CXL: Complications

Prof. Paolo Vinciguerra, M.D. 1, 2
Riccardo Vinciguerra, M.D. 1-3

1 Humanitas University
1 Humanitas Clinical and Research Center IRCS
2 Columbus, Ohio State University
3 University of Insubria, Varese
What we should avoid... from perfect technology to disaster
Before to speak about complication...

Which are the results we should expect?
Corneal Cross-Linking as a Treatment for Keratoconus

Four-Year Morphologic and Clinical Outcomes with Respect to Patient Age

Riccardo Vinciguerra, MD,1,2 Mario R. Romano, MD, PhD,1 Fabrizio I. Camesasca, MD,1 Claudio Azzolini, MD,2 Silvia Trazza,3 Emanuela Morenghi, PhD,1 Paolo Vinciguerra, MD1
Change in BSCVA Safety %

Loss > 1
- 52% (9-17)
- 44% (18-29)
- 0% (30-39)
- 4% (>40)

Gained ≥ 1
- 20% (9-17)
- 25% (18-29)
- 31% (30-39)
- 24% (>40)

24 mos post cxl

Pediatric:
- 18-29
- 30-39
- >40

unchanged
- 9%
- 35% (9-17)
- 22% (18-29)
- 8% (30-39)
- 35% (>40)
Sphere, Sph.Eq., Cyl overtime

- Sphere changes more than cyl
- Cyl reduce, but... has the coma reduces part of it is transformed in cyl
- The changes are taking years
- Patient report a constant improvement. The opposite of pre-op
Pediatric population:

- CXL halted the progression of disease
- Significant improvement of BCVA
- Morphological results showed a significant improvement of selected parameters and stability for all other indexes.
- A more aggressive disease in the pediatric population probably resulted in the observed reduced refractive and morphological improvement of CXL.
Population 18-28 and 29-39 years

- Significant improvement of BCVA till 36 months of follow up
- Morphological results showed an improvement of topographic indices like Simk1, Simk2, SAI, OSI and DSI up to a maximum of 36 months of follow-up.
- Significant reductions in total, comatic and spherical aberrations up to 36 months of follow-up.
- 18-39 years old -> best responder

Population >40 years

- CXL halted the progression of disease

- The limited improvement of CXL in this group is probably due to so-called “age-related crosslinks"
Changes by Curvature group

Curvature 45/50 D

- Better BCVA
- Better Curvature flattening
- Better Sph. Eq change
- Better Sph. change
- Better astigmatism
Outcomes by thinnest point value group….

Better outcome with respect of pre-op pachymetry:

- **BCVA gain** → between 400/500
- **Sph. Change** → less than 400
- **Cyl change** → greater than 450
- **Sph eq. change** → inferior 400
Reduction of the area/power of the keratoconus over time

1° examination: pre cxl

1 mos post-

3 mos post op

6 mos post

-5.17 D

12 mos post

-6.08 D

24 mos post

-6.61 D

pt n° 138 Differential map from pre cxl to 24 mos post cxl
Are we looking at proper parameter in the outcomes judgement of Cross Linking (CXL)

NO!

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Why?

- Cross linking aim to change the structure of corneal tissue
- Only tissue properties should be evaluated
- Refractive and aberrometric changes are desirable but are side effect of tissue changes
- Topography changes can be highly influenced by tears and epi-changes
- Many factors can change refraction

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Which are the parameter to judge a CXL?

**Primary:**
- Depth of demarcation line at the OCT
- Biomechanical Improvement
- Scheimpflug or OCT based Tomography elevation changes
- Pachymetry changes
- Epithelial Changes

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Demarcation line

- The deeper the demarcation line at the AS-OCT the more tissue is involved
- The deeper the stronger the cornea
- Deeper $\rightarrow$ long term stability
- Deeper $\rightarrow$ more refractive changes
Standard Demarcation line in Epi off CXL

328µ in cornea
CXL Epi on demarcation line variable depth and less homogeneous

This is a complication!!
Postoperative Complications

Causes

1. Inappropriate patient selection
2. Surgical technique errors
   - Lack of sterility/antisepsis
   - Erroneous UV source calibration
   - Erroneous UV focusing
   - Inadequate impregnation
   - Inadequate irradiation
   - Inadequate corneal wetting
3. Inadequate follow up
Postoperative Complications

Immediate

• Corneal Burn
• Delay in re-epithelialization
• Infections and corneal melting
• Sterile Infiltrates
Immediate Postoperative Complications

- Erroneous UV calibration
- Inadequate UV focusing
  - Distance must be regularly verified
- Inadequate impregnation
  - Poor solution
  - Longer exposition to solution with secondary thinning
Impregnation with riboflavin using the ring
Safety Measures

Complications due to technical errors

1. Incorrect focusing / irradiation
2. Inadequate impregnation
3. Insufficient hydration
4. Home-made solutions
1. Incorrect Focusing

- Corneal Burns
  - Erroneous UV calibration
  - Inadequate UV focusing
    - Distance: verify regularly
    - UV rays: orthogonal to iris plane
Delay in Reepithelialization due to corneal burn
Corneal Burn: inadequate irradiation

Day 5, RE

Marked flattening
Corneal Burn: inadequate irradiation

Day 30, RE
Excessive Flattening

PRE CXL OD BSCVA: 0.8 -1,25@94

POST CXL OD BSCVA: 0.6 +7,00 -1,00@90

6 mos: disappearance of flattening and hyp
Immediate Postoperative Complications

- Delay in reepithelialization
  - Selection criteria
    - Avoid excessively steep corneas
  - Corneal wetting
  - Contact lens
  - Aminoacids pre-load
Immediate Postoperative Complications

Provide adequate hygiene instructions!

• Infections
  • CXL KILLS bacteria and fungi!
  • Lack of sterility/antisepsis
    • OR-like procedure
  • Home-made solutions
  • Daily check until reepithelialization
  • During epithelial healing cornea is vulnerable to infections
Immediate Postoperative Complications

- Acanthamoeba (melt, 5 days)  
  Rama P J Cataract Refract Surg, 2009
- Staph epi  
- Staph epi non-infective  
  Perez-Santonia JJ J Cataract Refract Surg, 2009
- Escherichia Coli (3 days)  
  Pollhammer M J Cataract Refract Surg, 2009
- Herpes simplex (5 days)  
- LASIK, ectasia and CXL: diffused anterior lamellar keratitis  
- Corneal melt  
- Staph epi non infective  
  Angunawela RI J Cataract Refract Surg, 2009
- Diclofenac-induced  
  Gokhale NS Cornea, 2009
- Sterile Infiltrates  
  Koller T J Cataract Refract Surg, 2009
Early/Late Postoperative Complications

• **Early** – First Three months
  • Stromal deep opacity (NOT haze !)
  • Night time glare and haloes
  • Variable improvement of UCVA during the first months

• **Late** – After Three months
  • Stromal opacity
  • Endothelial damage
Stromal opacity

• 1+ Haze (Hanna scale) (12.7%)
  • Intraoperative corneal dehydration
  • Inadequate corneal protection
    • Inadequate impregnation
    • Home-made solutions
Post PRK  
Haze: more superficial

Post CXL  
Stromal opacity: deeper
1. Intraoperative Pachimetry

**Pre op**
- 470.77 microns
- p<0.001

**Sine epi**
- 406.85 microns
- p<0.001

**20 min**
- 345.58 microns
- p<0.001

**Espans**
- 427.77 microns
- p<0.001

**Fine UVA**
- 452.67 microns
- p>0.2

Change percentages:
- -13.41% (1), p<0.001
- -28.94%
- -15.05%
- +5.14%
- +9.13%
- -3.84%

**Total change:**
- 453 pts
Opacity and Corneal Edema post CXL
How to avoid post-op opacities

- The corneal stroma, by dextran, is reduced in pachymetry
- If U.V. is applied when the pachymetry is less than 340 post op haze should be expected
- Always check intra-op pachymetry
- If < than 340 micron expand with hypotonic solutions
Early/Late Postoperative Complication: **Stromal Opacity**

extending to 60% of stromal depth (300μm)
- regression after one month with topical steroids regimen
  - relative resistance to steroids
  - higher tendency with more advanced keratoconus
- frequently fade or disappears within a year

Vinciguerra et al. Ophthalmology 2009; Mar
Vinciguerra et al. J Refract Surg 2009; Sep
Hafezi, Vinciguerra, Br J Ophthalmol accepted, 2010
Hermann et al. Ophthalmologe 2008;105
Early/Late Postoperative Complications

- Night time glare and halos
  - Change in refraction
  - Will subside after few weeks
- Variable improvement of UCVA
Early/Late Postoperative Complications

- **Endothelial damage**
  - To be expected with corneal thickness of less than 400 μm
  - Inadequate impregnation

- **Lens damage**
  - Three-year objective follow-up with Pentacam software
  - No lens damage or induction of opacity

- **Retinal damage**
  - One-year follow-up ON head with OCT
  - No ON damage

*Wollensak G Ophthalmic Res, 2003*
*Vinciguerra P, J of Cat and Ref Surgery*
*Vinciguerra P, personal data*
When everything was properly done but..

- The pts still progress and V.A. does not improve overtime as expected...
- What we should look for?
Eye rubbing
Conclusions 1°

- Complication rate: 2.9% at one year
- Expressed as visual loss of 2 Snellen lines of BSCVA
- Failure factor:
  - K above 58.00 D
- Risk factors:
  - Age older than 35
  - Preop BSCVA better than 20/25

Koller T J. Cataract Refract Surg 2009; Aug
Vinciguerra et al. Ophthalmology 2009; Mar
Conclusions 2°

• Cross-Linking is a generally very safe procedure

• Beware of technical errors!
Thank you. Arrivederci