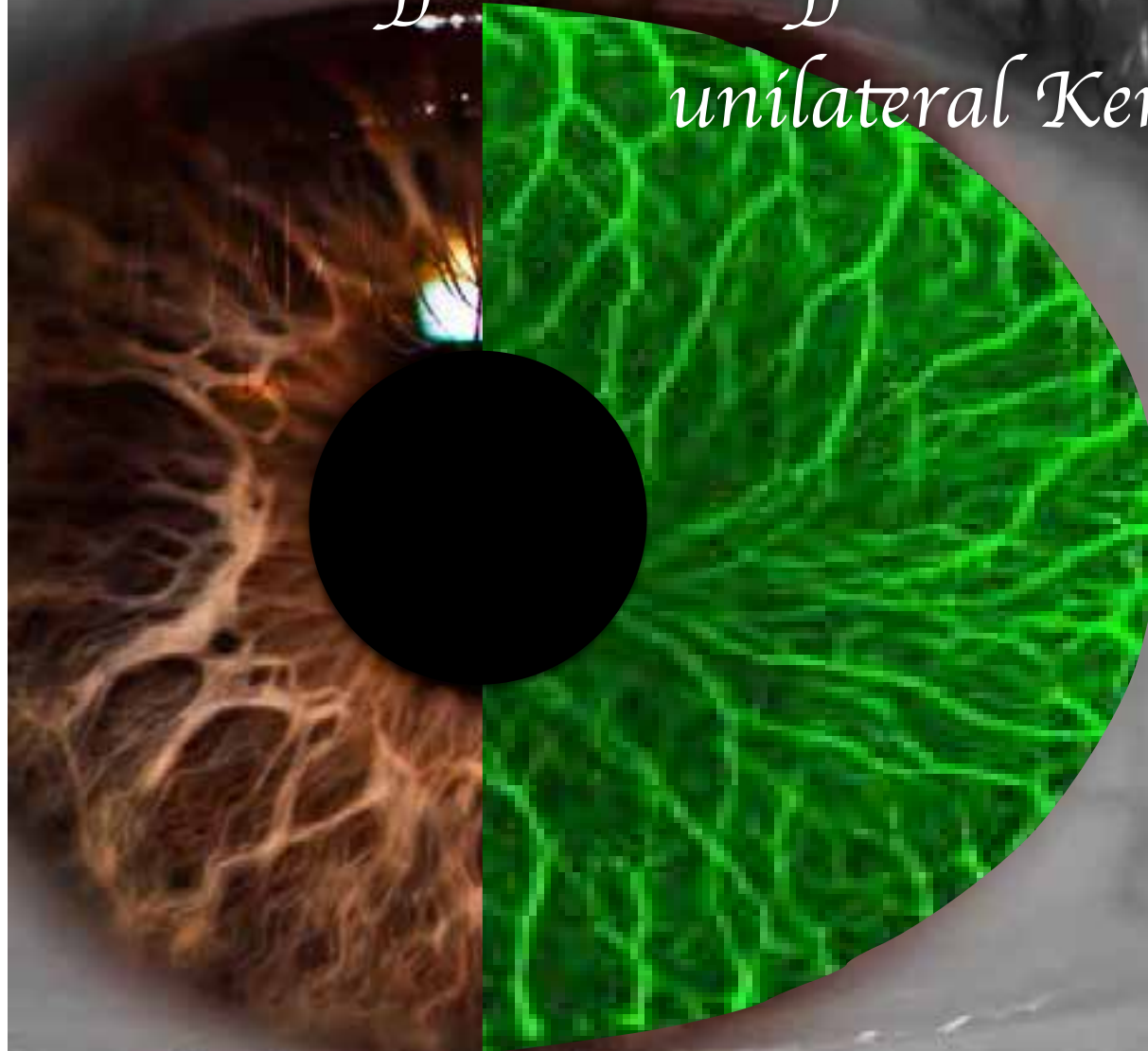


*Quantitative alterations in nerve morphology to
differentiate affected and unaffected eyes in
unilateral Keratoconus*

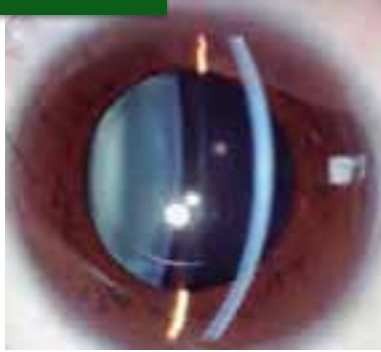


*Dr. Pallak Kusumgar
Fellow Cornea and refractive
Narayana Nethralaya,
Bangalore, India*

*Co-authors: Dr. Rohit Shetty
Dr. Natasha Pahuja
Dr. Kanchan Sinani*

No financial disclosure

Demographics and ocular examination



Current diagnostic parameters



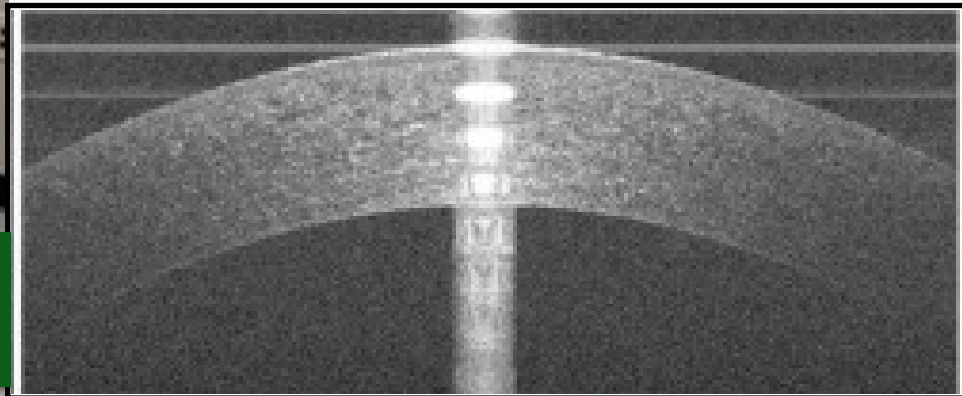
Topo/
tomography



ESTABLISHED KERATOCONUS



AS-OCT



Understanding the disease process



**In vivo Confocal
microscopy**

**No ideal animal
model**



Advanced KC

BUT!!!

Neuro

S

Unilateral KC



**Unaffected fellow eye - ideal control
(contributing risk factors are similar)**

The Scientific Journal of
The Royal College of Ophthalmologists
Eye (Lond). 2007 May;21(5):614-23. Epub 2006 Feb 24.

Quantitative analysis of corneal microstructure in keratoconus utilising in vivo confocal microscopy.

Weed KH¹, MacEwen C.J, Cox A, McGhee CN.

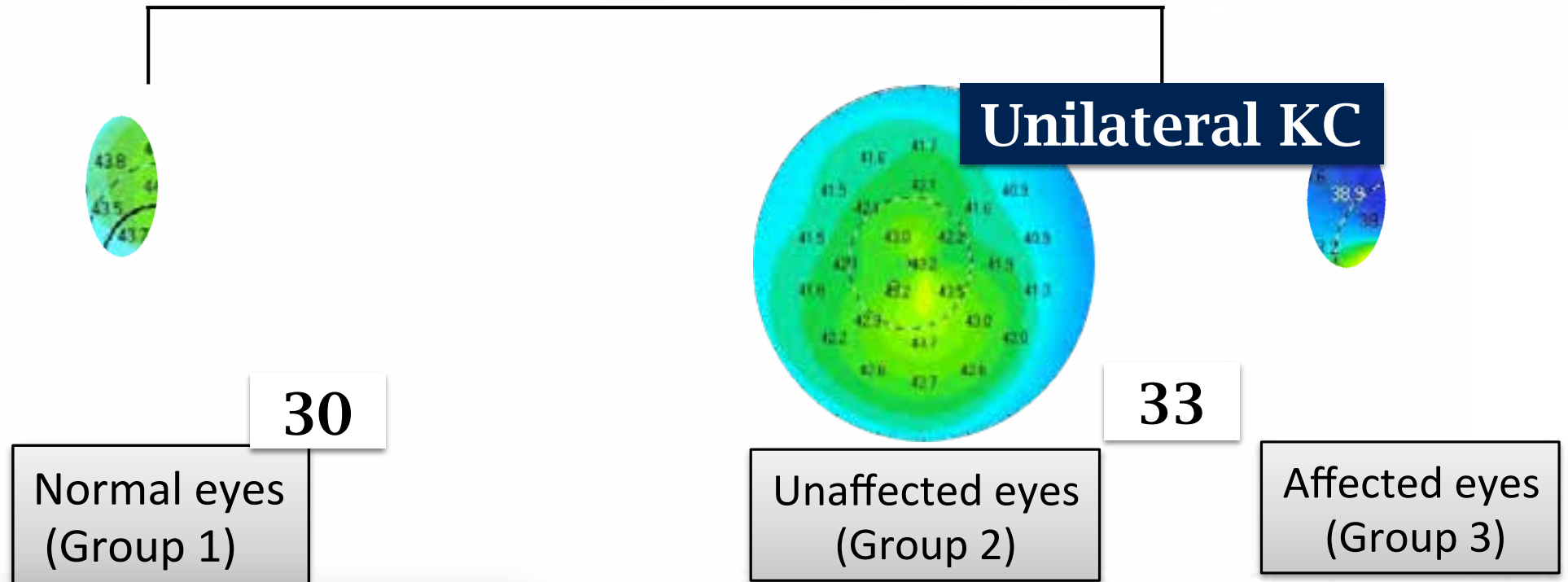


PURPOSE

- To study corneal nerve morphology in unilateral KC
- To determine its role in pathogenesis, diagnosis and as a marker for disease progression.

Material & Methods

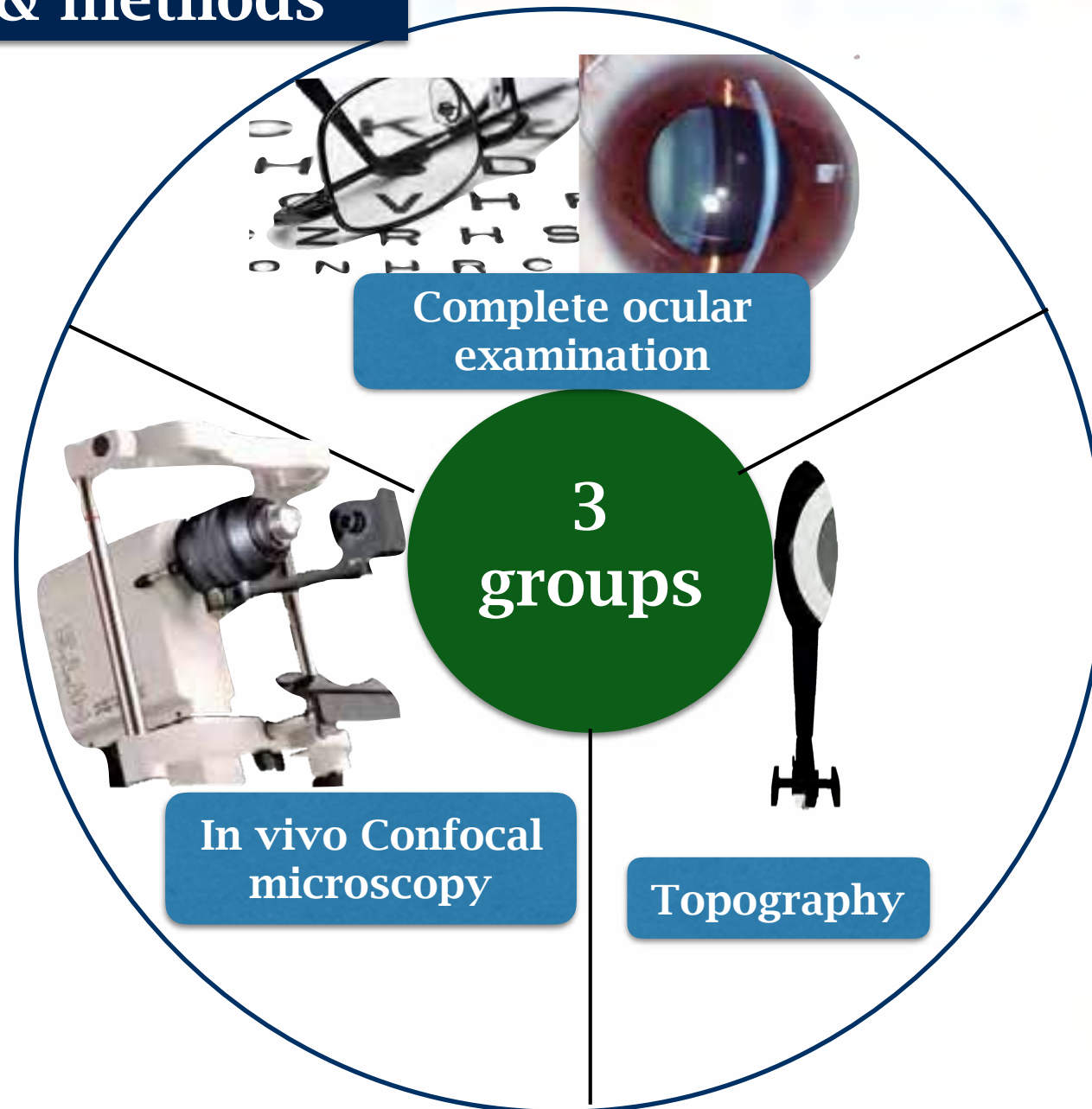
Prospective longitudinal study



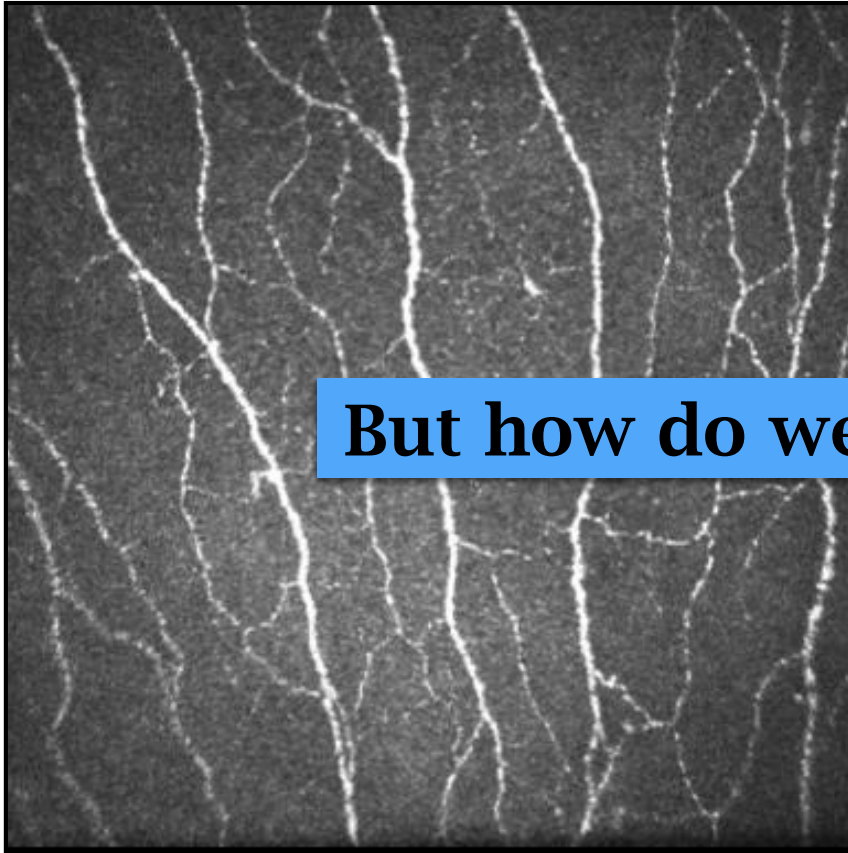
EXCLUSION CRITERIA

- Contact lens wearer
- Ocular trauma/surgery
- Bilateral KC

Materials & methods



IVCM images of corneal nerves



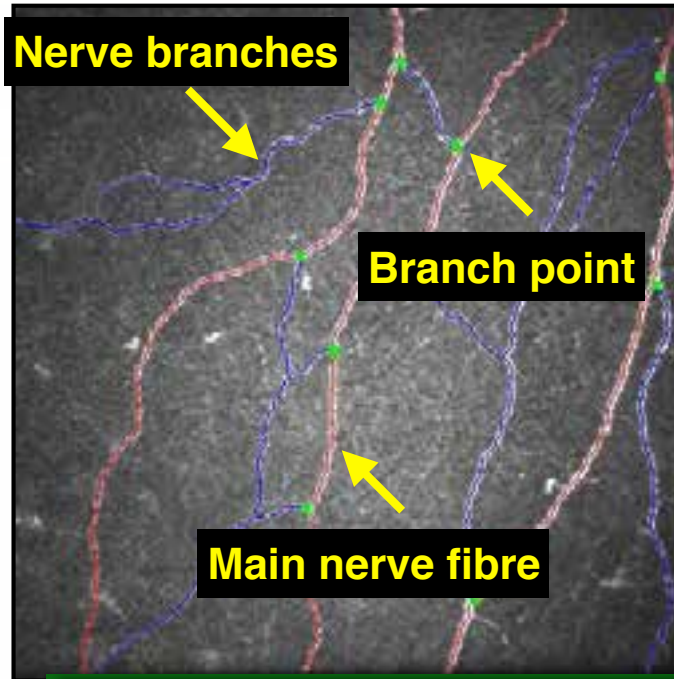
But how do we quantify the change??



They are different...!!

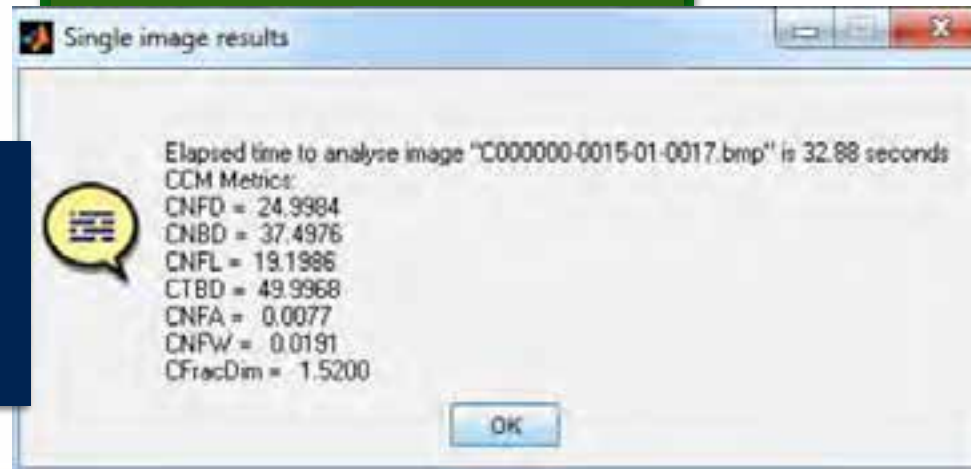
How are Nerves Analysed?

Automated
CCMetrics
software



Analysed image

Nerve parameters
calculated by CCmetrics
software (5 images
analyzed)



TOTAL 6 PARAMETERS QUANTIFIED & ANALYSED

1. Corneal nerve fiber density
(CNFD)

Number of nerve fibers/mm²

2. Corneal nerve branch density
(CNBD)

Number of branch points on
main nerve fibers/mm² ,

3. Corneal nerve fiber length
(CNFL)

Total length of nerve/mm²

4. Corneal total branch density
(CTBD)

Total number of branch points/
mm² ,

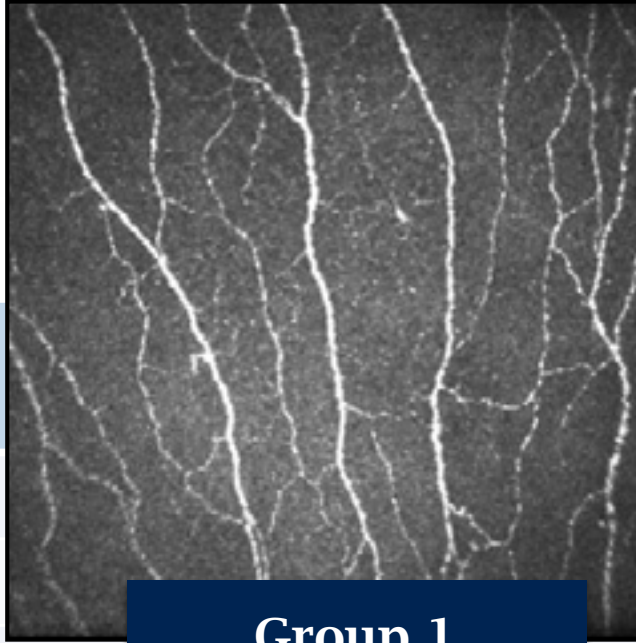
5. Corneal nerve fiber area
(CNFA)

Total nerve fiber area/mm²

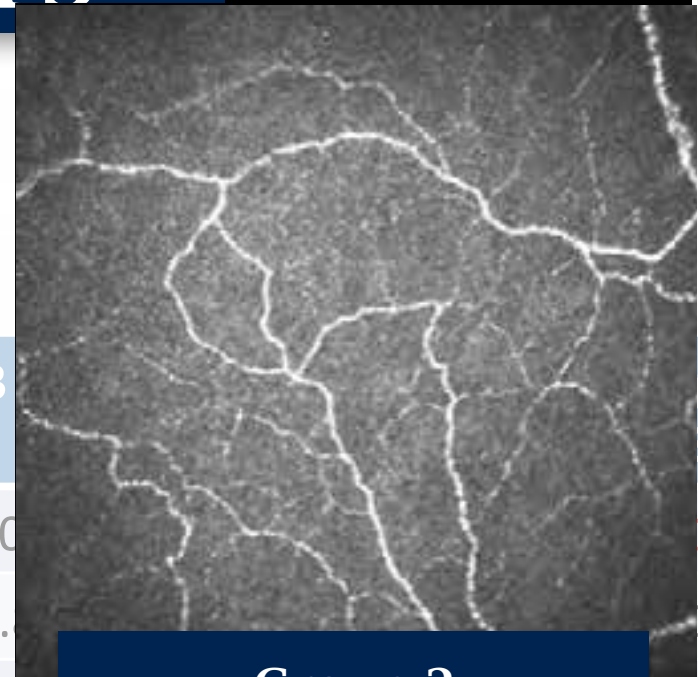
6. Corneal nerve fiber width
(CNFW)

Average nerve fiber width/mm² .

RESULTS



**Group 1
Normal eyes**



**Group 2
Unaffected fellow eye**

Nerve Parameters	Group 1 (n=33)	Group 2 (n=33)	Group 3 (n=33)
CNFD	17.54 ± 10.42	23.82 ± 8.01	49.05 ± 25.31
CNBD	19.73 ± 20.75	37.61 ± 19.11	49.05 ± 25.31
CNFL	17.54 ± 10.42	14.82 ± 3.61	49.05 ± 25.31
CNFW	0.01 ± 0.002	0.006 ± 0.001	0.021 ± 0.002
CNEM	0.02 ± 0.001	0.021 ± 0.002	0.021 ± 0.002

CNFD

p<0.001

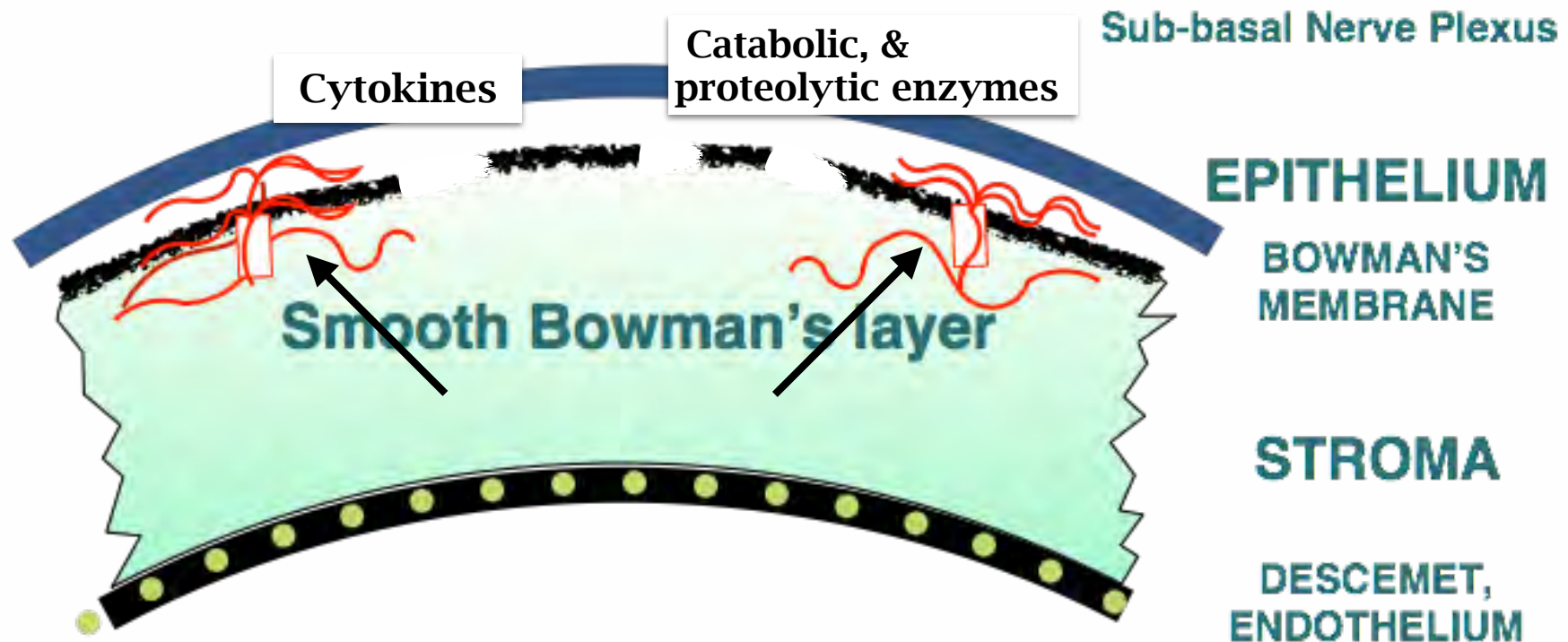
CNBD

p=0.05

CNFL

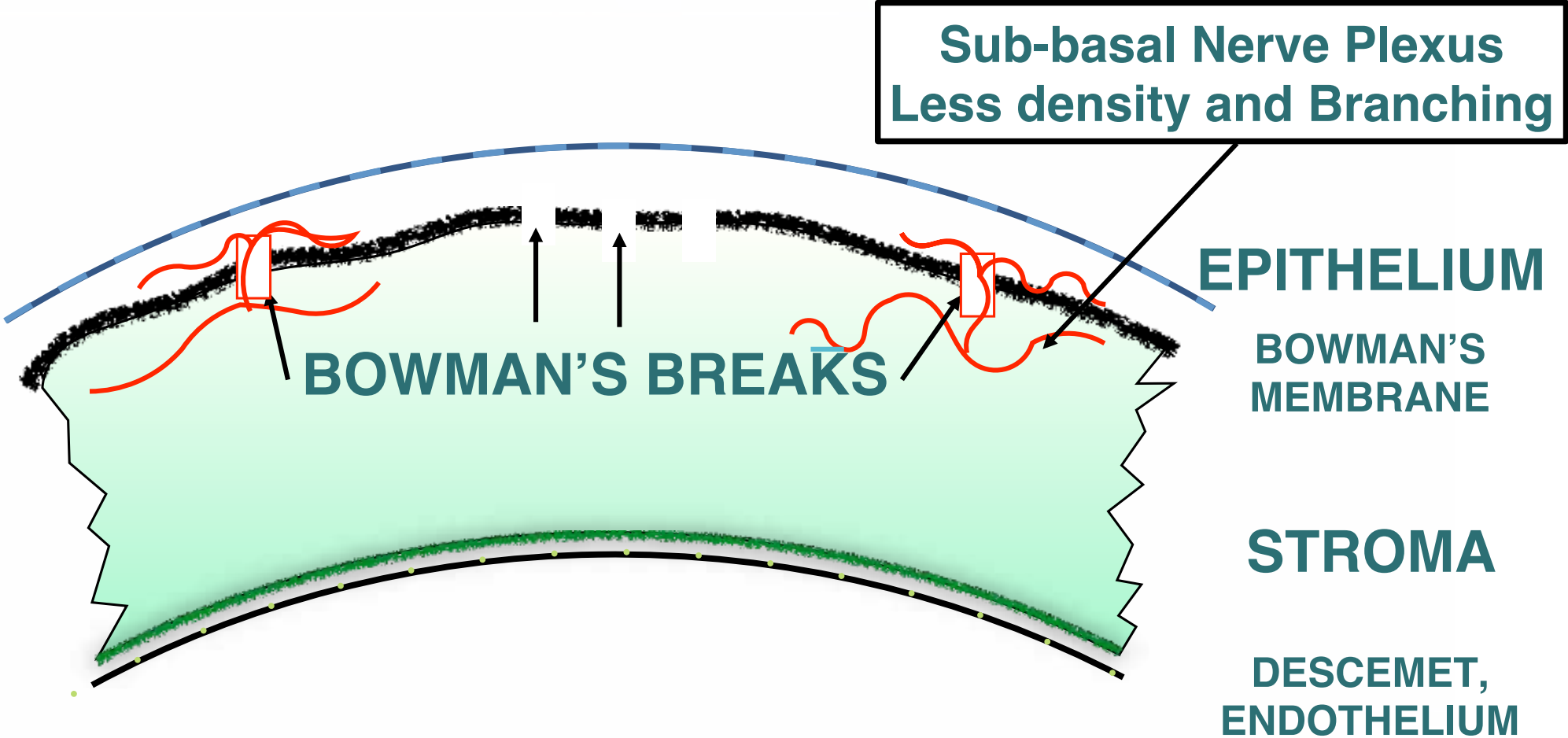
Early changes

Schematic of Normal Cornea



B. S. Shaheen, et al "Corneal nerves in health and disease," Survey of Ophthalmology, vol. 59, no. 3, pp. 263- 285, 2014.

Schematic of Cornea In Keratoconus



J.Müller et al, "Architecture of human corneal nerves," Investigative Ophthalmology and Visual Science, vol. 38, no. 5, pp. 985-994, 1997.



Longitudinal study of the normal eyes in unilateral keratoconus patients.

Li X¹, Rabinowitz YS, Rasheed K, Yang H.

⊕ Author information

Abstract

PURPOSE: To determine the rate at which clinically normal eyes in unilateral keratoconus (KC) patients progress to KC and to identify the risk factors that might predict the development of KC in a longitudinal study.

DESIGN: Prospective observational study.

PARTICIPANTS: We recruited 778 patients with KC and 252 normal controls in Los Angeles, California. One hundred sixteen of 778 patients (14.9%) were diagnosed with clinically unilateral KC at baseline.

METHODS: Both eyes of these unilateral KC patients were examined at baseline, and 85 patients were followed up with clinical evaluation and videokeratography for a period ranging from 6 months to 8 years.

MAIN OUTCOME MEASURES: Progression to clinical KC from previously normal fellow eyes. Quantitative and qualitative videokeratography variables, contact lens wear, and demographic variables were analyzed as potential predictive factors for this progression.

RESULTS: During the follow-up period, 30 of 85 (35.3%) clinically normal fellow eyes had KC develop, and 25 of these 30 (83.3%) had KC develop within the first 6 years after the initial KC diagnosis. By use of the time period from the patients' first diagnosis of unilateral KC to the end of the follow-up period (range, 6 months-41 years), the median time (estimated from the survival analysis) to the development of KC was 16.7 years (95% confidence interval, 11.34, 28.91). Fellow eyes with higher inferior-superior dioptric asymmetry value (I-S) or KC percentage index (logKISA) values had higher risk for KC developing (I-S, risk ratio [RR] = 1.348, P = 0.022; log(KISA), RR = 4.245, P = 0.003).

Asymmetric patterns also showed an increased risk for KC developing (P = 0.03), especially the asymmetric bowtie with skewed radial axes

CONCLUSIONS: Approximately 50% of clinically normal fellow eyes will progress to KC within 16 years. The greatest risk is during the first 6 years of the onset.

On going study

Varying grade of bilateral KC



Mass spectrometry



Altered expression
of 200 proteins

Unilateral KC



35

Potential molecular marker for
progression

Predicting progression in unaffected
fellow eye!!

What was known

- Clinical manifestations or topographical changes - diagnosis and management of KC
- No current diagnostic modalities that can predict early changes prior to them

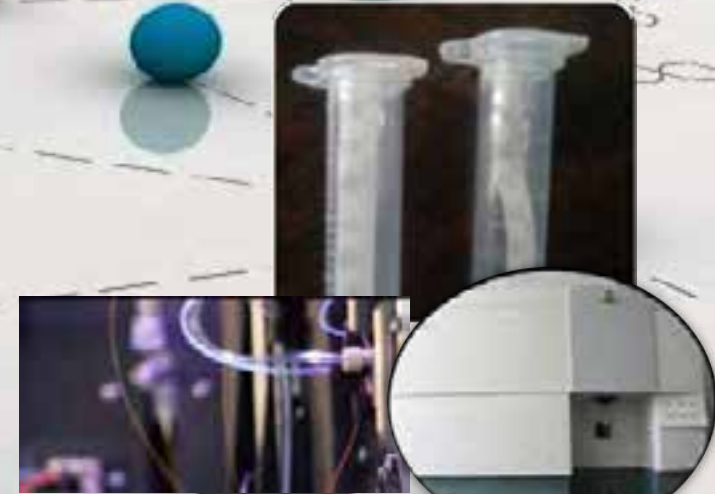
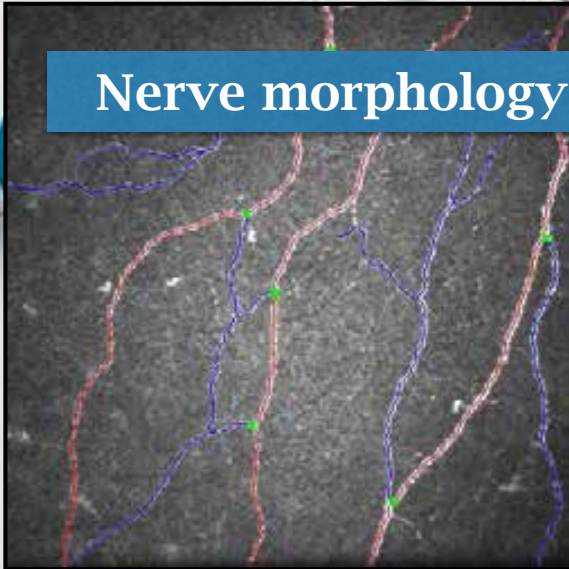
What this study adds

- Changes in the **SBNP** occur **early in disease**.
- **Quantitative analyses** - diagnosis of KC even before it is manifested clinically or topographically
- SBNP changes can also help in **monitoring disease progression**.
- Adding more parameters like **proteomic analysis** (from tears) - **increases predictability of progression**

Connecting DOTS.....

Current diagnostic modalities

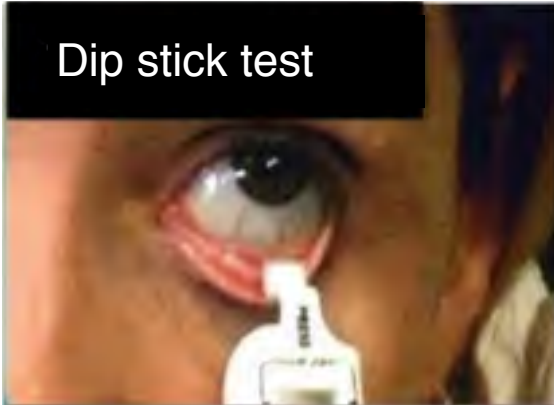
Nerve morphology



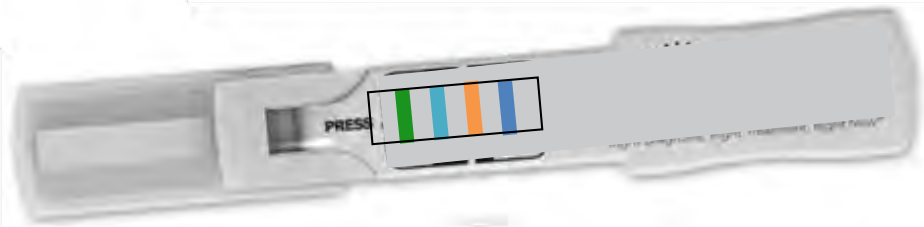
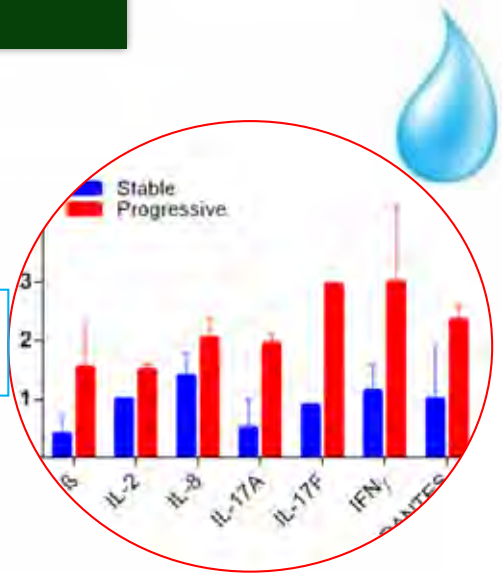
Proteomics and inflammatory markers

Understanding , predicting and controlling progression

Future Directions



Studying From Tears



Inflammatory markers
Proteins biomarkers

Prognostication
Treat inflammation
Close follow-up



**NARAYANA
NETHRALAYA**

*Thank
you*

your faith shall heal you...