Understanding Corneal Tomography: *A comprehensive course*

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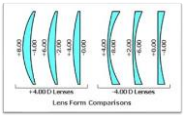
First, we need to understand How Elevation and Curvature Differ

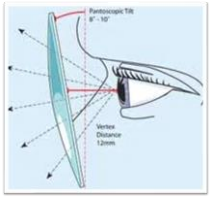
(The principals / examples apply to all tomographic devices (Scheimpflug / OCT)

- Curvature is analogous to measuring spectacle lens power.
  - It may be accurate, but tells you nothing about the shape of the lens

- Curvature is analogous to measuring spectacle lens power.
  - It may be accurate, but tells you nothing about the shape of the lens
    - i.e. multiple spectacle lenses *(different shapes)* can have the same power

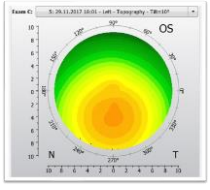


- Curvature & Power will change with orientation
  - Lens tilt and/or measurement axis
  - The same lens (shape) can have multiple powers

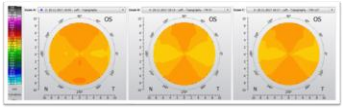


Keratoconus Misconceptions

- Inferior steepening is the hallmark on early ectatic change
  - Inferior steepening, IS values are late signs of disease and poor screening indices
  - Non-specific
    - Commonly seen in Normals

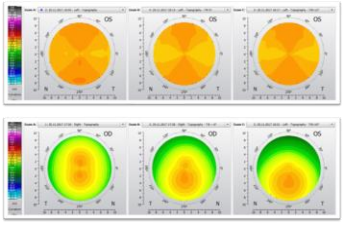


Limitations of Curvature



Astigmatic Test Object

Limitations of Curvature

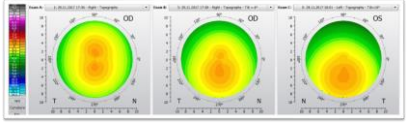


Aspheric Astigmatic Test Object

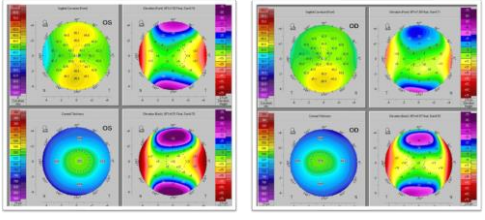
Limitations of Curvature

Human Cornea is Aspheric

This is NOT Keratoconus



Curvature False Positive

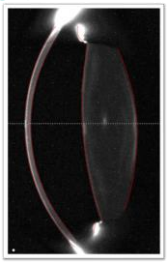


Elevation Data

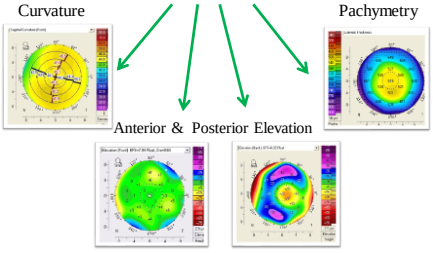
- Elevation represents TRUE shape
  - It is independent of axis, orientation or positioning.
    - *(Within normal limits)*
- All subsequent maps (curvature) can be derived from ACCURATE elevation data
  - Curvature is the second derivative of elevation

Scheimpflug Imaging *(OCT similar)*

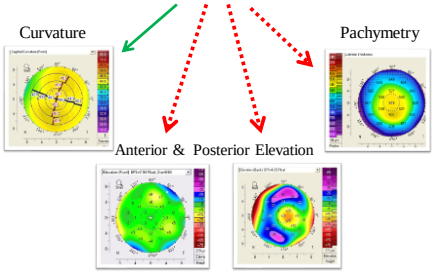
- Scheimpflug Imaging
  - Image edge detection
    - Anterior Cornea
    - Posterior Cornea
    - Anterior Lens
    - Posterior Lens
    - Anterior Iris



Elevation can derive

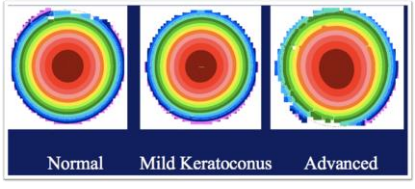


Curvature cannot

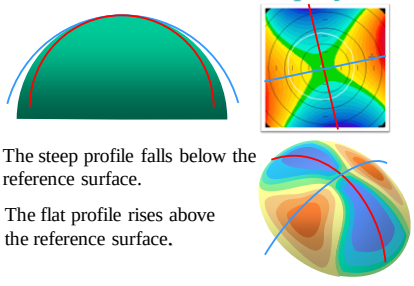


How is Elevation Data Displayed

- "RAW" elevation maps are rarely used

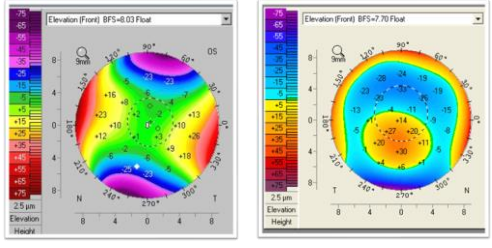


How Elevation is Displayed

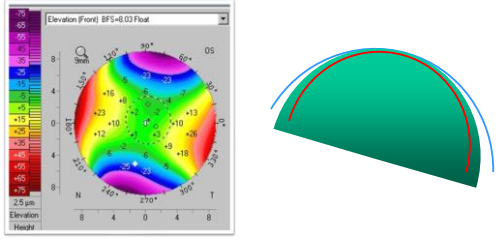


- The steep profile falls below the reference surface.
- The flat profile rises above the reference surface.

Astigmatism vs. Keratoconus

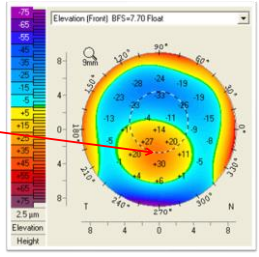


Astigmatism

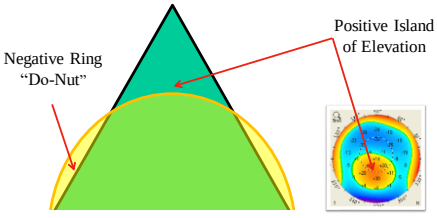


Keratoconus

We look for central or para-central *"Positive Islands of Elevation"*



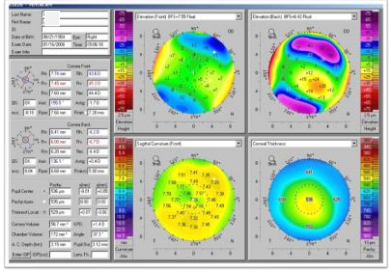
Derivation of Keratoconus Pattern



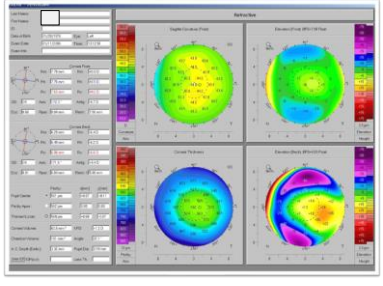
- The most significant advancement in corneal imaging is the change from a reflective system to an optical cross section

- New Imaging Systems (Scheimpflug & OCT) have the ability to look at both Anterior & Posterior Surfaces

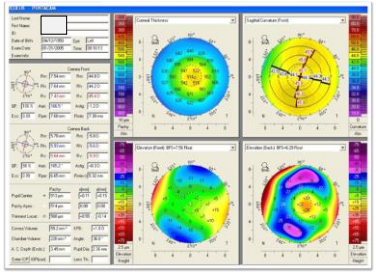
Isolated Abnormal Post Elevation



Normal Curvature

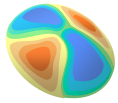


Normal Curvature *(Subclinical KCN)*

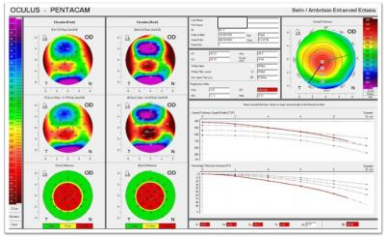


Why use a Best-Fit-Sphere ?

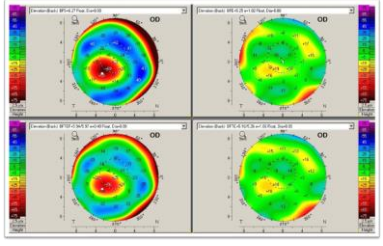
- A BFS (Sphere) conveys the most intuitive ***qualitative*** information about corneal shape
  - The differences are only qualitative as all maps are generated from the same raw elevation data.



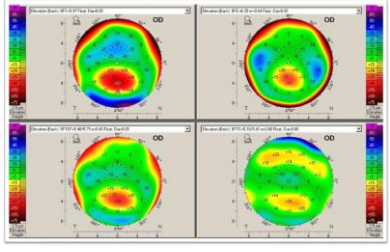
Sphere *vs* Ellipsoid *vs* Toric Ellipsoid Fixed *vs* Toric Ellipsoid



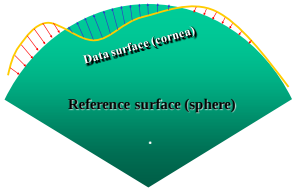
Sphere *vs* Ellipsoid *vs* Toric Ellipsoid Fixed *vs* Toric Ellipsoid



Sphere *vs* Ellipsoid *vs* Toric Ellipsoid Fixed *vs* Toric Ellipsoid

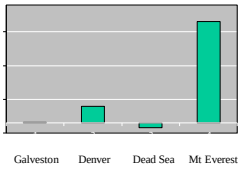


But What is the Best Reference Surface ?



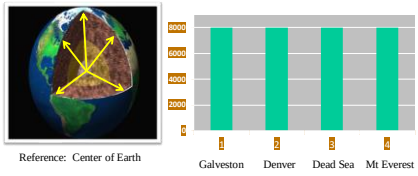
Reference Surface

A standardized REFERENCE SURFACE makes data interpretation easier.



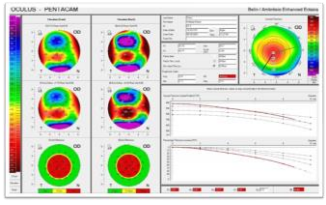
The Data is Identical…

…But the reference surface is not appropriate for qualitative inspection



Reference: Center of Earth

Derivation of the BAD Display



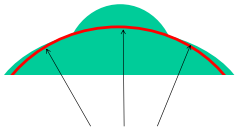
The "Best Fit Shape" below is essentially an average of the high and low elevations of the cornea.

"Average" Best Fit Shape

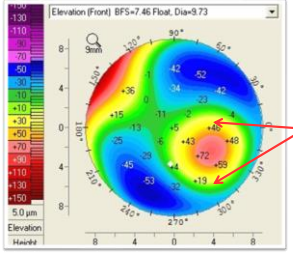
Map of the Earth

Reference Surface *(Sea Level)* is not a Best-Fit-Sphere

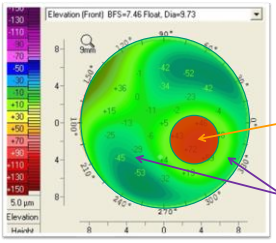
A TRUE "**Best *Reference* Shape**" would better approximate the normal cornea and accentuate the abnormal cone *(i.e., it would mimic "sea level").*



"BEST" Reference Shape



"BEST" Elevation reference shape is calculated using only data outside the cone.



3.0 – 4.0 mm diameter circle *(dynamic)* centered on point with smallest radius of curvature.

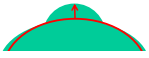
All elevation data within the red circle is excluded.

"BEST" Elevation reference shape (ENHANCED REFERENCE SURFACE) is calculated using only data outside the red circle.

Methods

Keratoconus fit with Best Fit Sphere

vs



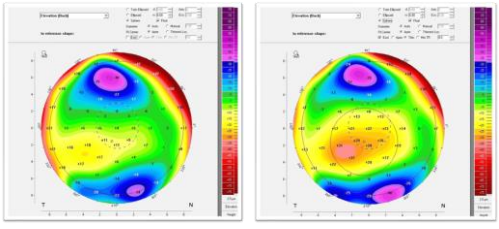
Keratoconus fit with New Reference Shape

Normal fit with Best Fit Sphere

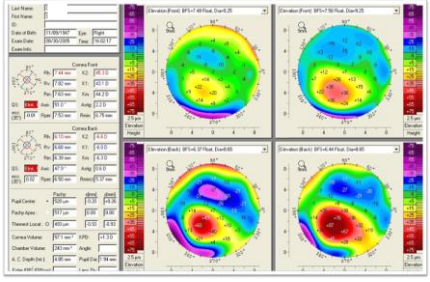
vs

Normal fit with new Reference Shape

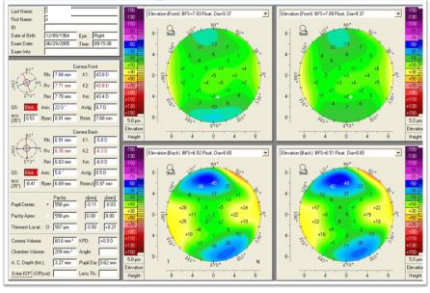
Before & After Exclusion Software



Keratoconus – Before / After



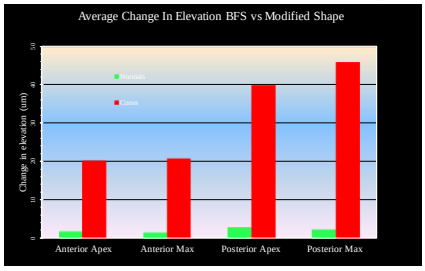
Normal Eye – Before / After



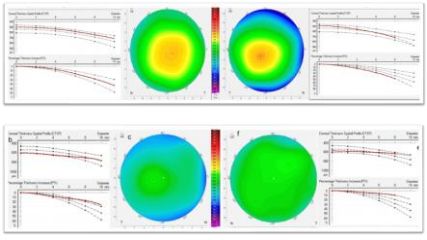
Results

- Comparing the BFS to the modified reference shape
  - Normal eyes showed an avg change in anterior apex and maximum elevation of 1.86±1.9µm and 1.63±1.4µm.
  - Keratoconus eyes showed anterior apex and maximum elevation changes of 20.4±23.1µm and 20.9±21.9µm.
    - *(P<.0001).*
  - Posteriorly, normal eyes showed an average change in apex and maximum elevation of 2.86±1.9µm and 2.27±1.1µm.
  - Keratoconus eys showed posterior apex and maximum elevation changes of 39.9±38.1µm and 45.7±35.9µm.
    - *(P<.0001).*

Enhanced Reference Shape



Pachymetric Progression



The "BAD" *Belin / Ambrosio III*

- Reports 5 "D" Values which are individual SD from the mean of:
  - "Df" STD - Anterior Elevation Change (Front)
  - "Db" STD - Posterior Elevation Change (Back)
  - "Dp" STD - Pachymetric Progression (Progression)
  - "Dt" STD - Thinnest Point Pachymetry (Thinnest)
  - "Da" STD – Relational Thickness
- Plus ARTmax, Ant & Post Elevation, Kmax
- Each of these **9** parameters are independently calculated based on established normal values

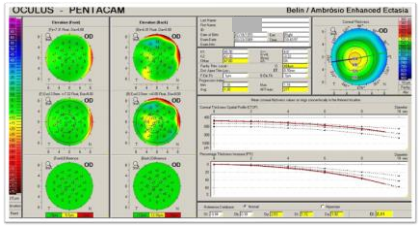
"BAD" *Belin / Ambrosio III*

- The individual "D" values and the additional 4 parameters are reported as SD from the mean and will change color to YELLOW at 1.6 SD from the norm and RED at 2.6 SD from the norm

"BAD" *Belin / Ambrosio III*

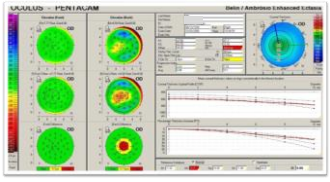
- The Final "**D**" is an overall reading of all the parameters based on a regression analysis. The individual "D" values have different weighting.
- Only the final "D" has statistical significance for separating normal from abnormal

Belin /Ambrosio III Enhanced Ectasia Display



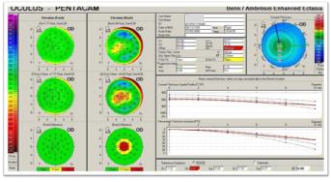
BAD Display

- The BAD display is designed for ***Refractive Screening***
- It separates "normal" from "abnormal"
- It does not specifically diagnose KCN



Using the Display

- May have individual YELLOW or RED but an overall final "D" that is within acceptable range
- You need to use other information to make a final clinical decision
  - Age
  - Ablation depth
  - Family history



Summary

- BAD III allows for a high specificity and sensitivity
  - Additional testing with Placido devices in unnecessary
  - You need to use other information to make a final clinical decision
    - Age
    - Ablation depth
    - Family history
    - Stability
    - Remember to compare both eyes for symmetry

ABCD Keratoconus Staging

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Why a new System

Global Consensus on Keratoconus and Ectatic Diseases

2015


Global Consensus on Keratoconus and Ectatic Diseases

What did they Conclude about Diagnosis

TABLE 2. Agreements Reached in the Definition/Diagnosis Panel

- The following findings are mandatory to diagnose keratoconus
  - Abnormal posterior elevation
  - Abnormal corneal thickness distribution
  - Clinical noninflammatory corneal thinning
- The best current and widely available diagnostic test to diagnose early keratoconus is tomography (Scheimpflug or optical coherence tomography)
- Posterior corneal elevation abnormalities must be present to diagnose early or subclinical keratoconus

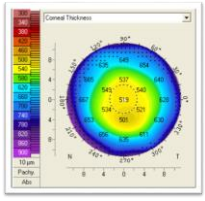
What we Need

- Recognition of full anatomical changes
  - Anterior cornea
  - Posterior cornea
  - Corneal thickness
- Simple Parameters
- Platform independent
  - Any tomographic device
- Easy to convey information

Limitations of Amsler-Krumeich

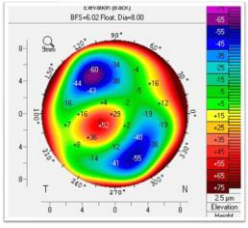
- Relies on apical thickness

STAGE I	Eccentric steepening Myopia / Astigmatism < 5.00 D Mean K < 48.0 D
STAGE II	Myopia / Astigmatism > 5.00 D but < 8.00 D Mean K < 53.0 D Absence of scarring Minimal apical corneal thickness > 400 um
STAGE III	Myopia / Astigmatism > 8.00 D but < 10.00 D Mean K > 53.0 D Absence of scarring Corneal thickness < 400 um but > 300 um
STAGE IV	Refraction not possible Mean K > 55.0 D Central corneal scarring Minimal apical corneal thickness < 300 um



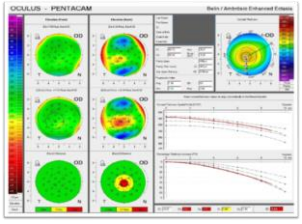
Limitations of Amsler-Krumeich

- Does not take posterior surface into account



Limitations of Amsler-Krumeich

- Does not recognize early (subclinical) disease



Would you treat these the same ?

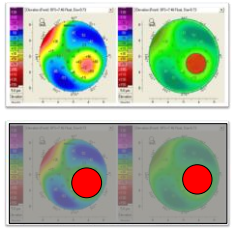
18 year old	47 year old
Pach 410	Pach 544
Mean K 52	Mean K 48.5
Rx – 8.0	Rx -5.25

Amsler/Krumeich grades them the Same

18 year old	STAGE I: Eccentric steepening Myopia / Astigmatism < 5.00 D Mean K < 48.0 D	47 year old
Pach 410	STAGE II: Myopia / Astigmatism > 5.00 D but < 8.00 D Mean K < 53.0 D Absence of scarring Minimal apical corneal thickness > 400 um	Pach 540
Mean K 52	STAGE III: Myopia / Astigmatism > 8.00 D but < 10.00 D Mean K > 53.0 D Absence of scarring Corneal thickness < 400 um but > 300 um	Mean K 48.5
Rx – 8.0	STAGE IV: Refraction not possible Mean K > 55.0 D Central corneal scarring Minimal apical corneal thickness < 300 um	Rx -5.25
Stage II		Stage II

"One Man's Trash, is Another Man's Treasure"

- The Enhanced Reference Surface works because the exclusion zone effectively removes the bulk of the cone and normalizes the reference surface.
- As opposed to removing the exclusion zone, we should examine the exclusion zone as it represents the ectatic region of the cornea



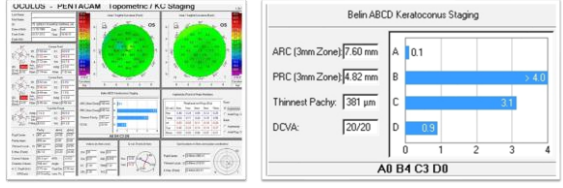
	Anterior Radius of Curvature (3 mm)	Posterior Radius of Curvature (3 mm)	Corneal Thickness at Thinnest Point (um)
Mean	7.65	6.26	534.2
Median	7.64	6.25	533
STD	0.236	0.214	30.36
Range	6.89 – 8.66	5.61 – 6.93	454 - 614

Because the Posterior cornea is a low power MINUS lens, we need to get comfortable with Radius of Curvature instead of Diopters in order to measure both Anterior and Posterior surfaces.

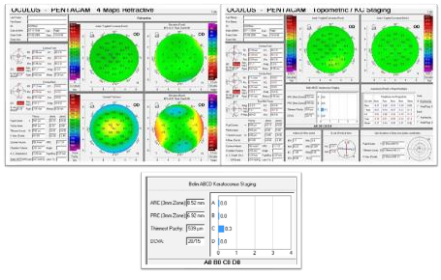
Belin ABCD Keratoconus Classification / Grading

ABCD Criteria	A	B	C	D	
	ARC (3 mm Zone)	PRC (3 mm Zone)	Thinnest Pach um	BDVA	Scarring
STAGE 0	> 7.25 mm (< 46.5 D)	> 5.90 mm	> 490 um	≥ 20/20 (≥ 1.0)	-
STAGE I	> 7.05 mm (< 48.0 D)	> 5.70 mm	> 450 um	< 20/20 (< 1.0)	-, +, ++
STAGE II	> 6.35 mm (< 53.0 D)	> 5.15 mm	> 400 um	< 20/40 (< 0.5)	-, +, ++
STAGE III	> 6.15 mm (< 55.0 D)	> 4.95 mm	> 300 um	< 20/100 (< 0.2)	-, +, ++
STAGE IV	< 6.15 mm (> 55.0 D)	< 4.95 mm	≤ 300 um	< 20/400 (< 0.05)	-, +, ++

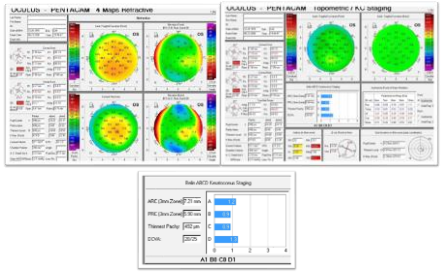
Currently part of the Topometric / KCN Staging Display



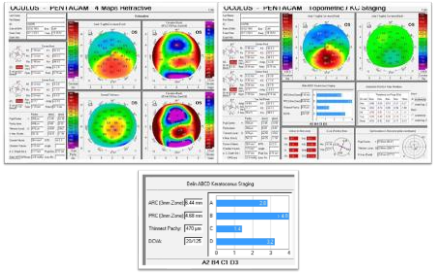
Normal Eye



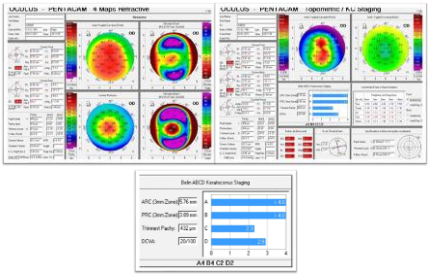
Very Early Ectatic Change



Moderately Advanced KCN



Advanced KCN



Belin ABCD Progression Display: *Before & After CXL*

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Consultant OCULUS GmbH, Avedro
CMO CXL Ophthalmics

Global Consensus on Keratoconus and Ectatic Diseases

2015

Ectasia Progression

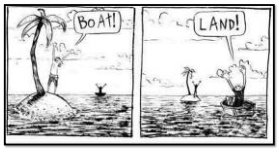
Global Consensus on Keratoconus and Ectatic Diseases

2015

- Currently, no consistent definition
- Consistent change in at least two of the following, where the change is above the normal measurement error
  - Steepening of the Anterior corneal surface
  - Steepening of the Posterior corneal surface
  - Progressive thinning or an increase in the rate of change from the periphery to the thinnest point

We Need a New Perspective

- The reliance on Kmax as both an efficacy parameter and an indicator of progression has resulted in irreversible loss of vision and delayed intervention
- *Kmax has never been statistically validated*



Prior Progression Parameters

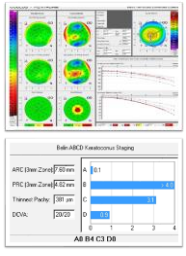
Suggested Parameter	Value Representing Progression
Spherical power, and higher order irregular astigmatism	Positive Rate of Change per Year
Spherical component, regular astigmatism,	Positive Rate of Change per Year
Kmax (steepest K)	≥1.00 D increase
Kmax – Kmin	≥1.00 D increase
Kmean (average of Kmax and Kmin)	≥0.75 D increase
Pachymetry	≥2% decrease in central thickness
Back optic zone radius of the best fitting contact lens	0.1 mm or more decrease
Increase in the central K power	≥ 1.50 D increase from baseline
Manifest cylinder	Increase of ≥ 1.00 D in 24 months
Manifest spherical equivalent change (MRSE)	≥0.50 D
ISV	Specific values for each KCN stage
IHA	Specific values for each KCN stage

None have been statistically validated

Suggested Parameter	Value Representing Progression	Validated
Spherical power, and higher order irregular astigmatism	Positive Rate of Change per Year	No
Spherical component, regular astigmatism,	Positive Rate of Change per Year	No
Kmax (steepest K)	≥1.00 D increase	No
Kmax – Kmin	≥1.00 D increase	No
Kmean (average of Kmax and Kmin)	≥0.75 D increase	No
Pachymetry	≥2% decrease in central thickness	No
Back optic zone radius of the best fitting contact lens	0.1 mm or more decrease	No
Increase in the central K power	≥ 1.50 D increase from baseline	No
Manifest cylinder	Increase of ≥ 1.00 D in 24 months	No
Manifest spherical equivalent change (MRSE)	≥0.50 D	No
ISV	Specific values for each KCN stage	No
IHA	Specific values for each KCN stage	No

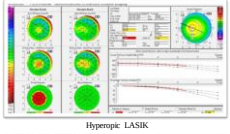
Why a Progression Display ?

- Can't we just follow the final "D" of the BAD ?
- Can't we just follow the parameters from the ABCD Staging/Grading System ?

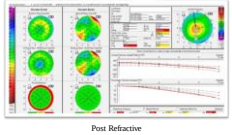


Why a new Progression Display ?

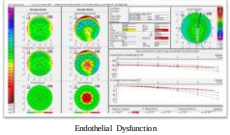
- Belin/Ambrosio Enhanced Ectasia Display (BAD)
  - Designed specifically to separate "normal" from "abnormal"



Hyperopic LASIK



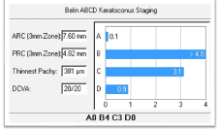
Post Refractive



Endothelial Dysfunction

Why a Progression Display ?

- Can't we just follow the parameters from the ABCD Staging/Grading System ?
- The ABCD is designed for population based studies, not to follow a single individual



Why a new Progression Display ?

- Belin ABCD Progression Display
  - Designed to follow and document progression of disease
  - Based on one-sided confidence intervals
  - Allows for documenting progression in spite of a stable anterior surface and/or stable Kmax
  - Evaluates each anatomical layer individually
  - Statistically validated

- Determine background noise for each parameter
  - Not determined for new parameters
- Staging / Progression display that *automatically* determines stage and significant change.

ABCD Criteria	A	B	C	D	
	ARC (3 mm Zone)	PRC (3 mm Zone)	Thinnest Pach um	BDVA	Scarring
STAGE 0	> 7.25 mm (< 46.5 D)	> 5.90 mm (< 57.25 D)	> 490 um	≥ 20/20 (≥ 1.0)	-
STAGE I	> 7.05 mm (< 48.0 D)	> 5.70 mm (< 59.25 D)	> 450 um	< 20/20 (< 1.0)	-, +, ++
STAGE II	> 6.35 mm (< 53.0 D)	> 5.15 mm (< 65.5 D)	> 400 um	< 20/40 (< 0.5)	-, +, ++
STAGE III	> 6.15 mm (< 55.0 D)	> 4.95 mm (< 68.5 D)	> 300 um	< 20/100 (< 0.2)	-, +, ++
STAGE IV	< 6.15 mm (> 55.0 D)	< 4.95 mm (> 68.5 D)	≤ 300 um	< 20/400 (< 0.05)	-, +, ++

Studied Populations
Normal & Abnormal *(Keratoconus)*

Why Study both Normals & Abnormals ?

- For older patients with clinically evident keratoconus the noise levels from the Keratoconic patient database is more appropriate for progression documentation
  - An older patient is less likely to exhibit rapid change and the risk of "waiting" is low
- A young patient with early or subclinical disease may change rapidly and their cornea more closely matches a normal population than a moderate to advanced keratoconic population
  - In a younger patient with normal vision and subclinical disease early detection of any change is paramount.
  - Here the risk of "waiting" is high

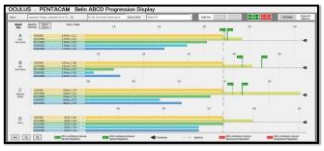
Progression Parameters
STD & Confidence Intervals

	Standard Dev	95% CI 1-tail	80% CI 1-tail
KCN ARC all (n=252)	0.062	0.102	0.052
KCN ARC OK (n=208)	0.062	0.102	0.052
NORM ARC (n=135)	0.015	0.024	0.012
KCN PRC all	0.062	0.102	0.052
KCN PRC OK	0.063	0.104	0.053
NORM PRC	0.050	0.083	0.042
KCN Min Pach all	6.03	9.92	5.07
KCN Min Pach OK	6.10	10.03	5.13
NORM Min Pach	4.79	7.88	4.03

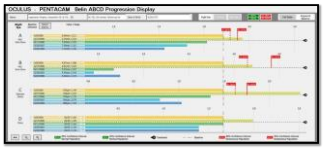
- One sided confidence intervals were chosen since progression is associated with a decrease in pachymetry and / or a decrease in radius of curvature of either the anterior or posterior surface
- Both 80% and 95% confidence intervals are reported to allow the surgeon to make a risk benefit analysis.

Belin KCN Progression Display *II*

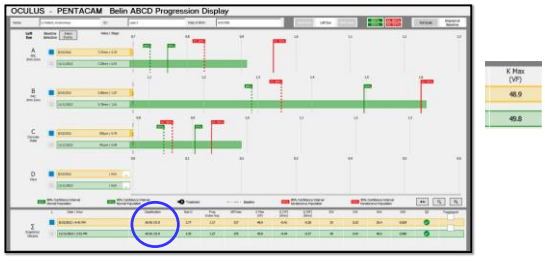
Normal Population



Keratoconus Population



16 yr old Progressive Subclinical Disease



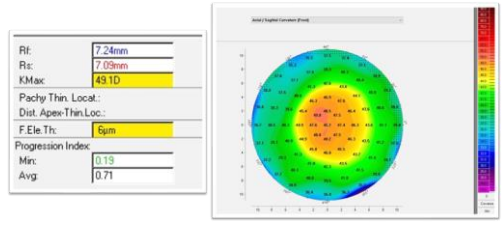
15 yr old very early KCN , 13 month f/u

(notice Kmax & anterior tabular parameters)

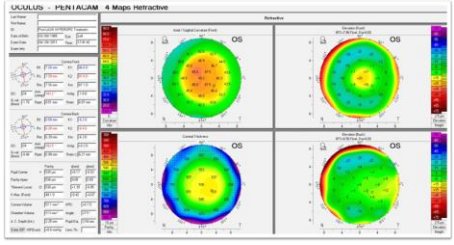
Progressive Advanced KCN with Stable Anterior Surface

BAD "D" > 7.0

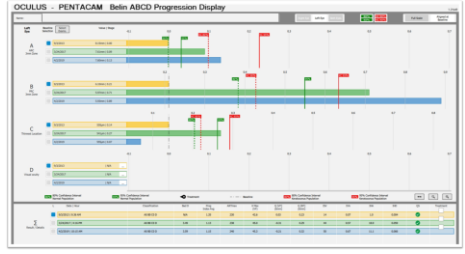
C/O Decrease UCVA post Hyperopic LASIK



Post Hyperopic LASIK



Post Hyperopic LASIK Ectasia



Diagnosing Progression of Keratoconus

- Dissociation of Clinical Progression with Changes in Kmax
- Tomographic based classification system recognizes all the anatomical layers
- Tomographic based progression display documents statistically significant change
  - One parameter @ 95% or two parameters @ 80%
    - "*Grain of salt*" for "C" parameter

How do you define Progression after CXL

- Progression parameters after CXL have been unknown
  - Currently, the confidence intervals on the ABCD Progression display are removed after you indicate CXL treatment

Post CXL Progression Study

- **Purpose**
  - Measure noise of post CXL eyes and evaluate whether these measurements can serve as progression determinants after CXL
- **Methods**
  - Patients from ELZA Institute (Switzerland) and Homburg Keratoconus Center (Germany) with a minimum 12 months post-CXL were enrolled.
    - We used two sites to compare since CXL is a surgical procedure with inherent user/site variability.
    - Three separate Pentacam measurements were taken, removing the patient between each exam. A minimum 7.5 mm of coverage and an acceptable quality score were required.
    - Both pooled variance and one-sided confidence intervals were computed. Site specific and time specific comparisons were made.

Post CXL Progression Study

- Demographics

	Combined	Zurich	Homburg
Eyes	60	38	22
Age (years)	29.5 ± 12.3 Range 11-62	29.9 ± 12.8 Range 11-62	28.8 ± 11.7 Range 17-56
Time since CXL (months)	26.1 ± 19.3 Range 12-115	16.6 ± 5.4 Range 12-28	42.6 ± 23.2 Range 16-115

Post CXL Progression Study

	95% CI 1-tail	80% CI 1-tail
KCN ARC *(n=252)*	0.102	0.052
NORMAL ARC *(n=135)*	0.024	0.012
POST CXL ARC *(n=60)*	0.055	0.028
KCN PRC	0.102	0.052
NORMAL PRC	0.083	0.042
POST CXL PRC	0.096	0.049
KCN Min Pach	9.92	5.07
NORMAL Min Pach	7.88	4.03
POST CXL Min PACH	7.20	3.68

Geographic Comparison

Geographical Location		N	Mean	Std. Deviation	Std. Error Mean
ARC3mmZone_mean	Zurich	38	6.8592	0.70333	0.11410
	Homburg	22	6.4032	0.57497	0.12258
PRC3mmZone_mean	Zurich	38	5.0926	0.70966	0.11512
	Homburg	22	4.5926	0.41934	0.08940
ThinnestPachy_mean	Zurich	38	450.4561	48.02548	7.79076
	Homburg	22	445.0758	39.49013	8.41932

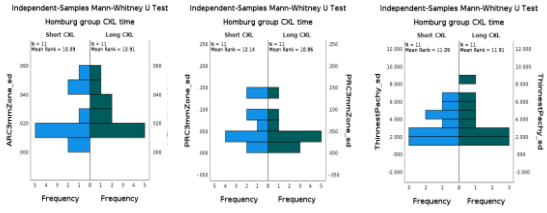
Populations have similar ABC values

Populations have similar noise measurements

Time Since CXL Comparison

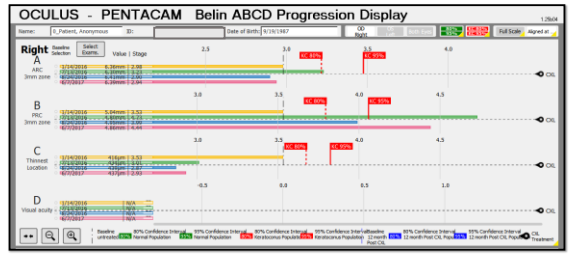
Short 1-3 years / Long >3 – 10 years

(Homburg Subjects)



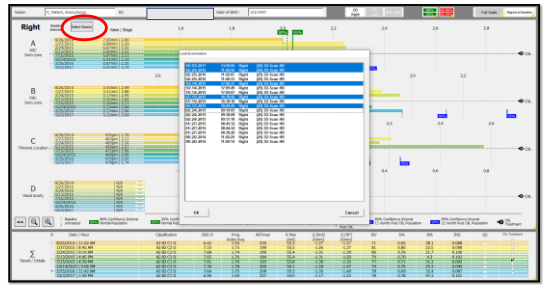
Belin ABCD Progression Display *III*

Post CXL gates only appear > 1 year

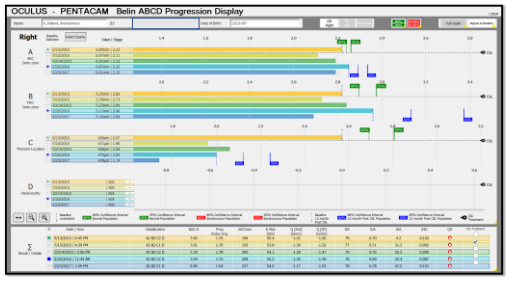


16 year-old, Selecting Green Gates

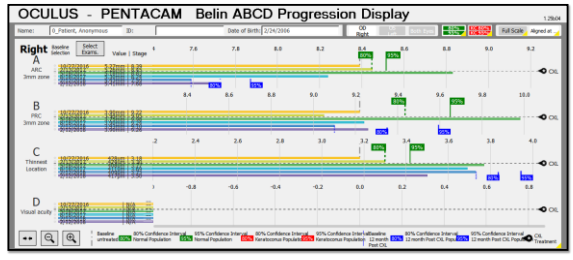
16 year-old, Post CXL Select Exam



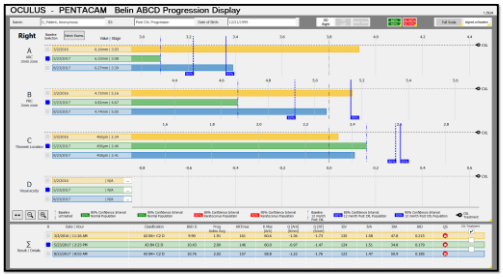
16 year-old, Post CXL Select Exam



Good Response to CXL



Possible Retreatment / Select Exams



Post CXL Progression Study

- **Conclusion**
  - Post CXL measurement variance (*noise*) can be used to determine progressive change
  - Noise measurements are consistent across different centers
  - Noise measurements are consistent > 12 months
  - New Post CXL confidence intervals added to current iteration of Belin ABCD Progression Display
    - *Belin ABCD Progression Display III*

Independent Validation

- Belin ABCD Progression Display Identifies Keratoconus Progression Earlier than Conventional Metrics. AJO 2022; 236:45-52
  - Identified progression 4 – 7 months earlier than Kmax
- Evaluating Keratoconus Progression prior to Crosslinking: maximum keratometry vs the ABCD grading system. J Cat Ref Surg 2021; 47:33-39
  - Identified progression on average 6 months earlier than Kmax
- ABCD progression display for keratoconus progression: a sensitivity-specificity study. EYE 2022
  - ABCD progression display can assess keratoconus progression with high sensitivity and specificity