

**Sequential versus Simultaneous
Photorefractive Keratectomy
And
Corneal Collagen Cross Linking
in Keratoconus Treatment**

Keratoconus

Keratoconus is a corneal ectatic disease that results in bilateral corneal distortion, altered refractive powers, and reduced vision.



Stabuc-Silih M, et al. Genetics and clinical characteristics of keratoconus. Acta Dermatovenerologica Alpina, Panonica, et Adriatica. 2010;19(2):3-10

Pathophysiology :

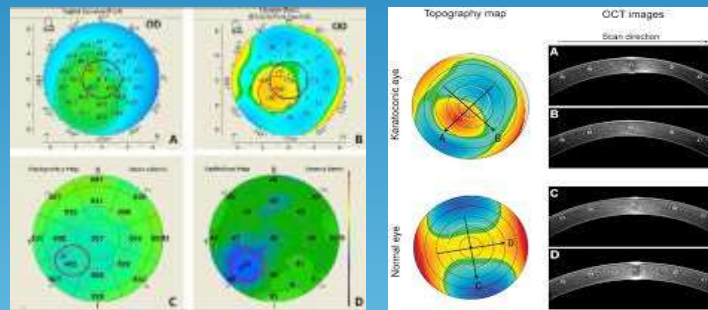
- The corneal epithelium shows central thinning**
- Irregular basement membrane**
- Defects in Bowman's layer .**

Sykakis E, Carley F, Irion L, et al. An in depth analysis of histopathological characteristics found in keratoconus. Pathology. 2012;44(3):234-239.

Diagnostic evaluation :

-Corneal topography is one of the most important diagnostic tools for keratoconus

-Newer devices such as optical coherence tomography (OCT) is useful in imaging early keratectasia.

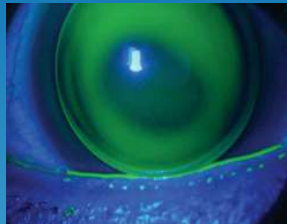


Matalia H. Swarup R. Imaging modalities in keratoconus. Indian J Ophthalmol. 2013 ; 61(8): 394–400.

TREATMENT

Visual rehabilitation

1.Contact lens fitting

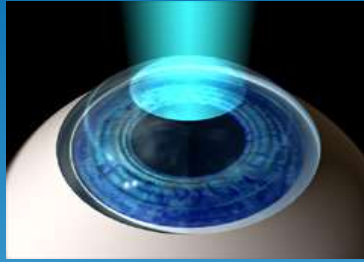


2 .Intrastromal corneal ring segments

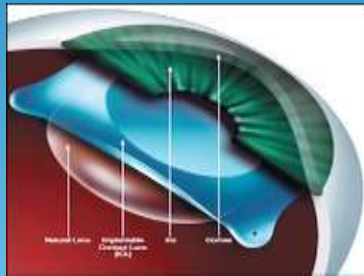


Chelala E, Rami HE, Dirani A, et al. Photorefractive keratectomy in patients with mild to moderate stable keratoconus: a five-year prospective follow-up study. ClinOphthalmol. 2013;7:1923–1928

3.PRK



4.Phakic intraocular lenses



Shape stablization

Collagen cross-linking

CXL technique using riboflavin and ultraviolet-A (UVA) light is developed to counteract the progressive corneal thinning and progression of keratoconus



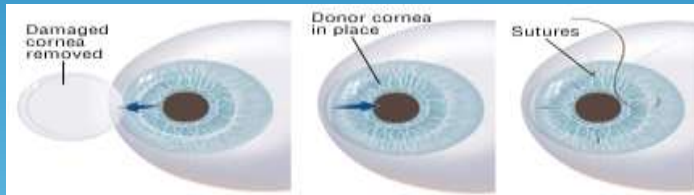
Meek KM, Tuft SJ, Huang Y, et al. Changes in collagen orientation and distribution in keratoconus corneas. Invest Ophthalmol Vis Sci. 2005;46:1948-56.

Conventional keratoconus management

Penetrating keratoplasty

-Penetrating keratoplasty (PK) achieves good visual outcomes.

-But graft survival declines rapidly with age.



Thompson RW, Jr, Price MO, Bowers PJ, et al. Long term graft survival after penetrating keratoplasty. *Ophthalmology*.2003;110:1396-1402.

Corneal Crosslinking

Corneal collagen cross linking (CXL) with riboflavin and ultraviolet – A irradiation increase corneal rigidity and stability of keratoconic corneas.

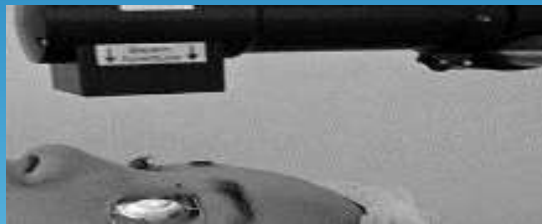


Cornea Saturated with Riboflavin

UV Light into the Cornea

Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-A-induced collagen crosslinking for the treatment of keratoconus. *Am J Ophthalmol.* 2003;135:620–7.

The goal of CXL is to inhibit the progression of the ectatic disease and to increase the rigidity and resistance of the cornea.



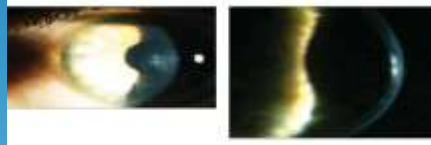
69.Hoyer A, et al. Collagen crosslinking with riboflavin and ultraviolet-A light in keratoconus: long-term results. *J Cataract Refract Surg.* 2008;34:796–801

Complications

(1) Postoperative infection



(2) Corneal haze



(3) Peripheral sterile infiltrates



Al-Qarni A. O, AlHarbi M. Herpetic Keratitis after Corneal Collagen Cross-Linking with Riboflavin and Ultraviolet-A for Keratoconus. Middle East Afr J Ophthalmol .2015;22(3): 389-392

(4) Herpes reactivation

(5) Endothelial damage

(6) Treatment failure

Al-Qarni A. O, AlHarbi M. Herpetic Keratitis after Corneal Collagen Cross-Linking with Riboflavin and Ultraviolet-A for Keratoconus. Middle East Afr J Ophthalmol .2015;22(3): 389-392 .

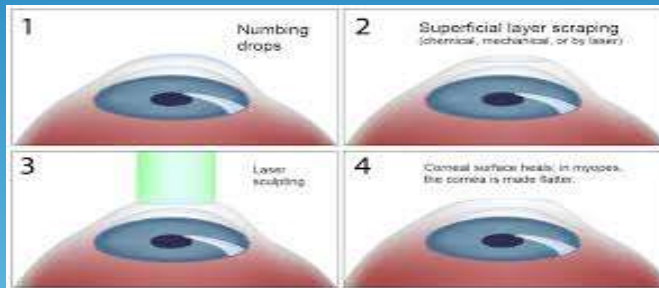
Photorefractive Keratectomy

Photorefractive keratectomy (PRK) is a procedure intended to correct refractive error reducing dependency on glasses .

Erie J.C. Corneal wound healing after photorefractive keratectomy: a 3-year confocal microscopy study. *Trans Am Ophthalmol Soc.* 2003;101:293-333.

Technique

- Ablate a small amount of tissue from the corneal stroma by excimer laser
- Produce stromal remodeling, and so inducing a change in corneal refraction.



Erie J.C. Corneal wound healing after photorefractive keratectomy: a 3-year confocal microscopy study. *Trans Am Ophthalmol Soc.* 2003;101:293-333.

Complications : Corneal haze

Corneal haze reduces corneal transparency at variable degrees.



Netto M.V., et al. Effect of prophylactic and therapeutic mitomycin C on corneal apoptosis, cellular proliferation, haze, and long-term keratocyte density in rabbits. *J Refract Surg.* 2006;22:562-574.

Corneal sensitivity and dry eye

Photoablation affects corneal nerves, disrupting the lacrimal function

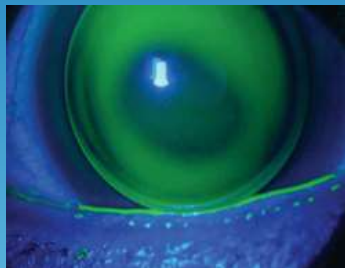


Stern M.E., et al. The role of the lacrimal functional unit in the pathophysiology of dry eye. *Exp Eye Res.* 2004;78:409–416.

Corneal reepithelialization after PRK

1. Bandage contact lenses

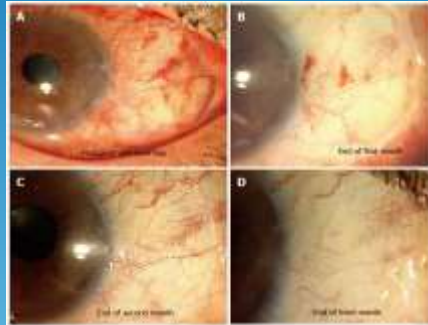
To ease off the postoperative pain and promote epithelial healing, bandage contact lenses are fitted for five days after surgery



-Razmjoo H., et al. Comparative study of two silicone hydrogel contact lenses used as bandage contact lenses after photorefractive keratectomy. *Int J Prev Med.* 2012;3:718–722.
 -Buzzonetti L., et al. A new transepithelial phototherapeutic keratectomy mode using the NIDEK CXIII excimer laser. *J Refract Surg.* 2009;25(1 Suppl.):S122–S124.

2. Amniotic membrane transplantation

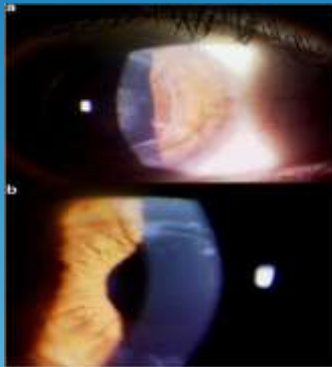
reduces the inflammation after PRK and stimulates corneal epithelialization



-Razmjoo H., et al. Comparative study of two silicone hydrogel contact lenses used as bandage contact lenses after photorefractive keratectomy. *Int J Prev Med.* 2012;3:718-722.
 -Buzzonetti L., et al. A new transepithelial phototherapeutic keratectomy mode using the NIDEK CXIII excimer laser. *J Refract Surg.* 2009;25(1 Suppl.):S122-S124.

3. Mitomycin-C

The wound healing response may be altered by mitomycin-C (MMC) immediately after the laser ablation to minimize myofibroblast activation



-Virasch V.V., et al. Reduced application time for prophylactic mitomycin C in photorefractive keratectomy. *Ophthalmology.* 2010;117:885-889.
 -Nien C.J., et al. Reducing peak corneal haze after photorefractive keratectomy in rabbits: prednisolone acetate 1.00% versus cyclosporine A 0.05% J *Cataract Refract Surg.* 2011;37:937-944.

4. Corticosteroids and non-steroidal anti-inflammatory agents (NSAIDs)

The most common treatment after PRK to avoid the corneal inflammation is the application of corticosteroids.



-Virasch V.V., et al. Reduced application time for prophylactic mitomycin C in photorefractive keratectomy. *Ophthalmology*. 2010;117:885-889.
-Nien C.J., et al. Reducing peak corneal haze after photorefractive keratectomy in rabbits: prednisolone acetate 1.00% versus cyclosporine A 0.05% J *Cataract Refract Surg*. 2011;37:937-944.

Combination of Photorefractive Keratectomy and Corneal Collagen Cross Linking in Keratoconus Treatment

Successful keratoconus treatment confronts two parameters:

- 1- Corneal biomechanical stability
- 2- Optical inefficiency of the irregular cornea .

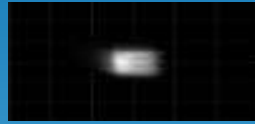
-Jhanji V, Sharma N, Vajpayee RB. Management of keratoconus: current scenario. Br J Ophthalmol. 2011;95:1044-50.
 -Raiskup-Wolf F, Hoyer A, Spoerl E et al. Collagen crosslinking with riboflavin and ultraviolet-A light in keratoconus: long-term results. J Cataract Refract Surg. 2008;34:796-801

So, CXL has been combined with topography-guided PRK with excellent results regarding safety and patient satisfaction

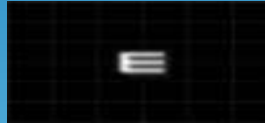


Parker JS, van Dijk K, Melles GR. Treatment options for advanced keratoconus: a review. Surv Ophthalmol. 2015;60(5):459-480.

Combined treatment of CXL/PRK normalize the cornea as much as possible to increase BSCVA .



VA before treatment show blurred vision



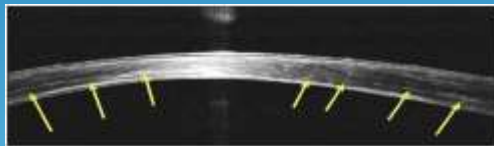
improved VA post TCAT treatment

Kanellopoulos AJ, Binder PS. Collagen cross-linking (CCL) with sequential topography-guided PRK: a temporizing alternative for keratoconus to penetrating keratoplasty .Cornea 2007;26(7):891-895

Approaches of combination surgeries

1- Two-steps sequential approach in the form of CXL then after interval of stability PRK is done.

2- Simultaneous procedures done in the form of same day PRK followed by CXL



Corneal OCT demonstrates hyperreflective intercorneal stromal lines (arrows) corresponding with clinical presence of CXL demarcation line in patient with simultaneous PRK and CXL

Kanellopoulos AJ. Comparison of sequential vs same-day simultaneous collagen cross linking and topography-guided PRK for treatment of keratoconus. J Refract Surg. 2009;25:S812-8

Limitations with the sequential approach

First the stiffened crosslinked cornea is removed in a second step by the PRK so decreasing benefits of CXL

Second ablation rate could be different in cross-linked cornea than in the virgin cornea (this lead to unpredictable refractive results)

Third increased possibility of post-PRK haze

Kymionis GD, Diakonis VF, Kalyvianaki M, et al. One-year follow-up of corneal confocal microscopy after corneal crosslinking in patients with post laser in situ keratosmleusis ectasia and keratoconus. Am J Ophthalmol 2009;147(5):774-78.

SO PRK followed by CXL simultaneously in a single surgical procedure is better for treating keratoconus

Kymionis GD, Diakonis VF, Kalyvianaki M, et al. One-year follow-up of corneal confocal microscopy after corneal crosslinking in patients with post laser in situ keratosmleusis ectasia and keratoconus. Am J Ophthalmol 2009;147(5):774-78.

Take Home Message

A comparison of sequential versus simultaneous PRK and CXL for treatment of keratoconus in terms of:

- Topography
 - Keratometry
 - corneal haze
 - Manifest refraction
 - Ectatic progression
 - Endothelial cell count
 - Central corneal thickness

shows that **the same day** procedure performs better in all parameters

