



STATE BOARD OF OPTOMETRY
2450 DEL PASO ROAD, SUITE 105, SACRAMENTO, CA 95834
P (916) 575-7170 F (916) 575-7292 www.optometry .ca.gov



Continuing Education Course Approval Checklist

Title:

Provider Name:

- Completed Application
 - Open to all Optometrists? Yes No
 - Maintain Record Agreement? Yes No
- Correct Application Fee
- Detailed Course Summary
- Detailed Course Outline
- PowerPoint and/or other Presentation Materials
- Advertising (optional)
- CV for EACH Course Instructor
- License Verification for Each Course Instructor
 - Disciplinary History? Yes No



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CONTINUING EDUCATION COURSE APPROVAL APPLICATION

\$50 Mandatory

Pursuant to California Code of Regulations (CCR) § 1536, the Board will approve continuing education (CE) courses after receiving the applicable fee, the requested information below and it has been determined that the course meets criteria specified in CCR § 1536(g).

In addition to the information requested below, please attach a copy of the course schedule and topical outline of the subject matter. Applications must be submitted 45 days prior to the course presentation date.

Please type or print clearly.

FEE PAID

Course Title <u>STAR WARS: GO RO BUE</u> <u>Corneal Crosslinking "The Lightsaber for Corneal Ectasia."</u>	Course Presentation Date <u>7:45 AM - 11:35 AM</u> <div style="display: flex; justify-content: space-around;"> 1 2 / 1 8 / 2 0 1 6 </div>
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Course Provider Contact Information		
Provider Name <u>Coastal Vision Medical Group</u> <u>Gina</u> <small>(First)</small>	<u>Valdemar</u> <small>(Last)</small>	 <small>(Middle)</small>

Provider Mailing Address		
Street <u>743 S. Main St. #100</u>	City <u>Orange</u>	State <u>CA</u> Zip <u>92880</u>

Provider Email Address <u>gina.valdemar@coastal-vision.com</u>

Will the proposed course be open to all California licensed optometrists?	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
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Do you agree to maintain and furnish to the Board and/or attending licensee such records of course content and attendance as the Board requires, for a period of at least three years from the date of course presentation?	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
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Course Instructor Information

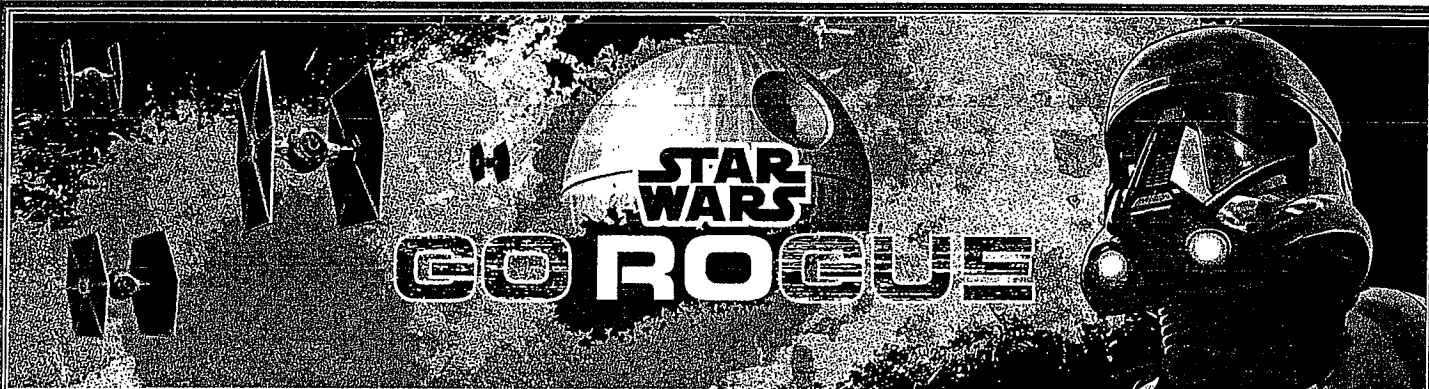
Please provide the information below and attach the curriculum vitae for each instructor or lecturer involved in the course. If there are more instructors in the course, please provide the requested information on a separate sheet of paper.

Instructor Name		
<u>Jennifer</u> <small>(First)</small>	<u>Wu</u> <small>(Last)</small>	 <small>(Middle)</small>
License Number <u>117309</u>	License Type <u>M.D.</u>	
Phone Number <u>(714) 746-9679</u>	Email Address _____	

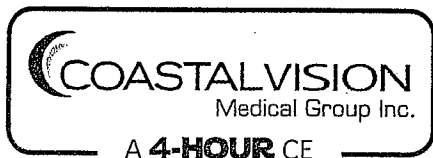
I declare under penalty of perjury under the laws of the State of California that all the information submitted on this form and on any accompanying attachments submitted is true and correct.

Signature of Course Provider

11/11/16
 Date



IN A TIME OF CELEBRATION, A GROUP OF UNLIKELY HEROES BAND TOGETHER ON A MISSION TO LEARN MORE ABOUT OPTOMETRY, THEIR CHOSEN WEAPON.



WHEN:
 Sunday, December 18th
 Registration opens at 6:45am
 7:45am-11:35am (4-hour CE followed by the movie)

WHERE:
 AMC Downtown Disney
 Downtown Disney District
 1565 Disneyland Drive
 Anaheim, CA 92802

Hyperdrive of Toys

Bring any new, unwrapped toy, to benefit Toys for Tots, and receive a movie ticket for you and a guest for Rogue One: A Star Wars Story. Movie to follow CE. Additional tickets available for purchase.



Downtown Disney Parking: First 2 hours are free; additional 2 hours free with AMC-validation (Disneyland parking lots may be available for all day parking prices; parking is responsibility of attendee)

For registration information please visit our Affiliate Portal:
coastalvisionmedical.com/site/ces.htm

AGENDA

6:45 am	Check-in (pastries and coffee provided)	
7:45 am	Welcome - Opening Remarks	
7:50 am	Lisa Garbutt, MD	Symfony and Symfomy Toric: The Best of Both Galaxies
8:15 am	Jennifer Wu, MD	Corneal Crosslinking "The Lightsaber for Corneal Ectasia"
8:40 am	Raj Rathod, MD	Retina One: A Story of Systemic Discovery
9:05 am	Dan Tran, MD	Combining Laser Corneal Refractive Surgery and Intraocular Lens Technology - The Force Is Strong
9:30 am	Break	
9:55 am	Vincent Hau, MD	Retina Jeopardy...From a Galaxy, Far, Far Away
10:20 am	Betsy Nguyen, MD	MIGS Episode III: Cypass Micro-Stent, A New Hope
10:45 am	Madhu Agarwal, MD	Eye Rebel: Waging War on Orbital Disease
	Dan Tran, MD	
11:10 am	Lisa Garbutt, MD	Rogue Diagnosis: Case Presentations
	Betsy Nguyen, MD	
	Jennifer Wu, MD	
11:35 am	Conclusion	
11:45 am	Movie: <i>Rogue One: A Star Wars Story</i>	

*CE and movie ticket registration is based on first-come, first-served basis. Seating is limited.



November 5, 2016

State Board of Optometry
2450 Del Paso Road, Ste. 105
Sacramento, CA 95834

RE: Late submission of CE course approval; Star Wars: Go Rogue Symposium-Symfony and Symphony Toric; The Best of Both Galaxies, Corneal Crosslinking "The Lightsaber for Corneal Ectasia", Retina One: A Story of Systemic Discovery, Combining Laser Refractive Surgery and Intraocular Lens Technology-The force is strong, Retina Jeopardy, MIGS Episode III: Cypass Micro-Stent, A New Hope, Eye Rebel: Waging War on Orbital Disease, Rogue Diagnosis: Case Presentations.

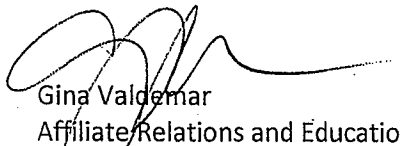
Dear Practice and Education committee,

I am writing this letter in regards to late submission for the multi-course symposium titled "Star Wars; Go Rogue" scheduled for presentation on 12/18/16. We are just shy of the 45 day submission request, and wanted to include a letter for late submission with our CE approval application.

We continue to work diligently to get all required items to the board needed for CE approval in a timely manner. Due to multiple speakers at the upcoming CE, we had difficulty obtaining all the lectures to meet the submission requirement timeline and would appreciate your consideration of our continuing education approval request.

Please feel free to reach out to us with any other questions. We look forward to continued relations with the State Board of Optometry and the practice and education committee.

Sincerely,



Gina Valdemar
Affiliate Relations and Education Director
Coastal Vision Medical Group
ginavaldemar@coastal-vision.com

Coastal Vision Irvine
15825 Laguna Canyon Rd., Ste. 201, Irvine, CA 92618
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Coastal Vision Orange
293 S. Main St., Ste. 100, Orange, CA 92868
Tel: (714) 771-1213 • Fax: (714) 771-7126

Coastal Vision Long Beach
709 E. Anaheim St., Long Beach, CA 90813
Tel: (562) 591-7700 • Fax: (562) 591-1311

Star Wars: Go Rogue 4 hour CE

Course Title: Corneal Crosslinking “The Lightsaber for Cornea Etasia”

Course Presentation date: 12/18/2016

Speaker: Jennifer Wu, MD

Target Audience: This lecture is intended for optometrist seeking continuing education

Course Description:

This lecture seeks to provide optometrists with information regarding cornea crosslinking for ectasia. Discussion includes how corneal crosslinking works and reviews of scientific data. Corneal crosslinking treatment applies to keratoconus as a safe and effective treatment for progressive keratoconus and provides a goal of halting its progression, while strengthening the cornea and avoids the need for corneal transplant. The lecture will include information regarding the FDA approved Avdro Crosslinking system and FDA trails. This lecture also provides the OD patient education regarding the need for hard contact lens fittings and that crosslinking is not a refractive procedure.

CE Credit: .50 CE Unit

1  **CORNEAL CROSSLINKING:
"THE LIGHTSABER FOR CORNEA ECTASIA"**

JENNIFER LEE WU, MD
CORNEA, ANTERIOR SEGMENT, REFRACTIVE SPECIALIST
COASTAL VISION MEDICAL GROUP

2  **OBJECTIVES**

- LEARN HOW CORNEAL CROSS LINKING (CXL) WORKS AND REVIEW THE SCIENTIFIC DATA
- LEARN HOW CORNEAL CROSS LINKING TREATMENT APPLIES TO KERATOCONUS
- LEARN ABOUT THE AVEDRO CROSS LINKING SYSTEM AND FDA TRIALS

3  **CASE #1**

- 18 YO MALE, RAPID CHANGING GLASSES RX FOR LAST 3 YEARS
- UNABLE TO IMPROVE BCVA BEYOND 20/70 AT LAST OPTOMETRIST VISIT
- REFERRED FOR KERATOCONUS SUSPECT EVALUATION

4  **STANDARD TREATMENTS REGIMENTS**

- MEDICAL
 - VISION CORRECTION (RIGID GAS-PERMEABLE OR SCLERAL CONTACT LENS)
- SURGICAL
 - CORNEAL TRANSPLANT FOR CONTACT LENS INTOLERANCE OR CORNEAL SCARRING

5  **CORNEA CROSS-LINKING (CXL)**

- COMBINES THE USE OF ULTRA-VIOLET (UV) LIGHT AND RIBOFLAVIN (VITAMIN B2) DROPS
- THE ABSORPTION OF UVA BY RIBOFLAVIN GENERATES RADICAL RIBOFLAVIN AND SINGLET OXYGEN TO FORM CROSS-LINKS¹
- CROSS-LINKING²:
 - CREATES NEW CORNEAL COLLAGEN AND GLYCOSAMINOGLYCAN CROSS-LINKS
 - RESULTS IN A SHORTENING AND THICKENING OF THE COLLAGEN FIBRILS
 - LEADS TO THE STIFFENING OF THE CORNEA

6  **LAYERS OF THE CORNEA**

7  **IDEAL CANDIDATES FOR KCN CXL**

- YOUNG KERATOCONUS PATIENTS (14 TO 40 YEARS) WITH DOCUMENTATION OF PROGRESSION OVER 6 MONTH PERIOD
 - > 1D CHANGE IN REFRACTION
 - TOPOGRAPHIC STEEPENING (INCREASE IN KMAX)
 - DECREASE IN MEAN CENTRAL CORNEAL THICKNESS OR THINNING OF POSTERIOR CORNEA
- GOAL IS TO HALT PROGRESSION, STRENGTHEN CORNEA, AND AVOID NEED FOR CORNEAL TRANSPLANT, NOT REFRACTIVE PROCEDURE!
- VISION IS ACCEPTABLE WITH GLASSES OR CONTACT CORRECTION

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8  **CONTRAINDICATION FOR KCN CXL**

- CORNEAL SCARRING (APICAL OR HYDROPS)
- CENTRAL CORNEAL THICKNESS < 400UM (CONCERN FOR DAMAGE TO ENDOTHELIUM AND LENS)
- HISTORY OF VIRAL CORNEAL INFECTION (CONCERN FOR REACTIVATION WITH UV LIGHT)
- MAXIMUM CORNEAL TOPOGRAPHY > 58D

9  **CORNEAL CROSS-LINKING (CXL) PROTOCOL**

BASED ON DRESDEN PROTOCOL¹:

- 1) REMOVAL OF CORNEAL EPITHELIUM IN 9MM ZONE
- 2) INSTILL 1 DROP OF RIBOFLAVIN SOLUTION 0.146% TOPICALLY EVERY 2 MINUTES X 30 MINUTES
- 3) CHECK FOR YELLOW FLARE IN THE ANTERIOR CHAMBER, IF NOT PRESENT, ADD RIBOFLAVIN EVERY 2 MINUTES UNTIL YELLOW FLARE DETECTED
- 4) CHECK CORNEAL PACHYMETRY >400UM
- 5) UV-A IRRADIATION APPLIED AT 3MW/CM² X 30 MINUTES AT 5CM WITH CONTINUOUS APPLICATION OF RIBOFLAVEN SOLUTION EVERY 2 MINUTES
- 6) PLACE BANDAGE CONTACT LENS OVER CORNEA

10  **CORNEAL CXL FOR KCN: HISTORY AND RESULTS**

- FIRST PERFORMED AT DRESDEN UNIVERSITY OF TECHNOLOGY (GERMANY) IN 1998¹
 - SEVERAL ARTICLES SHOW EFFECTIVENESS OF KXL FOR STOPPING PROGRESSION OF KCN
 - MANY PATIENTS ALSO HAD FLATTENING OF CENTRAL CORNEAL CURVATURE
 - 10-YEAR RESULTS OF CORNEAL COLLAGEN CROSSLINKING (CXL) FOR PROGRESSIVE KERATOCONUS FROM DRESDEN: 34 EYES (FROM 24 PATIENTS) TREATED FROM 2000 TO 2004
 - MEAN APICAL KERATOMETRY (K) VALUE (61.5 DIOPTERS (D) PREOPERATIVELY AND 55.3 D 10 YEARS POSTOPERATIVELY) ($P < .001$)
 - MEAN KMAX (53.2 D AND 49.56 D, RESPECTIVELY) AND KMIN (47.5 D AND 45.5 D, RESPECTIVELY) ($P < .001$)
 - MEAN CORRECTED DISTANCE VISUAL ACUITY (CDVA) IMPROVED BY 0.14 LOGMAR OVER PREOPERATIVELY ($P = .002$)
 - ENDOTHELIAL CELL COUNT (ECC) WAS UNCHANGED POSTOPERATIVELY
-
-

11  **COMPLICATIONS**

- PERSISTENT SUBEPITHELIAL/STROMAL HAZE- MAKE TAKE UP TO 12 MONTHS TO RESOLVE
 - APPROXIMATELY 4.5% IN 6-MONTH FOLLOW-UP¹
- PERSISTENT EPITHELIAL DEFECT
- CORNEA ULCER
- FEW PATIENTS SHOW PROGRESSION AFTER CXL (2 OF 33 EYES), FOUND IN ADVANCED KCN $K_{MAX} > 60^2$

12  **CORNEAL CXL IN THE US**

- AVEDRO AND CXL-USA COMPANIES BEGAN CORNEA COLLAGEN CROSS-LINKING CLINICAL TRIALS IN THE US IN 2008 FOR FDA APPROVAL
- APRIL 2016 AVEDRO KXL SYSTEM + PHOTOENHANCERS RECEIVES FDA APPROVAL FOR TREATMENT OF PROGRESSIVE KERATOCONUS
- JULY 2016 AVEDRO KXL SYSTEM + PHOTOENHANCER RECEIVES FDA APPROVAL FOR TREATMENT OF CORNEA ECTASIA FOLLOWING REFRACTIVE SURGERY

13  **Photrexa® Viscous**

(riboflavin 5'-phosphate in 20% dextran ophthalmic solution) 0.146%

Photrexa®

(riboflavin 5'-phosphate ophthalmic solution) 0.146%

and the KXL® System

Corneal Cross-linking for Progressive Keratoconus

14  **AVEDRO PHASE III STUDY DESIGN**

- AVEDRO'S NDA SUBMISSION ENCOMPASSED DATA FROM THREE PROSPECTIVE, RANDOMIZED, PARALLEL-GROUP, OPEN-LABEL, PLACEBO-CONTROLLED, 12-MONTH TRIALS CONDUCTED IN THE UNITED STATES TO EVALUATE THE SAFETY AND EFFECTIVENESS OF RIBOFLAVIN OPHTHALMIC SOLUTION/UVA IRRADIATION FOR PERFORMING CORNEAL COLLAGEN CROSS-LINKING.
- THE TRIALS INCLUDED:
 - STUDY 1: 58 PATIENTS WITH PROGRESSIVE KERATOCONUS.
 - STUDY 2: 147 PATIENTS WITH PROGRESSIVE KERATOCONUS.
- SCHEDULE OF ASSESSMENTS:
 - SCREENING/BASELINE, DAY 0 (RANDOMIZATION/TREATMENT DAY), 1 DAY, 1 WEEK, AND 1, 3, 6 AND 12 MONTHS AFTER TREATMENT.
- PRIMARY ENDPOINT WAS K_{MAX} , AS MEASURED BY KERATOMETRY

15  **EFFICACY ANALYSIS:**

MEAN CHANGE FROM BASELINE K_{MAX}, CXL AND SHAM

- IN THE STUDIES, TREATED EYES SHOWED IMPROVEMENT IN K_{MAX} AT 12 MONTHS, WHILE IN UNTREATED EYES K_{MAX} CONTINUED TO WORSEN.
- AT MONTH 12, CXL TREATED EYES HAD AN AVERAGE K_{MAX} REDUCTION OF 1.4 AND 1.7 DIOPTER IN STUDY 1 AND STUDY 2, RESPECTIVELY WHILE THE SHAM EYES HAD AN AVERAGE INCREASE OF 0.5 AND 0.6 DIOPTER IN STUDY 1 AND STUDY 2, RESPECTIVELY.
- PATIENTS SHOULD BE MONITORED FOR RESOLUTION OF EPITHELIAL DEFECTS AS ULCERATIVE KERATITIS CAN OCCUR.

16  **ACCELERATED CXL**

- ACCELERATED CXL BASED ON THE BUNSEN-ROSCOE LAW: RATE OF THE PHOTOCHEMICAL AND PHOTOBIOLOGICAL REACTION IS DIRECTLY PROPORTIONAL TO THE TOTAL DOSE OF RADIATION ENERGY
- DRESDEN PROTOCOL 3MW/CM² FOR 30 MINUTES, TOTAL UVA ENERGY DELIVERED TO

THE CORNEAL IS 5.4 J/CM²

- AVEDRO SPONSORED ACCELERATED CXL TRIAL FOR FDA SUBMISSION USING 30MV/CM² FOR 4 MINUTES (2012-2014)
- AECOS (AMERICAN-EUROPEAN CONGRESS OF OPHTHALMIC SURGERY) SPONSORED ACCELERATED CXL STUDY USING AVEDRO'S RIBOFLAVEN AND KXL SYSTEM (2012-2015)
 - THREE DOSES OF IRRADIATION TESTED:
 - 15 MW/CM² FOR 8 MINUTES
 - 30 MW/CM² FOR 4 MINUTES
 - 45 MW/CM² FOR 2 MINUTES AND 40 SECONDS
- ONE STUDY USING 6 MW/CM² UVA FOR 15 MINUTES, SHOWED INCREASED RATE OF SUBEPITHELIAL CORNEAL HAZE 25% AT 2 YEARS, PERFORMED IN POLAND.¹

17  **COST EFFECTIVENESS OF CXL**

- CORNEAL CROSS-LINKING FOR PROGRESSIVE KCN IS CURRENTLY NOT COVERED BY INSURANCE
- CASH PAY FOR TREATMENT, CARE CREDIT AVAILABLE
- PROGRESSIVE KCN AFFECTS PATIENTS EARLY TEENS THROUGH 40 YEARS OLD (MOST ACTIVE AND PRODUCTIVE YEARS)
- SIGNIFICANT VISUAL MORBIDITY
- HALTING DISEASE PROGRESSION MAY ELIMINATE THE NEED FOR A CORNEAL TRANSPLANT

18  **PRE-OPERATIVE PATIENT EDUCATION**

- SET THE EXPECTATION THAT CROSS-LINKING IS NOT REFRACTIVE SURGERY
 - CONTACT LENSES AND/OR SPECTACLES STILL REQUIRED
- EDUCATE PATIENTS REGARDING THE TIME COURSE OF THE POST-OPERATIVE HEALING PROCESS.
 - ON AVERAGE, STEEPENING OF KMAX IS OBSERVED AT 1 MONTH POSTOPERATIVELY, FOLLOWED BY FLATTENING THROUGH 12 MONTHS.
 - IN 1-2% OF PATIENTS, CORNEAL EPITHELIUM DEFECT, CORNEAL EDEMA, CORNEAL OPACITY AND CORNEAL SCAR CONTINUED TO BE OBSERVED AT 12 MONTHS

19  **POST-OPERATIVE MANAGEMENT**

20  **CLINICAL EFFECT OF CXL**

- CROSS-LINKING IS SUCCESSFUL IN STOPPING THE DISEASE FROM PROGRESSING IN CLOSE TO 98 PERCENT OF PATIENTS
- 70% MEAN KERATOMETRY REGRESSION OF 2 D AT THE CORNEAL PLANE AND A REGRESSION OF 1.14 D OF THE MANIFEST SPHERICAL EQUIVALENT REFRACTIVE ERROR
- VISUAL ACUITY IMPROVED SLIGHTLY IN 65% OF THE EYES
- CXL AFFECT CAN CONTINUE TO EVOLVE OVER TIME

21  **SUMMARY**

- CORNEAL CROSS-LINKING IS A SAFE AND EFFECTIVE TREATMENT FOR PROGRESSIVE KERATOCONUS
- GOAL IS TO HALT PROGRESSION, STRENGTHEN CORNEA, AND AVOID NEED FOR CORNEAL TRANSPLANT, NOT REFRACTIVE PROCEDURE!
- COMMON COMPLICATIONS INCLUDE DELAYED EPITHELIAL HEALING AND PERSISTENT SUBEPITHELIAL/STROMAL HAZE THAT MAKE TAKE UP TO 12 MONTHS TO RESOLVE
- PATIENTS NEED HARD CONTACT LENS REFITTING AFTER CXL
-
-
-
-

22  **THANK YOU!**

QUESTIONS?
JENNYWU@COASTAL-VISION.COM

CORNEAL CROSSLINKING: "THE LIGHTSABER FOR CORNEA ECTASIA"

JENNIFER LEE WU, MD
CORNEA/ ANTERIOR SEGMENT, REFRACTIVE SPECIALIST
COASTAL VISION MEDICAL GROUP

OBJECTIVES

- LEARN HOW CORNEAL CROSS LINKING (CXL) WORKS AND REVIEW THE SCIENTIFIC DATA
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STANDARD TREATMENTS REGIMENTS

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 - CORNEAL TRANSPLANT FOR CONTACT LENS INTOLERANCE OR CORNEAL SCARRING

CORNEA CROSS-LINKING (CXL)

- COMBINES THE USE OF ULTRA-VIOLET (UV) LIGHT AND RIBOFLAVIN (VITAMIN B2) DROPS
- THE ABSORPTION OF UVA BY RIBOFLAVIN GENERATES RADICAL RIBOFLAVIN AND SINGLET OXYGEN TO FORM CROSS-LINKS*
- CROSS-LINKING?
 - CREATES NEW CORNEAL COLLAGEN AND GLYCOSAMINOGLYCAN CROSS-LINKS
 - RESULTS IN A SHORTENING AND THICKENING OF THE COLLAGEN FIBRILS
 - LEADS TO THE STIFFENING OF THE CORNEA

1- standard application of UVA and Riboflavin (UVA)

2- Production of pyrimid radicals

3- Production of radical cross-links

4- Cross-linking

UV-A

UV-B

UV-C

UV-D

UV-E

UV-F

UV-G

UV-H

UV-I

UV-J

UV-K

UV-L

UV-M

UV-N

UV-O

UV-P

UV-Q

UV-R

UV-S

UV-T

UV-U

UV-V

UV-W

UV-X

UV-Y

UV-Z

UV-A

UV-B

UV-C

UV-D

UV-E

UV-F

UV-G

UV-H

UV-I

UV-J

UV-K

UV-L

UV-M

UV-N

UV-O

UV-P

UV-Q

UV-R

UV-S

UV-T

UV-U

UV-V

UV-W

UV-X

UV-Y

UV-Z

*Reference: P. Friedman, MD, Sherr J, Miller D. Photochemical kinetics of normal cross-linking with riboflavin. Invest Ophthalmol Vis Sci. 2013;54:3236-7. National Eye Institute. Chemical and physical properties of normal cross-linking agents. Available at: <http://www.nei.nih.gov/oculist>

LAYERS OF THE CORNEA

IDEAL CANDIDATES FOR KCN CXL

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- MAXIMUM CORNEAL TOPOGRAPHY > 58D

CORNEAL CROSS-LINKING (CXL) PROTOCOL

BASED ON DRESDEN PROTOCOL¹:

- 1) REMOVAL OF CORNEAL EPITHELIUM IN 9MM ZONE
- 2) INSTILL 1 DROP OF RIBOFLAVIN SOLUTION 0.1-0.46% TOPICALLY EVERY 2 MINUTES X 30 MINUTES
- 3) CHECK FOR YELLOW FLARE IN THE ANTERIOR CHAMBER, IF NOT PRESENT, ADD RIBOFLAVIN EVERY 2 MINUTES UNTIL YELLOW FLARE DETECTED
- 4) CHECK CORNEAL PACHYMETRY > 400UM
- 5) UV-A IRRADIATION APPLIED AT 3MW/CM² X 30 MINUTES AT 5CM WITH CONTINUOUS APPLICATION OF RIBOFLAVEN SOLUTION EVERY 2 MINUTES
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CORNEAL CXL FOR KCN: HISTORY AND RESULTS

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 - MEAN KMAX (53.2 D AND 49.54 D, RESPECTIVELY) AND KMIN (47.5 D AND 45.5 D, RESPECTIVELY) (P<0.01)
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 - ENDOTHELIAL CELL COUNT (ECC) WAS UNCHANGED POSTOPERATIVELY

1. Wollastik, G, et al. Fluorescein-riboflavin-induced collagen crosslinking for the treatment of keratoconus. American Journal of Ophthalmology, 2005; 139:690-697.
2. Bhatnagar P, et al. Corneal collagen crosslinking with riboflavin and ultraviolet light to progressive keratoconus: long-term results. J. Cataract Refract Surg, 2015; 41(1):14-18

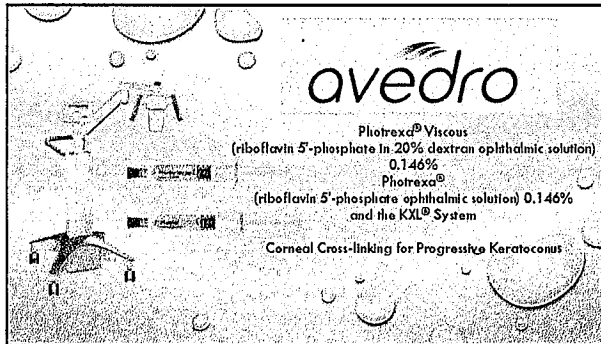
COMPLICATIONS

- PERSISTENT SUBEPITHELIAL/STROMAL HAZE- MAKE TAKE UP TO 12 MONTHS TO RESOLVE
 - APPROXIMATELY 4.5% IN 6-MONTH FOLLOW-UP¹
- PERSISTENT EPITHELIAL DEFECT
- CORNEA ULCER
- FEW PATIENTS SHOW PROGRESSION AFTER CXL (2 OF 33 EYES), FOUND IN ADVANCED KCN K_{max} > 60²

1. Caporaso A, Mazzotta C, Belschi L, Caporaso L. Long-term results of riboflavin-uv-a corneal collagen cross-linking for keratoconus in Italy: the first 175 cases study. The American Journal of Ophthalmology, 2010; 149(1):185-192.
2. Mollnes, Sorenson G, Paulsen A, et al. Long-term results after corneal collagen cross-linking in children with progressive keratoconus. Acta Ophthalmol, 2016, Apr 19. (In press)

CORNEAL CXL IN THE US


- AVEDRO AND CXL-USA COMPANIES BEGAN CORNEA COLLAGEN CROSS-LINKING CLINICAL TRIALS IN THE US IN 2008 FOR FDA APPROVAL
- APRIL 2016 AVEDRO KXL SYSTEM + PHOTOENHANCER RECEIVES FDA APPROVAL FOR TREATMENT OF PROGRESSIVE KERATOCONUS
- JULY 2016 AVEDRO KXL SYSTEM + PHOTOENHANCER RECEIVES FDA APPROVAL FOR TREATMENT OF CORNEA ECTASIA FOLLOWING REFRACTIVE SURGERY



avedro
 Photrex[®] Viscous
 (riboflavin 5'-phosphate in 20% dextran ophthalmic solution) 0.146%
 Photrex[®]
 (riboflavin 5'-phosphate ophthalmic solution) 0.146%
 and the KXL[®] System
 Corneal Cross-linking for Progressive Keratoconus

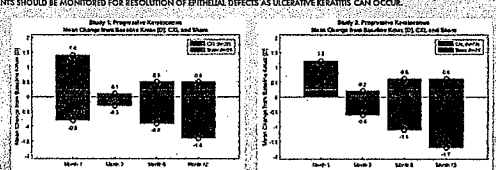
AVEDRO PHASE III STUDY DESIGN

- AVEDRO'S NDA SUBMISSION ENCOMPASSED DATA FROM THREE PROSPECTIVE, RANDOMIZED, PARALLEL-GROUP, OPEN-LABEL, PLACEBO-CONTROLLED, 12-MONTH TRIALS CONDUCTED IN THE UNITED STATES TO EVALUATE THE SAFETY AND EFFECTIVENESS OF RIBOFLAVIN OPHTHALMIC SOLUTION/UVA IRRADIATION FOR PERFORMING CORNEAL COLLAGEN CROSS-LINKING.
- THE TRIALS INCLUDED:
 - STUDY 1: 58 PATIENTS WITH PROGRESSIVE KERATOCONUS.
 - STUDY 2: 147 PATIENTS WITH PROGRESSIVE KERATOCONUS.
- SCHEDULE OF ASSESSMENTS:
 - SCREENING/BASELINE, DAY 0 (RANDOMIZATION/TREATMENT DAY), 1 DAY, 1 WEEK, AND 1, 3, 6 AND 12 MONTHS AFTER TREATMENT.
 - PRIMARY ENDPOINT WAS K_{max} AS MEASURED BY KERATOMETRY.



EFFICACY ANALYSIS: MEAN CHANGE FROM BASELINE KMAX, CXL AND SHAM

- IN THE STUDIES, TREATED EYES SHOWED IMPROVEMENT IN K_{max} AT 12 MONTHS, WHILE IN UNTREATED EYES K_{max} CONTINUED TO WORSEN.
- AT MONTH 12, CXL TREATED EYES HAD AN AVERAGE K_{max} REDUCTION OF 1.4 AND 1.7 DIOPTER IN STUDY 1 AND STUDY 2, RESPECTIVELY WHILE THE SHAM EYES HAD AN AVERAGE INCREASE OF 0.5 AND 0.6 DIOPTER IN STUDY 1 AND STUDY 2, RESPECTIVELY.
- PATIENTS SHOULD BE MONITORED FOR RESOLUTION OF EPITHELIAL DEFECTS AS ULCERATIVE KERATITIS CAN OCCUR.



Study 1: Progressive Keratoconus
 Mean Change from Baseline Kmax (D) CXL and Sham

Month	CXL (Mean Change)	Sham (Mean Change)
Month 1	-0.4	0.4
Month 3	-0.4	0.2
Month 6	-0.4	0.2
Month 12	-1.4	0.5

Study 2: Progressive Keratoconus
 Mean Change from Baseline Kmax (D) CXL and Sham

Month	CXL (Mean Change)	Sham (Mean Change)
Month 1	-0.4	0.4
Month 3	-0.4	0.2
Month 6	-0.4	0.2
Month 12	-1.7	0.6


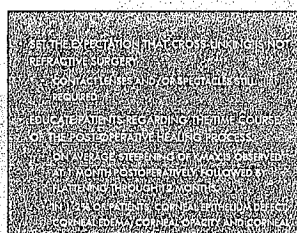
ACCELERATED CXL

- ACCELERATED CXL BASED ON THE BUNSEN-ROSCOE LAW: RATE OF THE PHOTOCHEMICAL AND PHOTOBIOLOGICAL REACTION IS DIRECTLY PROPORTIONAL TO THE TOTAL DOSE OF RADIATION ENERGY.
- DRESDEN PROTOCOL 3MW/CM² FOR 30 MINUTES, TOTAL UVA ENERGY DELIVERED TO THE CORNEAL IS 5.4 J/CM²
- AVEDRO SPONSORED ACCELERATED CXL TRIAL FOR FDA SUBMISSION USING 30MW/CM² FOR 4 MINUTES (2012-2014)
- AECOS (AMERICAN-EUROPEAN CONGRESS OF OPHTHALMIC SURGERY) SPONSORED ACCELERATED CXL STUDY USING AVEDRO'S RIBOFLAVIN AND KXL SYSTEM (2012-2015)
 - THREE DOSES OF IRRADIATION TESTED:
 - 15 MW/CM² FOR 8 MINUTES
 - 30 MW/CM² FOR 4 MINUTES
 - 45 MW/CM² FOR 2 MINUTES AND 40 SECONDS
 - ONE STUDY USING 6 MW/CM² UVA FOR 1.5 MINUTES, SHOWED INCREASED RATE OF SUBEPITHELIAL CORNEAL PLATE 25% AT 2 YEARS, PERFORMED IN POLAND!

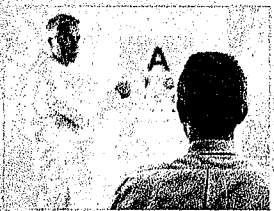
COST EFFECTIVENESS OF CXL

- CORNEAL CROSS-LINKING FOR PROGRESSIVE KCN IS CURRENTLY NOT COVERED BY INSURANCE
- CASH PAY FOR TREATMENT, CARE CREDIT AVAILABLE
- PROGRESSIVE KCN AFFECTS PATIENTS EARLY TEENS THROUGH 40 YEARS OLD (MOST ACTIVE AND PRODUCTIVE YEARS)
- SIGNIFICANT VISUAL MORBIDITY
- HALTING DISEASE PROGRESSION MAY ELIMINATE THE NEED FOR A CORNEAL TRANSPLANT

PRE-OPERATIVE PATIENT EDUCATION

POST-OPERATIVE MANAGEMENT



- Wound Care
- Post-operative treatment similar to cataract surgery
- Extended follow-up
- Care of epithelial debridement
- Bandage contact lens
- Patient education
- Initial recheck 1-2 weeks
- Gradual flattening
- May have persistent haze up to 1 year
- Contact Lens Refitting

CLINICAL EFFECT OF CXL

- CROSS-LINKING IS SUCCESSFUL IN STOPPING THE DISEASE FROM PROGRESSING IN CLOSE TO 98 PERCENT OF PATIENTS
- 70% MEAN KERATOMETRY REGRESSION OF 2 D AT THE CORNEAL PLANE AND A REGRESSION OF 1.14 D OF THE MANIFEST SPHERICAL EQUIVALENT REFRACTIVE ERROR
- VISUAL ACUITY IMPROVED SLIGHTLY IN 65% OF THE EYES
- CXL EFFECT CAN CONTINUE TO EVOLVE OVER TIME

Wolbarsht G, Spindt E, Saha T. Efficacy of corneal crosslinking for the treatment of keratoconus. Am J Ophthalmol. 2013; 154:254-17

SUMMARY

- CORNEAL CROSS-LINKING IS A SAFE AND EFFECTIVE TREATMENT FOR PROGRESSIVE KERATOCONUS
- GOAL IS TO HALT PROGRESSION, STRENGTHEN CORNEA, AND AVOID NEED FOR CORNEAL TRANSPLANT, NOT REFRACTIVE PROCEDURE!
- COMMON COMPLICATIONS INCLUDE DELAYED EPITHELIAL HEALING AND PERSISTENT SUBEPITHELIAL/STROMAL HAZE THAT TAKE UP TO 12 MONTHS TO RESOLVE
- PATIENTS NEED HARD CONTACT LENS REFITTING AFTER CXL

THANK YOU!

QUESTIONS?
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Education:

- 2005 B.S. in Molecular, Cellular, Developmental Biology
Yale College, New Haven, Connecticut
- 2009 M.D.
Yale University School of Medicine, New Haven, Connecticut

Postdoctoral Training:

- 2009-10 Internship in Internal Medicine
Yale New Haven Hospital, New Haven, Connecticut
- 2010-13 Residency in Ophthalmology
Doheny Eye Institute/LAC-USC Medical Center, Los Angeles, California
- 2013-14 Clinical Fellowship in Cornea and External Disease
Doheny Eye Institute/University of Southern California, Los Angeles, California

Board Certification:

- 2014 Diplomate, American Board of Ophthalmology

Medical Licensure:

- 2011 California
- 2014 Oklahoma

Academic Appointments:

- 2014- 16 Clinical Assistant Professor in Cornea and External Disease and Refractive
Dean McGee Eye Institute, University of Oklahoma Health Sciences Center,
Oklahoma City, Oklahoma
- 2013-14 Clinical Instructor in Ophthalmology
Keck Medical Center at University of Southern California, Los Angeles,
California

Private Practice:

- 2016-Present Coastal Vision Medical

Teaching Experience:

- Teaching medical students, residents, and fellows in the eye clinic and operating room
- Presenting lectures on cornea and external disease to ophthalmology residents

Mentoring Experience:

- Mentoring multiple medical students and residents in clinical research project design and manuscript preparation resulting in publications and conference presentations
- Participating faculty mentor for American Medical Women's Association at University of Oklahoma- role model for female medical students and undergraduate pre-medical students

Honors and Awards:

- 2005 Edgar Boell Prize, Yale College
Awarded best senior thesis in the Health Sciences
- 2009 Farr Research Scholar, Yale University School of Medicine
Awarded honors medical thesis
- 2012 ARVO National Eye Institute Travel Grant, National Eye Institute
Awarded grant for outstanding research abstract
- 2012 Henry & Lilian Nesburn Award, Henry & Lilian Nesburn Foundation
Awarded best resident research manuscript
- 2013 Doheny Resident Research Award, Doheny Eye Institute
Awarded exceptional ARVO presentation

Peer Reviewed Publications:

Articles

1. Mckay T, Hjortdal J, Sejersen J, Asara J, **Wu JL** and Karamichos D. Endocrine and Inflammatory Factors in Keratoconus: Role of Hormones in the Stromal Microenvironment. *EMBO reports*. Accepted for publication April 2016.
2. Royer D, Gurung H, Jinkins J, Geltz J, **Wu JL**, Halford W, and Carr DJ. A Highly Efficacious HSV-1 Vaccine Blocks Viral Pathogenesis and Prevents Corneal Immunopathology Via Humoral. *Journal of Virology*. Accepted for publication March 2016.
3. **Lee JC**, Wang MY, Damodar D, Sadun AA, Satta SR. Headache and whiteout vision as the presenting symptoms in a case of Takayasu Retinopathy. *Retinal Cases & Brief Reports*. 2014; 8(4):273-275.
4. **Lee JC**, Chiu G, Bach D, Irvine J, Heur JM. Functional and visual improvement of the Prosthetic Replacement of the Ocular Surface Ecosystem (PROSE) for irregular astigmatism. *Cornea*. 2013; 32(12):1540-1543.
5. **Lee JC**, Wong B, Srinivas S, Satta SR, Huang D, Fawzi, AA. Doppler Fourier-domain optical coherence tomography measurement of the effect of panretinal photocoagulation on retinal blood flow in poorly controlled diabetic proliferative diabetic retinopathy. *Invest Ophthalmol Vis Sci*. 2013; 54(9):6104-6111.

6. Khine, K, Lee, JC, Hwang, J, Francis, BA, Boyer, DS. Methyl-Sulfonyl-Methane (MSM)-Induced Acute Angle Closure. *Journal of Glaucoma*. 2013; November 14. (Epub ahead of print)
7. Lee JC and Shields MB. Horizontal Deviation of Retinal Nerve Fiber Layer Peak Thickness with Stratus Optical Coherence Tomography in Glaucoma Patients and Glaucoma Suspects. *Journal of Glaucoma*. 2010; 19:299-303.
8. Lee JC, Prado HS, Diniz JB, Miguel EC, Leckman JF, Rosario MC. Perfectionism and Sensory Phenomena: Possible Phenotypic Components of Obsessive-Compulsive Disorder. *Comprehensive Psychiatry*. 2009; 50:431-436.
9. Lee JC and Salchow DJ. Myelinated retinal nerve fibers associated with hyperopia and amblyopia. *Journal of AAPOS*. 2008; 12: 418-419.
10. Prado HS, Rosario MC, Lee JC, Hounie AG, Shavitt RG, Miguel EC. Sensory Phenomena in Obsessive-Compulsive Disorder and Tic Disorders: a review of the literature. *CNS Spectrums*. 2008; 13: 425-432.

Presentations:

1. ARVO 2016, Seattle, Washington
2. ARVO 2013, Fort Lauderdale, Florida
3. ARVO 2012, Fort Lauderdale, Florida
4. Yale Medical School Student Research Day 2009, New Haven, Connecticut

Professional Memberships:

American Academy of Ophthalmology (AAO)
Association for Research in Vision and Ophthalmology (ARVO)
Cornea Society
American Society of Cataract and Refractive Surgery (ASCRS)
Oklahoma Academy of Ophthalmology (OAO)

Languages:

- Fluent in Spanish (Spoken)
- Fluent in Chinese (Mandarin) (Spoken)

Community Service:

Volunteer Alumni Interviewer for Yale College Admissions