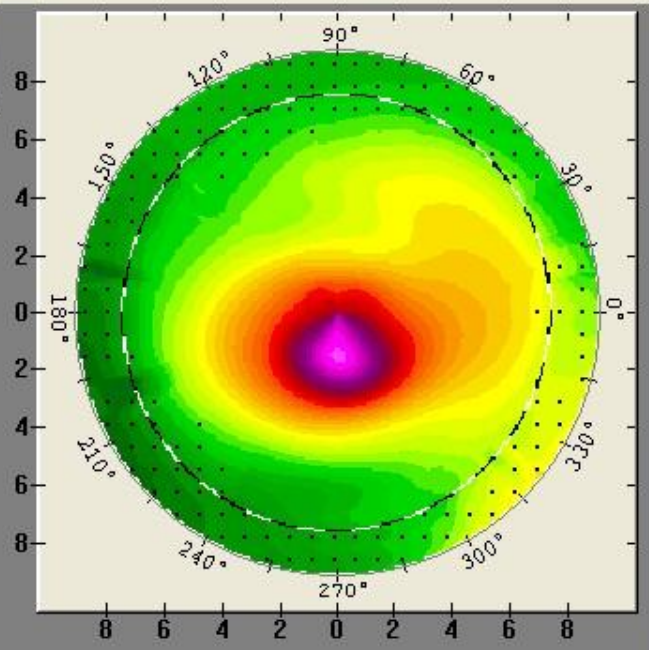

OCULUS - KERATOGRAPH
Paziente Esame Visualizza Lenti a contatto Impostazioni Varie
JPG Stampa
Nome:
Data di n.:
Occhio:
Data es.:
Data tie.:
L.A. 27ys ♀ - RE
12 ms after CXL Epi-On TE
K max value 2D less
Dati keratometrici : meridiani perpendicolari principali
K1: 50.6D
K2: 54.0D
Ast.: 3.5D
Asse: 179.3°
Ecc.: 1.23
HH: 11.2
269.3°
89.3°
179.3°
359.3°
AA:71%
38.5
36.0
32.6
40.9
40.5
48.3
42.8
37.6
32.1
47.9
30.8
31.0
1.00D
Tangen.
Relativ

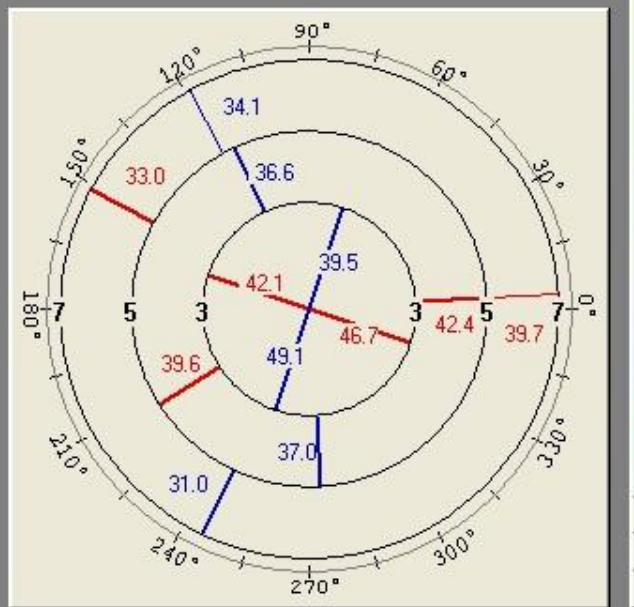
OCULUS - KERATOGRAPH

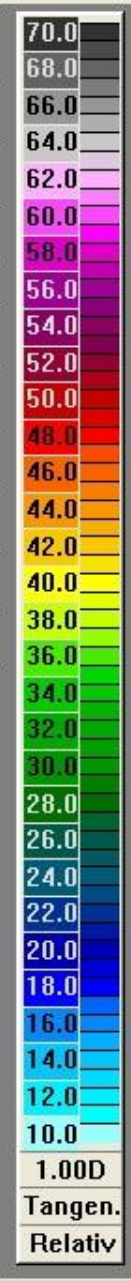
Paziente Esame Visualizza Lenti a contatto Impostazioni Varie JPG Stampa

Nome: Data es.:

Data di n.: Occhio: Data tie.:







Dati keratometrici : meridiani perpendicolari principali

K1: 47.6D

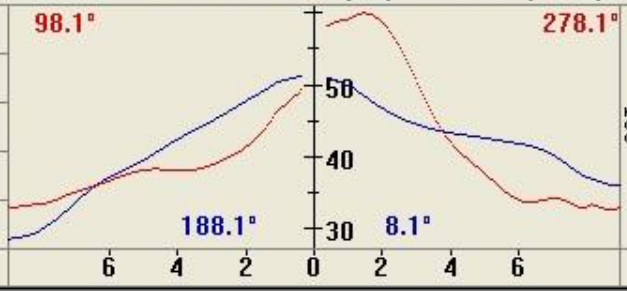
K2: 48.8D

Ast.: 1.2D

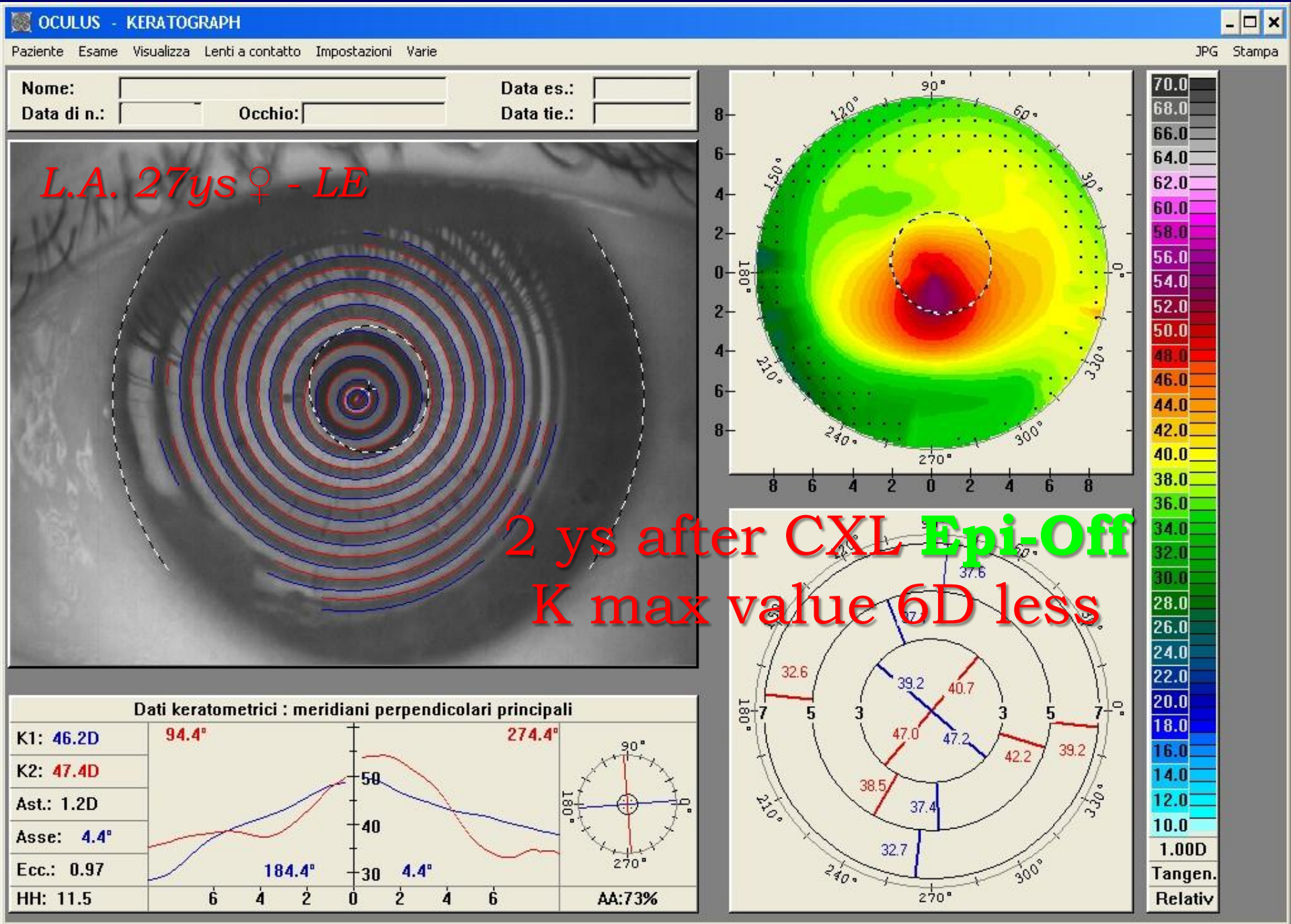
Asse: 8.1°

Ecc.: 1.03

HH: 11.5



AA:69%


OCULUS - KERATOGRAPH
Paziente Esame Visualizza Lenti a contatto Impostazioni Varie
JPG Stampa
Nome:
Data di n.:
Occhio:
Data es.:
Data tie.:
L.A. 27ys ♀ - LE
2 ys after CXL Epi-Off
K max value 6D less
Dati keratometrici : meridiani perpendicolari principali
K1: 46.2D
K2: 47.4D
Ast.: 1.2D
Asse: 4.4°
Ecc.: 0.97
HH: 11.5
94.4°
274.4°
184.4°
4.4°
AA:73%
1.00D
Tangen.
Relativ

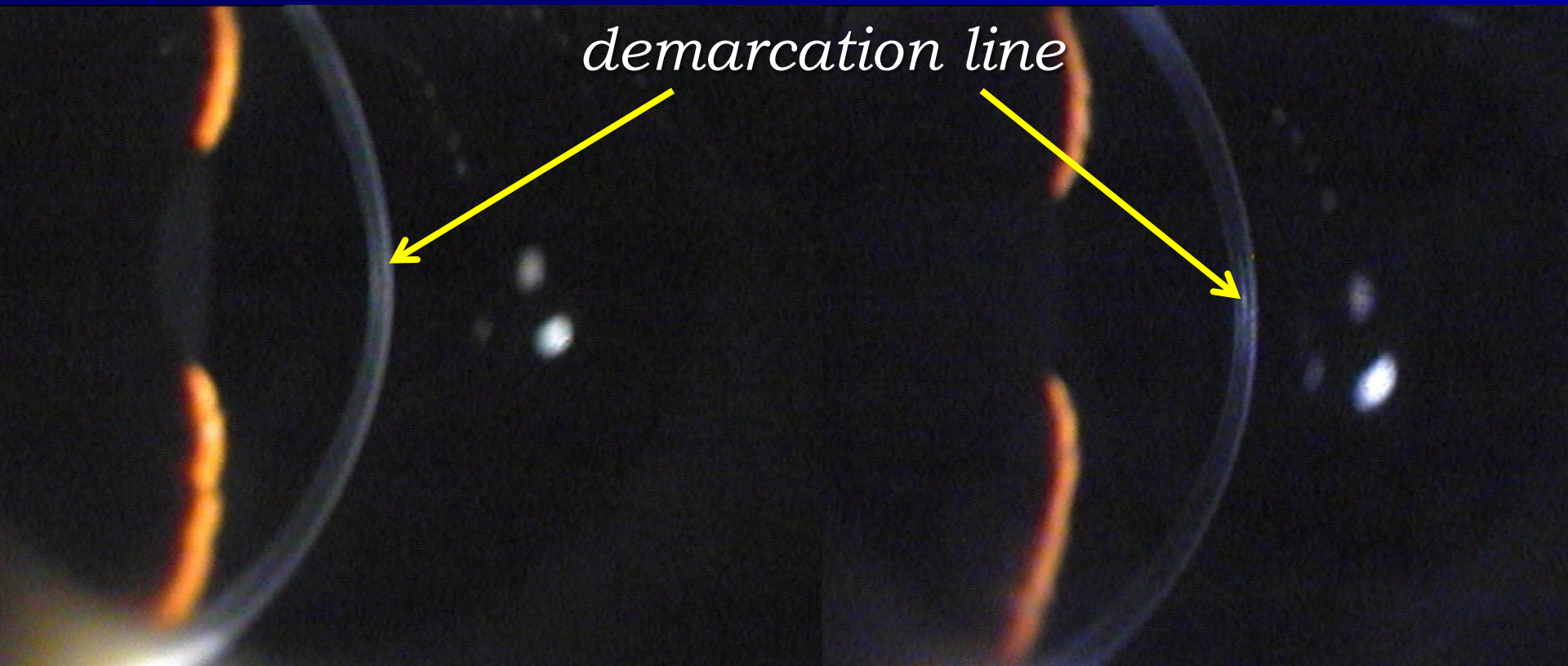
L.A. 27ys ♀

Pre CXL **Epi-On** TE
RE +1sf=-1.75(90°) 20/40

Pre CXL **Epi-Off**
LE -0.50sf=-1.75(40°) 20/30

12 ms after CXL **Epi-On** TE
RE +2sf=-3(100°) 20/30

2 ys after CXL **Epi-Off**
LE +1.75sf=-2.25(180°)
20/20



CXL Epi-On Results at 2 yrs FU

*Transepithelial **Epi-On** CXL procedure showed a relative instability with a regression of functional outcomes returning to baseline at 24 months of f-up*

(Caporossi A, EVER 2012)

CXL Epi-Off Vs CXL Epi-On

- More effective
- Shorter riboflavin loading time
- Solid laboratory and theoretical evidence
- Very long experimentation and follow-up

- Easier technique
- Less complications
- Also for thin corneas (<400mm)
- Shorter recovery time
- Absence of post-treatment pain
- Less intensive postop management
- Better patient compliance
- Usefull in pediatrics
- Regression of functional outcomes?

CXL Epi-Off Vs CXL Epi-On

- **More effective**
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- **Less complications**
- **Also for thin corneas (<400mm)**
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- Usefull in pediatrics
- Regression of functional outcomes?

CXL Epi-Off Vs CXL Epi-On

- **More effective**
- Shorter riboflavin loading time
- Solid laboratory and theoretical evidence
- Very long experimentation and follow-up

- Easier technique
- **Less complications**
- **Also for thin corneas (<400mm)**
- Shorter recovery time
- Absence of post-treatment pain
- Less intensive postop management
- Better patient compliance
- Usefull in pediatrics
- ***Regression of functional outcomes?***

CXL Epi-Off Vs CXL Epi-On


Thanks
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