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: Taste of the Islands: Crosslinking for Corneal Ectasia

Provider Name: Coastal Vision Medical Group c/o Ms. Gina Valdemar

☑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

CALIFORNIA STATE BOARD OF OPTOMETRY

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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.

Course Title "Taste of the Islands CE" Crosslinking for Corneal Ectasia	**Course Presentation Date** 9am - 4:30pm 04/30/2017

Course Provider Contact Information

Provider Name Coastal Vision Medical Group

Gina (First) Valdemar (Last) _____ (Middle)

Provider Mailing Address

Street 323 S. Main St. #100 **City** Orange **State** CA **Zip** 92868

Provider Email Address ginavaldemar@coastal-vision.com

Will the proposed course be open to all California licensed optometrists?	☒ YES ☐ NO
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?	☒ YES ☐ NO

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

Jennifer (First) Wu (Last) Lee (Middle)

License Number 117309	**License Type** MD
Phone Number (714) 746-9679	**Email Address** ginavaldemar@coastal-vision.com

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.

_____ 3-30-17

Signature of Course Provider ***Date***

COASTALVISION
Technique. Technology. Trust.

March 23, 2017

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

RE: Late submission of CE course approval-Taste of the Islands 8 Hour CE-April 30, 2017: Five Retinal Diagnoses You Don't Want to Miss; Cataract Surgery in Patients with Corneal Pathology; Buried Treasure: Connecting the Dots to Treating Binocular Misalignment; Patient-reported Outcomes with Lasik: Interpreting the PROWL study; What We Know about Topography Guided Refractive Surgery: Case Studies in Clinical Practice; Do You See What I See?; Crosslinking for Corneal Ectasia: The Evolution of Sclera Lenses; Blink and You'll Miss It: Dry Eye in the Cosmetic Patient; Is the Symfony Toric Lens the Answer for Every Eye Condition; Should My Glaucoma Patient with a Cataract have a MIGS Surgery; Vitreous: Friend or Foe; Is it Cancer? The Optometrist Role in the Diagnosis and Management of Periocular Skin Cancer; Oral Presentations of Systemic Disease: Case Presentations; Glaucoma Management: What Should I do Next?

Dear Practice and Education committee,

I am writing this letter in regards to late submission for the multi-course symposium titled "Taste of the Islands CE" scheduled for presentation on 04/30/2017. We are short 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 appreciation 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

Schedule of Events:

7:00 am-7:50 am	Registration & Breakfast	
7:50 am-8:00 am	Dan B. Tran, MD	Welcome & Opening Remarks
8:00 am-8:25 am	Timothy You, MD	5 Retinal Diagnoses You Don't Want to Miss
8:25 am-8:50 am	Jennifer Lee Wu, MD	Cataract Surgery in Patients with Corneal Pathology
8:50 am-9:15 am	Gary Lovcik, OD	Buried Treasure: Connecting the Dots to Treating Binocular Misalignment
9:15 am-9:40 am	Elizabeth Hofmeister, MD, MC, USN	Patient-reported Outcomes with LASIK: Interpreting the PROWL Study
9:40 am-10:05 am	Dan B. Tran, MD	What We Know about Topography Guided Refractive Surgery: Case Studies in Clinical Practice
10:05 am-10:30 am	Madhu Agarwal, MD	Do You See What I See?
10:30 am-11:00 am	Break	
11:00 am-11:50 am	Jennifer Lee Wu, MD	Crosslinking for Corneal Ectasia
11:50 am-12:15 pm	Justin Kwan, OD, FAAO	The Evolution of Sclera Lenses
12:15 pm-12:40 pm	Jeffrey Joseph, MD	Blink and You'll Miss It: Dry Eye in the Cosmetic Patient
12:40 pm-1:50 pm	Lunch/Luau	
1:50 pm-2:15 pm	Dan B. Tran, MD	Is the Symfony Toric Lens the Answer for Every Eye Condition?
2:15 pm-2:40 pm	Betsy Nguyen, MD	Should My Glaucoma Patient with a Cataract have a MIGS Surgery?
2:40 pm-3:05 pm	Raj Rathod, MD, MBA	Vitreous: Friend or Foe
3:10 pm-3:35 pm	Jeffrey Joseph, MD	Is it Cancer? The Optometrist's Role in the Diagnosis and Management of Periocular Skin Cancer
3:35pm-3:40 pm	Lisa D. Garbutt, MD	Ocular Presentations of Systemic Disease: Case Presentations
4:00 pm-4:25 pm	Betsy Nguyen, MD	Glaucoma Management: What Should I Do Next?
4:25 pm-4:30 pm	Closing Remarks/Raffle	

*At time of print, pending CA Board of Optometry approval. Topics and speakers are subject to change.

COASTALVISION
Medical Group Inc.

Taste of the Islands 8 hour CE
(7 of 15 lectures) 50 minutes

Course Title: Crosslinking for Corneal Ectasia

Course Presentation date: 4/30/17

Speaker: Jennifer Lee Wu, MD

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

Course Description: This lecture provides the attendee with the clinical presentation and diagnosis of Keratoconus. It discusses recently approved crosslinking with Avdero and FDA data. It also explores new treatment options for moderate to severe Keratoconus patients, cornea ectasias and advanced cornea transplant options.

CE Credit: 1 CE Unit

1 **CORNEAL CROSS-LINKING FOR CORNEA ECTASIA**

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

2 **OBJECTIVES**

- UNDERSTAND THE CLINICAL PRESENTATION AND DIAGNOSIS OF KERATOCONUS (KCN)
- REVIEW THE DEFINITION FOR CORNEA ECTASIA
- LEARN HOW CORNEAL CROSS LINKING (CXL) WORKS AND REVIEW THE SCIENTIFIC DATA
- LEARN HOW CORNEAL CROSS LINKING TREATMENT APPLIES TO KERATOCONUS AND POST-REFRACTIVE ECTASIA
- LEARN ABOUT THE AVEDRO CROSS LINKING SYSTEM AND FDA TRIALS
- LEARN ABOUT REFRACTIVE TREATMENT OPTIONS IN COMBINATION WITH CORNEAL CROSS LINKING FOR CORNEA ECTASIAS
-
-

3 **LAYERS OF THE CORNEA**

4 **CORNEA ECTASIA**

- DEFINITION- THINNING OF THE CORNEA COUPLED WITH STEEPENING (CENTRAL, PARACENTRAL, PERIPHERAL, DIFFUSE)
  - KERATOCONUS
  - PELLUCID MARGINAL DEGENERATION
  - POST-LASIK (REFRACTIVE) ECTASIA
  - TERRIEN'S MARGINAL DEGENERATION
  - KERATOGLOBUS

5 **BACKGROUND- KERATOCONUS**

- DISORDER OF PROGRESSIVE THINNING AND BULGING OF CENTRAL/PARACENTRAL STROMA RESULTING IN CONE SHAPE
- PREVALENCE ~1 IN 2000 (0.05%) UP TO 1 IN 500 (0.2%)
- USUALLY BILATERAL, BUT CAN BE ASYMMETRICAL
- DISEASE STARTS IN PUBERTY (EARLY TEENS) WITH PROGRESSION TO MID-30S
- VISUAL MORBIDITY FROM IRREGULAR ASTIGMATISM, HIGH MYOPIA, CORNEAL SCARRING

6 **HISTOPATHOLOGY**

- HISTOPATHOLOGY SHOWS
  - FRAGMENTATION OR BREAKS IN BOWMAN LAYER
  - COLLAGEN DISORGANIZATION/THINNING
  - SCARRING
  - FOLDS OR BREAKS IN DESCEMET'S MEMBRANE
  -
-

7 **PATHOPHYSIOLOGY- WHAT CAUSE KCN?**

1 • GENETIC
- PREDOMINANTLY AUTOSOMAL DOMINANT INHERITANCE
- FOUND IN ALL ETHNICITIES, MORE FREQUENTLY IN SOUTH ASIANS
- SEVERAL GENE LOCI ASSOCIATED WITH KCN (VARIANTS OF LYSYL OXIDASE)

• ENVIRONMENT
- STRONG ASSOCIATION WITH EYE RUBBING AND ATOPY
- LINKED TO SUN EXPOSURE AND GEOGRAPHY- OXIDATIVE STRESS WEAKENS CORNEA STRUCTURE
- LOCAL RELEASE OF PROTEOLYTIC ENZYMES THAT DEGRADE STROMAL COLLAGEN TO THIN THE CORNEA

8 **PATHOPHYSIOLOGY- EVOLVING UNDERSTANDING**

• CELLULAR- INFLAMMATORY COMPONENT
- OVER EXPRESSION OF PRO-INFLAMMATORY CYTOKINES AND INTERLEUKINS FOUND IN TEARS AND CORNEA OF KCN PATIENTS
- DIABETES OR HIGH GLUCOSE IS PROTECTIVE AGAINST CORNEA ECTASIA

• INTERPLAY BETWEEN ENVIRONMENT AND GENETIC (HORMONE LEVELS PLAY A ROLE)
- 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.

9 **HOW TO DIAGNOSE KERATOCONUS?**

• 1) CLASSIC CLINICAL SIGNS- CORNEAL THINNING
• 2) TOPOGRAPHY
• 3)RAPIDLY CHANGING REFRACTION

10 **KCN DISEASE STAGING**

11 **CLASSIC CLINICAL SIGNS**

12

1 KERATOCONUS
2 PELLUCID MARGINAL DEGENERATION
3 • CLASSIC "CRAB-CLAW" APPEARANCE ON TOPOGRAPHY
• K_{MAX} INFERIOR TO CORNEAL APEX
• THINNEST PACHYMETRY POINT IS INFERIOR TO K_{MAX}
•
4 • INFERIOR STEEPENING ON TOPOGRAPHY
• K_{MAX} CLOSE TO CORNEAL APEX, USUALLY SLIGHTLY INFERIOR-TEMPORAL
• THINNEST PACHYMETRY POINT CORRESPONDS TO K_{MAX}
•

13

1 KERATOCONUS
2 PELLUCID MARGINAL DEGENERATION

14 **RISK FACTORS FOR POST-LASIK ECTASIA**

- EVIDENCE OF FORM FRUSTE KERATOCONUS ON TOPOGRAPHY (ASYMMETRY BETWEEN SUPERIOR AND INFERIOR TOPOGRAPHY)
- ASYMMETRY IN ASTIGMATISM
- LOW RESIDUAL STROMAL BED (<250UM)/LOW PRE-OPERATIVE CORNEAL THICKNESS
- MULTIPLE ENHANCEMENTS
- HIGH MYOPIA (> 8 DIOPTERS PREOPERATIVELY)/HIGH CYLINDER CORRECTION
- YOUNG PATIENT AGE (< 24 YEARS AT TIME OF TREATMENT)
- THE ECTASIA RISK SCORE SYSTEM DESIGNED BY RANDLEMAN
-

15 **POST-REFRACTIVE SURGERY ECTASIA**

- FEARED COMPLICATION OF LASER REFRACTIVE SURGERY
- POST-LASIK, POST-PRK, POST-RK
- DEFINITION- CHANGE IN VISION OR REFRACTION AFTER LASER REFRACTIVE SURGERY
  - INCREASING MYOPIA, WITH OR WITHOUT INCREASING ASTIGMATISM
  - LOSS OF UNCORRECTED VISUAL ACUITY
  - KERATOMETRIC STEEPENING
  - TOPOGRAPHIC EVIDENCE OF ASYMMETRIC INFERIOR CORNEAL STEEPENING
- THE INCIDENCE RATE OF 0.04% TO 0.6% FOR LASIK HAS BEEN REPORTED WITH OLDER SCREENING TECHNOLOGY

16

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

17 **DISEASE STAGING**

18

19 **STANDARD TREATMENTS FOR ECTASIA**

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

20 **SCLERAL LENS**

- VAULTS THE ENTIRE CORNEA AND RESTS ON THE SCLERA

- BATHES THE ENTIRE CORNEAL SURFACE IN FLUID
-
-
-

21 **CORNEAL SCARRING IN KCN**

1 APICAL SCARRING
2 HYDROPS

22 **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[1]
- CROSS-LINKING[2]:
  - 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

23 **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
- POST-LASIK ECTASIA, DO NOT NEED TO SHOW PROGRESSION
- GOAL IS TO HALT PROGRESSION, STRENGTHEN CORNEA, AND AVOID NEED FOR CORNEAL TRANSPLANT, NOT REFRACTIVE PROCEDURE!
- VISION IS ACCEPTABLE WITH GLASSES OR CONTACT CORRECTION
-

24 **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

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

BASED ON DRESDEN PROTOCOL[1]:

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

26 **COMPLICATIONS- WHAT CAN GO WRONG?**

- PERSISTENT SUBEPITHELIAL/STROMAL HAZE- MAKE TAKE UP TO 12 MONTHS TO RESOLVE
  - APPROXIMATELY 4.5% IN 6-MONTH FOLLOW-UP[1]
- PERSISTENT EPITHELIAL DEFECT
- CORNEA ULCER
- FEW PATIENTS SHOW PROGRESSION AFTER CXL (2 OF 33 EYES), FOUND IN ADVANCED KCN K_{MAX} >60[2]
-

27 **TRANSEPITHELIAL CXL FOR PROGRESSIVE KCN**

- TRANSEPITHELIAL CXL- THE DIFFUSION OF RIBOFLAVIN INTO THE STROMA IS LIMITED BY CORNEAL EPITHELIAL TIGHT JUNCTIONS
  - USE BENZALKONIUM CHLORIDE (BAK) TO ENHANCE STROMAL PENETRATION
  - IONTOPHORESIS- USES A SMALL ELECTRIC CURRENT TO ENHANCE THE DELIVERY OF RIBOFLAVIN WHICH IS NEGATIVELY CHARGED
- STUDY 1 (2016)- USING BAK ENHANCED RIBOFLAVIN, 26 PATIENTS
  - PROGRESSION (DEFINED BY AN INCREASE IN KMAX GREATER THAN 1.00 DIOPTER OCCURRED IN 46% OF EYES AT 12 MONTHS.
  - CORNEAL EPITHELIAL DEFECTS WERE OBSERVED IN 46% OF THE PATIENTS

28 **TRANSEPITHELIAL VERSUS EPITHELIUM-OFF CXL**

1 EPITHELIUM-OFF-CXL
2 TRANSEPITHELIAL-CXL (BAK+TETRACAINE)
3 • KMAX DECREASED BY MEAN 2.4D
  • PROGRESSION RATE 0%
4 • KMAX INCREASED BY MEAN 1.1D
  • PROGRESSION RATE 55%

29 **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/CM^2 FOR 30 MINUTES, TOTAL UVA ENERGY DELIVERED TO THE CORNEAL IS 5.4 J/CM^2
- AVEDRO SPONSORED ACCELERATED CXL TRIAL FOR FDA SUBMISSION USING 30MV/CM^2 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/CM^2 FOR 8 MINUTES

- 30 MW/CM^2 FOR 4 MINUTES
- 45 MW/CM^2 FOR 2 MINUTES AND 40 SECONDS

- ONE STUDY USING 6 MW/CM^2 UVA FOR 15 MINUTES, SHOWED INCREASED RATE OF SUBEPITHELIAL CORNEAL HAZE 25% AT 2 YEARS, PERFORMED IN POLAND.[1]

30 **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

31 **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

32 **PHASE III STUDY DESIGN**

- THE TRIALS INCLUDED
  - 205 PATIENTS WITH PROGRESSIVE KERATOCONUS.
  - 179 PATIENTS WITH CORNEAL ECTASIA FOLLOWING REFRACTIVE SURGERY.
- 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
- NO SUBJECTS ENROLLED IN THE CLINICAL STUDIES WERE 65 YEARS OF AGE OR OLDER
-
-

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

34 **COST EFFECTIVENESS OF CXL**

- CORNEAL CROSS-LINKING FOR PROGRESSIVE KCN AND POST-LASIK ECTASIA 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

35

36 **CXL FOR DIURNAL FLUCTUATION AFTER RK**

- 9 EYES IN 6 PATIENTS WITH UP TO 12 MONTHS FOLLOW-UP
- RESULTS:
  - 8/9 EYE HAD DISCONTINUATION OF DIURNAL VISUAL FLUCTUATIONS BETWEEN 6 AND 12 MONTHS AFTER CXL
  - MEAN K PRE-OPERATIVE AND 12 MONTHS WAS 40.1 AND 39.1 DIOPTERS
- CONCLUSIONS: PROCEDURE IS SAFE, SOME OF THE EFFECTS WERE BLUNTED AT 12 MONTHS

37 **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
  -
  -
  -
-

38 **POST-OPERATIVE MANAGEMENT**

39 **RISK FACTORS FOR DELAYED EPITHELIAL HEALING**

- VERY STEEP CORNEA >KMAX 56, BANDAGE CONTACT LENS RUBS THE APEX AND PREVENTS EPITHELIZATION
- PATIENTS WITH SEVERE DRY EYE
- POOR MEDICATION COMPLIANCE

40

41

42

43 **MORE DATA NEEDED**

3/2013

- K READINGS:
  RT: 43.25@004/45.25 @94
  LT:43.50@170/46.00@80
- MRX:
  RT: +0.25 -1.00 X 005 DVA 20/25
  LT: +0.25 -1.50X 163 DVA 20/25
-
-

-

44 **DISEASE STAGING**

45 **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

46 **AVEDRO CXL DRESDEN PROTOCOL RESULT**

1. BASELINE (KMAX 47.4)
2. POM 2.5 (KMAX 46.1)

47 **AVEDRO CXL RESULT**

1. PRE-OPERATIVE AS-OCT
2. POM 2.5 AS-OCT

48 **SUMMARY**

- CORNEAL CROSS-LINKING IS A SAFE AND EFFECTIVE TREATMENT FOR PROGRESSIVE KERATOCONUS ANS POST-LASIK ECTASIA
- GOAL IS TO HALT PROGRESSION, STRENGTHEN CORNEA, AND AVOID NEED FOR CORNEAL TRANSPLANT, NOT REFRACTIVE PROCEDURE!
- THIS IS A MEDICALLY NECESSARY PROCEDURE, BUT NOT CURRENTLY COVERED BY INSURANCE
- PATIENTS NEED HARD CONTACT LENS REFITTING AFTER CXL
-
-
-
-

49 **THANK YOU!**

QUESTIONS?

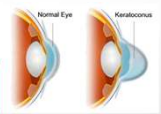
JENNYWU@COASTAL-VISION.COM

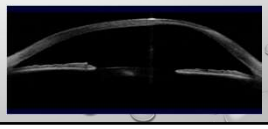
CORNEAL CROSS-LINKING FOR CORNEA ECTASIA

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

CORNEA ECTASIA

- DEFINITION- THINNING OF THE CORNEA COUPLED WITH STEEPENING (CENTRAL, PARACENTRAL, PERIPHERAL, DIFFUSE)
  - KERATOCONUS
  - PELLUCID MARGINAL DEGENERATION
  - POST-LASIK (REFRACTIVE) ECTASIA
  - TERRIEN'S MARGINAL DEGENERATION
  - KERATOGLOBUS

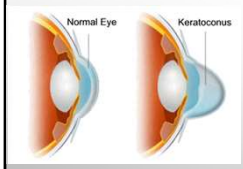




OBJECTIVES

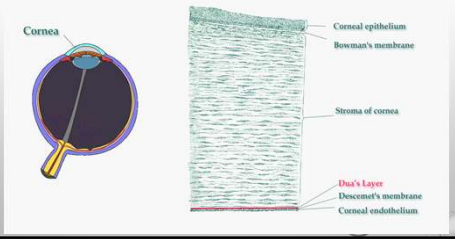
- UNDERSTAND THE CLINICAL PRESENTATION AND DIAGNOSIS OF KERATOCONUS (KCN)
- REVIEW THE DEFINITION FOR CORNEA ECTASIA
- LEARN HOW CORNEAL CROSS LINKING (CXL) WORKS AND REVIEW THE SCIENTIFIC DATA
- LEARN HOW CORNEAL CROSS LINKING TREATMENT APPLIES TO KERATOCONUS AND POST-REFRACTIVE ECTASIA
- LEARN ABOUT THE AVEDRO CROSS LINKING SYSTEM AND FDA TRIALS
- LEARN ABOUT REFRACTIVE TREATMENT OPTIONS IN COMBINATION WITH CORNEAL CROSS LINKING FOR CORNEA ECTASIAS

BACKGROUND- KERATOCONUS



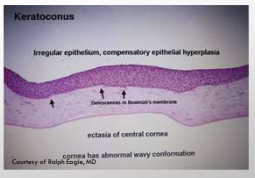
- DISORDER OF PROGRESSIVE THINNING AND BULGING OF CENTRAL/PARACENTRAL STROMA RESULTING IN CONE SHAPE
- PREVALENCE ~1 IN 2000 (0.05%) UP TO 1 IN 500 (0.2%)
- USUALLY BILATERAL, BUT CAN BE ASYMMETRICAL
- DISEASE STARTS IN PUBERTY (EARLY TEENS) WITH PROGRESSION TO MID-30S
- VISUAL MORBIDITY FROM IRREGULAR ASTIGMATISM, HIGH MYOPIA, CORNEAL SCARRING

LAYERS OF THE CORNEA



HISTOPATHOLOGY

- HISTOPATHOLOGY SHOWS
  - FRAGMENTATION OR BREAKS IN BOWMAN LAYER
  - COLLAGEN DISORGANIZATION/THINNING
  - SCARRING
  - FOLDS OR BREAKS IN DESCEMET'S MEMBRANE



PATHOPHYSIOLOGY- WHAT CAUSE KCN?

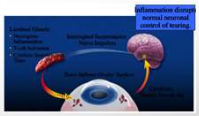
- GENETIC
  - PREDOMINANTLY AUTOSOMAL DOMINANT INHERITANCE
  - FOUND IN ALL ETHNICITIES, MORE FREQUENTLY IN SOUTH ASIANS
  - SEVERAL GENE LOCI ASSOCIATED WITH KCN (VARIANTS OF LYSYL OXIDASE)
- ENVIRONMENT
  - STRONG ASSOCIATION WITH EYE RUBBING AND ATOPY
  - LINKED TO SUN EXPOSURE AND GEOGRAPHY- OXIDATIVE STRESS WEAKENS CORNEA STRUCTURE
  - LOCAL RELEASE OF PROTEOLYTIC ENZYMES THAT DEGRADE STROMAL COLLAGEN TO THIN THE CORNEA

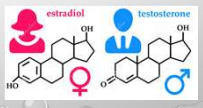
KCN DISEASE STAGING

Stage	Topography	Keratometry	Pachymetry	Clinical Findings
Forme Fruste	Minimal inferior steepening, <5D astigmatism	Kmax <48D	May be normal >500	None
Mild	Inferior steepening apparent, 5-8D of astigmatism	Kmax <53D	>400um	Fleisher Ring, Vogt's Strea
Moderate	8-10D of irregular astigmatism	Kmax <55D	200 to 400um	Fleisher Ring, Vogt's Strea
Severe	>10D astigmatism	Kmax >55D	<200um	Apical scarring or hydrops

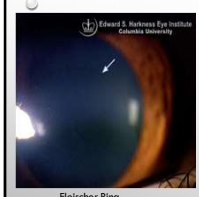
PATHOPHYSIOLOGY- EVOLVING UNDERSTANDING

- CELLULAR- **INFLAMMATORY COMPONENT**
  - OVER EXPRESSION OF PRO-INFLAMMATORY CYTOKINES AND INTERLEUKINS FOUND IN TEARS AND CORNEA OF KCN PATIENTS
  - DIABETES OR HIGH GLUCOSE IS PROTECTIVE AGAINST CORNEA ECTASIA
- INTERPLAY BETWEEN ENVIRONMENT AND GENETIC (HORMONE LEVELS PLAY A ROLE)
  - 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.





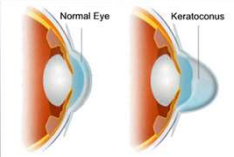
CLASSIC CLINICAL SIGNS



Fleischer Ring

Munson Sign

HOW TO DIAGNOSE KERATOCONUS?



- **1) CLASSIC CLINICAL SIGNS- CORNEAL THINNING**
- **2) TOPOGRAPHY**
- **3)RAPIDLY CHANGING REFRACTION**

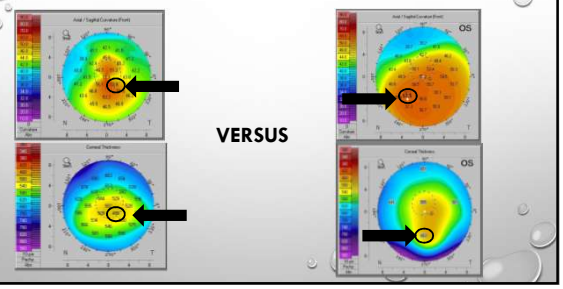
KERATOCONUS VERSUS PELLUCID MARGINAL DEGENERATION

- INFERIOR STEEPENING ON TOPOGRAPHY
- K_{MAX} CLOSE TO CORNEAL APEX, USUALLY SLIGHTLY INFERIOR-TEMPORAL
- THINNEST PACHYMETRY POINT CORRESPONDS TO K_{MAX}

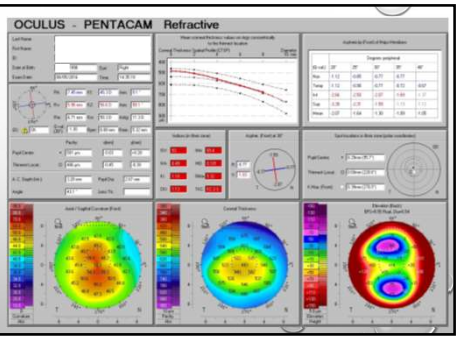
- CLASSIC "CRAB-CLAW" APPEARANCE ON TOPOGRAPHY
- K_{MAX} INFERIOR TO CORNEAL APEX
- THINNEST PACHYMETRY POINT IS INFERIOR TO K_{MAX}

KERATOCONUS

PELLUCID MARGINAL DEGENERATION



VERSUS



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

Kmax 55.2, Pachy 490

RISK FACTORS FOR POST-LASIK ECTASIA

- EVIDENCE OF FORM FRUSTE KERATOCONUS ON TOPOGRAPHY (ASYMMETRY BETWEEN SUPERIOR AND INFERIOR TOPOGRAPHY)
- ASYMMETRY IN ASTIGMATISM
- LOW RESIDUAL STROMAL BED (<250UM)/LOW PRE-OPERATIVE CORNEAL THICKNESS
- MULTIPLE ENHANCEMENTS
- HIGH MYOPIA (> 8 DIOPTERS PREOPERATIVELY)/HIGH CYLINDER CORRECTION
- YOUNG PATIENT AGE (< 24 YEARS AT TIME OF TREATMENT)
- THE ECTASIA RISK SCORE SYSTEM DESIGNED BY RANDLEMAN

Randleman et al. Risk factors and prognosis for corneal ectasia after LASIK. Ophthalmology. 2003. 267-275.

DISEASE STAGING

Stage	Topography	Keratometry	Pachymetry	Clinical Findings
Forme Fruste	Minimal inferior steepening, <5D astigmatism	Kmax <48D	May be normal	None
Mild	Inferior steepening apparent, 5-8D of astigmatism	Kmax <53D	>400um	Fleisher Ring, Vogt's Strea
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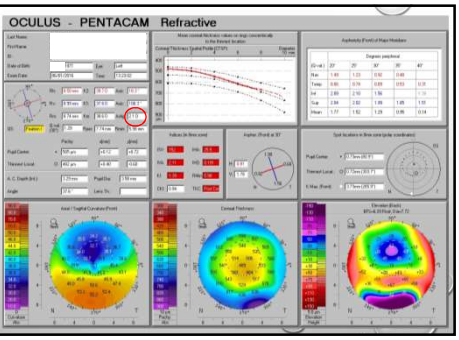
Severe	>10D astigmatism	Kmax >55D	<200um	Apical scarring or hydrops

POST-REFRACTIVE SURGERY ECTASIA

- FEARED COMPLICATION OF LASER REFRACTIVE SURGERY
- POST-LASIK, POST-PRK, POST-RK
- DEFINITION- CHANGE IN VISION OR REFRACTION AFTER LASER REFRACTIVE SURGERY
  - INCREASING MYOPIA, WITH OR WITHOUT INCREASING ASTIGMATISM
  - LOSS OF UNCORRECTED VISUAL ACUITY
  - KERATOMETRIC STEEPENING
  - TOPOGRAPHIC EVIDENCE OF ASYMMETRIC INFERIOR CORNEAL STEEPENING
- THE INCIDENCE RATE OF 0.04% TO 0.6% FOR LASIK HAS BEEN REPORTED WITH OLDER SCREENING TECHNOLOGY



CASE #1

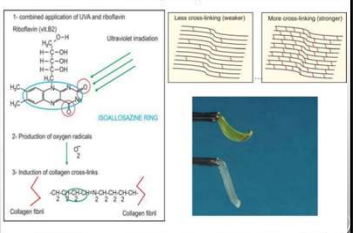
- 45 YO MALE, PROGRESSIVE CHANGE IN VISION OVER LAST 2 YEARS
- S/P MYOPIC LASIK OU 2001
- SERIAL TOPOGRAPHY SHOWS PROGRESSION OVER LAST 6 MONTHS
- VASC 20/50

STANDARD TREATMENTS FOR ECTASIA

- **CORNEAL CROSS-LINKING**
- MEDICAL
  - VISION CORRECTION (GLASSES, RIGID GAS-PERMEABLE OR SCLERAL CONTACT LENS)
- SURGICAL
  - CORNEAL TRANSPLANT FOR CONTACT LENS INTOLERANCE OR CORNEAL SCARRING

CORNEA CROSS-LINKING (CXL)

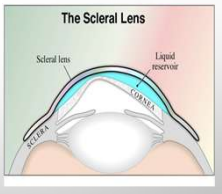
- COMBINES THE USE OF ULTRA-VIOLET (UV) LIGHT AND RIBOFLAVIN (VITAMIN B2) DROPS
- THE ABSORPTION OF UVA BY RIBOFLAVIN GENERATES RADICAL RIBOFLAVIN AND SINGLET OXYGEN TO FORM CROSS-LINKS[1]
- CROSS-LINKING[2]:
  - CREATES NEW CORNEAL COLLAGEN AND GLYCOSAMINOGLYCAN CROSS-LINKS
  - RESULTS IN A SHORTENING AND THICKENING OF THE COLLAGEN FIBRILS
  - LEADS TO THE STIFFENING OF THE CORNEA



[1]Kamaev P, Friedman MD, Sherr E, Muller D. Photochemical kinetics of corneal cross-linking with riboflavin. Invest Ophthalmol Vis Sci. 2012;53:2360–7.
[2]Bestwari IM, O'Donnell C, Radhakrishnan H. Biomechanical properties of corneal tissue after ultraviolet-A-riboflavin cross-linking. J Cataract Refract Surg. 2013;39(3):451–62.

SCLERAL LENS

- VAULTS THE ENTIRE CORNEA AND RESTS ON THE SCLERA
- BATHES THE ENTIRE CORNEAL SURFACE IN FLUID



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.

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
- POST-LASIK ECTASIA, DO NOT NEED TO SHOW PROGRESSION
- GOAL IS TO HALT PROGRESSION, STRENGTHEN CORNEA, AND AVOID NEED FOR CORNEAL TRANSPLANT, NOT REFRACTIVE PROCEDURE!
- VISION IS ACCEPTABLE WITH GLASSES OR CONTACT CORRECTION

CORNEAL SCARRING IN KCN

APICAL SCARRING

HYDROPS

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

CORNEAL CROSS-LINKING (CXL) PROTOCOL

BASED ON DRESDEN PROTOCOL[1]:

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

[1]Wollensak, G. et al. Riboflavin/ultraviolet-a-induced collagen crosslinking for the treatment of keratoconus. American Journal of Ophthalgology. 2003;135:620-627

TRANSEPITHELIAL VERSUS EPITHELIUM-OFF CXL

Study 2 (2015)- 3 year follow-up results for progressive KCN, 34 patients per group

EPITHELIUM-OFF-CXL
- KMAX DECREASED BY MEAN 2.4D
- PROGRESSION RATE 0%

TRANSEPITHELIAL-CXL (BAK+TETRACAINE)
- KMAX INCREASED BY MEAN 1.1D
- PROGRESSION RATE 55%

Fayez et al. Cornea. 2015 Oct;34 Suppl 10:S53-6.

COMPLICATIONS- WHAT CAN GO WRONG?

- PERSISTENT SUBEPITHELIAL/STROMAL HAZE- MAKE TAKE UP TO 12 MONTHS TO RESOLVE
  - APPROXIMATELY 4.5% IN 6-MONTH FOLLOW-UP[1]
- PERSISTENT EPITHELIAL DEFECT
- CORNEA ULCER
- FEW PATIENTS SHOW PROGRESSION AFTER CXL (2 OF 33 EYES), FOUND IN ADVANCED KCN K_{MAX} >60[2]

[1]Caporossi A., Mazzotta C., Baiocchi S., Caporossi T. Long-term results of riboflavin ultraviolet a corneal collagen cross-linking for keratoconus in Italy: the siena eye cross study. *The American Journal of Ophthalmology*. 2010;149(4):585–593.
[2]Scheerch K, Tappeiner C, Frueh BE. Analysis of pseudoprogression after corneal cross-linking in children with progressive keratoconus. Acta Ophthalmol. 2016 Apr 29. (Epub ahead of print)

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/CM^2 FOR 30 MINUTES, TOTAL UVA ENERGY DELIVERED TO THE CORNEAL IS 5.4 J/CM^2
- AVEDRO SPONSORED ACCELERATED CXL TRIAL FOR FDA SUBMISSION USING 30MV/CM^2 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/CM^2 FOR 8 MINUTES
  - 30 MW/CM^2 FOR 4 MINUTES
  - 45 MW/CM^2 FOR 2 MINUTES AND 40 SECONDS
- ONE STUDY USING 6 MW/CM^2 UVA FOR 15 MINUTES, SHOWED INCREASED RATE OF SUBEPITHELIAL CORNEAL HAZE 25% AT 2 YEARS, PERFORMED IN POLAND.[1]

[1]Waszczykowska, A and P Jurowski. Two-Year Accelerated Corneal Cross-Linking Outcome in Patients with Progressive Keratoconus. Biomed Res Int. 2015;2015: 325157.

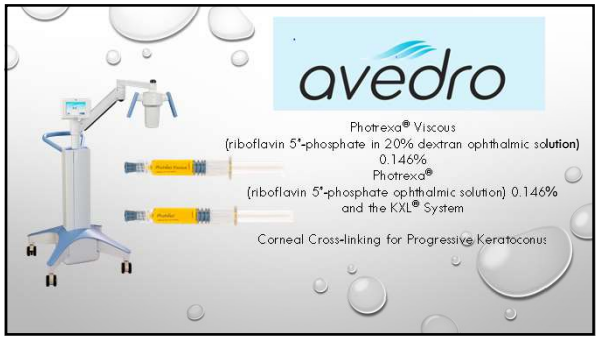
TRANSEPITHELIAL CXL FOR PROGRESSIVE KCN

- TRANSEPITHELIAL CXL- THE DIFFUSION OF RIBOFLAVIN INTO THE STROMA IS LIMITED BY CORNEAL EPITHELIAL TIGHT JUNCTIONS
  - USE BENZALKONIUM CHLORIDE (BAK) TO ENHANCE STROMAL PENETRATION
  - IONTOPHORESIS- USES A SMALL ELECTRIC CURRENT TO ENHANCE THE DELIVERY OF RIBOFLAVIN WHICH IS NEGATIVELY CHARGED
- STUDY 1 (2016)- USING BAK ENHANCED RIBOFLAVIN, 26 PATIENTS
  - PROGRESSION (DEFINED BY AN INCREASE IN KMAX GREATER THAN 1.00 DIOPTER OCCURRED IN 46% OF EYES AT 12 MONTHS.
  - CORNEAL EPITHELIAL DEFECTS WERE OBSERVED IN 46% OF THE PATIENTS

Gatzioufas et al. J Refract Surg. 2016;32:372-377).

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

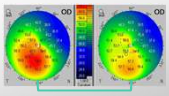


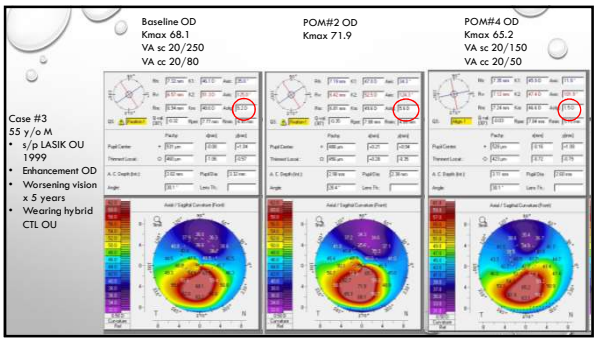
COST EFFECTIVENESS OF CXL

- CORNEAL CROSS-LINKING FOR PROGRESSIVE KCN AND POST-LASIK ECTASIA 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

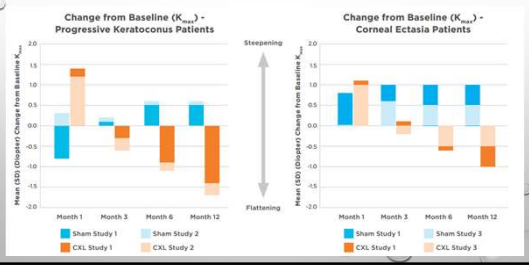
PHASE III STUDY DESIGN

- THE TRIALS INCLUDED
  - 205 PATIENTS WITH PROGRESSIVE KERATOCONUS.
  - 179 PATIENTS WITH CORNEAL ECTASIA FOLLOWING REFRACTIVE SURGERY.
- 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
- NO SUBJECTS ENROLLED IN THE CLINICAL STUDIES WERE 65 YEARS OF AGE OR OLDER





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



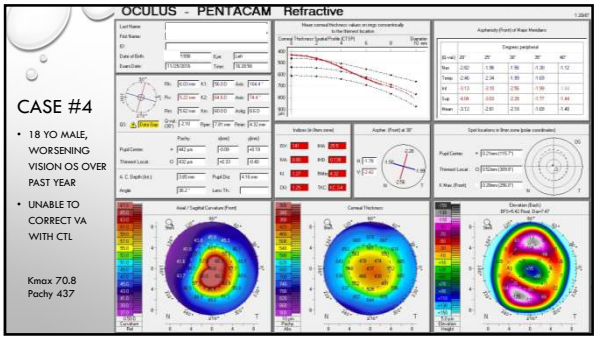
CXL FOR DIURNAL FLUCTUATION AFTER RK

- 9 EYES IN 6 PATIENTS WITH UP TO 12 MONTHS FOLLOW-UP
- RESULTS:
  - 8/9 EYE HAD DISCONTINUATION OF DIURNAL VISUAL FLUCTUATIONS BETWEEN 6 AND 12 MONTHS AFTER CXL
  - MEAN K PRE-OPERATIVE AND 12 MONTHS WAS 40.1 AND 39.1 DIOPTERS
- CONCLUSIONS: PROCEDURE IS SAFE, SOME OF THE EFFECTS WERE BLUNTED AT 12 MONTHS

Elbaz, U et al. Collagen crosslinking after radial keratotomy. Cornea. 2014 Feb;33(2):131-6.

PRE-OPERATIVE PATIENT EDUCATION

- SET THE EXPECTAT ON THAT CROSS L NK NG S NOT REFRACT VE SURGERY
  - CONTACT LENSES AND/OR SPECTACLES ST LL REQU RED
- EDUCATE PAT ENTS REGARD NG THE T ME COURSE OF THE POST OPERATIVE HEAL NG PROCESS.
  - ON AVERAGE STEEPEN NG OF KMAX S OBSERVED AT 1 MONTH POSTOPERAT VELY FOLLOWED BY FLATTEN NG THROUGH 12 MONTHS
  - N 1 2% OF PAT ENTS CORNEAL EP THEL UM DEFECT CORNEAL EDEMA CORNEAL OPAC TY AND CORNEAL SCAR CONT NUED TO BE OBSERVED AT 12 MONTHS



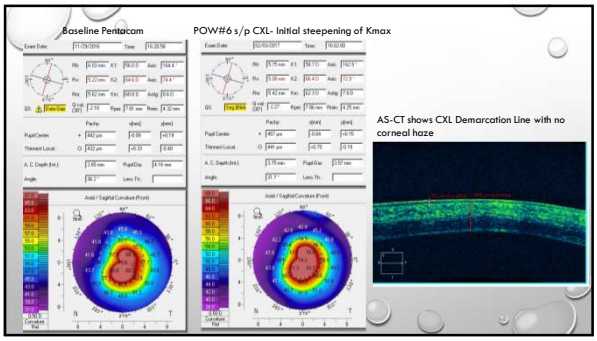
CASE #4

- 18 YO MALE, WORSENING VISION OS OVER PAST YEAR
- UNABLE TO CORRECT VA WITH CTL

Kmax 70.8
Pachy 437

POST-OPERATIVE MANAGEMENT

- Post operative Care
  - Post operative regimen similar to care after PRK, except longer healing time
  - Care of epithelial debridement
  - Bandage contact lens
- Contact Lens Refitting



RISK FACTORS FOR DELAYED EPITHELIAL HEALING

- VERY STEEP CORNEA >KMAX 56, BANDAGE CONTACT LENS RUBS THE APEX AND PREVENTS EPITHELIZATION
- PATIENTS WITH SEVERE DRY EYE
- POOR MEDICATION COMPLIANCE

CASE #5

- 12 YO FEMALE, WORSENING VISION OS OVER PAST YEAR
- CHANGE IN MRX OVER PAST 6 MONTHS

Kmax 47.2
Pachy 494

MORE DATA NEEDED

3/2013
- K READINGS:
  RT: 43.25@004/45.25 @94
  LT:43.50@170/46.00@80
- MRX:
  RT: +0.25 -1.00 X 005 DVA 20/25
  LT: +0.25 -1.50X 163 DVA 20/25

4/2015
K readings:
RT42.75@ 006/46.00@96
LT 43.00 @170/46.50@80

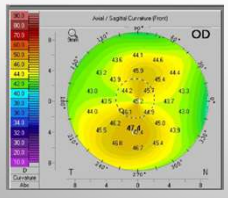
Mrx:
RT: plano -1.25 x 010 DVA 20/25
LT: -0.25 -2.25 x 165 DVA 20/30

12/2016
K readings:
RT 42.75@004/45.25@94
LT 42.50@171/47.25@81

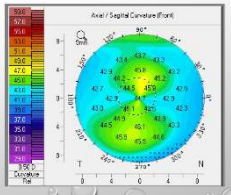
MRx:
RT:-0.75-1.50x13 DVA 20/25
LT: -0.25-3.00x169 DVA 20/30

AVEDRO CXL DRESDEN PROTOCOL RESULT

BASELINE (KMAX 47.4)



POM 2.5 (KMAX 46.1)



DISEASE STAGING

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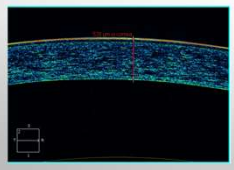
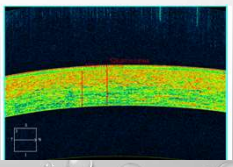
Severe	>10D astigmatism	Kmax >55D	<200um	Apical scarring or hydrops

AVEDRO CXL RESULT

PRE-OPERATIVE AS-OCT



POM 2.5 AS-OCT



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

Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-a-induced collagen cross linking for the treatment of keratoconus. Am J Ophthalmol. 2003;135:620-627.

SUMMARY

- CORNEAL CROSS-LINKING IS A SAFE AND EFFECTIVE TREATMENT FOR PROGRESSIVE KERATOCONUS ANS POST-LASIK ECTASIA
- GOAL IS TO HALT PROGRESSION, STRENGTHEN CORNEA, AND AVOID NEED FOR CORNEAL TRANSPLANT, NOT REFRACTIVE PROCEDURE!
- THIS IS A MEDICALLY NECESSARY PROCEDURE, BUT NOT CURRENTLY COVERED BY INSURANCE
- 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 Diplomat, 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, Sadda 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, Sadda 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