

## Improving decision making in crosslinking treatments

### *The DUtch Crosslinking for Keratoconus (DUCK) score*

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# Financial disclosure

Unrestricted grants from the Dr. Fischer Foundation



# When is a CXL treatment indicated?

- Global consensus (Delphi method): perform CXL when progression is documented: “no matter what age or level of vision”

SPECIAL ARTICLE

## Global Consensus on Keratoconus and Ectatic Diseases

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François Malecaze, MD, PhD,\*\* Kohji Nishida, MD,†† and Virender 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.

**Purpose:** This project aimed to reach consensus of ophthalmology experts from around the world regarding keratoconus and ectatic diseases, focusing on their definition, concepts, clinical management, and surgical treatments.

**Methods:** The Delphi method was followed with 3 questionnaire rounds and was complemented with a face-to-face meeting. Thirty-six panelists were involved and allocated to 1 of 3 panels: definition, diagnosis, non-surgical management, or surgical treatment. The level of agreement considered for consensus was two thirds.

**Results:** Numerous agreements were generated in definitions, methods of diagnosing, and management of keratoconus and other ectatic diseases. Non-surgical and surgical treatments for these conditions, including the use of corneal cross-linking and corneal transplantsations, were presented in a stepwise approach. A flowchart describing a logical management sequence for keratoconus was created.

**Conclusions:** This project resulted in definitions, statements, and recommendations for the diagnosis and management of keratoconus

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

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

(Cornea 2015;34:359-369)

Keratoconus and ectatic corneal diseases have been recognized for more than 150 years.<sup>1,2</sup> Over the last 2 decades, there has been a revolution in the knowledge related to the diagnosis and management of these conditions. In terms of diagnosis, the advent of corneal topography, and more recently corneal tomography, has increased the ability of ophthalmologists to identify corneal ectasia at a much earlier stage than was previously possible.<sup>3</sup> As a result, the previously established prevalence of keratoconus of approximately 1/2000 among the general population<sup>4</sup> has been challenged with much higher prevalence rates found in many parts of the world.<sup>5,6</sup>

The surgical treatment for keratoconus reflects this evolution.<sup>7</sup> Alternative procedures, such as the use of intrastromal corneal ring segment(s) (ICRS),<sup>8,9</sup> corneal cross-linking (CXL),<sup>10-12</sup> therapeutic excimer laser treatments including phototherapeutic keratectomy<sup>13</sup> and photorefractive



# How should we define progressive keratoconus?

- >1 D progression in keratometry ( $K_{\max}/K_{\text{mean}}$ ) is the Word<sup>1-3</sup>
- Pros:
  - Easy to use parameters with adequate repeatability<sup>4-5</sup>
- Cons:
  - Visual acuity, refractive errors, contact lens tolerability, associated symptoms are now not considered
  - Where is the patients perspective? Should we treat the patient or their topograms?

1. O'Brart DPS, Chan E, Samaras K, et al. A randomised, prospective study to investigate the efficacy of (...) corneal collagen cross-linkage. Br J Ophthalmol 2011;95:1519–24.

2. Hersh PS, Greenstein SA, Fry KL. Corneal collagen crosslinking for keratoconus and corneal ectasia : One-year results. J Cataract Refract Surg 2011;37:149–160.

3. Wittig-Silva C, Chan E, Islam FM a, et al. A Randomized, Controlled Trial of Corneal Collagen Cross-Linking in Progressive Keratoconus: Three-Year Results. Ophthalmology 2014;121:812–821

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# Consequences of treating topograms

*Acta Ophthalmologica*

ACTA OPHTHALMOLOGICA 2016

## **Nationwide reduction in the number of corneal transplantations for keratoconus following the implementation of cross-linking**

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## **Is only half of the equation!**



1. Godefrooij DA, de Wit GA, Mangen MJ, Wisse RPL. Comment on "Cost effectiveness of collagen crosslinking for progressive keratoconus in the UK NHS." *Eye*. 2016;1-2.
2. L. Klotz. Prostate cancer overdiagnosis and overtreatment. *Curr Opin Endocrinol Diabetes Obes*, 20 (3) (2013), pp. 204–209

# What is needed?

- A rational weighted compound score that
  - Encompasses relevant clinical domains in progressive KC
  - Takes the patients perspective in consideration
  - Is easy to use
- The **DU**tch **C**rosslinking for **K**eratoconus score
  - Age
  - Subjective changes in quality of vision
  - Changes in UDVA
  - Changes in Refraction (SE)
  - Changes in Keratometry ( $K_{\max}$ )
- 0, 1 or 2 points per item, lead to a 0-10 point score



## Conclusion of study results (n=332 eyes)

- Evaluation of longitudinal 2-year cohort of all KC patients
- When applying a 5/10 DUCK score vs.  $>1D$  of  $K_{\max}$  threshold

18% lower rate of treatment

11% reduction of under-treatment

13% lower failure rate



# Methods

- Inclusion/exclusion criteria for analysis:
  - All keratoconus patients referred between Jan 1<sup>st</sup> 2012 & July 1<sup>st</sup> 2014
  - No cases unsuitable for CXL treatment (too thin, scars etc)
- Data collection
  - UDVA/CDVA, manifest refraction, Scheimpflug tomography
  - Patient experiences / remarks / complaints
  - Treatment characteristics
- Three measurements in time
  1. First consultation
  2. Progression analysis
  3. 12mo after CXL or after last consultation



# Results

			K <sub>max</sub> progression				
			<1D		≥1D		
			CXL		CXL		
			No	Yes	No	Yes	
DUCK- score	<5	Stable	55	42	12	23	132
		Progressive	62	18	4	8	92
	≥5	Stable	5	5	20	45	75
		Progressive	9	5	4	13	31
			131	70	40	89	*332

- 159 / 332 eyes underwent CXL (48%)

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- 106 treatments based on DUCK score >5 (18%↓)



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- 159 / 332 eyes underwent CXL (48%)
- 129 treatments based on K<sub>max</sub> >1D in one year
- 106 treatments based on DUCK score >5 (18%↓)
- 14 cases of progressive KC treated with DUCK (11%)



# Discussion

- Large cohort of 332 consecutive KC cases with adequate follow-up
- The DUCK score was evaluated in retrospect
  - CXL treatments were not necessarily based on either criterion
  - Natural course of disease could not be incorporated
- All eyes of all patients were included
  - Complex statistics
  - Multiple imputation used to complete the dataset
- Validation of findings mandatory
  - Multicenter data acquisition to compare & pool data
  - Collaboration with Maastricht & Antwerp



# Summary

- Defining keratoconus progression is fundamental in clinical decision making in CXL
- Targeting the right patient for therapy
  - Prevents unnecessary exposure to treatment risks, and
  - Increases overall cost-effectiveness
- Adhering to the DUCK-score as a weighted compound measurement of keratoconus progression lead to
  - 18% less treatments performed in likely low-risk cases
  - 11% more treatments performed in potential progressive cases
  - 13% lower treatment failure rates due to a higher threshold



# References

1. O'Brart DPS, Chan E, Samaras K, et al. A randomised, prospective study to investigate the efficacy of riboflavin/ultraviolet A (370 nm) corneal collagen cross-linkage to halt the progression of keratoconus. Br J Ophthalmol 2011;95:1519–24.
2. Hersh PS, Greenstein SA, Fry KL. Corneal collagen crosslinking for keratoconus and corneal ectasia : One-year results. J Cataract Refract Surg 2011;37:149–160.
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