Crosslinking of corneal collagen and its applications

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Crosslinking of the cornea

- Forme fruste keratectasia
- Crosslinking
- Clinical applications
keratectasia

• starts usually between 10 and 20 years of age

• can stop at any time and is then called forme fruste keratoconus (Amsler)

• incidence approx. 5:1000, formes frustes 3 to 5 times more frequent

• VSX1-gene mutation is responsible for 9% of the cases

• other predisposing factors: rubbing (oculodigital syndrome, allergy) chromosome aberrations
• **Diagnosis:**

  *classical signs: Munson, Fleischerring Vogtstriae*

  *corneal topography*

• **The biomechanical strength of the keratoconus cornea is approx. 2 times smaller compared to that of the normal cornea**
keratectasia

• subentities: keratoconus, keratotorus, pellucid marginal cornea degeneration, with floating transitions
13 eyes of 8 forme frustes keratoconus patients were treated with customized surface ablation based on Zernike approximation of the difference elevation map.

- **aim**: visual rehabilitation
- **parameter**: Z3 (Schwiegerling)

- The diagnosis „forme fruste“ was based on anamnesis and earlier topographies if available.
- The patients were followed for at least 1 year up to 3 years.
Die Zukunft im Auge

BSCVA 20/25

BSCVA 20/16
• Z3 was reduced by 41% \((p<0.001)\)
• ghosting was reduced in all eyes
• 7 out of 13 eyes gained 1 or more lines, none lost one line or more
• topography was stable within the follow-up
• sphere and cylinder was reduced significantly

The goal of visual rehabilitation was achieved in all eyes
Crosslinking of the cornea

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• crosslinking is a standard technique in der material science

• induction of additional chemical bonds increases the mechanical and the chemical resistance
crosslinking of human collagen is a physiologic process, the stiffening of connective tissue is well known in diabetes and aging.

- Diabetes is a protection factor against keratoconus.
- Crosslinking can be managed by several methods: enzymatically, with aldehydes, and by irradiation.
Die Zukunft im Auge
Die Zukunft im Auge

Dehnung in %

Spannung in $10^5\,\text{Pa}$

menschliche Hornhaut

behandelt

unbehandelt

Dehnung in %
Die Zukunft im Auge

UV / Riboflavin | Glutaraldehyde | Aldehyde sugar (14 days)

<table>
<thead>
<tr>
<th>UV / Riboflavin</th>
<th>Glutaraldehyde</th>
<th>Aldehyde sugar (14 days)</th>
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<tbody>
<tr>
<td>254 nm / 20 min</td>
<td>Glycolaldehyd</td>
<td>Glycolaldehyd</td>
</tr>
<tr>
<td>365 nm / 45 min</td>
<td>Methylglyoxa</td>
<td>Ribose</td>
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<tr>
<td>365 nm / 30 min</td>
<td>Glyceraldehyd</td>
<td>Glukose</td>
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<tr>
<td>436 nm / 45 min</td>
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<tr>
<td>0,1 % / 10 min</td>
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<td>0,075 % / 10 min</td>
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<td>0,075 % / 20 min</td>
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Spannungszunahme in %
1. Combined application of UVA and riboflavin

**riboflavin (vit. B2)**  **Ultraviolet irradiation**

2. Production of oxygen radicals

\[ \text{O}_2^- \]

3. Induction of collagen cross-links

\[ \text{-CH}_2\text{-CH}_2\text{-CH}=\text{NH}\cdot\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-} \]

collagen fibril

collagen fibril
Crosslinking of the cornea

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26 eyes of 25 keratoconus patients were treated with an abrasion of the cornea, imbibited with riboflavin 0.1% - drops, and irradiated with UV-light at a wavelength of 365 nm for 30 minutes.

Preoperative progression of the keratoconus was verified in any case.

The patients were followed for at least 2 years up to 5 years (36 ± 13 months).
Die Zukunft im Auge
• healing of the epithelium was uneventful
• according to corneal topography, progression halted in every case
• maximal K-readings were significantly reduced in 65% of the cases
Results

Quantitative results of the keratoconus study

- VA-improvement of 1,3 lines (p< 0,01)

- decrease of the max. K-value by 1,38 dpt (p<0,01)

- follow-up: 5 years maximum
  35,2 ± 9,4 Monate

- no side effects or complications
Conclusion

• A progressive keratoconus can be transferred into a forme fruste keratoconus by means of collagen crosslinking

• With customized surface ablation forme fruste corneas can be visually rehabilitated
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HansPeter Iseli

Institut für Refraktive und Ophthalmo-Chirurgie (IROC)
3 months after LASIK with DLK

Floating, systemic and topic antibiotic, antimycotic and steroid therapy

In-patient service

before crosslinking
3 months after LASIK with DLK

Floating, systemic and topical antibiotic, antimycotic and steroid therapy

In-patient service

5 days after crosslinking
Die Zukunft im Auge
- crosslinking of the sclera in progressive myopia
To demonstrate the immediate biomechanical effect of corneal crosslinking we developed a new measurement technique:

Time-of-flight (TOF) measurement of ultrasound velocity

Avg. 1.8x increase, p=0.002