Early Stage Investigator Lecture

Early Detection and Prevention of Angle Closure Glaucoma Using OCT and Artificial Intelligence

Presented by:
Benjamin Xu, M.D., Ph.D.
University of Southern California Roski Eye Institute

NIH National Institutes of Health
Office of Disease Prevention

Financial Disclosures

- Funding sources
  - NIH R01 EY035677
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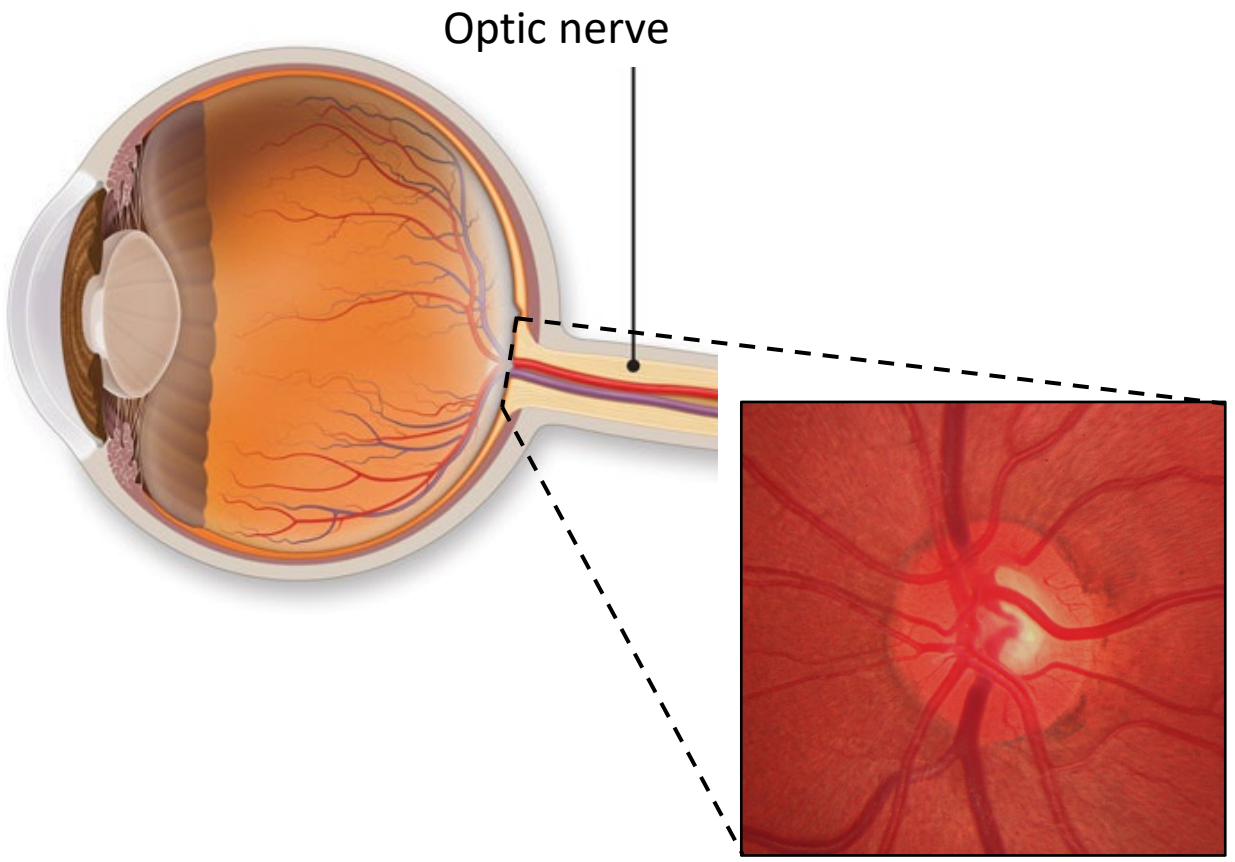
  - DHS-USC Safety Net Innovation Award
  - USC AI4Health Award
- Research support
  - Heidelberg Engineering
  - Ocular Therapeutix
  - ArcScan

Glaucoma Facts

- Most common cause of irreversible vision loss
- 80 million cases of glaucoma worldwide
- IOP is primary modifiable risk factor



Source: American Academy of Ophthalmology.

Glaucoma Facts

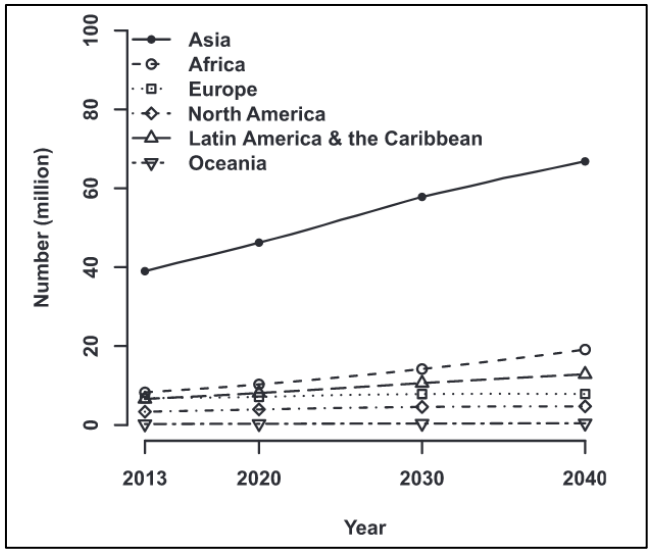
- Most common cause of irreversible vision loss
- 80 million cases of glaucoma worldwide
- IOP is primary modifiable risk factor

Global Prevalence of Glaucoma and Projections of Glaucoma Burden through 2040

A Systematic Review and Meta-Analysis

Yih-Chung Tham, BSc Hons,[1,2,] Xiang Li, BSc,[1,3,*] Tien Y. Wong, FRCS, PhD,[1,2] Harry A. Quigley, MD,[4] Tin Aung, FRCS (Ed), PhD,[1,2] Ching-Yu Cheng, MD, PhD[1,2,5,6]*

Source: *Ophthalmology*, 2017



Source: *Ophthalmology*, 2017

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Glaucoma Facts

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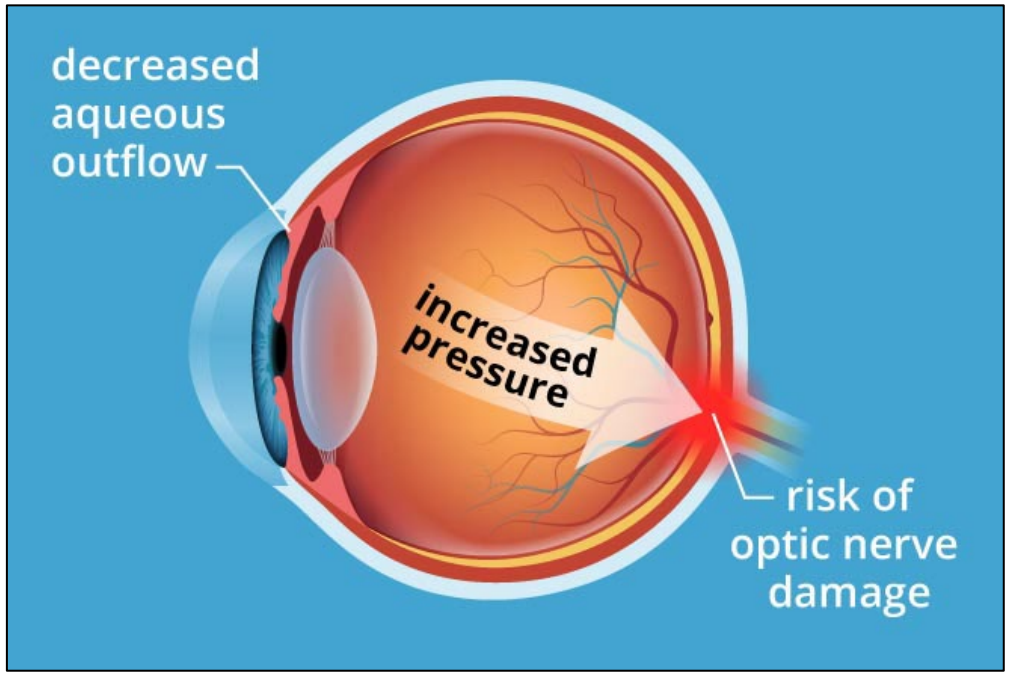
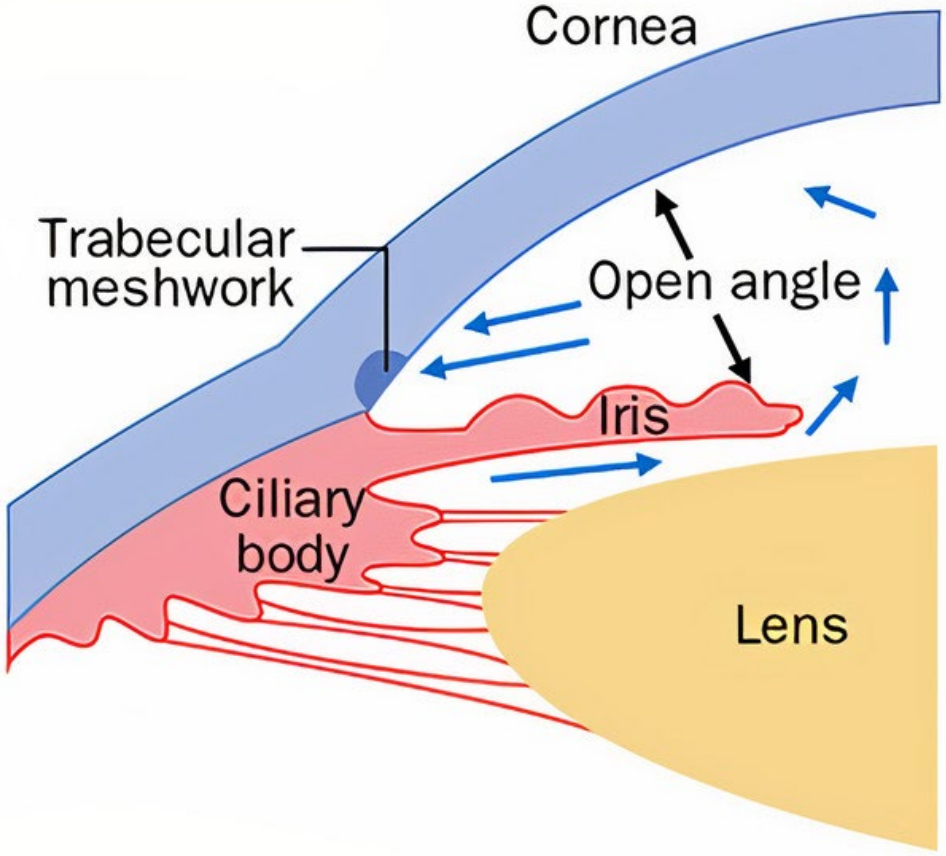
Intraocular Pressure (IOP)



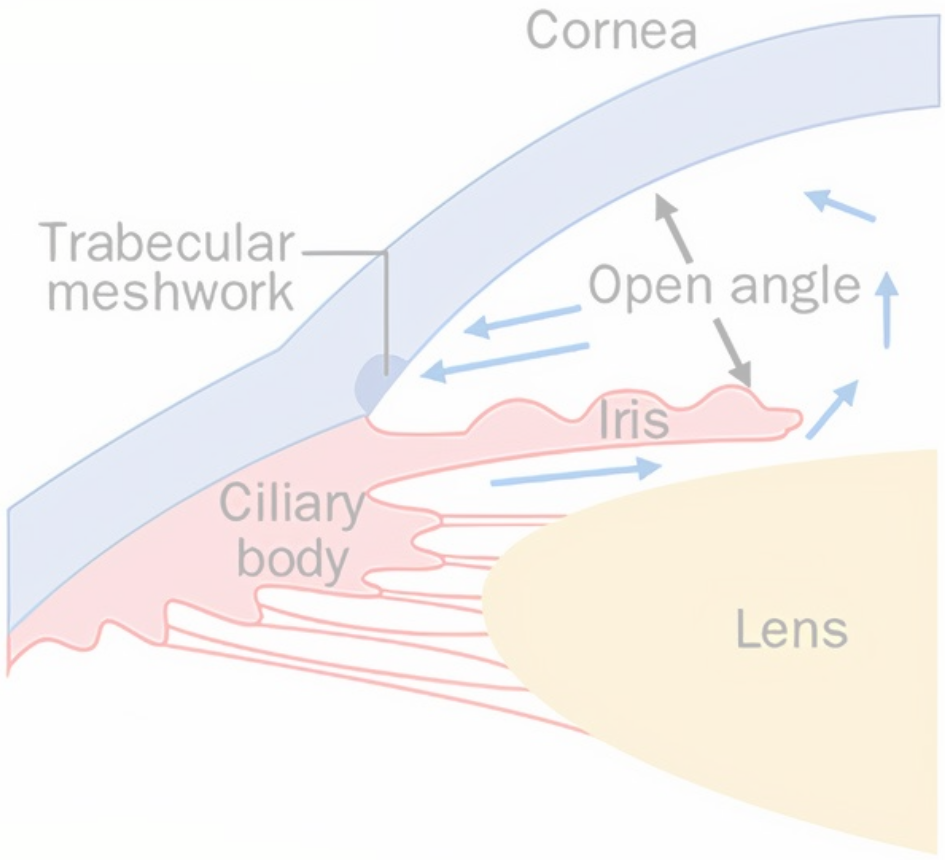
Source: www.allaboutvision.com

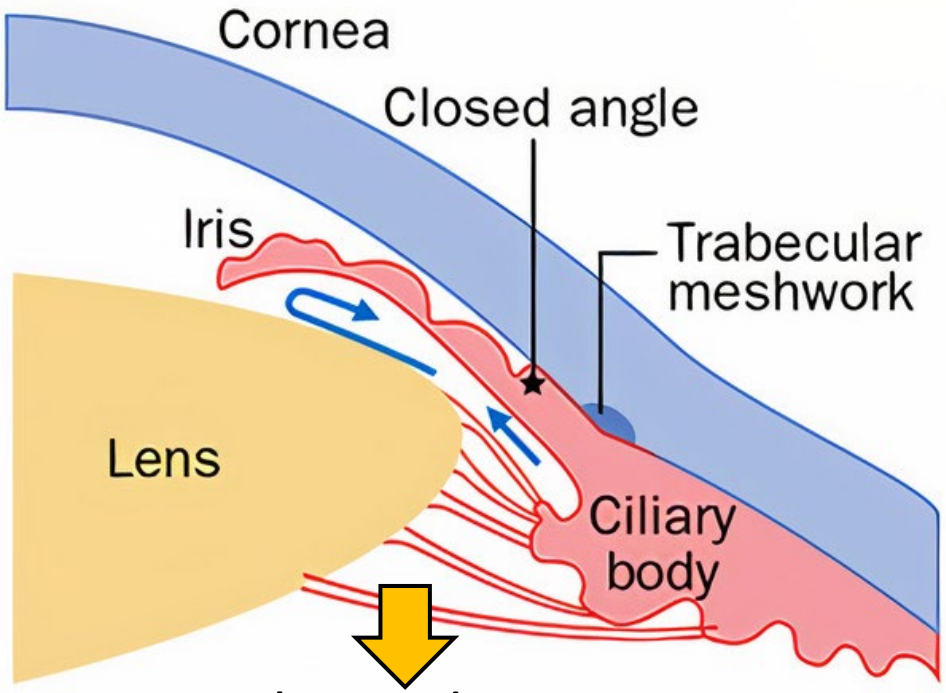
Conventional Aqueous Outflow



Source: NIH

Angle Closure





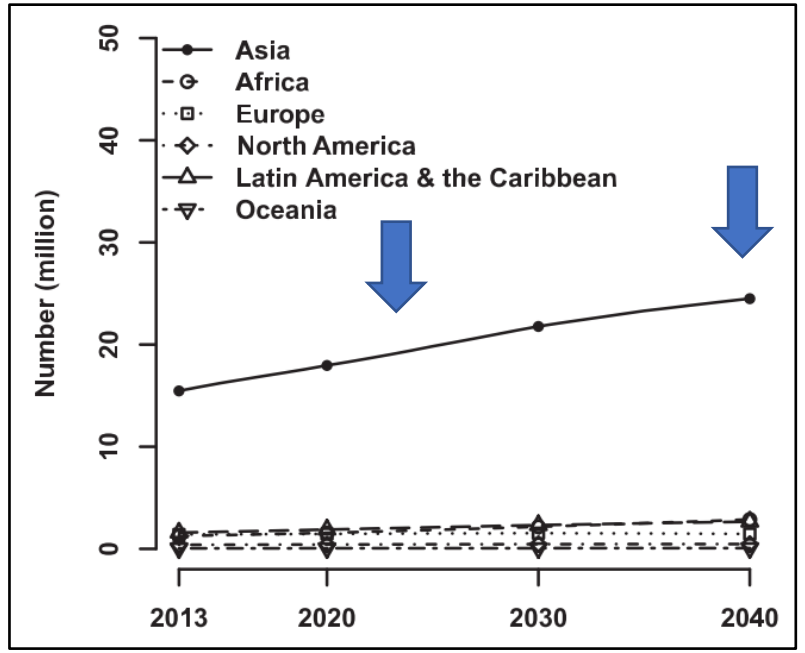
Elevated IOP

Angle Closure Glaucoma

Source: NIH

Primary Angle Closure Glaucoma (PACG)

- 24 million cases worldwide
  - 75% in Asia
- 34 million cases by 2040
- 2.4 times higher odds of blindness compared to POAG (George et al, *Eye*, 2021)



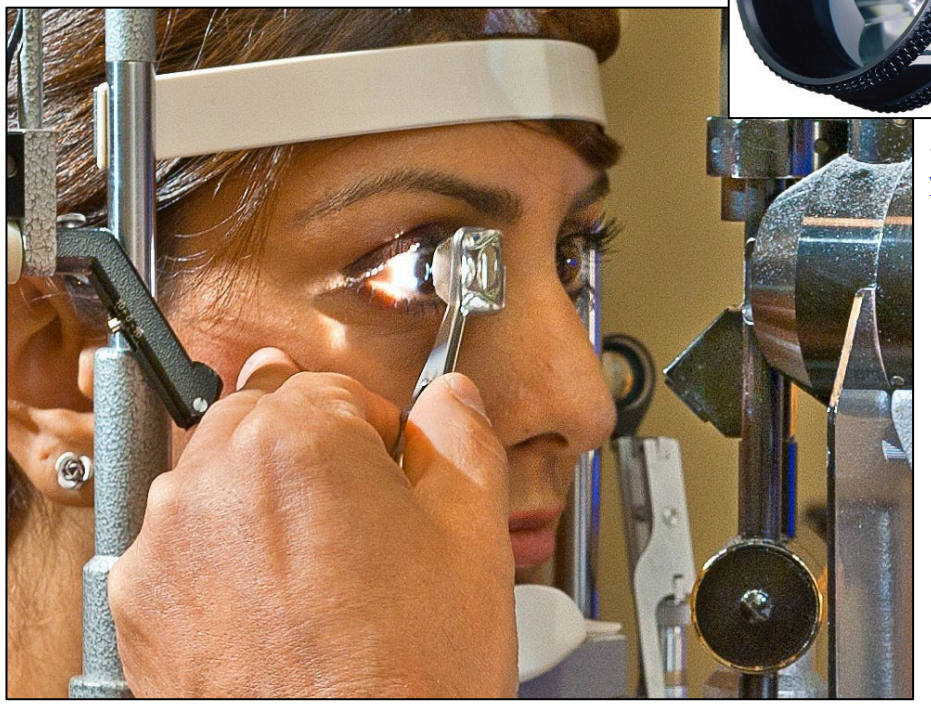
Source: Tham et al, *Ophthalmology*, 2014

Gonioscopy

- Clinical standard for evaluating the angle

- Visualize the pigmented trabecular meshwork

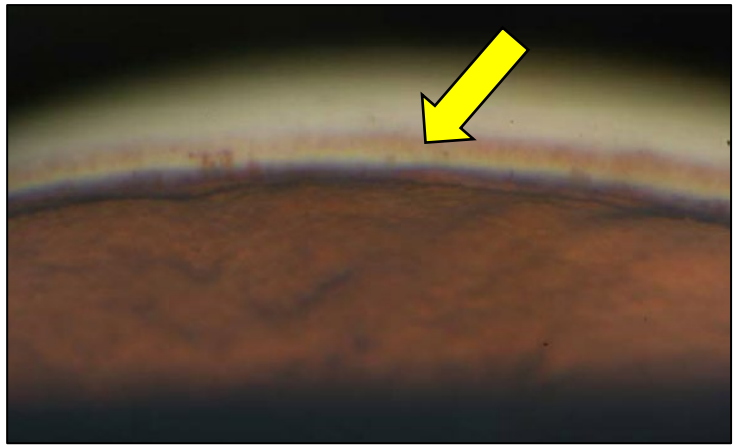
Source: www.midoptic.com



Source: www.visivite.com

Gonioscopy

- Clinical standard for evaluating the angle



Open

Source: Current Diagnosis and Management of Angle-Closure Glaucoma. R. Castaneda-Diez et al.

- Visualize the pigmented trabecular meshwork

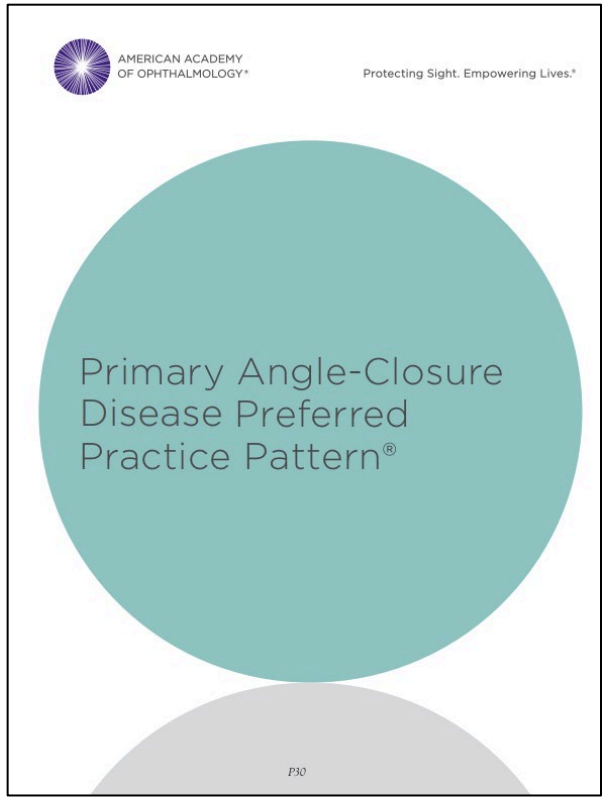
Closed

Source: https://decisionmakerplus.net/case-report-post/narrow-angle-glaucoma-2/

AAO Preferred Practice Pattern Guidelines

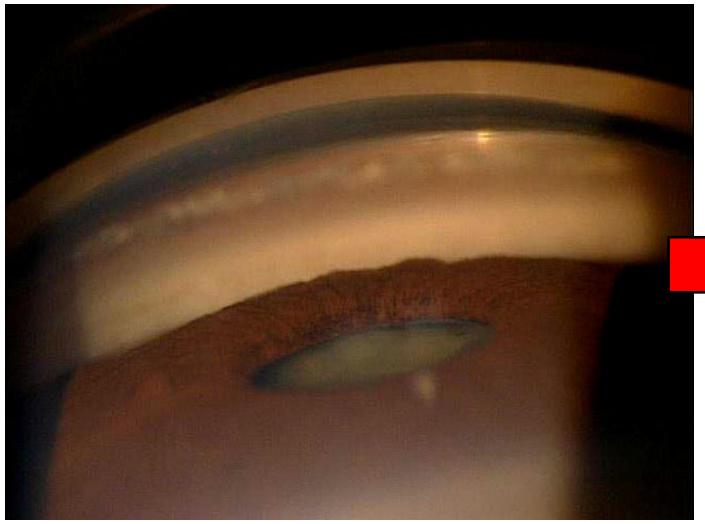
Gonioscopy should be performed in **ALL**:

1. Suspected glaucoma
2. Suspected angle closure
3. Incisional glaucoma surgery



Primary Angle Closure Disease (PACD)

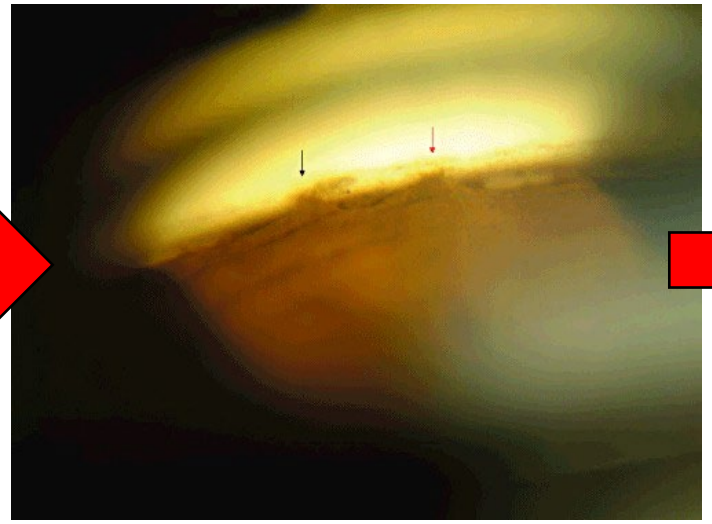
Primary Angle Closure Suspect (PACS)



Angle closure in 2+ quadrants

Low risk of PACG

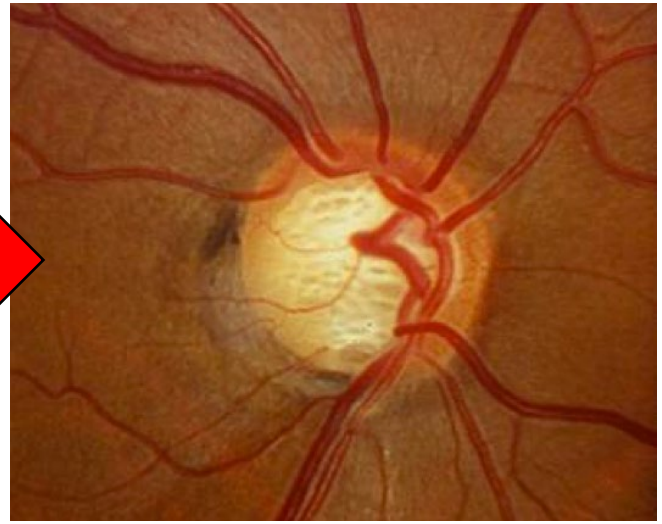
Primary Angle Closure (PAC)



PAS or elevated IOP

High risk of PACG

Primary Angle Closure Glaucoma (PACG)



Optic nerve ± visual field changes

Foster et al, *BJO*, 2002

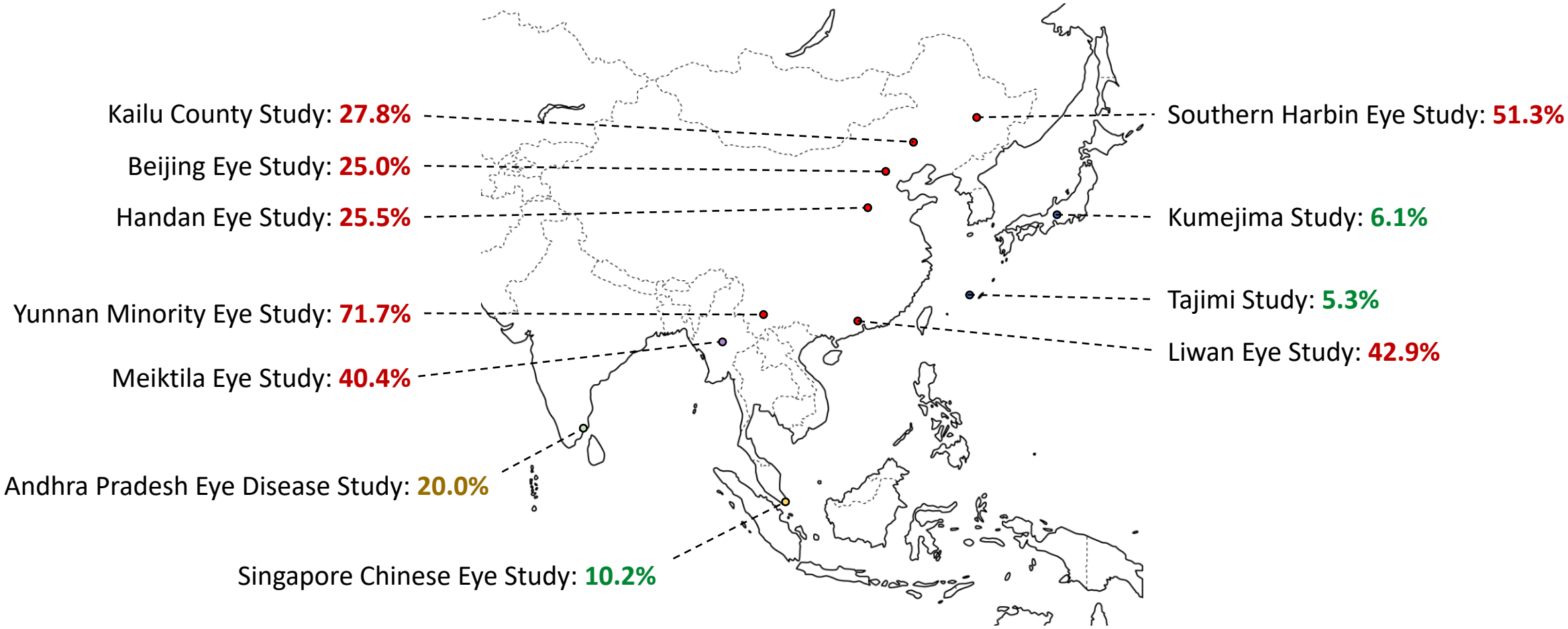
Limitations of Gonioscopy

- Subjective and expertise-dependent
- Moderate inter-examiner reproducibility
  (Randhawa et al, *BJO*, 2021)
- Uncomfortable and time-consuming

Major Issue #1

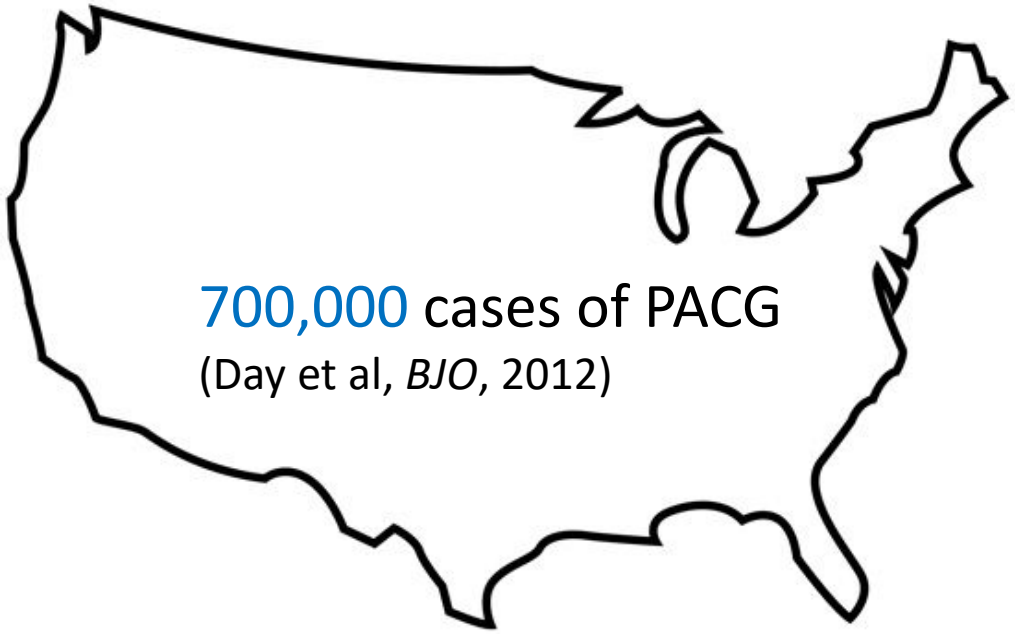
PACG often remains undetected and untreated until after severe vision loss has occurred

Blindness in PACG

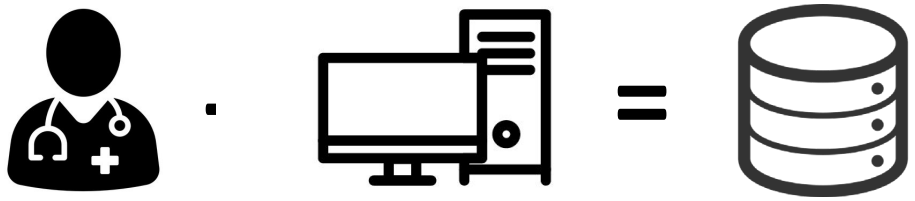


PACG in the United States

Big Healthcare Data in the United States



Source: Day et al, BJO, 2012



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OPTUM

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Aidan Lee

Utilization of Gonioscopy

- Optum Database: 65 million patients
- 198,995 patients undergoing initial glaucoma evaluation (2009-2020)
- 29.5% had record of gonioscopy within 6 months
- Lower odds of gonioscopy among POAG than PACG (OR=0.12)

AJO, 2024

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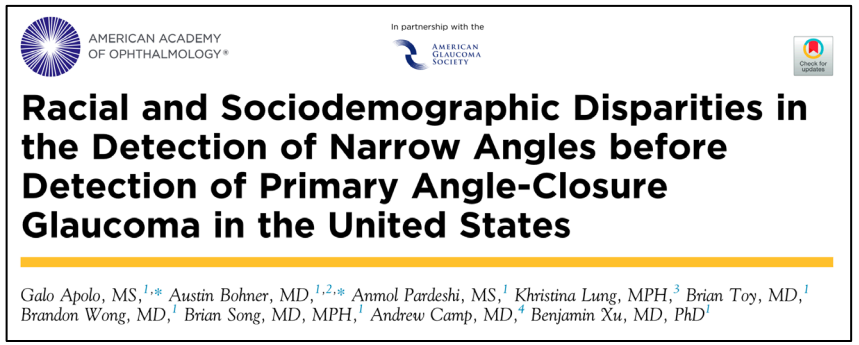
Patterns in Angle Closure Detection

Galo Apolo

- Optum Database: 65 million patients
- 31,044 patients newly diagnosed with PACG (2009-2020)
- 75.2% lacked previous diagnosis of angle closure
- Late detection more common among Black Americans (OR=1.3)

OPTUM



AMERICAN ACADEMY OF OPHTHALMOLOGY®

In partnership with the AMERICAN GLAUCOMA SOCIETY

Racial and Sociodemographic Disparities in the Detection of Narrow Angles before Detection of Primary Angle-Closure Glaucoma in the United States

Galo Apolo, MS,[1,] Austin Bohner, MD,[1,2,*] Anmol Pardeshi, MS,[1] Khristina Lung, MPH,[3] Brian Toy, MD,[1] Brandon Wong, MD,[1] Brian Song, MD, MPH,[1] Andrew Camp, MD,[4] Benjamin Xu, MD, PhD[1]*

Ophthalmology Glaucoma, 2023

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PACG-related Blindness

Sona Shah

- IRIS Registry: 73 million patients
- 49,183 patients newly diagnosed with PACG (2015-2019)
- 12.4% blind in at least one eye
- Higher risk among Black (OR=1.5) and Hispanic (OR=1.3) Americans
- Higher risk with late detection (OR = 1.8)

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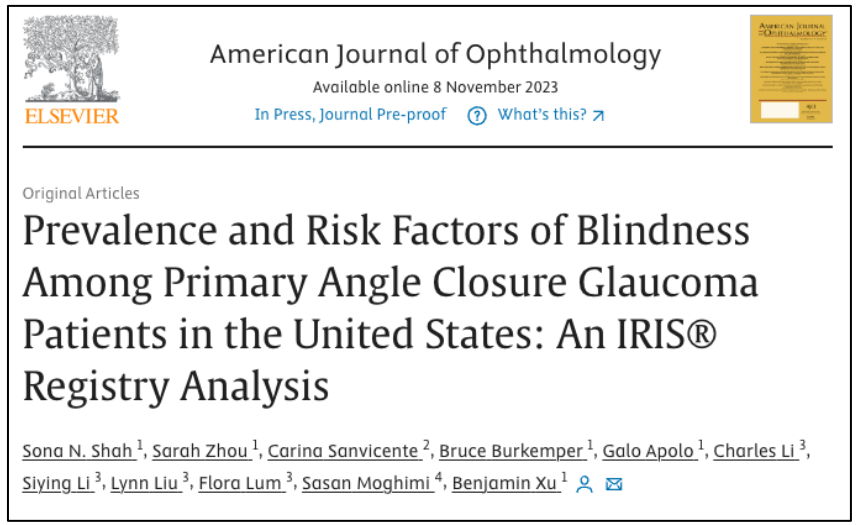

ELSEVIER

American Journal of Ophthalmology
Available online 8 November 2023
In Press, Journal Pre-proof What's this?

Original Articles

Prevalence and Risk Factors of Blindness Among Primary Angle Closure Glaucoma Patients in the United States: An IRIS® Registry Analysis

Sona N. Shah [1], Sarah Zhou [1], Carina Sanvicente [2], Bruce Burkemper [1], Galo Apolo [1], Charles Li [3], Siying Li [3], Lynn Liu [3], Flora Lum [3], Sasan Moghimi [4], Benjamin Xu [1]

AJO, 2023

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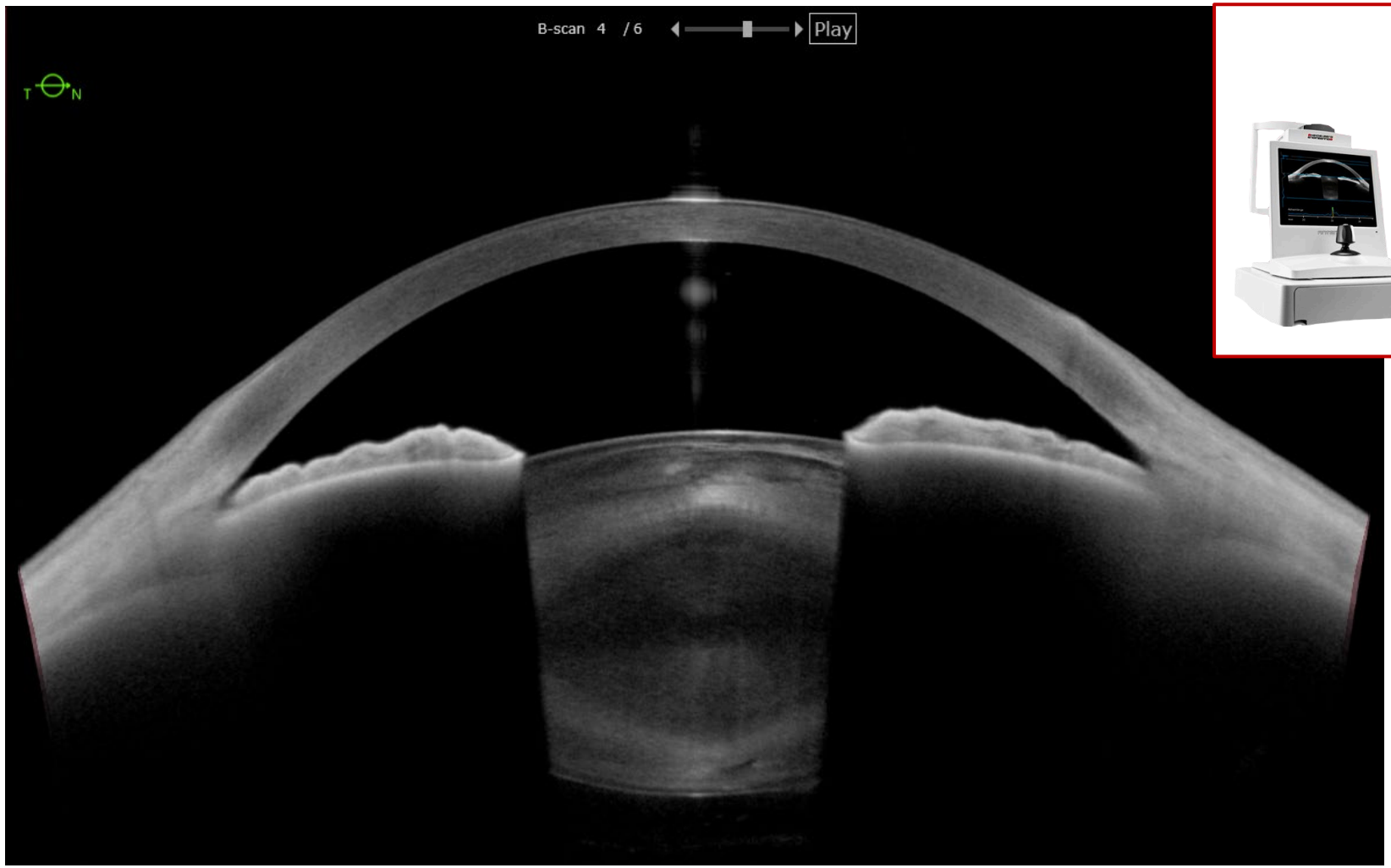
Urgent Need #1

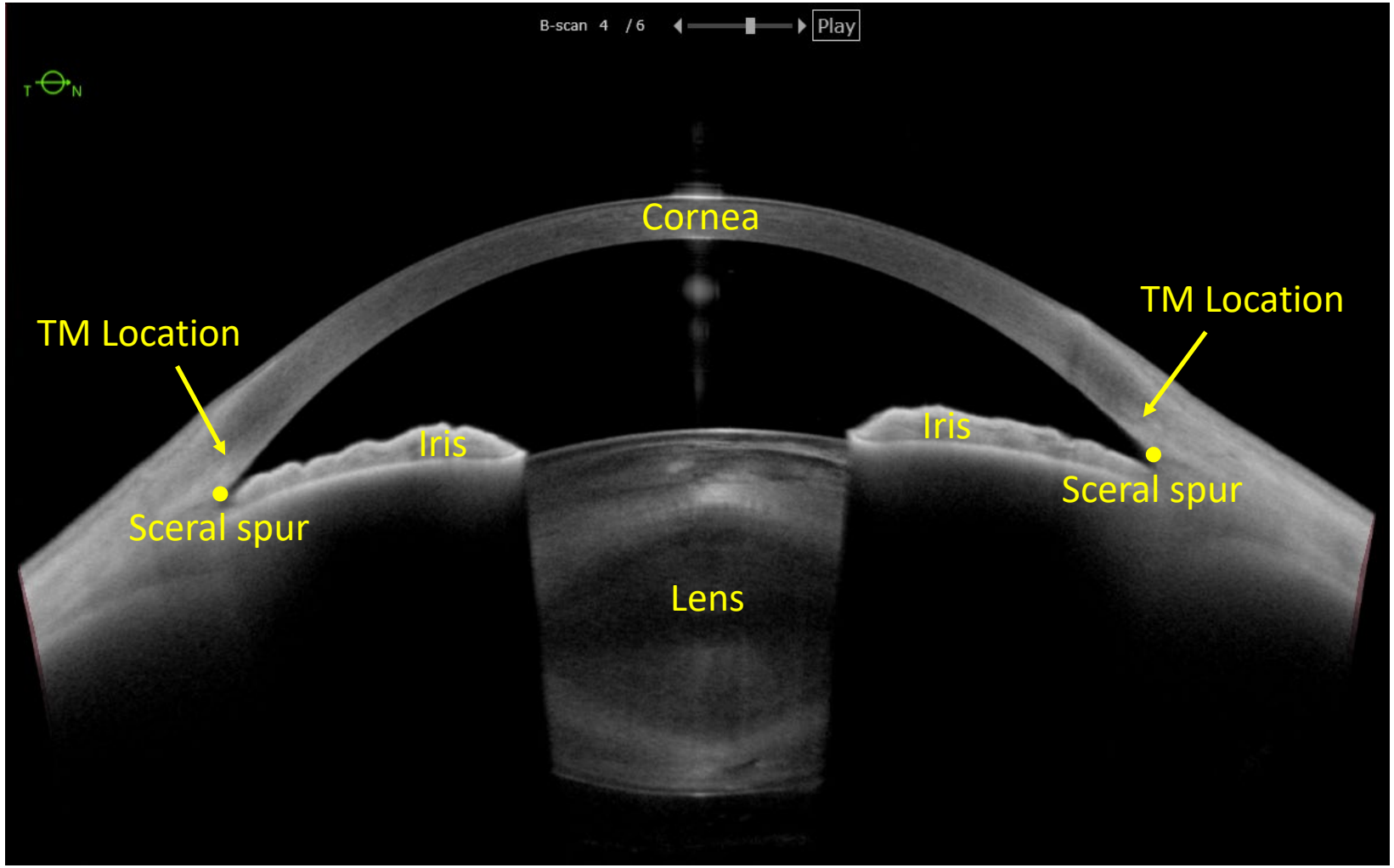
Convenient and equitable method to detect patients at risk for PACG

Optical Coherence Tomography (OCT)



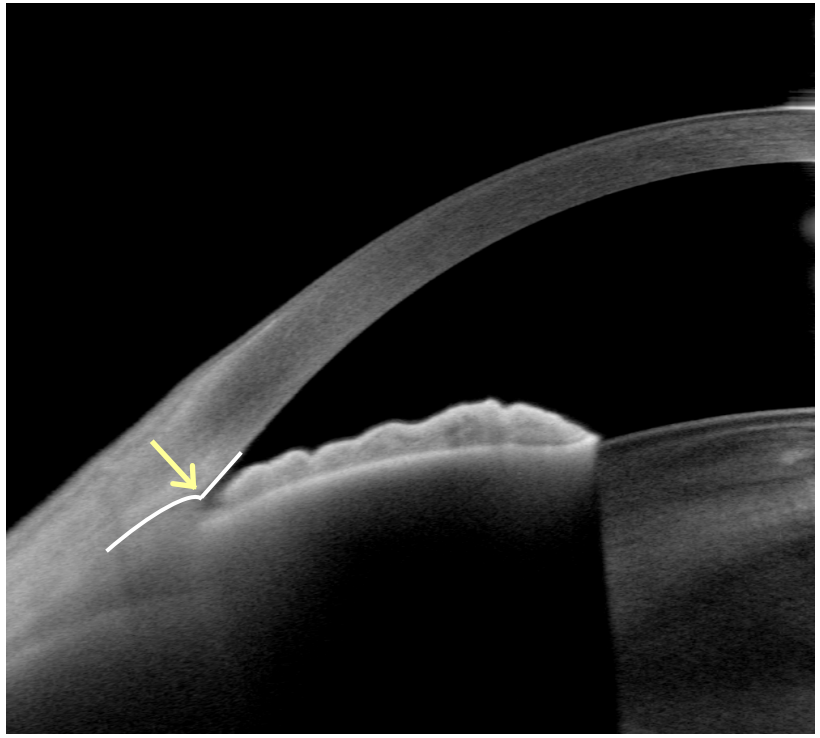
Source: www.djapplelab.com

Anterior Segment OCT (AS-OCT)

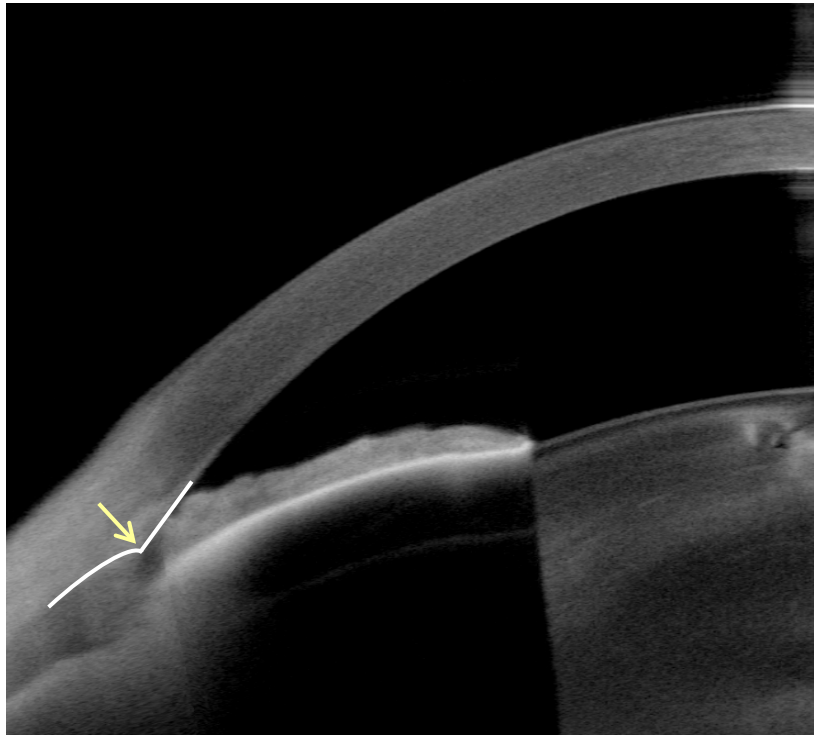


Angle Closure Detection

Open Angle



Angle Closure



Question

Can analysis of AS-OCT images be automated to detect gonioscopic angle closure?

ARTIFICIAL INTELLIGENCE (AI)

AI in Healthcare

- Computers are taught cognitive functions (e.g. analyze images, detect disease)
- Revolutionize healthcare
- Increase access and reduce costs

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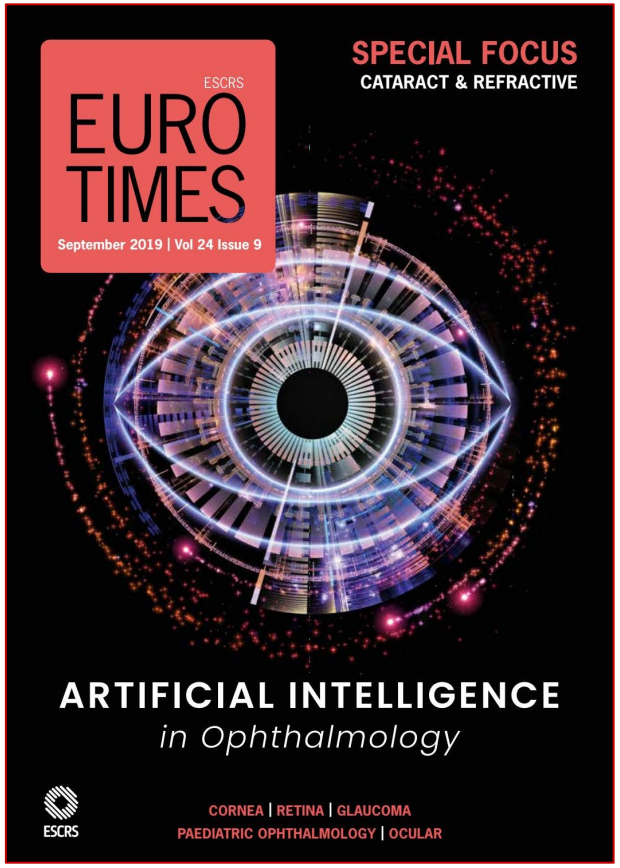
Deep Learning (DL)

- DL is a popular form of AI
- DL has been widely used to automate image analysis for disease detection



Gonioscopic Angle Closure Detection

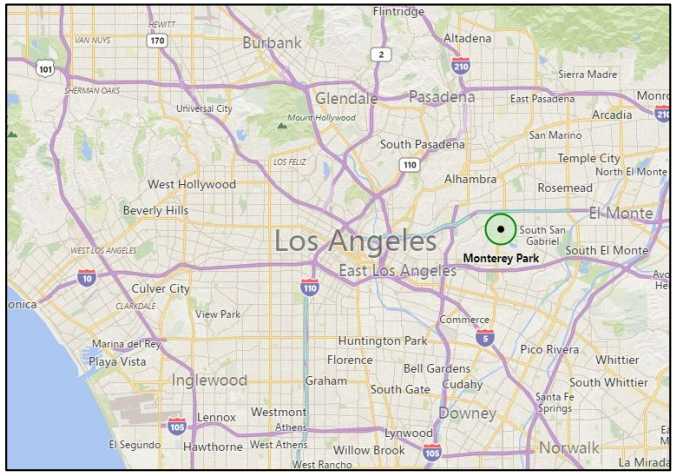
Deep Learning Classifiers for Automated Detection of Gonioscopic Angle Closure Based on Anterior Segment OCT Images

BENJAMIN Y. XU, MICHAEL CHIANG, SHREYASI CHAUDHARY, SHRADDHA KULKARNI, ANMOL A. PARDESHI, AND ROHIT VARMA

AJO, 2019

National Eye Institute

CHINESE AMERICAN EYE STUDY
美國華裔眼科健康調查



- 4,570 Chinese Americans
- Gonioscopy and AS-OCT imaging

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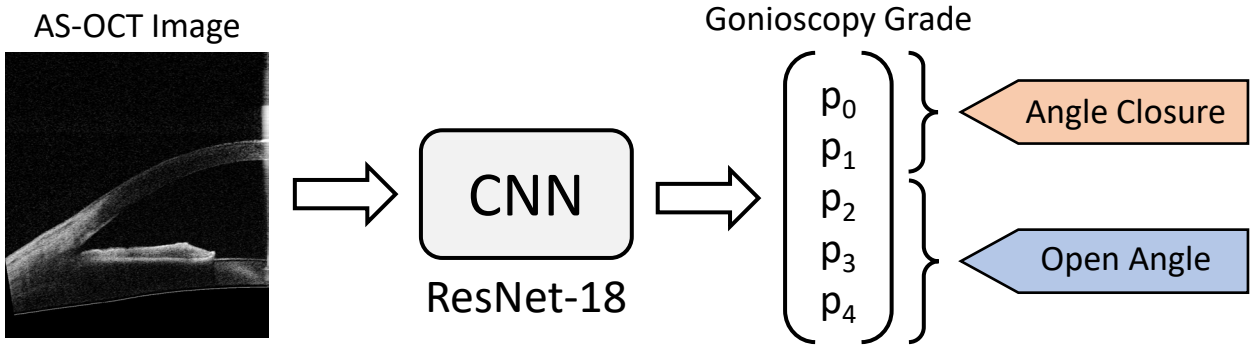
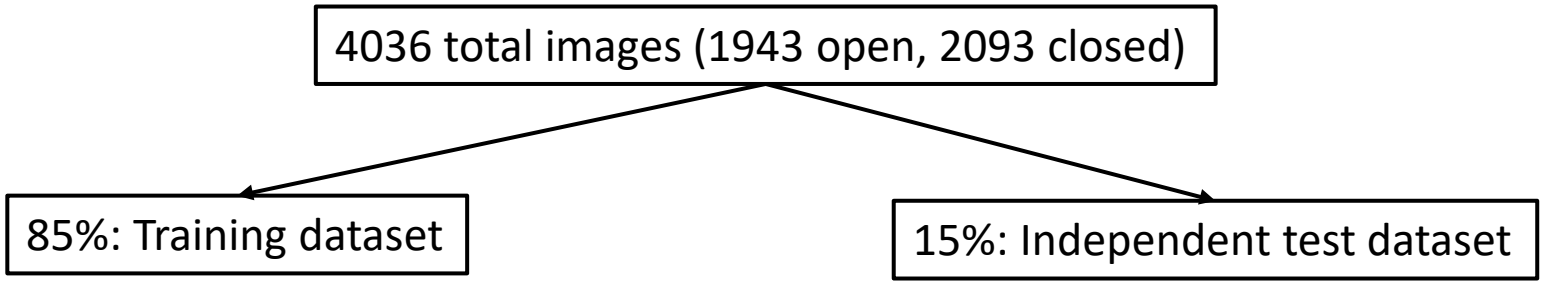
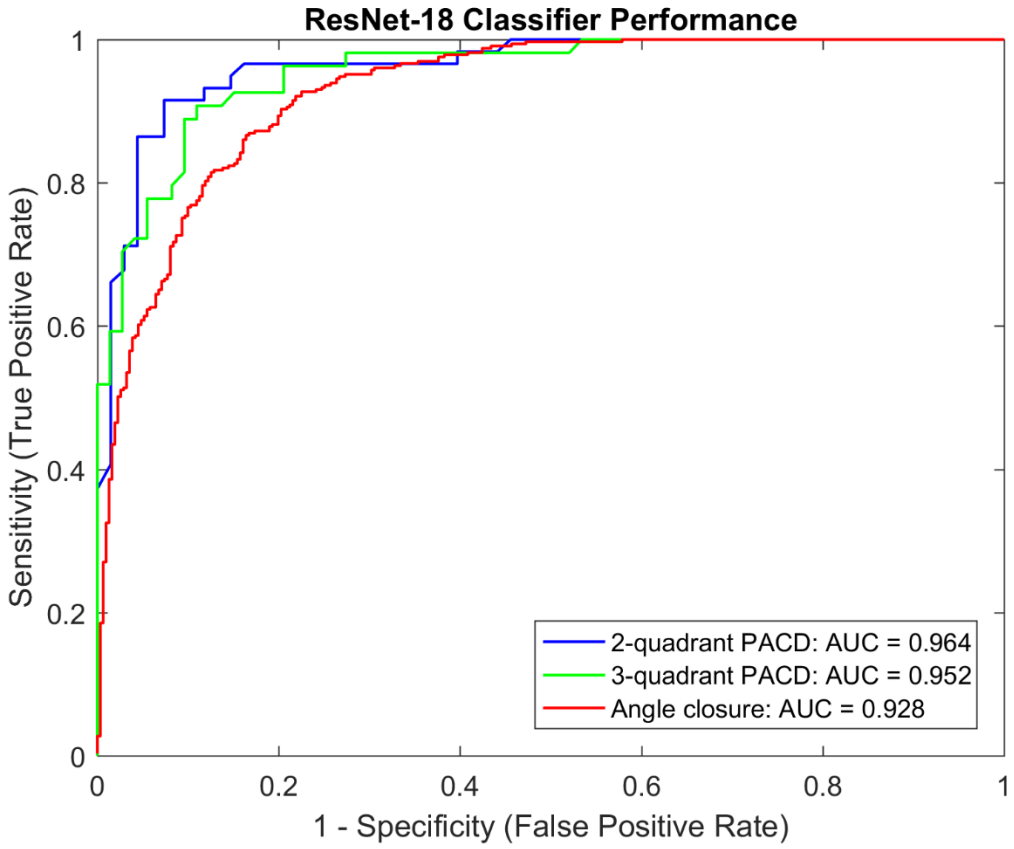
Methods





Performance (1)



Jasmeen Randhawa

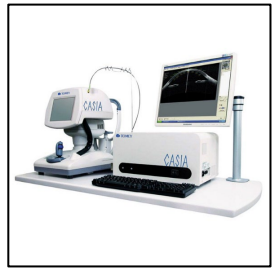
Algorithm Generalizability

Generalisability and performance of an OCT-based deep learning classifier for community-based and hospital-based detection of gonioscopic angle closure

Jasmeen Randhawa,[1] Michael Chiang,[2] Natalia Porporato,[3] Anmol A Pardeshi,[2] Justin Dredge,[2] Galo Apolo Aroca ,[2] Tin A Tun,[3] Joanne HuiMin Quah,[4] Marcus Tan,[5] Risa Higashita,[6] Tin Aung,[3,5] Rohit Varma,[7] Benjamin Y Xu [1]

BJO, 2021

CASIA SS-1000



CHINESE AMERICAN EYE STUDY 美國華裔眼科健康調查

1 Ophthalmologist

Polyclinics SingHealth

1 Glaucoma Specialist

USC Roski Eye Institute

1 Glaucoma Specialist
1 Ophthalmologist

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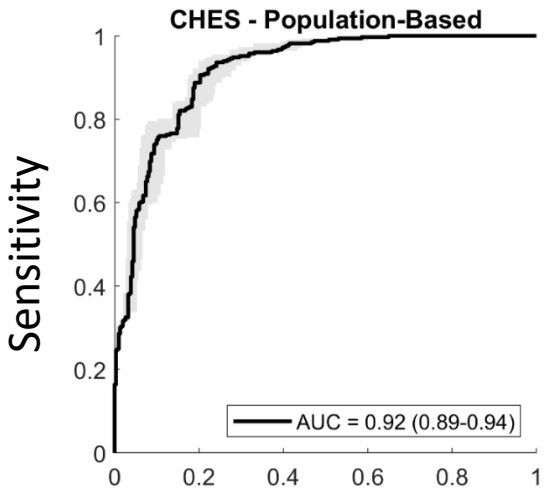
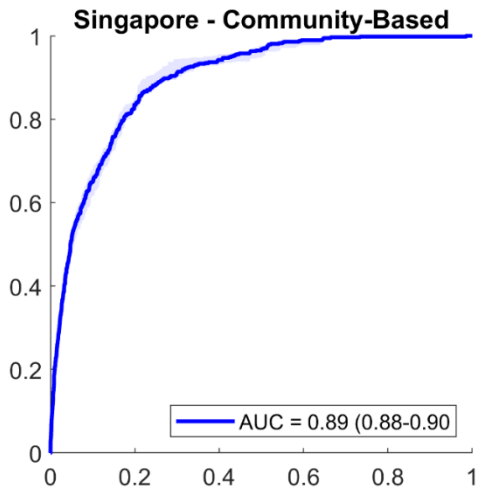
Performance (2)

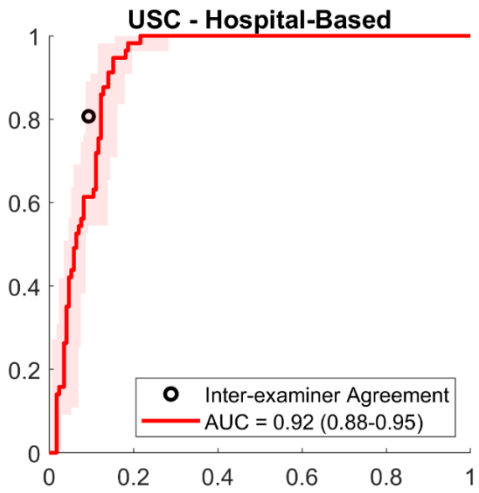
Chinese Americans
(N = 138)



Singaporean Chinese
(N = 1318)



Mixed Race
(N = 40)



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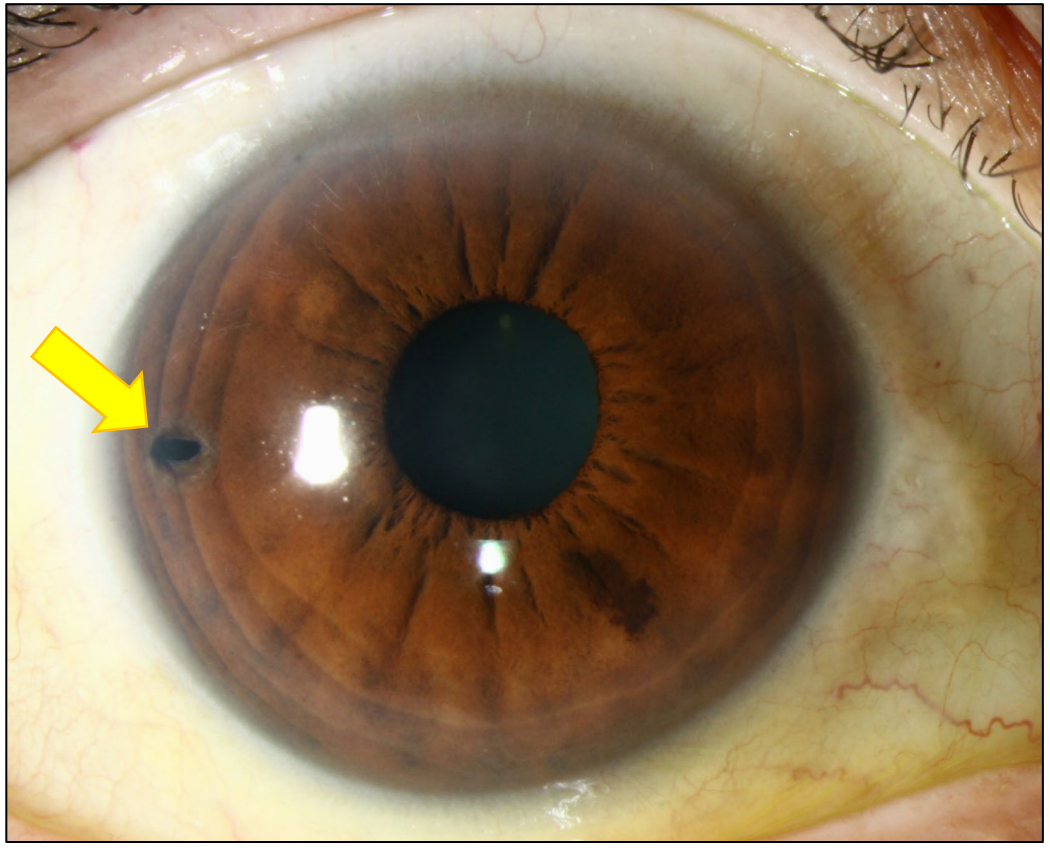
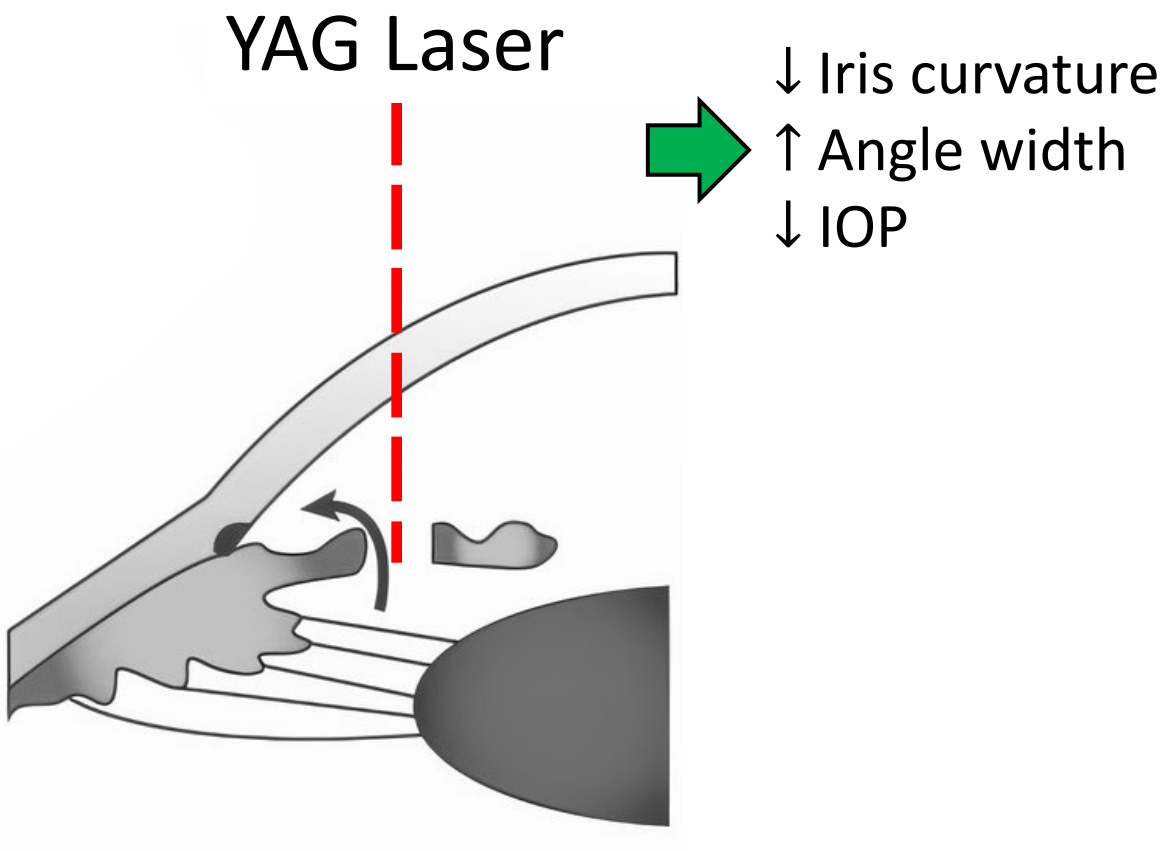
Major Issue #2

It is unclear which PACS eyes will benefit from prophylactic treatment

Laser Peripheral Iridotomy (LPI)





Source: The Best Approach for Narrow-Angle Patients, by Michelle Stephenson.
https://www.reviewofophthalmology.com/article/the-best-approach-for-narrowangle-patients

LPI Benefits in PAC/PACG

- IOP lowering in angle closure eyes with high IOP (EAGLE Trial, *Lancet*, 2017)

Effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma (EAGLE): a randomised controlled trial

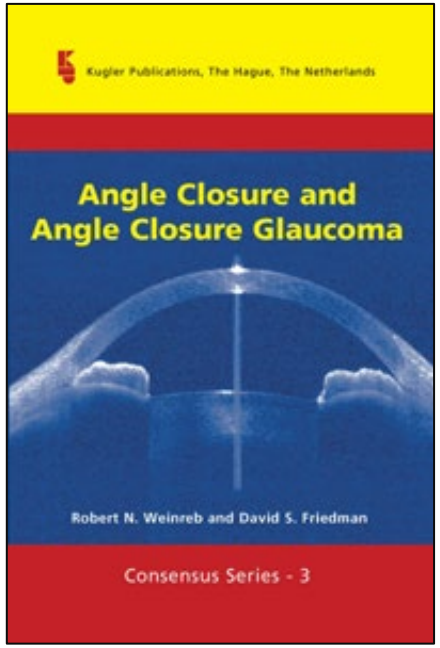
Augusto Azuara-Blanco, Jennifer Burr, Craig Ramsay, David Cooper, Paul J Foster, David S Friedman, Graham Scotland, Mehdi Javanbakht, Claire Cochrane, John Norrie, for the EAGLE study group

The Lancet, 2017

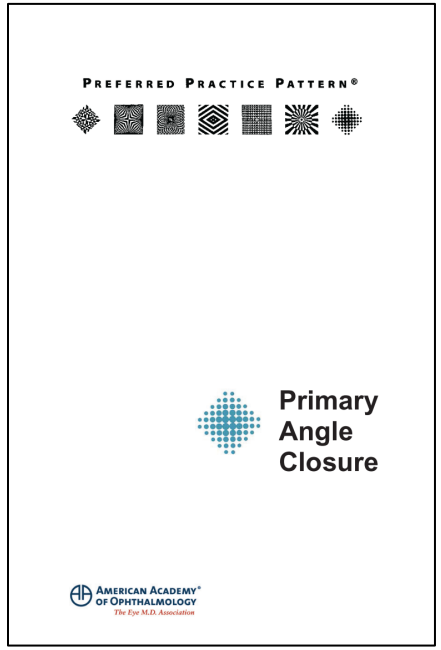
- Break pupillary block and acute angle closure attacks

LPI for PAC and PACG

CONSENSUS: LPI is indicated for eyes with PAC and PACG



WGA 2006



AAO 2020

Distribution of PACD

Prevalence and Clinical Characteristics of Glaucoma in Adult Chinese: A Population-Based Study in Liwan District, Guangzhou

Mingguang He,[1,2] Paul J. Foster,[1,3] Jian Ge,[2] Wenyong Huang,[2] Yingfeng Zheng,[2] David S. Friedman,[4] Pak Sang Lee,[1] and Peng T. Khaw[1,3]

IOVS, 2006

	N	PACS	PAC	PACG
Men and women				
50–59	466	3.7 (1.9–5.4)	1.1 (0.1–2.0)	0 (–)
60–69	398	11.6 (8.4–14.7)	2.9 (1.3–4.6)	1.2 (0.4–2.9)
70–79	408	14.0 (10.6–17.3)	2.9 (1.3–4.5)	3.3 (1.8–5.5)
80–93	100	20.0 (12.0–28.0)	3.7 (0.8–7.3)	1.9 (0.2–6.5)
All	1372	10.2 (8.6–11.8)	2.4 (1.6–3.1)	1.5 (0.9–2.1)

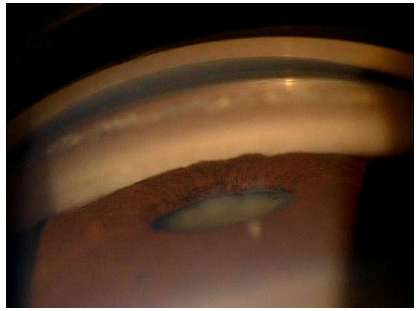
Zhongshan Angle-Closure Prevention (ZAP) Trial

Laser peripheral iridotomy for the prevention of angle closure: a single-centre, randomised controlled trial

Mingguang He, Yuzhen Jiang, Shengsong Huang, Dolly S Chang, Beatriz Munoz, Tin Aung, Paul J Foster, David S Friedman**

The Lancet, 2019

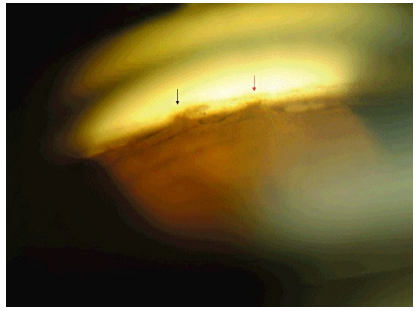
Bilateral PACS



889 participants
Age 50-70
Mainland Chinese
LPI in one eye

6 years

PAC



PAS, IOP > 24 mmHg, AAC

ZAP Trial: Results

	Laser peripheral iridotomy (n=889)	Control (n=889)	p value
Reach primary endpoint	19 (4·19 per 1000 eye-years)	36 (7·97 per 1000 eye-years)	0·021
2 weeks	1	1	..
6 months	5	3	..
18 months	5	6	..
36 months	3	6	..
54 months	2	11	..
72 months	3	9	..

TREATED WITH LPI

0.42% per eye year

UNTREATED

0.80% per eye year

Cost Effectiveness

- 44: eyes needed to treat to prevent one case of PAC
- 126: eyes needed to treat to prevent one case of PACG

Study Conclusion

"Efforts to identify (using gonioscopy) and treat (PACS) with iridotomy on a population basis probably are not the best use of resources…"

- ZAP Trial Authors

Kristy Yoo

Utilization of LPI

- 52,045 patients newly diagnosed with angle closure *without* glaucoma (2009-2020)
- 27.7% received LPI treatment
- Higher odds among Asian and Hispanic Americans (OR≥1.2)

OPTUM

ELSEVIER

American Journal of Ophthalmology

Available online 11 January 2024

In Press, Journal Pre-proof What's this?

Original Articles

Practice Patterns and Sociodemographic Disparities in the Clinical Care of Anatomical Narrow Angles in the United States

Kristy Yoo [1], Galo Apolo [2], Khristina Lung [3], Brian Toy [2], Benjamin Xu [2]

AJO, 2024

USC Roski Eye Institute
Keck Medicine of USC

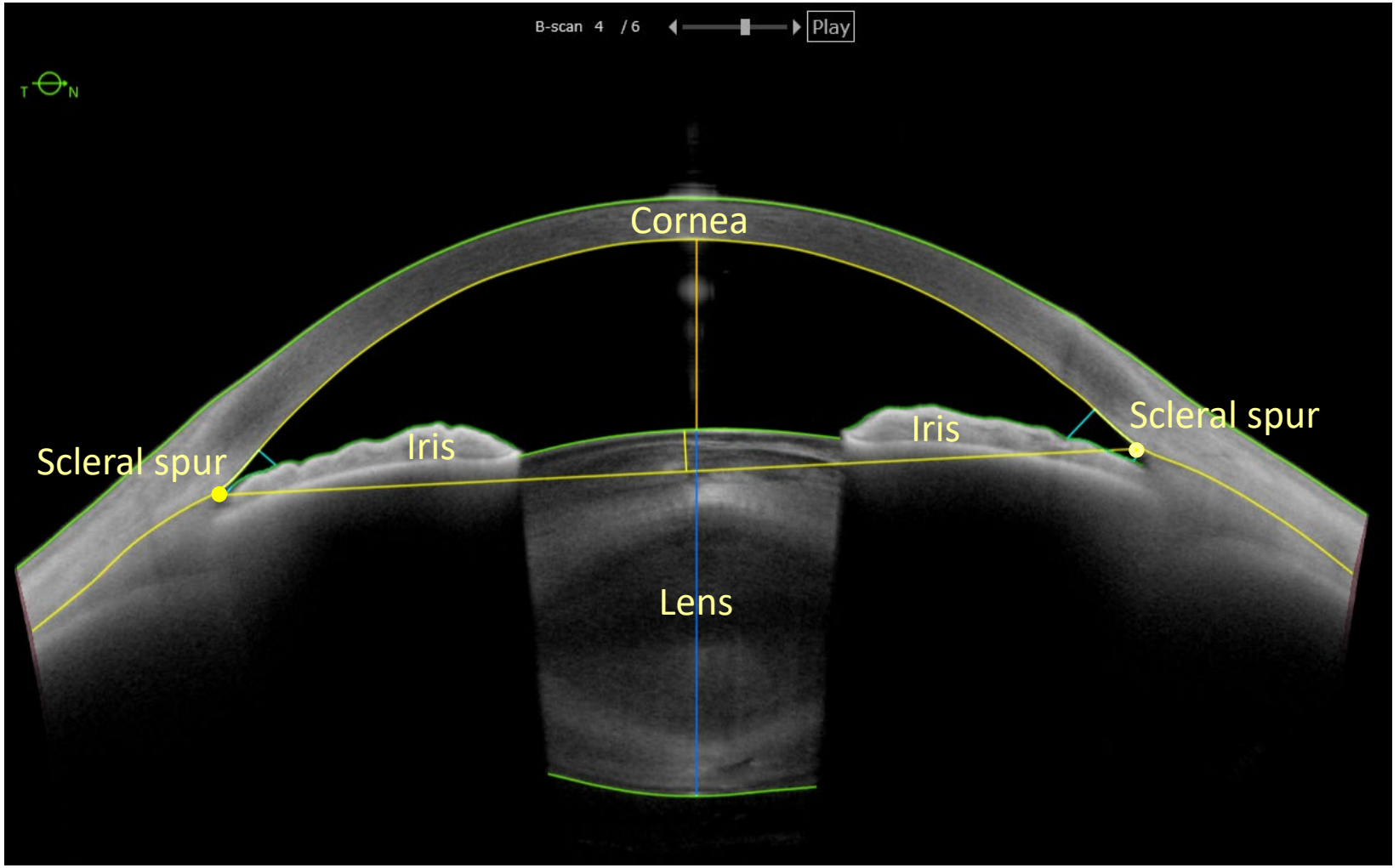
Children's Hospital Los Angeles
We Treat Kids Better

LAC+USC Healthcare Network

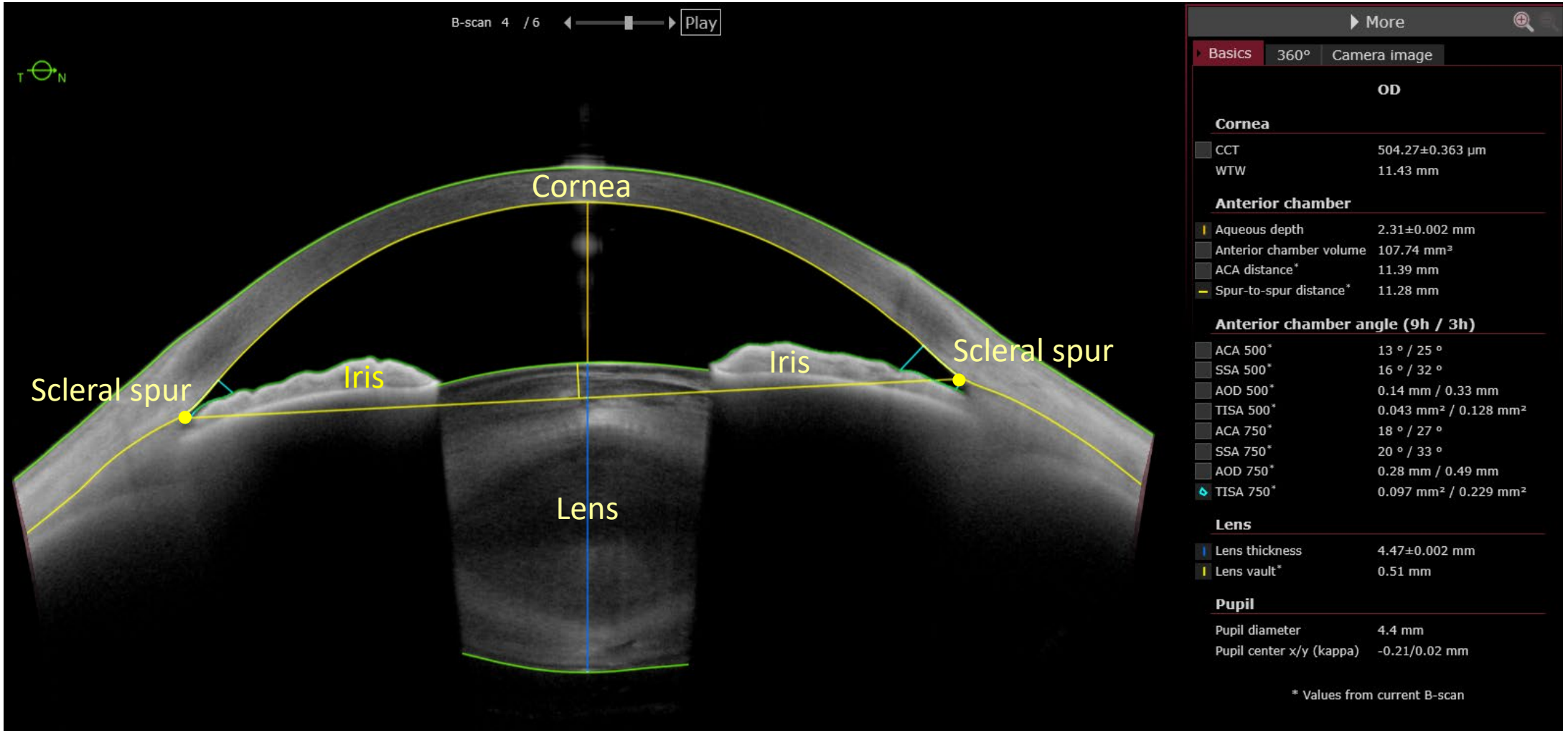
Urgent Need #2

Precise and reproducible method to identify high-risk PACS eyes that should receive LPI

Quantitative AS-OCT



Quantitative AS-OCT



Question

Are AS-OCT measurements predictive of IOP and angle closure outcomes?

Angle Width and IOP

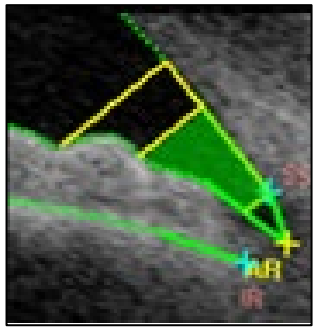
Correlation between Intraocular Pressure and Angle Configuration Measured by OCT

The Chinese American Eye Study

Benjamin Y. Xu, MD, PhD,[1] Bruce Burkemper, PhD,[1] Juan Pablo Lewinger, PhD,[2] Xuejuan Jiang, PhD,[1,2] Anmol A. Pardeshi, MS,[1] Grace Richter, MD, MPH,[1] Mina Torres, PhD,[1] Roberta McKean-Cowdin, PhD,[1,2] Rohit Varma, MD, MPH[1,2]

Ophthalmology Glaucoma, 2018

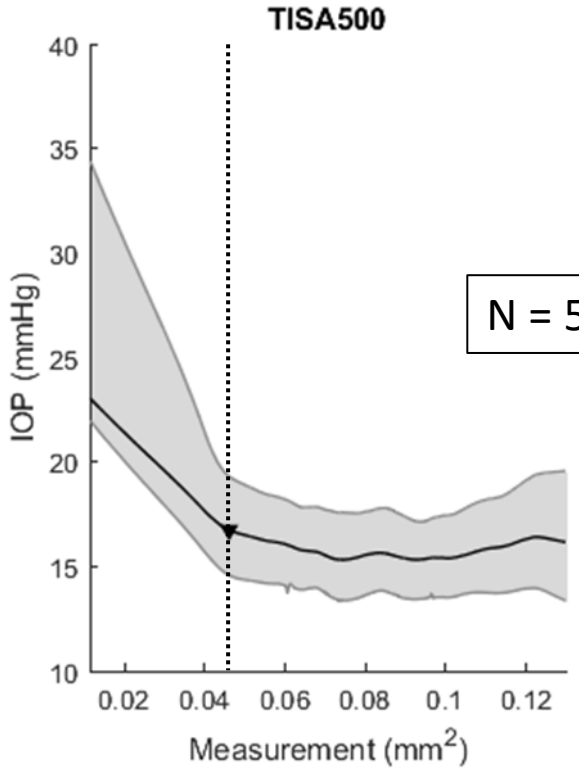
CHINESE AMERICAN EYE STUDY
美國華裔眼科健康調查



TISA

R = -0.698
P < 0.001

R = -0.049
P = 0.401



N = 555

Source: Correlation between Intraocular Pressure and Angle Configuration Measured by OCT, The Chinese American Eye Study

USC Roski Eye Institute
Keck Medicine of USC
Children's Hospital Los Angeles
We Treat Kids Better
LAC+USC Healthcare Network

UNTREATED Angle Closure Progression

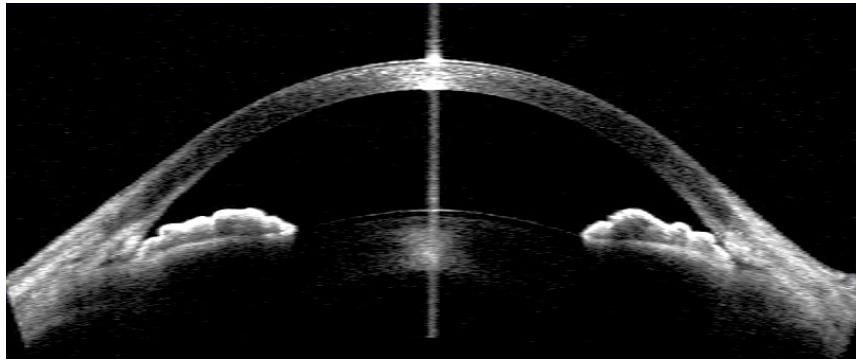
Ocular Biometric Risk Factors for Progression of Primary Angle Closure Disease

The Zhongshan Angle Closure Prevention Trial

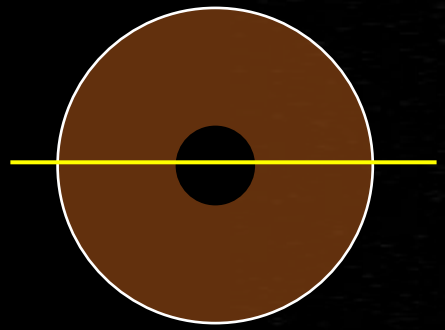
Benjamin Y. Xu, MD, PhD,[1] David S. Friedman, MD, PhD,[2] Paul J. Foster, PhD, FRCS(Ed),[3] Yu Jiang, MD,[4] Natalia Porporato, MD,[5] Anmol A. Pardeshi, MS,[1] Yuzhen Jiang, MD, PhD,[4] Beatriz Munoz, MS,[6] Tin Aung, PhD, FRCS(Ed),[5] Mingguang He, MD, PhD[4]

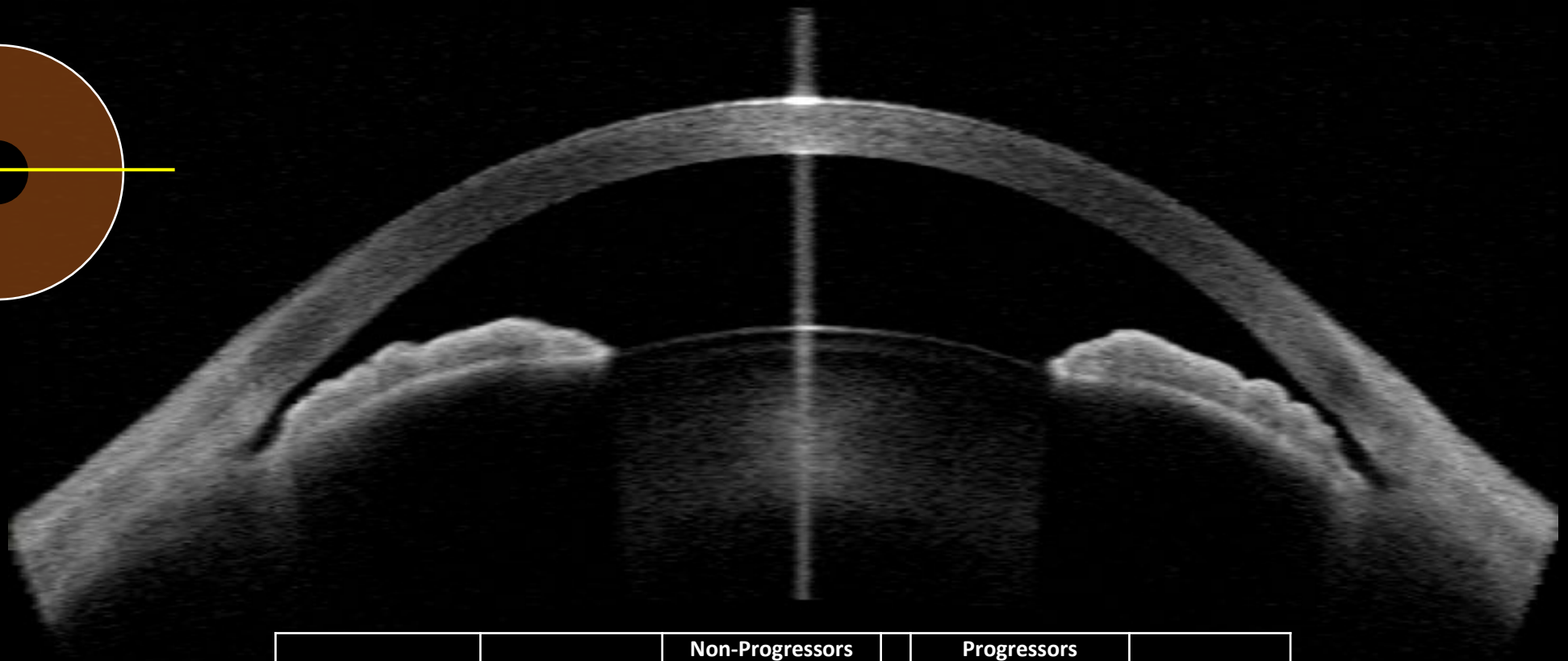
Ophthalmology, 2022

- 643 untreated PACS eyes
- Gonioscopy and AS-OCT at baseline
- Outcome: PACS to PAC



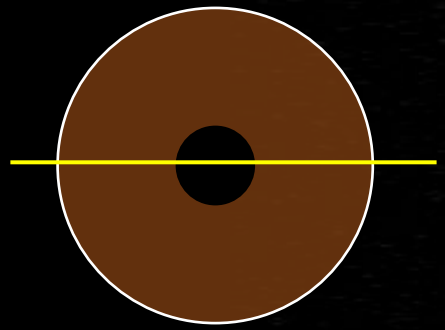
Results: Baseline Demographic and Biometric Differences

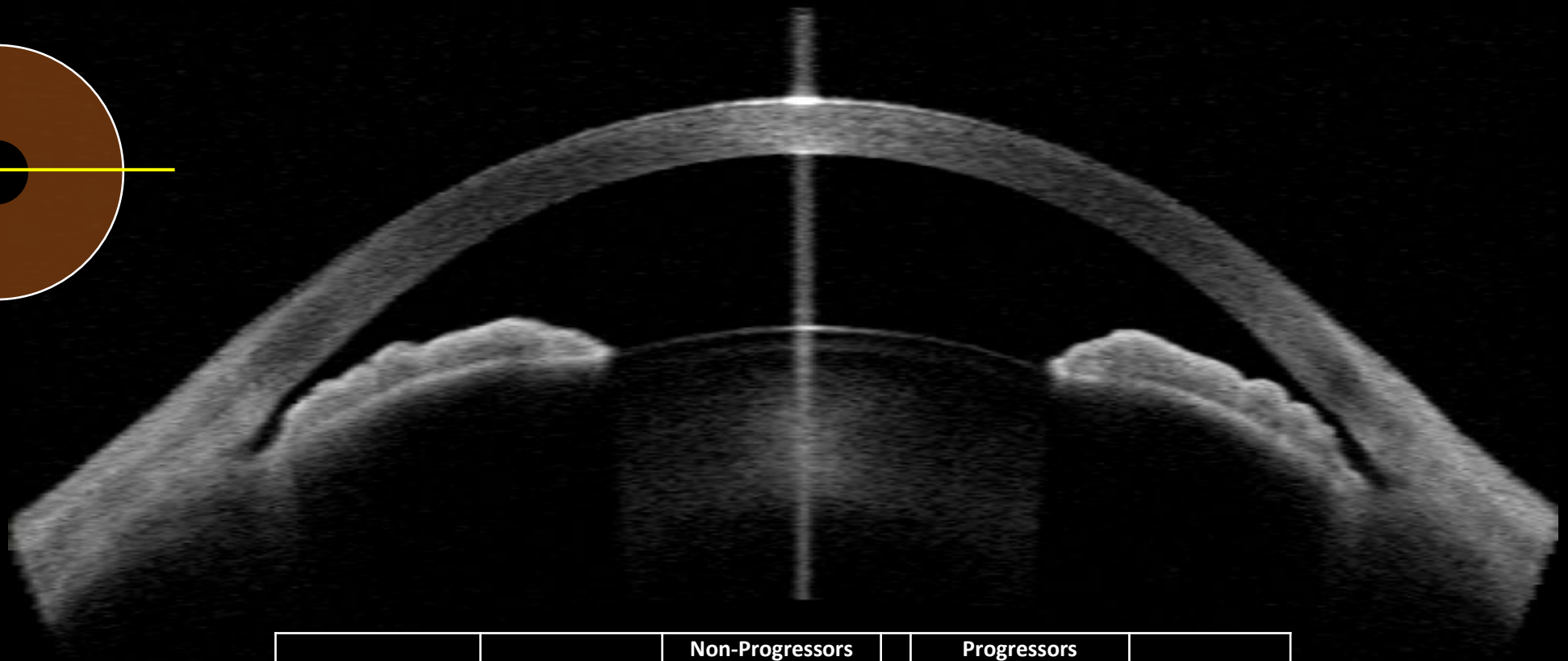


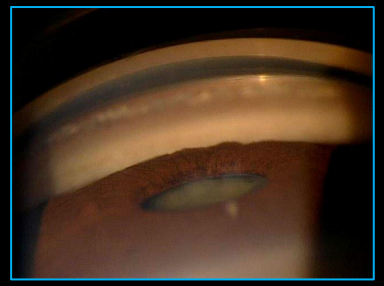


		Non-Progressors (N = 609)		Progressors (N = 34)	
Parameter	Units	Mean (STD)		Mean (STD)	P-value
Age	Years	58.567 (4.977)		60.294 (5.681)	0.051
Sex	Male/Female	110/499		6/28	1.000
IOP	mmHg	15.170 (2.873)		16.303 (2.974)	**0.028**

Results: Baseline Demographic and Biometric Differences







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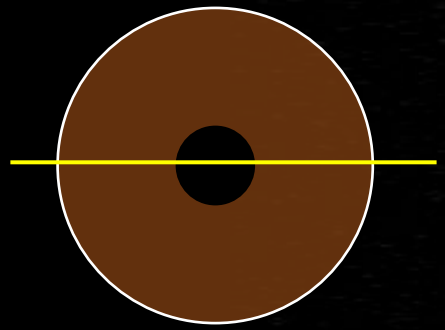
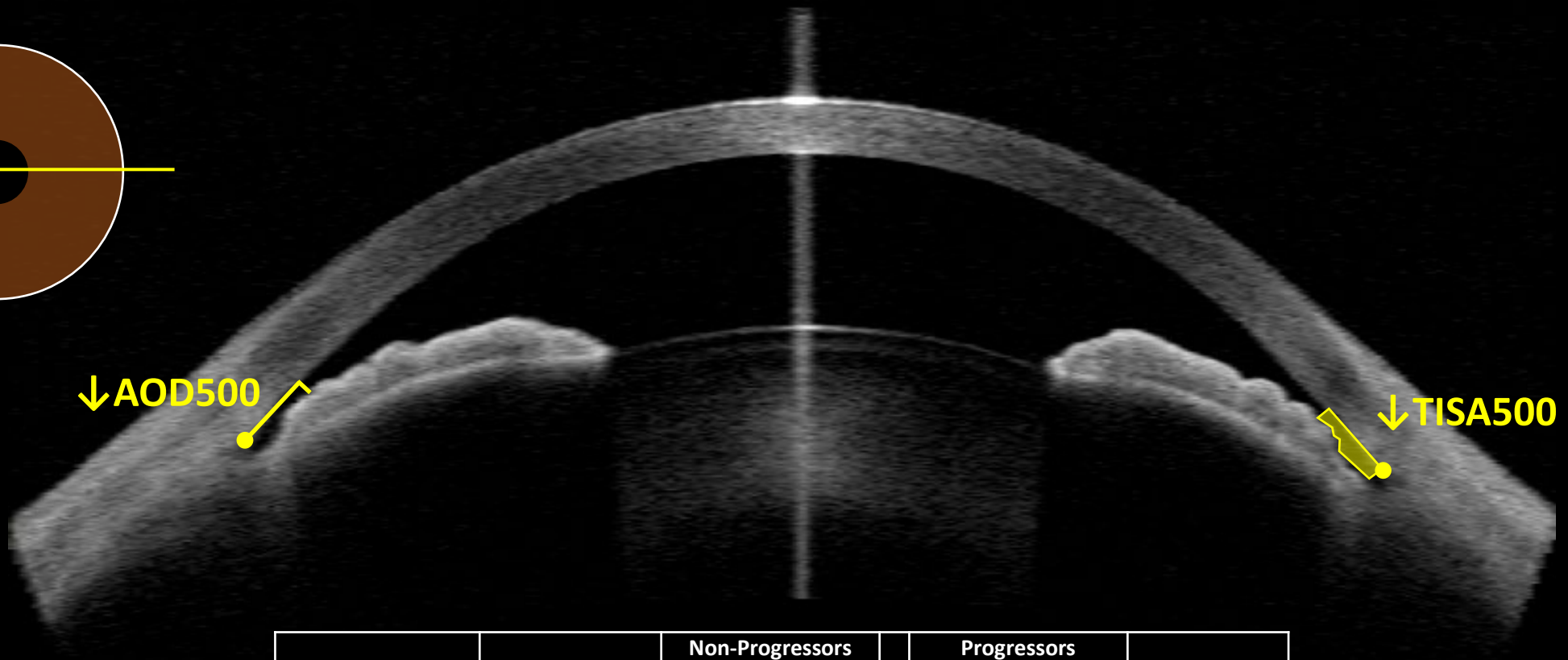
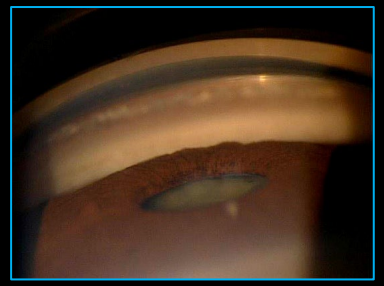
Sex	Male/Female	110/499		6/28	1.000
IOP	mmHg	15.170 (2.873)		16.303 (2.974)	**0.028**
Goniscopy score	mShaffer grade	3.584 (1.476)		3.296 (1.336)	0.265

Results: Baseline Demographic and Biometric Differences







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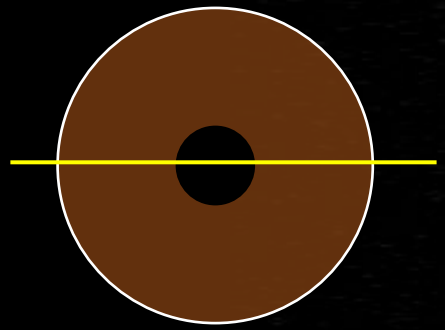
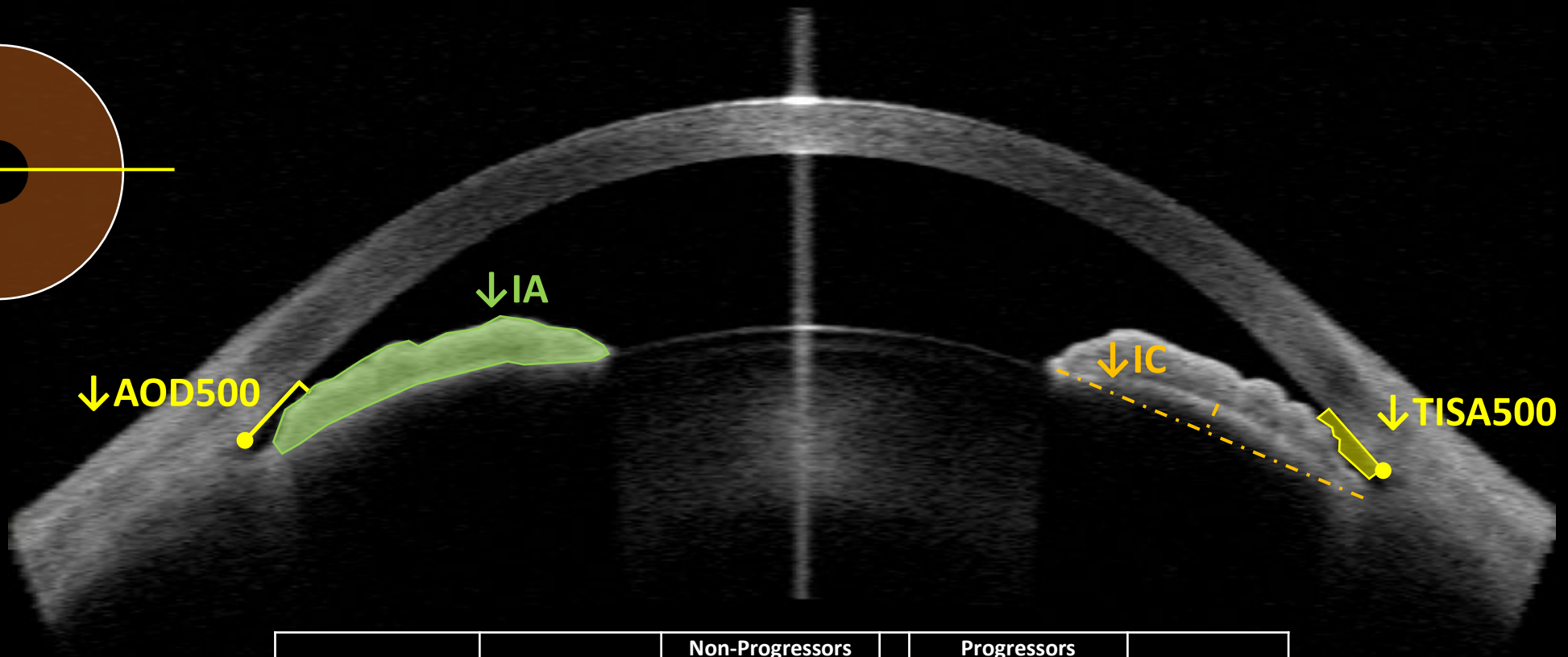
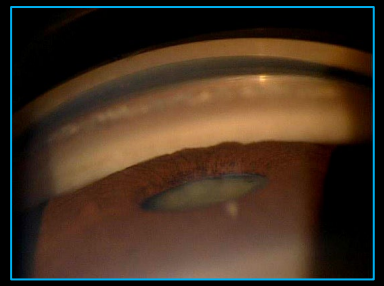
Goniscopy score	mShaffer grade	3.584 (1.476)		3.296 (1.336)	0.265
AOD500	mm	0.088 (0.053)		0.057 (0.050)	**0.001**
TISA500	mm^2	0.055 (0.034)		0.033 (0.021)	**<0.001**

Results: Baseline Demographic and Biometric Differences







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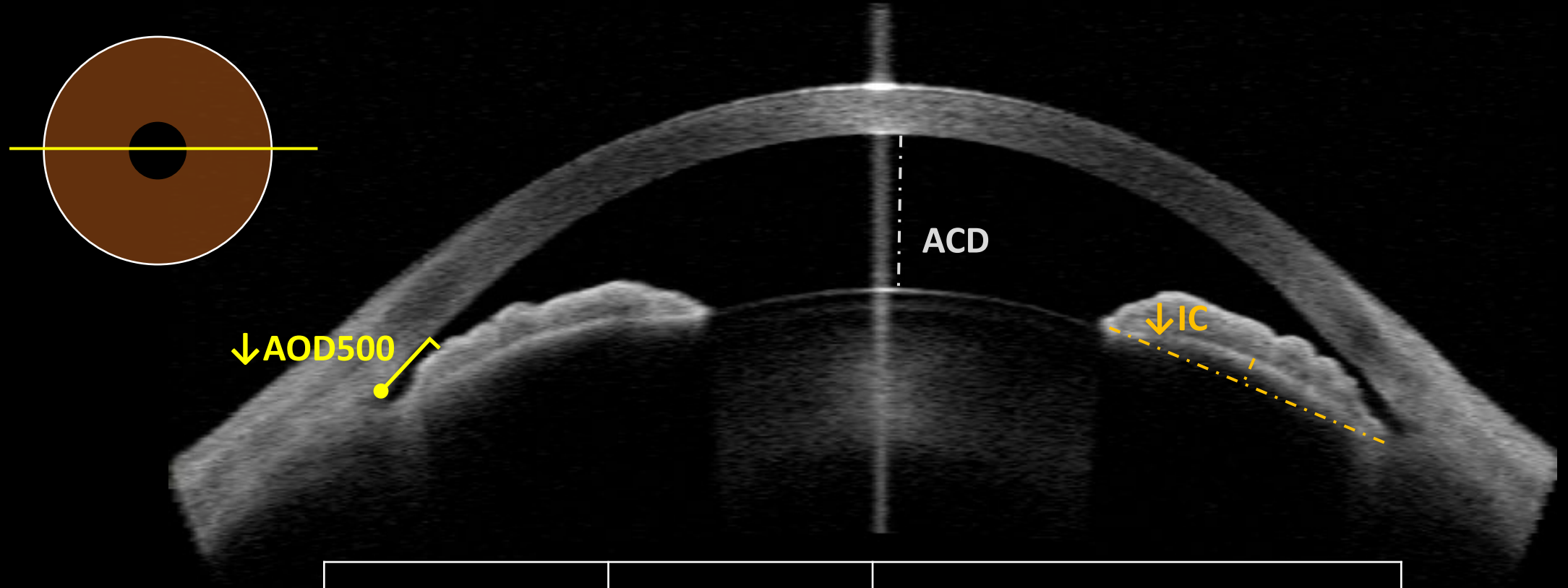
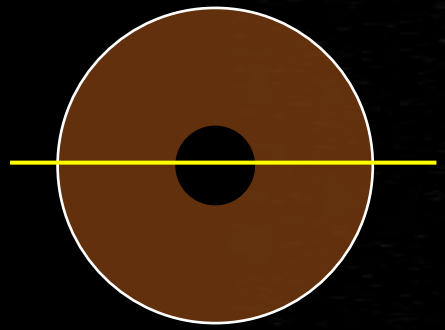
Sex	Male/Female	110/499		6/28	1.000
IOP	mmHg	15.170 (2.873)		16.303 (2.974)	**0.028**
Goniscopy score	mShaffer grade	3.584 (1.476)		3.296 (1.336)	0.265
AOD500	mm	0.088 (0.053)		0.057 (0.050)	**0.001**
TISA500	mm^2	0.055 (0.034)		0.033 (0.021)	**<0.001**
IA	mm^2	1.606 (0.216)		1.526 (0.145)	**0.045**
IC	mm	0.391 (0.088)		0.351 (0.089)	**0.016**

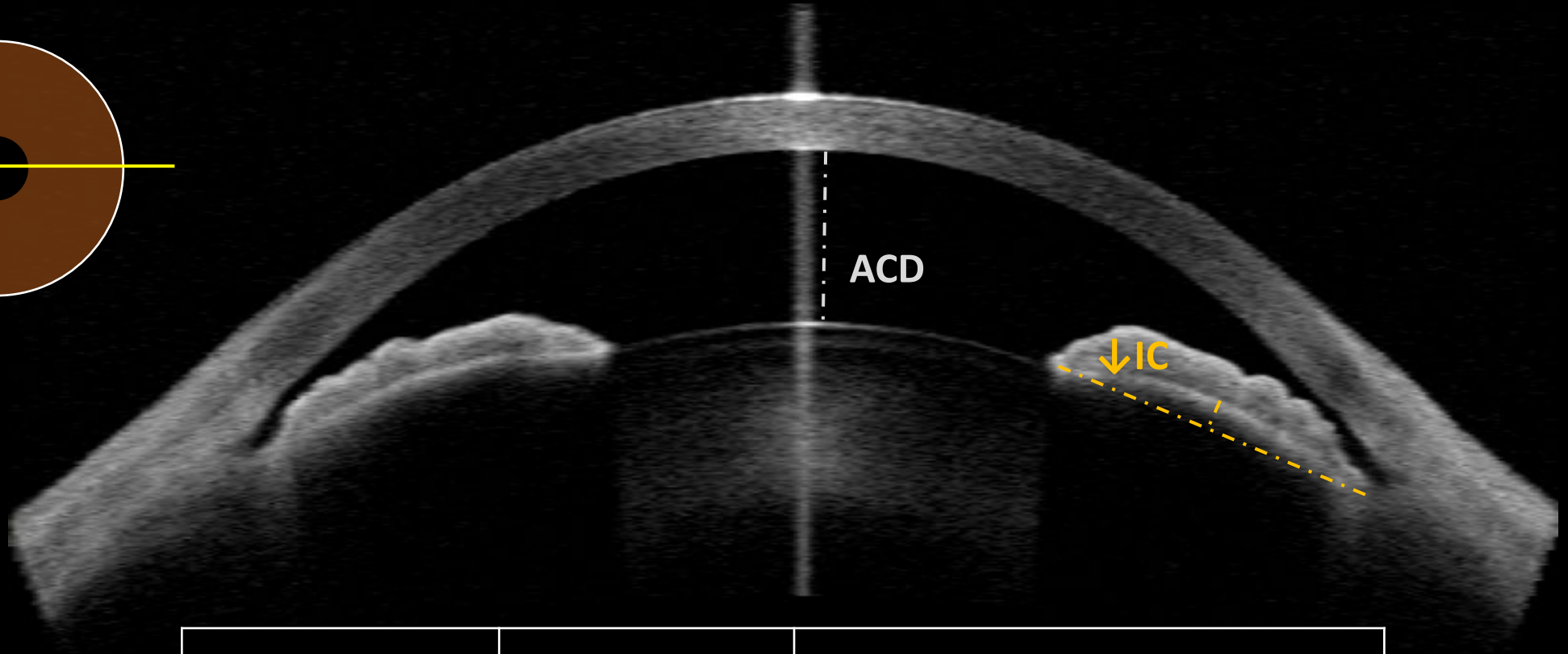
Results: Multivariable Predictors of Progression – AOD500

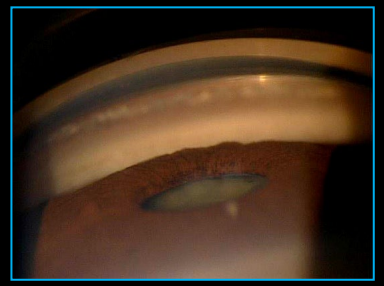


		Multivariable	
Parameter	Units	OR (95% CI)	P-value
Age	1 year older	1.11 (1.03-1.20)	**0.007**
AOD500	0.01 mm lower	1.10 (1.01-1.19)	**0.027**
IC	0.1 mm lower	1.96 (1.19-3.23)	**0.010**
ACD	0.1 mm lower	1.15 (0.94-1.41)	0.162

Results: Multivariable Predictors of Progression – Gonioscopy Score







		Multivariable	
Parameter	Units	OR (95% CI)	P-value
Age	1 year increase	1.11 (1.03-1.20)	**0.006**
Gonioscopy score	1 grade decrease	1.06 (0.82-1.37)	0.665
IC	0.1 mm decrease	2.22 (1.39-3.70)	**0.001**
ACD	0.1 mm decrease	1.22 (1.00-1.49)	0.056

Precision Care With AS-OCT

Role of Static and Dynamic Ocular Biometrics Measured in the Dark and Light as Risk Factors for Angle Closure Progression

AUSTIN CHO, BENJAMIN Y. XU, DAVID S. FRIEDMAN, PAUL J. FOSTER, YU JIANG, ANMOL A. PARDESHI, YUZHEN JIANG, TIN AUNG, AND MINGGUANG HE

AJO, 2023

JAMA Ophthalmology | Original Investigation

Biometric Risk Factors for Angle Closure Progression After Laser Peripheral Iridotomy

Yicheng K. Bao, MD; Benjamin Y. Xu, MD, PhD; David S. Friedman, MD, PhD; Austin Cho, BA; Paul J. Foster, PhD; Yu Jiang, MD; Natalia Porporato, MD, PhD; Anmol A. Pardeshi, MS; Yuzhen Jiang, MD, PhD; Beatriz Munoz, MS; Tin Aung, PhD; Mingguang He, MD, PhD

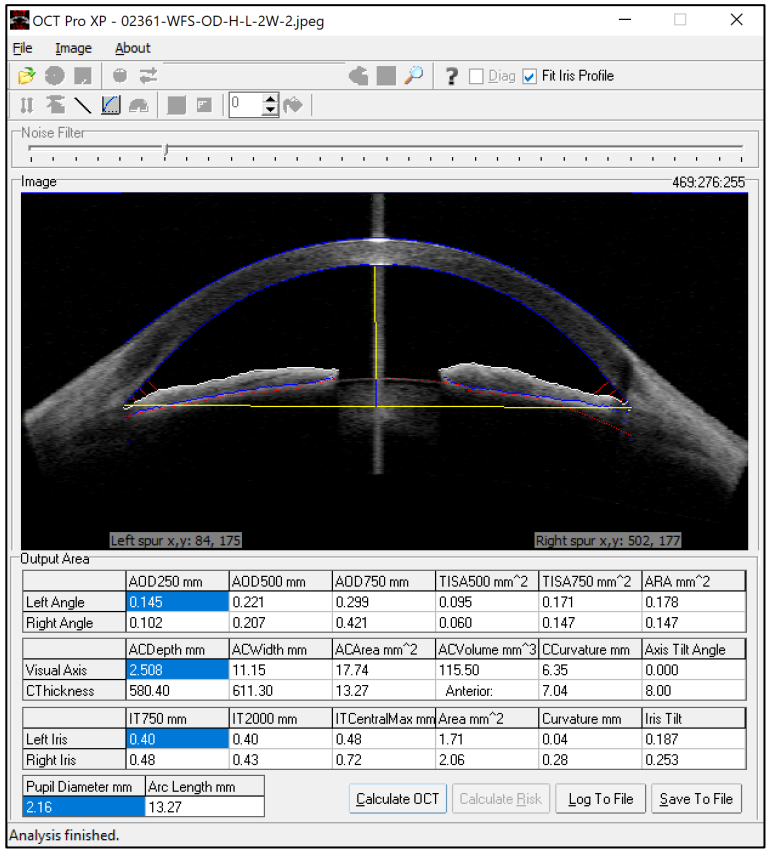
JAMA Ophthalmology, 2023

Anatomic Changes and Predictors of Angle Widening after Laser Peripheral Iridotomy

The Zhongshan Angle Closure Prevention Trial

Benjamin Y. Xu, MD, PhD,[1] David S. Friedman, MD, PhD,[2] Paul J. Foster, FRCS(Ed), PhD,[3] Yu Jiang, MD,[4] Anmol A. Pardeshi, MS,[1] Yuzhen Jiang, MD, PhD,[4] Beatriz Munoz, MS,[5] Tin Aung, FRCS(Ed), PhD,[6] Mingguang He, MD, PhD[4]

Ophthalmology, 2022



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Children's Hospital Los Angeles
We Treat Kids Better
LAC+USC Healthcare Network

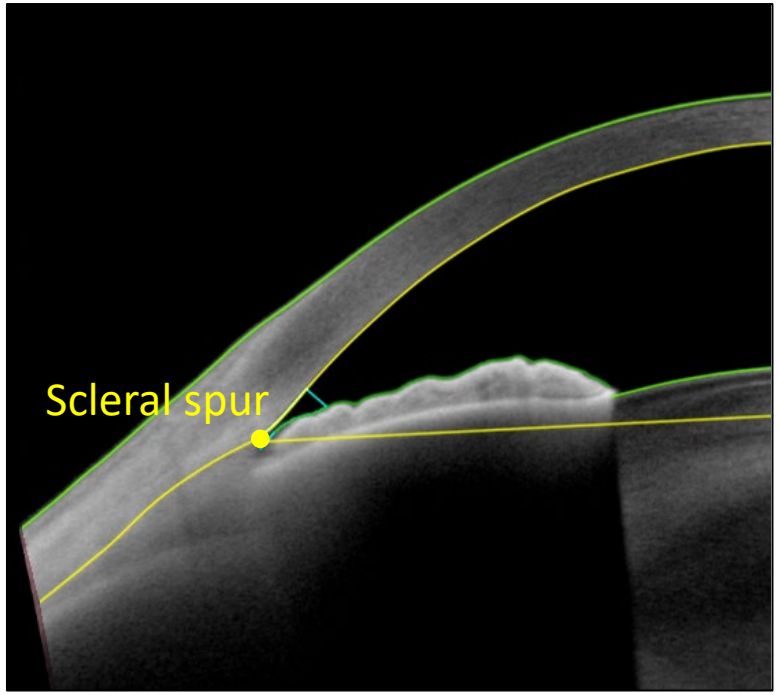
Precise Risk-Stratification → Early Treatment → PACG Prevention

Source: *https://www.sermoncentral.com/sermons/looking-ahead-new-years-premium-sermon-on-future-hope-40000341*

Barriers to Clinical Implementation

Barrier #1

Most eye care providers don’t have the time or expertise to manually analyze AS-OCT images



Automated Scleral Spur Detection

Tomey CASIA SS-1000

tvst

Special Issue

Deep Neural Network for Scleral Spur Detection in Anterior Segment OCT Images: The Chinese American Eye Study

Benjamin Y. Xu[1], Michael Chiang[2], Anmol A. Pardeshi[1], Sasan Moghimi[3], and Rohit Varma[4]

TVST, 2020

CHINESE AMERICAN EYE STUDY
美國華裔眼科健康調查

USC Roski Eye Institute
Keck Medicine of USC

Children's Hospital LOS ANGELES
We Treat Kids Better

LAC+USC HEALTHCARE NETWORK

Kyle Bolo

Automated Biometric Analysis

ANTERION

Clinical science

Automated expert-level scleral spur detection and quantitative biometric analysis on the ANTERION anterior segment OCT system

Kyle Bolo [1], Galo Apolo Aroca [1], Anmol A Pardeshi,[1,2] Michael Chiang,[1] Bruce Burkemper,[1,2] Xiaobin Xie,[3] Alex S Huang,[4] Martin Simonovsky,[5] Benjamin Y Xu [1]

BJO, 2023

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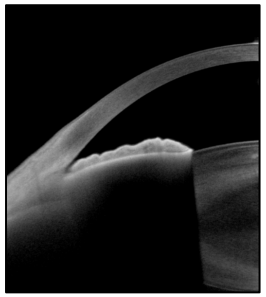
ANTERION Scleral Spur Detection

ANTERION AS-OCT Image



CNN

M2U-Net

Scleral spur location
(X- and Y-coordinates)

4,038 AS-OCT images + scleral spur locations

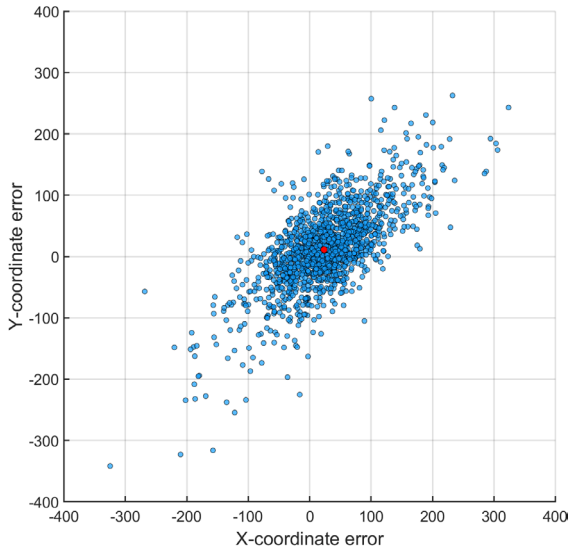
80%: Training dataset

20%: Test dataset

Scleral Spur Detection

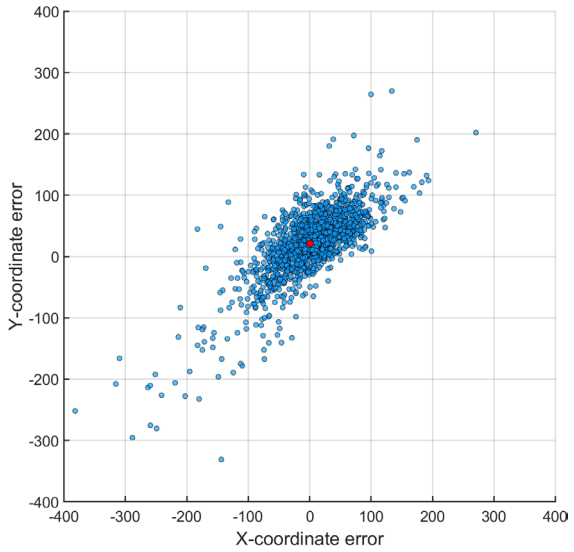
DATASET:
1,308 images
2,616 spurs

Human-Human Agreement



Median Error = 61.1 µm

Human-Machine Agreement

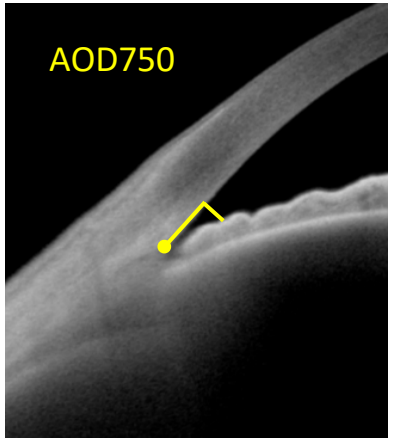


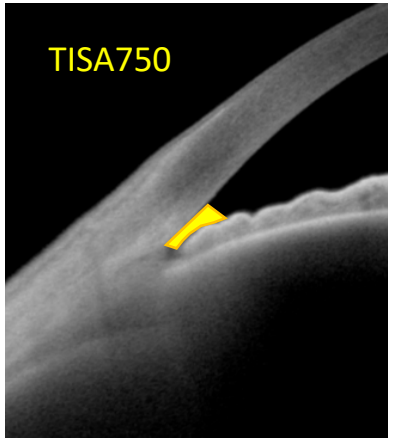
Median Error = 55.5 µm

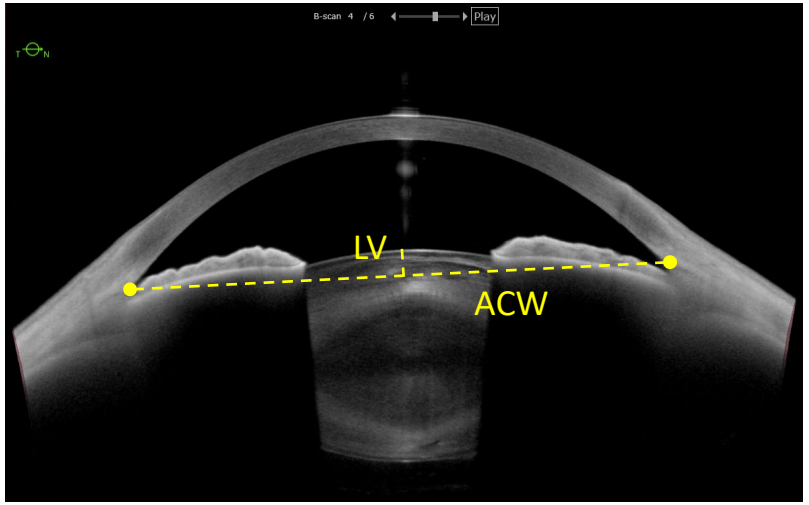
Error (µm) = Reference – Predicted Scleral Spur Coordinates

Source: Automated expert-level scleral spur detection and quantitative biometric analysis on the Anterion anterior segment OCT system by Kyle Bolo et al.

Inter-Grader Reproducibility of Biometric Measurements







	Glaucoma Specialist	Deep Learning
	Intraclass Correlation Coefficient (ICC)	
AOD500	0.961	0.963
AOD750	0.976	0.975
TISA500	0.965	0.968
TISA750	0.974	0.976
ACW	0.966	0.978
LV	0.996	0.996

Barrier #2

AS-OCT devices are relatively uncommon and expensive

Modern Biometers

Heidelberg ANTERION

Alcon ARGOS

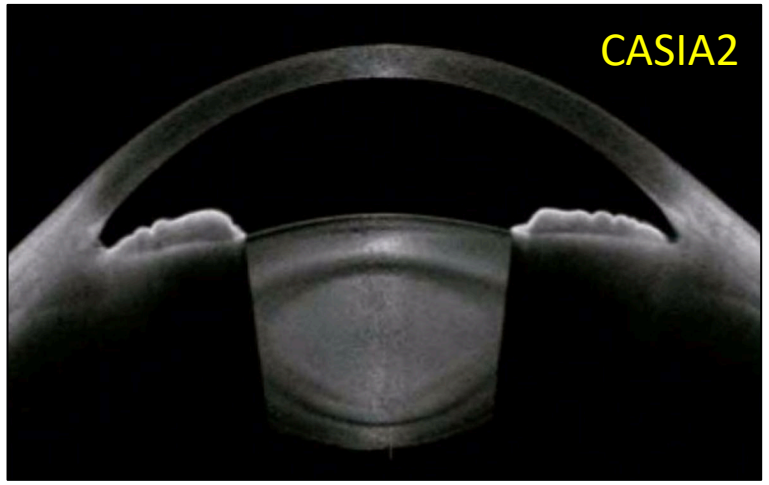
Tomey CASIA2

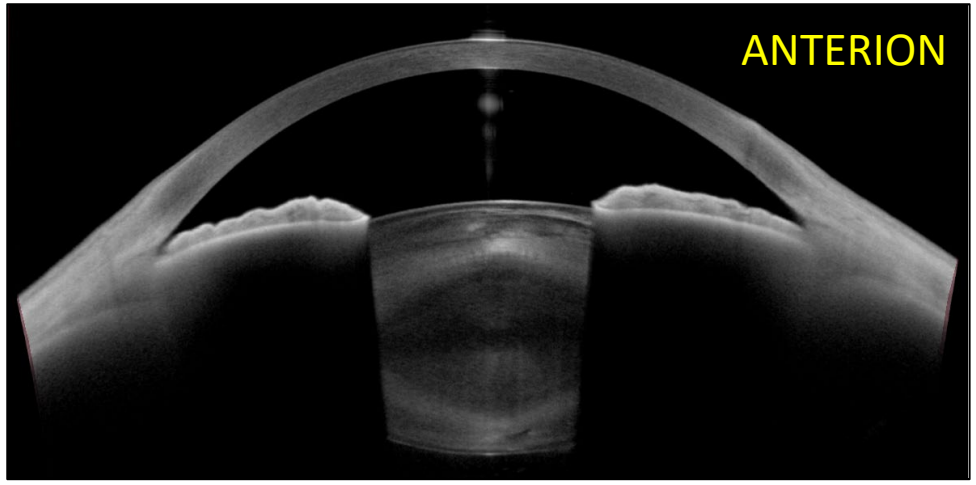
Low-cost OCT technology is needed for resource-limited settings

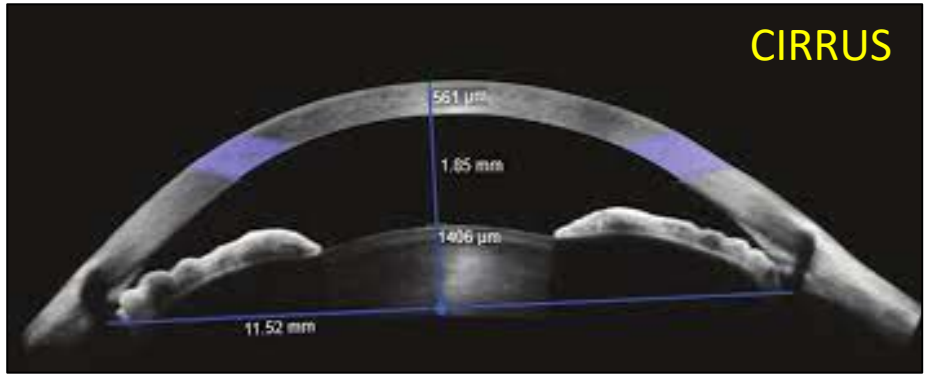
Barrier #3

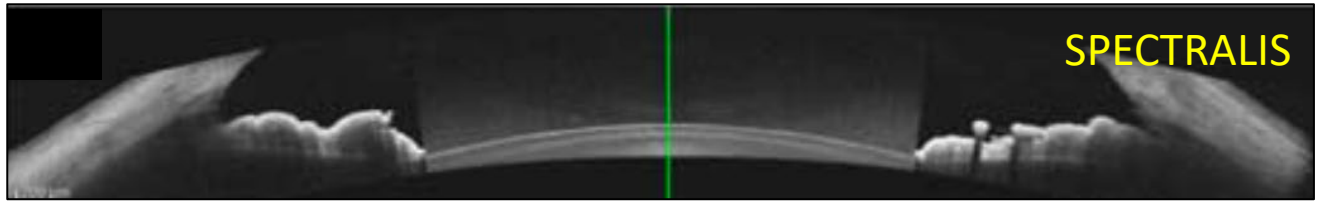
There is a lack of standardization between AS-OCT systems and images

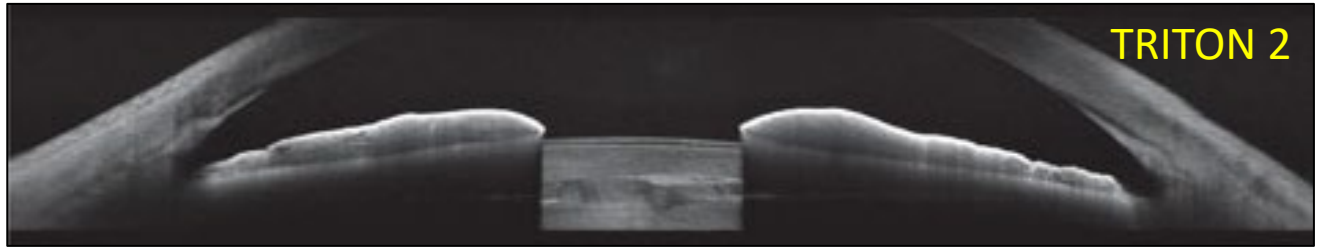
Image Appearance and Refraction Correction









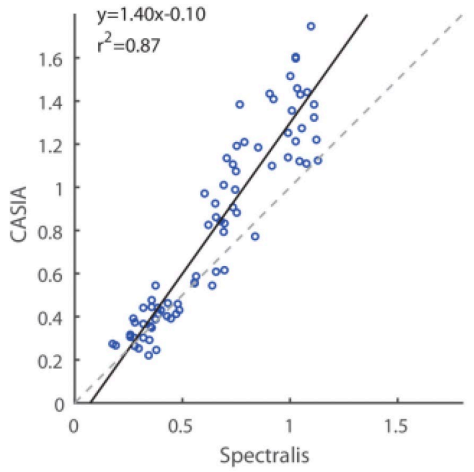


Inter-Device Agreement of Measurements

Reproducibility and Agreement of Anterior Segment Parameter Measurements Obtained Using the CASIA2 and Spectralis OCT2 Optical Coherence Tomography Devices

Benjamin Y. Xu, MD, PhD, Derek D. Mai, MD, Rafaella C. Penteado, MD, Luke Saunders, PhD, and Robert N. Weinreb, MD

Journal of Glaucoma, 2017



AOD500

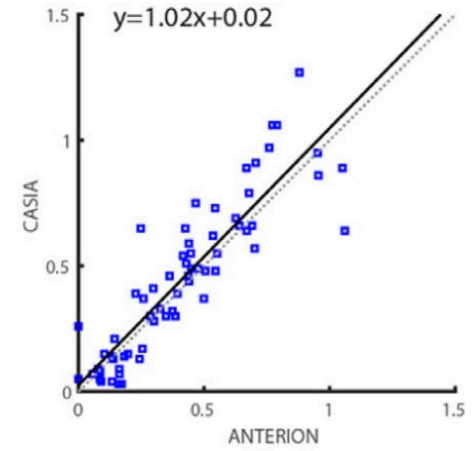
tvst

Article

Intradevice Repeatability and Interdevice Agreement of Ocular Biometric Measurements: A Comparison of Two Swept-Source Anterior Segment OCT Devices

Anmol A. Pardeshi[1], Abe E. Song[1], Naim Lazkani[1], Xiaobin Xie[2,3], Alex Huang[3], and Benjamin Y. Xu[1]

TVST, 2022



AOD750

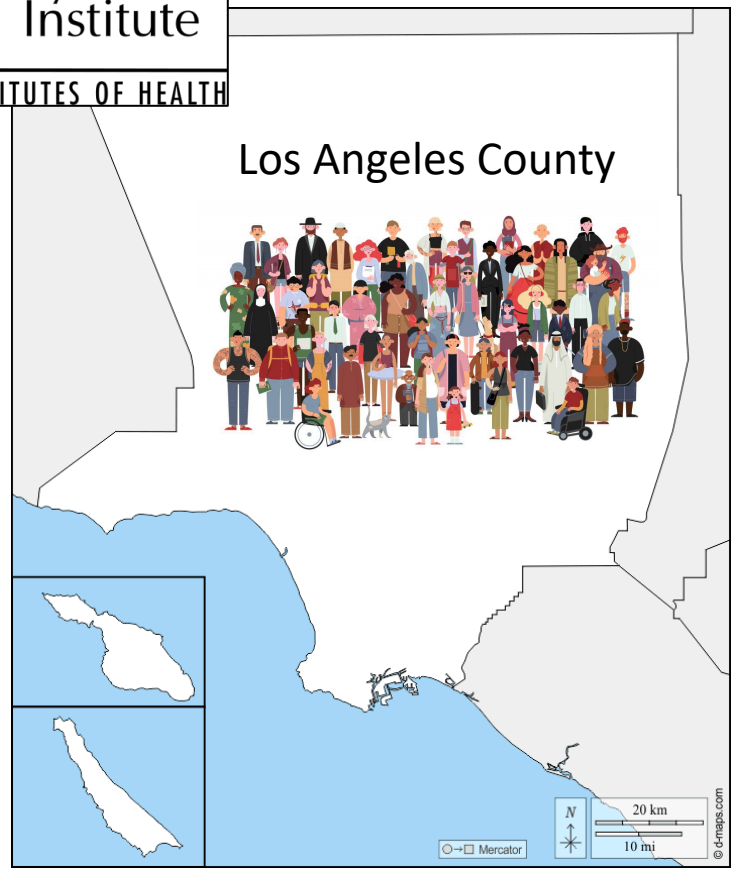
Barrier #4

Little is known about angle anatomy and PACG pathogenesis outside of Asian populations

Multiracial Angle-Closure Progression Study: MAPS

National Eye Institute
NATIONAL INSTITUTES OF HEALTH

R01 EY035677



1. Why are some racial groups at higher risk of PACG?
2. Can we establish an OCT-based definition of “narrow angles”?
3. Can we identify novel OCT-based risk factors for PACG?

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Summary

- PACG is a visually devastating disease
- AS-OCT can identify high-risk angle closure whereas gonioscopy cannot
- AI can help address shortcomings of AS-OCT
- More work is needed to overcome implementation barriers and improve clinical outcomes

The Xu Lab

@BenXuLab

SCAN ME

BIOMEDICAL ENGINEERING

Galo Apolo

Chifeng Chang

COMPUTER SCIENCE

Sreenidhi Iyengar

Shriya Nagrath

OPHTHALMOLOGY RESIDENTS

Sona Shah

Austin Bohner

Yicheng Bao

Kyle Bolo

Aidan Lee

Kendra Hong

EPDEMIOLOGY AND STATISTICS

Anmol Pardeshi

Bruce Burkemper

HEALTY POLICY

Daniel Guth

Khristina Ipapo

MEDICAL STUDENTS

Sarah Zhou

Kristy Yoo

Austin Cho

Ryan Shean

USC Roski Eye Institute
Keck Medicine of USC

Children's Hospital Los Angeles
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LAC+USC Healthcare Network