

# Keratoconus Update

## Diagnosis of Keratoconus

**Sheraz Daya**  
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## Diagnosis of Keratoconus

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## Anatomy of the normal cornea

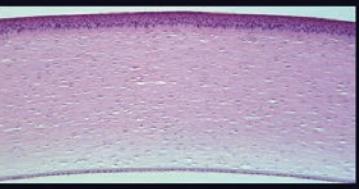
• Epithelium 75 microns

• Bowman's layer 10 microns

• Stroma 450 microns

• Descemet's membrane 10 microns

• Endothelium 5 microns



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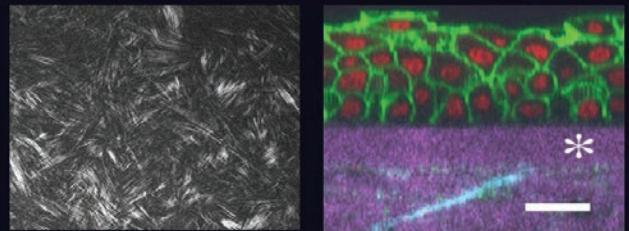
## Collagen



Source: Campbell, HA. Biologie 1996. Éditions du Renouveau Pédagogique Inc. 30.Laurel.

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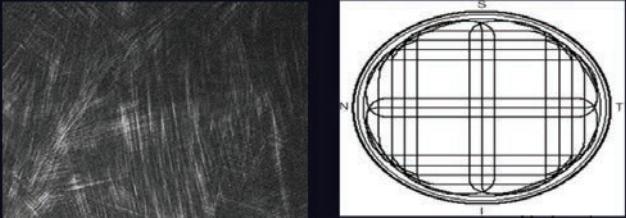
## Anterior stroma structure



Jester et al.

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## Posterior stromal structure



Jester et al.

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## Keratoconus

### Defined:

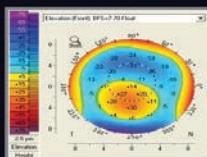
- Progressive, non-inflammatory thinning disorder of the cornea, leading to altered shape adversely affecting visual performance
- Variety of ectasias
  - Keratoconus
  - Pellucid Marginal Degeneration
  - Keratoglobus



## Keratoconus

### Keratoconus Facts

- 50 to 230 cases per 100,000
- Strong association with Atopy
- Why ?
  - Inflammation, influences elasticity ?
  - Eye Rubbing
- Definite rationale for:
  - Aggressive treatment of Allergic Conjunctivitis
    - Mast cell stabilisers
    - Steroids



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## Keratoconus

- Asymmetric
- Usual onset during puberty
- Progressive myopia + irregular astigmatism
- Corneal thinning with conical deformation
- Association
  - Atopy
  - eye rubbing
  - Down's syndrome
  - Marfan's syndrome

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# 'Diagnosis of Keratoconus'

(slides 1-8)

Sheraz Daya  
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## Keratoconus

- Epithelial thinning
- Fragmentation of Bowmans
- Apical scarring
- Fleischer ring
- Stromal thinning
- Posterior stromal / Descemet's folds (Vogt's)
- Descemet's tear - hydrops

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## KERATOCONUS - Pathogenesis

Atopy	CTL	Hormonal	Systemic Conditions
Inflammation IL-1 $\alpha$ IL-1 IL-6 TNF $\alpha$	Proteases MMP 9 Reduction in inhibitors TIMP's A Proteinase A2 macroglobulin	E.Oxidative Nitric Oxide Superoxide dismutase Reduction of Enzymes Aldehyde dehydrogenases	Apoptosis Programmed cell death P53 Proliferation Differentiation

Degradation and altered synthesis of corneal tissue

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Courtesy Jesus Merayo, Oviedo, Spain

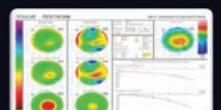
### Balance of Degradation vs Regeneration



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## Diagnosis

- Clinical
- Topographic
  - Pentacam – more sensitive and specific
    - Belin-Ambrosio
- Corneal Hysteresis
  - Corneal strength



## Keratoconus

- CLINICAL
  - Astigmatism – increasing
  - Retinoscopy/ retroillumination
    - Droplet appearance – red reflex
    - Scissoring
  - Munson Sign



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## Rizzuti's Sign



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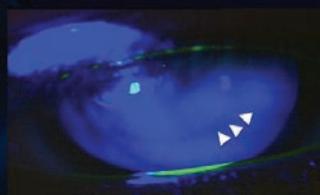
## DIAGNOSIS - Clinical

### Keratoconus

- Thinning
- Apical scarring
- Vogt's striae



## DIAGNOSIS - Clinical



Fleischer Ring

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# 'Diagnosis of Keratoconus'

(slides 9-24)

## Vogt's Striae



## Hydrops



## Pellucid Marginal Degeneration

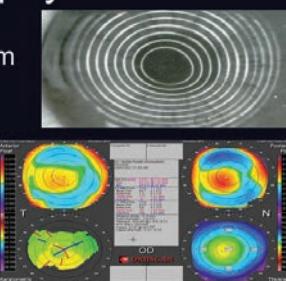


## Keratoglobus

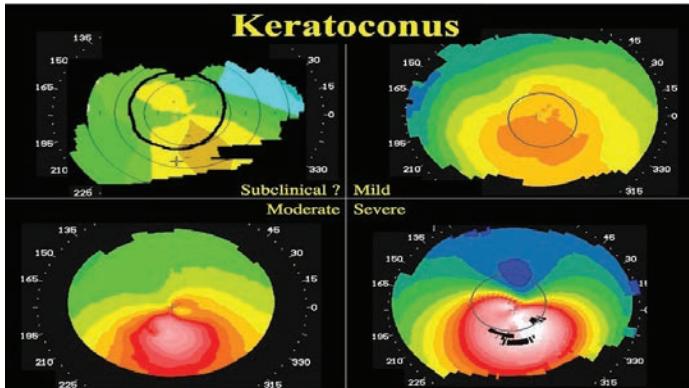


## DIAGNOSIS: Corneal Topography

- Steep cornea
- Non-orthogonal astigmatism
- Inferior steepening
- Coinciding point:
  - Anterior elevation
  - Posterior elevation
  - Thinnest spot on cornea



## Keratoconus

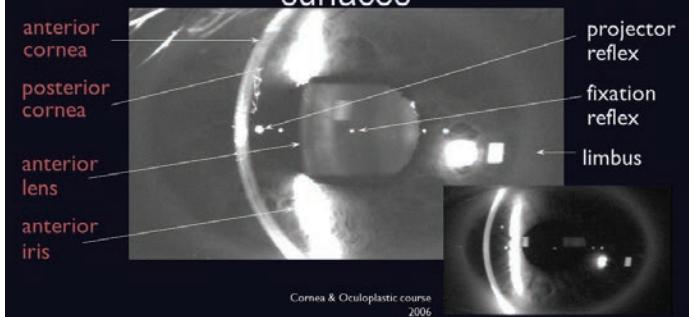


## 3-Dimensional Topography

- Slit beam – Orbscan
- Scheimpflug
  - Pentacam (*Oculus*)
  - Gallilei (*Zeiss*)
  - Sirius (CSO)
- OCT
  - Casia 2 (*Tomey*)
  - MS 39 (CSO)
  - Antereon (*Heidelberg*)

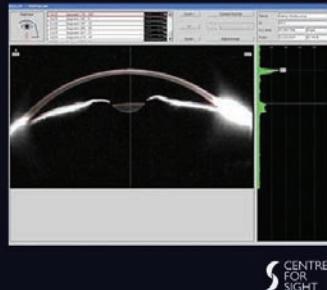
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## Scanning slits measure several surfaces

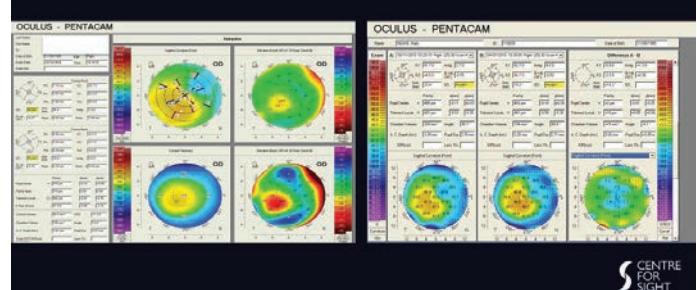


## Scheimpflug imaging

- Pentacam (Oculus, Inc)
- Two integrated cameras:
  - Central: size and orientation of the pupil, and fixation
  - Rotating Scheimpflug camera
- 50 Scheimpflug images during one scan in less than 2 seconds

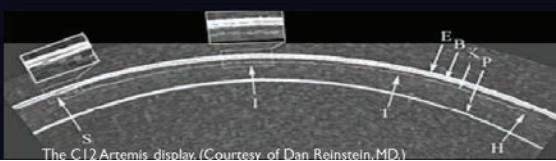


## Scheimpflug imaging

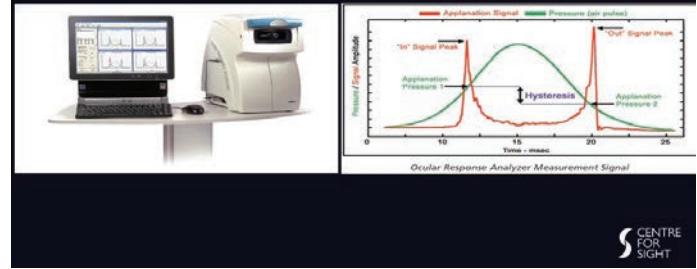


## Ultrasound digital topography

- High-frequency ultrasound scanning
- Thickness of corneal layers with high precision.
- Post refractive surgery.
- Not limited to optically transparent tissue.



## Corneal Biomechanics



## CORVIS - Corneal Deformation

### KERATOCONUS

- Deforms earlier  
Increased
- Deformation
  - Oscillation

*Courtesy Renato Ambrosio*

## Keratoconus Diagnosis

- Clinical
  - Oblique or ATR astigmatism
  - Increasing astigmatism
  - Scissoring
- Diagnostics
  - 3-D tomography – gold standard
  - Hysteresis - useful

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## Treatment options

### TRADITIONAL

- Spectacles
- Contact lenses
  - Soft; toric; RGP;
- Corneal graft
  - Penetrating keratoplasty
  - Lamellar keratoplasty

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## Management of Keratoconus 2017

- Collagen Crosslinking (CXL)
  - +/- topo guided PRK
- Intracorneal Rings
- Myoring
- Toric Phakic Lenses (ICL or Artisan)
- Corneal Transplantation

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# 'Diagnosis of Keratoconus'

## (slides 25-32)

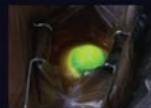
# Keratoconus Update

## Corneal Collagen CrossLinking for Keratoconus

Marcela Espinosa  
MD



## Collagen Crosslinking for Keratoconus



Marcela Espinosa-Lagana MD

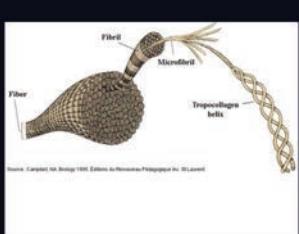
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## Collagen Crosslinking (CXL)

- Riboflavin
  - Large Molecule
  - Does not penetrate epithelial tight junctions
- Traditional Method of CXL
  - Epithelial Removal
- Transepithelial CXL
  - Tetracaine
  - Transepithelial Riboflavin solutions
- Epithelial Disruption CXL
  - Alternative option
  - Breaks in epithelium allow Riboflavin to penetrate

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## Collagen



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## Collagen Cross Linking

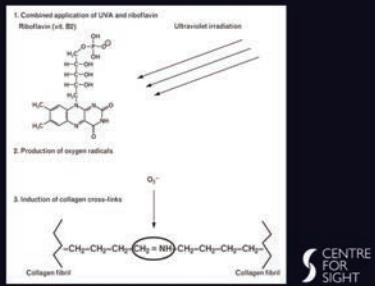
- Natural
  - Ageing
- Pathogenic
  - Diabetes Mellitus – chronic hyperglycaemia
- Artificial
  - Strengthen collagenous valves - Cardiac Surgery
  - Cornea for Keratoconus !



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## Collagen Cross Linking

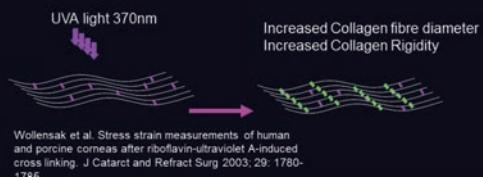
- Mechanism
  - Riboflavin
  - UVA light exposure
  - Formation of free radicals
  - Oxidation reaction with development of cross-links in collagen



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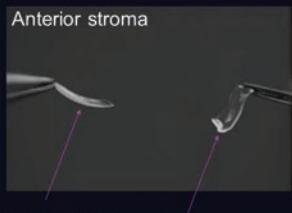
## Cross Linking

- Increases Tensile rigidity in Human Cornea by 328% (stress testing)
- Young's Modulus increases 4.5 times



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## Basic research



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## Epithelial Disruption - Method

- Topical Anaesthesia
- Topical Antibiotic
- Topical Pilocarpine (2%)
- Epithelial Disruption (Daya Disruptor)
- Riboflavin instillation (45 mins)



Check penetration at Slit Lamp



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# 'Corneal Collagen CrossLinking' (slides 1-16)

Marcela Espinosa  
MD

## Corneal "Cross linking"

UV light exposure (370nm)  
3mW/cm<sup>2</sup>  
Variable aperture  
30 minutes



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## RESULTS - different

Bandage CTL – removed by 48 hours

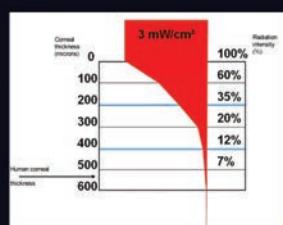
Persistent Epithelial Defect	0
Infectious Keratitis	0
Sterile Infiltrates	0
Pain – day of procedure	111

Demarcation line or Anterior Haze 61%

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## Safety

Corneal thickness must be 400μm  
If thinner use riboflavin without dextran  
Measure before treatment!



Irradiance is reduced by 95% at endothelium

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## Postop CXL – 1 month



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## CXL – 1 month postop Demarcation

61%



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## Corneal "Cross Linking"

- Retrospective Study
- Keratoconus
- Analysis of Results Centre for Sight
- 154 Consecutive eyes 2011-2016

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## Collagen Crosslinking (CXL)

### Procedures

- 30min UV exposure 41 procedures
  - 39 Epithelial disruption
  - 2 Epithelial removal
- 10min UV exposure 113 procedures
  - 63 Epithelial disruption
  - 50 Epithelial removal

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## Collagen Crosslinking (CXL)

### Follow Up

-1m	141
-6m	131
-1y	99
-2y	48
-3y	27

Ave 1.5 (0.1 – 5.1)

STD 1.2

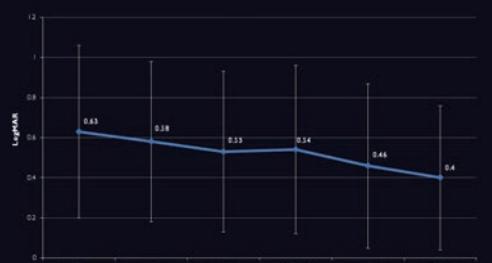


## Corneal “Cross Linking”

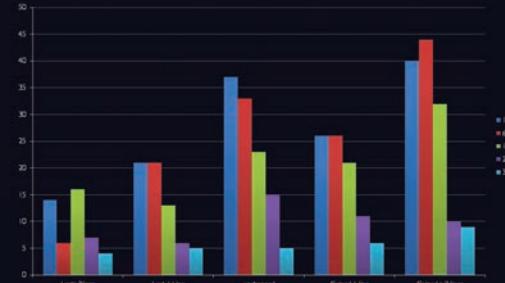
### VISUAL OUTCOMES



### UCVA



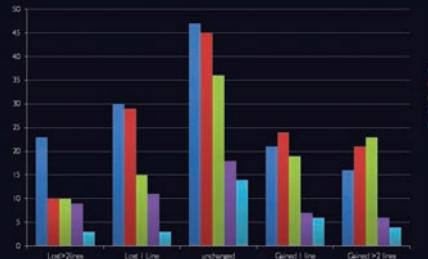
### UCVA CHANGE



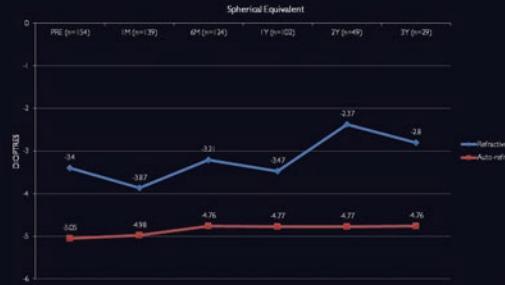
### BCVA



### BCVA CHANGE



### SPHERICAL EQUIVALENT



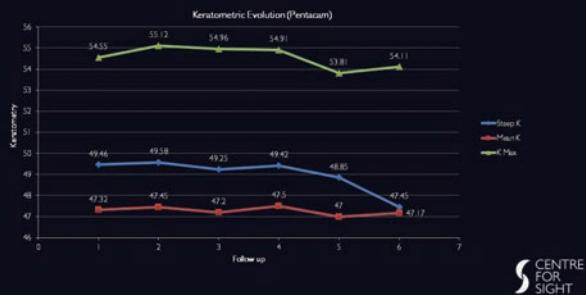
### ASTIGMATISM- REFRACTIVE



# ‘Corneal Collagen CrossLinking’ (slides 17-30)

Marcela Espinosa  
MD

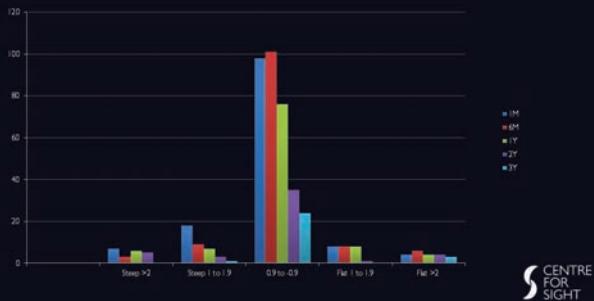
## KERATOMETRIC EVOLUTION (PENTACAM)



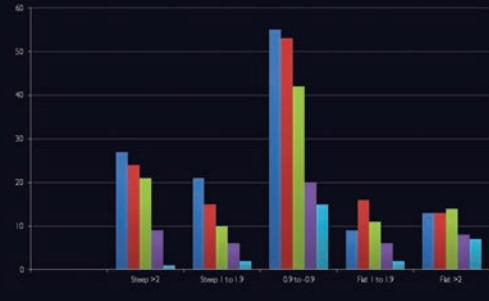
## STEEPEST KERATOMETRY (PENTACAM)



## MEAN KERATOMETRY (PENTACAM)



## KMAX CHANGE (PENTACAM)



## RESULTS

- Bandage CTL – removed by 48 hours
- Persistent Epithelial Defect 0
- Infectious Keratitis 0
- Sterile Infiltrates 0
- Pain – day of procedure
- Demarcation line or Anterior Haze 61%

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Thank you



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# Keratoconus Update

## Intracorneal rings for Keratoconus

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## Intracorneal Rings for Keratoconus

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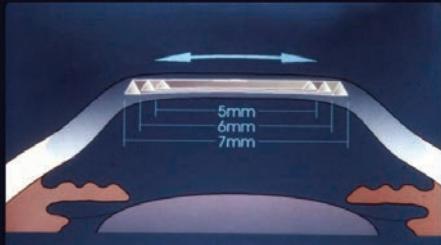
## Rings – How do they work ?



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## Rings – How do they work ?

### Function of Diameter and Thickness



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## Rings – how do they work?

- Corneal remodeling through addition technique: preserves corneal integrity
- Corneal topography regularization restoring/preserving natural prolate profile
- Improving contact lens tolerance
- Displace corneal apex towards centre
- Corneal stabilization, delaying or eliminating the need for corneal transplantation

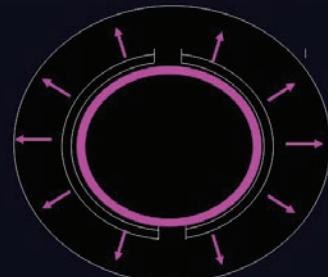
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## Intracorneal rings - insertion techniques

- Conventional - manual lamellar tunnel creation; fixed diameter
- Femtosecond laser - quicker, easier, customizable channel parameters

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## Rationale for Smaller Outer Diameter



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## Intracorneal rings

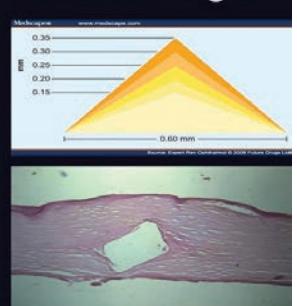
### 3 TYPES

- Ferrara / Kerarings
- Intacs
- Myoring

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## Intracorneal rings - Ferrara rings

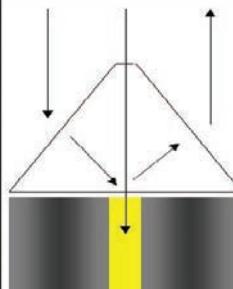
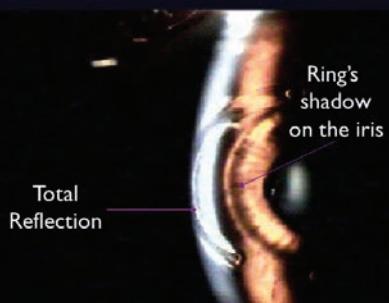
- 5.0/6.0mm PMMA micro-inserts
- 600/800 microns wide – triangular cross section
- 160 (90-210) degree segments  
– 0.15mm to 0.35mm
- First implanted 1994



# 'Intracorneal Rings for Keratoconus' (slides 1- 8)

Sheraz Daya  
MD FACP FRCS(Ed) FRCOphth

### Ferrara Ring - Prismatic Effect



### Intracorneal rings - INTACS

- 7mm diameter PMMA micro-inserts
- 6.0mm (SK)
- 150-210 degree segments - 0.21mm to 0.45mm
- Hexagonal cross section
- Can treat corneas up to 55D



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### Intracorneal rings - INTACS SK

- Smaller - 6mm diameter PMMA micro-inserts
- 90 to 150 degree segments - 0.21mm to 0.50mm
- For more severe cases – up to 62D
- Elliptical profile

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### Intracorneal rings - indications

- Spectacle / contact lens intolerance
- Keratometry up to 62D
- Clear visual axis
- Pachymetry > 400 microns

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### Intracorneal rings - indications

- MUST HAVE REALISTIC EXPECTATIONS
- Aim is to restore contact lens tolerance and improve BCVA - NOT UCVA
- Long recovery period – fluctuating vision for up to 18 months

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### Intracorneal rings - procedure

- Daycase / Topical anaesthesia
- Bandage contact lens for 24hrs
- Topical triple therapy for 1 month
  - G. Chloramphenicol Q2H
  - G. Levofloxacin Q2H
  - G. FML qds tapering by one drop weekly

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## Intralase Insertion of Intacs

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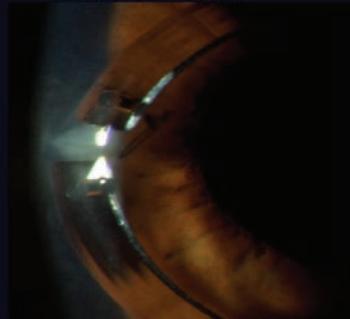
# 'Intracorneal Rings for Keratoconus' (slides 9-24)

## INTACS - complications

- Infection
- Extrusion
- Perforation - mechanical > femto
- Channel deposits
- Inadequate effect

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## Infection



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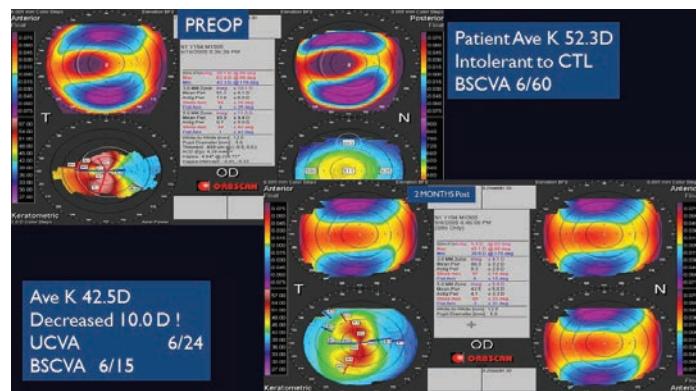
## Infection



## Extrusion



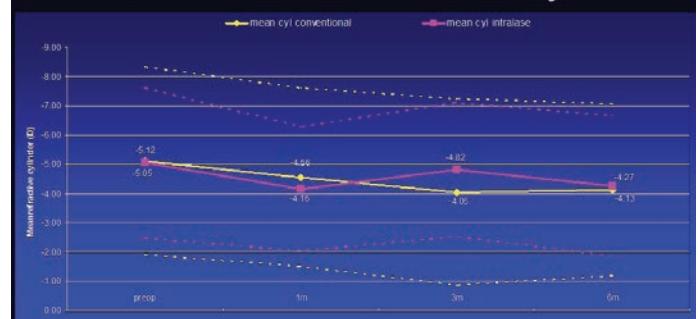
## Channel deposits



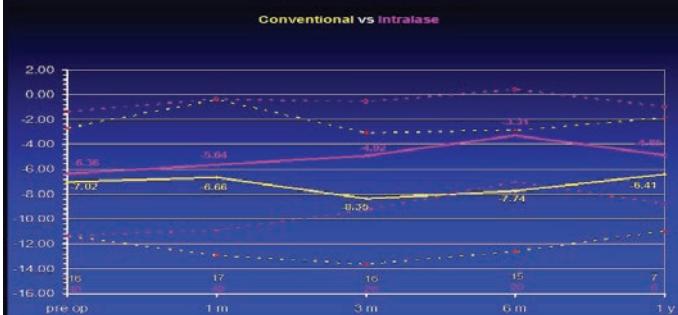
## Results - Change In Keratometry



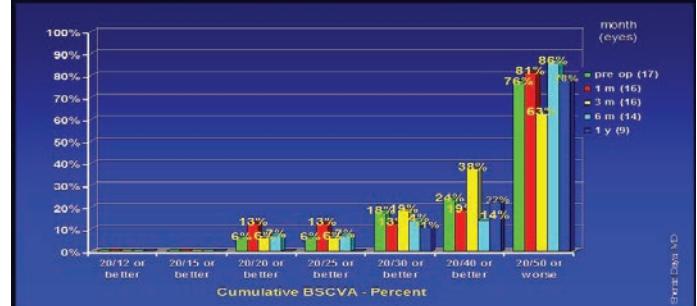
## Results - Mean Refractive Cylinder



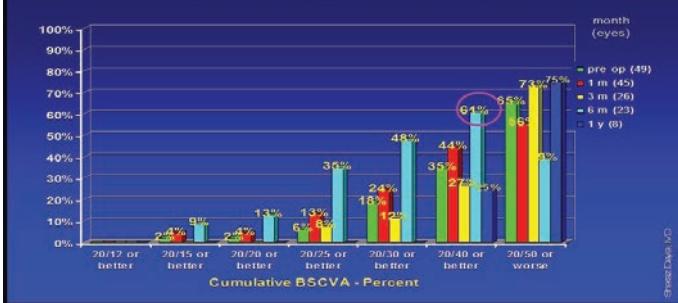
## Results - Spherical Equivalent



## Results - BSCVA -mechanical



## Results - BSCVA - Femtosecond



## RESULTS - Ferrara literature

	BSCVA	MEAN KERATOMETRY	MEAN REF CYL	SPHERICAL EQUIV
PESANDO ET AL EUR J OPHTH 2010 130 EYES	Improved in 97.6%	Decreased by 4.59D		Decreased by 5.51D
FERRARA +TORQUETTI JCRS 2009 80 EYES	Improved in 86.4%	Decreased by 4.64D		Decreased by 2.96D
KWITKO/SEVERO JCRS 2004 51 EYES	Improved in 86.4%	Decreased by 5.59D	Decreased by 1.66D	Decreased by 1.53D
MIRANDA ET AL JRS 2003 36 EYES	Improved in 80.6%	Decreased by		Decreased by 2.49D

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## Results - INTACS literature

	BSCVA	MEAN KERATOMETRY	MEAN REF CYL	SPHERICAL EQUIV
SANSANAYUDH ET AL JCRS 2010 10 EYES-5K	Mean improved from -0.51 to -0.24 D logmar	Decreased by 7.87D	Decreased by 1.15D	Decreased by 3.05D
RODRIGUEZ ET AL JCRS 2009 7 EYES-8K	Improved in 86.4%	Decreased by 5.23D	Decreased by 1.66D	Decreased by 11.74D
WACHLER ET AL, OPHTHALMOLOGY 2003 12 EYES	Improved in 45%			Decreased by 1.53D
J COLIN JCRS 2006 57 EYES	Improved by 2 lines or more in 63%	Decreased by 3.7D	Decreased by 2.94D	Decreased by 2.49D

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## Intracorneal rings - conclusions

Improves contact lens tolerance and BSCVA

Reduction in SE, Mean K & Astigmatism

Femtosecond better than mechanical

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## Intracorneal rings

- Can be performed in conjunction with CXL
  - Early data
  - MORE effect
  - Less fluctuation

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Thank you !

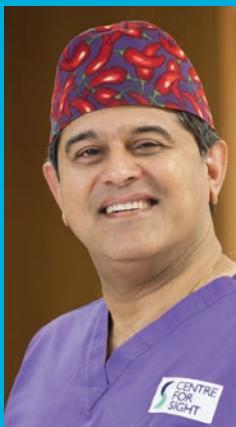
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# ‘Intracorneal Rings for Keratoconus’ (slides 25-32)

# Keratoconus Update

## Phakic Intraocular Lenses

**Sheraz Daya**  
MD FACP FRCS(Ed) FRCOphth



## PHAKIC INTRAOCULAR LENSES

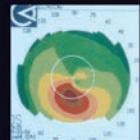


SHERAZ DAYA  
MD FACP FACS FRCS(Ed)



## LENS SURGERY

- Additive
- Reversible
- Optically – advantageous
  - Hyperopia / Myopia
  - Toricity
  - ? Future – Multifocality
- Astigmatism
  - Application in KERATOCONUS



## INDICATIONS

- Any Refractive Error
  - Myopia to -18.00 (ICL), Artisan (-23.00)
  - Hyperopia to +10.00 (ICL), Artisan (+12.00)
  - Astigmatism 6.00D
- AC Depth > 2.8mm
- Endothelial Cell Count >2000 cells/mm<sup>2</sup>
- KERATOCONUS
  - Stable Refraction
  - Good Refraction with Glasses



## PHAKIC IOL - Options

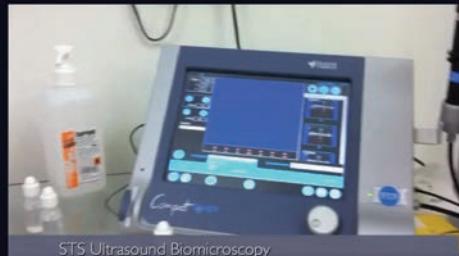
- VISION ICL
  - implantable contact lens
- ARTISAN / ARTIFLEX
- (Veriseyes/Veriflex)



## Anterior Segment Biometry



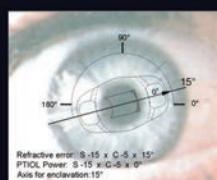
## STS Ultrasound Biomicroscopy



## ARTISAN/ARTIFLEX IOL

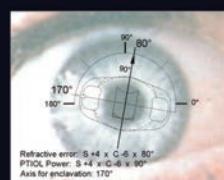


## ARTISAN Toric IOL AXIS of Toricity 90 or 180



Refractive error: S-15 x C-5 x 15°  
PTIOL Power: S-15 x C-5 x 0°  
Axis for encavitation: 15°

PTIOL - 0

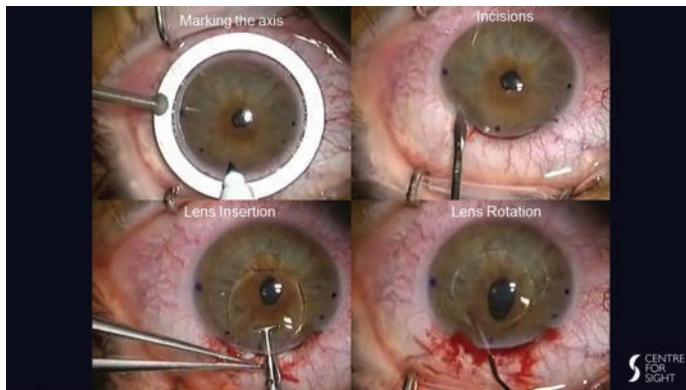


Refractive error: S-4 x C-6 x 80°  
PTIOL Power: S-4 x C-6 x 90°  
Axis for encavitation: 170°

PTIOL - 90



# 'Phakic Intraocular Lenses' (slides 1-16)



**The ICL**

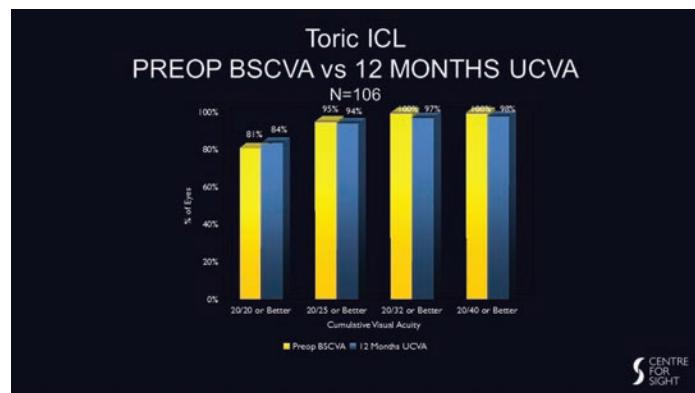
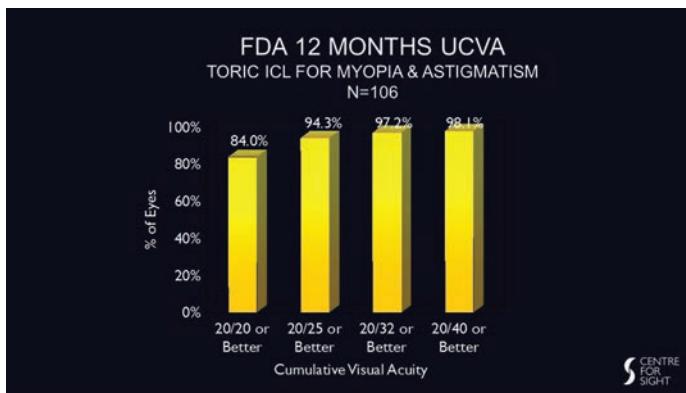
- Implantable Contact Lens (ICL)
- CE mark 1997 and FDA approval in 2005
- Sold in more than 60 countries world wide
- More than 2 million ICLs implanted

**CENTRE FOR SIGHT**

### FDA STUDY

- 207 Eyes of 123 Patients
- Spherical Equivalent
  - ♦ Mean: -9.37D
  - ♦ Range: -2.38D to -19.50D SEQ
- Refractive Cylinder
  - ♦ Mean: 1.94D
  - ♦ Range: 1.0D to 4.0D
- Mean Age: 35 years
- 45% Male, 55% Female

**CENTRE FOR SIGHT**



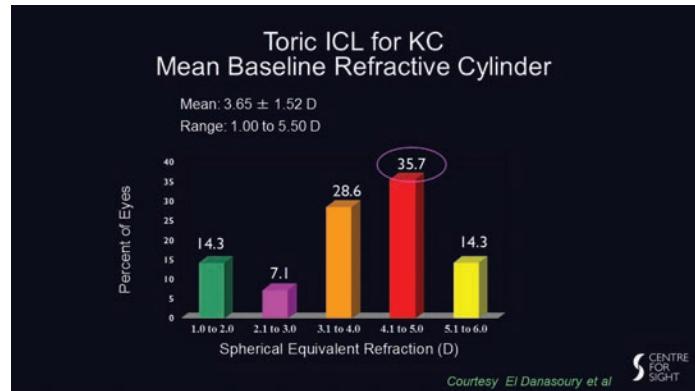
### Toric ICL for KC

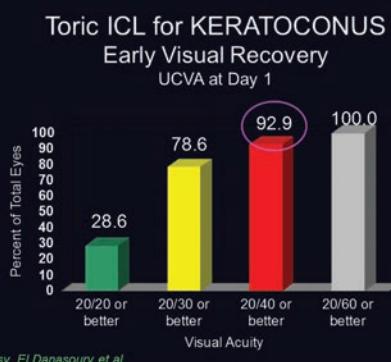
#### Demographics

- 37 eyes of 23 patients.
- Mean age:  $35.2 \pm 3.1$  years (range; 21 to 45 yrs)
- 68.3% were males.
- Follow-up rate:
  - 26 eyes (70.3%) completed 3 months.
  - 21 eyes (56.8%) completed 6 months.
  - 14 eyes (37.8%) completed 12 months.

*Courtesy El Danasouri et al*

**CENTRE FOR SIGHT**





**Toric ICL for KERATOCONUS**  
**SAFETY:** BSCVA - lines gained or lost  
Baseline Vs Postoperative



**Personal Data - Keratoconus**



**NEW ICL**

- V4C
  - No peripheral iridotomy required
  - Simpler for Patient & Surgeon



**When is ICL indicated ?**

- Inform every patient about possible options:
  - LASIK and ICL / Toric ICL
- Suspicious cornea
  - Form fruste Keratoconus (with good spectacle vision)
  - Thin cornea
  - Dry eye
- Post LASIK / PRK; RK etc:
  - ICL as secondary procedure

**S** CENTRE FOR SIGHT

**Summary**

- Superior Quality of Vision
  - Less HOA
  - Gain in retinal size image
- Can be reversed
  - In case refraction changes
  - In case of need
- No change in axial length readings
- High level of Patient Satisfaction

**S** CENTRE FOR SIGHT

Thank you

**S** CENTRE FOR SIGHT

# 'Phakic Intraocular Lenses'

(slides 17-23)

**Sheraz Daya**  
MD FACP FRCS(Ed) FRCOphth

# Keratoconus Update

## Keratoconus - An Algorithmic approach

**Sheraz Daya**  
MD FACP FRCS(Ed) FRCOphth



# Keratoconus An Algorithmic Approach

SHERAZ DAYA

MD, FACP, FACS, FRCS(Ed), FRCOphth



## Delphi Panel – Collaboration of International Corneal Societies

SPECIAL ARTICLE

### Global Consensus on Keratoconus and Ectatic Diseases

José A. P. Gomes, MD, PhD,\* Donald Tan, MD, PhD,† Christopher J. Rapuano, MD,‡ Michael W. Belin, MD,§ Renato Ambrosio, Jr, MD, PhD,¶ José L. Guell, MD,|| François Malecze, MD, PhD,\*\* Kohji Nishida, MD,†† and Virinder S. Sangwan, MD,‡‡, The Group of Panelists for the Global Delphi Panel of Keratoconus and Ectatic Diseases

**Background:** Despite extensive knowledge regarding the diagnosis and management of keratoconus and ectatic corneal diseases, many controversies still exist. For that reason, there is a need for current guidelines for the diagnosis and management of these conditions.

and other ectatic diseases. It also provides an insight into the current worldwide treatment of these conditions.

**Key Words:** keratoconus, corneal ectasia, consensus, corneal cross-linking, corneal transplantation



## Financial Disclosure

Company	Code	
1. Abbott Medical Optics Inc.	S	C = Consultant / Advisor
2. Bausch + Lomb	C,L	E = Employee
3. Carl Zeiss Meditec	C	I = Lecture Fees
4. Clavista	C	O = Equity Owner
5. Ellex	L	P = Patents / Royalty
6. Excellens	C,O	S = Grant Support
7. LinCor Biosciences	C	
8. Lumensis	C	
9. Medicem	C	
10. Nidek, Inc.	C,L	
11. Omeros	C	
12. Physiol	L	
13. PRN	O	
14. STAAR Surgical	C,O	
15. StrathSpey Crown	C	
16. Scope Pharmaceuticals	C	
17. Rayner	C	



Selection of Experts  
Email invitations: 40  
No. of participants: 36

Study Design & questionnaires  
(literature review, list of items)

Three panels  
(12 experts each)

DEFINITION/  
DIAGNOSIS      NON-SURGICAL  
MANAGEMENT      SURGICAL  
MANAGEMENT

1st round      1st round      1st round  
14 items (n=12)      14 items (n=12)      43 items (n=12)

2nd round      2nd round      2nd round  
7 items (n=12)      9 items (n=12)      19 items (n=12)

3rd round &  
discussion      3rd round &  
discussion      3rd round &  
discussion  
3 items (n=11)      5 items (n=7)      10 items (n=11)

Final meeting (open discussion of results)

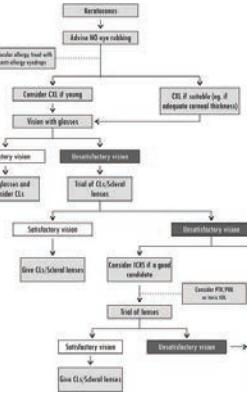
4th round      4th round  
2 items (n=12)      10 items (n=12)



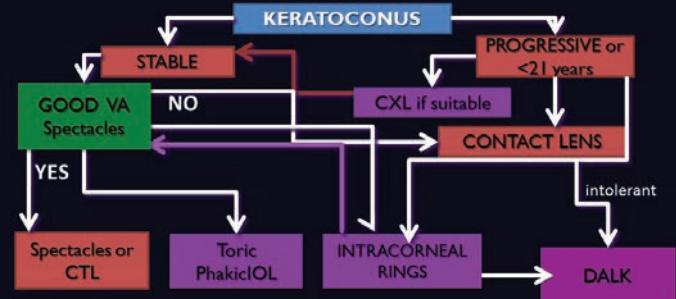
TABLE 1. Coordinators and Expert Panel by Major Topic		
Definition/Diagnosis	Non-surgical Management	Surgical Management
Coordinators	Coordinators	Coordinators
Renato Ambrosio (Brazil)	José Gomes (Portugal)	Jed Gull (USA)
Michael Belin (United States)	François Malecze (France)	Christopher Rapuano (United States)
Koichi Nishida (Japan)	Veronica Sangwan (India)	David Tan (Singapore)
Panellists	Panellists	Panellists
Jean Abad (Colombia)	Peregrine Abdell (United States)	Amit H. Dandona (United States)
Roberto Alberici (Argentina)	Aldo Caporaso (Italy)	Richard Davidson (United States)
Deborah Jacobs (United Kingdom)	Danielle de Freitas (Brazil)	Sheraz Daya (United Kingdom)
Detlef Knecht (Germany)	Farhad Hafezi (Switzerland)	Enrique Grana (Argentina)
Hamidreza Darvishi (United Kingdom)	Deborah Jacobs (United States)	Hernandez (Mexico)
Robert Feder (United States)	Stephen Kasthuri (United States)	Luiz Lapinsky Jr (Portugal)
Pauline Goto (United States)	Francesco Leonardi (France)	Ganga Kansagara (United States)
Naweed Mistry (India)	Premra Padmanabhan (India)	Eduardo Sancilio (Brazil)
Indbir Malhi (Singapore)	Victor Peres (United States)	Shagot Shammas (Israel)
Genet Setton (Australia)	Daniel Sonett (Argentina)	Wolf Winterberg (Sweden)



## Delphi Panel Consensus on KC 2014/2015



## Management of Keratoconus 2015



# 'Keratoconus - An Algorithmic approach' (slides 1-7)

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