

# Corneal Cross-Linking (CXL) – Wann und wie?

Prof. Dr. Dr. Farhad Hafezi  
ELZA Institute, Zürich, Schweiz



ELZA



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# ESCRS

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Chef des  
ESCRS Forschungs-Komitees  
seit 1.1.2025

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CLINICAL AND EXPERIMENTAL OPHTHALMOLOGY  
<https://doi.org/10.1093/ceio/01/14/022.008813>



RESEARCH

Trends in research on corneal cross linking from 2001 to 2020: a bibliometric analysis

Shaopei Wang<sup>1</sup>, Kaili Yang<sup>1</sup>, Yawen Wang<sup>1</sup>, Liyan Xu<sup>1</sup>, Yuwei Gu<sup>1</sup>, Qi Fan<sup>1</sup>, Meng Zhu<sup>1</sup>, Qing Wang<sup>1</sup>, Kai Guo<sup>1</sup>, Shengwei Ren<sup>1</sup> and Dongqing Zhao<sup>1\*</sup>

Table 3. Top 10 productive authors and co-cited authors on CXL study from 2001 to 2020.

Rank	Author	Count	Co-cited Author	Count
1	Hafezi F	62	Wollensak G	2963
2	Kymionis GD	43	Spoerl E	1191
3	Vinciguerra P	30	Kymionis GD	1087
4	Vinciguerra P	27	Kanellopoulos AJ	1007
5	Hashemi H	26	Caporossi A	706
6	Shetty R	25	Mazzotta C	692
7	Vinciguerra R	25	Vinciguerra P	620
8	Lai JY	24	Rabinowitz YS	560
9	Randleman JB	24	Hafezi F	486
10	Grentzelos MA	23	Lai JY	427

Int Ophthalmol  
<https://doi.org/10.1007/s10792-022-02334-1>

ORIGINAL PAPER

A bibliometric analysis of the top 100 most-cited articles on keratoconus

Kaili Yang · Liyan Xu · Meng Zhu · Shaopei Wang · Qi Fan · Yuwei Gu · Yawen Wang · Qing Wang · Kai Guo · Chenjia Pang · Shengwei Ren

Supplementary Table 4 First and corresponding authors with multiple articles(N≥2) in the top 100 most-cited articles

ID	First author	No of articles	Corresponding author	No of articles
1	Rabinowitz, YS	4	Rabinowitz, YS	5
2	Caporossi, A	3	Mazzotta, C	4
3	Maeda, N	3	Hafezi, F	3
4	Ambrosio, R	2	KLYCE, SD	3
5	Amir, M	2	Ambrosio, R	2
6	Colin, J	2	Colin, J	2
7	Hafezi, F	2	Hersh, PS	2
8	Kanellopoulos, AJ	2	Kanellopoulos, AJ	2
9	Lema, I	2	Lema, I	2
10	Mazzotta, C	2	Raiskup, F	2

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## 2. GLOBALE DEFINITION «KERATOKONUS» 2025



Renato Ambrosio  
Brasilien



José Alvaro Gomes  
Brasilien



Farhad Hafezi  
Schweiz



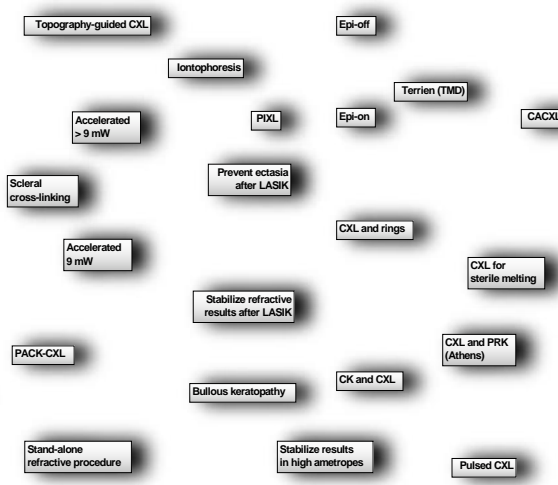
7

**ELZA**  
KORNEA FOCUS GROUP OF THE FUTURE



**ESCRS**

## «MEER DER PROTOKOLLE»



CV & Info

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EUROPEAN LEAGUE OF LASER ASSOCIATIONS

WIT-Lasers in Health    UNIVERSITÄT ZÜRICH  
LIGHT    ESCRS

# Dresden-Protokoll

## Die Anfänge



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### Die Anfänge



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Dresden & Zurich 1999-2003



2<sup>nd</sup> International Congress of Corneal Cross Linking  
Hotel Hilton Airport, Zurich/ Switzerland  
December the 8<sup>th</sup> and 9<sup>th</sup>, 2006

**CCL**  
[www.ccl-congress.ch](http://www.ccl-congress.ch)



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WILLGANGS  
FORSCHUNG

LIGHT

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UNIVERSITÄT  
DUISBURG  
ESSEN

UNIVERSITY OF  
SOUTH ALABAMA

# ?

**30 min @ 3 mW/cm<sup>2</sup>**

=

**10 min @ 9 mW/cm<sup>2</sup>**

=

**5 min @ 18 mW/cm<sup>2</sup>**

=

**3 min @ 30 mW/cm<sup>2</sup>**

5.4 J/cm<sup>2</sup>

**Bunson Roscoe**

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**Cornea**

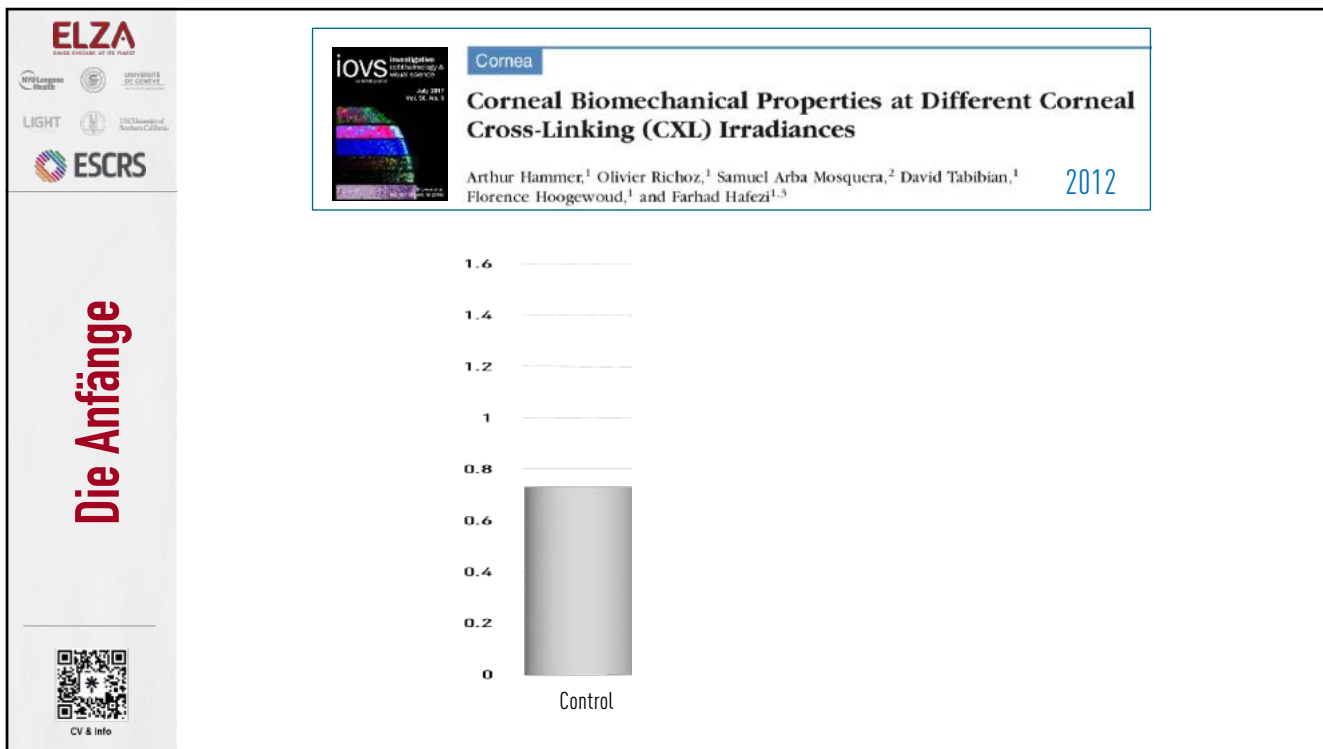
**Corneal Biomechanical Properties at Different Corneal Cross-Linking (CXL) Irradiances**

Arthur Hammer,<sup>1</sup> Olivier Richo,<sup>1</sup> Samuel Arba Mosquera,<sup>2</sup> David Tabibian,<sup>1</sup> Florence Hoogewoud,<sup>1</sup> and Farhad Hafezi<sup>1,3</sup>

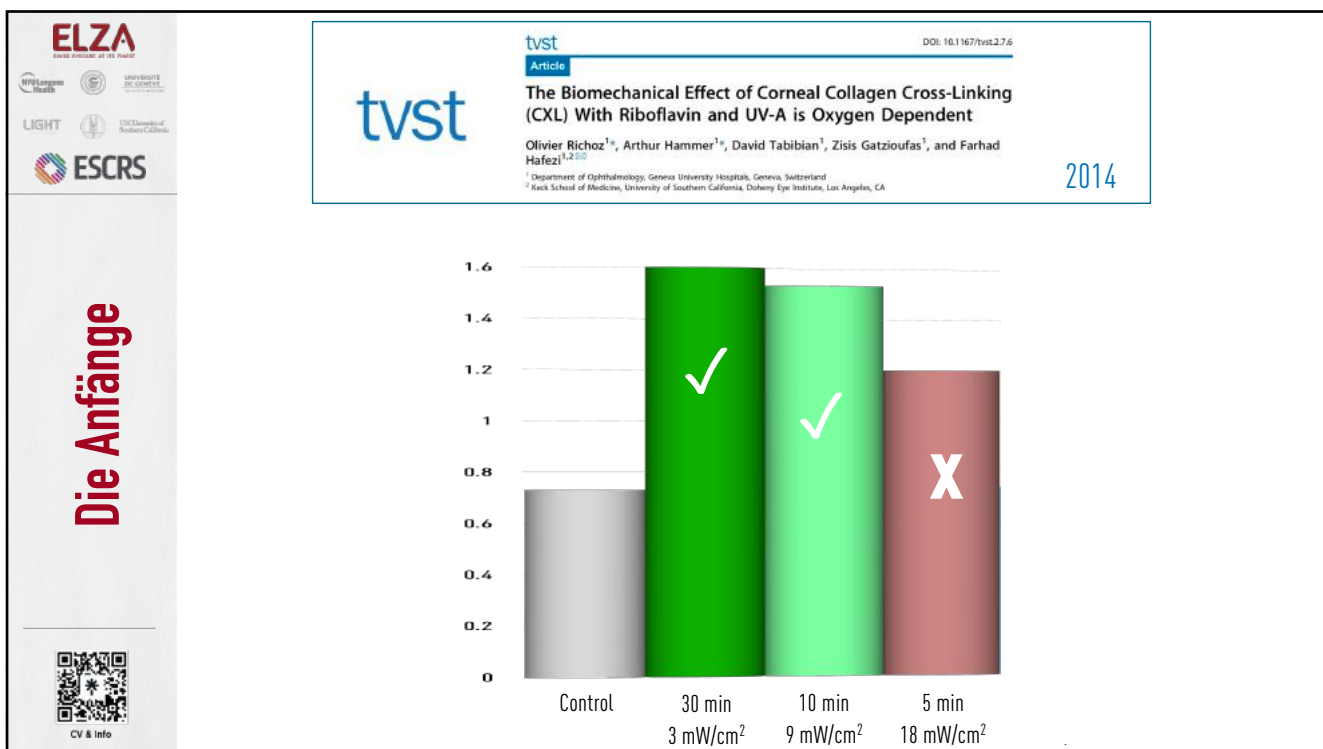
2012

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12



13



14




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UNIVERSITY OF SOUTHERN CALIFORNIA

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**Starke Progression**



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### High-Fluence Accelerated Epithelium-Off Corneal Cross-Linking Protocol Provides Dresden Protocol-Like Corneal Strengthening

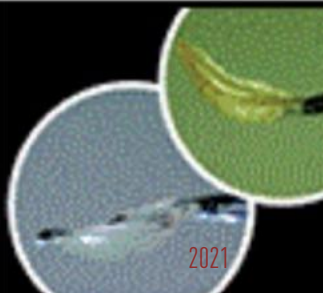
Reyhaneh Abrishamchi<sup>1-3,\*</sup>, Hormoz Abdshahzadeh<sup>1-3,\*</sup>, Mark Hillen<sup>3</sup>, Nikki Hafezi<sup>3</sup>, Emilio A. Torres-Netto<sup>1,2,4,5</sup>, Ioannis M. Aslanides<sup>6,7</sup>, Shihao Chen<sup>6</sup>, J. Bradley Randleman<sup>8</sup>, and Farhad Hafezi<sup>1-3,6,9</sup>

2021

Special Issue

tvst

2021



Therapeutic Applications of Corneal and Scleral Crosslinking

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UNIVERSITY OF GENOVA

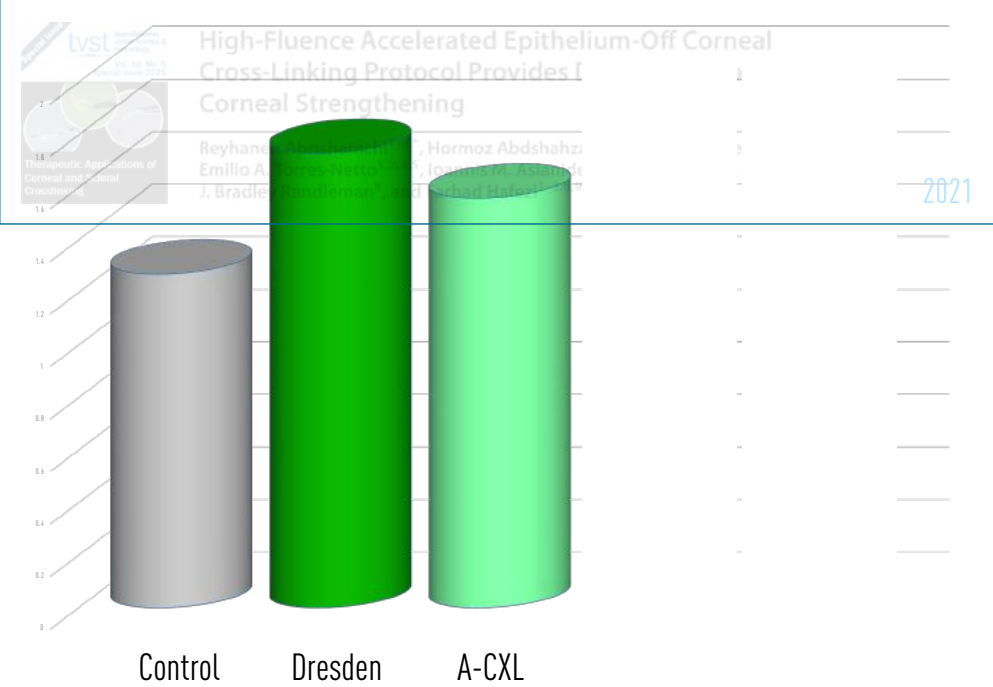
UNIVERSITY OF SOUTHERN CALIFORNIA

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**Starke Progression**



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Group	Strengthening Value (approx.)
Control	10.5
Dresden	13.5
A-CXL	12.5

High-Fluence Accelerated Epithelium-Off Corneal Cross-Linking Protocol Provides Dresden Protocol-Like Corneal Strengthening

Reyhaneh Abrishamchi<sup>1-3,\*</sup>, Hormoz Abdshahzadeh<sup>1-3,\*</sup>, Mark Hillen<sup>3</sup>, Nikki Hafezi<sup>3</sup>, Emilio A. Torres-Netto<sup>1,2,4,5</sup>, Ioannis M. Aslanides<sup>6,7</sup>, Shihao Chen<sup>6</sup>, J. Bradley Randleman<sup>8</sup>, and Farhad Hafezi<sup>1-3,6,9</sup>

2021

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EARLY INTERVENTION AT THE PEARL

WILLERGEN Health

LIGHT

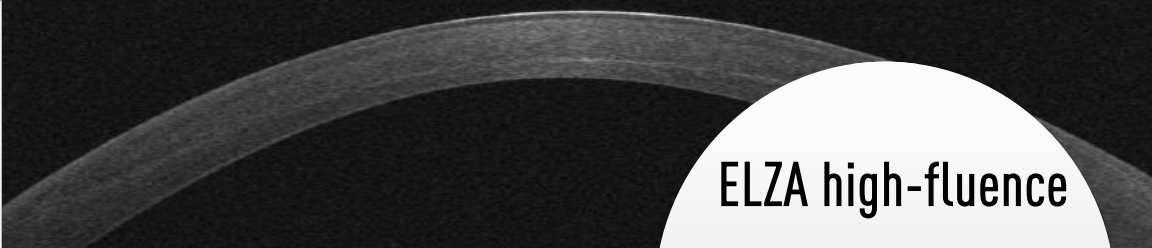
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**Starke Progression**



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## Clinical Study ELZA



**ELZA high-fluence**

18 mW/cm<sup>2</sup> für 9 Min 15 Sek  
10.0 J/cm<sup>2</sup> epi-off

Genauso stark wie Dresden

- 50 Augen
- 1 Jahr
- 10 J/cm<sup>2</sup>
- Demarkation

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EARLY INTERVENTION AT THE PEARL

WILLERGEN Health

LIGHT

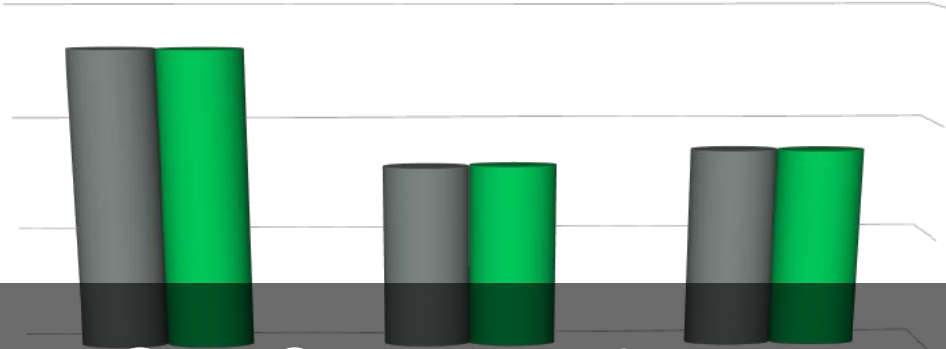
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**Strong Progression**



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## Klinische Studie ELZA



Corneal thickness (µm)    Epithelial thickness (µm)    max (D)

■ as line    ■ 12 months post-operative

# 94% Erfolg

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# Sofortiges CXL ?



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Kinder und Jugendliche unter 20 Jahren



**Progression of Keratoconus and Efficacy of Pediatric Corneal Collagen Cross-linking in Children and Adolescents**

Nico Chatzis, DDS; Farhad Hafezi, MD, PhD

2012

Ektasie nach LASIK (Laserchirurgie)



**Corneal collagen crosslinking with riboflavin and ultraviolet A to treat induced keratectasia after laser in situ keratomileusis**

Farhad Hafezi, MD, John Kanellopoulos, MD, Rainer Wiltfang, MD, Theo Seiler, MD, PhD

2007



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# Normale Progression

## A-CXL epi-off (9 mW/cm<sup>2</sup> for 10 min)

## ELZA epi-on CXL



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## A-CXL epi-off (9 mW/cm<sup>2</sup> for 10 min)

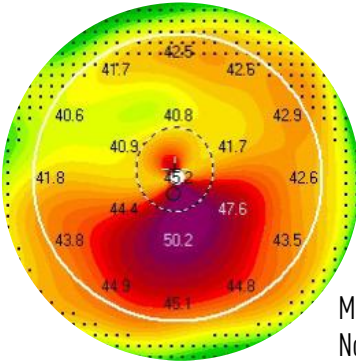


**Eye and Vision**


Long term results of accelerated 9 mW corneal crosslinking for early progressive keratoconus: the Siena Eye-Cross Study 2

Cosimo Mazzotta<sup>1,2</sup>, Frederik Raskup<sup>3</sup>, Fahad Hafed<sup>4,5,6,7</sup>, Emilio A Torres-Netto<sup>4,5,8</sup>, Ashraf Armia Balamoun<sup>9</sup>, Giuseppe Giannacare<sup>10</sup> and Simone Alex Bagaglia<sup>1</sup>

2021



Male, 28 years  
Normal progression



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UNIVERSITY OF GREECE

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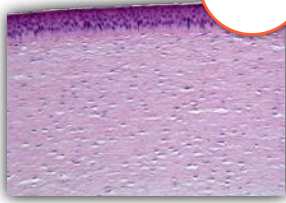
**Epi-on CXL**



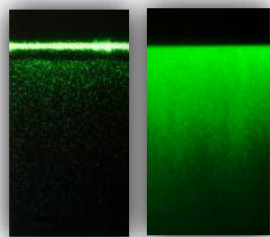
CV & Info

## Challenges epi-on

**-20%**

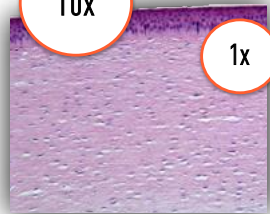


UV penetration



RIBO saturation

**10x**



1x

O<sub>2</sub> consumption

epi-on CXL

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**Epi-on CXL**



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**5x**



Supplemental oxygen

**10x**



Iontophoresis



- UV attenuation
- O<sub>2</sub> consumption
- RIBO saturation

epi-on CXL

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**Epi-on CXL**

2018 |

Oxygen

Iontophoresis

UV-A

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**Epi-on CXL**

2018 |

Iontophoresis

UV-A

Oxygen

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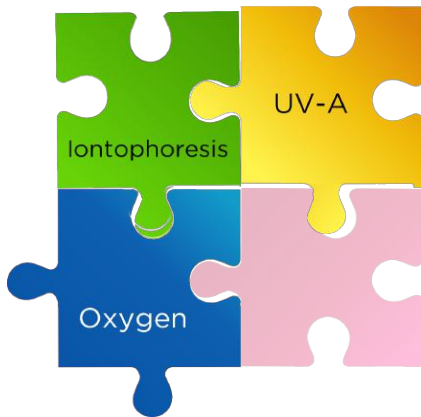


### Iontophoresis Corneal Cross-linking With Enhanced Fluence and Pulsed UV-A Light: 3-Year Clinical Results


Cosimo Mazzotta, MD, PhD; Simone Alex Bagaglia, MD; Arianna Sgheri, MD; Alessandro Di Maggio, MD; Mario Fruschelli, MD; Andrea Romani, MD; Riccardo Vinciguerra, MD; Paolo Vinciguerra, MD; Gian Marco Tosi, MD, PhD



2020



**Epi-on CXL**



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WILLIGSEN HEALTH

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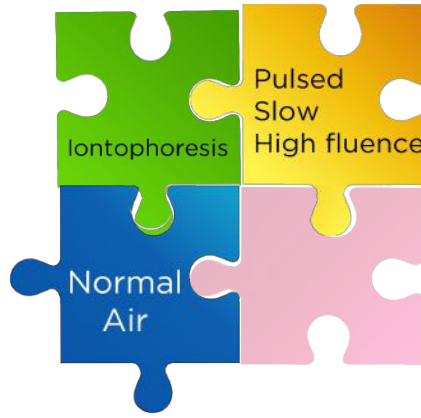
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### Iontophoresis Corneal Cross-linking With Enhanced Fluence and Pulsed UV-A Light: 3-Year Clinical Results

Cosimo Mazzotta, MD, PhD; Simone Alex Bagaglia, MD; Arianna Sgheri, MD; Alessandro Di Maggio, MD; Mario Fruschelli, MD; Andrea Romani, MD; Riccardo Vinciguerra, MD; Paolo Vinciguerra, MD; Gian Marco Tosi, MD, PhD

2020



**Epi-on CXL**




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2nd Generation Penetration Enhancers

Pulsed Slow High fluence

Normal Air




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WILLERSON HEALTH UNIVERSITY OF GENEVE  
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**A Transepithelial Corneal Cross-linking (CXL) Protocol Providing the Same Biomechanical Strengthening as Accelerated Epithelium-off CXL**


*Nan-Ji Lu, MD, PhD, MSc; Emilio A. Torres-Netto, MD, PhD; M. Enes Aydemir, MD; Sabine Kling, MSc, PhD; Nikki Hafezi, MASIP ETHZ; Léonard Kollros, MSc, FSLs; Farhad Hafezi, MD, PhD, FARVO*

2025

2nd Generation Penetration Enhancers

Pulsed Slow High fluence

Normal Air



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UNIVERSITÄT ST. GEMEIN


LIGHT

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**Epi-on CXL**



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**ELZA epi-on**

18 mW/cm<sup>2</sup> for 15 min  
 8.1 J/cm<sup>2</sup>, pulsed

No addy'l oxygen  
 No iontophoresis

**Anesthesia**      **Penetration Enhancers**      **Ribo-Ker**      **Irradiation**



**3 min**      **10 min + 5 min wait**      **20 min**      **15 min**

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LIGHT

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**Epi-on CXL**



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## PARADIGMENWECHSEL

1. Risikoprofil extrem tief.
2. Können wir proaktiver werden?

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LASER PIONEER AT THE PEARL

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LIGHT    ESCRS

**Epi-on CXL**

**TECHNOLOGIE**



EMAGINE  
emagine-eye.com

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**ELZA**  
LASER PIONEER AT THE PEARL

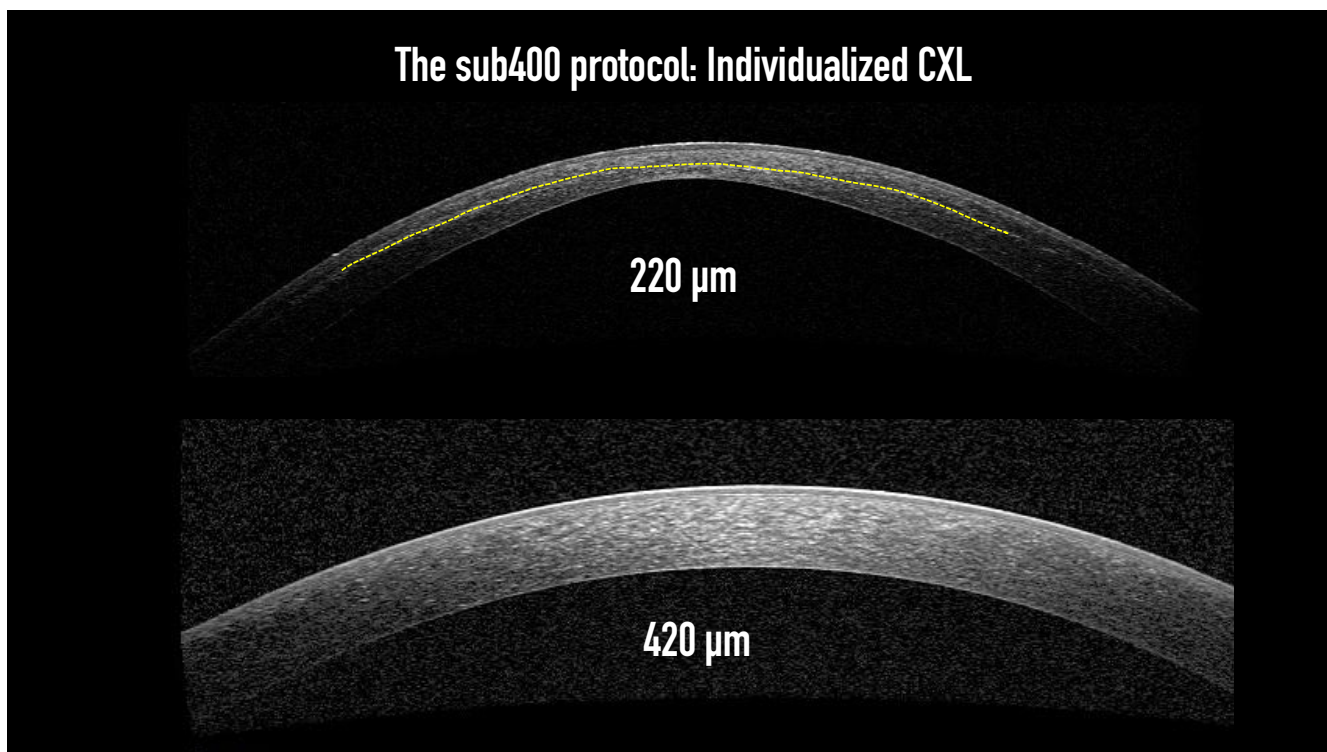
WILLERSON Health    UNIVERSITÄT ST. GALLEN  
LIGHT    ESCRS

**Fortgeschrittener KK**

**ELZA sub400**

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Ultrathin corneas: sub400 |

2009

**JCRS**  
Journal of Cataract & Refractive Surgery

**Collagen crosslinking with ultraviolet-A and  
hypoosmolar riboflavin solution in thin corneas**

Farhad Hafezi, MD, PhD, Michael Mrochen, PhD, Hans Peter Iseli, MD, Theo Seiler, MD, PhD

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**Until 2021**

**ADAPT THE CORNEA  
TO MY TECHNIQUE**

**ELZA sub400**

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**Until 2021**


**ADAPT THE CORNEA  
TO MY TECHNIQUE**

**Since 2021: sub400**


**ADAPT THE CORNEA  
TO MY TECHNIQUE**

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ELZA sub400



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## Until 2021

# ADAPT THE CORNEA TO MY TECHNIQUE


## Since 2021: sub400

# ADAPT MY TECHNIQUE TO THE CORNEA

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ELZA sub400



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Step 1  
Develop algorithm



Kling & Hafezi, JRS, 2017


### Ultrathin corneas: sub400

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LIGHT  
UNIVERSITY OF Southern California  
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**ELZA sub400**

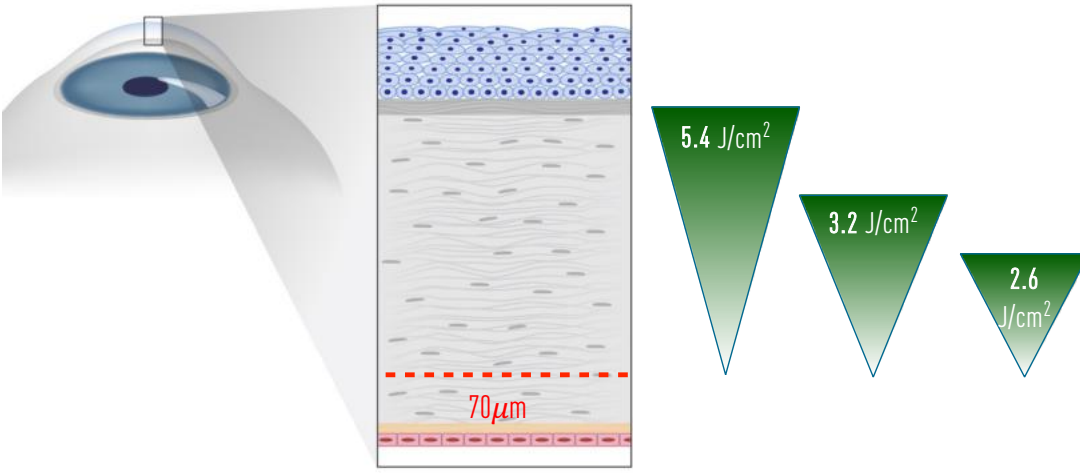


CV & info

American Journal of Ophthalmology

**Individualized Corneal Cross-linking With Riboflavin and UV-A in Ultrathin Corneas: The Sub-400 Protocol**

FABRIZIO HATZEL, SABINE ALING, FRANCESCA CALABONDI, NOBA HIRAZI, HANR HUISEN, BISHWANATH ARISHIVAMACHARI, JONAS ALVARO P. LONDEL, CESARINO MAZZOTTA, I. BRAGLEY MANGUNAN, AND EMERIO A. TORRES-NEVO



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Determine thickness |




**sub400 integrated into EMAGine's C-eye device**

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EARLY LINKAGE AT THE PUPIL

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LIGHT  
UNIVERSITY of Southern California  
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**ELZA sub400**

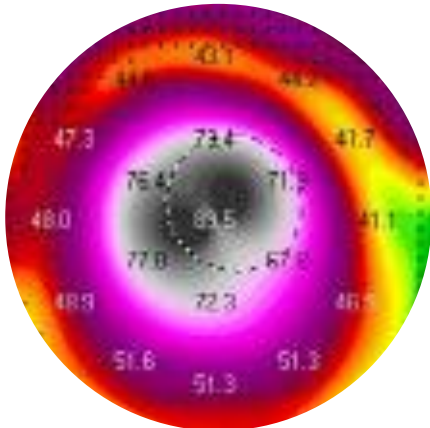
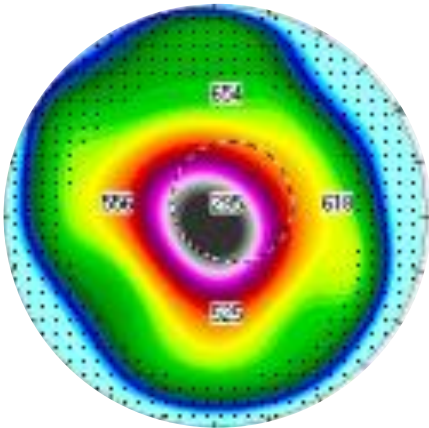


CV & Info

Individualized Corneal Cross-linking With Riboflavin and UV-A in Ultrathin Corneas: The Sub400 Protocol

FARHAD HAFEZI, SABINE ELING, FRANCESCA CALABOCCA, NIKKI HAFEZI, JAMES HELLER, BRYANSH ABRAHAMAM, JESSIE ALVARO P. GOMEZ, COSIMO MAZZOTTA, J BRADLEY RANDLEMAN, AND EMILIO A. TORRES-NETTO

Sub400  
1st gen





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**ELZA**  
EARLY LINKAGE AT THE PUPIL

WILLIAMS Institute  
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LIGHT  
UNIVERSITY of Southern California  
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**ELZA sub400**




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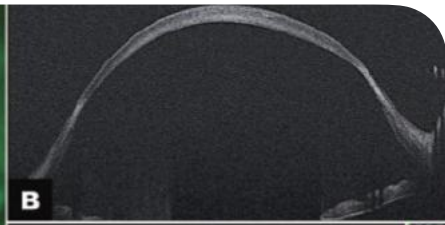
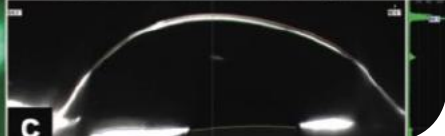
sub400: Generation 1

## Corneal Cross-linking for Keratoglobus Using Individualized Fluence

Farhad Hafezi, MD, PhD; Emilio A. Torres-Netto, MD, PhD; J. Bradley Randleman, MD; Nikki L. Hafezi, MAS IP ETHZ; Cosimo Mazzotta, MD, PhD; Renato Ambrósio, Jr, MD, PhD; Léonard Kollros, BSc Clin Optometry

Sub400  
1st gen



46

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WITzenberg Health UNIVERSITY OF GENEVA  
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# Sehkraft verbessern

## ...mit Brille

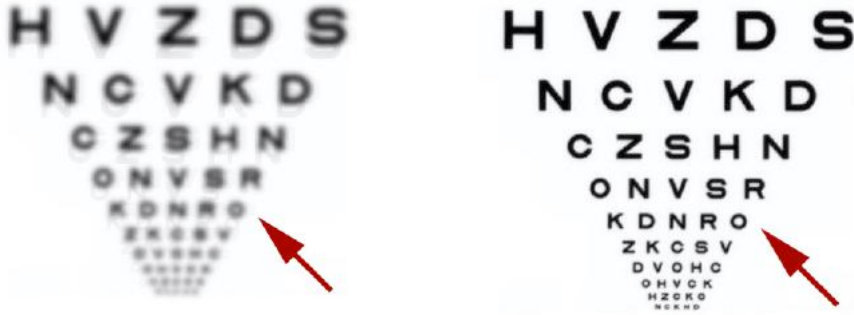


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LIGHT USC University of Southern California  
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H V Z D S  
N C V K D  
C Z S H N  
O N V S R  
K D N R O  
Z K C S V  
D V O H C  
H Z O S O  
N E K H O

### Sehschärfe und Bildqualität



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# Sehkraft verbessern

## Wellenfrontgeführte transPRK



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WILLERSON HEALTH UNIVERSITY OF GOSWARTH

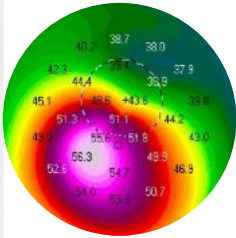
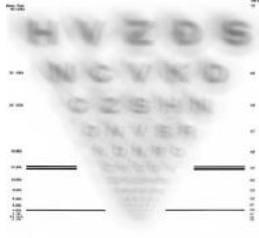
LIGHT UNIVERSITY OF SOUTHERN CALIFORNIA

ESCRS

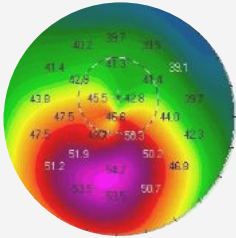
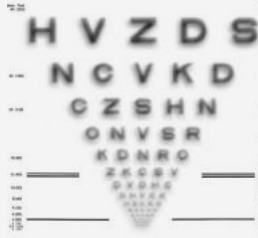
### PREOPERATIVE

OD: +3.00 -6.00 081°  
CDVA 0.2


OD: -1.5 -2.75 120°  
CDVA 0.5p

### POSTOPERATIVE

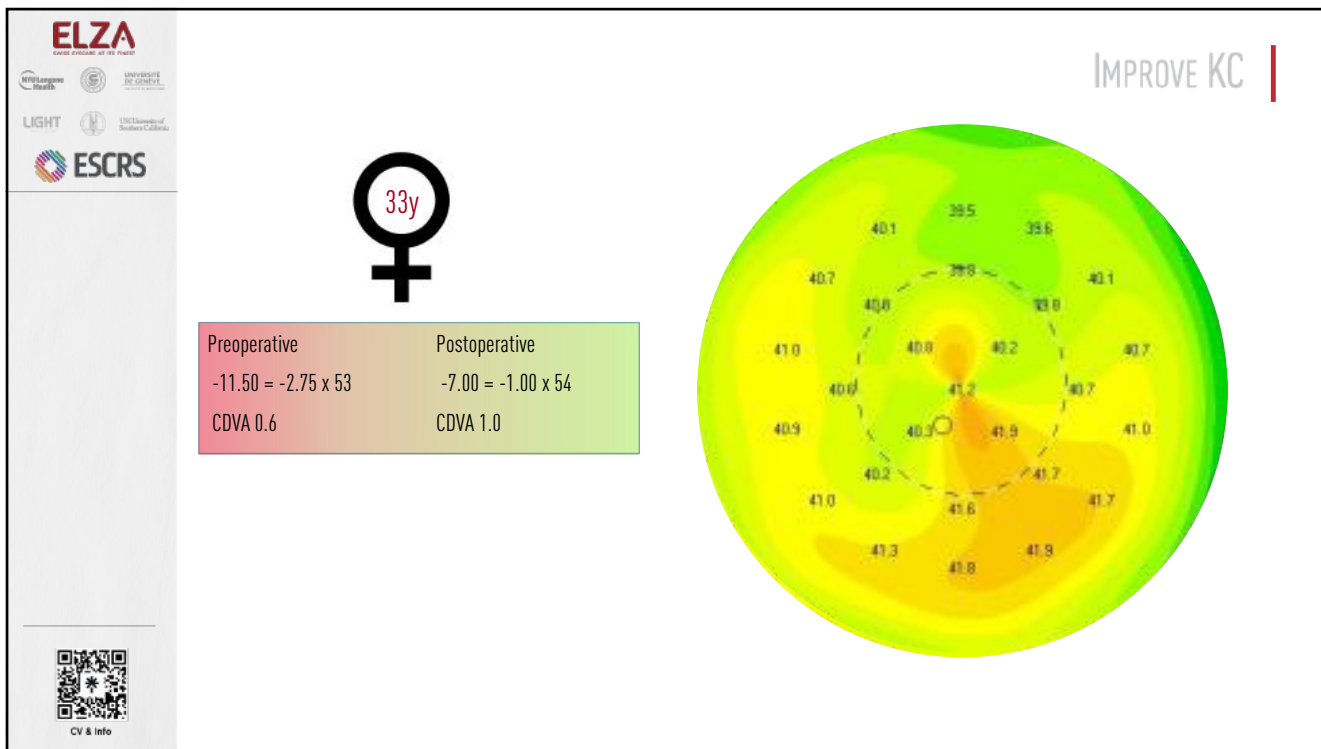



Wellenfrontgeführte transPRK



CV & Info

50



51

**ELZA**  
LARGE EYE CARE AT THE PACE

WU Langens Health | UNIVERSITY OF GRAZ  
LIGHT | ESCRS

IMPROVE KC

# Sehkraft verbessern

## ELZA-PACE

CV & Info

52

**ELZA**  
LASER PROGRAM AT THE FACULTY

WILLERSON  
LIGHT  
ESCRS

UNIVERSITY OF GUELPH  
UNIVERSITY OF SOUTHERN CALIFORNIA

**ELZA-PACE**

CV & Info

1 + 2 + 3



**SCHWIND**  
eye-tech-solutions



**EMAGINE**



**CSO**

53

**ELZA**  
LASER PROGRAM AT THE FACULTY

WILLERSON  
LIGHT  
ESCRS

UNIVERSITY OF GUELPH  
UNIVERSITY OF SOUTHERN CALIFORNIA

**ELZA-PACE**

CV & Info

**ELZA-PACE**



54

**ELZA**  
LARGE EPICENTRE AT THE PACE

WILLIAMS  
LIGHT  
ESCRS

UNIVERSITY OF GENEVA  
UNIVERSITY OF SOUTHERN CALIFORNIA

**ELZA-PACE**



ELZA  
epi-on



**A Transepithelial Corneal Cross-linking (CXL) Protocol Providing the Same Biomechanical Strengthening as Accelerated Epithelium-off CXL**

*Nan-Ji Lu, MD, PhD, MSc; Emilio A. Torres-Netto, MD, PhD; M. Enes Aydemir, MD; Sabine Kling, MSc, PhD; Nikki Hafezi, MASIP ETHZ; Léonard Kollros, MSc, FSLs; Farhad Hafezi, MD, PhD, FARVO*

JRS, 2025



CV & Info

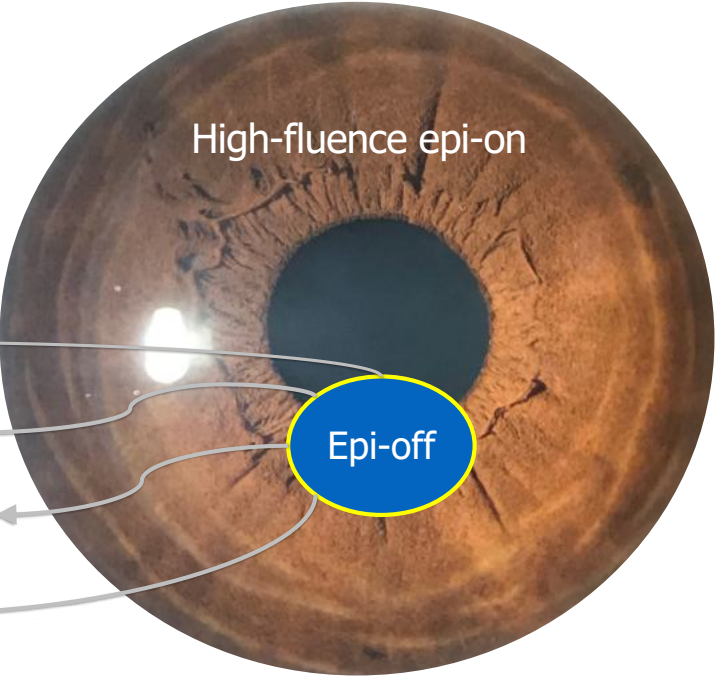
55

**ELZA**  
LARGE EPICENTRE AT THE PACE

WILLIAMS  
LIGHT  
ESCRS


UNIVERSITY OF GENEVA  
UNIVERSITY OF SOUTHERN CALIFORNIA

**ELZA-PACE**



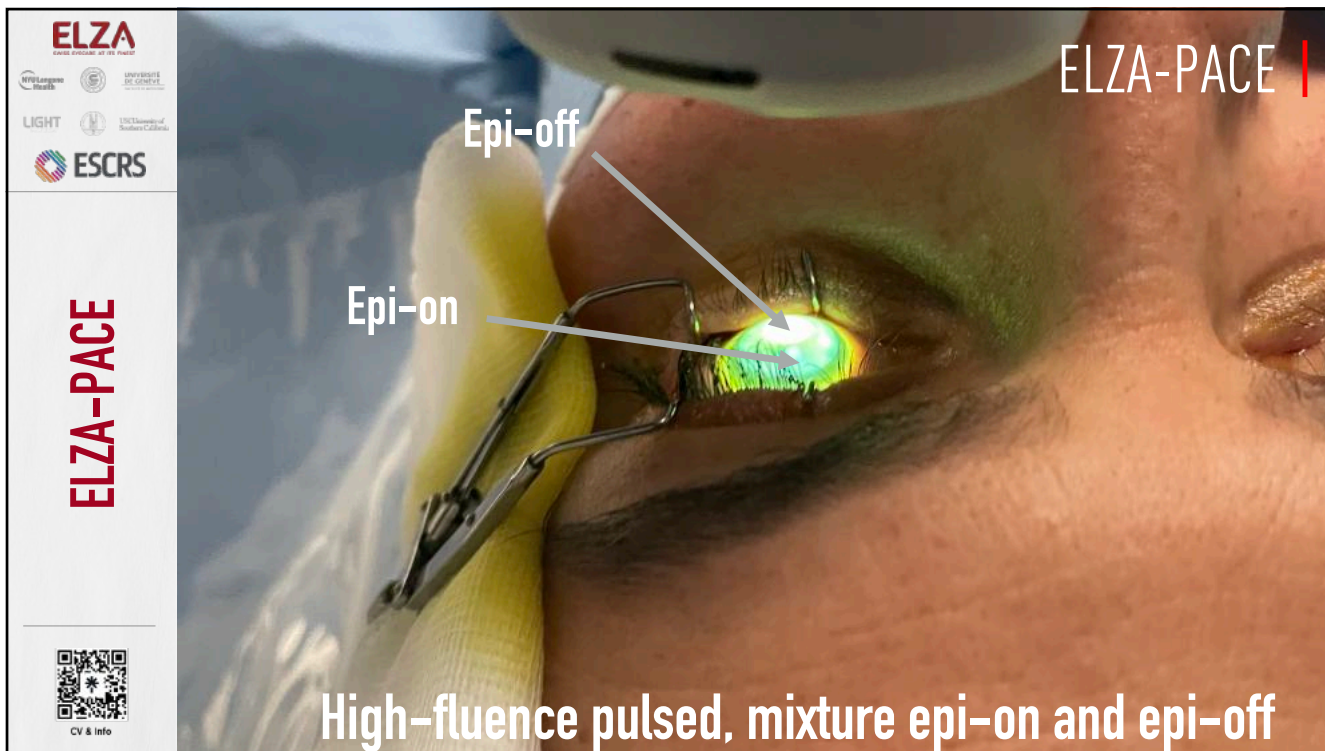
High-fluence epi-on

- 1
20% more UV light
- 2
More oxygen availability
- 3
More riboflavin saturation
- 4
Additional fluence

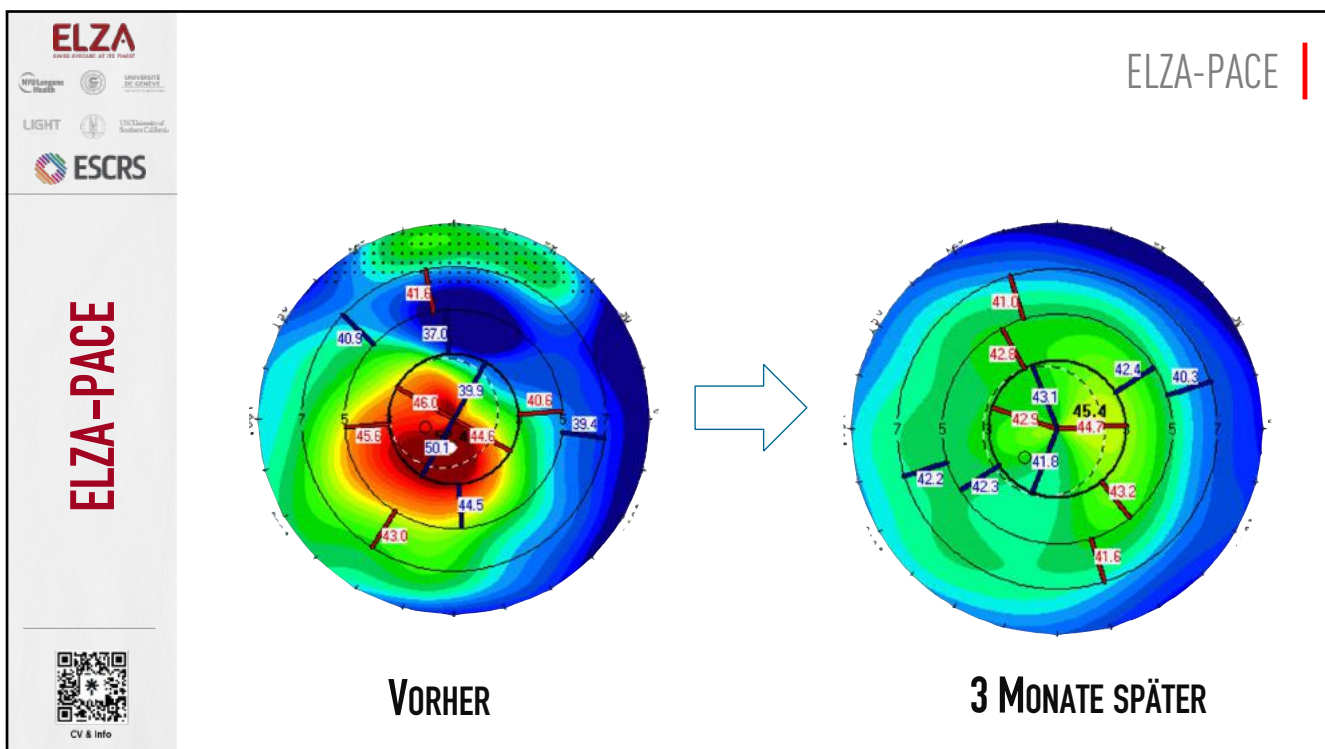


CV & Info

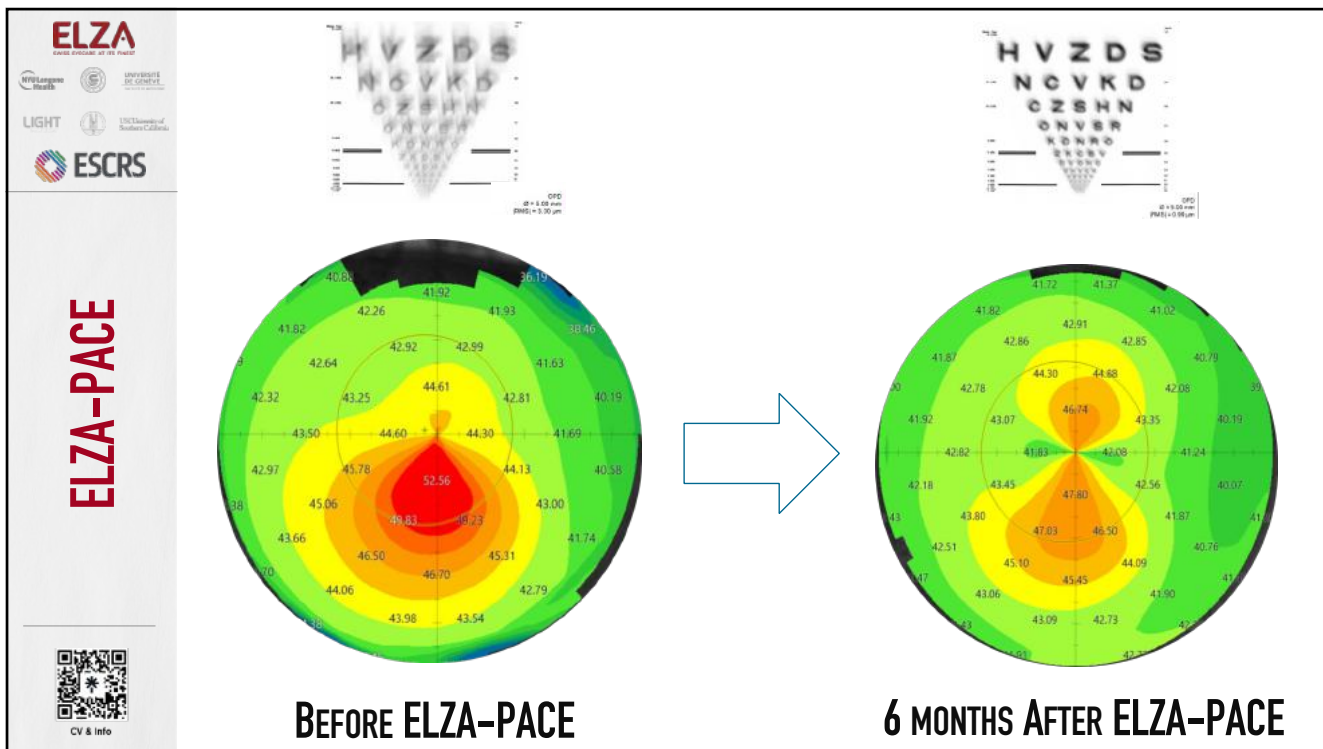
56



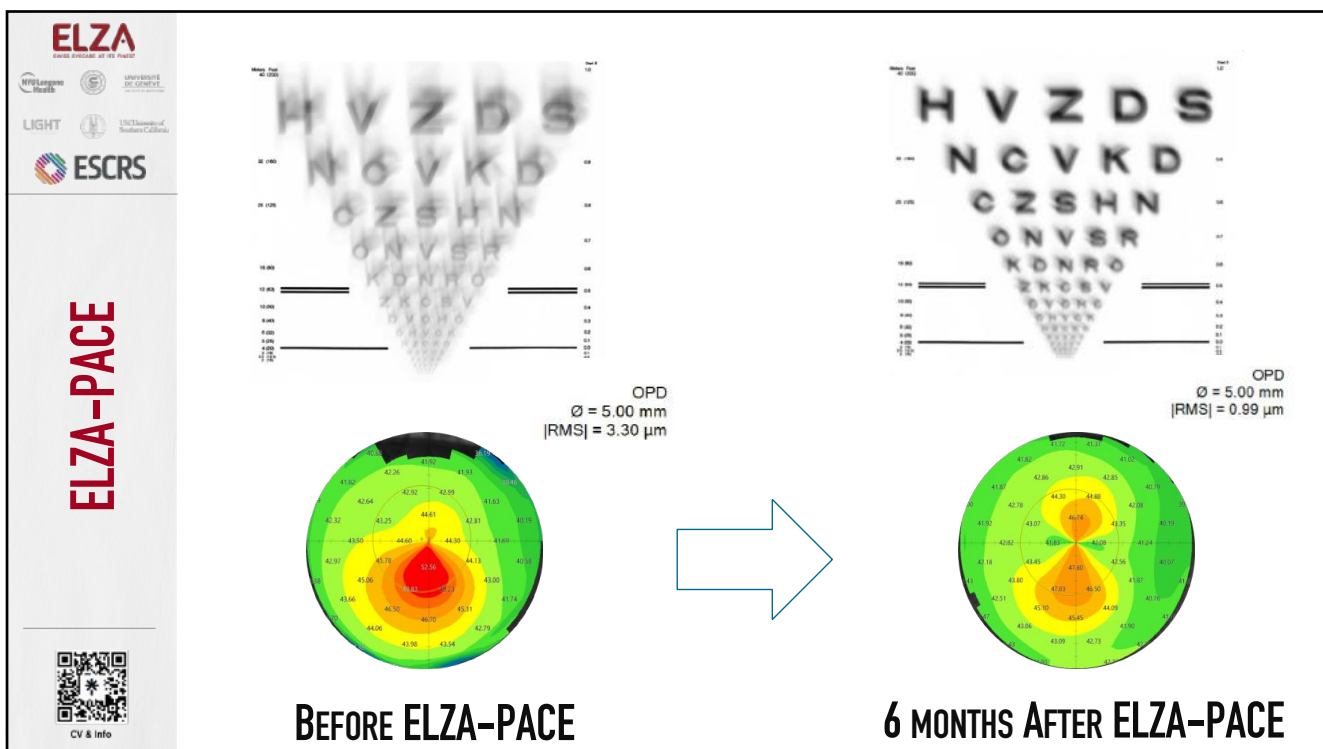
57



58



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**ELZA**  
EUROPEAN LEADER IN THE FIELD

Wittgenstein Institute UNIVERSITY OF GÖTTINGEN  
LIGHT ESCRS ESCI University of Southern California

# Sehkraft verbessern ECO-CAIRS




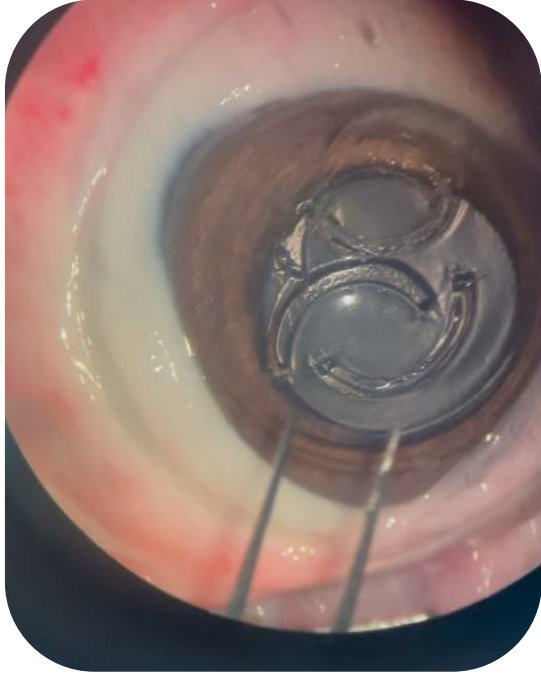


CV & Info

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**ELZA**  
EUROPEAN LEADER IN THE FIELD

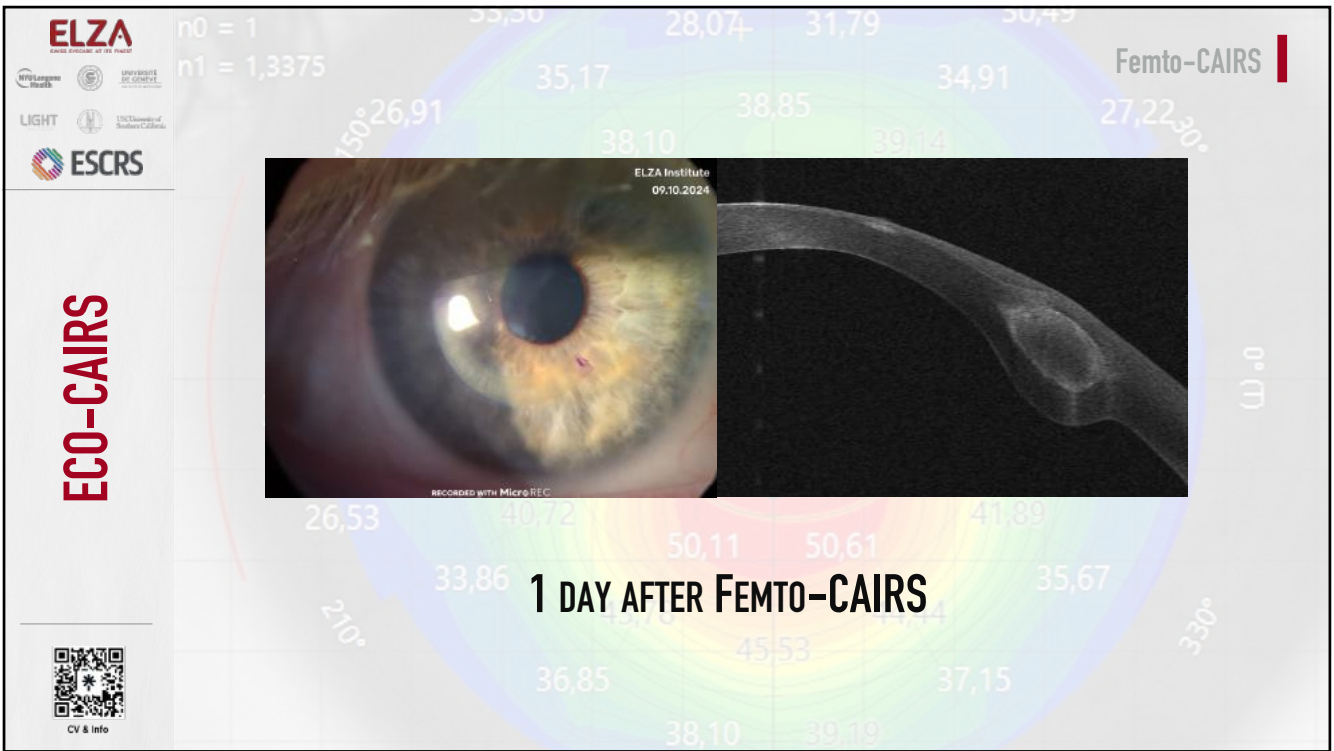
Wittgenstein Institute UNIVERSITY OF GÖTTINGEN  
LIGHT ESCRS ESCI University of Southern California

## ECO-CAIRS

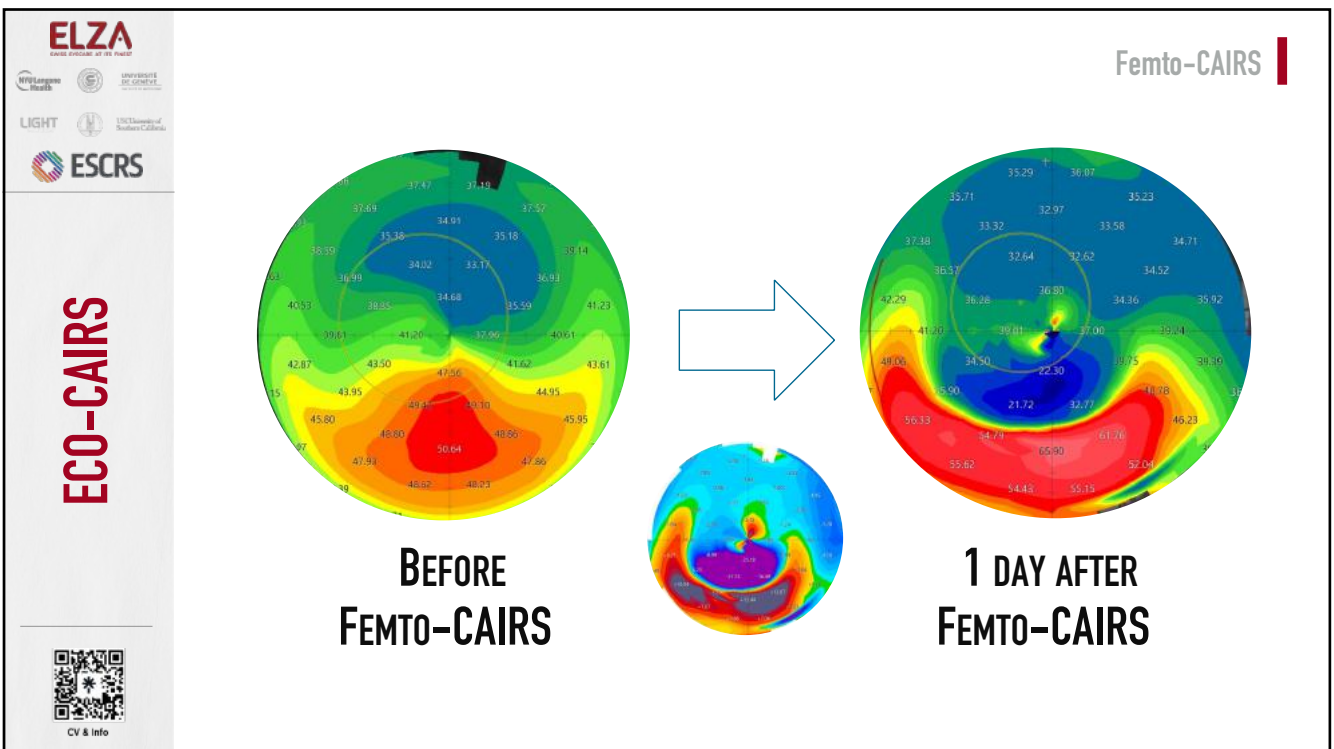


CV & Info


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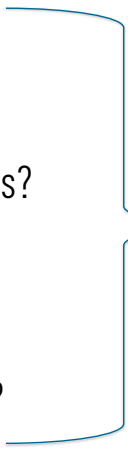
64




2023

## Femto-CAIRS


- 1) Wie das Einsetzen vereinfachen?
- 2) Hat mein Spender\*in Keratokonus?
- 3) Wie eine Infektion verhindern?
- 4) Wie eine Abstossung verhindern?



## Cross-Linking


CV & Info


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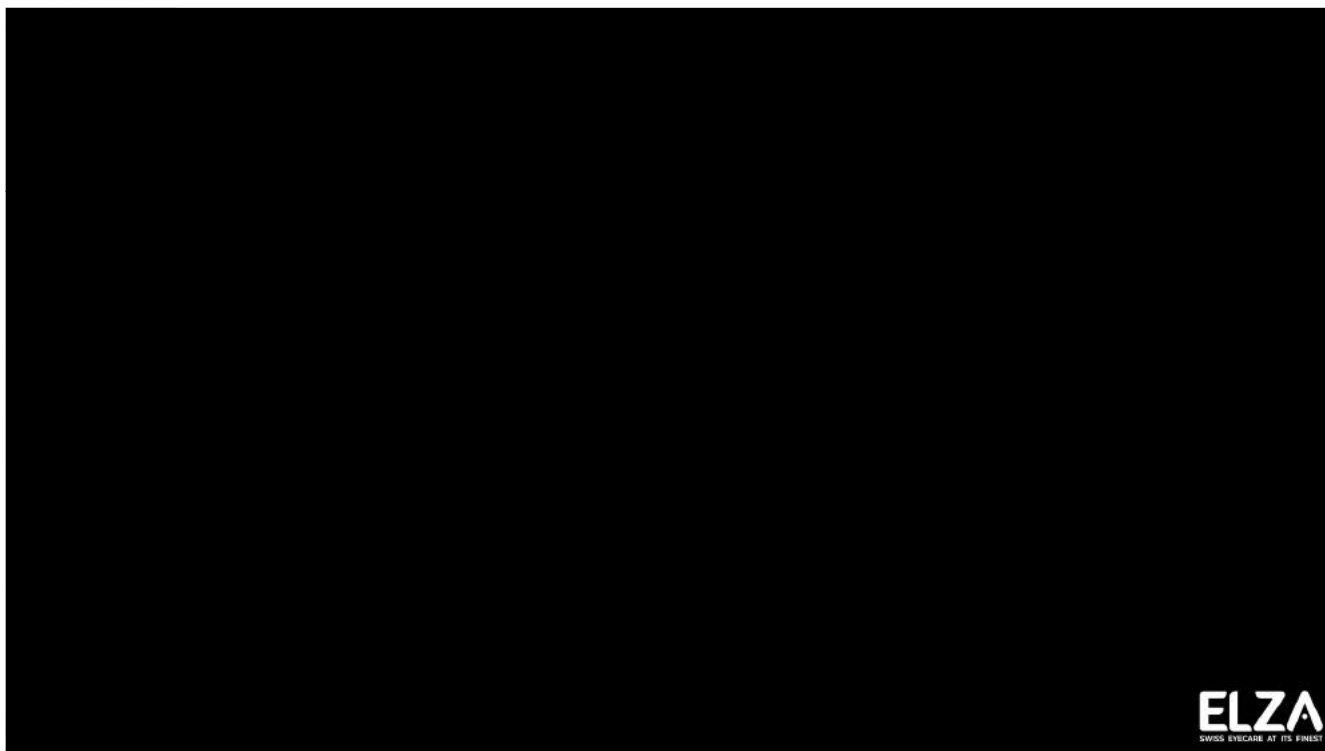
# ECO-CAIRS

Ultra high-fluence **ExtraCO**rporeal CXL

for optimization of **CAIRS**.


CV & Info

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The infographic is titled "ELZA'S APPROACH TO IMPROVE VISION IN KERATOCONUS" in a green banner at the top. On the left side, there is a vertical grey bar containing the ELZA logo, logos for "WILLERGEN Health", "UNIVERSITÄT ST. GALL", "LIGHT", and "ESCRS", and the text "ECO-CAIRS" in large red letters. Below this bar is a QR code labeled "CV &amp; Info". The main content area features two circular corneal topography maps: a smoother one at the bottom and a more irregular one at the top. A green arrow points upwards between them, labeled "Irregularity (Kmax)". To the right, two large, light blue curved arrows point towards the top right.

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**ELZA**  
EARLY LESIONS AT THE PEARL

WILLINGER HAMBURG  
UNIVERSITÄT ST. GEREON  
LIGHT  
ESCERS  
UNIVERSITY OF SOUTHERN CALIFORNIA

# Kontakt




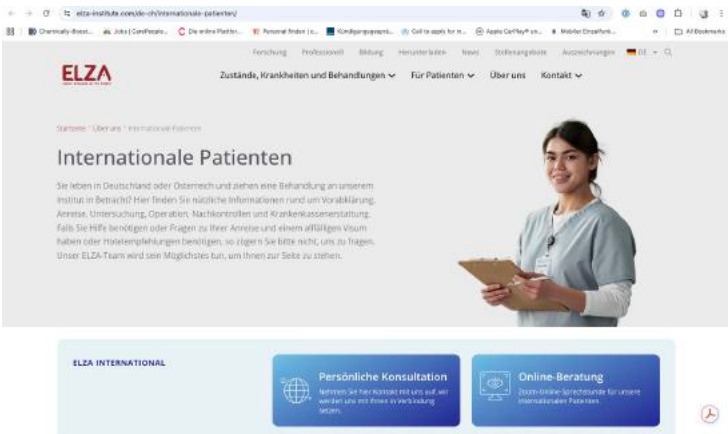
CV & Info

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**ELZA**  
EARLY LESIONS AT THE PEARL

WILLINGER HAMBURG  
UNIVERSITÄT ST. GEREON  
LIGHT  
ESCERS  
UNIVERSITY OF SOUTHERN CALIFORNIA

# international@elza-institute.com









**Kontakt**




CV & Info


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# international@elza-institute.com



Kontakt



CV & Info

KRANKENKASSEN. DEUTSCHLAND

Gesetzliche Krankenkassen

Private Krankenversicherung

Krankenkassen-Mitgliedsbeiträge

Krankenkassen-Vergleiche

Zusatzversicherungen

MCHP Krankenkasse

Aus dem Ausland kommen

Im Ausland gehen

Auslandskrankenversicherungen

Europäische Krankenversicherungskarte

COVID-19-Zertifikat der EU

Certificate of Entitlement

Ausländerbeiträge

Länder

Reisen und Gesundheit

E-Krankenscheine

Portabile Dokumente

EU-Sozialrecht

Drittstaaten

Krankenkassen-Überrichter

Gesundheit-Links

iM-News

Krankenkassen-Geschäftsstellen

Krankenkassen-Garantie > Im Ausland gehen > Portabile Dokumente > **Portabile Dokumente - S2**

Portabile Dokumente - S2: Anspruch auf eine geplante Behandlung im EU-Ausland

Krankenversicherung nur übernommen, wenn der Versicherte von ihr zuvor eine Genehmigung eingeholt hat

Geplante **medizinische Behandlungen** im EU-Ausland werden von der gesetzlichen Krankenkasse übernommen, wenn der Versicherte von ihr zuvor eine Genehmigung eingeholt hat. Ist eine **notwendige medizinische Behandlung** in dem Staat der Krankenversicherung nicht rechtzeitig möglich, muss die Krankenkasse die Behandlung im Ausland genehmigen. Nachweise für den Anspruch ist das "Portabile Dokumente" S2. Um die Genehmigung vor, werden die Kosten der stationären und der ambulanten Versorgung übernommen.

Versicherte können das Formular bei ihrer Krankenkasse beantragen. Es muss von der Abreise vorliegen. Das Portabile Dokument S2 muss selbst der Krankenkasse in dem Staat der Behandlung vorgelegt werden. Müssen Versicherte bereits während der Antragstellung von ihrer Krankenkasse, welcher Träger im Ausland die richtige Kontaktstelle ist.


**Fallbeispiel:**  
Herr Markus Mustermann ist in Deutschland krankenversichert, will aber in Polen eine Zahnbehandlung vornehmen lassen. Er wendet sich an seine Krankenkasse. Diese stellt ihm das Portabile Dokument S2 aus. Dieses legt er einer Krankenkasse seiner Wahl in Polen vor. Die Behandlung wird vorgenommen und seine deutsche Krankenkasse übernimmt die Kosten.

**Wichtig:** Während die Krankenkassen einiger Mitgliedsstaaten bereits auf das neue Format der Portablen Dokumente umgestellt haben, verwenden andere Mitgliedsstaaten noch die alten E-Formulare.

**Downloads**

- Portables Dokument S2: Formular (207K, 14, pdf)
- Informationsheet zum Portablen Dokument S2 (2024, 10, pdf)

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