Belin ABCD Staging & Progression Display:

Can we demonstrate Progression Earlier than Kmax?

RIO Memorial Lecture

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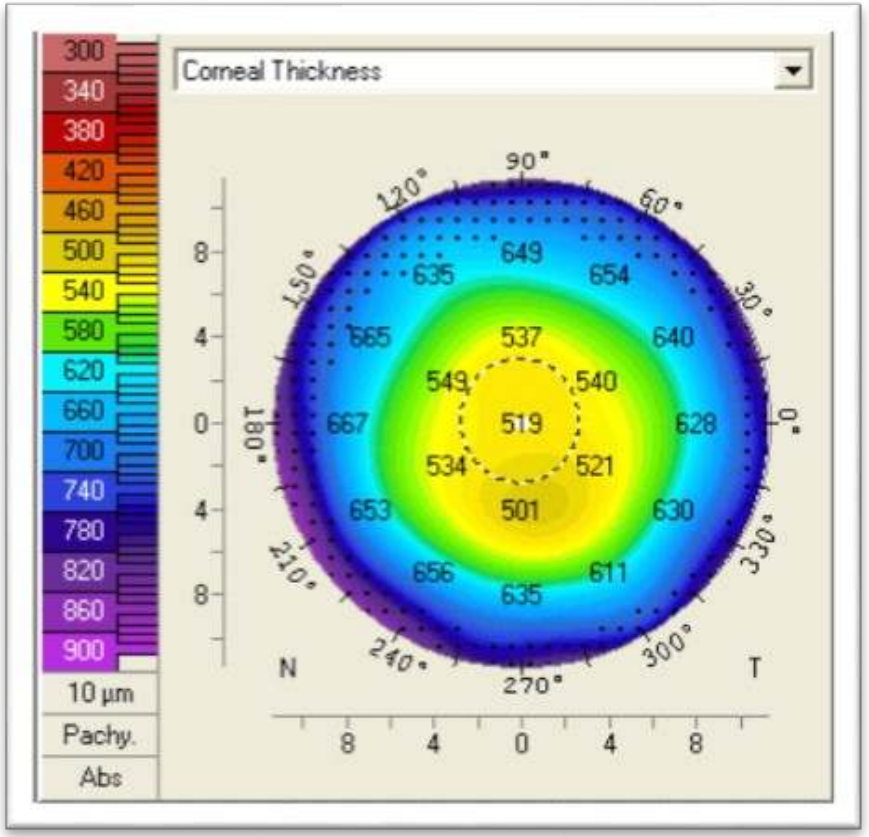
CMO - EPION Therapeutics

Limitations of Amsler-Krumeich

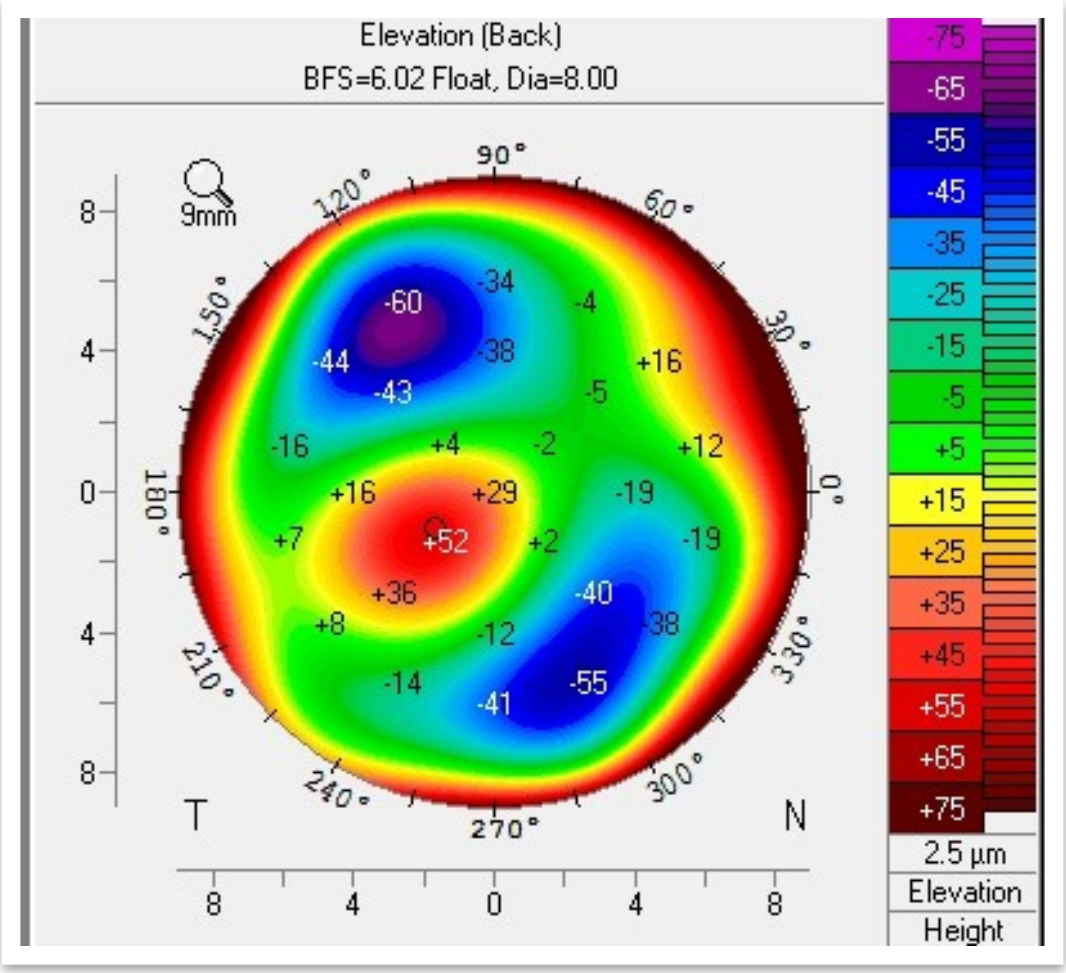
- Relies on apical thickness

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



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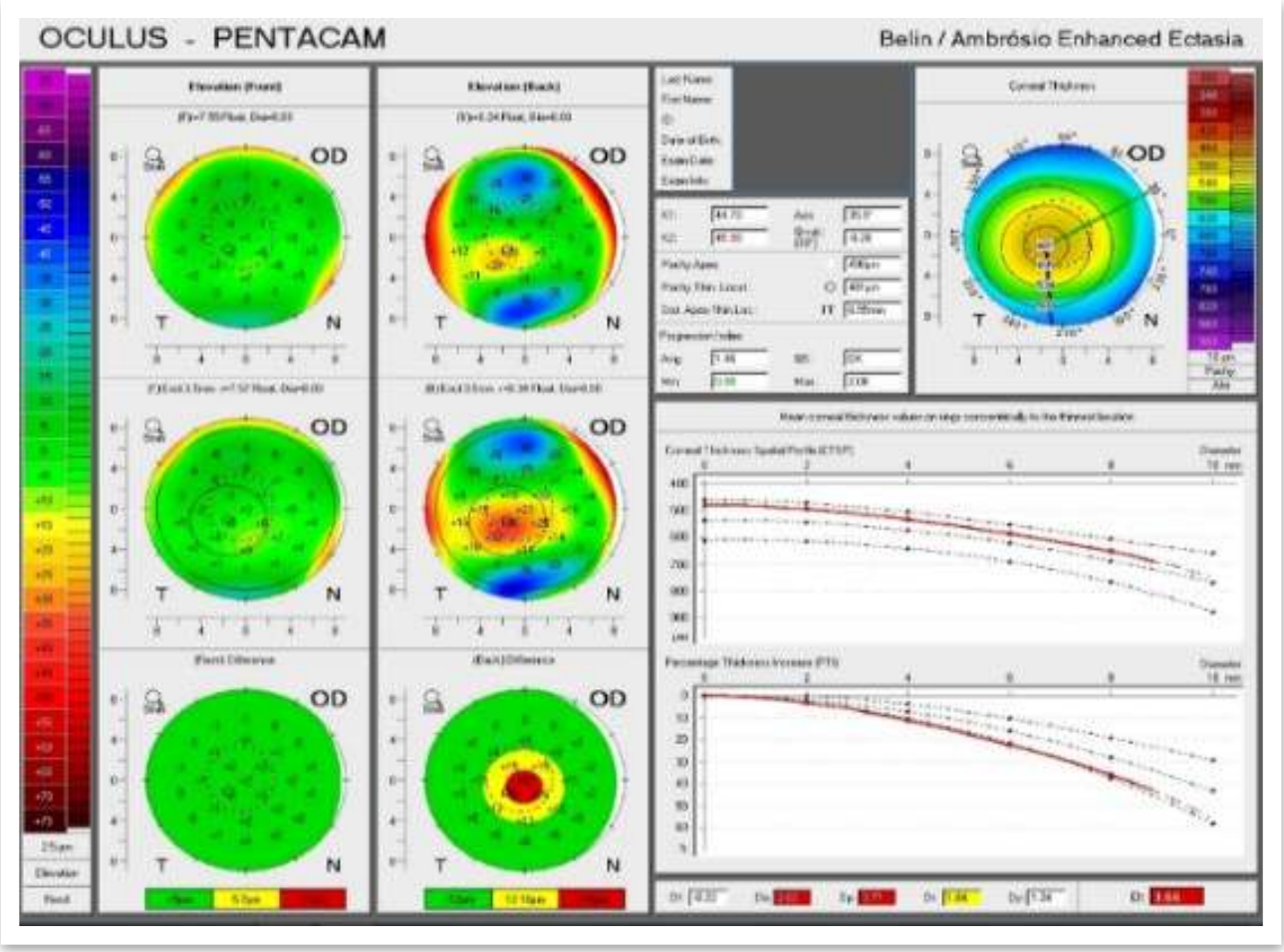
Limitations of Amsler-Krumeich

- Does not recognize early (subclinical) disease



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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

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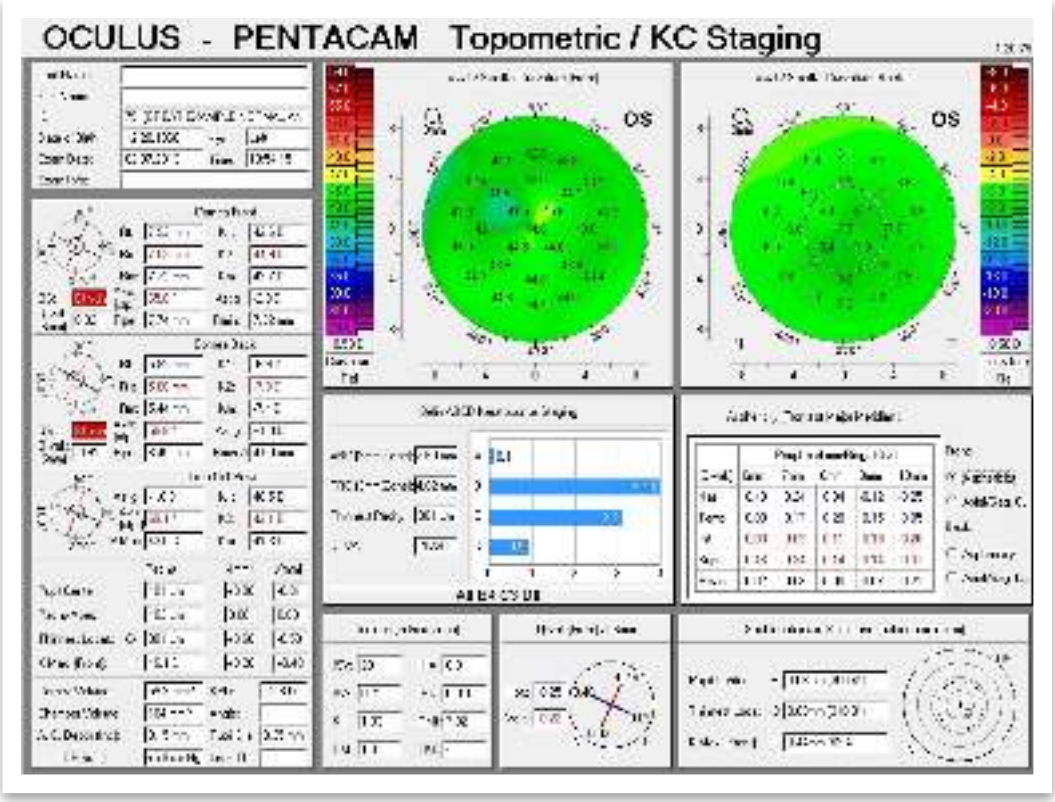
	Anterior Radius of Curvature (3 mm)	Posterior Radius of Curvature (3 mm)	Corneal Thickness at Thinnest Point (um)
Mean	7.65	6.26	534.2
Median	7.64	6.25	533
STD	0.236	0.214	30.36
Range	6.89 – 8.66	5.61 – 6.93	454 - 614

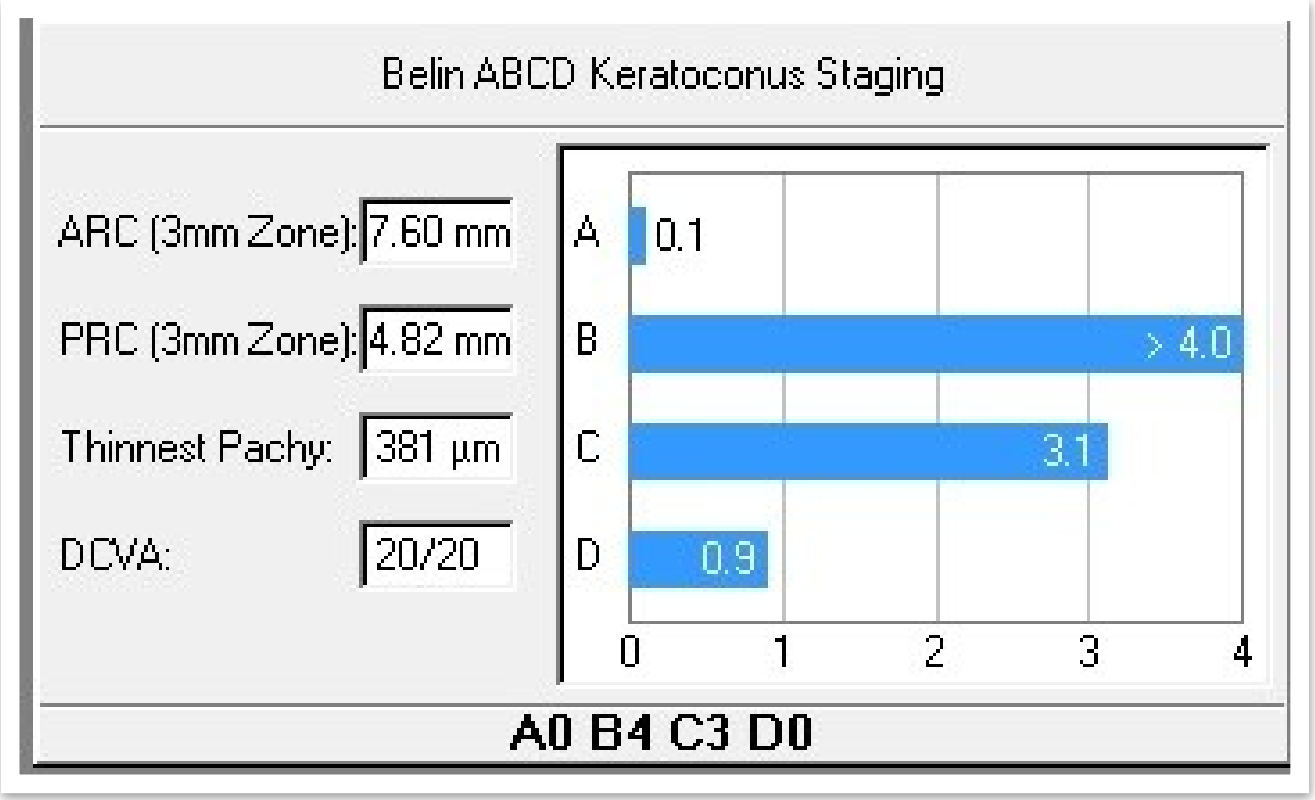
Because the Posterior cornea is a low power MINUS lens, we need to get comfortable with Radius of Curvature instead of Diopters in order to measure both Anterior and Posterior surfaces.

Belin ABCD Keratoconus Classification / Grading

ABCD Criteria	A	B	C	D
	ARC (3 mm Zone)	PRC (3 mm Zone)	Thinnest Pach um	BDVA
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





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Why a new Progression Display

Global Consensus on
Keratoconus and
Ectatic Diseases

2015

Definition of Ectasia Progression

Currently, there is no consistent or clear definition of ectasia progression. This led the Definition/diagnosis group to use 2 additional questionnaire rounds in an attempt to better define ectasia progression: "Ectasia progression" is defined by a consistent change in at least 2 of the following parameters where the magnitude of the change is above the normal noise of the testing system:

1. Steepening of the anterior corneal surface
2. Steepening of the posterior corneal surface
3. Thinning and/or an increase in the rate of corneal thickness change from the periphery to the thinnest point."

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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

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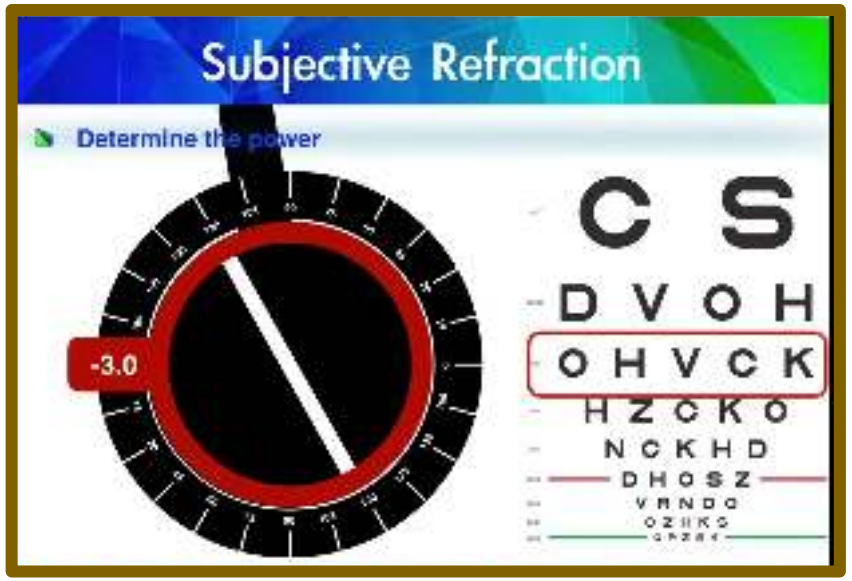
Subjective Refraction End Points

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



Back Optic Zone of RGP

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
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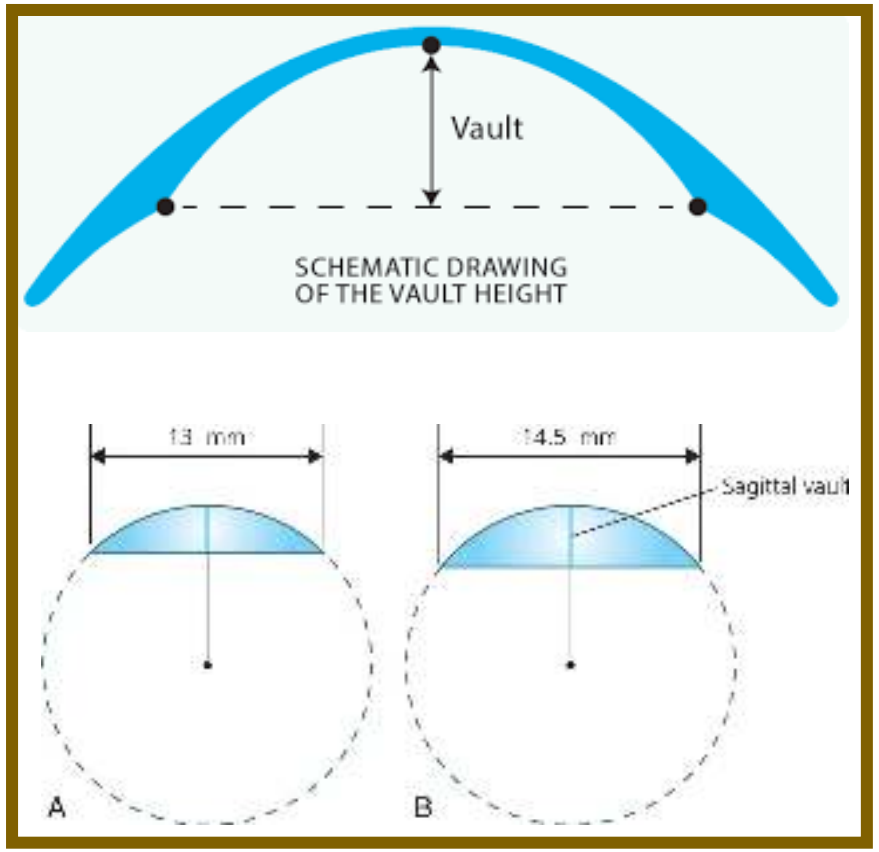

Which leaves us with K*max* and other Anterior Surface Parameters

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
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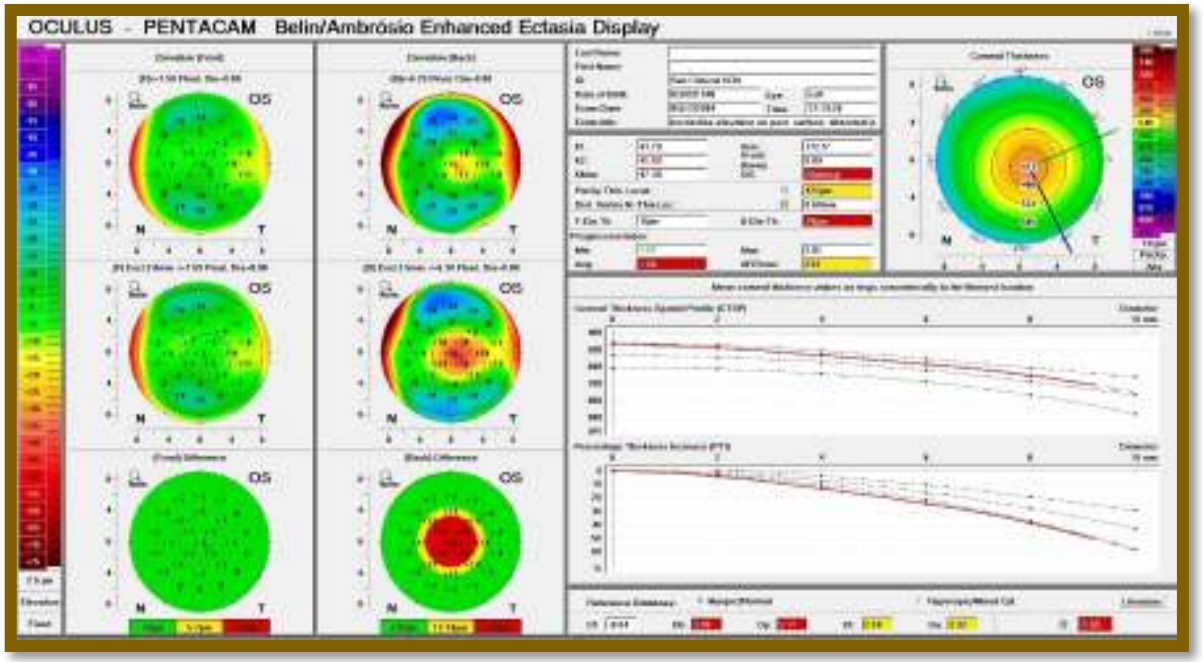

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Why a Progression Display ?

- 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

Studied 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

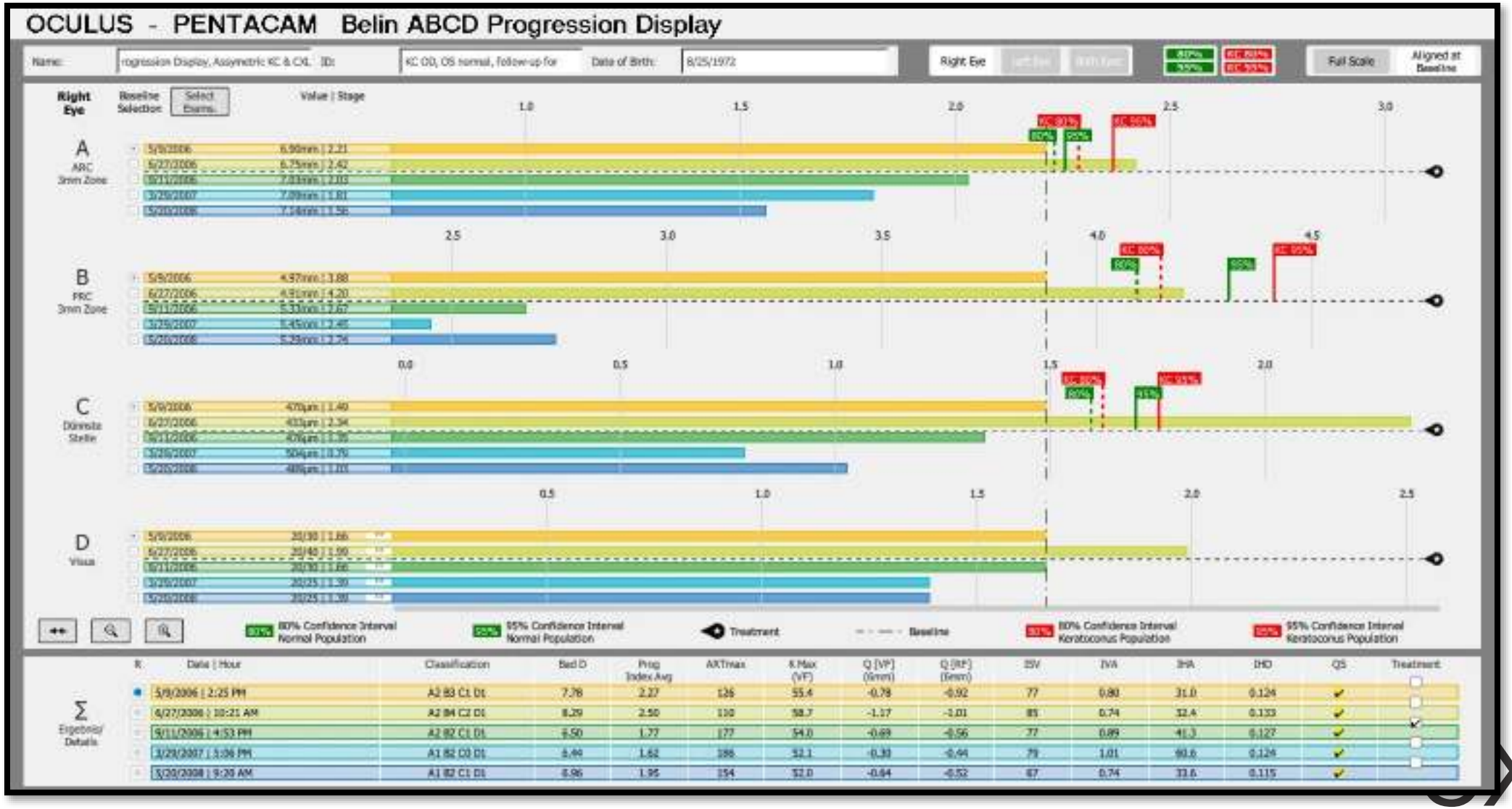
Progression Parameters

STD & Confidence Intervals

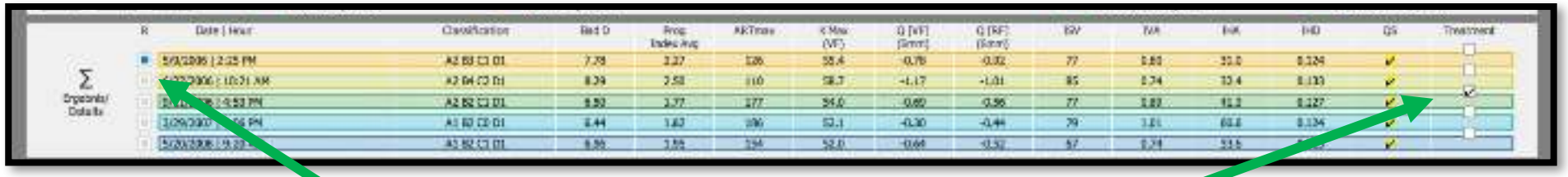
	Standard Dev	95% CI 1-tail	80% CI 1-tail
KCN ARC all (n=252)	0.062	0.102	0.052
KCN ARC OK (n=208)	0.062	0.102	0.052
NORM ARC (n=135)	0.015	0.024	0.012
KCN PRC all	0.062	0.102	0.052
KCN PRC OK	0.063	0.104	0.053
NORM PRC	0.050	0.083	0.042
KCN Min Pach all	6.03	9.92	5.07
KCN Min Pach OK	6.10	10.03	5.13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



Belin KCN Progression Display II



Identify Baseline & Treatment

Choose Comparison Population

(Defaults to Both)

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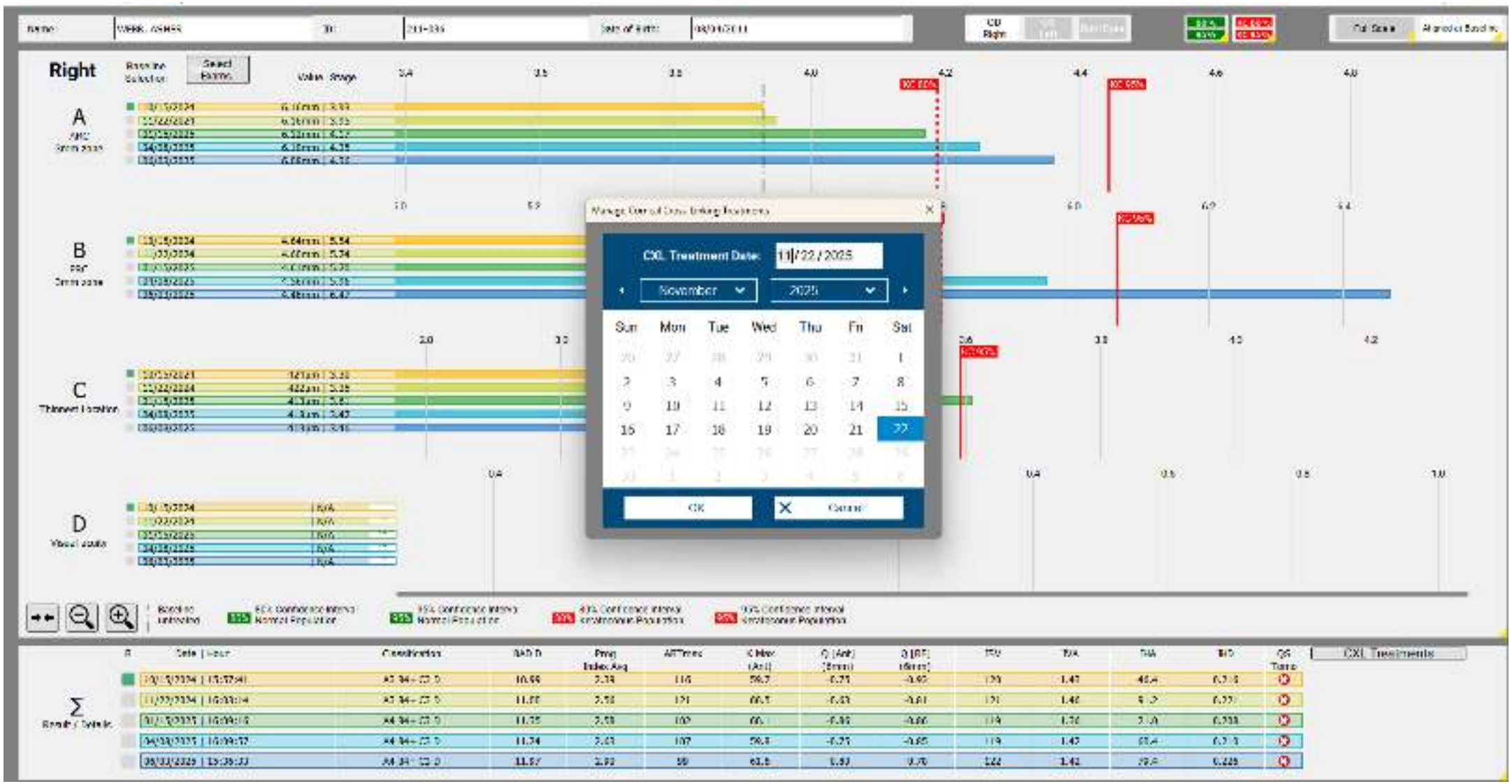
Select Date of Treatment (CXL)



Confidence Intervals: Removed after Treatment

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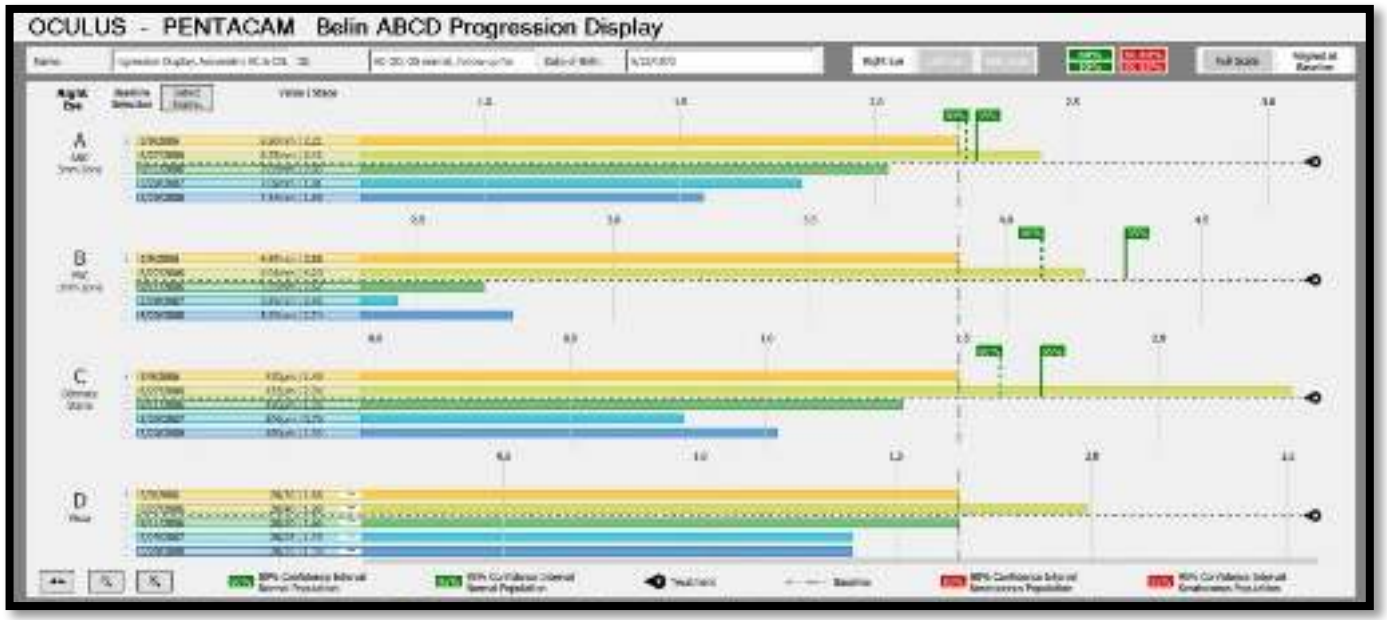
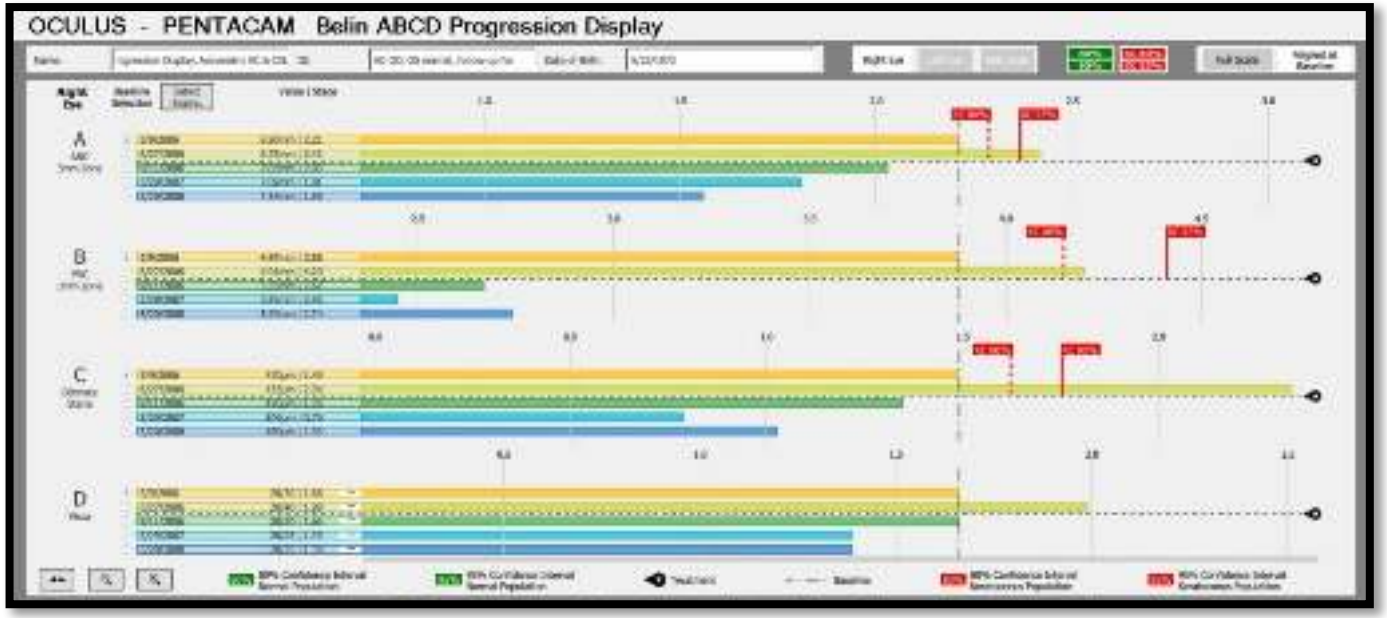
Normal Population



Keratoconus Population



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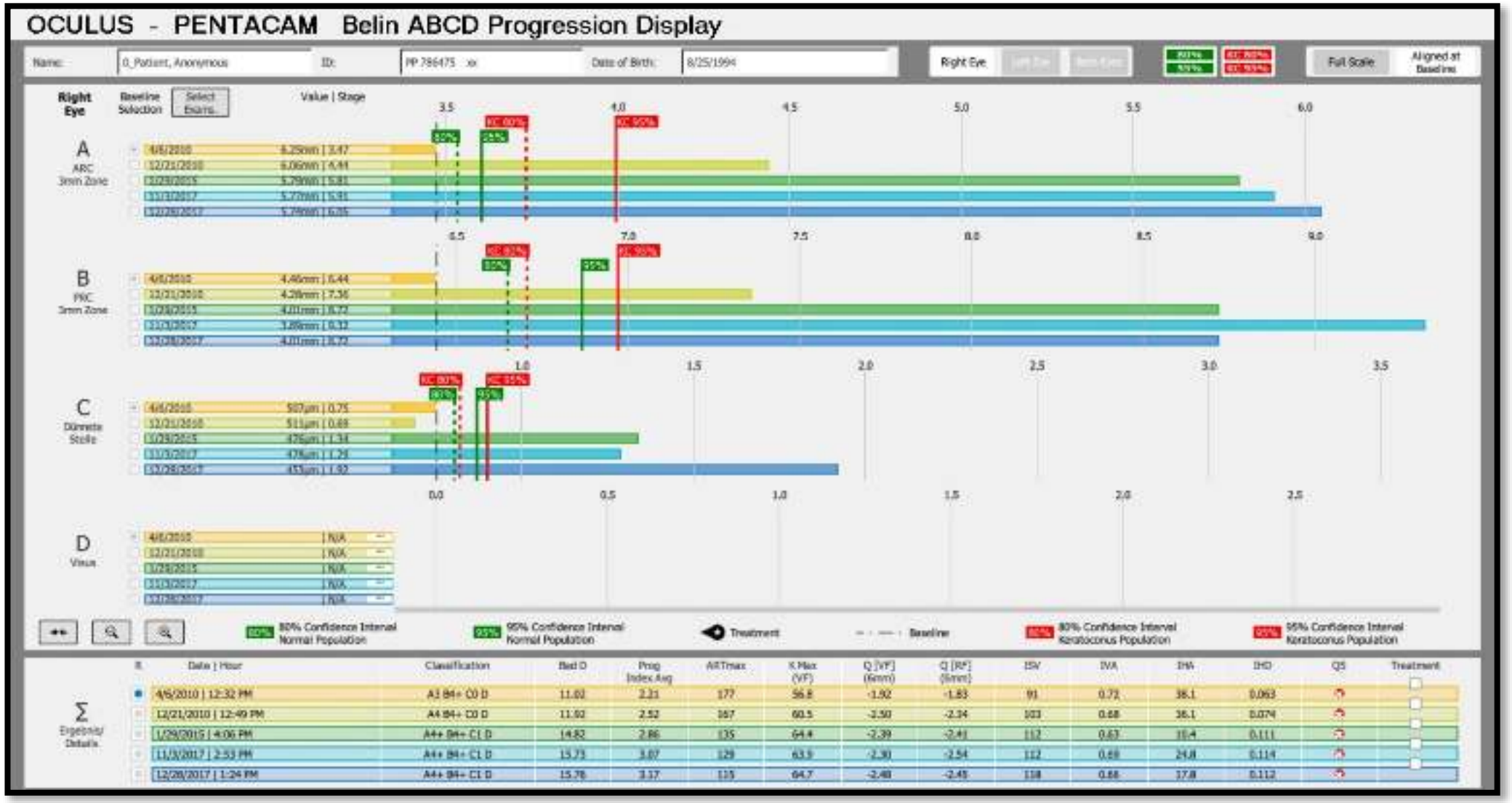
CLINICAL CASES

15 yr old advanced kcn , 7 year f/u



K Max (VF)
56.8
60.5
64.4
63.9
64.7

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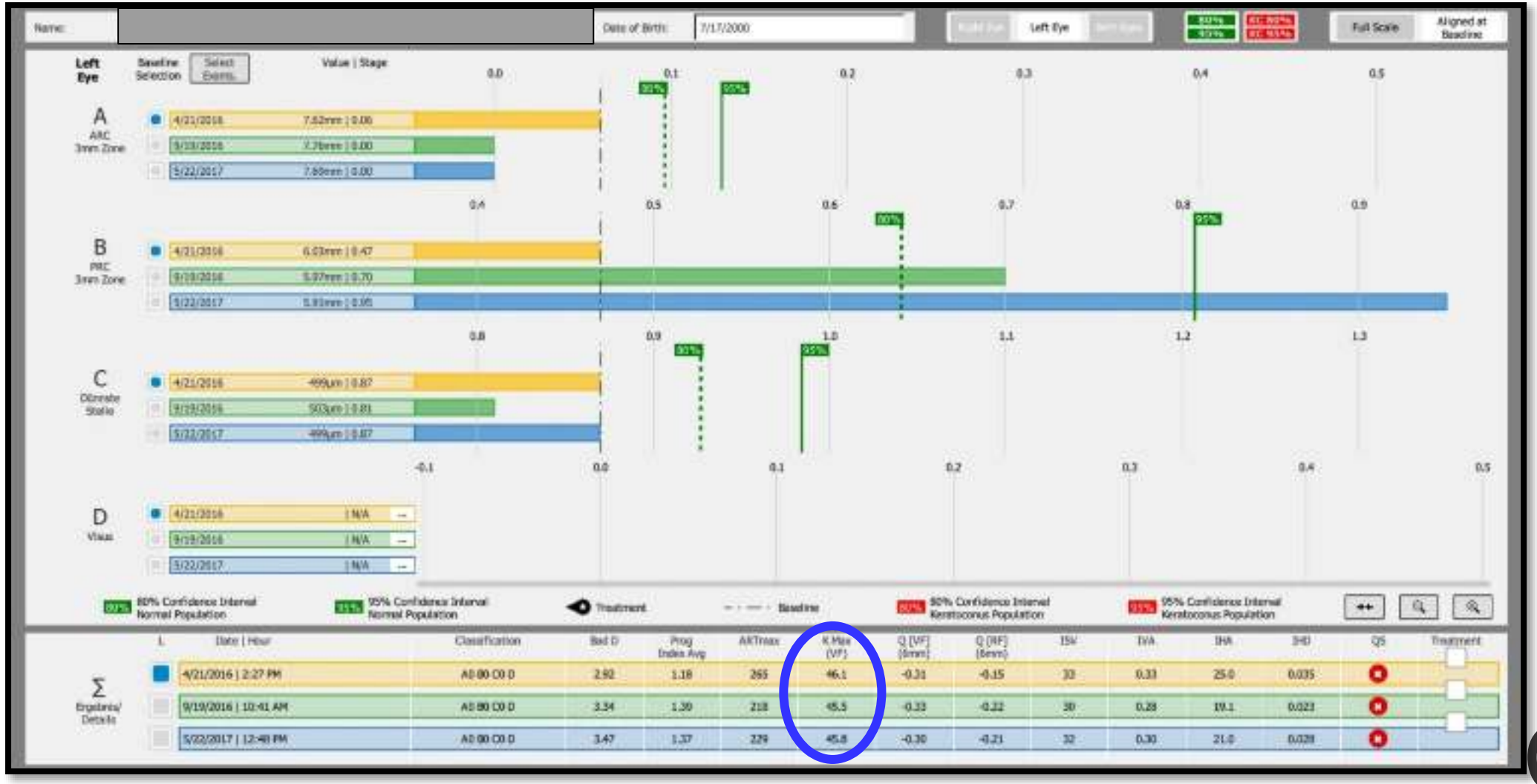
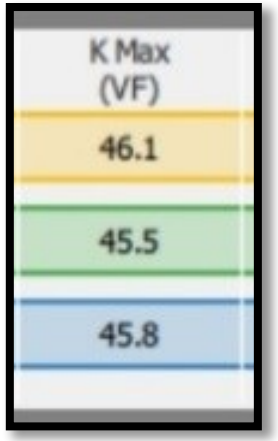
15 yr old very early KCN , 13 month f/u

(notice Kmax & anterior tabular parameters)





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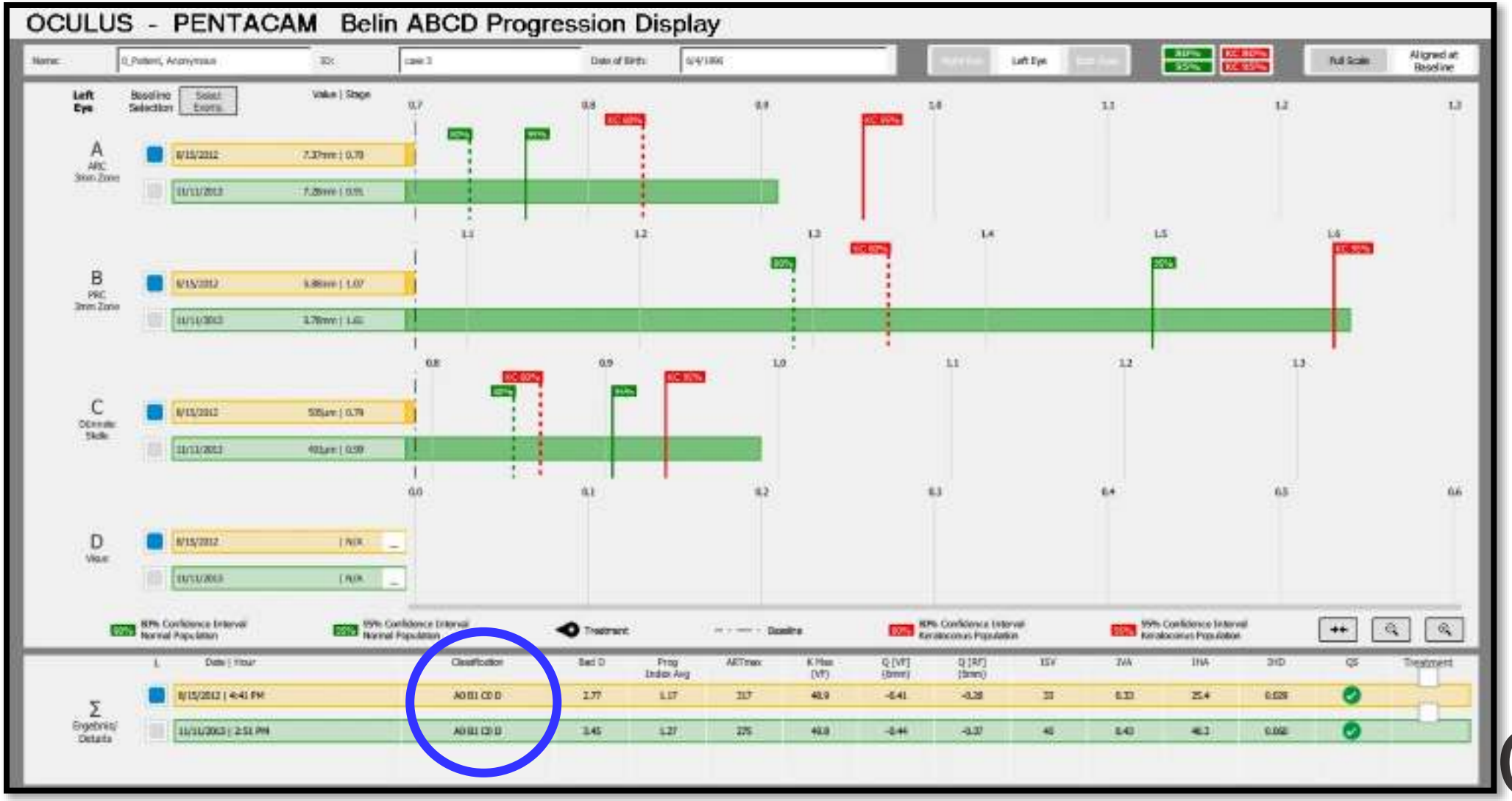
16 yr old Progressive Subclinical Disease



K Max (VF)
48.9
49.8

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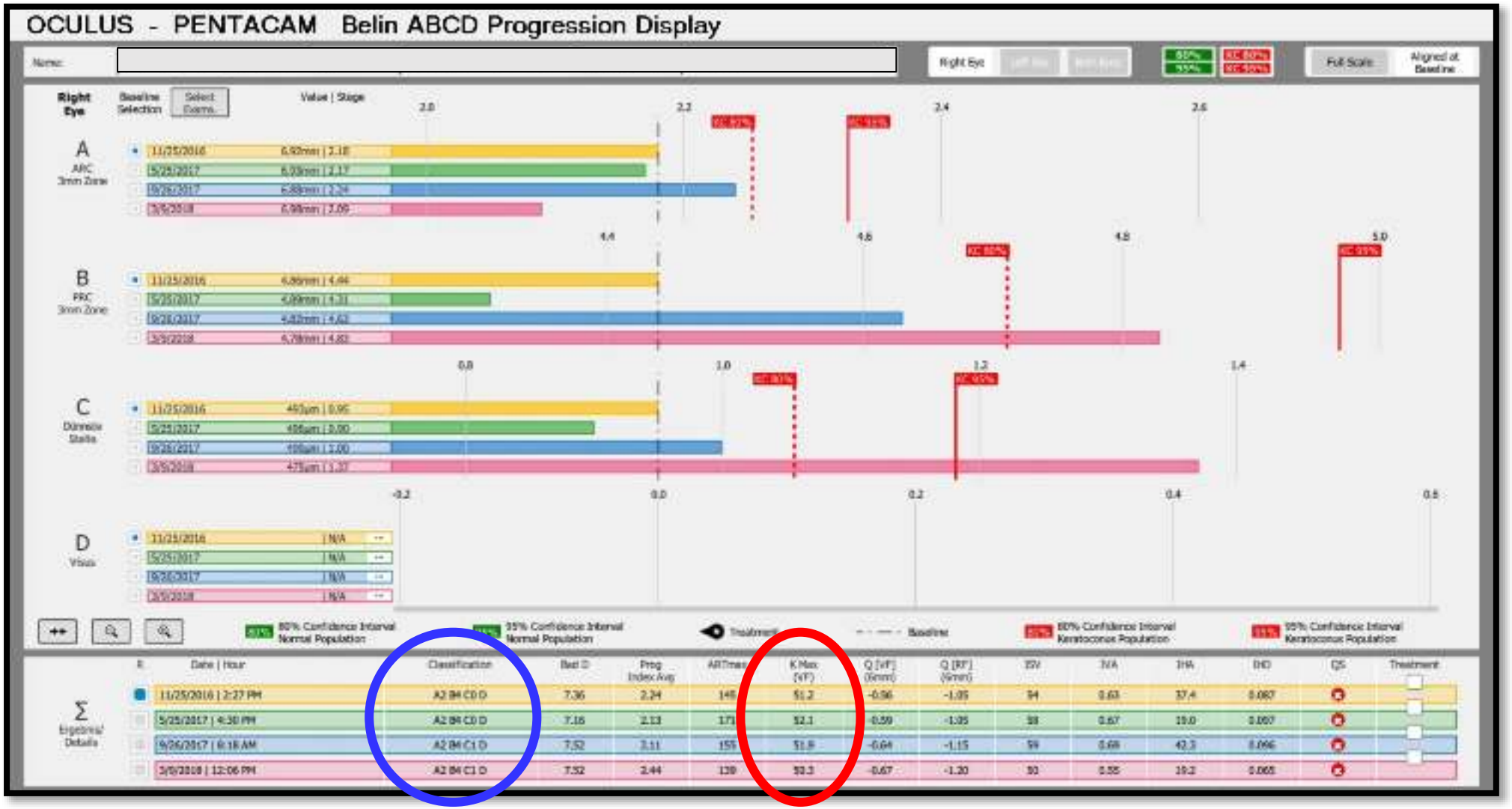
Progressive Advanced KCN with Stable Anterior Surface



BAD "D" > 7.0

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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

Progression after CXL

- Version II - The confidence intervals on the Belin ABCD Progression display were 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.

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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

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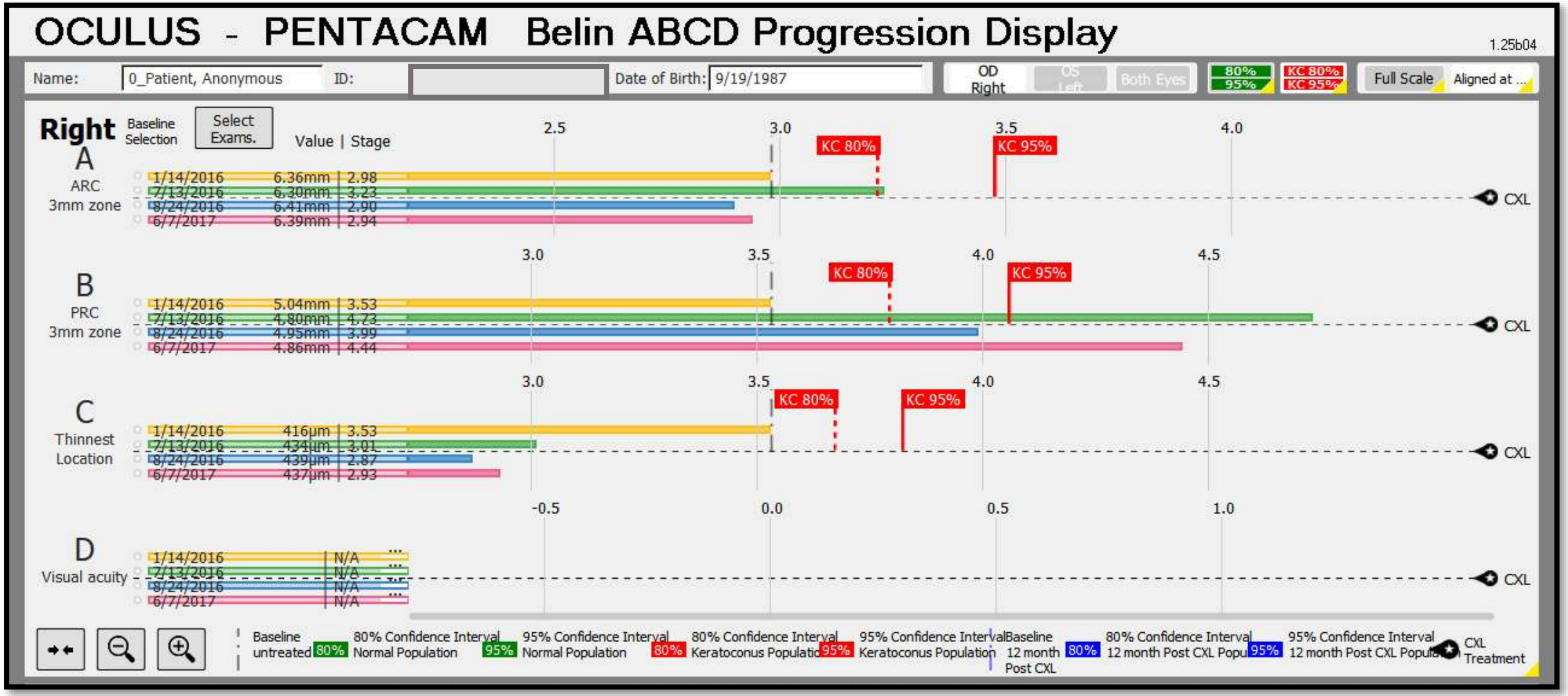
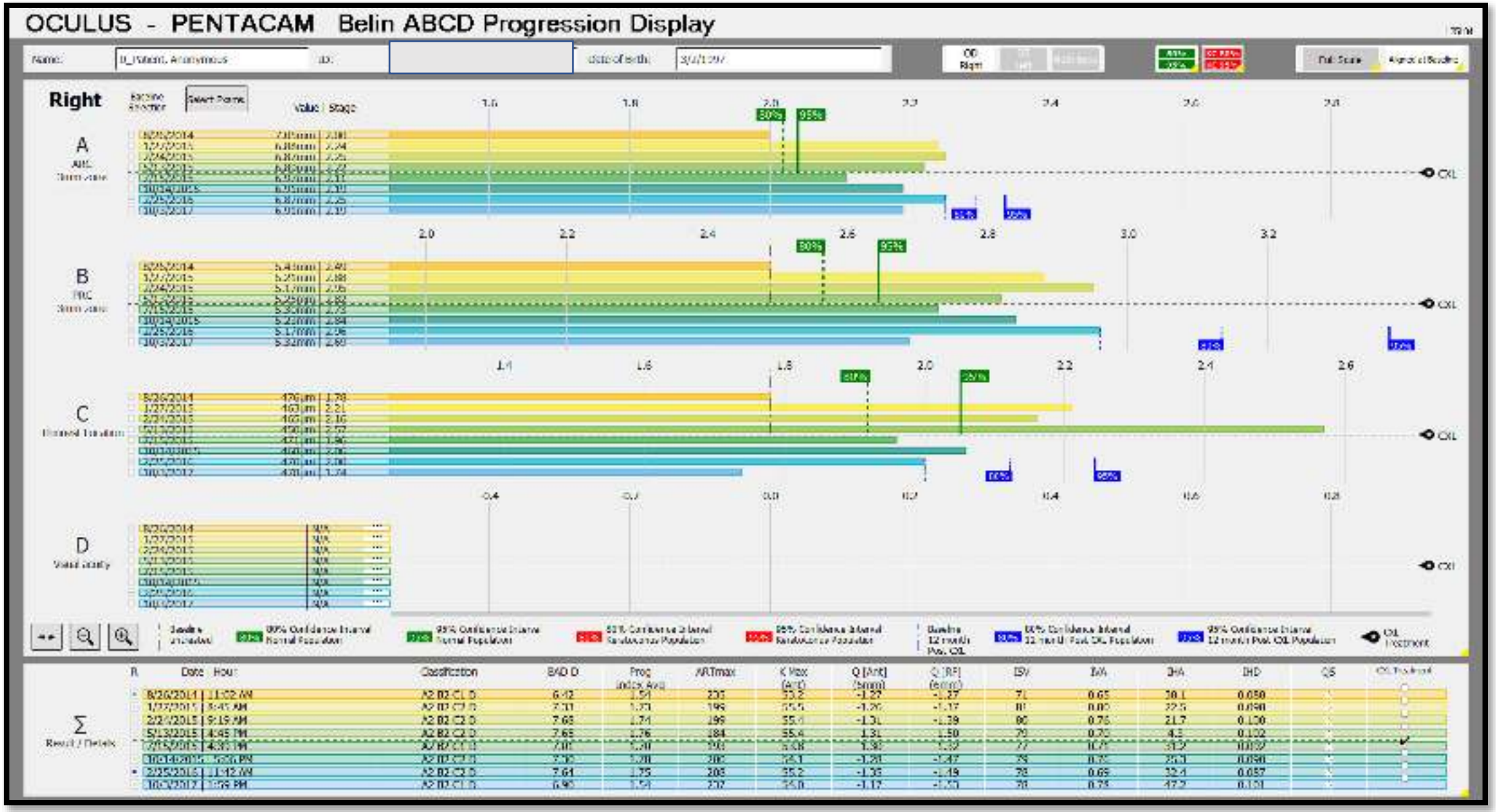
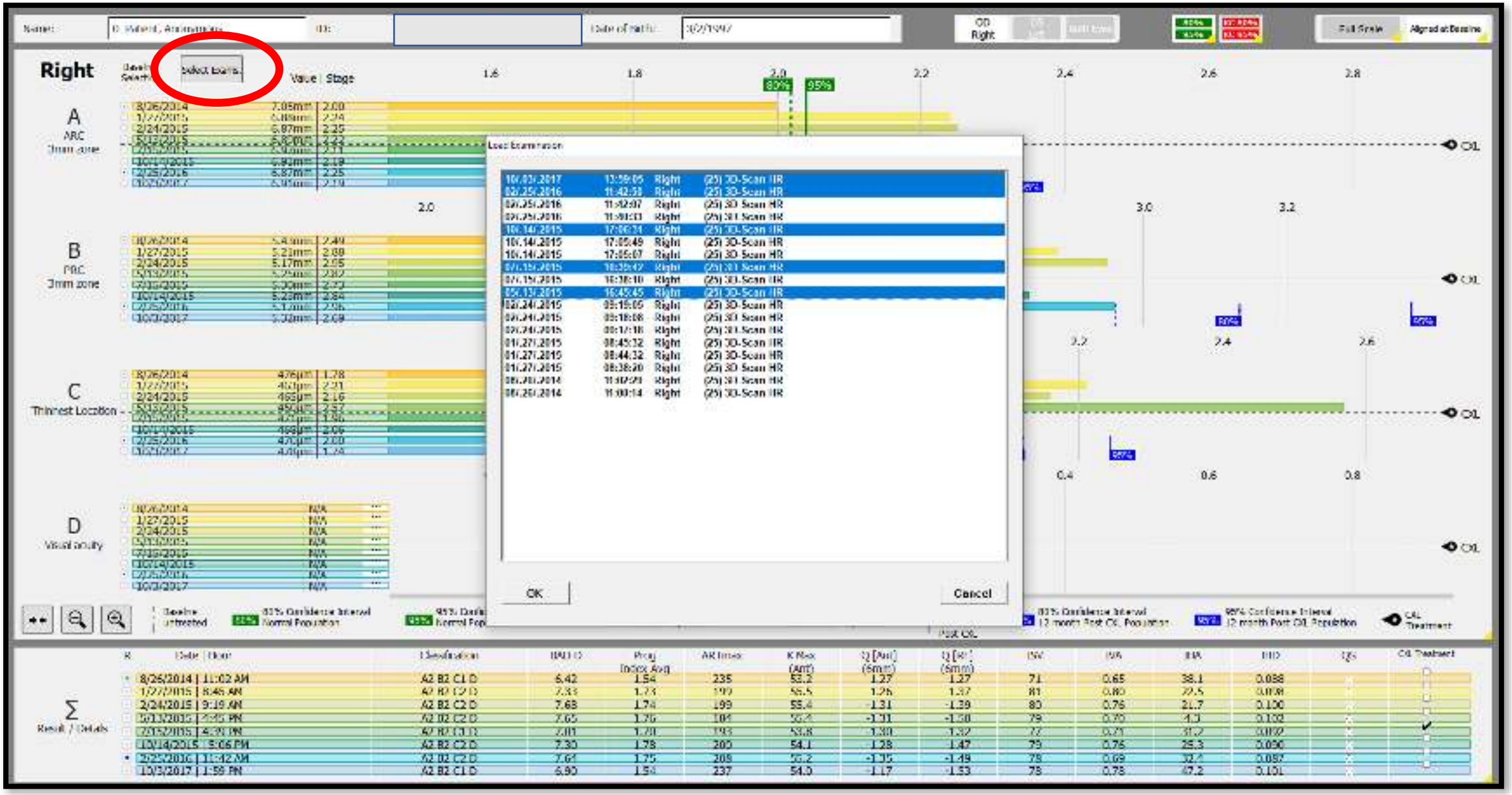
Belin ABCD Progression Display ///
Post CXL gates only appear > 1 year



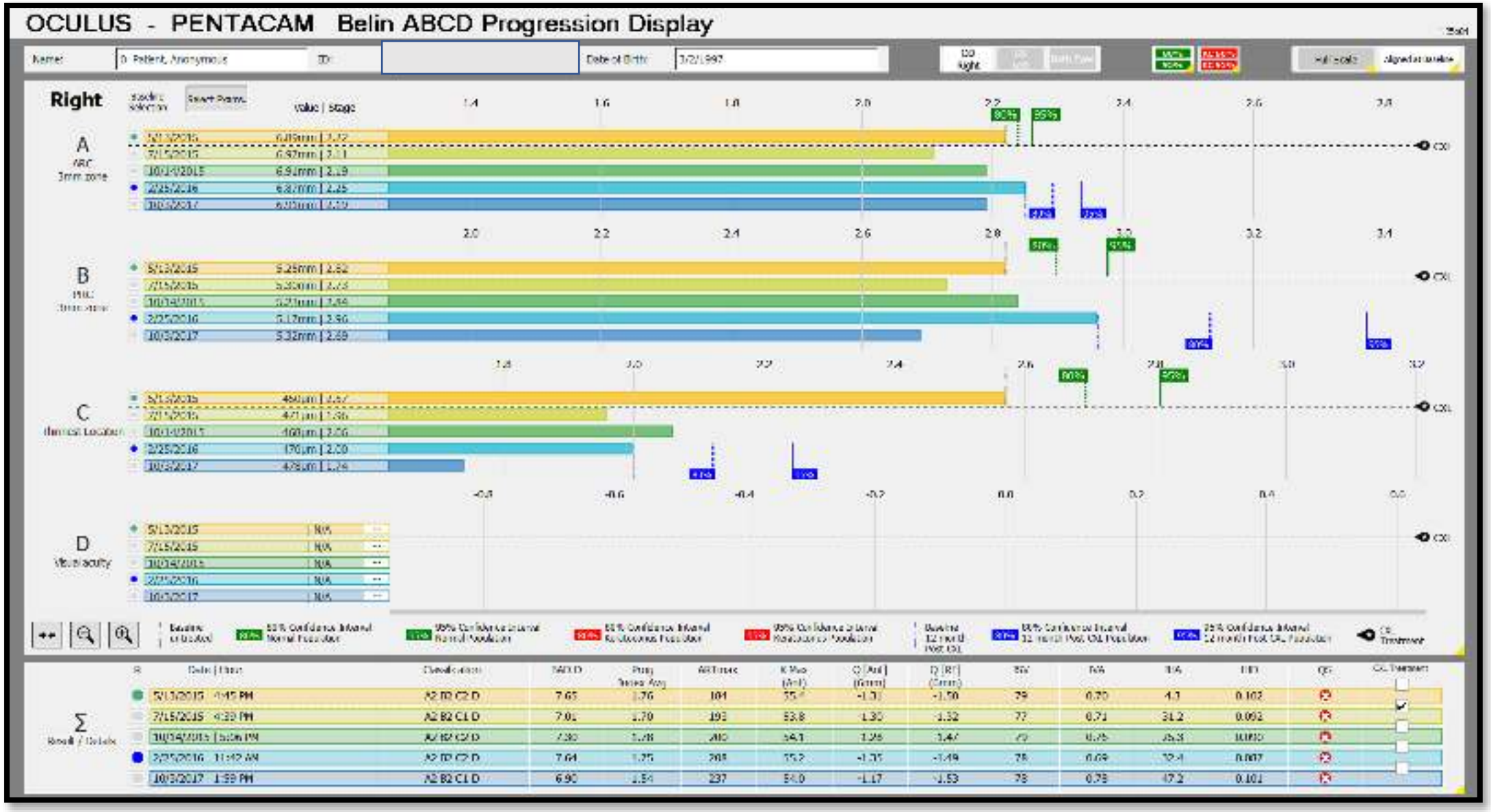
16 year-old, Selecting Green Gates



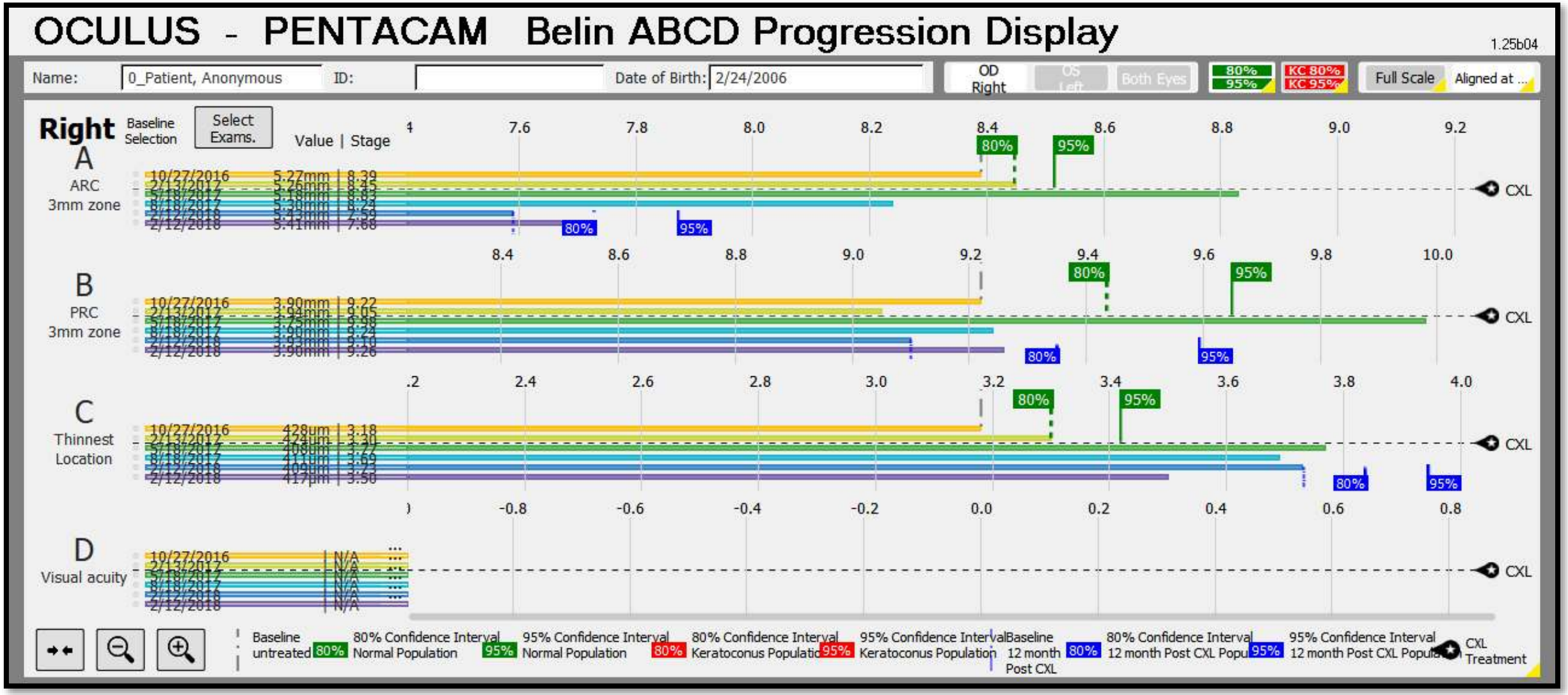
16 year-old, Post CXL Select Exam



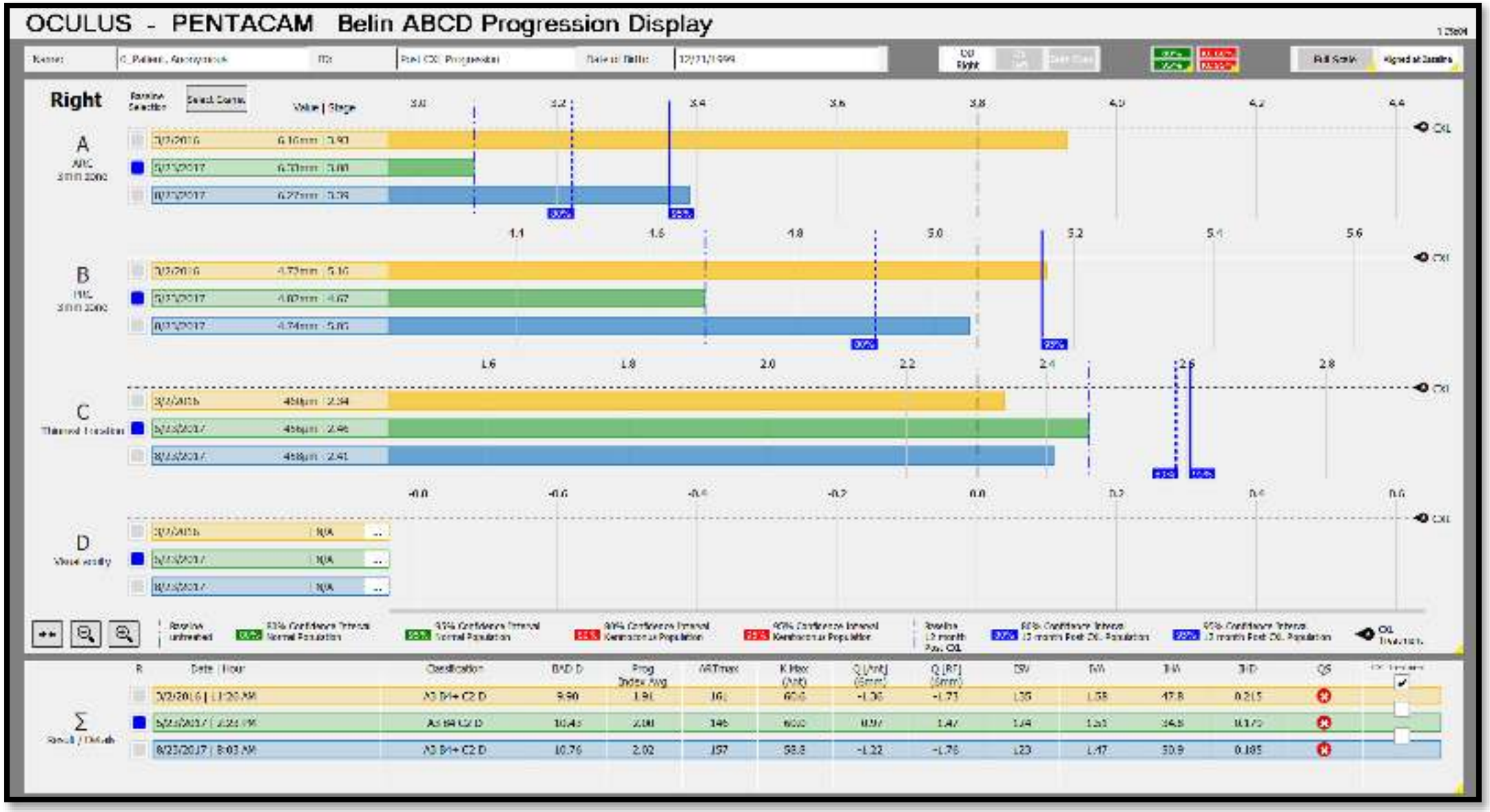
16 year-old, Post CXL Select Exam



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*

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Independent verification of the Belin ABCD Progression Display

- Changes in ABCD Keratoconus Grade following Intracorneal Ring Implantation. CORNEA 2018; 37:1431-1437
- Anatomical and Visual Effects of the MyoRing Implantation Measured by the ABCD Keratoconus Grading System. Eye & Contact Lens 2019; 23
- Evaluating Keratoconus Progression prior to Crosslinking: Kmax versus the ABCD grading system. J Cat Refract Surg 2021; 47:33-39
- Corneal stability and visual acuity one year after corneal cross-linking assessed using the ABCD Keratoconus Staging system. J Refract Surg 2021; 37:700-706
- Keratoconus Progression Classification One Year After Performed Crosslinking Method Based on ABCD Keratoconus Grading System. Acta Inform Med. 2020 Mar; 28(1): 18–23
- The ABCD Keratoconus Grading System: A Useful Tool to Estimate Keratoconus Progression in the Pediatric Population. Cornea. 2021 Oct 1;40(10):1322-1329
- Comparison of variables measured with a Scheimpflug device for evaluation of progression and detection of keratoconus. Sci Rep. 2020 Nov 9;10(1):19308
- Corneal Cross-linking for Progressive Keratoconus: Up to 13 Years of Follow-up. J Refract Surg 2020; 36:838-843
- Belin ABCD Progression Display identifies Keratoconus Progression earlier than conventional metrics. Am J Ophthalmol 2022; 236:45-52

Belin ABCD Progression Display Detects Progression 6 Months Earlier then Kmax

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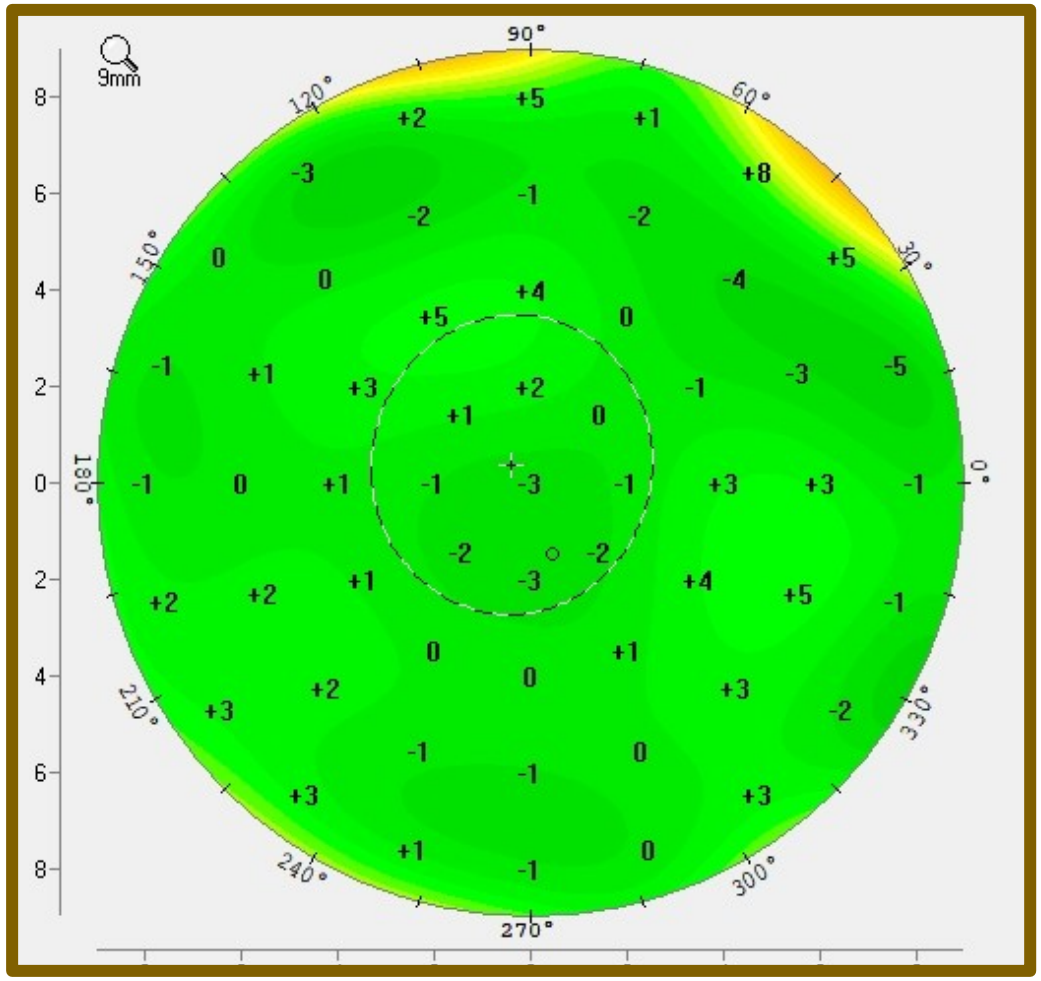
Reference Shape: BFS *vs* Toric Ellipsoid



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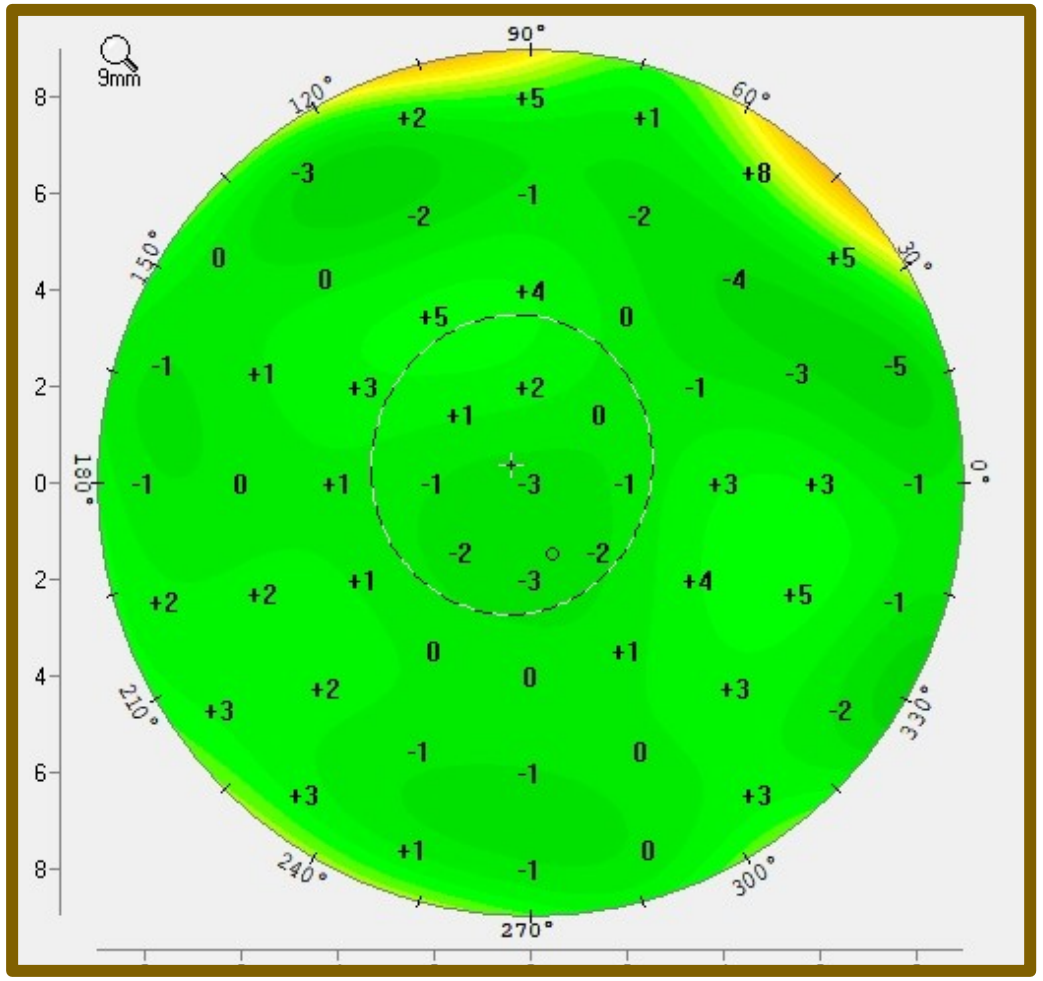
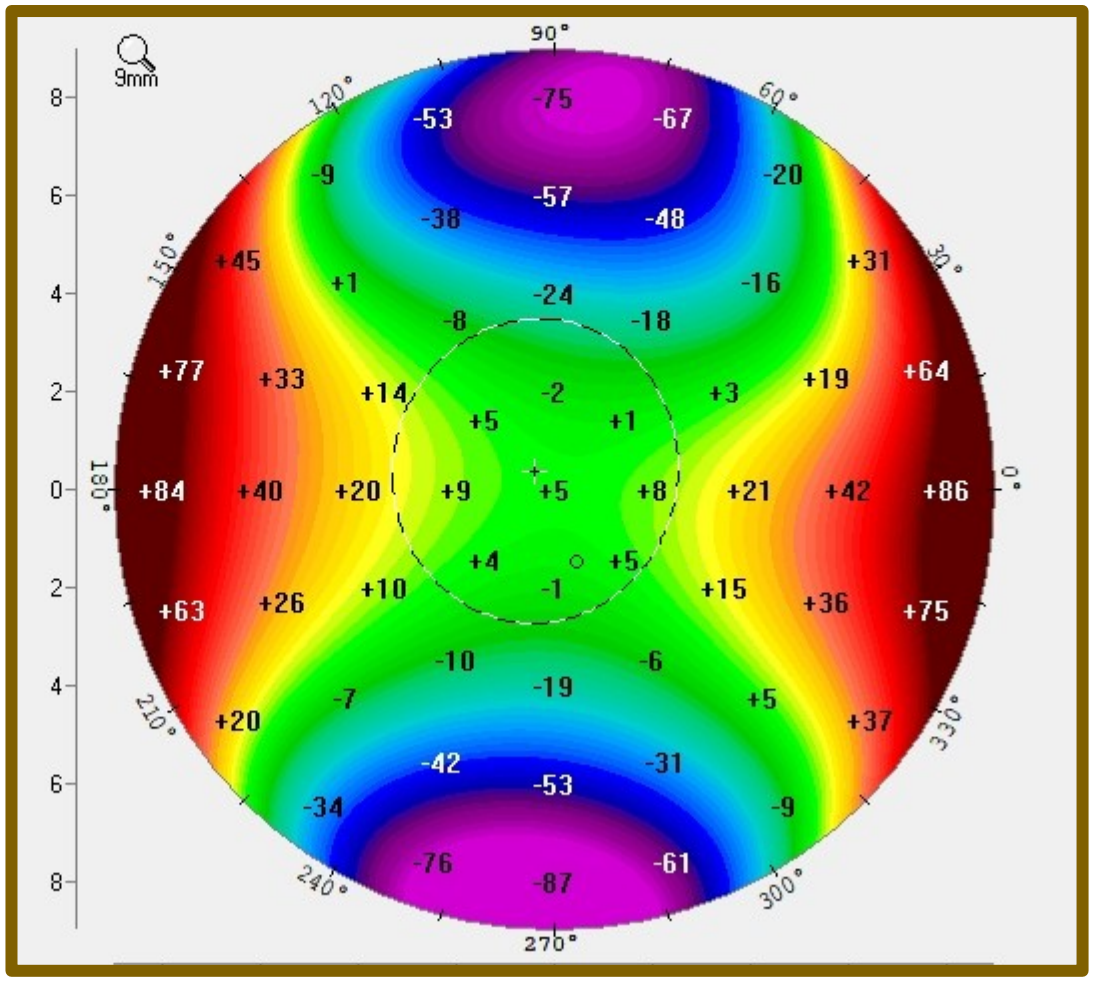
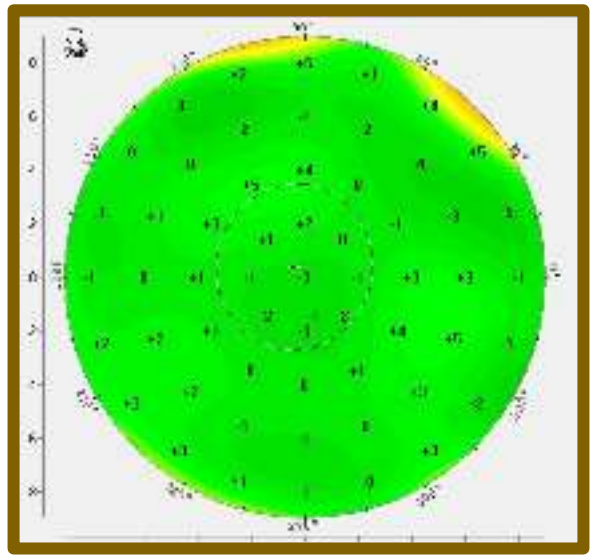
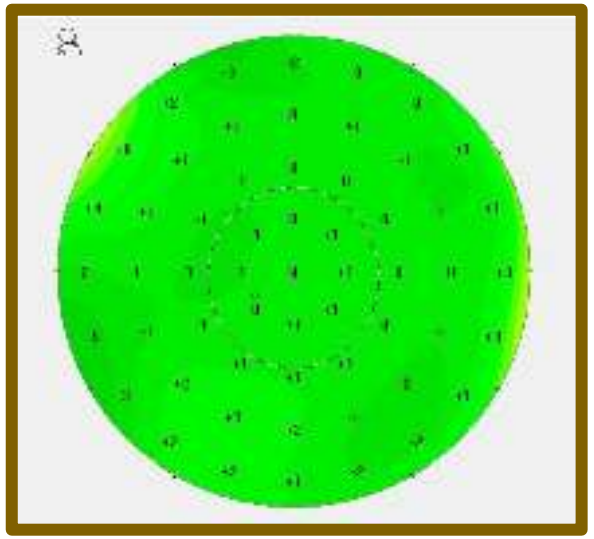


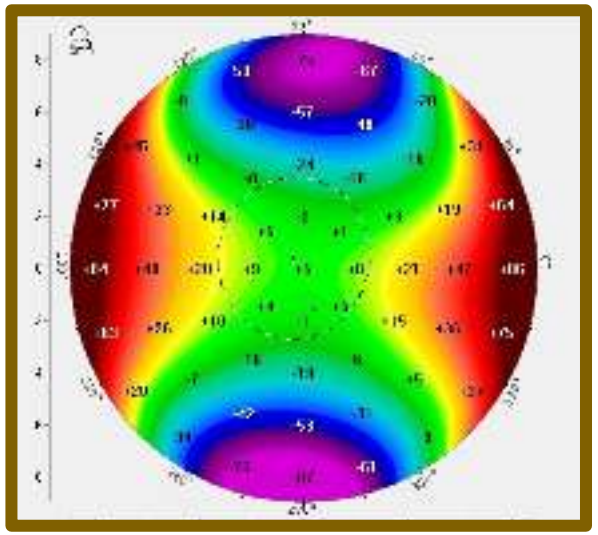


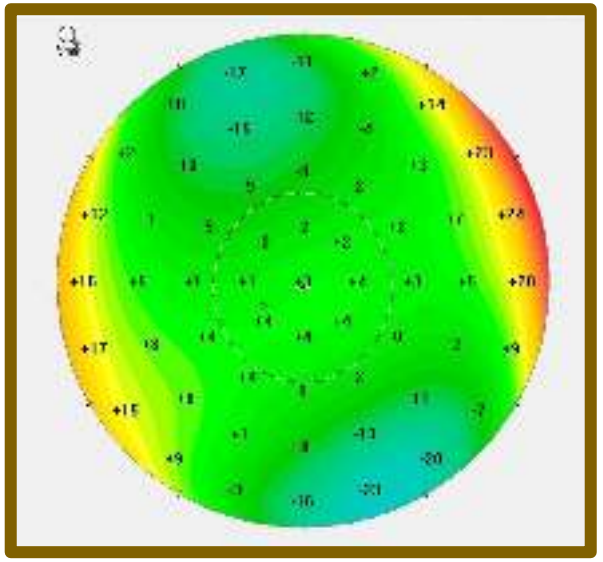
Reference Shape: BFS *vs* Toric Ellipsoid

Toric Ellipsoid









BFS

Thank You