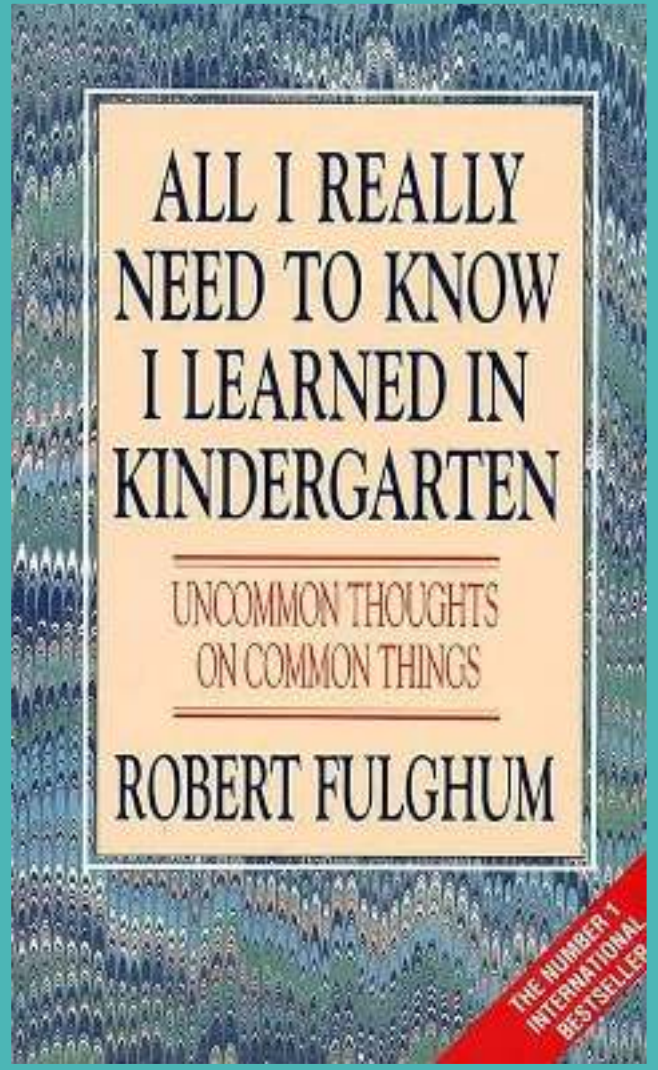

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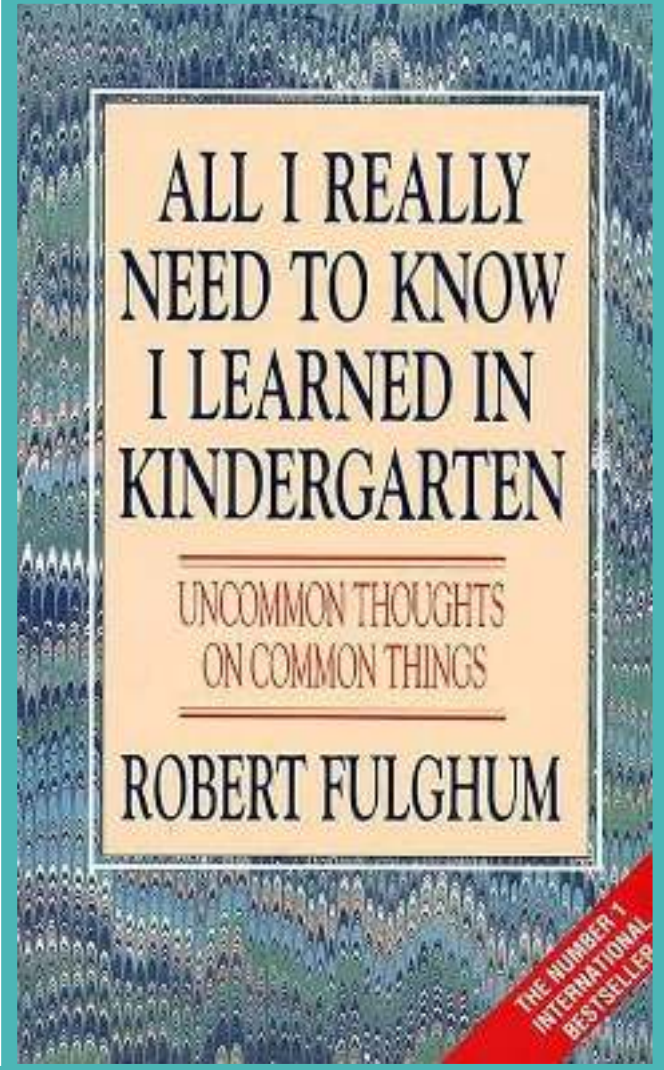

- *Scheimpflug Technology*
- *How Elevation Data is Displayed*
- Pellucid Marginal Degeneration
- Sensitivity vs Specificity
- Measuring Corneal Thickness

Scheimpflug Technology

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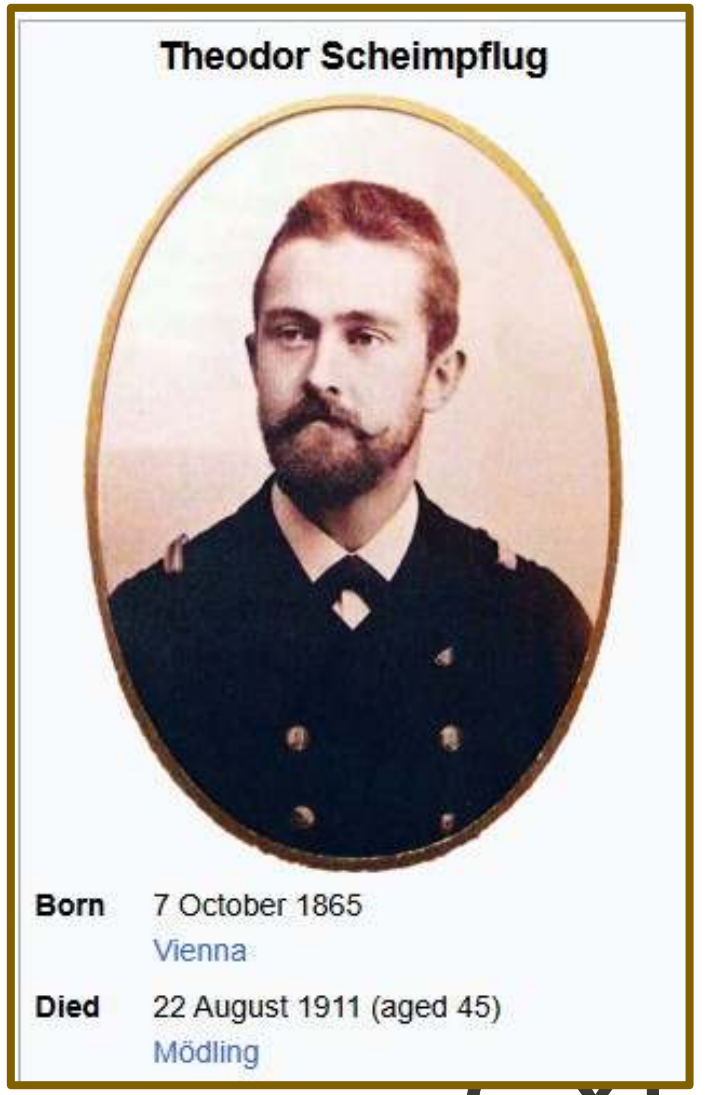
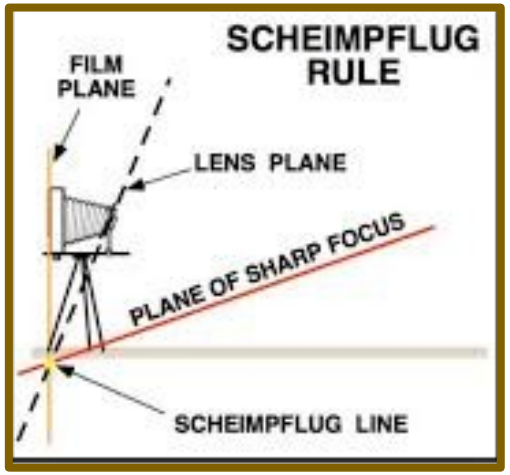
Scheimpflug Photography

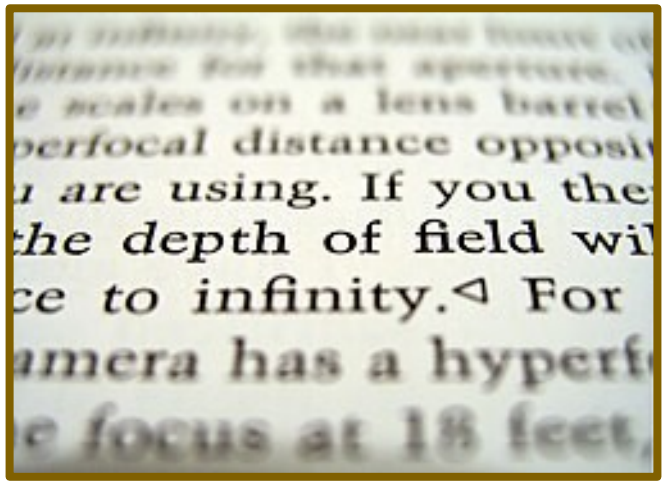
- The principle is named after Austrian army/navy Captain Theodor Scheimpflug, who used it in devising a method and apparatus for correcting distortion in aerial photographs



Scheimpflug Principal

- In a conventional camera, the lens plane and the image plane (sensor or film) are parallel, meaning only subjects parallel to the image plane can be rendered entirely sharp.
- The Scheimpflug principle states that if the object plane, the lens plane, and the image plane all intersect along a single common line (known as the Scheimpflug line), then the entire object plane will be in sharp focus.

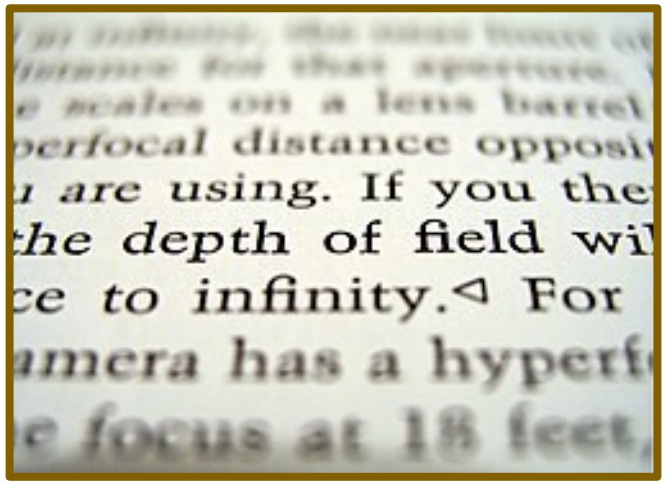




CXL

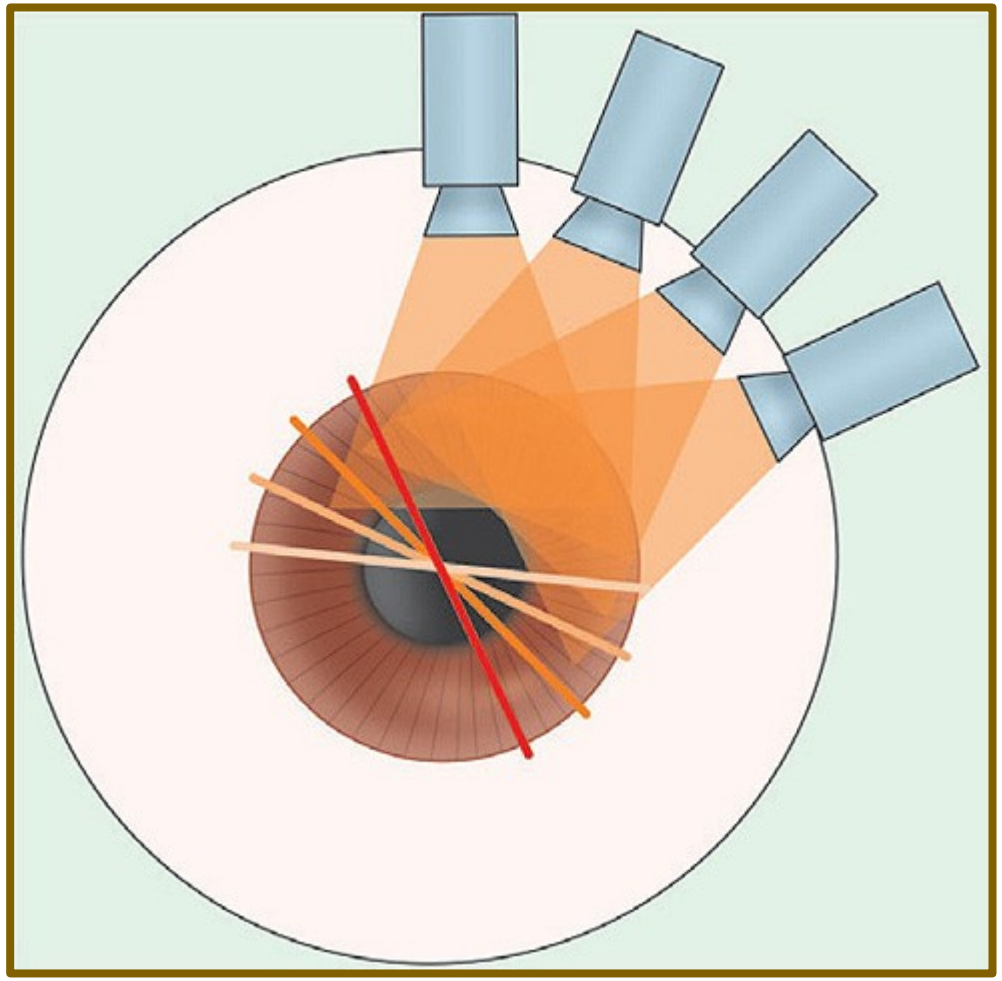
Scheimpflug Principal

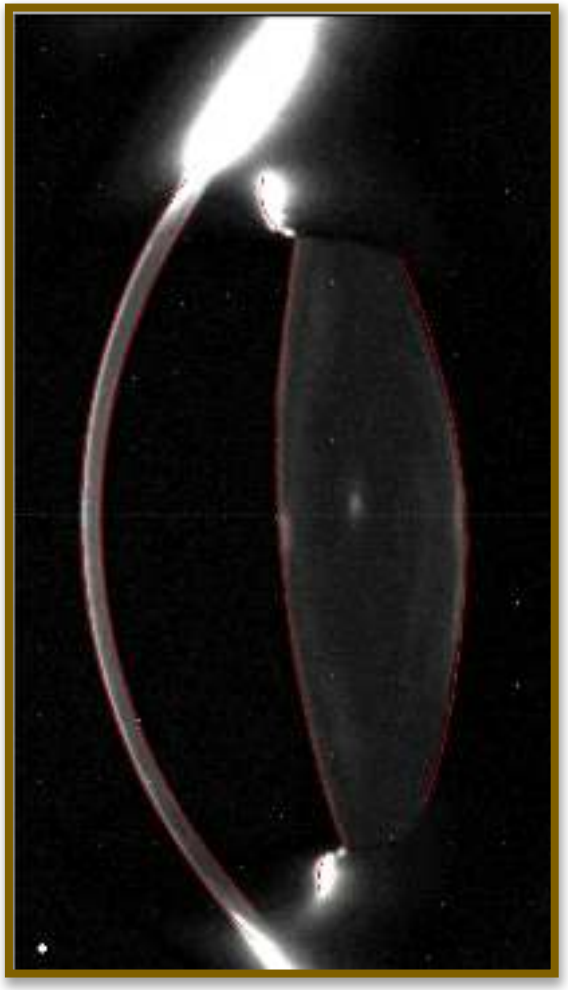
- **EXTENDED DEPTH OF FIELD** – allows for a vast depth of field across an oblique field without needing to use a very small aperture, which avoids image degradation from diffraction and **allows for faster shutter speeds**



Scheimpflug Imaging in Medicine

- Non-invasive technique that uses a rotating camera to create a cross-section, 3D image of the anterior segment of the eye.
- Provides detailed data on the cornea, anterior chamber, lens and angle
- Limited to Ophthalmology as requires optical cross-section



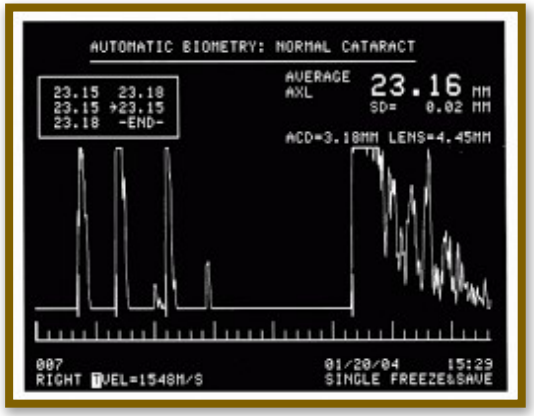


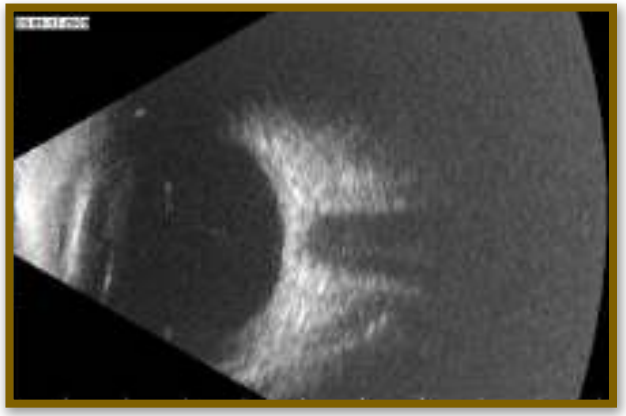
Scheimpflug *vs* OCT

- Total Scan Time vs Image Acquisition Time
  - OCT has faster Scan acquisition time
    - < 0.125 seconds vs 2 seconds
  - Scheimpflug has faster Image acquisition time
    - < 0.001 seconds vs 0.125 seconds

Scheimpflug *vs* OCT

- Similar to comparing A-scan to B-scan.
- A-scan is better at “measuring”
  - (axial length)
- B-scan is better at “imaging”





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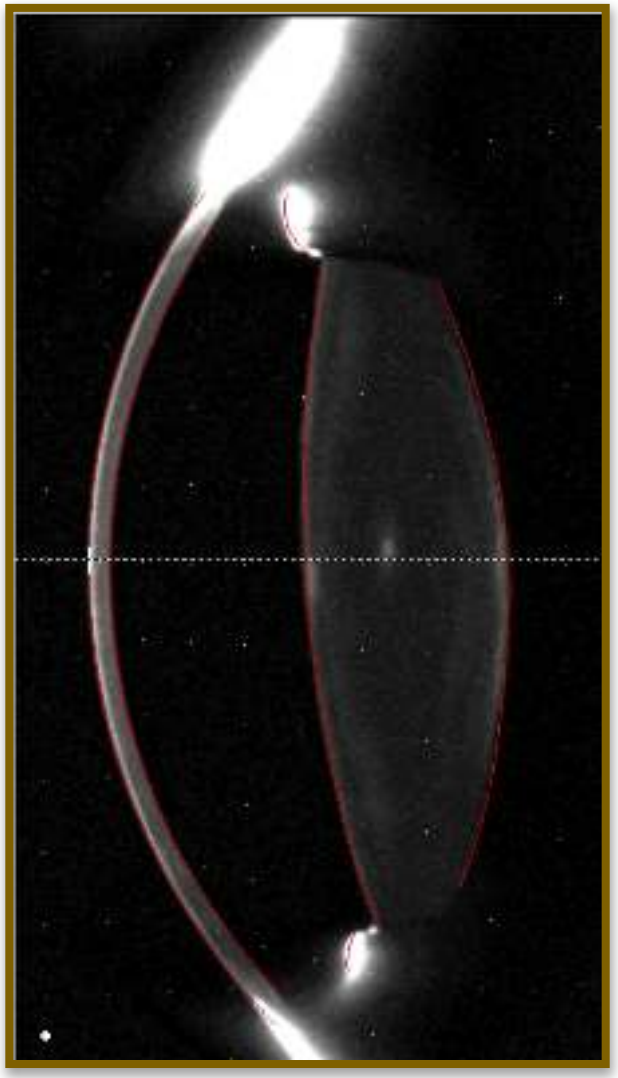
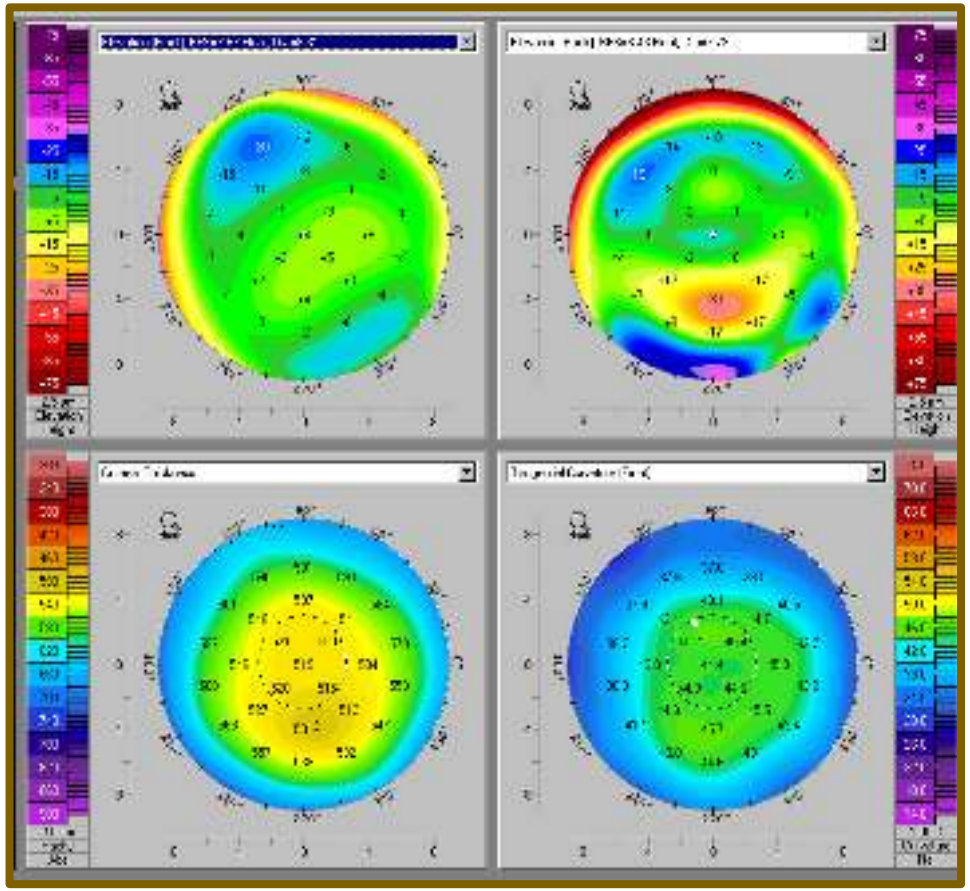
3 – Dimensional Analysis

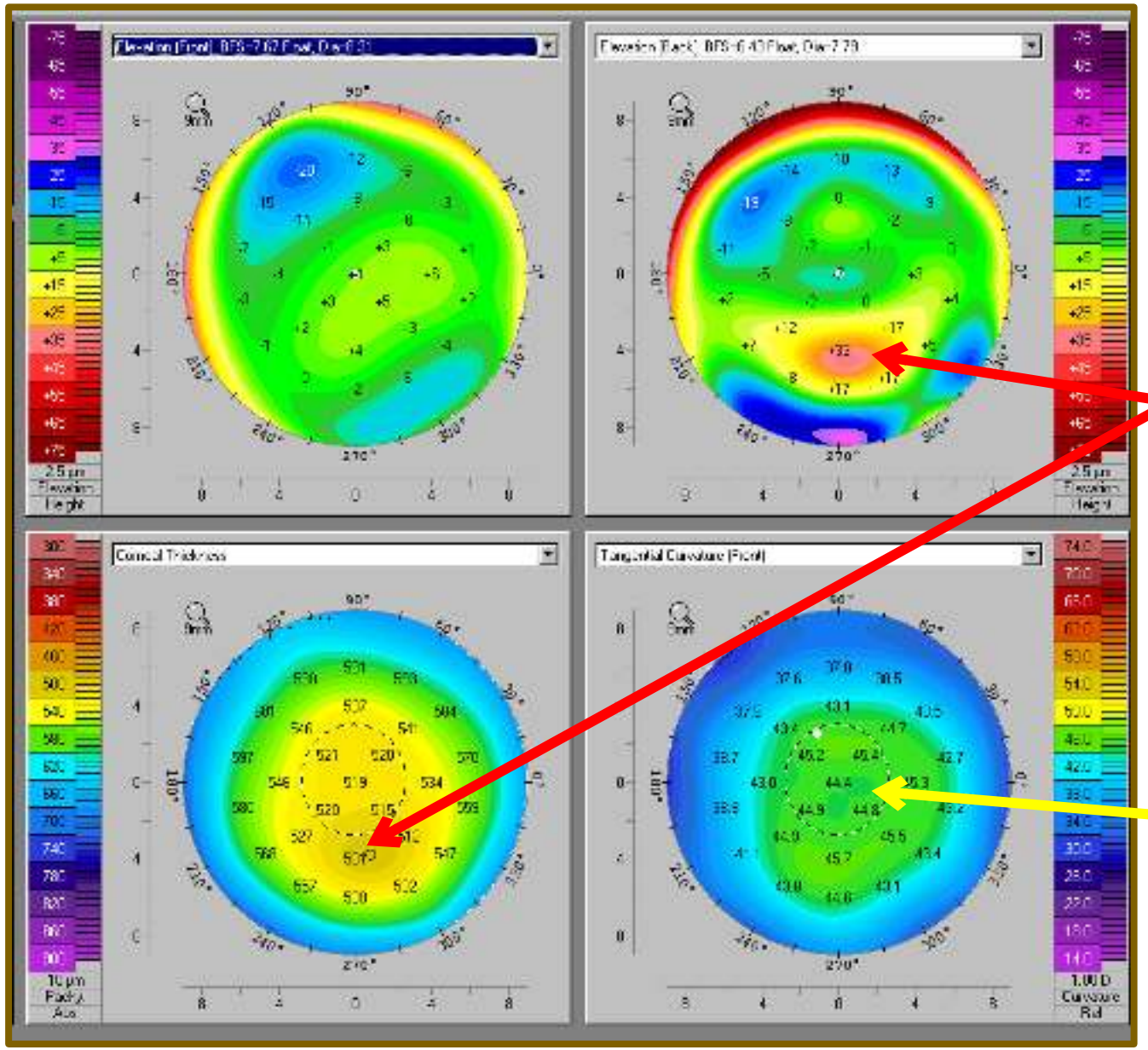
- The major advance of complete anterior segment analysis is the ability to measure the posterior corneal surface and a full corneal thickness map



What is "*Subclinical*" Keratoconus ?

- It is TRUE Keratoconus
  - It is not "*suspect*"
- Corneas are abnormal
  - Abnormal posterior elevation
  - Abnormal pachymetric progression
  - But normal anterior curvature
    - Patients retain good vision
      - "subclinical Keratoconus"

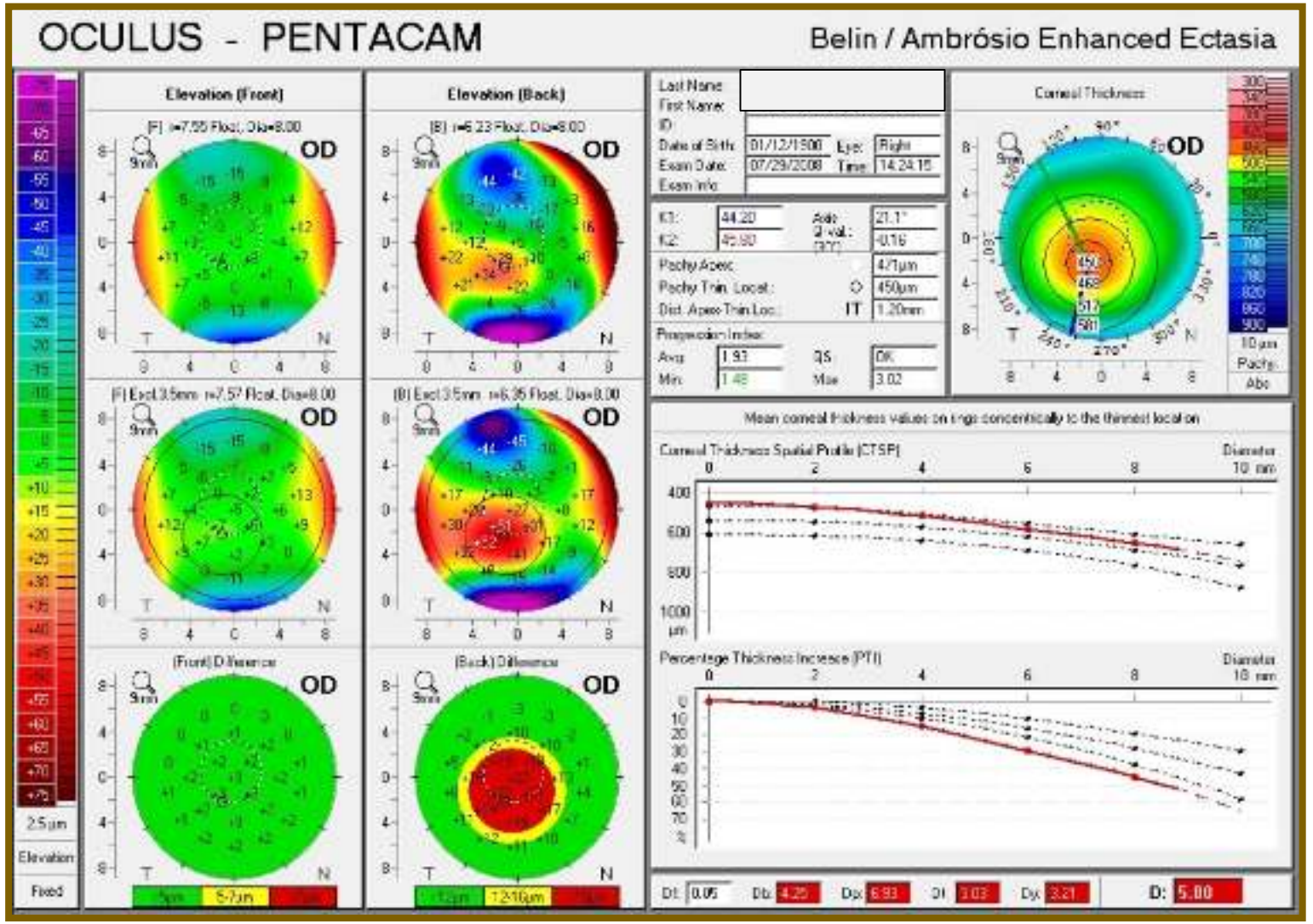




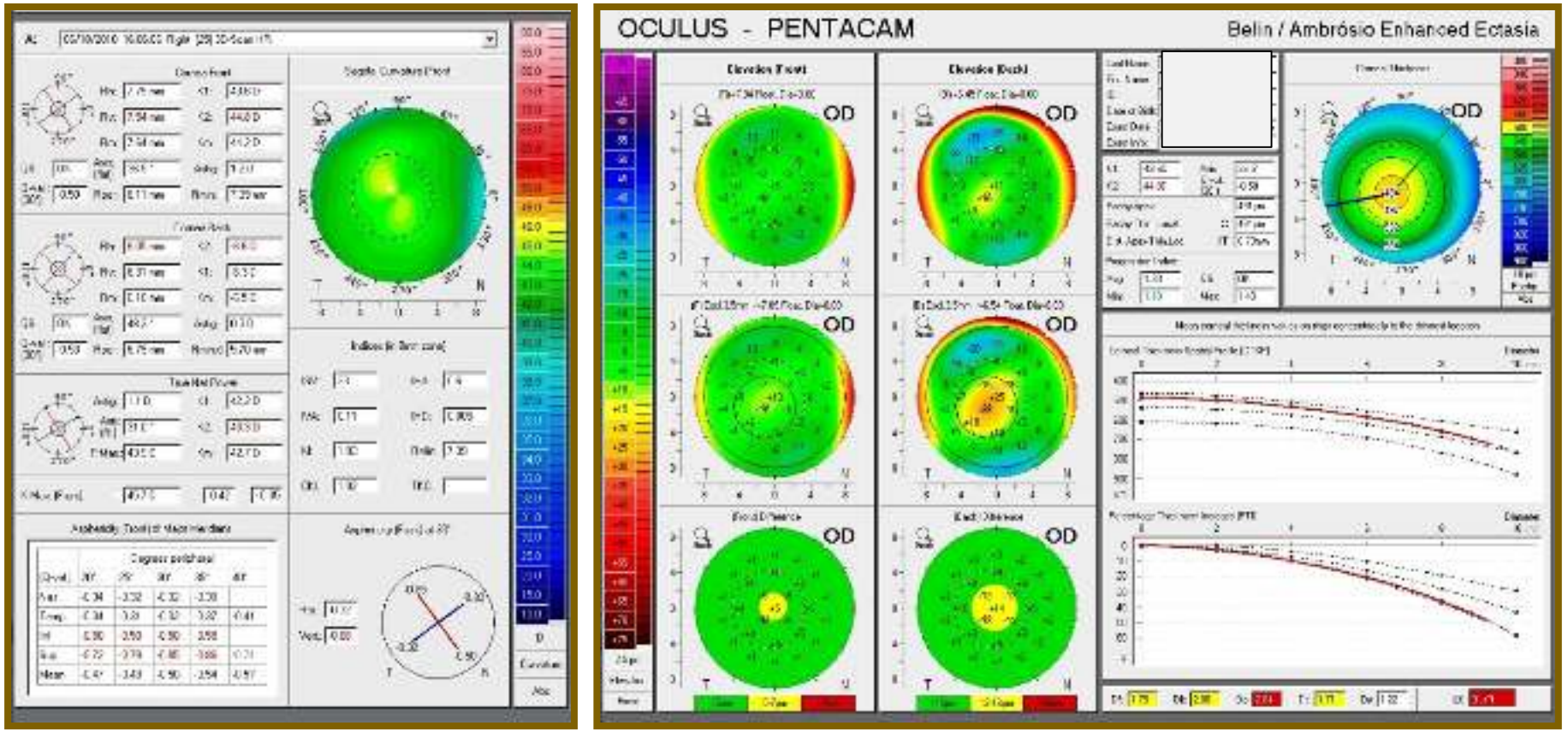
Abnormal posterior elevation & pachymetric progression

Normal anterior curvature

"Subclinical" Keratoconus



Advantages of Tomography



Normal by Curvature - Clearly Abnormal by Tomography

Anterior *vs* Posterior Cornea KCN Detection

Parameter	Cut-off	AUC	Sensitivity	Specificty	*p*
Ele_F_BFS_8mm_Apex_	> 3	0.834	70.1	94.5	0.0001
Ele_F_BFS_8mm_Max._4mm_Zone_	> 12	0.957	87.6	96.5	0.0001
Ele_F_BFS_8mm_Thinnest_	> 5	0.973	91.5	99.0	0.0001
Ele_B_BFS_8mm_Apex_	> 6	0.858	72.3	93.5	0.0001
Ele_B_BFS_8mm_Max._4mm_Zone_	> 22	0.976	92.7	97.0	0.0001
Ele_B_BFS_8mm_Thinnest_	> 12	0.983	94.4	98.0	0.0001

Fernando Faria-Correia, Isaac Ramos, Bernardo Lopes, Marcella P. Salomão, Allan Luz, Rosane O. Correa, Lívia Faria Jordão, Belin MW, Renato Ambrósio Jr, Int J Kerat Ect Cor Dis 2012; 1(2):92-99

Central Pachymetry *vs* Full Pachymetric

Parameter	Cut-off	AUC	Sensitivity	Specificity	*p*
Pach Apex	≤ 517	0.932	85.9	87.0	0.0001
Pach Min	≤ 494	0.956	81.9	97.5	0.0001
PI *avg*	> 1.05	0.996	97.7	99.0	0.0001
PI *max*	> 1.42	0.996	95.5	100	0.0001

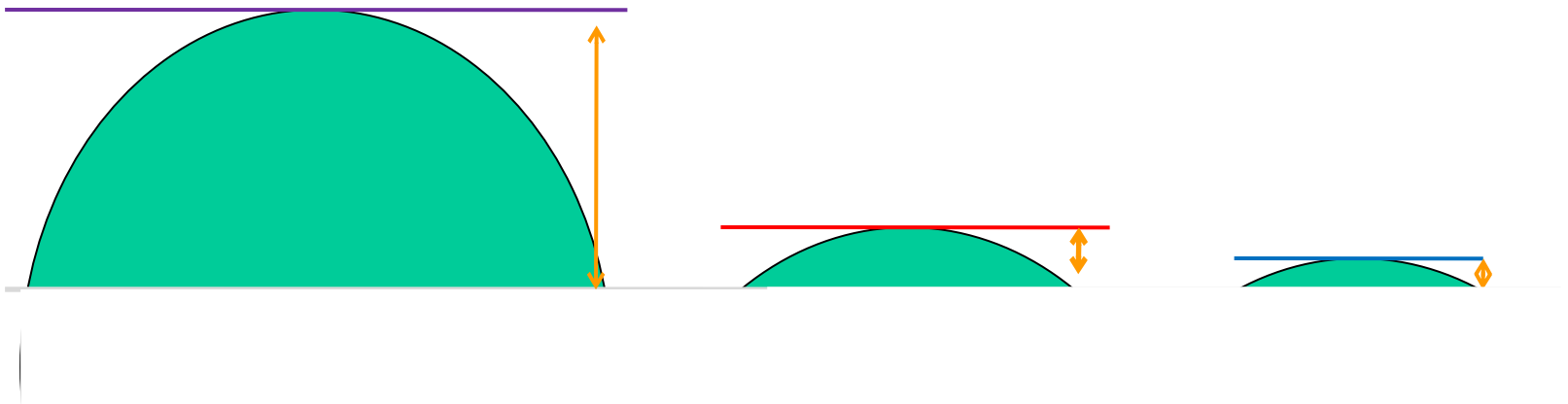
Fernando Faria-Correia, MD, Isaac Ramos, MD; Bernardo Lopes, MD; Marcella P. Salomão, MD; Allan Luz, MD; Rosane O. Correa, MD; Lívia Faria Jordão, MD; Renato Ambrósio Jr, MD, PhD

Can Elevation based systems derive accurate curvature ?

Truth vs Myth

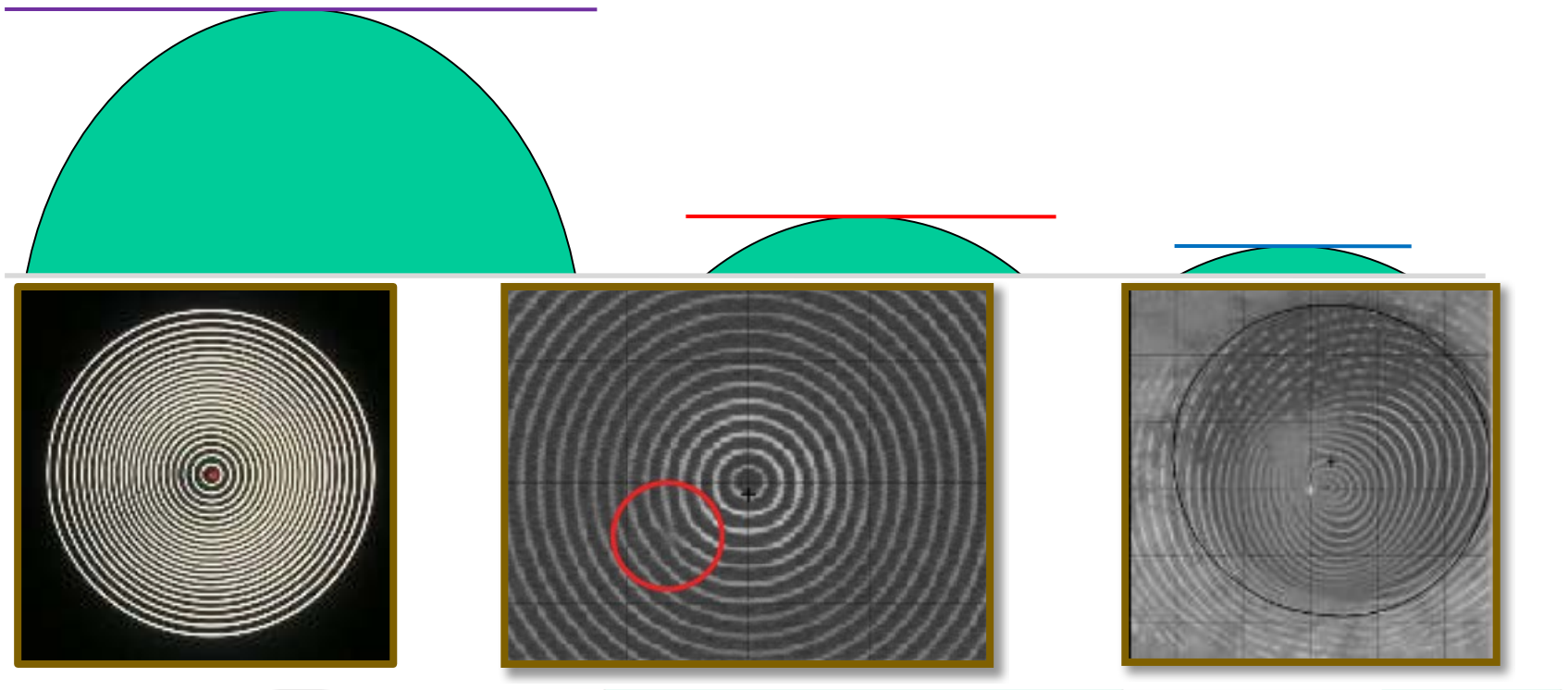
Placido *vs* Elevation

- Assertion that Elevation is not as sensitive as Placido is incorrect

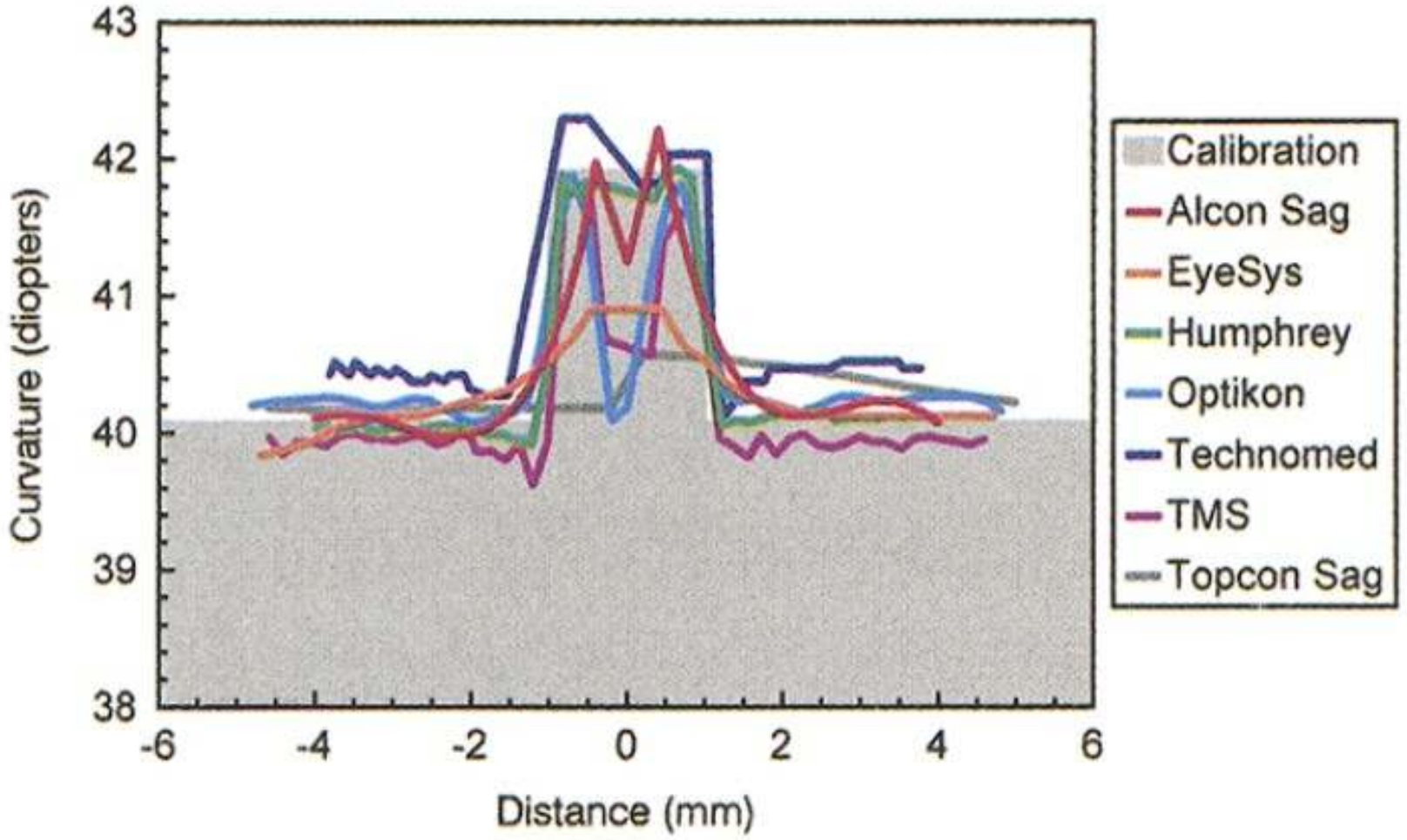


Small Elevation Change but Equal Curvature

Placido systems cannot read minute changes because this would require the rings to be very thin and close causing them to merge (*cross*) and become unreadable with normal levels of distortion.

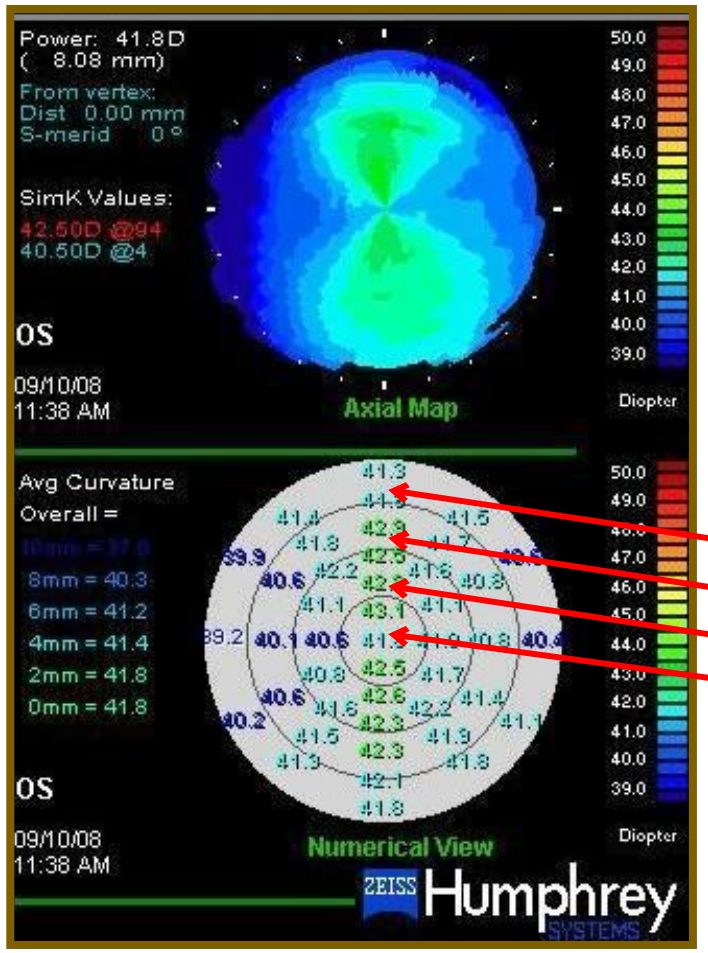


- The assertion that Elevation systems are not as sensitive as Placido systems is incorrect
- Testing was/is done on highly reflective spherical test objects – *Ball Bearings*
  - ANSI / FDA standard testing
    - Testing on Spherical test objects has limited clinical relevance

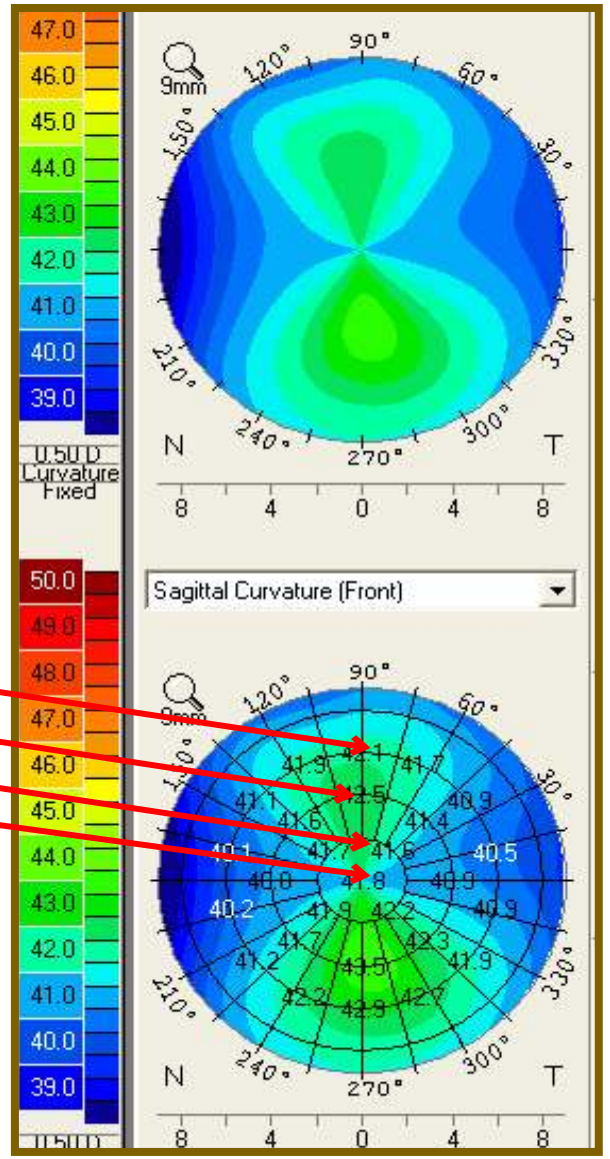


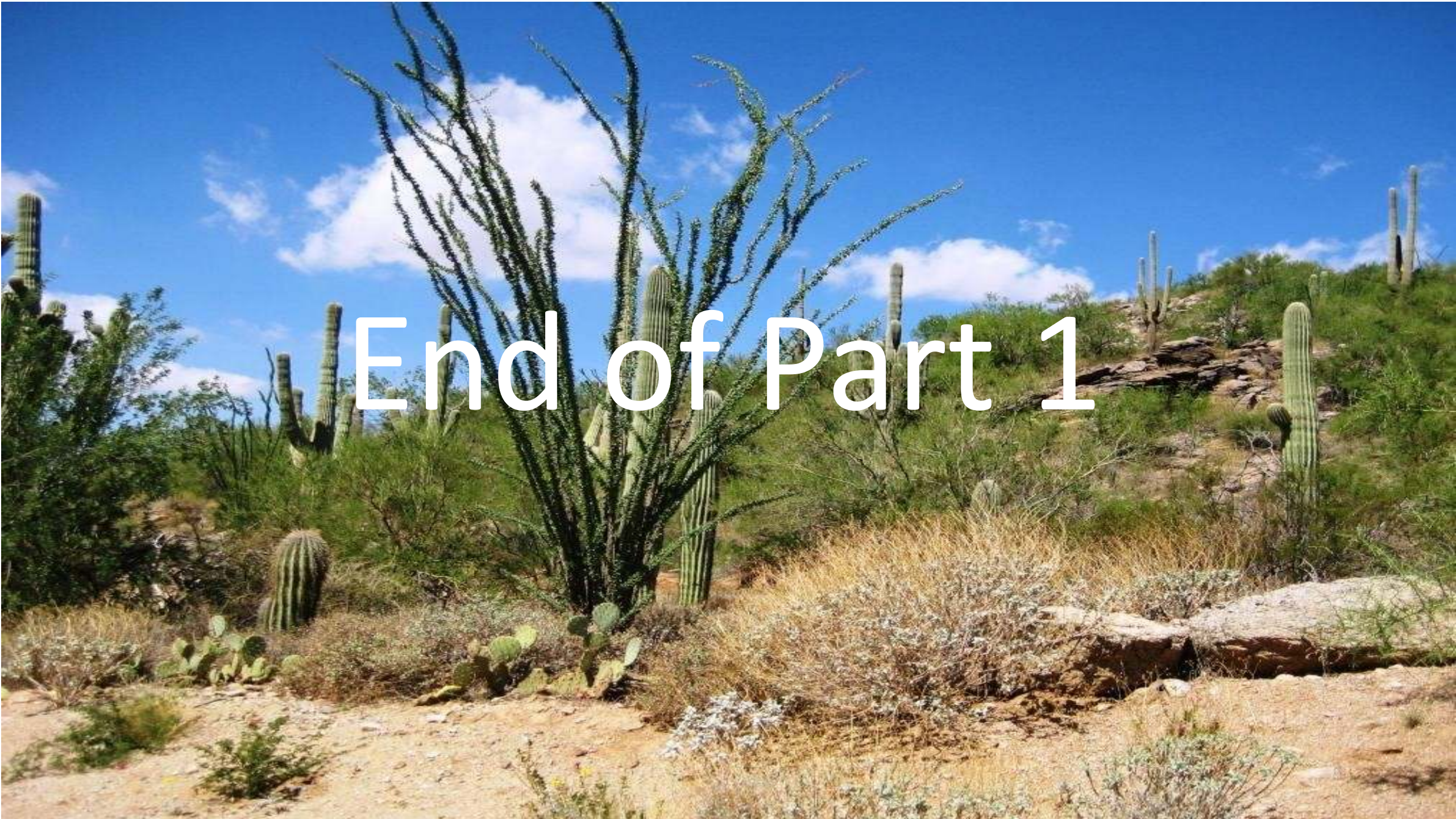
Belin MW, Ratliff CD: Evaluating Data Acquisition and Smoothing Functions of Currently Available Videokeratoscopes. J Cataract Refract Surg 22:421-426, 1996.

Curvature Comparison



Compared Average K values at the 0mm, 2mm, 4mm, and 6mm zones




End of Part 1

How Elevation Data is Displayed

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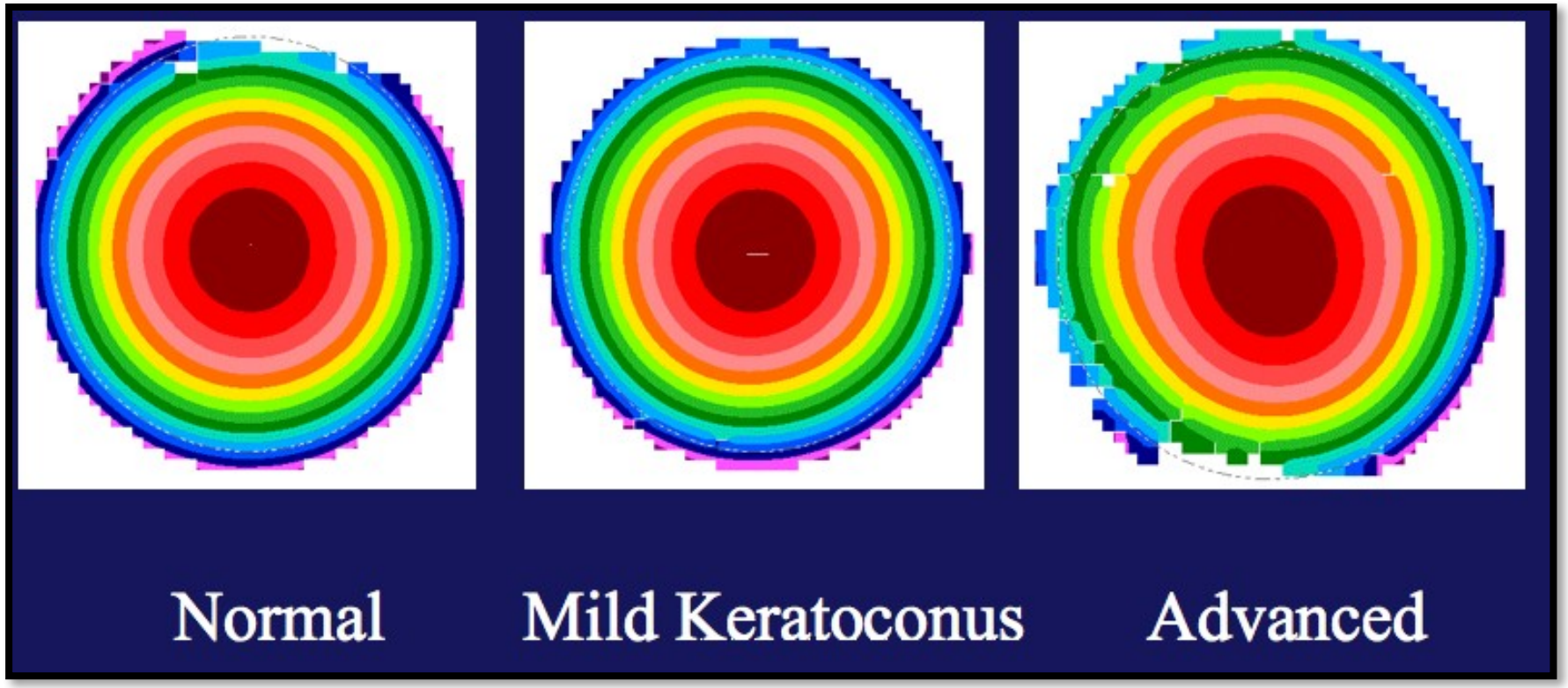
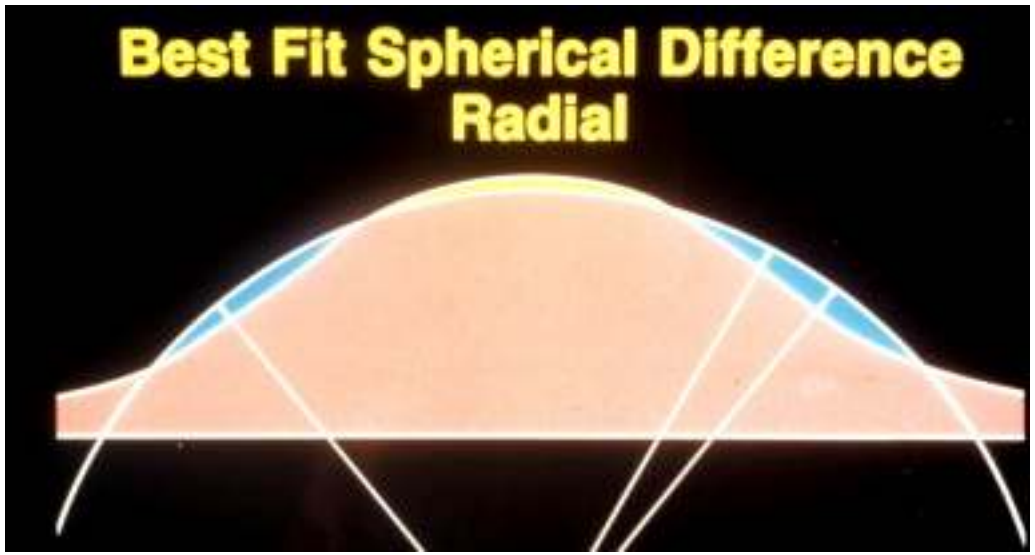
How is Elevation Data Displayed

- "RAW" elevation maps are rarely used

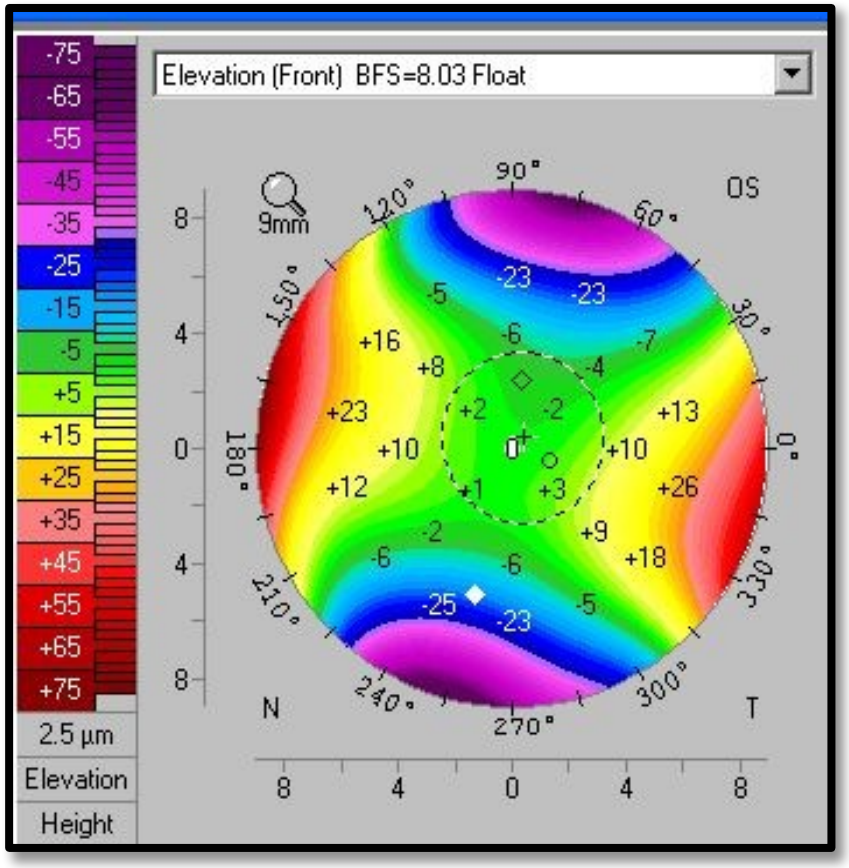


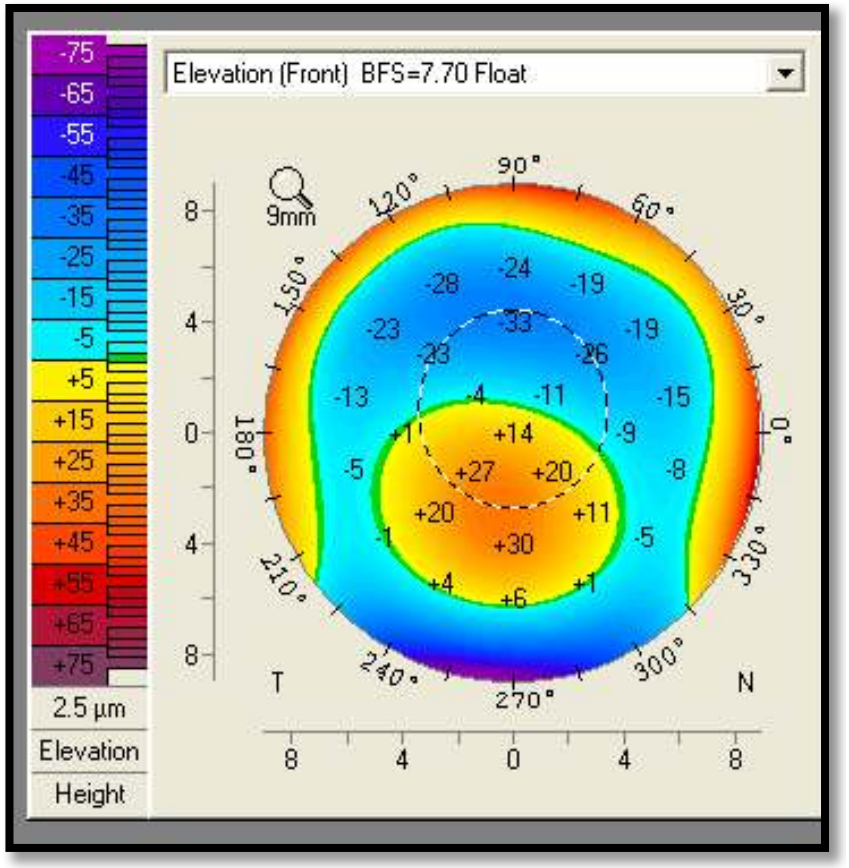
How is Elevation Data Displayed

- The most common method is to compare (*amplify*) the raw elevation data against some common shape
  - The most common shape used is the Best Fit Sphere (BFS)
    - Other shapes can also be used
      - Ellipse
      - Toric Ellipsoid

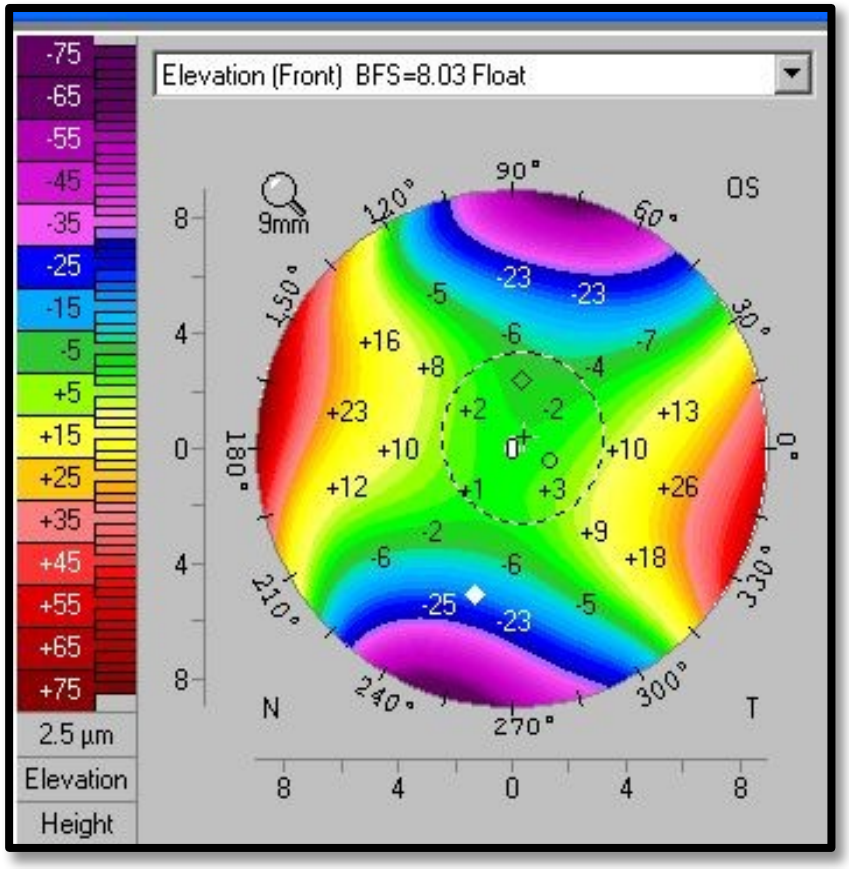


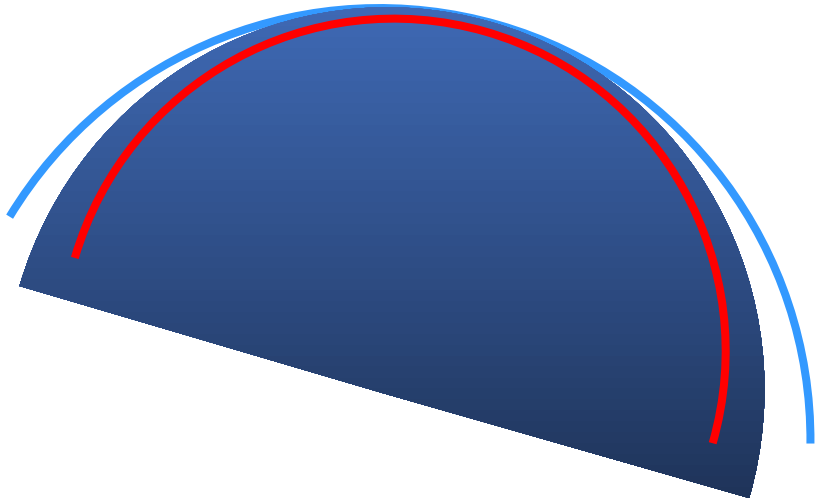
Astigmatism vs. Keratoconus





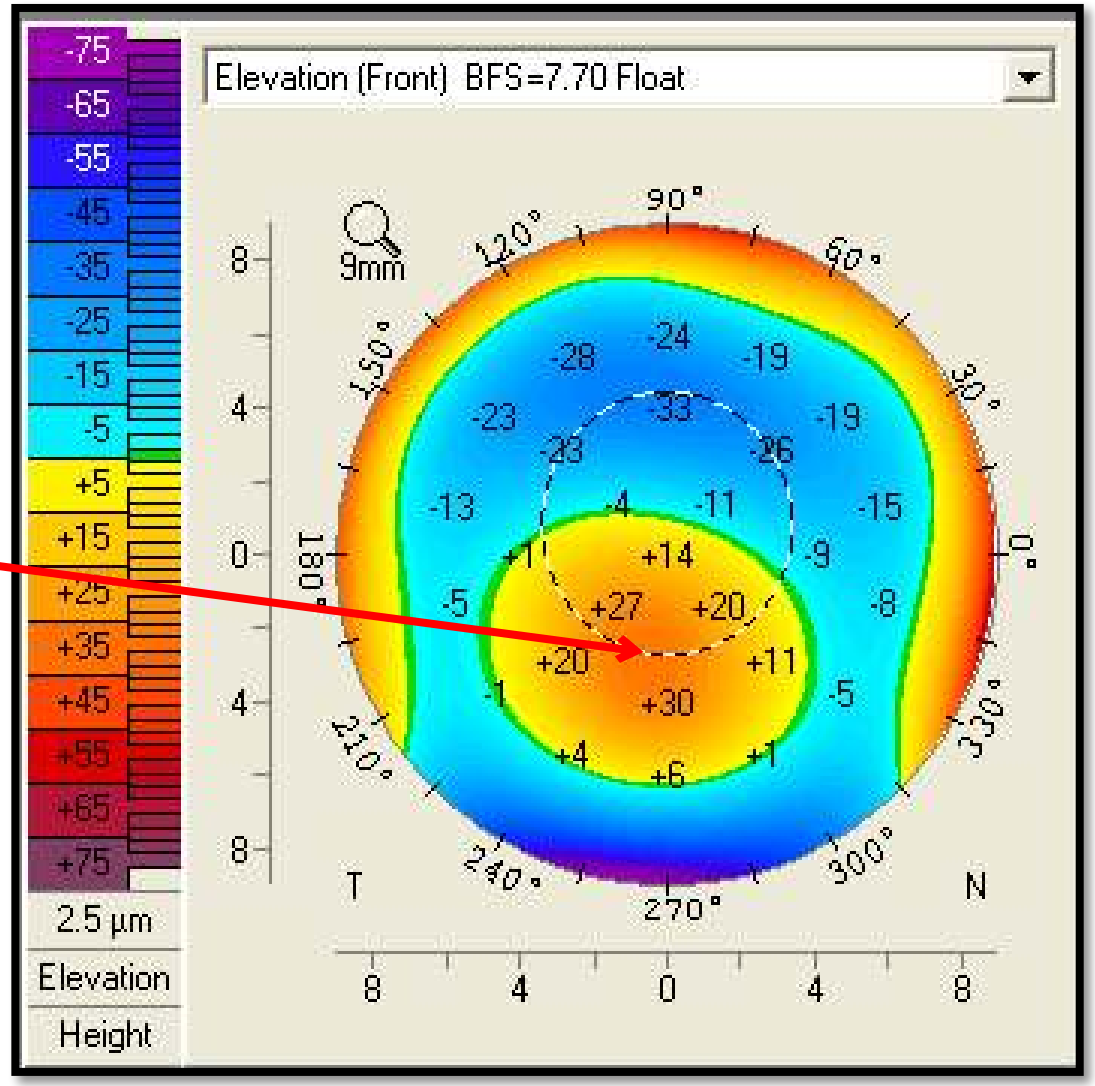
Astigmatism



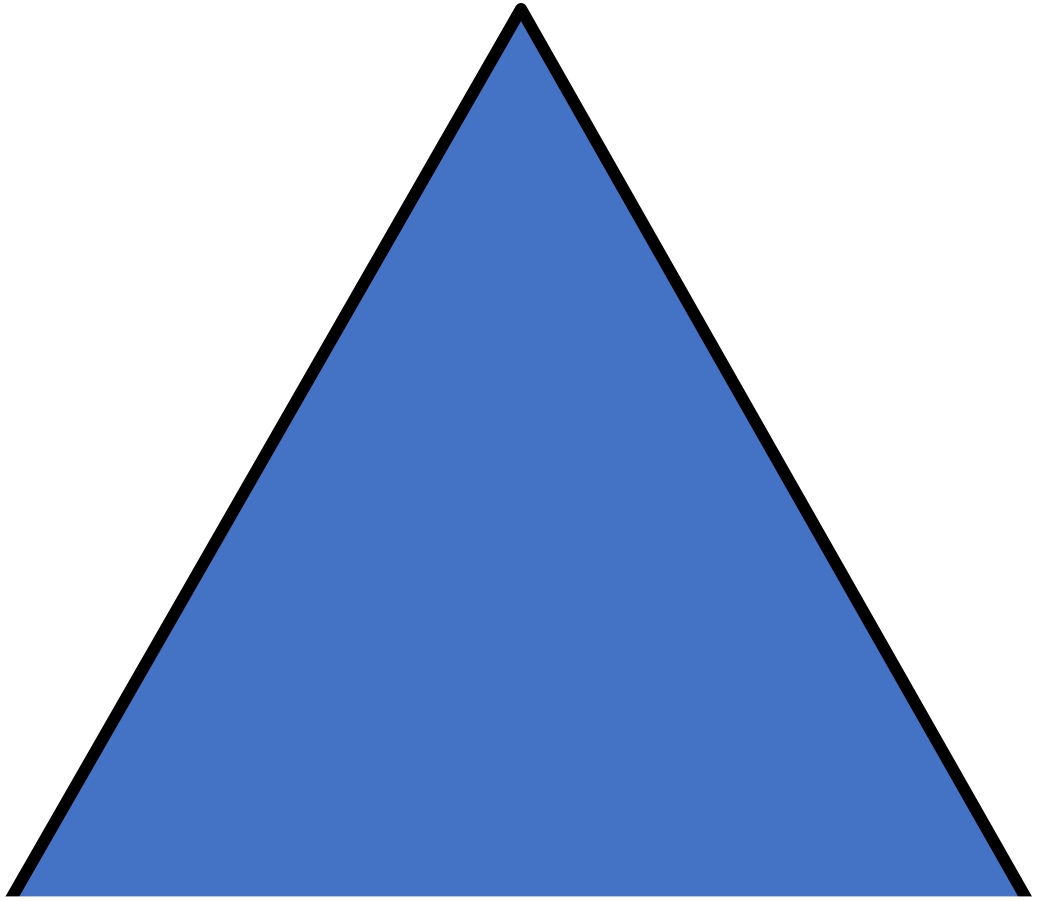


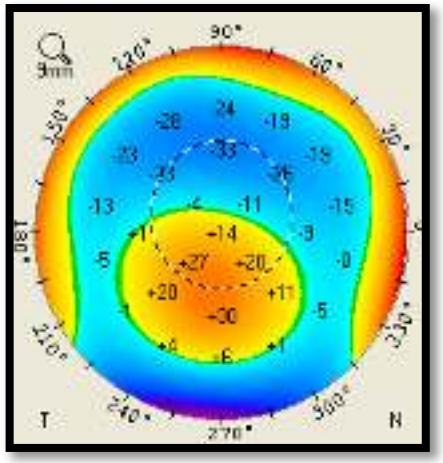
Keratoconus

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



Derivation of Keratoconus Pattern





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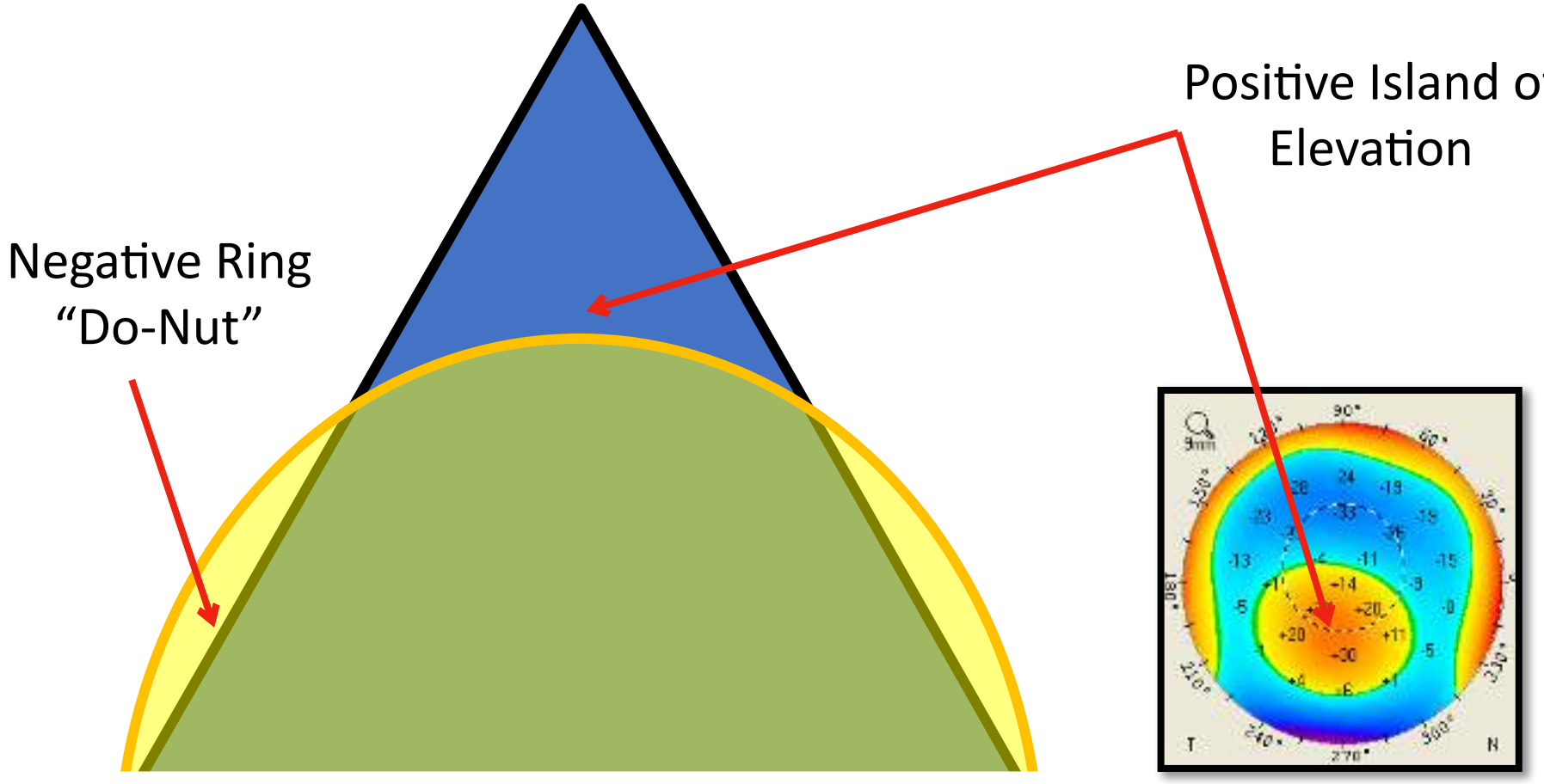
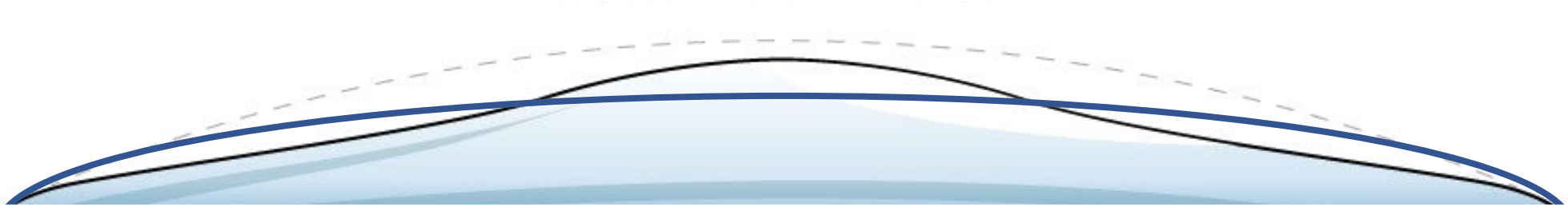
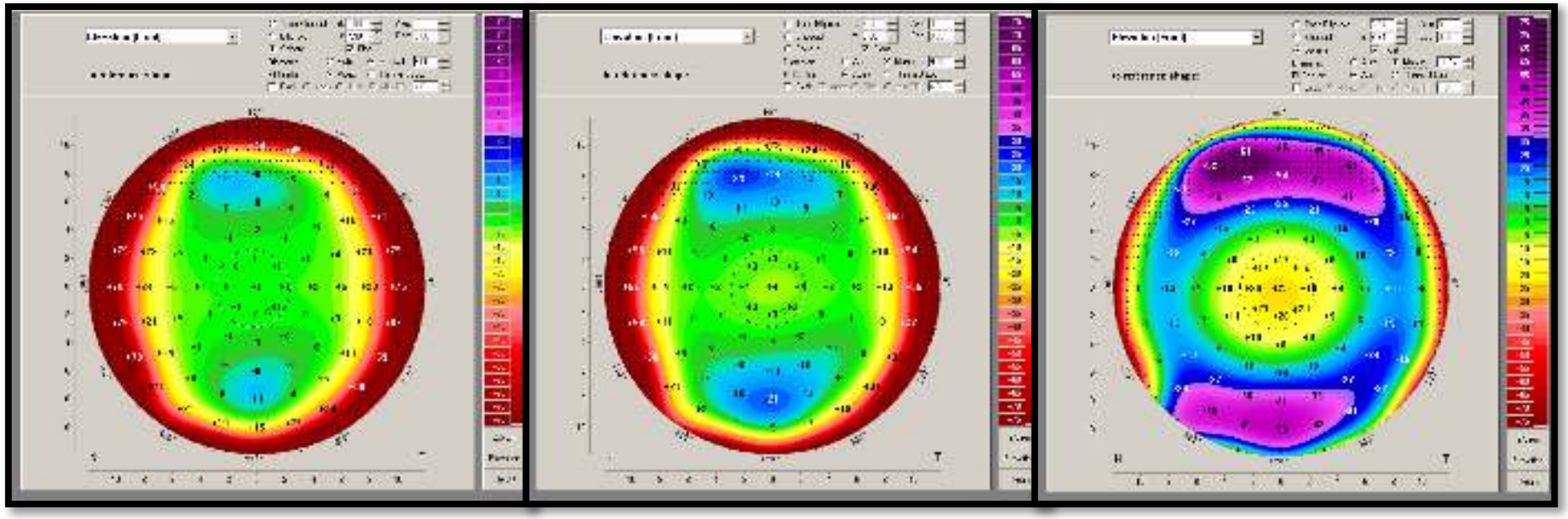


Problem Normal Eye is Aspheric



A “normal” eye will show a “positive island of elevation” if compared against a best-fit-sphere utilizing the entire cornea

Why do we use an 8.0 mm optical zone for the BFS



Diameter = 7.0 mm Diameter = 9.0 mm Diameter = 11.94 mm

A BFS from the central 8.0 mm hides the normal asphericity of the cornea

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End of Part 2

Pellucid Marginal Degeneration

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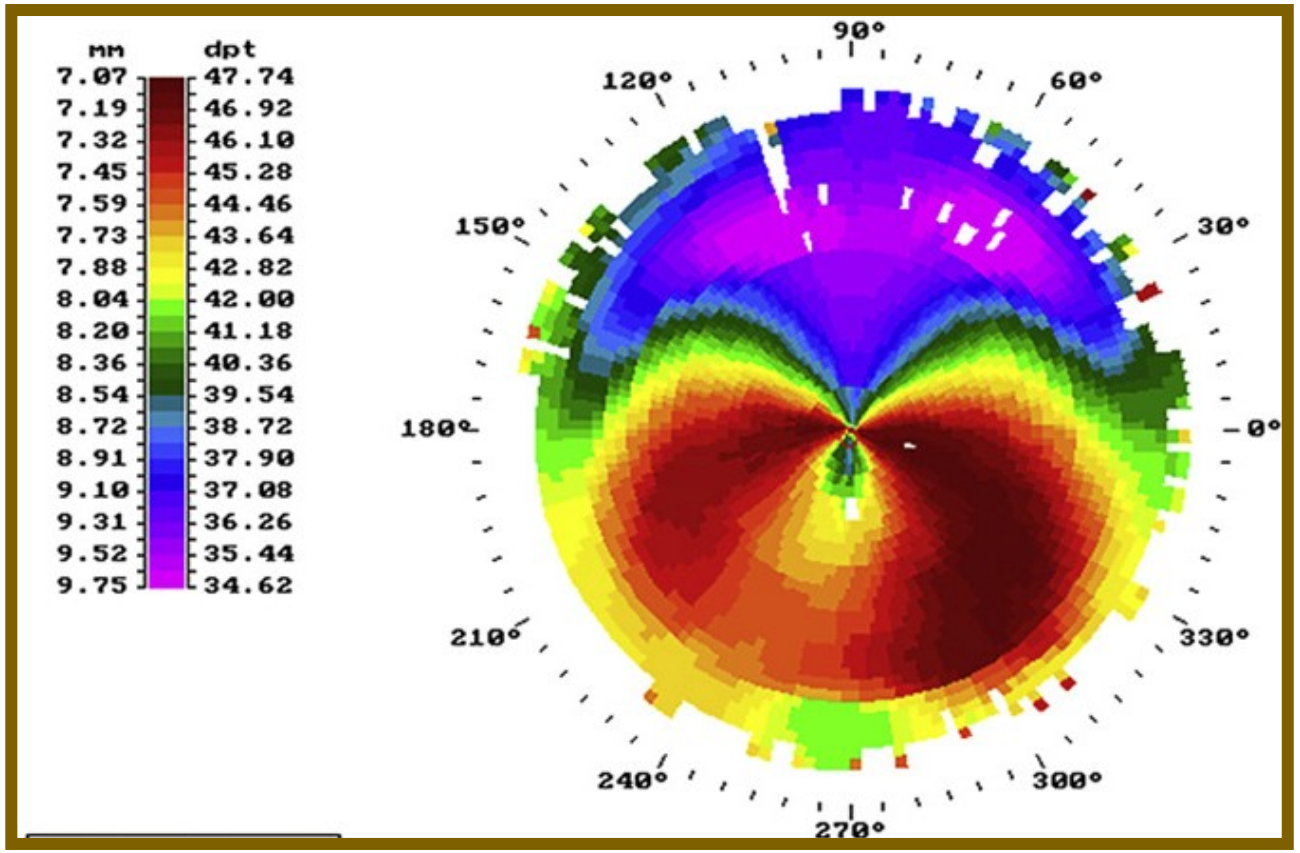
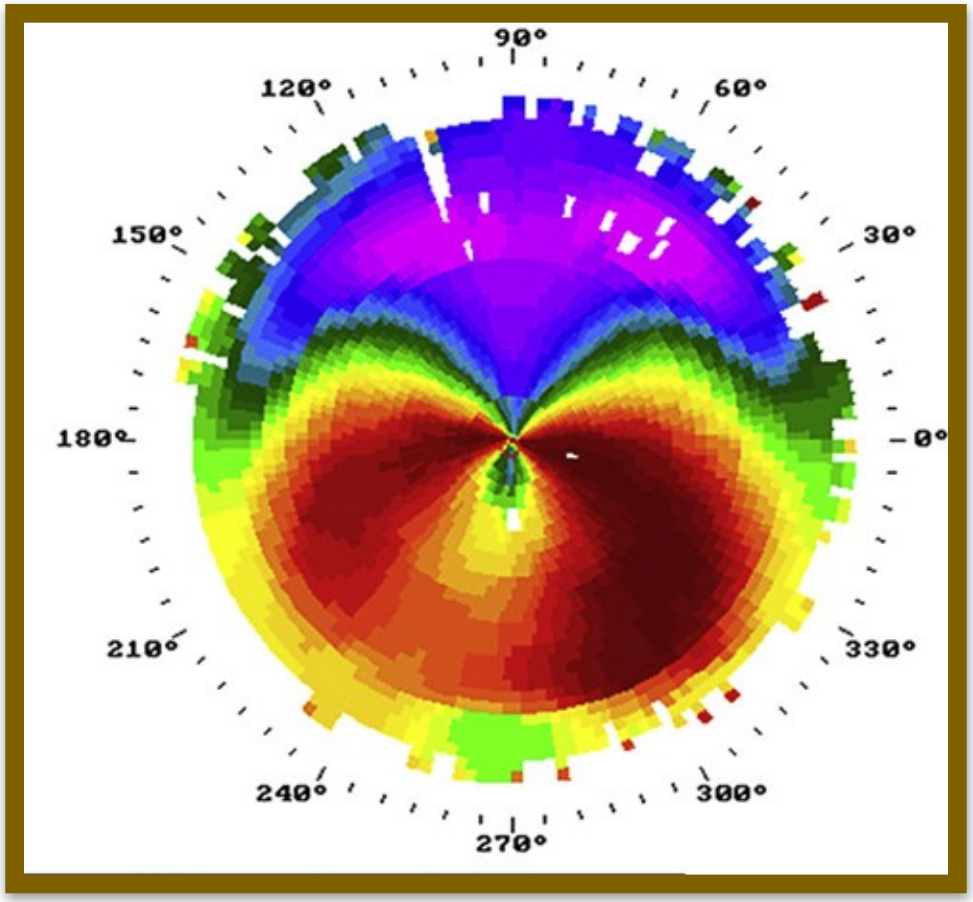
How to Diagnose Pellucid Marginal Degeneration

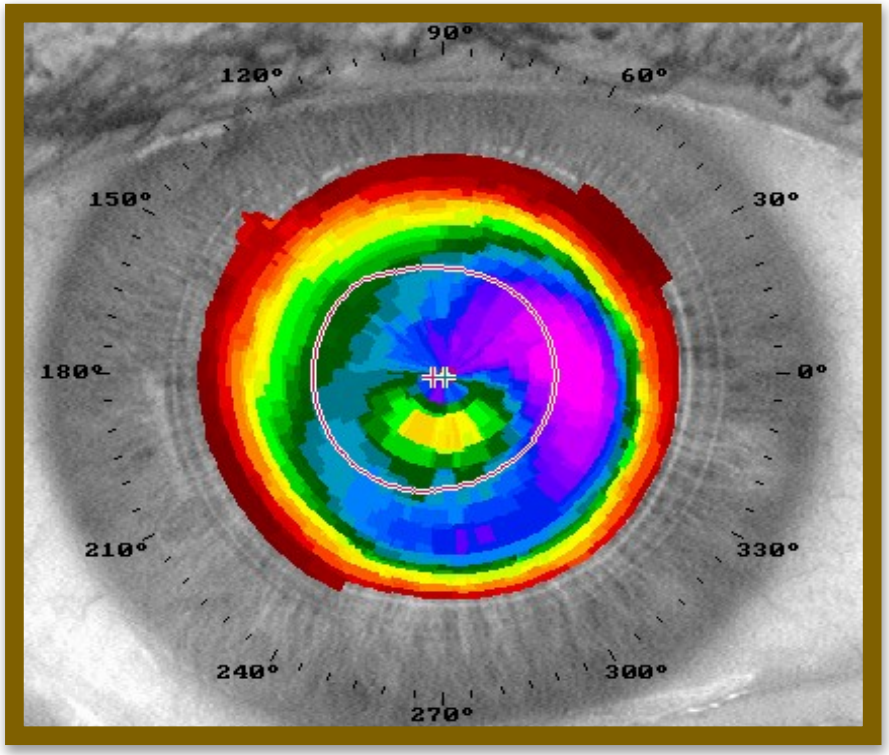


- Curvature patterns such as “*Crab Claw*” are measurement (curvature) anomalies and do not represent peripheral shape changes
  - Almost all “topographic” PMD is just inferior keratoconus



Pseudo PMD

- Placido systems are limited to covering < 60% of the cornea surface under optimal conditions
  - Cannot image where pathology is
    - Pellucid (PMD)
  - Limited by the eye



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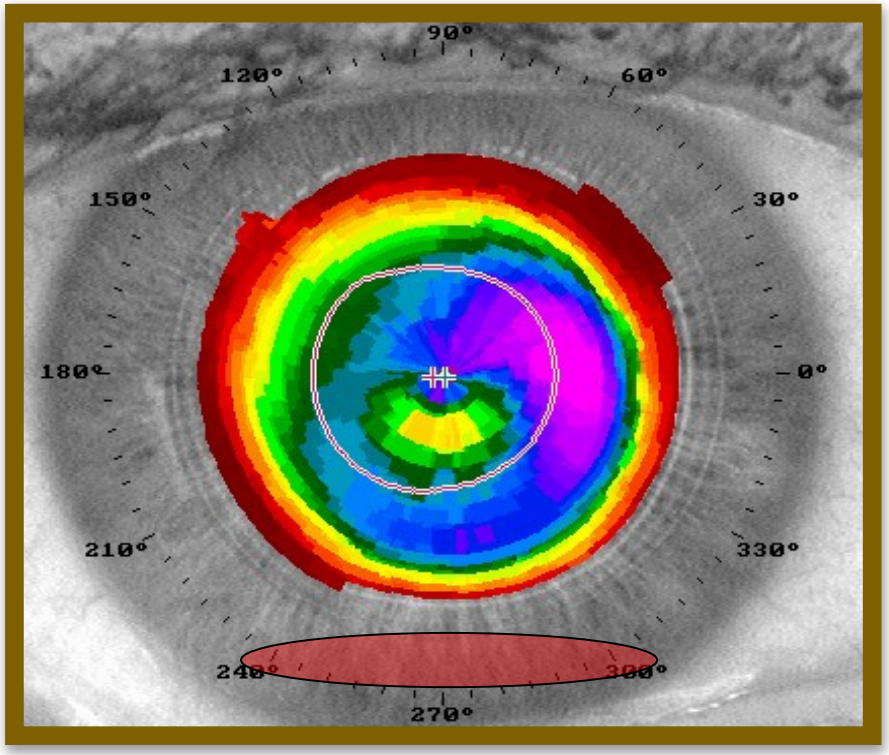
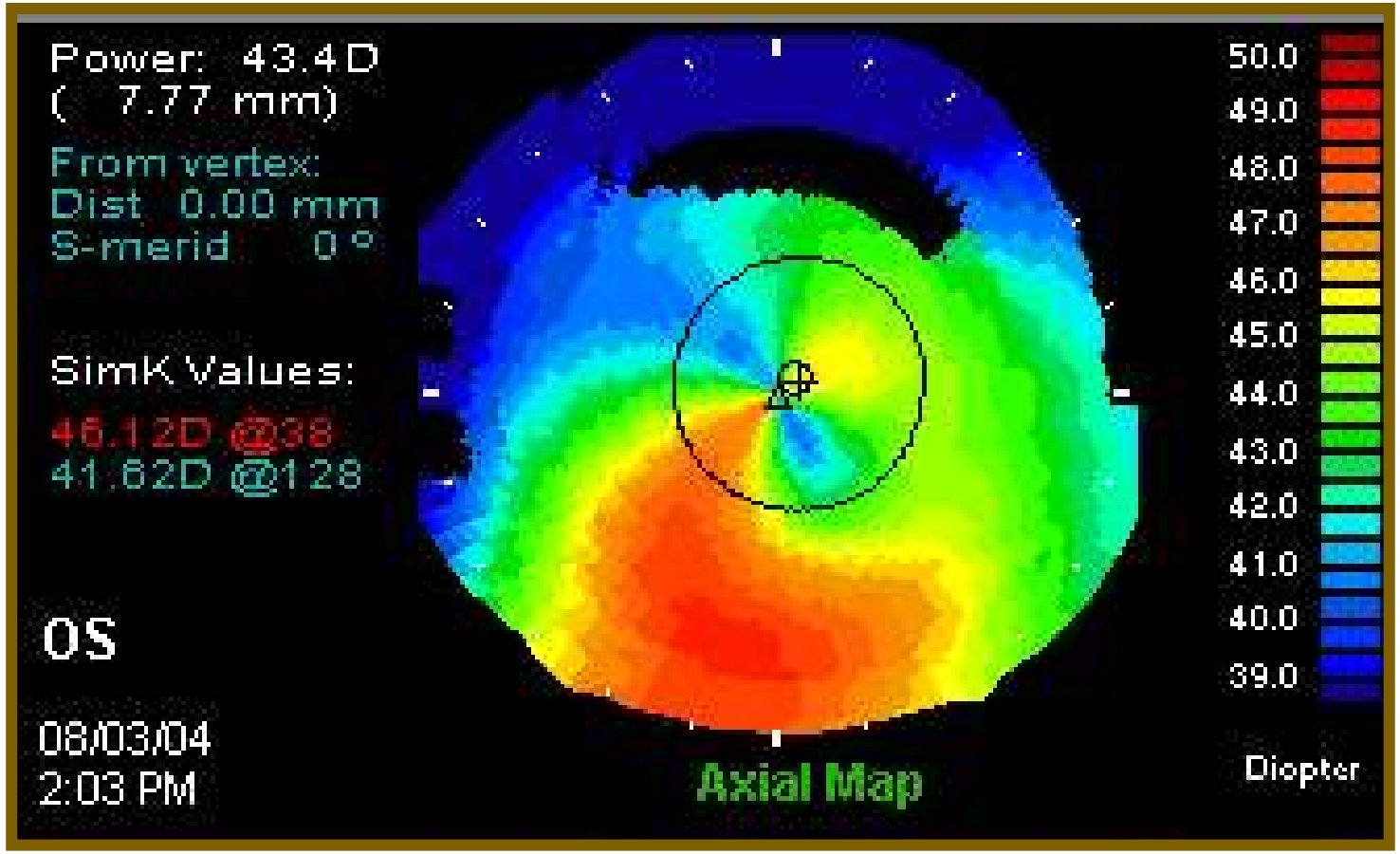
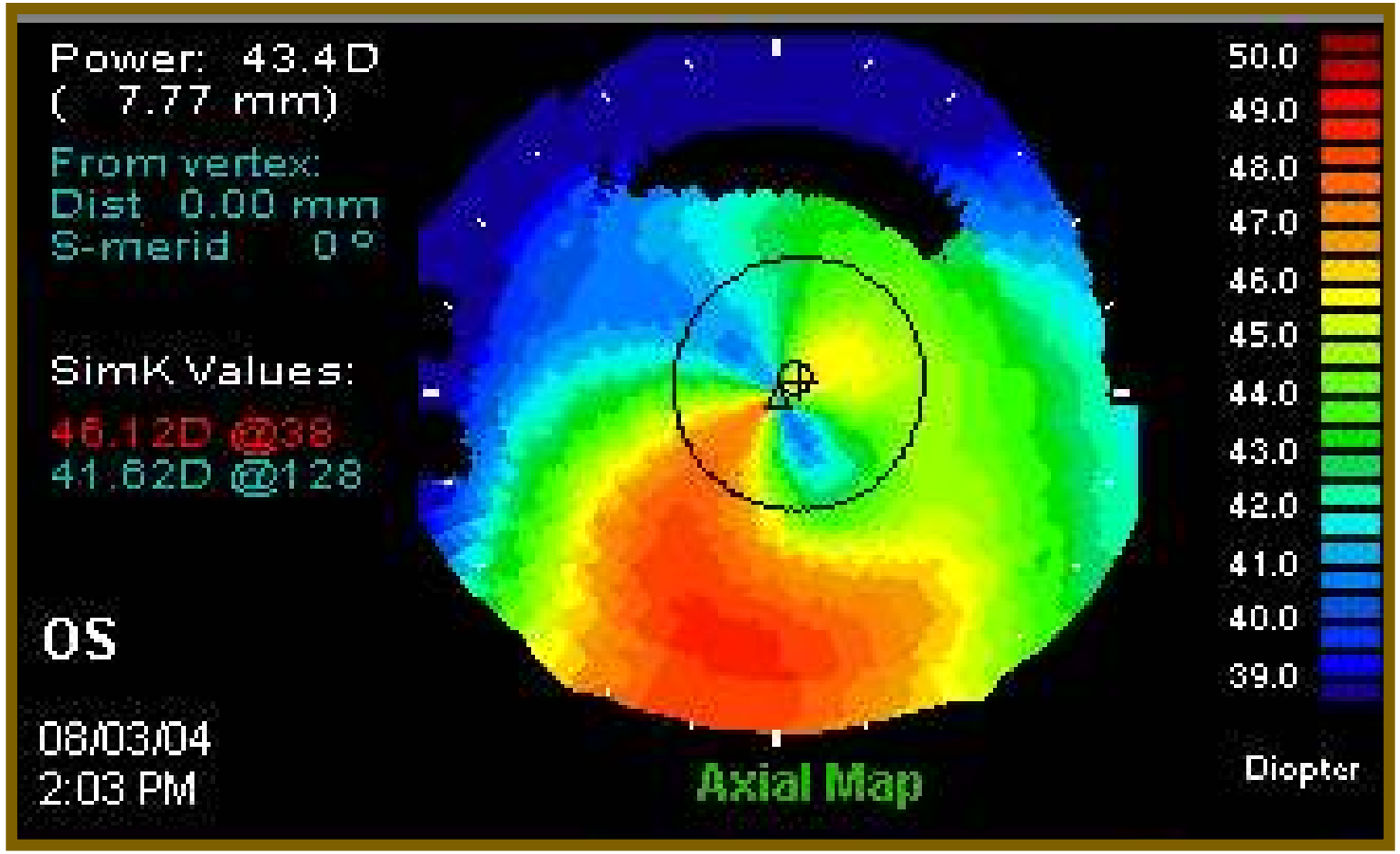


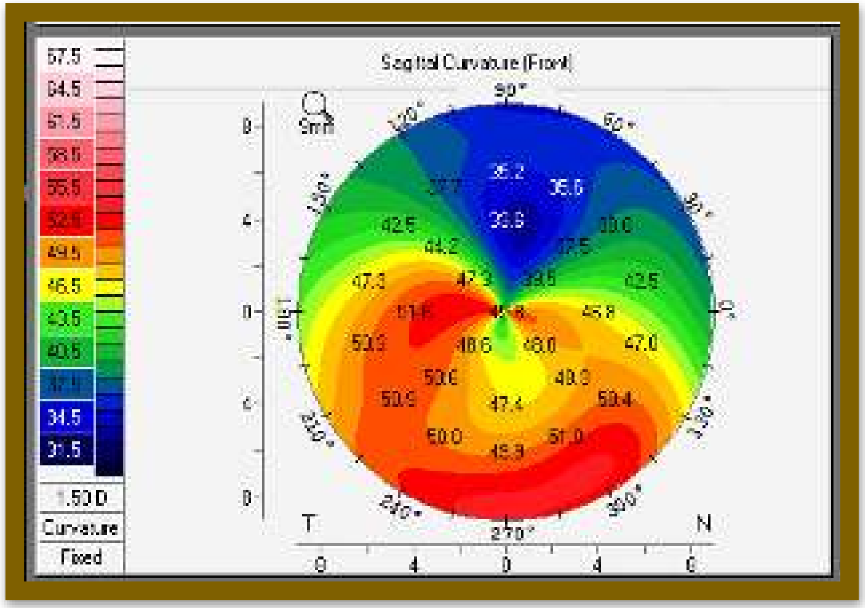
PMD, more often than not, equals



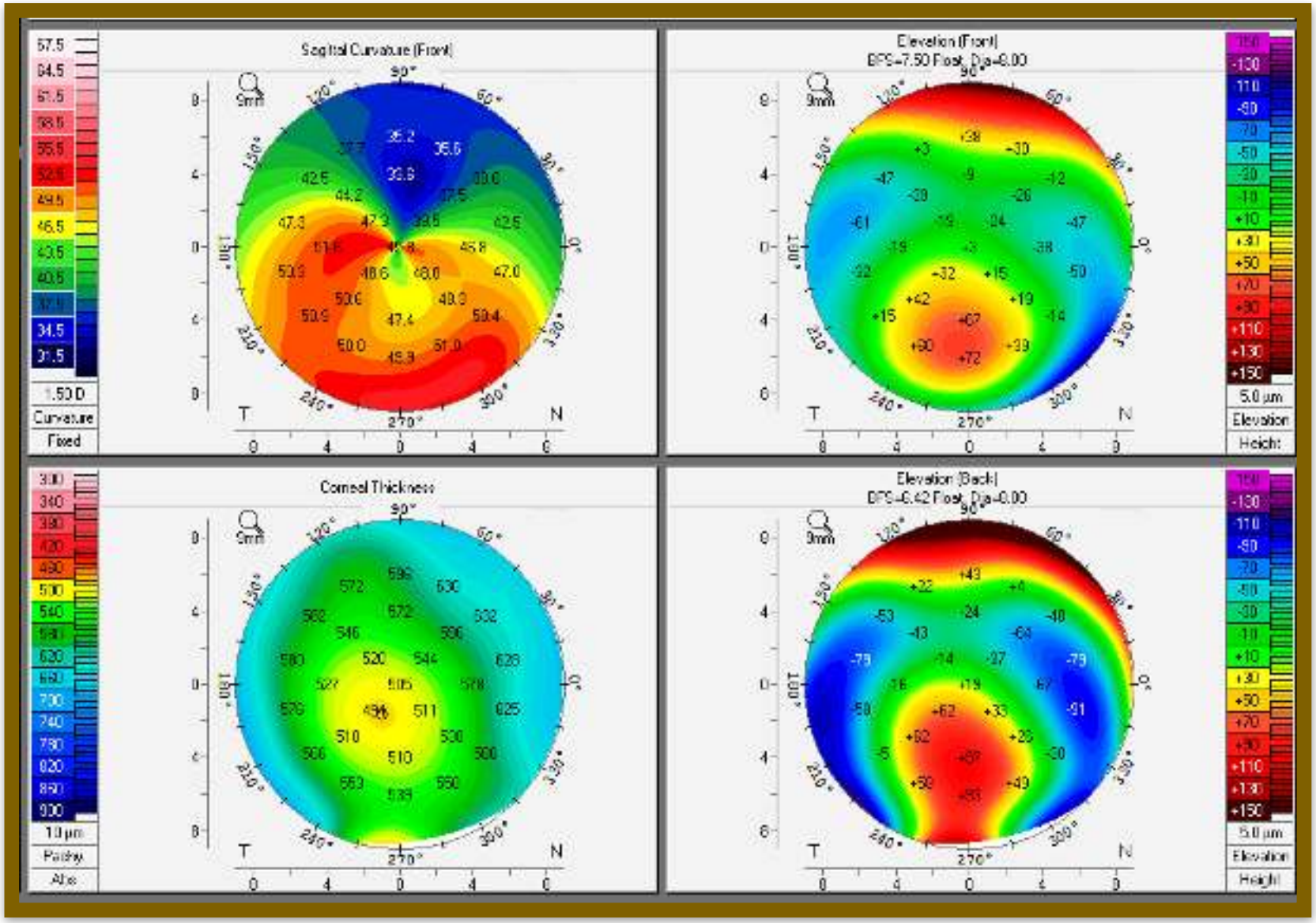
"Placido Marginal Degeneration"



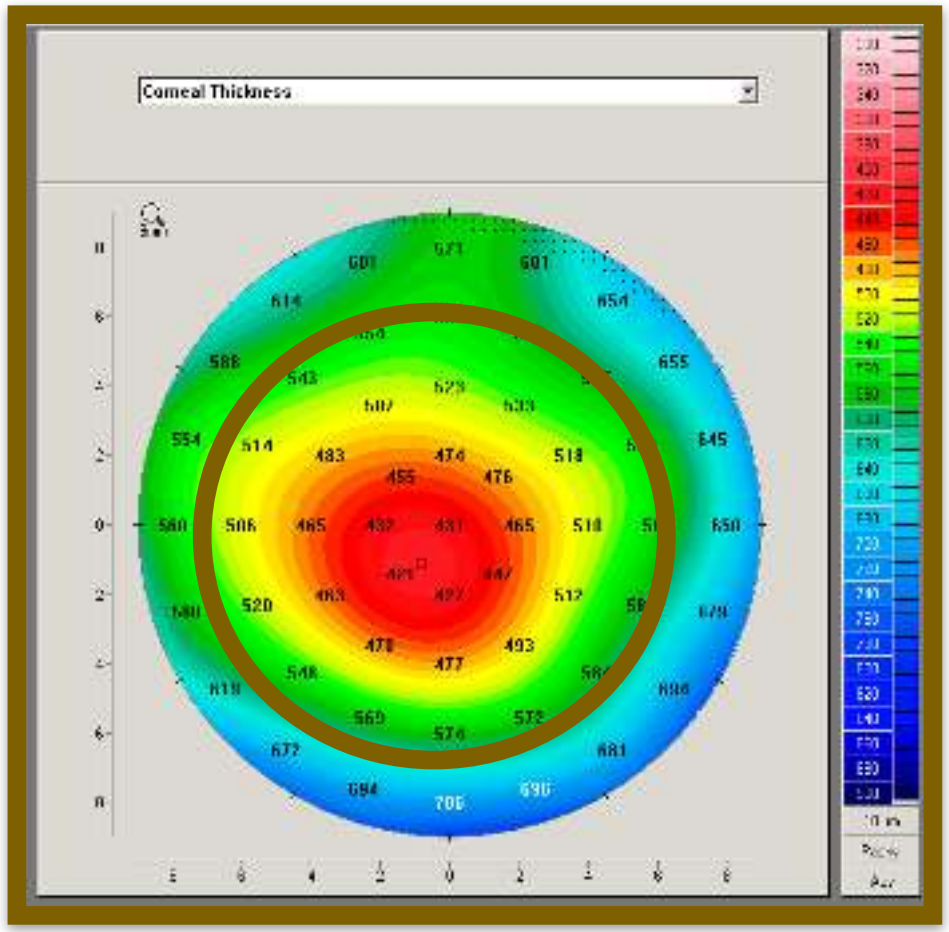
Pseudo PMD

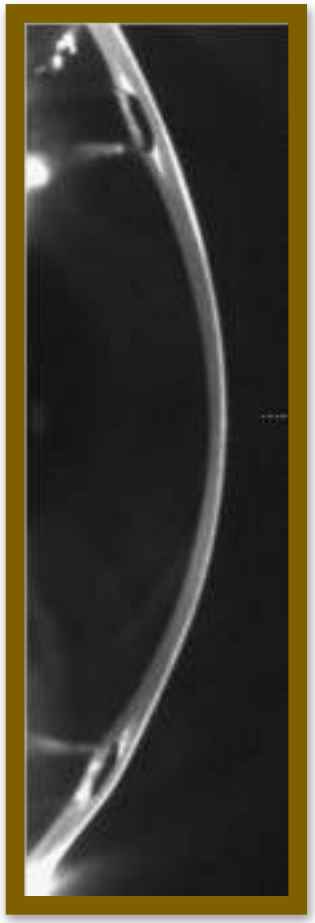


Pseudo PMD

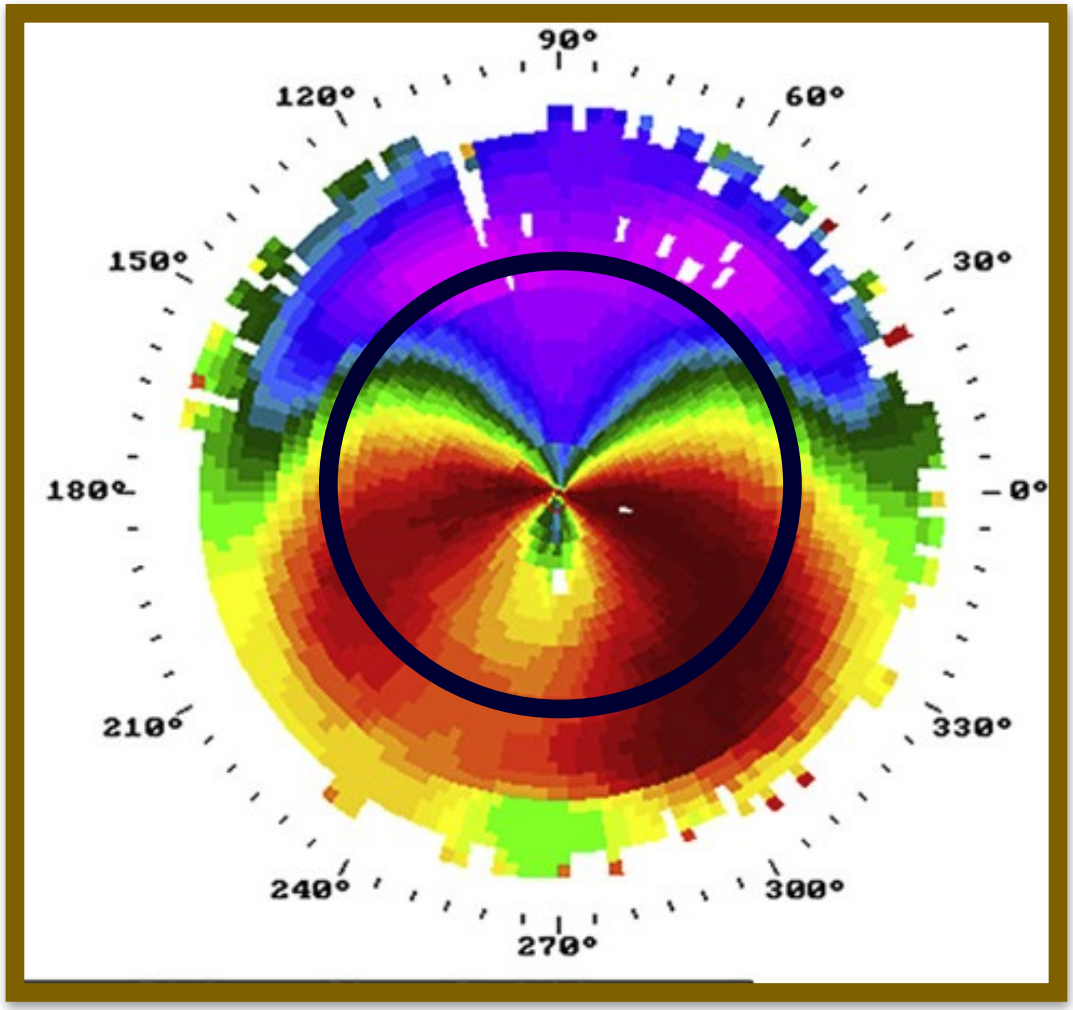

Sagittal Curvature (Front)
Elevation (Front)
Corneal Thickness
Elevation (Back)
T
N

ICR in True KCN

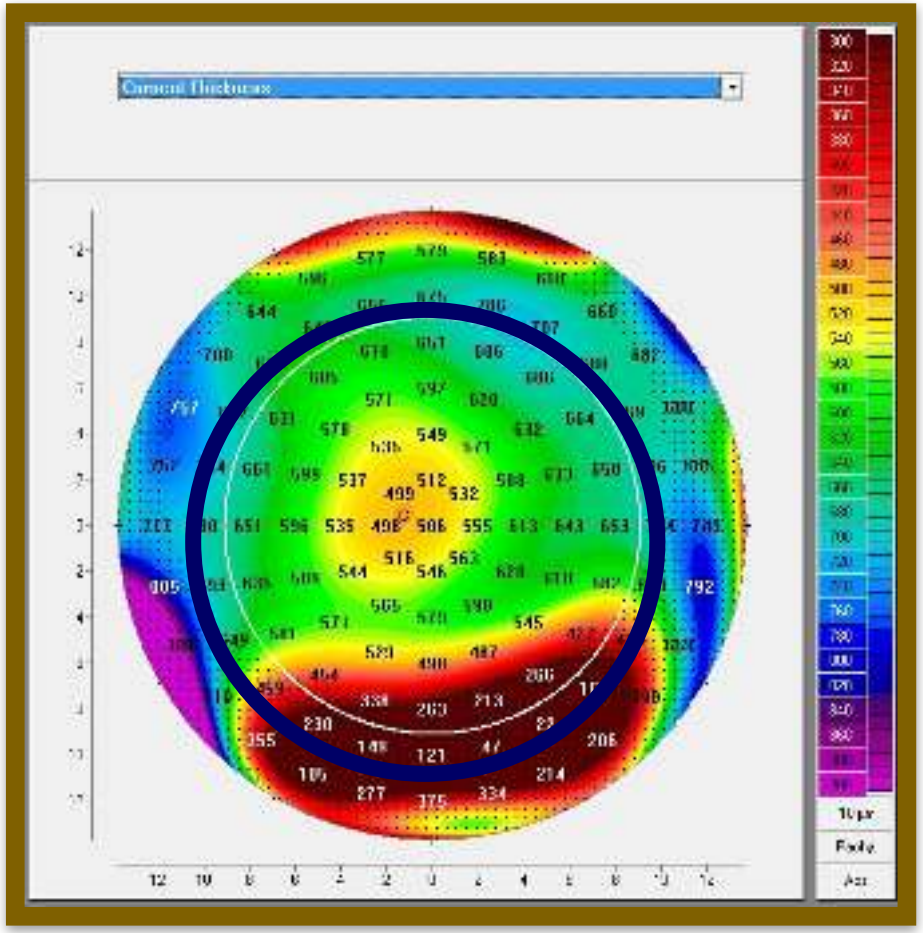


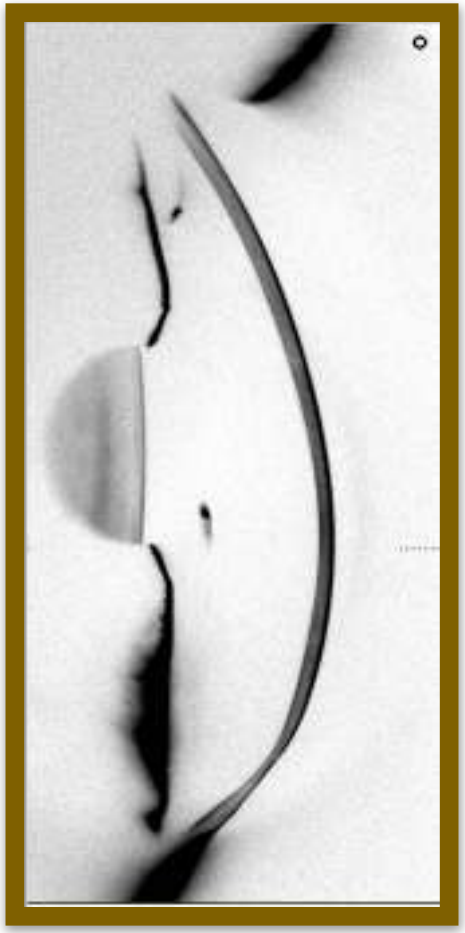


People suggest ICR in PMD

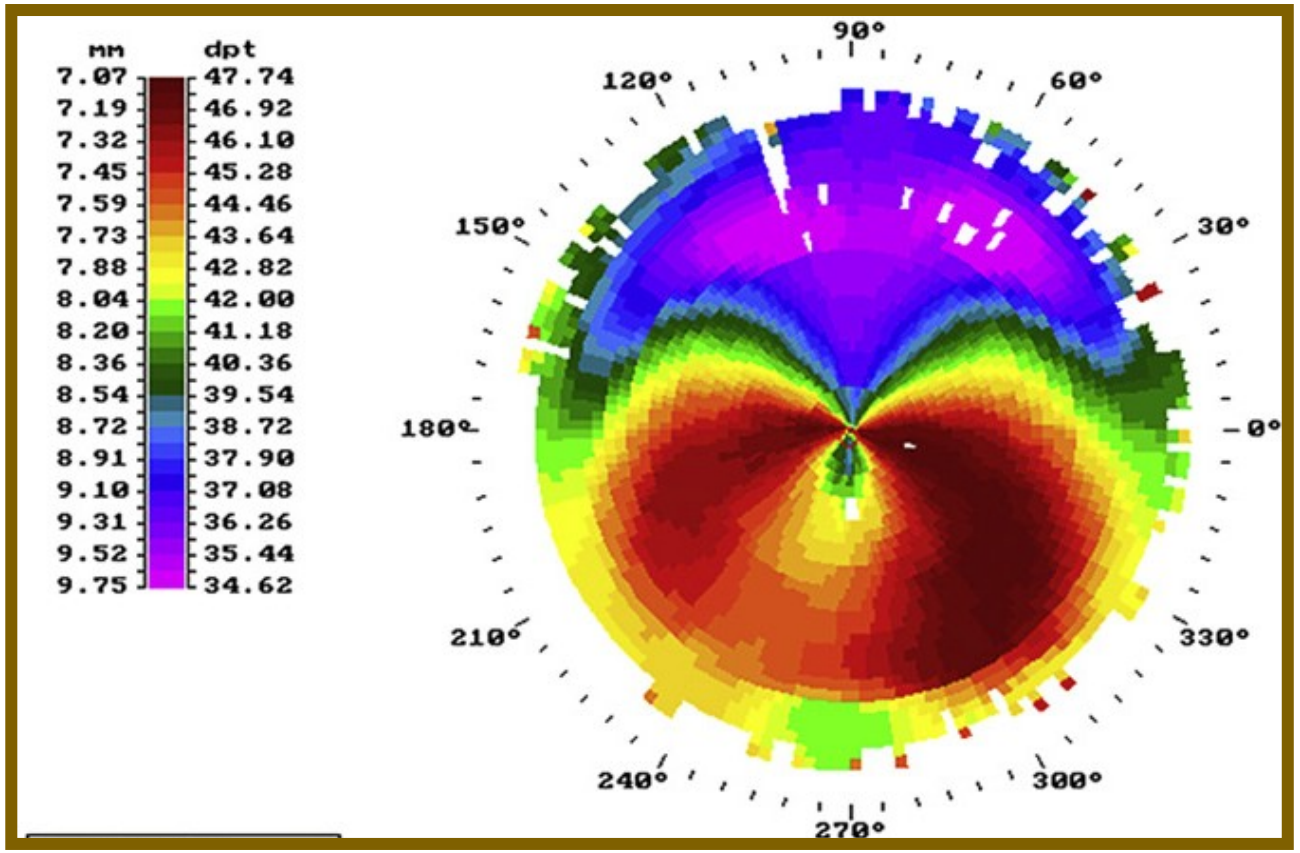


ICR in True PMD Contraindicated

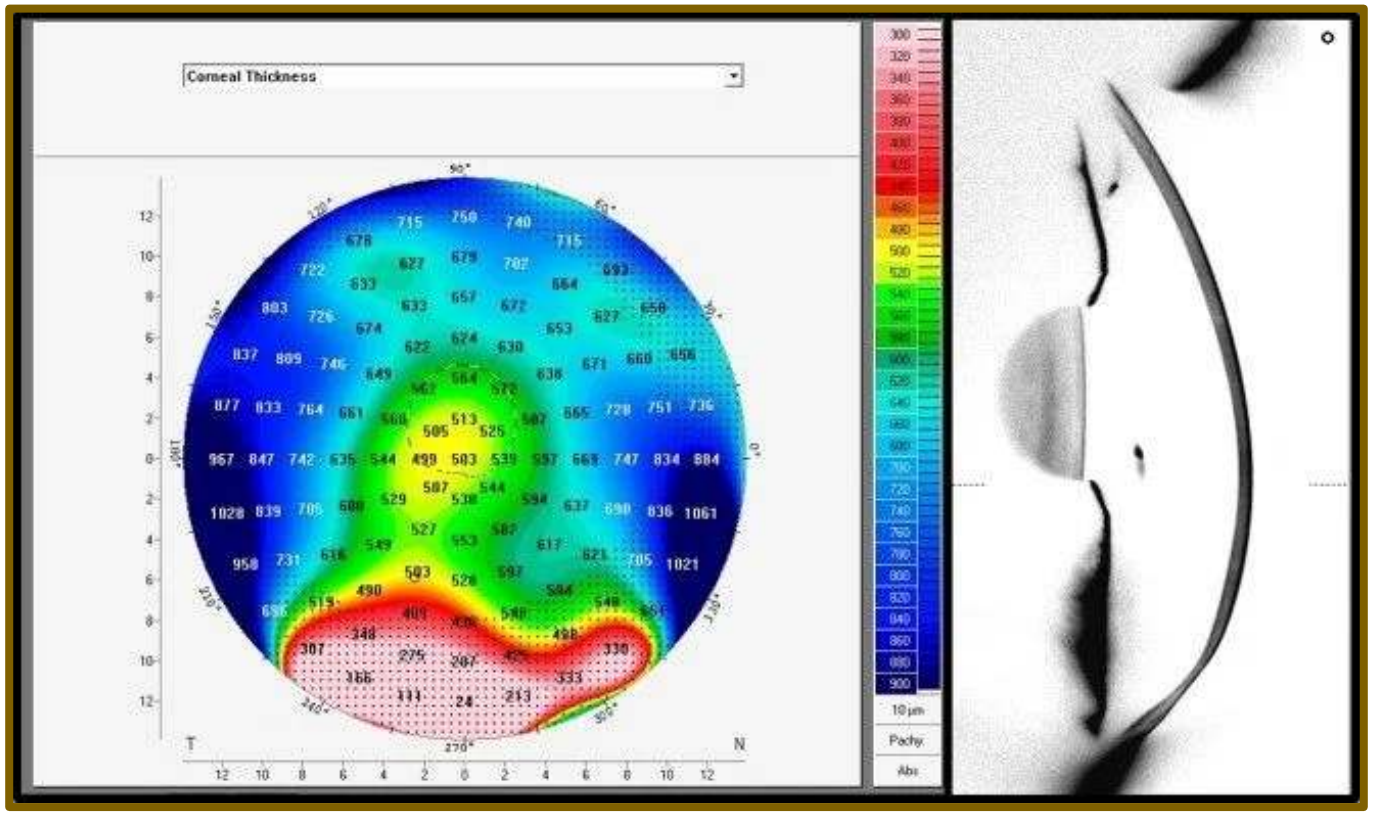




How to Diagnose Pellucid Marginal Degeneration



How to Diagnose Pellucid Marginal Degeneration

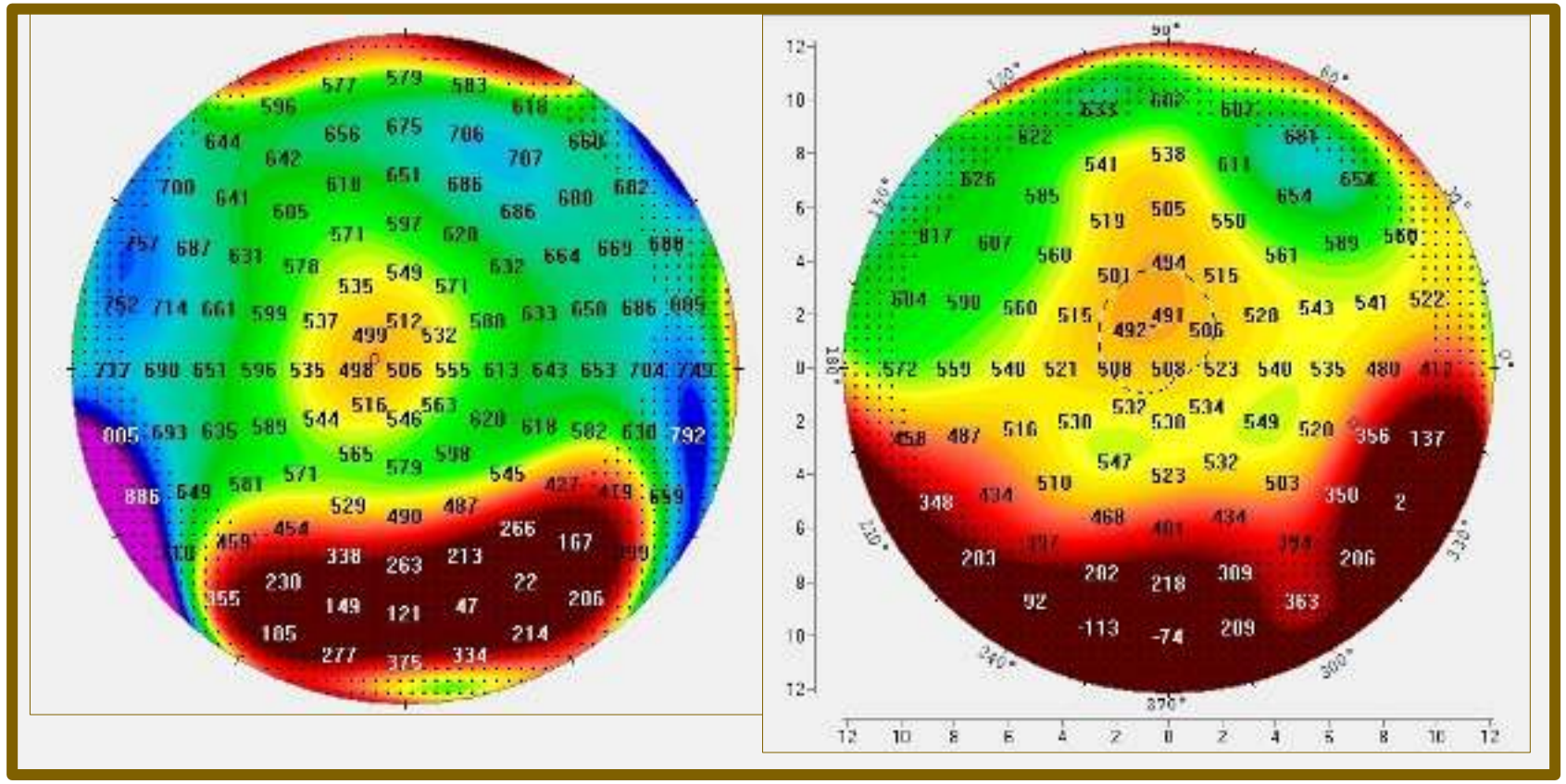


You need to look at a FULL PACYMETRIC map opened up to 12 mm

Walker RN, Khackikian SS, Belin MW.

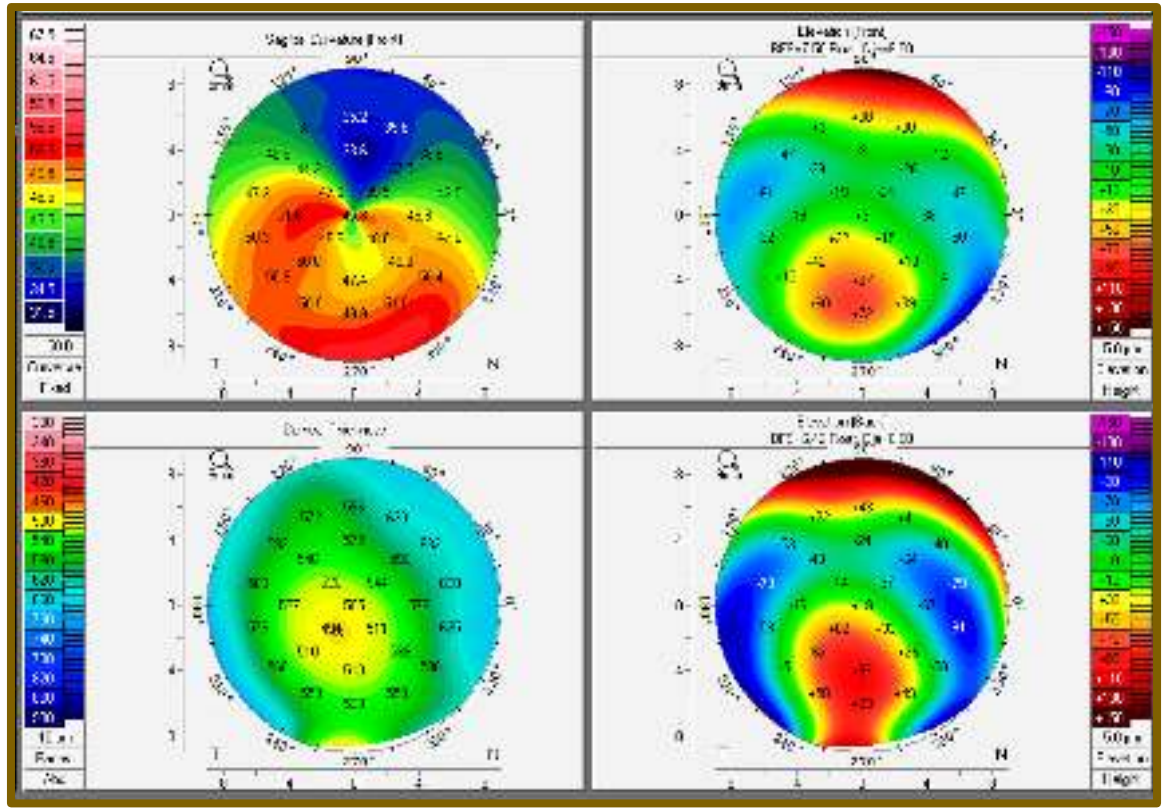
Scheimpflug Imaging of Pellucid Marginal Degeneration.

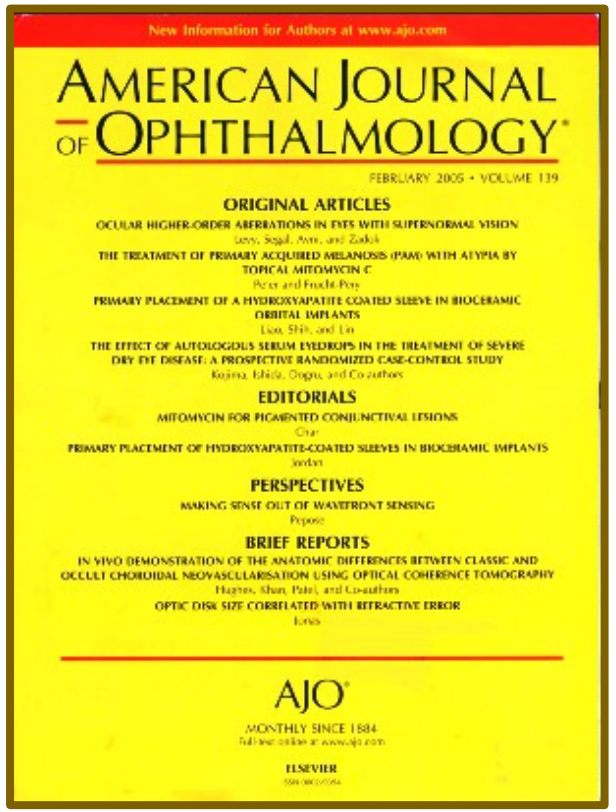
CORNEA 2008 Sep; 27(8):963-6



What's in a Name: *Keratoconus, Pellucid Marginal Degeneration, and Related Thinning Disorders*

Belin MW, Asota IM, Ambrosio R, Khachikian SS. Am J Ophthalmol 2011; ; 152(2): 157-162





Even a single Scheimpflug image can be misleading

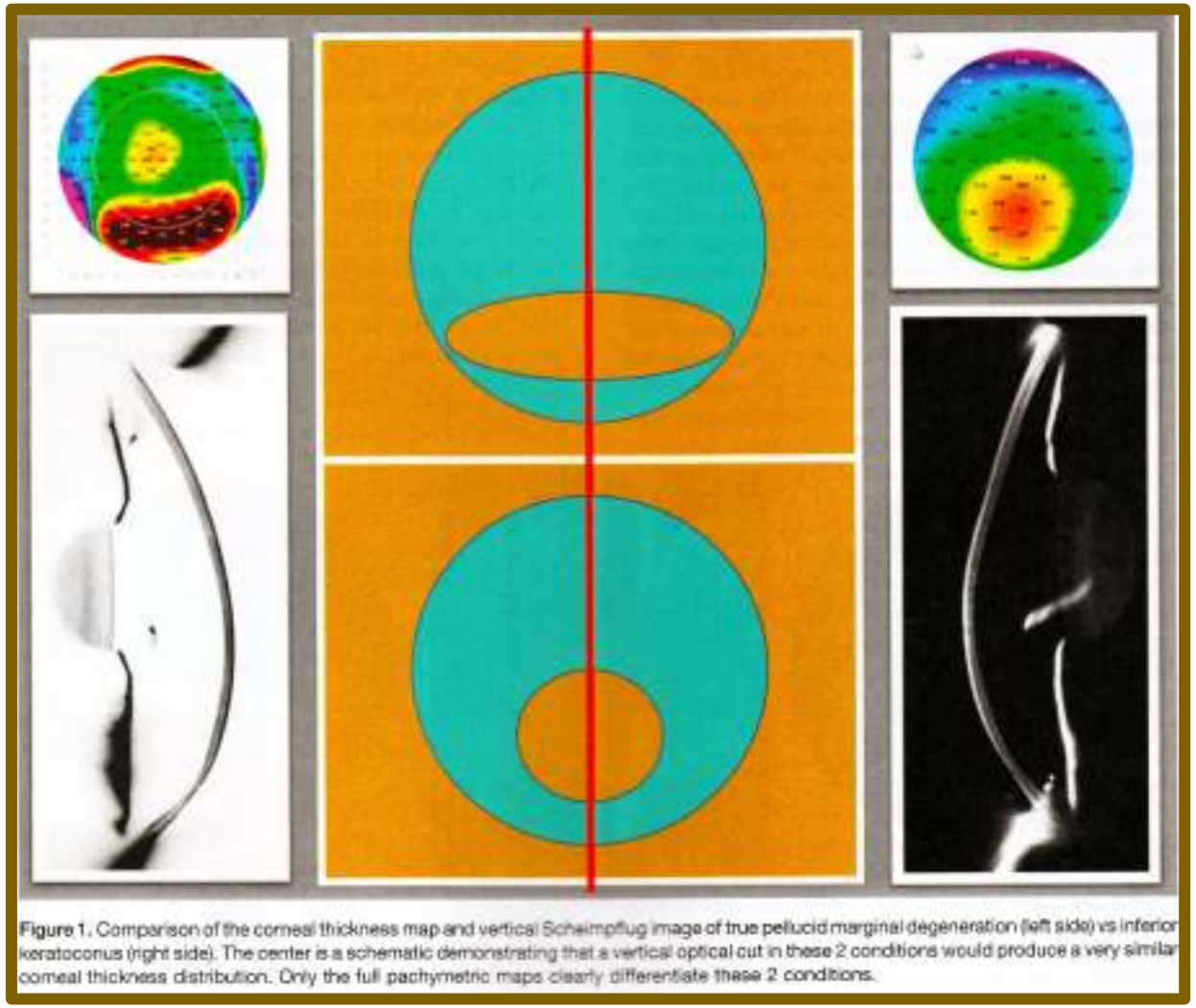
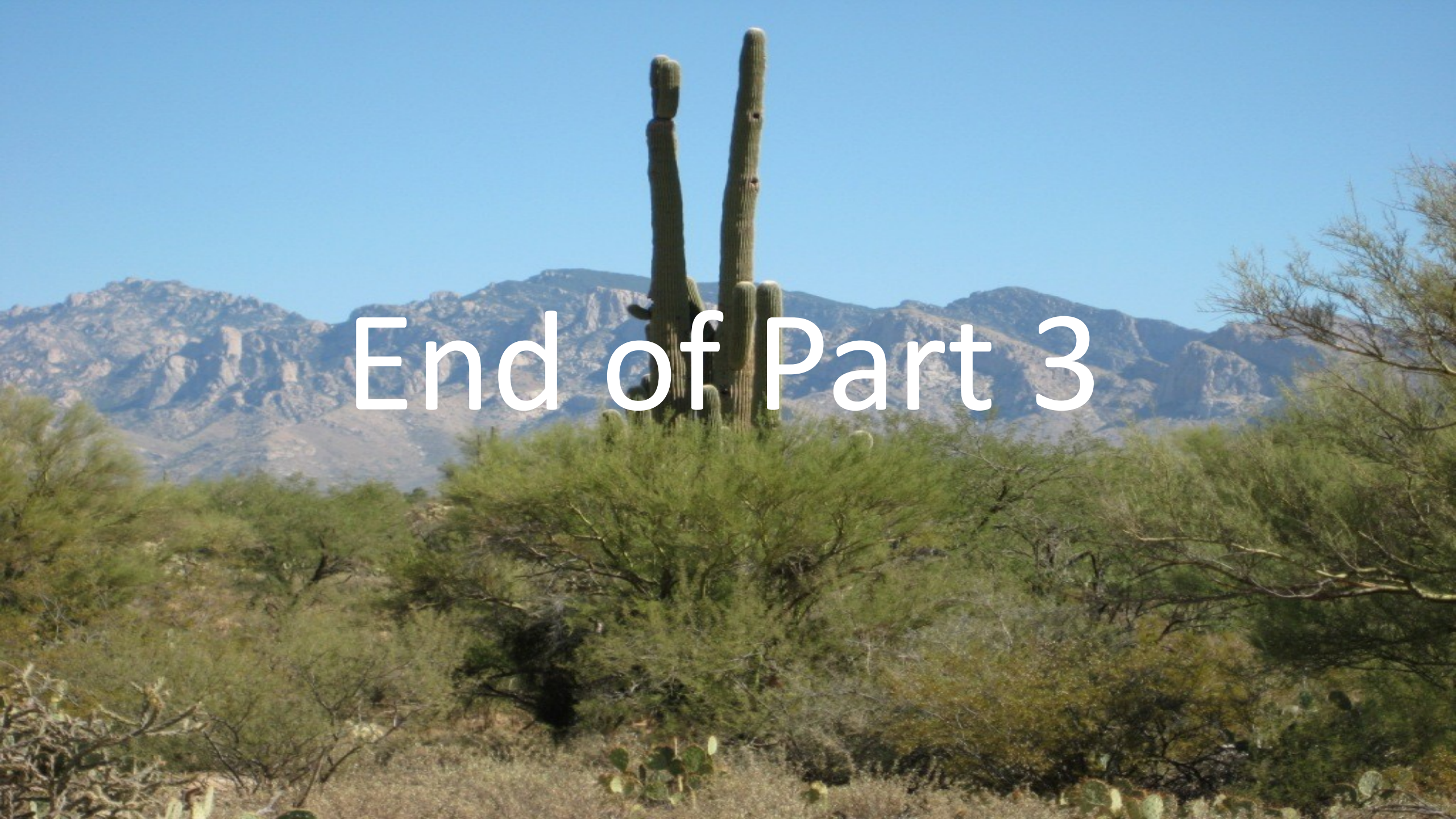


Figure 1. Comparison of the corneal thickness map and vertical Scheimpflug image of true pellucid marginal degeneration (left side) vs inferior keratoconus (right side). The center is a schematic demonstrating that a vertical optical cut in these 2 conditions would produce a very similar corneal thickness distribution. Only the full pachymetric maps clearly differentiate these 2 conditions.

Belin MW, Boyd BM, Ambrosio R Jr. Pellucid marginal degeneration vs inferior keratoconus: why it matters. J Cat Refract Surg. 2020;46: 325-326


End of Part 3

Sensitivity vs Specificity :
Which is more important

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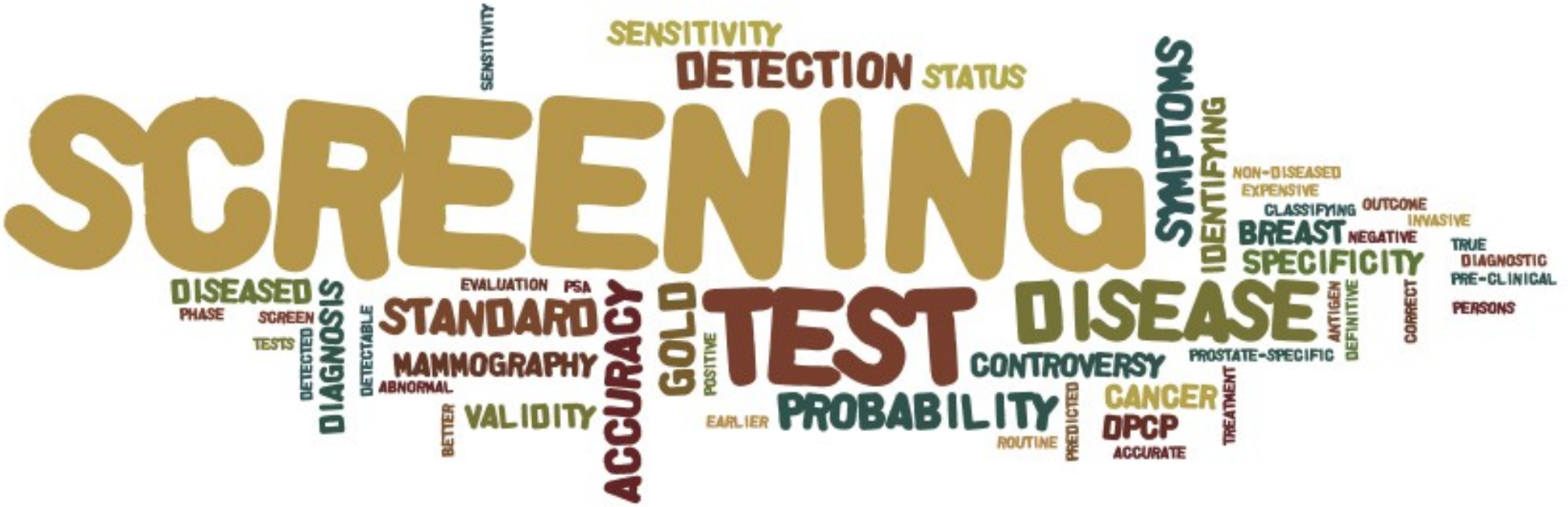
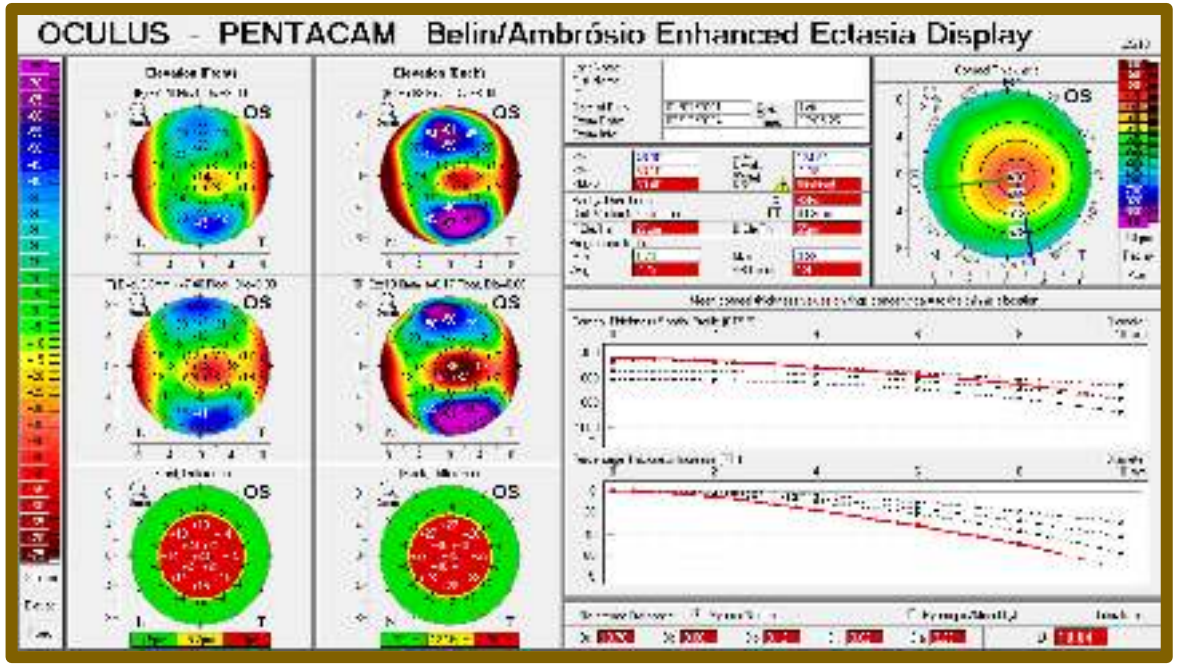
Screening vs Diagnosing

- We need to understand the difference between screening for a disease and diagnosing a disease.



Refractive Screening *vs* KCN Diagnosis

- The goal of refractive screening is to evaluate “RISK”
  - Eliminate those patients at risk for developing post-refractive ectasia
    - A 5% false positive rate is considered acceptable
      - Sensitivity over specificity
- Diagnosing Keratoconus
  - Specificity is most important



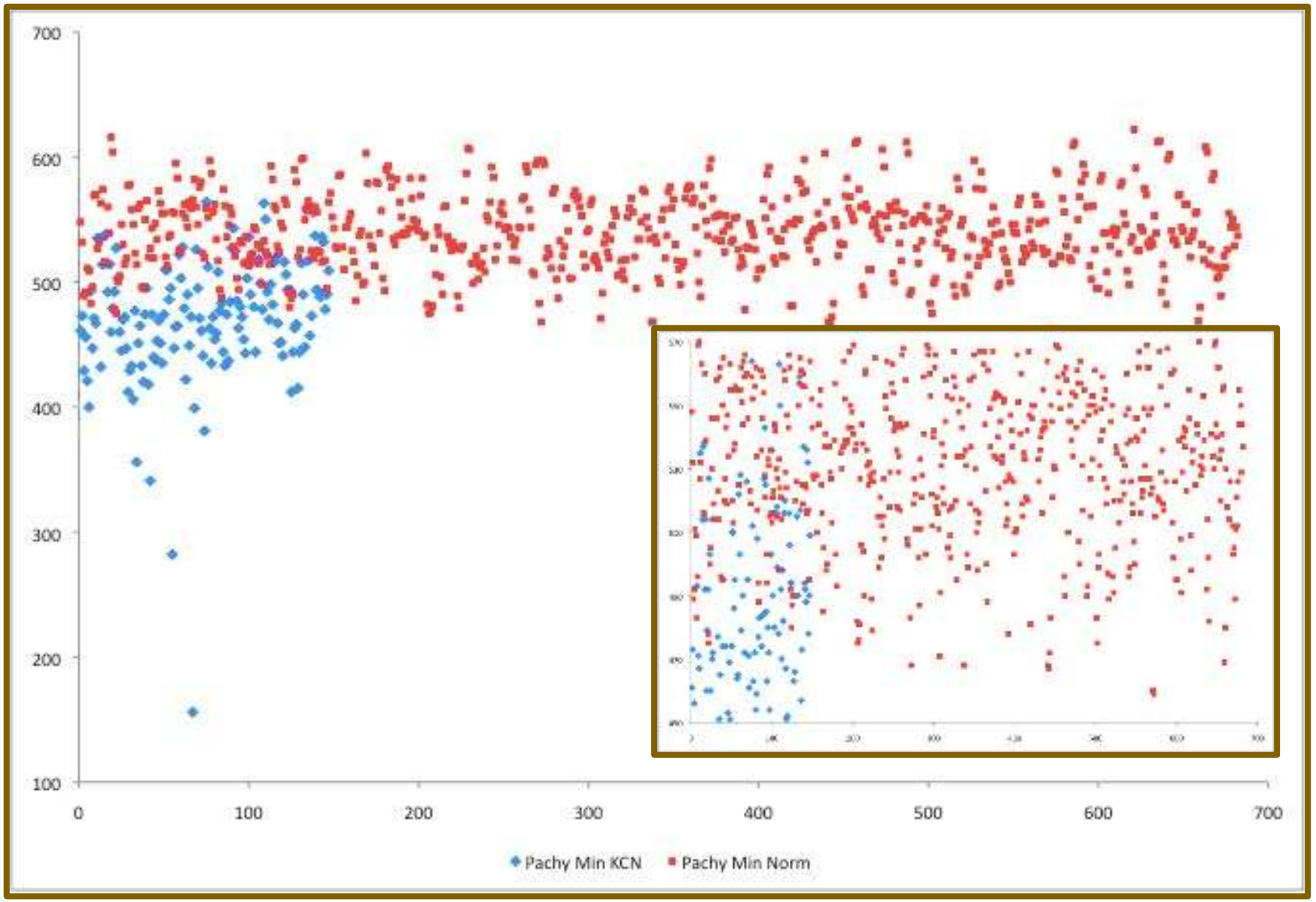
Refractive Screening Sample

	95% CI / % KCN included	97.5% CI / % KCN included
Minimal Pach	489 / 38 %	480 / 44 %
Kmax	47.7 / 9.5 %	48.1 / 10 %
Df	1.66 / 6.8 %	2.14 / 10 %
Db	1.63 / 11 %	2.05 / 15 %
Elev Front Thinnest	4.0 / 4.8 %	5.0 / 6.1 %
Elev Back Thinnest	12.0 / 6.1 %	13.0 / 6.1 %
Plavg	1.14 / 4.1 %	1.18 / 6.1 %
ARTmax	353 / 4.8 %	332 / 8.8 %
Final “D”	1.65 / 0.7 %	1.88 / 0.7 %

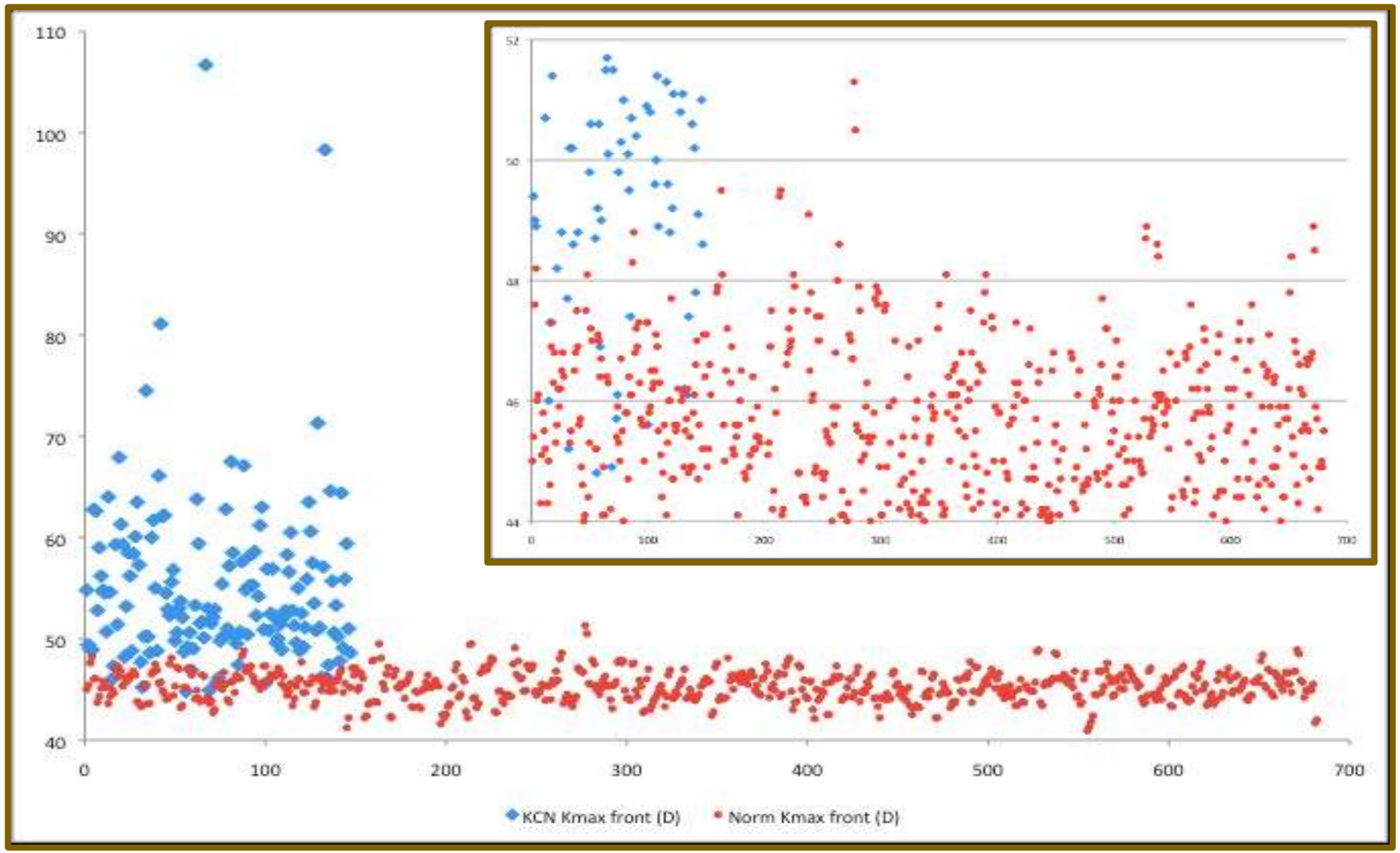
Keratoconus Inclusion Criteria

	95% CI / % Normal Inc	97.5% CI / % Normal Inc
Minimal Pach	538 / 49 %	558 / 73 %
Kmax	46.1 / 31 %	45.3 / 55 %
Df	1.43 / 8.2 %	-0.2 / 50 %
Db	1.0 / 13 %	0.48 / 23 %
Elev Front Thinnest	4.3 / 3.5 %	-1.7 / 98.2 %
Elev Back Thinnest	11.3 / 5.7 %	6.3 / 25.0 %
PIavg	1.17 / 3.2 %	1.08 / 12 %
ARTmax	354 / 5.3 %	376 / 11 %
Final “D”	2.69 / 0 %	2.26 / 0.6 %

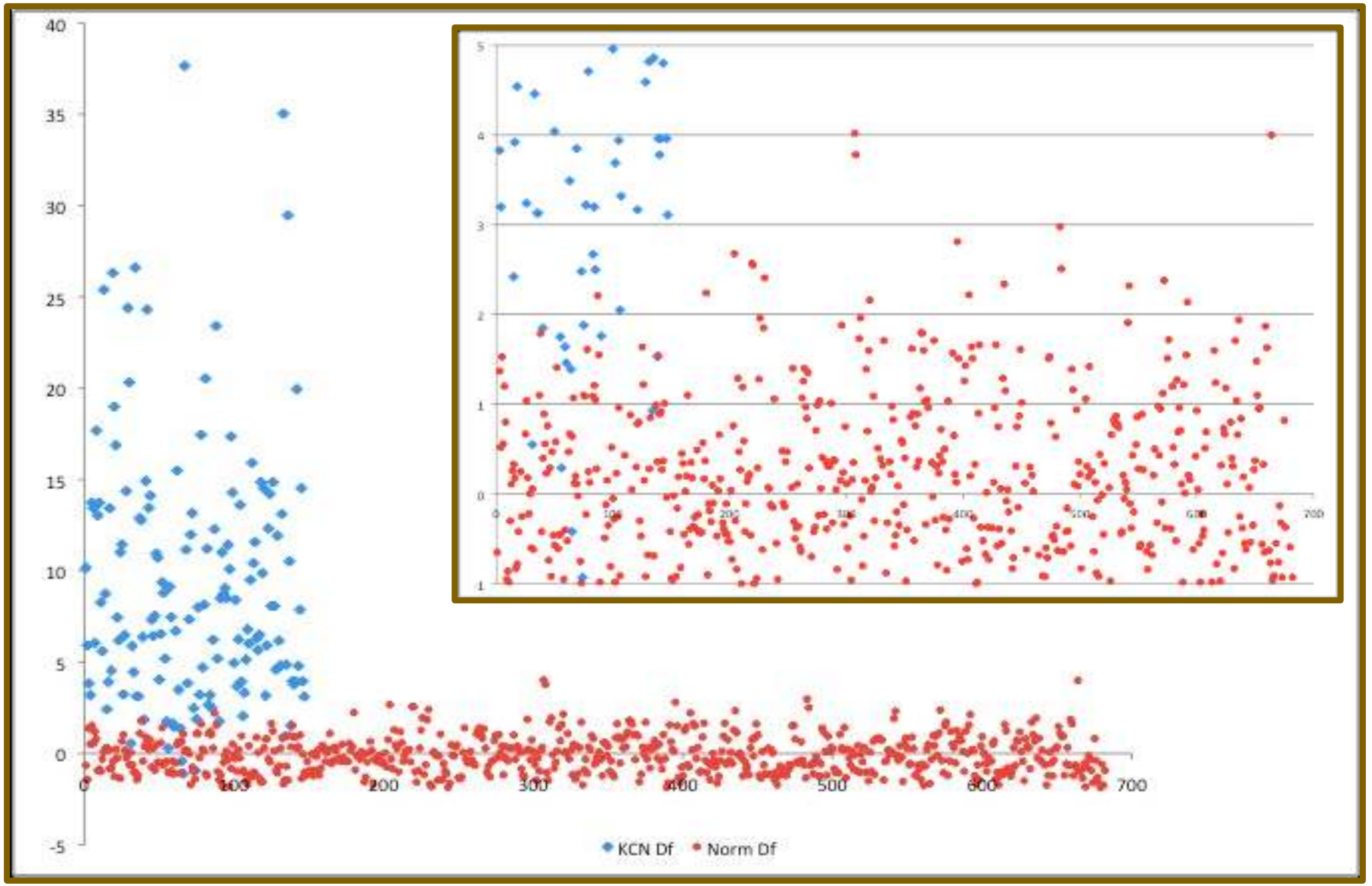
Minimal Central Pachymetry



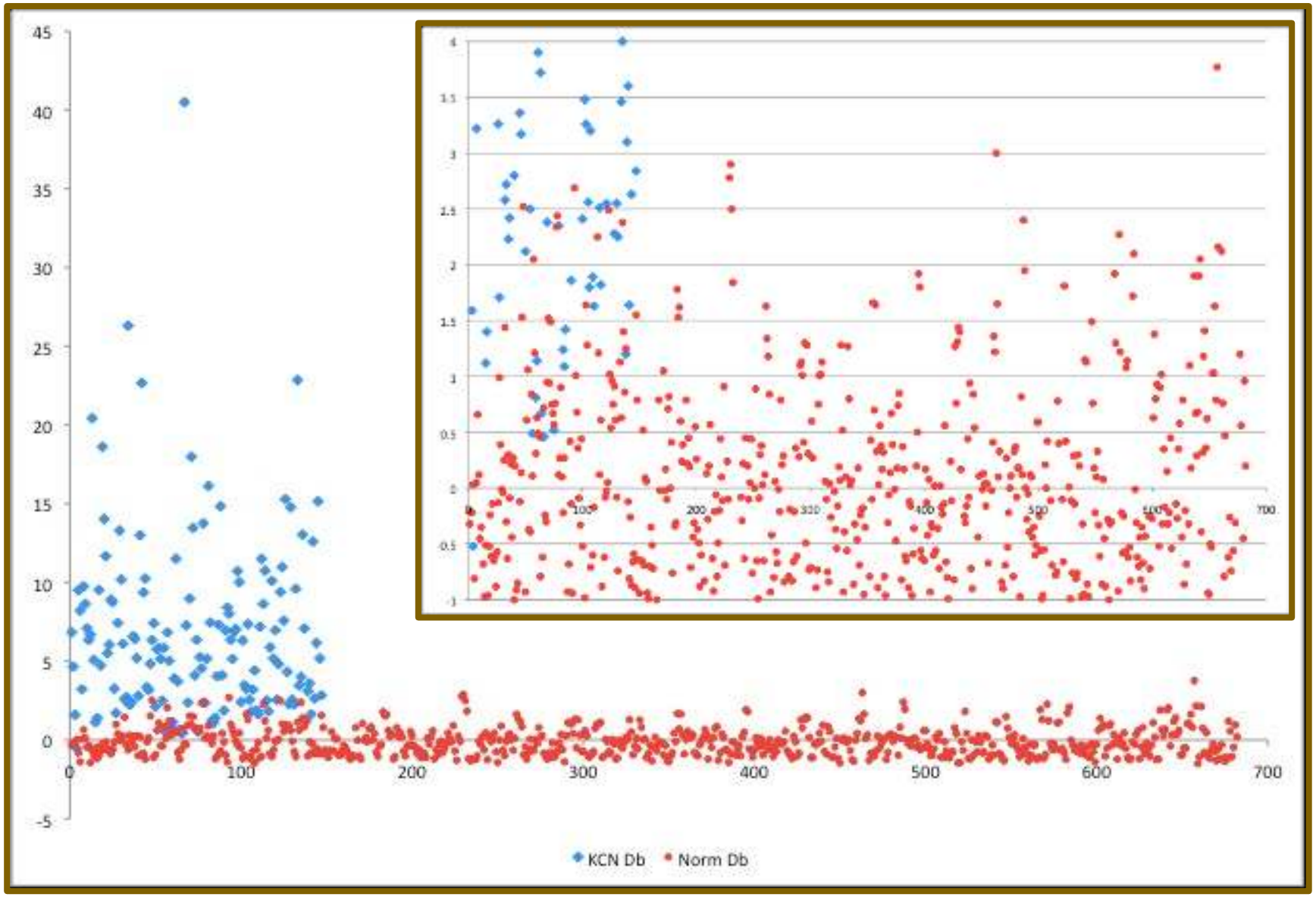
Kmax


110
100
90
80
70
60
50
40
0
100
200
300
400
500
600
700
KCN Kmax front (D)
Norm Kmax front (D)

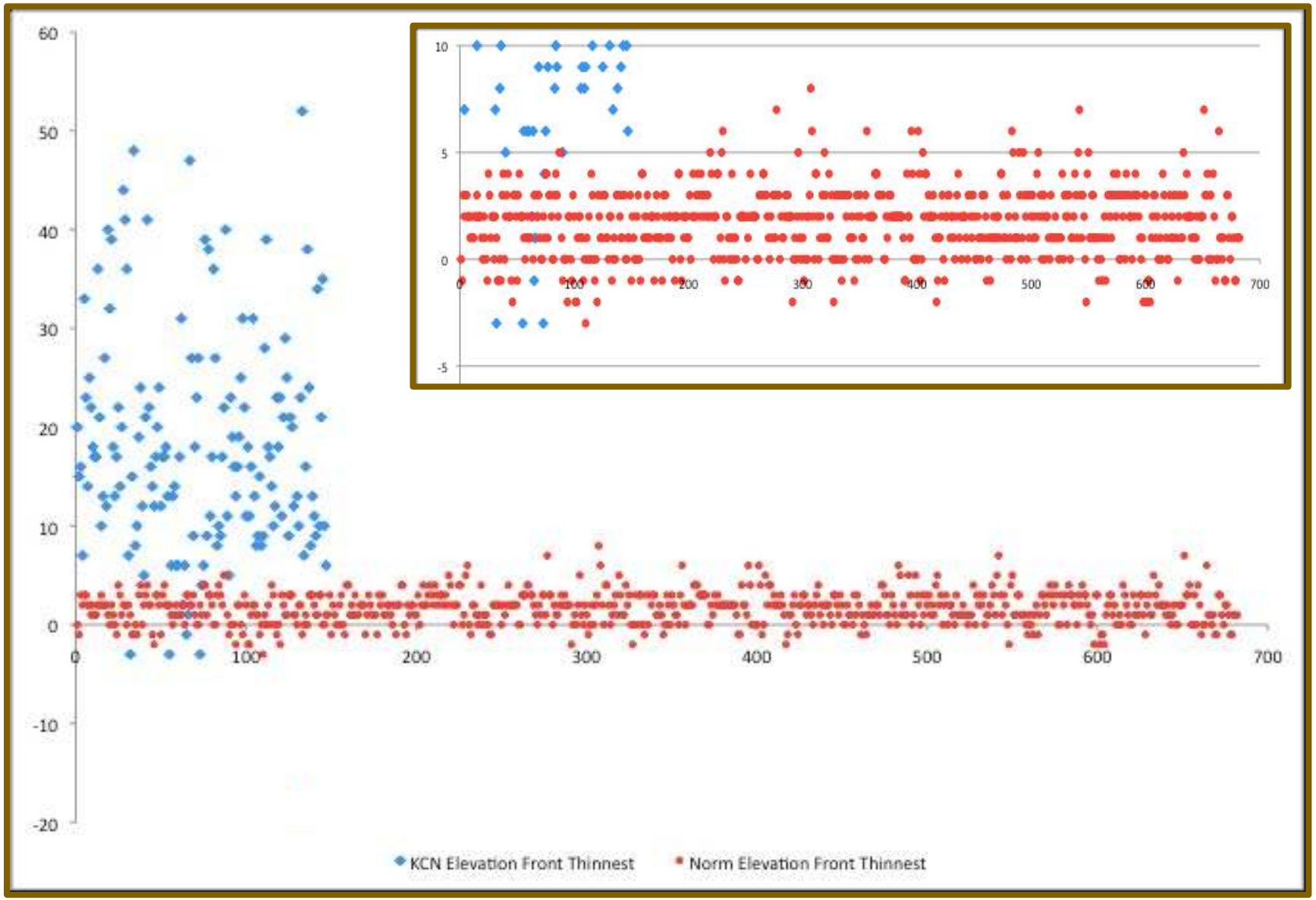
Df (front elevation difference)



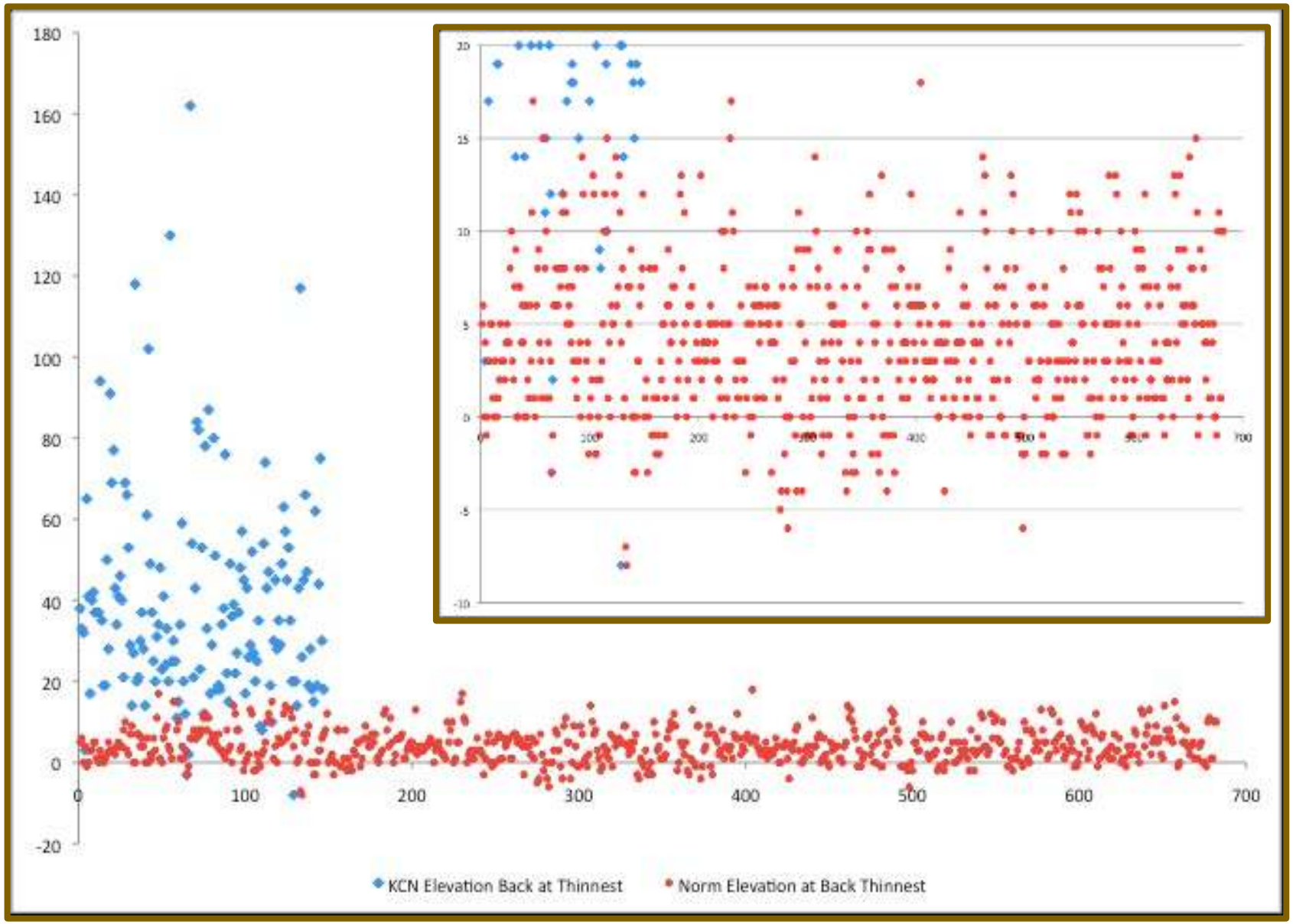
Db (back elevation difference)



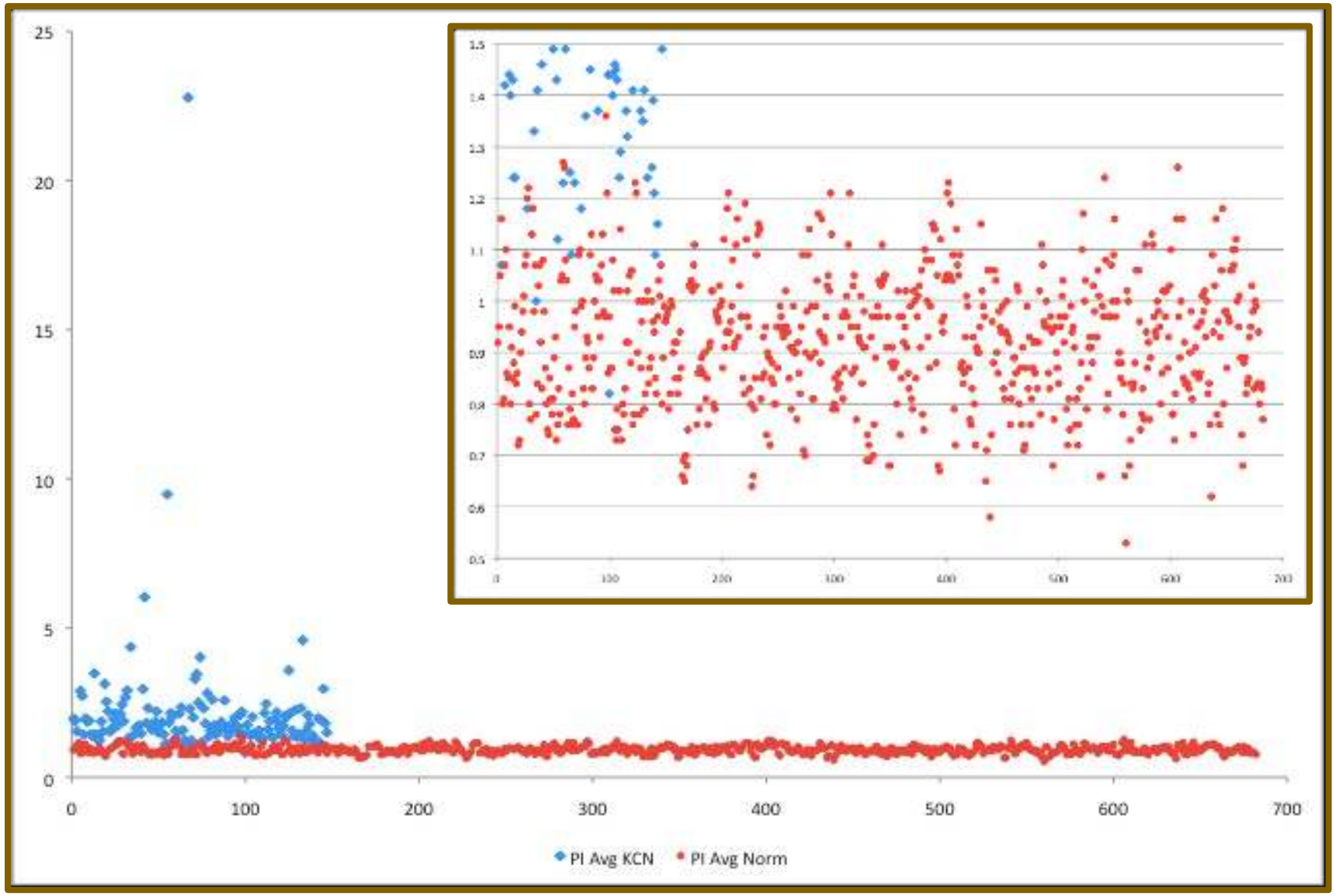
Elevation Front Thinnest



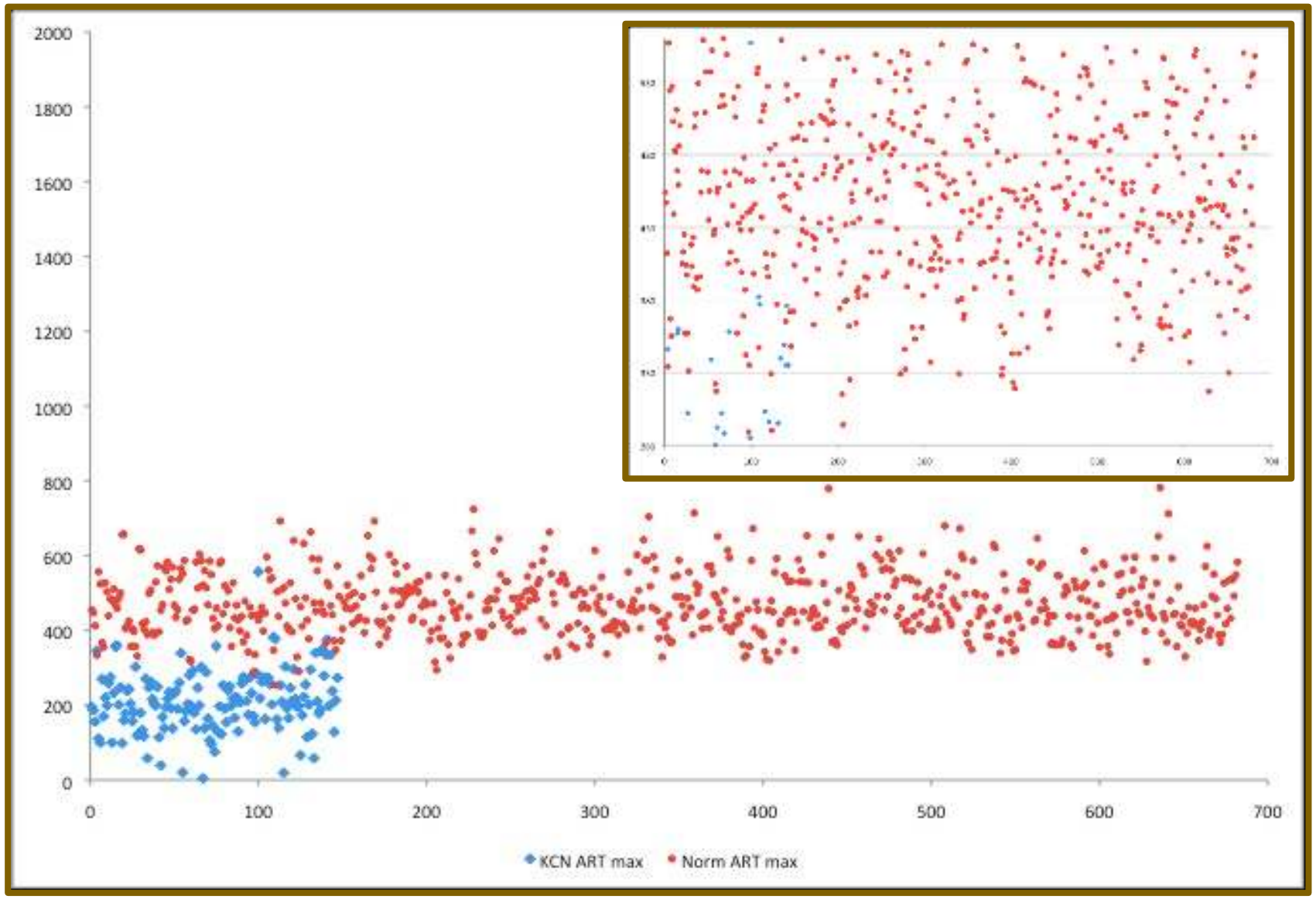
Elevation Back Thinnest



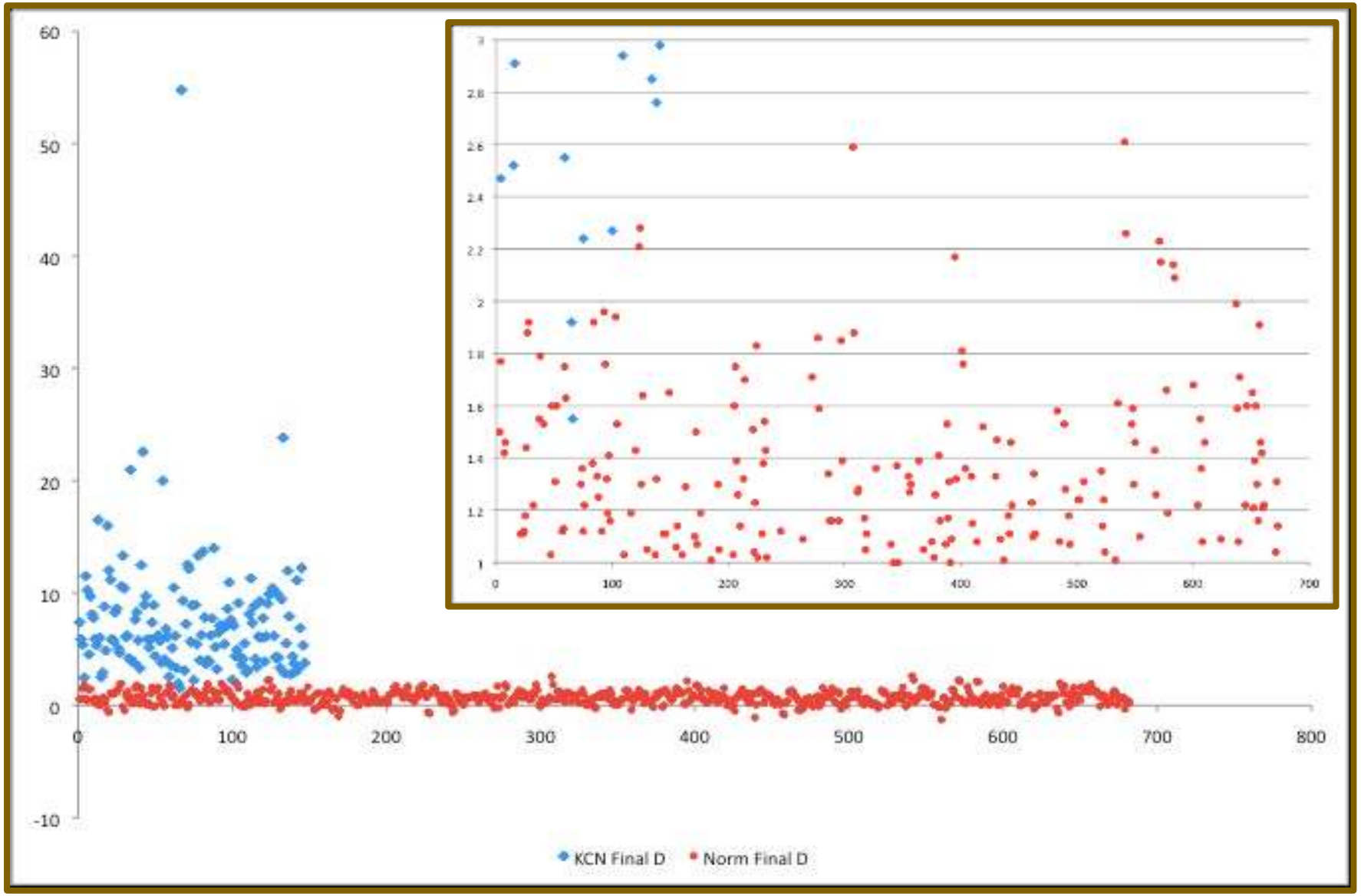
PIavg (progression index)



ARTmax (Ambrosio relational thickness)



“D” (final D based on all parameters)



What’s the Problem ?

Why is eliminating False Positives Important ?

- While it is easily appreciated that false negatives can have major consequences
  - Performing surgery on an unknown keratoconic

Why is eliminating False Positives Important ?

- While it is easily appreciated that false negatives can have major consequences
  - Performing surgery on an unknown keratoconic
- It is less appreciated that false positives have significant consequences
  - Reports of safe elective refractive surgery in eyes that are incorrectly diagnosed with Keratoconus

Single Best Inclusion Parameter

	95% CI / % Normal Inc	97.5% CI / % Normal Inc
Minimal Pach	538 / 49 %	558 / 73 %
Kmax	46.1 / 31 %	45.3 / 55 %
Df	1.43 / 8.2 %	-0.2 / 50 %
Db	1.0 / 13 %	0.48 / 23 %
Elev Front Thinnest	4.3 / 3.5 %	-1.7 / 98.2 %
Elev Back Thinnest	11.3 / 5.7 %	6.3 / 25.0 %
Plavg	1.17 / **3.2 %**	1.08 / 12 %
ARTmax	354 / 5.3 %	376 / 11 %
Final "D"	2.69 / 0 %	2.26 / 0.6 %

This single parameter has been reported as having excellent sensitivity and specificity

Keratoconus Inclusion Criteria

	95% CI / % Normal Inc	97.5% CI / % Normal Inc
Minimal Pach	538 / 49 %	558 / 73 %
Kmax	46.1 / 31 %	45.3 / 55 %
Df	1.43 / 8.2 %	-0.2 / 50 %
Db	1.0 / 13 %	0.48 / 23 %
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Plavg	1.17 / **3.2 %**	1.08 / 12 %
ARTmax	354 / 5.3 %	376 / 11 %
Final "D"	2.69 / 0 %	2.26 / 0.6 %

If we assume a 1:1000 rate a 3.2% false positive rate means that you will have 32 "normal" misdiagnosed as diseased for every true Keratoconus patients.

This makes determining the true efficacy of many studies on early disease difficult to analyze (believe)

Keratoconus Inclusion Criteria

	95% CI / % Normal Inc	97.5% CI / % Normal Inc
Minimal Pach	538 / 49 %	558 / 73 %
Kmax	46.1 / 31 %	45.3 / 55 %
Df	1.43 / 8.2 %	-0.2 / 50 %
Db	1.0 / 13 %	0.48 / 23 %
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Plavg	1.17 / 3.2 %	1.08 / 12 %
ARTmax	354 / 5.3 %	376 / 11 %
Final “D”	2.69 / 0 %	2.26 / **0.6 %**

If we assume a 1:1000 rate a 0.6% false positive rate means that you will have 6 “normal” misdiagnosed as diseased for every true Keratoconus patients.

This still makes determining true efficacy difficult to analyze

Keratoconus Inclusion Criteria

	95% CI / % Normal Inc	97.5% CI / % Normal Inc
Minimal Pach	538 / 49 %	558 / 73 %
Kmax	46.1 / 31 %	45.3 / 55 %
Df	1.43 / 8.2 %	-0.2 / 50 %
Db	1.0 / 13 %	0.48 / 23 %
Elev Front Thinnest	4.3 / 3.5 %	-1.7 / 98.2 %
Elev Back Thinnest	11.3 / 5.7 %	6.3 / 25.0 %
Plavg	1.17 / 3.2 %	1.08 / 12 %
ARTmax	354 / 5.3 %	376 / 11 %
Final "D"	**2.69 / 0 %**	2.26 / 0.6 %

If we assume a 1:1000 rate a 0.6% false positive rate means that you will have 6 "normal" misdiagnosed as diseased for every true Keratoconus patients.

This still makes determining true efficacy difficult to analyze

We need to approach a zero false positive rate.

Many CXL+ studies enroll patients that have been excluded from refractive surgery due to “suspicious” maps

If you use a 95% CI from refractive screening that means that 2% of your treated subjects are likely to have true disease

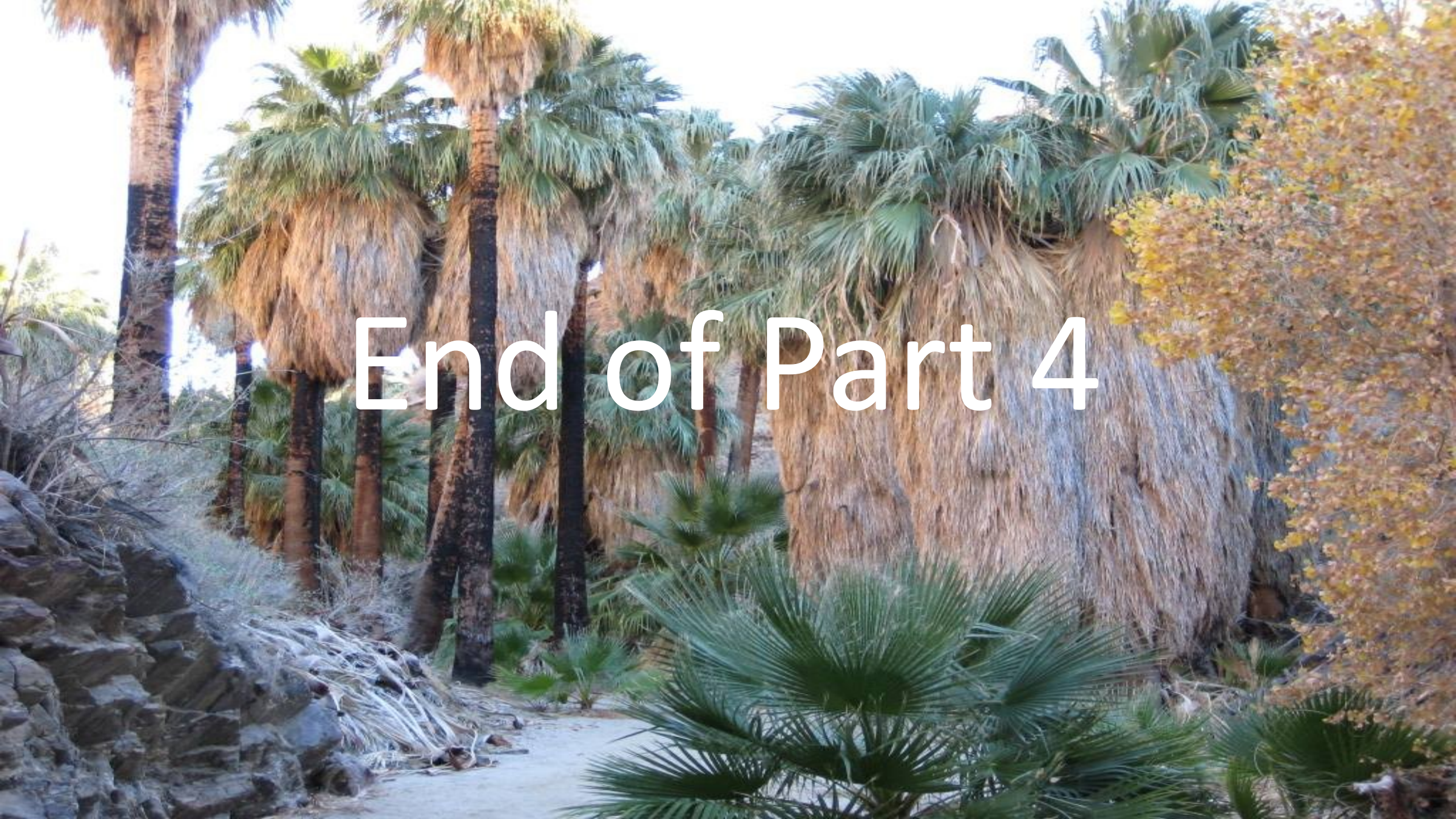
This makes analyzing the data almost impossible

Positive Predictive Value

	95% CI / % Normal Inc	97.5% CI / % Normal Inc
Minimal Pach	538 / 49 %	558 / 73 %
Kmax	46.1 / 31 %	45.3 / 55 %
Df	1.43 / 8.2 %	-0.2 / 50 %
Db	1.0 / 13 %	0.48 / 23 %
Elev Front Thinnest	4.3 / 3.5 %	-1.7 / 98.2 %
Elev Back Thinnest	11.3 / 5.7 %	6.3 / 25.0 %
Pavg	1.17 / 3.2 %	1.08 / 12 %
ARTmax	354 / 5.3 %	376 / 11 %
Final "D"	2.69 / 0 %	2.26 / 0.6 %

- Proportion of patients who test positive who actually have the disease
- If we assume a 1:1000 rate a 3.2% false positive rate means that you will have 32 "normal" misdiagnosed as diseased for every true Keratoconus patients.
- Positive Predictive Value = 1/32

CXL


End of Part 4

Measuring Corneal Thickness

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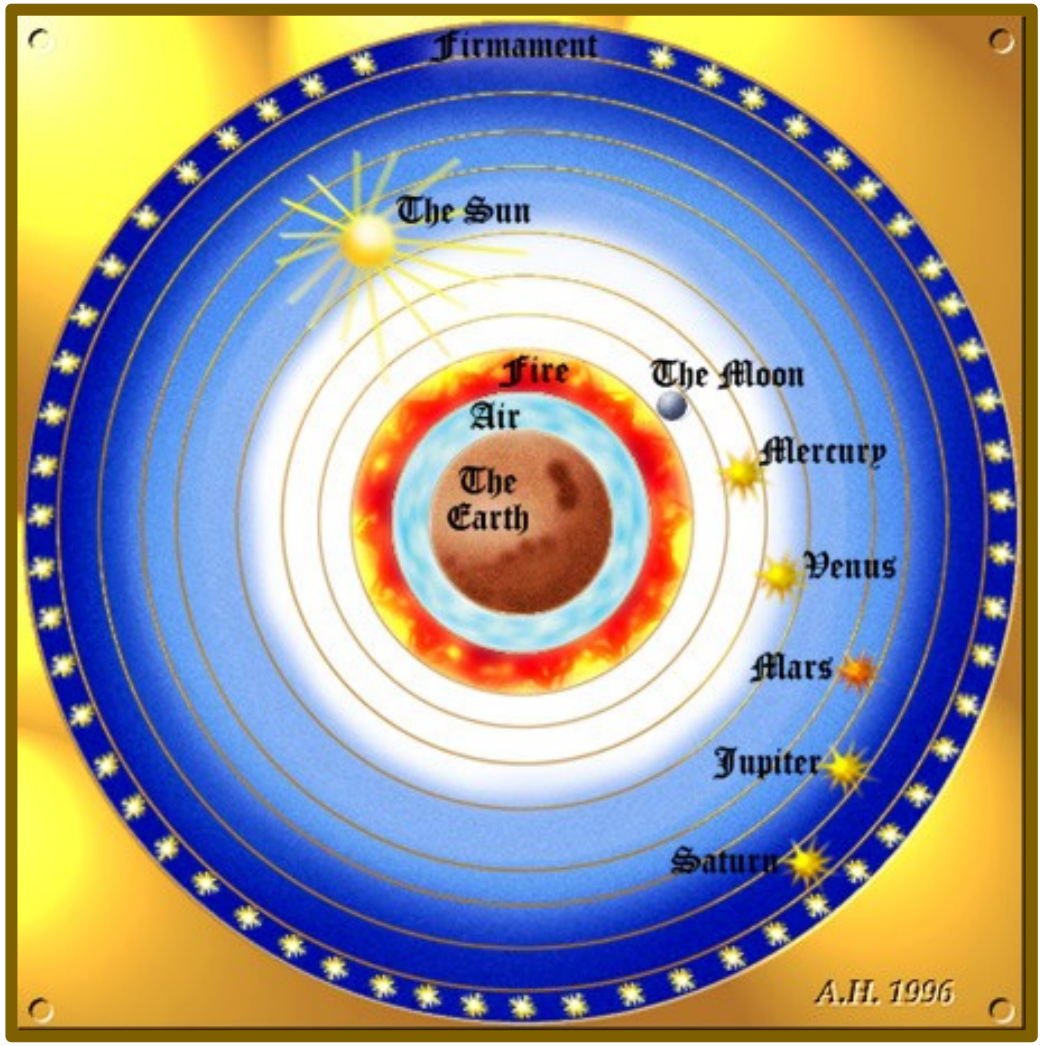
- This is really a discussion on how we look at things
  - Most people are used to visualizing things in 2 dimensions



2 Dimensional Thought

- In 1983 (42 years ago) KAL # 007 was shot down when it strayed over Soviet airspace

The New York Times

U.S. SAYS SOVIET DOWNED KOREAN AIRLINER; 269 LOST; REAGAN DENOUNCES 'WANTON' ACT

Begin's Party Chooses Shamir as New Leader

A FRUITLESS SEARCH

President Calls Meeting of National Security Council for Today

U.S. Positioning 2,000 Marines Off Beirut Coast

MOSCOW CONFIRMS TRACKING OF PLANE

President Demands Explanation For 'Horrifying Act of Violence'

Heart Attack Kills Sen. Jackson

Strategic Soviet Region

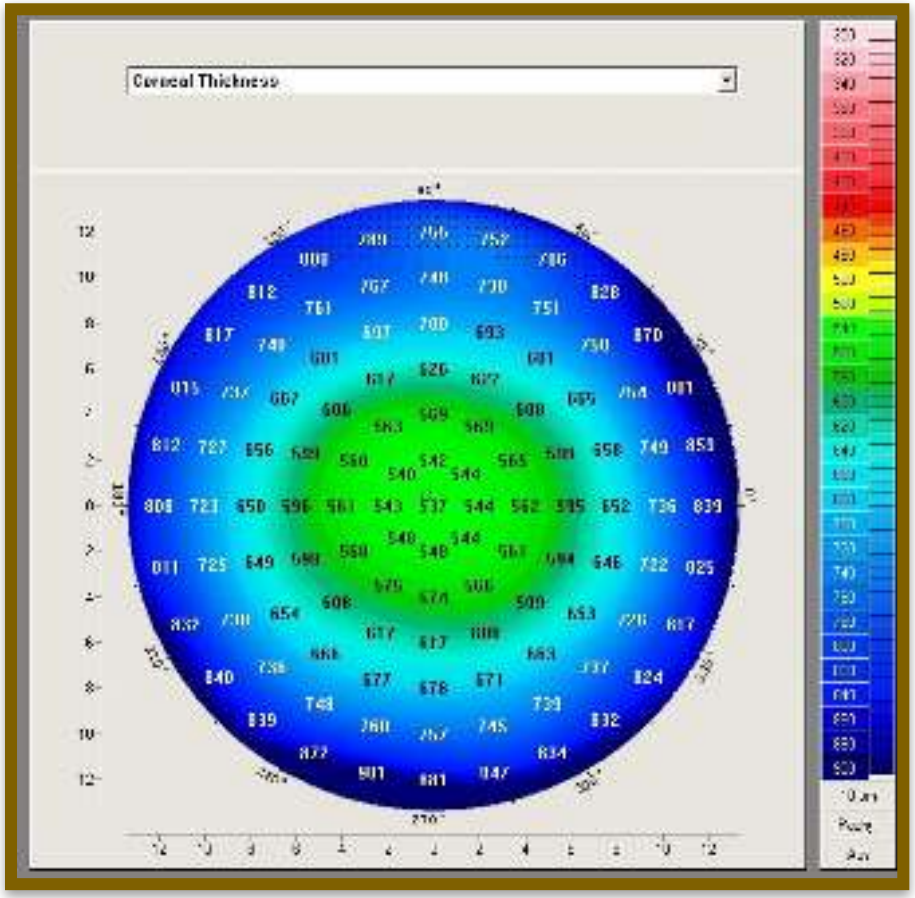
It was a Heyday for Conspiracy Theorists

Two-Dimensional Thinking

Problem of 2D Visualization

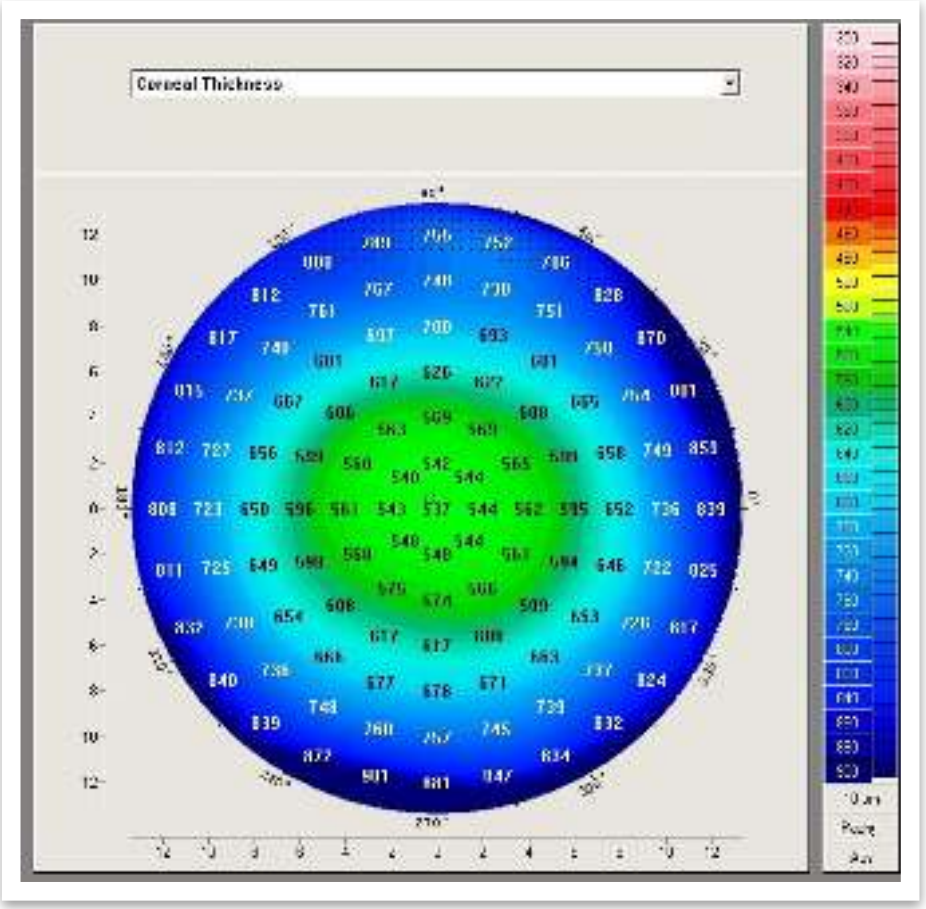
Corneal Thickness

- I would like to address Corneal Thickness
  - One of the more "*Concrete*" Properties
- Thickness is not an optical property
- Physical property described in microns



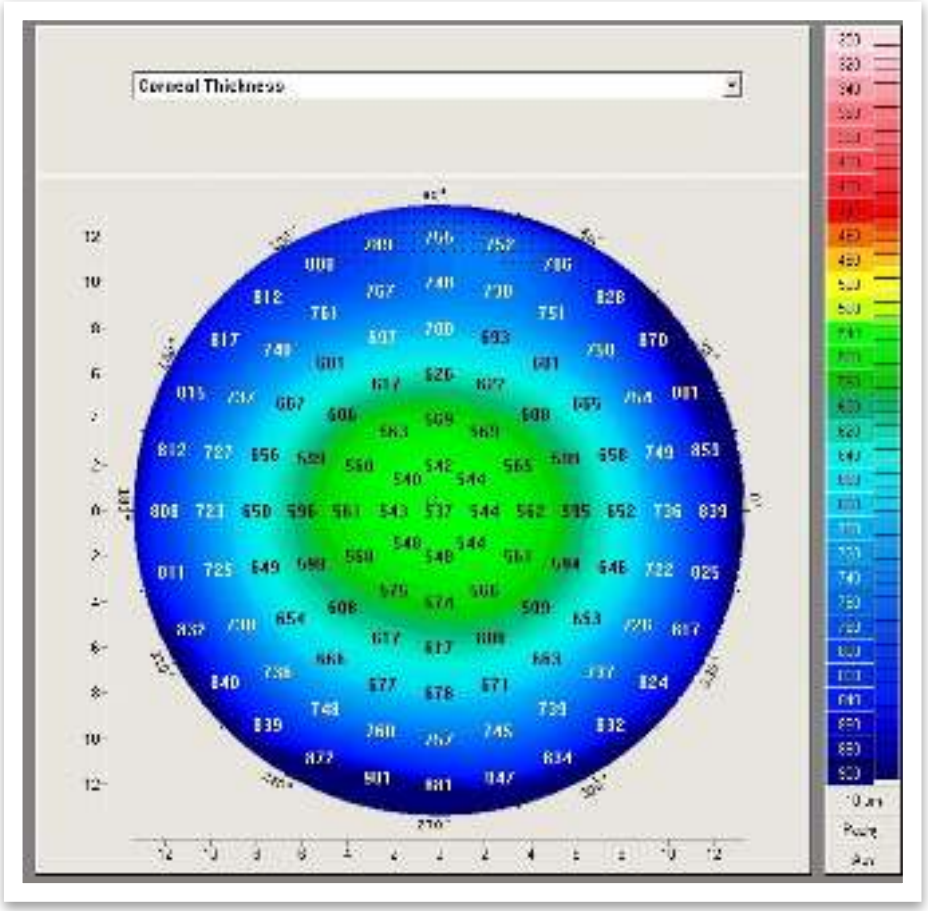
Corneal Thickness Map

- Multiple papers compare different instruments measuring corneal thickness
  - Ultrasound, Optical Pachymetry, Scheimpflug, OCT, Confocal, etc.



Corneal Thickness Map

- We assume they're all measuring the same thing and concentrate on machine variability
  - Ultrasound, Optical Pachymetry, Scheimpflug, OCT, Confocal, etc.



How far is it from Cairo to Alexandria ?

How far is it from Cairo to Alexandria ?

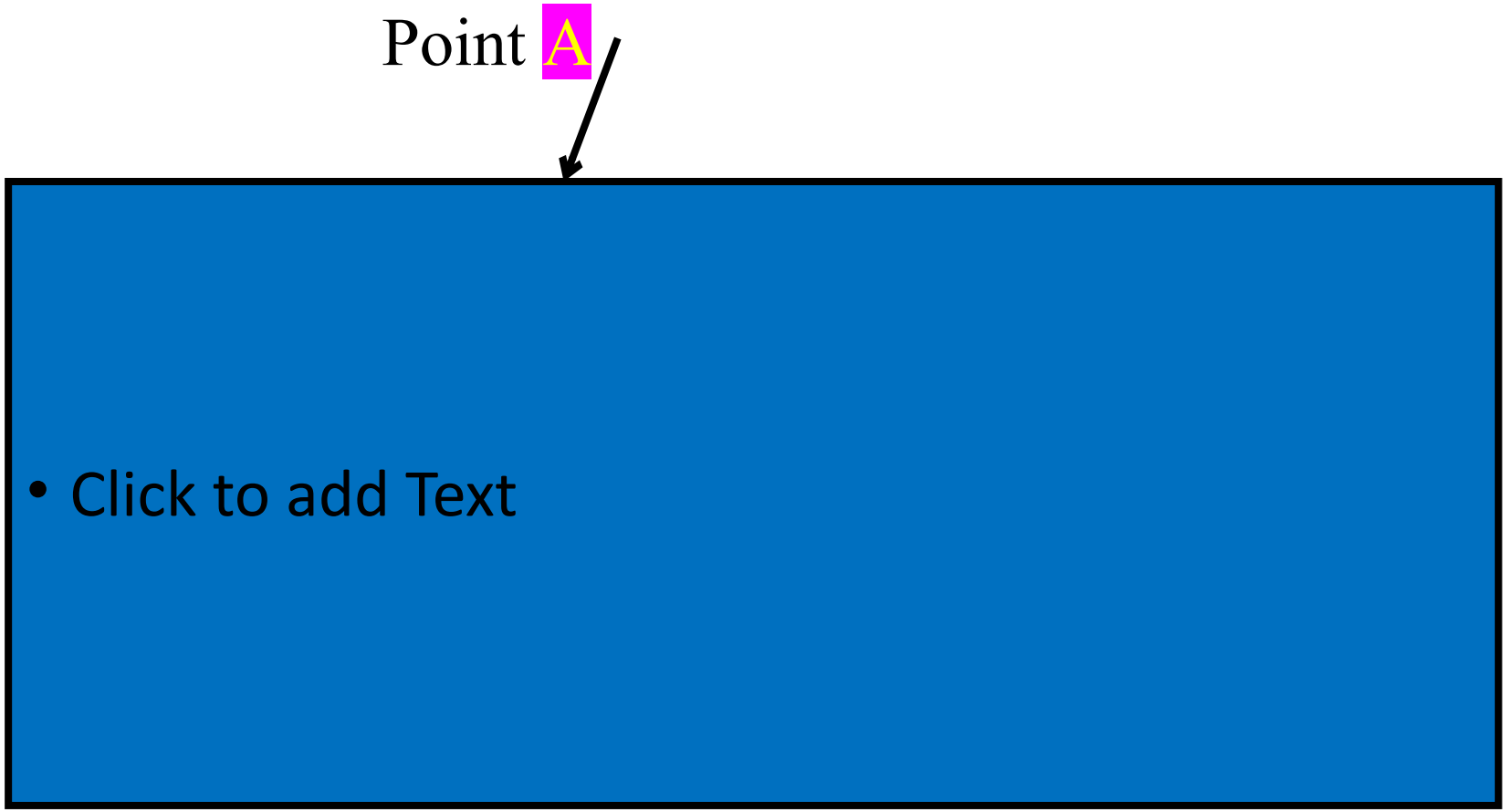
218 Km
(131 miles)

How far is it from Alexandria to Cairo ?

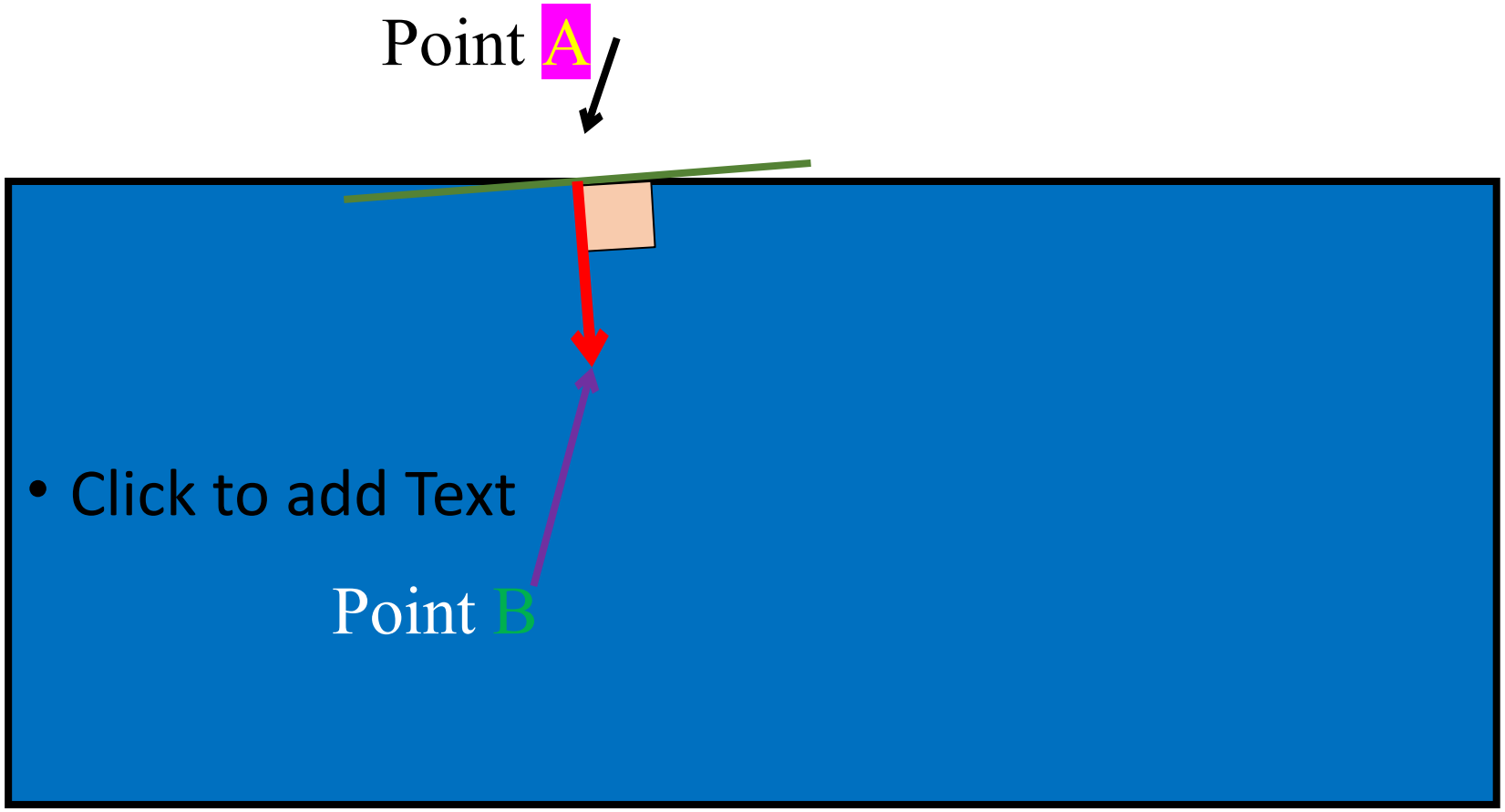
How far is it from Alexandria to Cairo ?

It’s a Trick Question

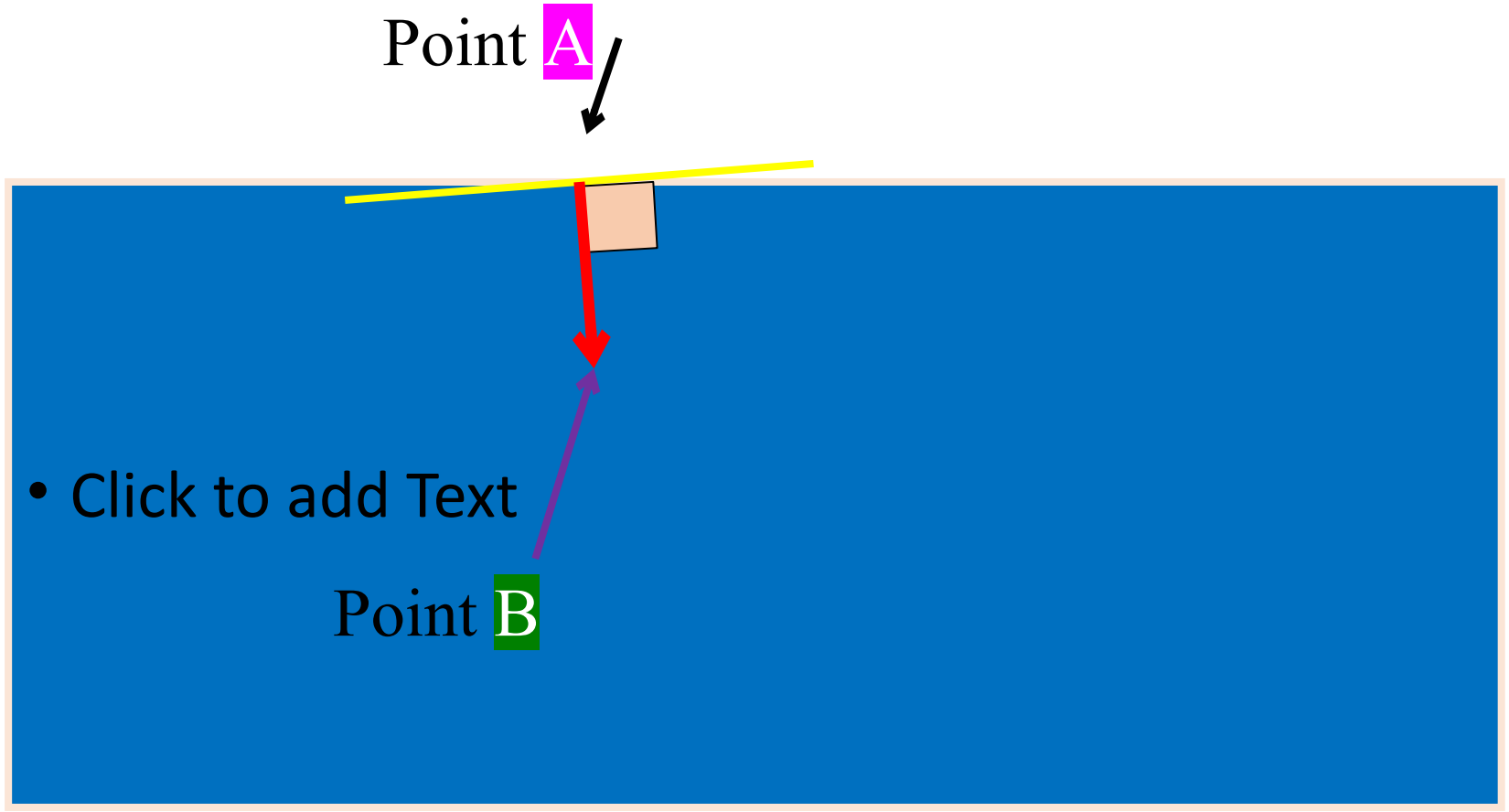
How Thick is the Cornea at Point A



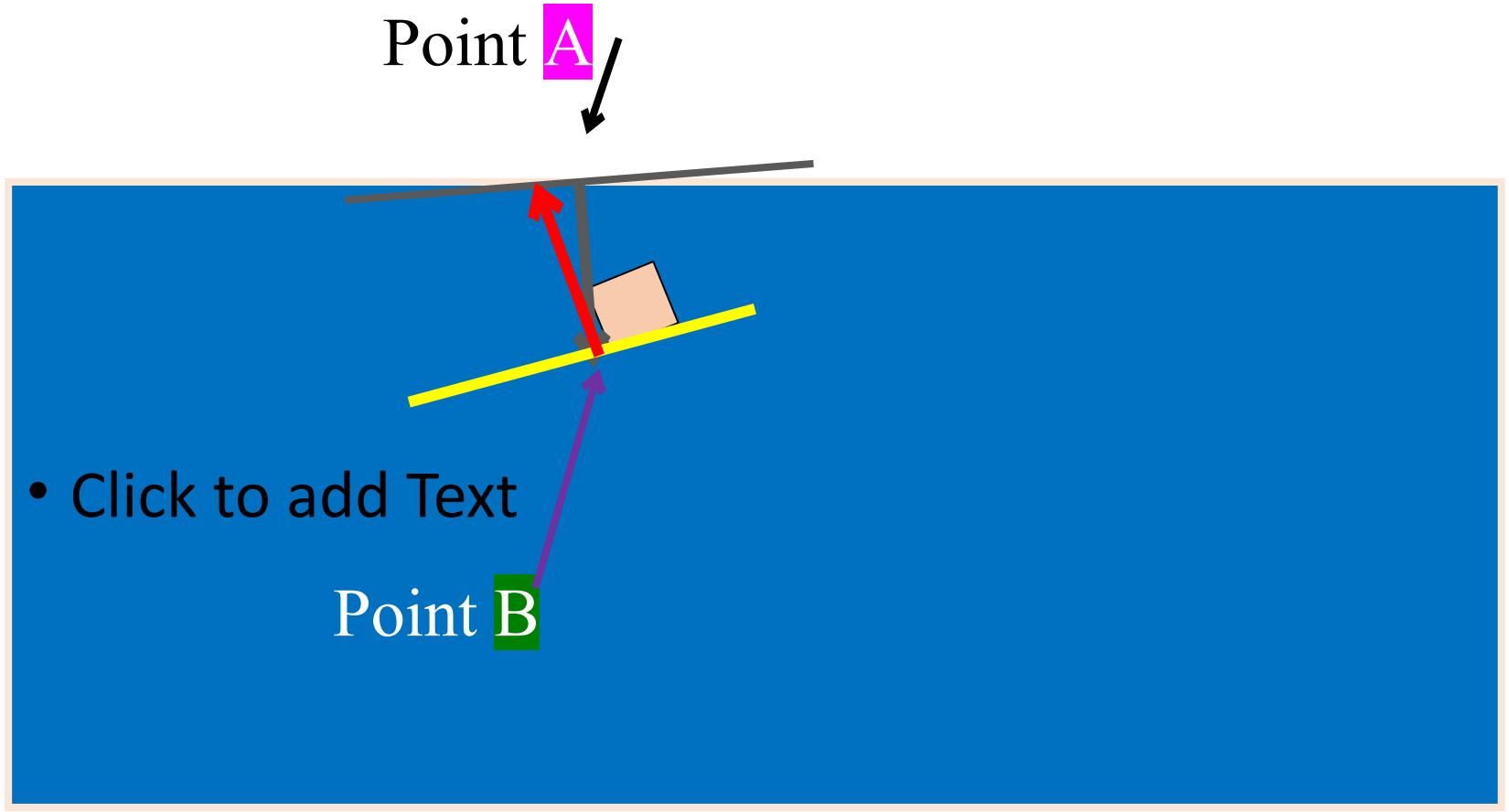
How Thick is the Cornea at Point A



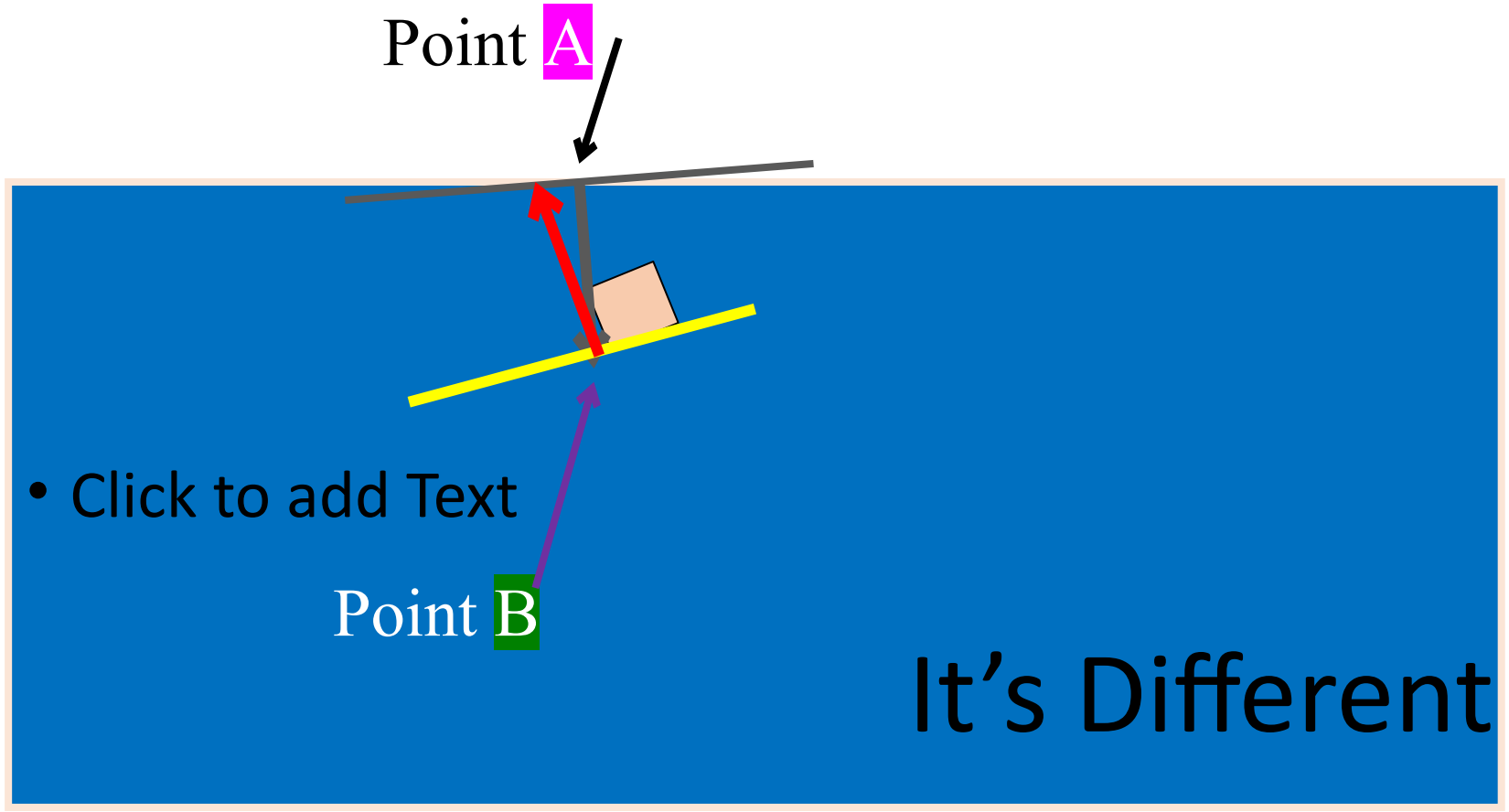
How Thick is the Cornea at Point B



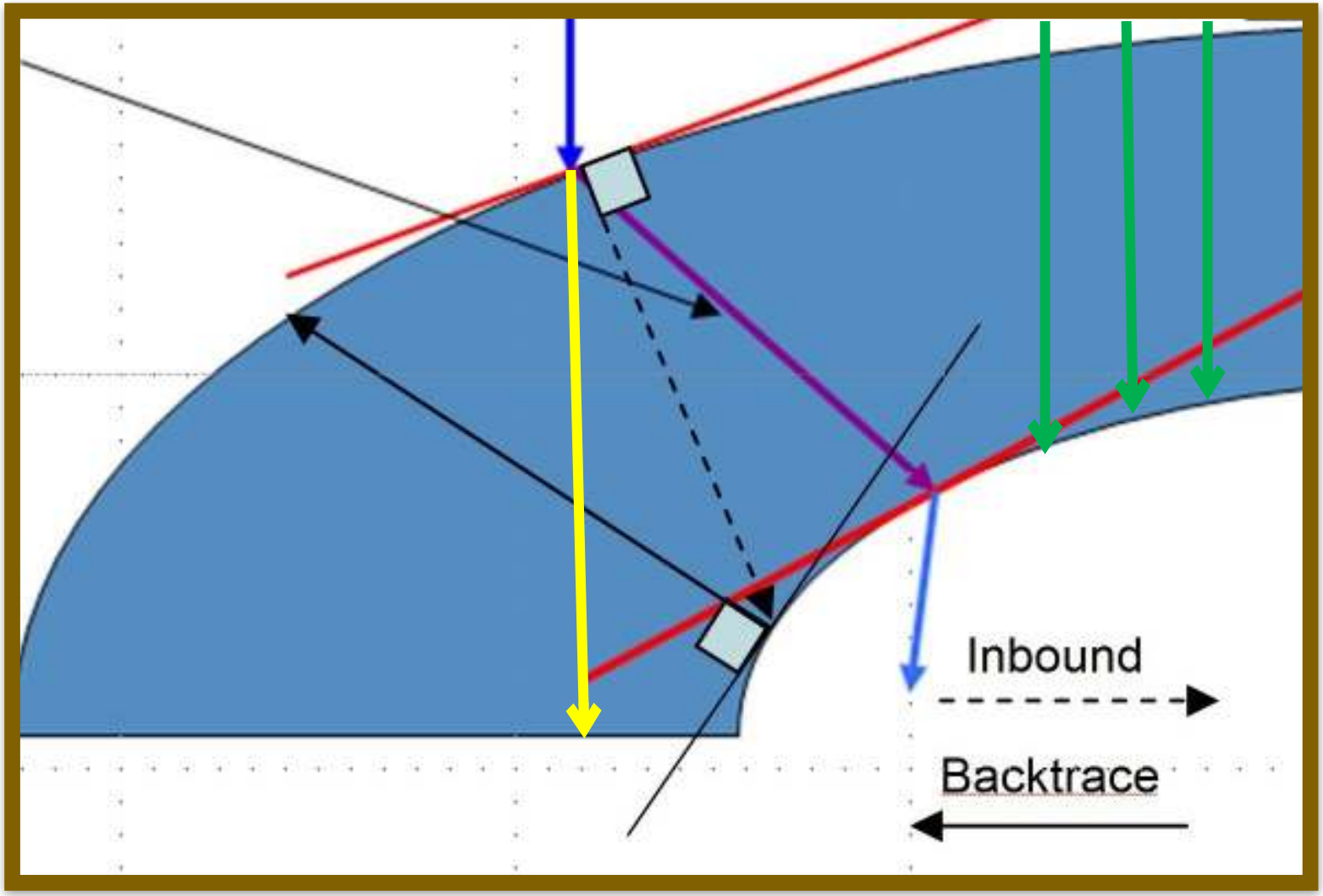
How Thick is the Cornea at Point B



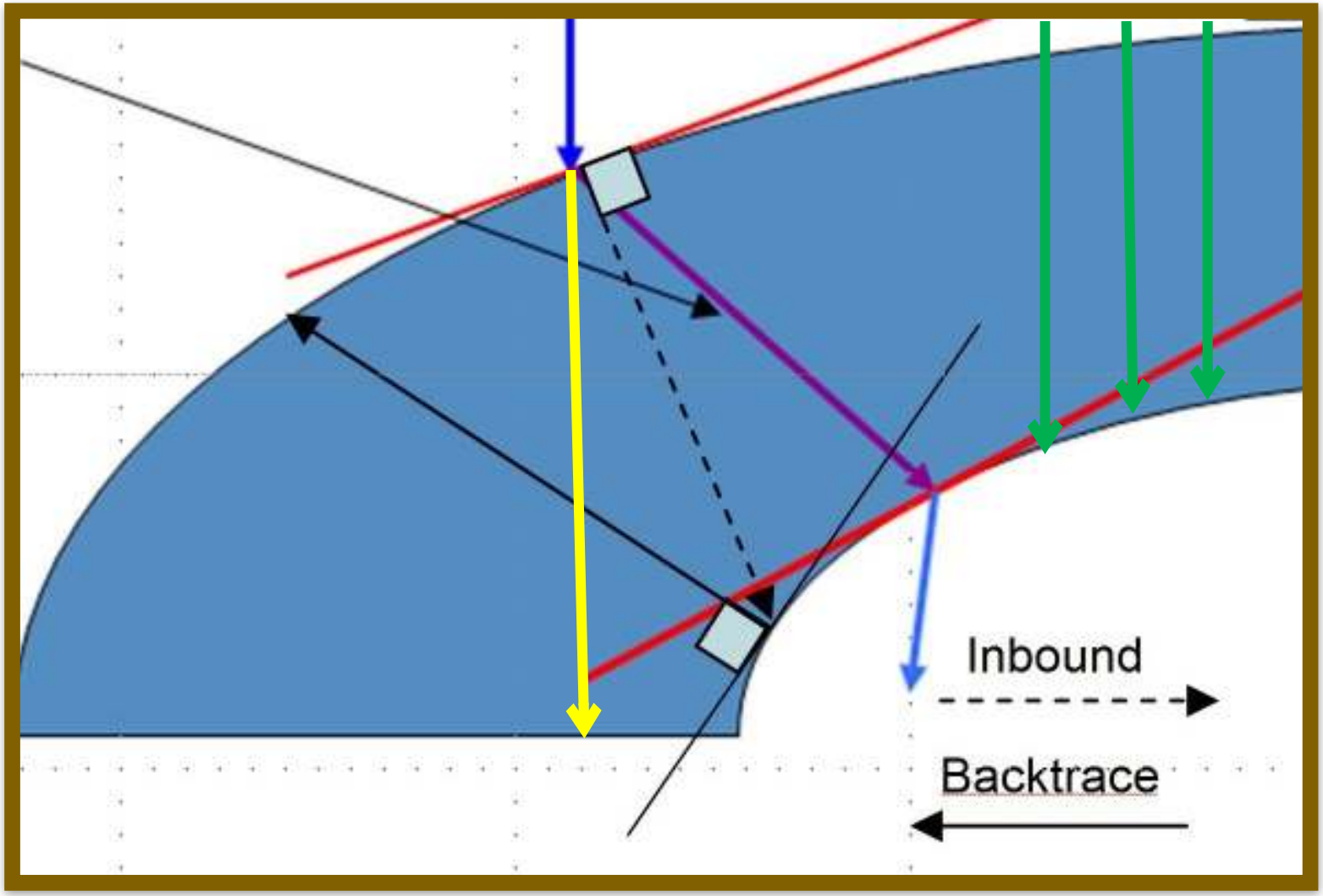
How Thick is the Cornea at Point B



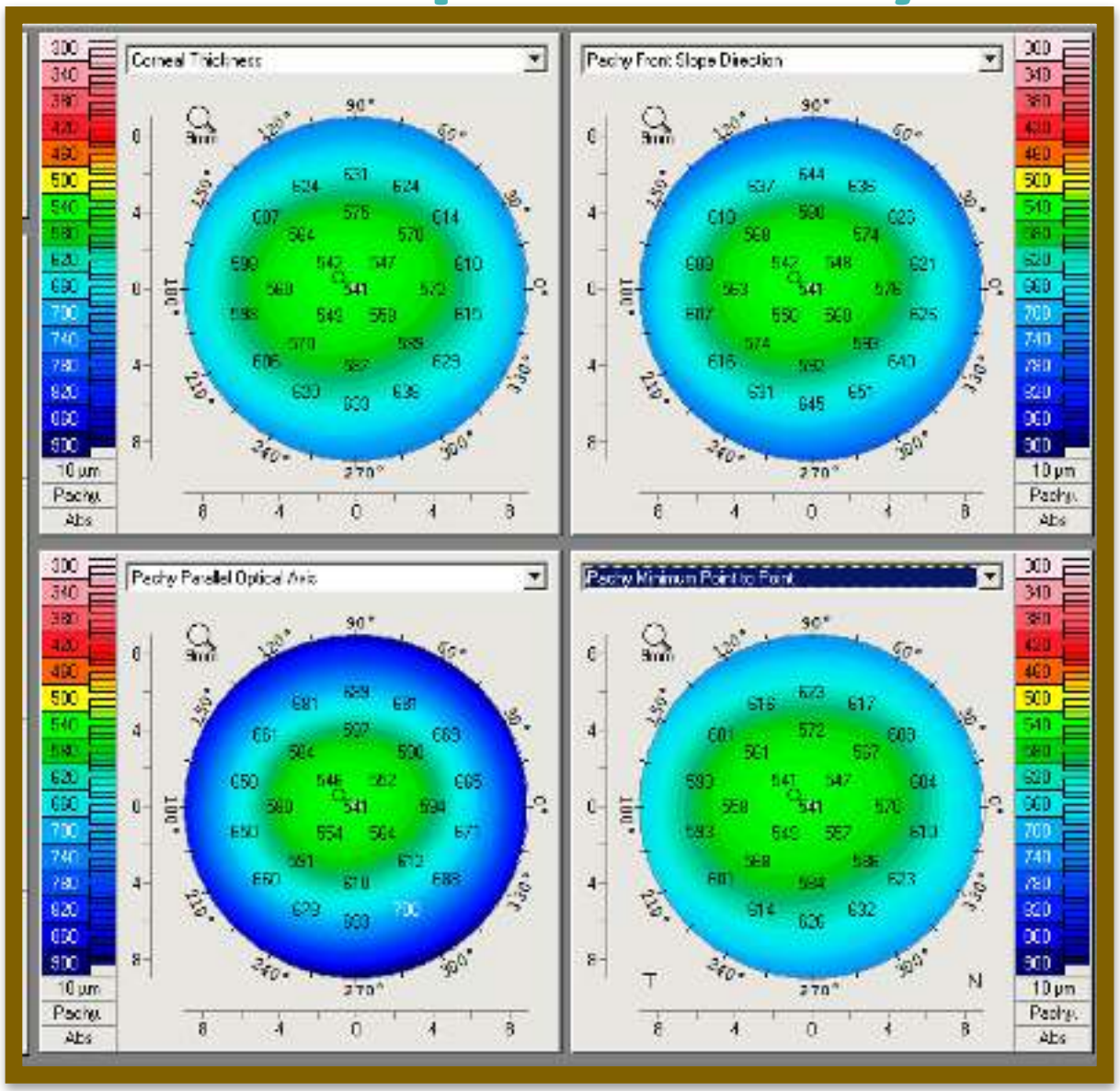
Multiple ways to measure Thickness



We typically only think of one

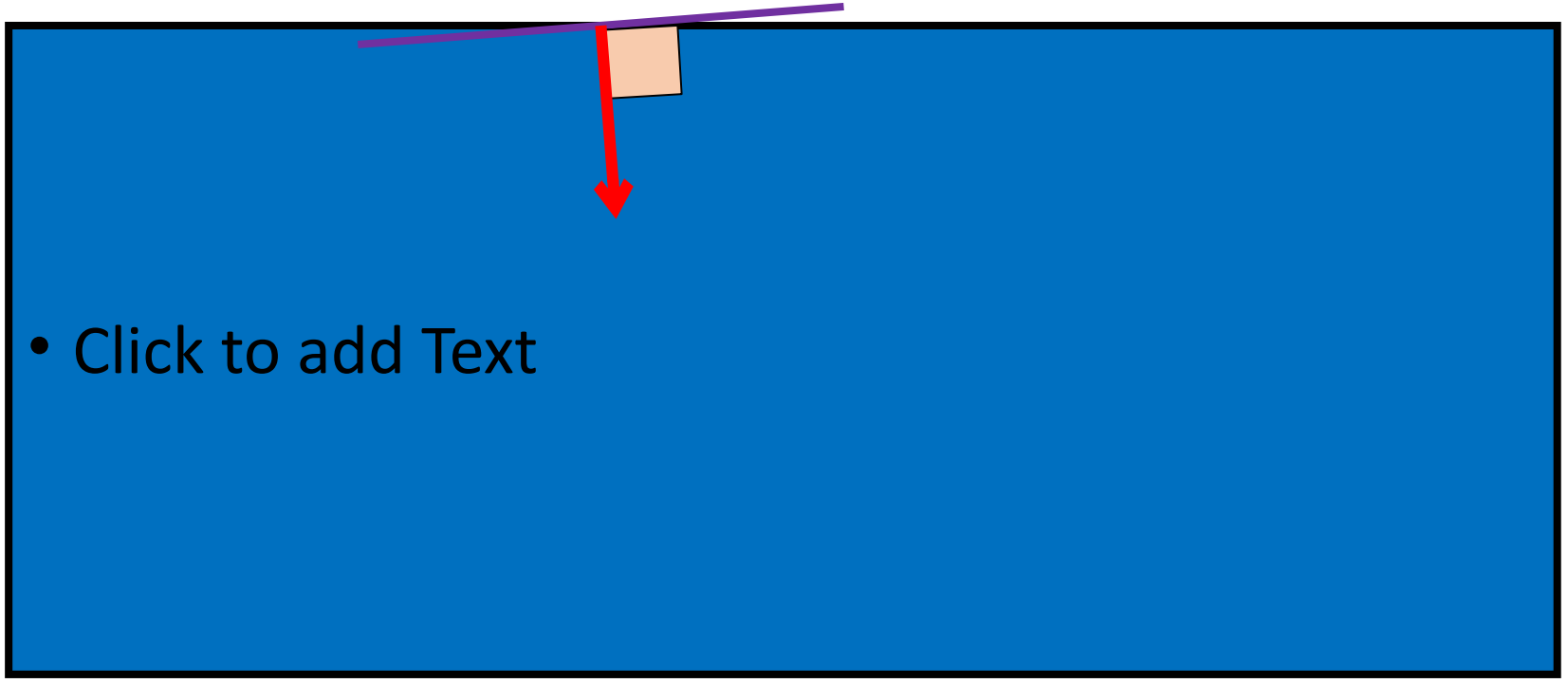


Multiple Ways

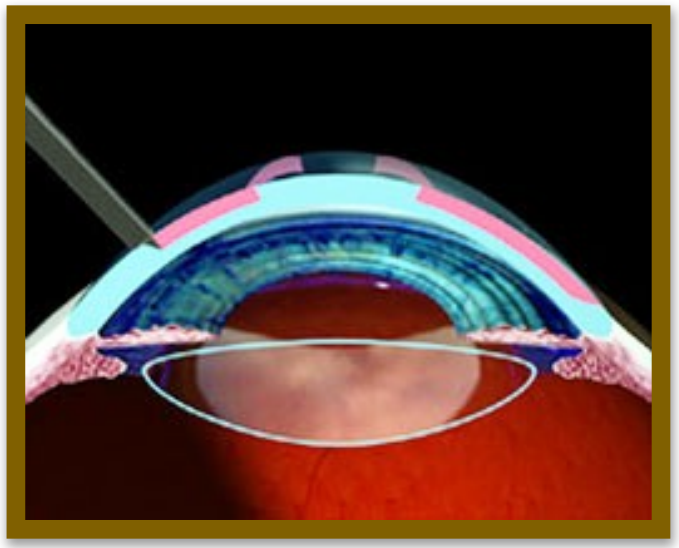


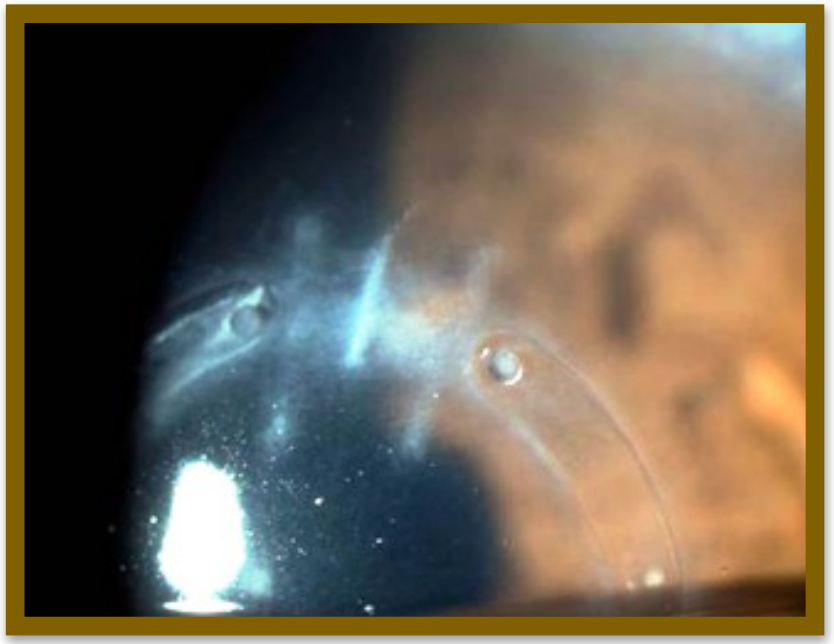
Normal to the Anterior Surface Tangent

This is what most of us think is being measured

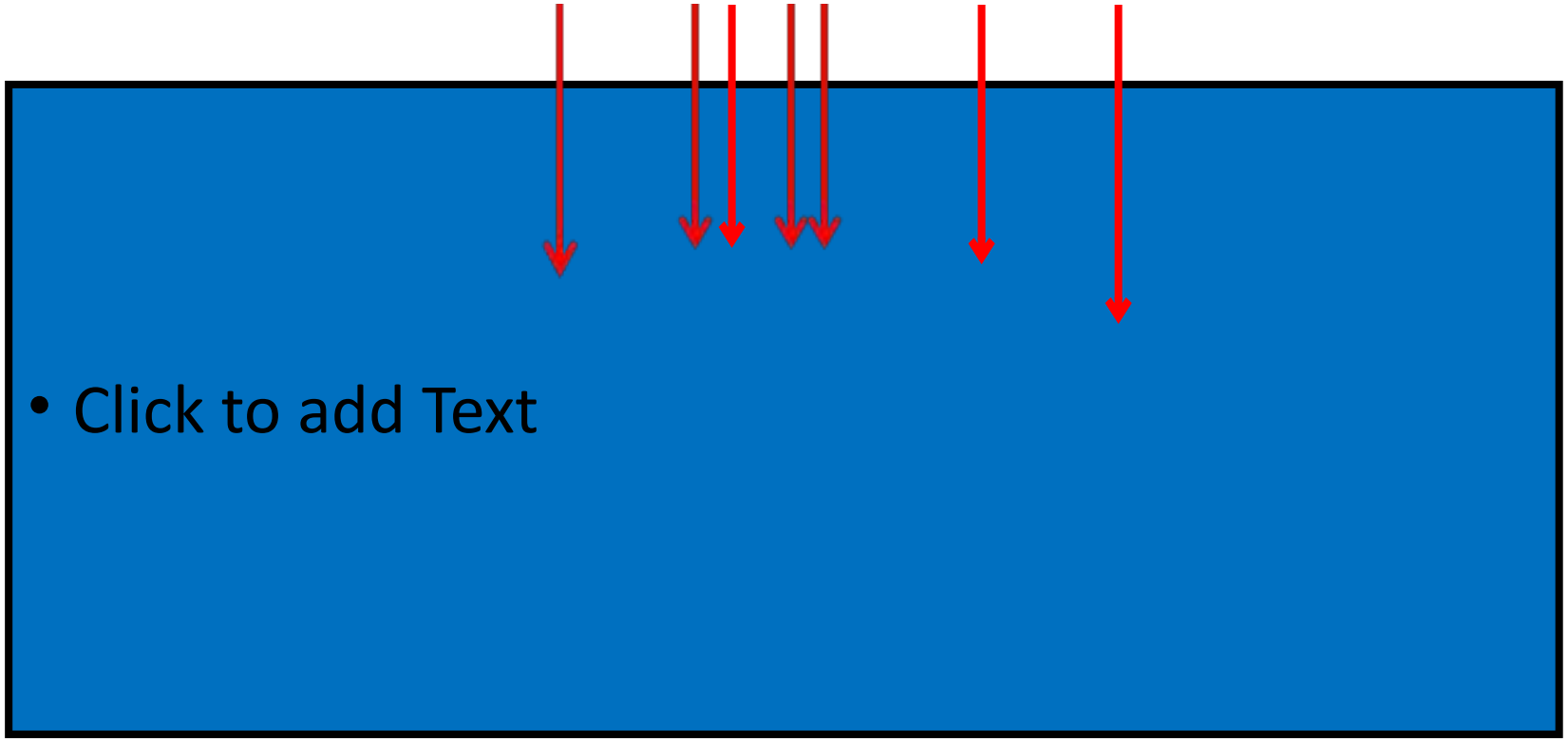


Normal to the Surface Tangent





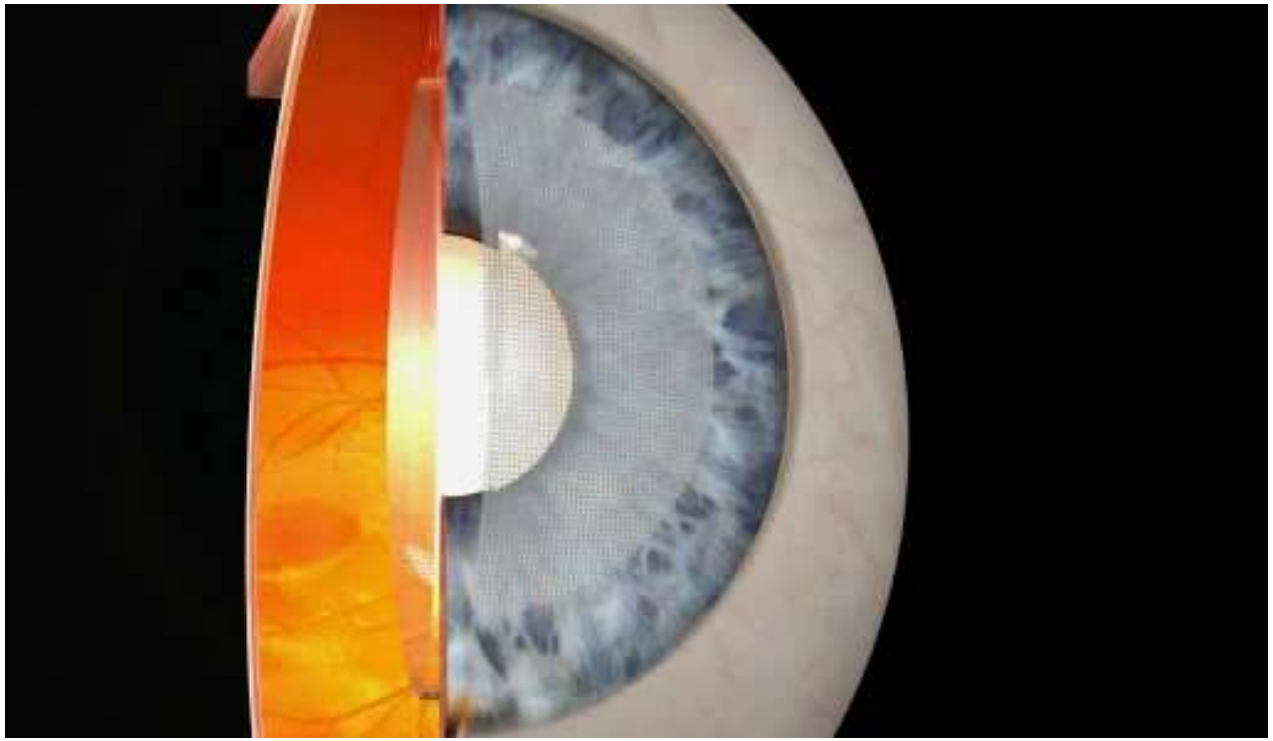
Parallel Vertical Cuts



Similar to an Egg Slicer

Ophthalmic Analogy

- Translational femtosecond laser
  - Ziemer LDV



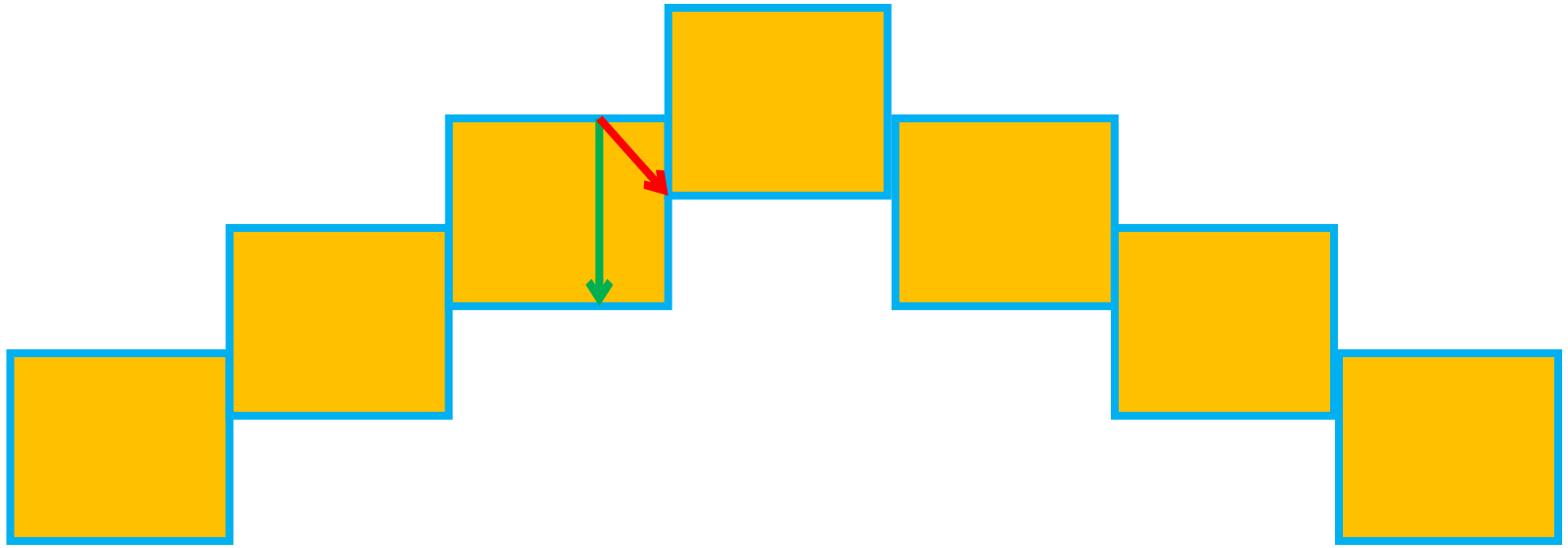
Searching for Minimal Thickness

GREEN is how you currently do it by taking the normal to the surface

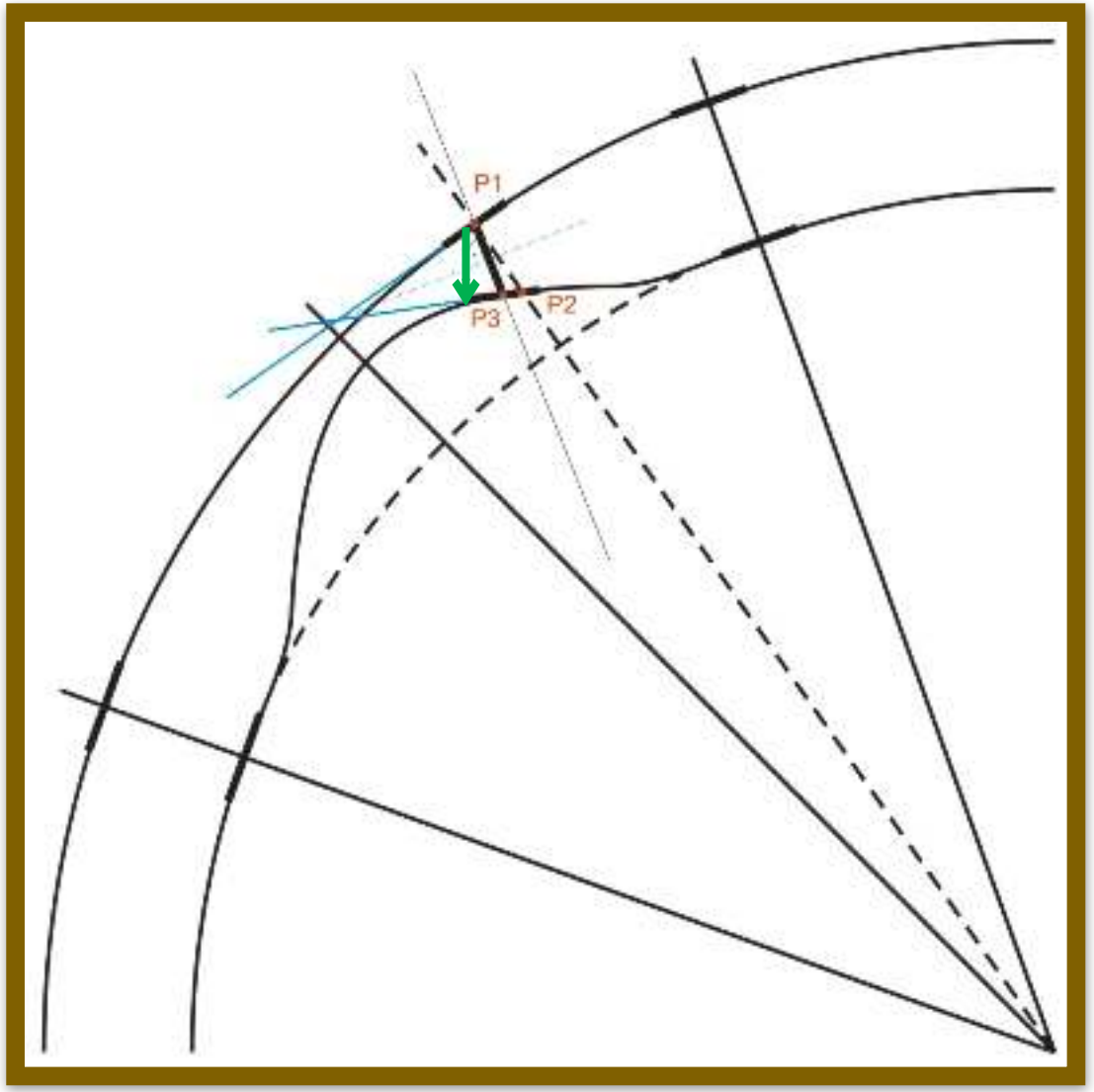
Searching for Minimal Thickness

GREEN is how you currently do it by taking the normal to the surface

RED by looking for the closest posterior point regardless of orientation

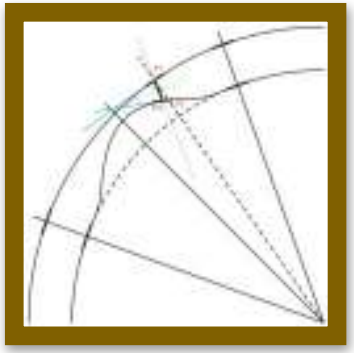


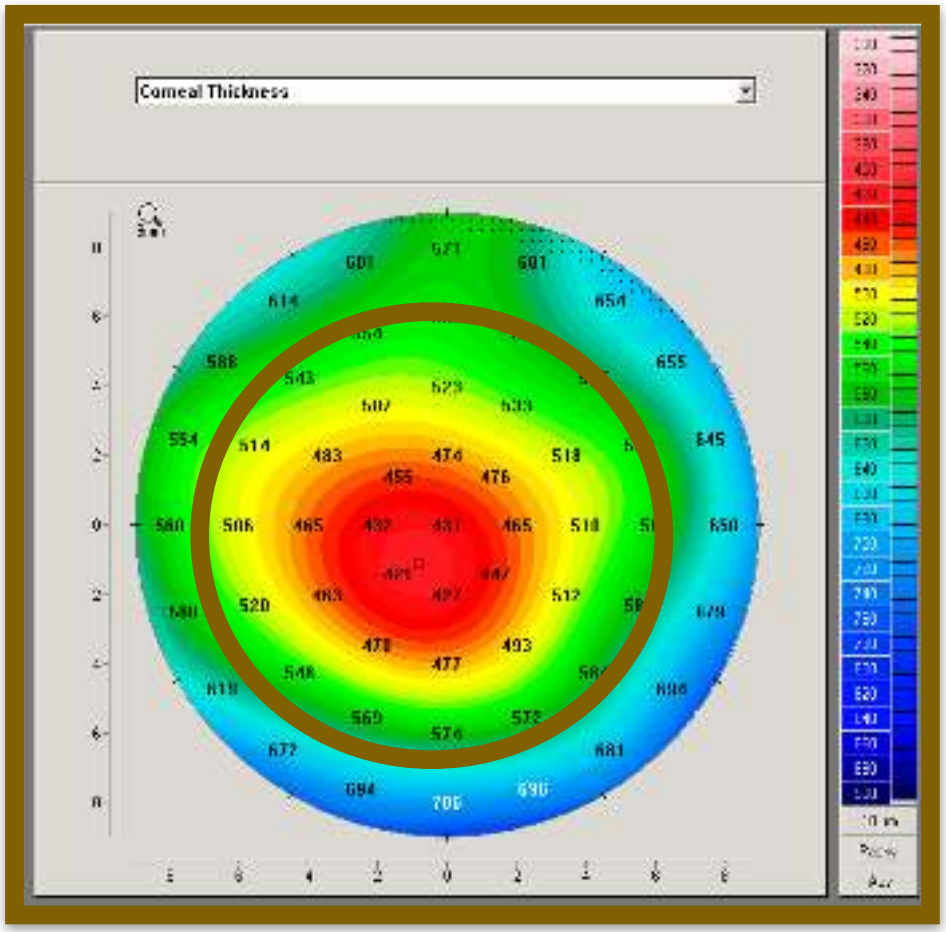
Minimal Distance vs Normal to Tangent



Sonar - Minimal Distance is Critical

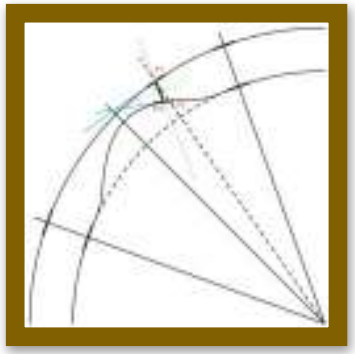
ICR Surgical Planning Channel Depth

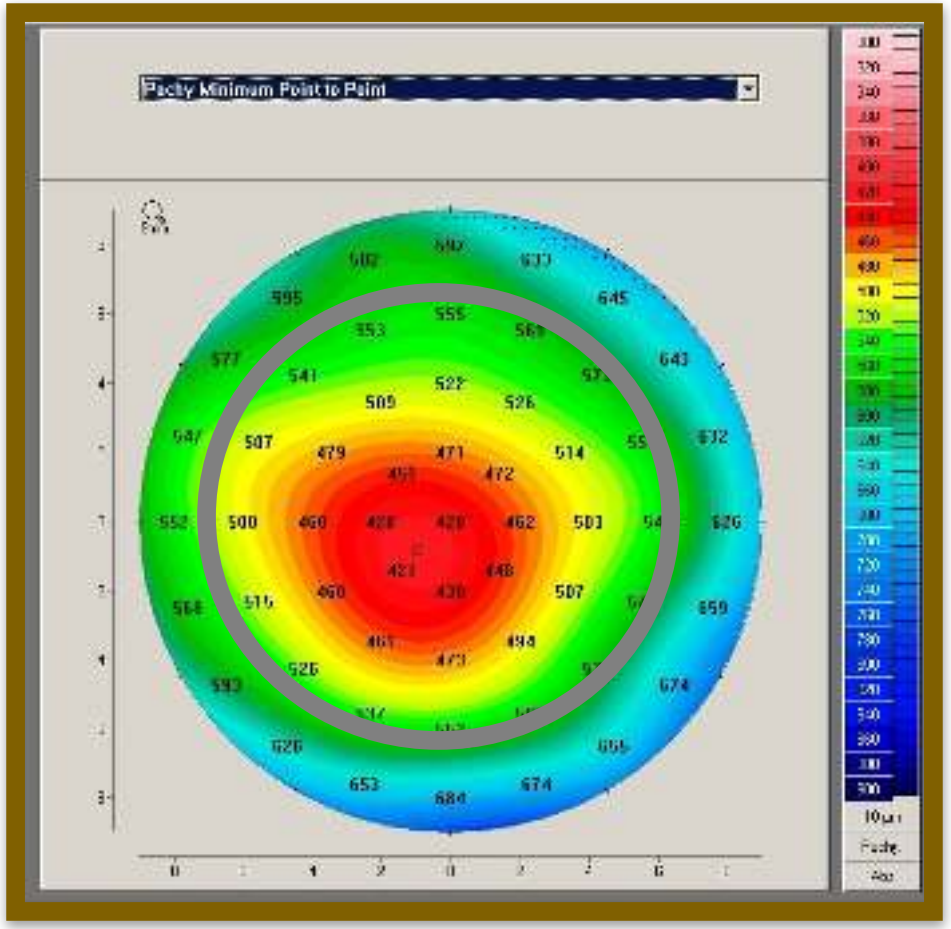




Standard Pachymetry

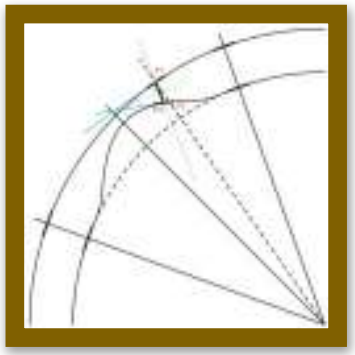
Minimal Distance Method

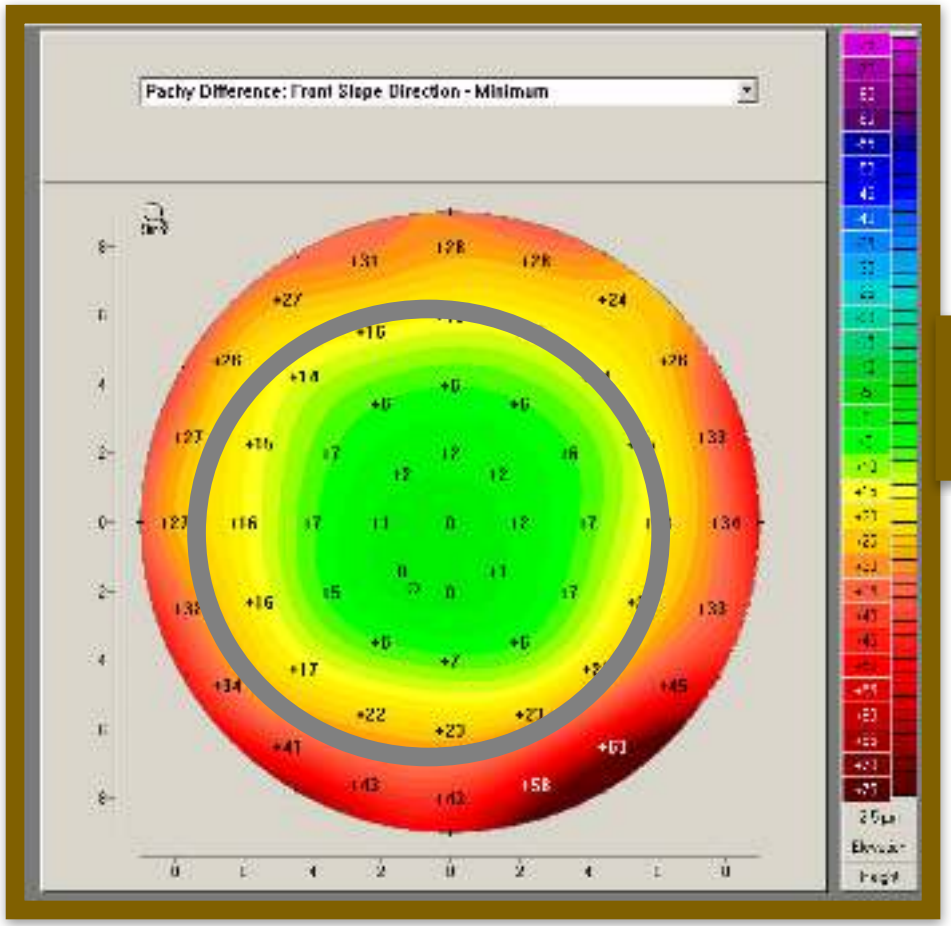




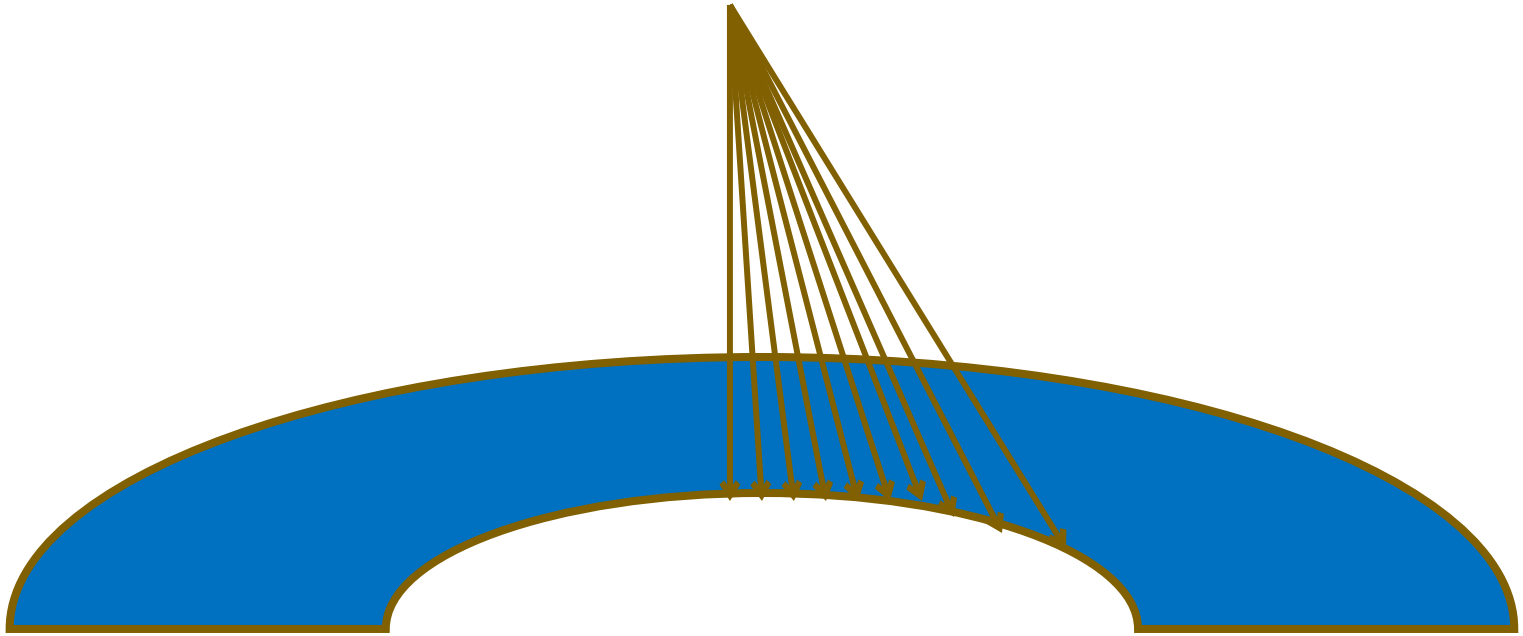
Minimal Distance Method

As much as a 35-micron difference between Minimal & Standard Methods

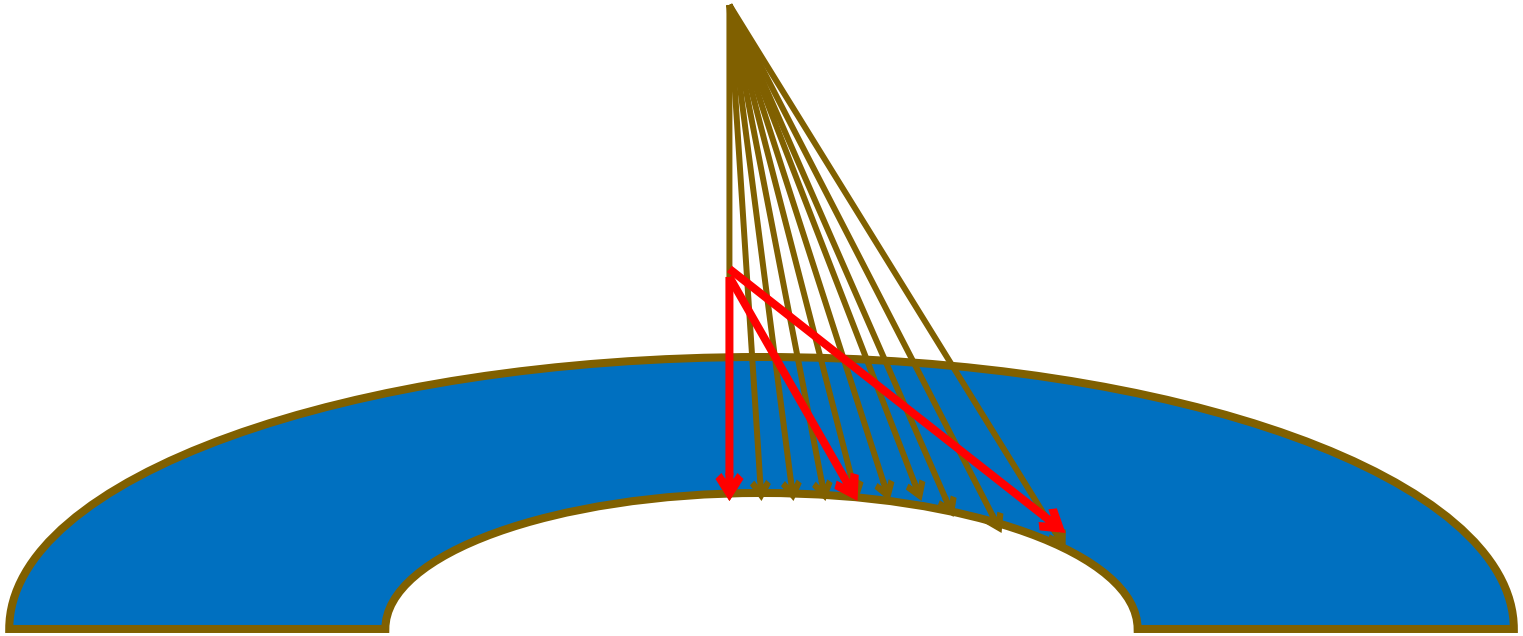




Thickness from 1 fixed point



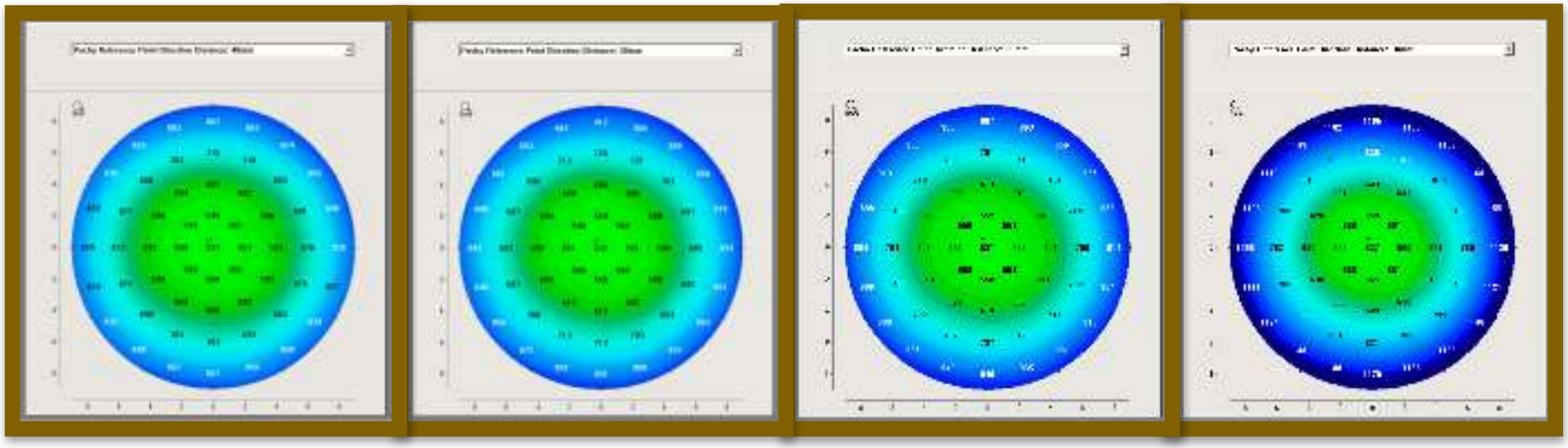
Thickness from 1 fixed point



This will vary based on the distance from the Apex

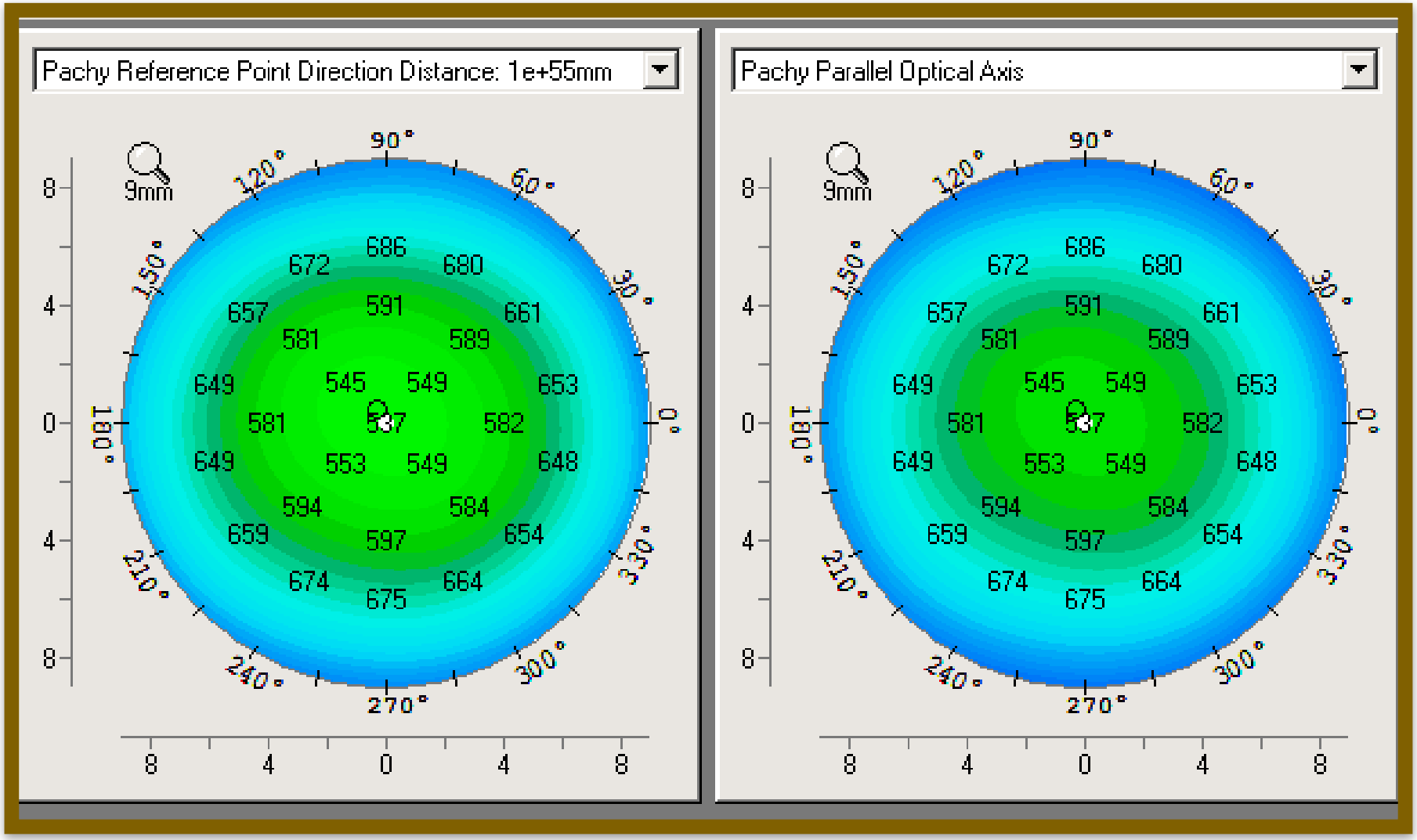
Most Current Refractive Lasers

Distance set by the focal Length of the Delivery System

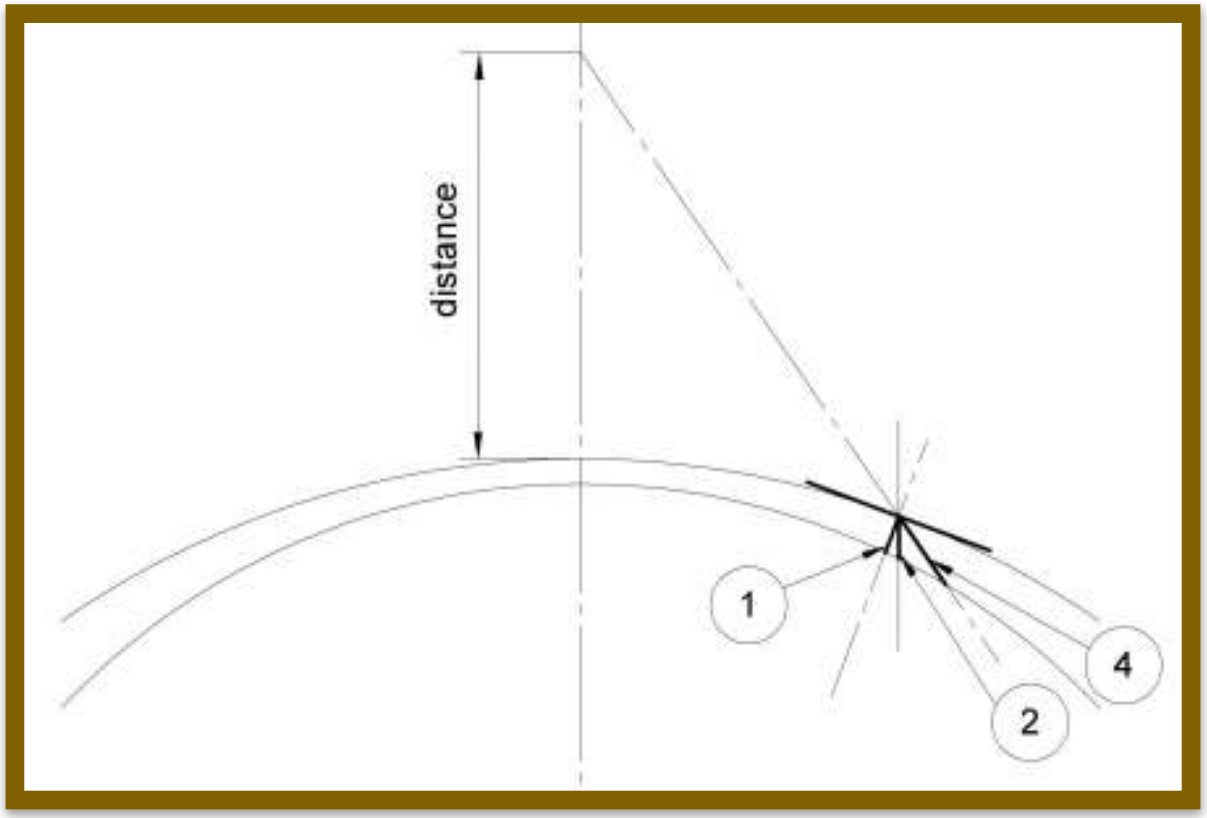


40 microns 30 microns 20 microns 10 microns

Working distance at infinity should be the same as parallel cuts



Measurements / Information can Vary



It is important to know exactly how the measurements are being made


Thank You