Characterization of retinal nerve fiber layer and ganglion cell layer inner plexiform thickness in the Ocular Hypertension Treatment Study (OHTS 3) 20-year follow-up.

Evan Walker

Christopher Bowd, Robert N. Weinreb,
Mae O. Gordon, Michael A. Kass,
Keri Dirkes, Suzanne Vega,
Linda M. Zangwill
(for the Ocular Hypertension Treatment Study Group)

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OHTS Resource Centers

Visual Field Reading Center

Chris A. Johnson, Ph.D. (Iowa)

John L. Keltner, M.D. (UC Davis)

Optic Disc Reading Center

Richard Parrish, M.D. (Bascom Palmer/Miami)

Optical Coherence Tomography Reading Center

Linda M. Zangwill PhD. (UCSD)

Keri Dirkes, MPH (UCSD)

Suzanne Vega, MPH. (UCSD)

Endpoint Committee

Dale K. Heuer, M.D. (Doheny/UCLA)

Eve Higginbotham, M.D. (Pennsylvania)

Richard Parrish, M.D. (Bascom Palmer/Miami)

Coordinating Center

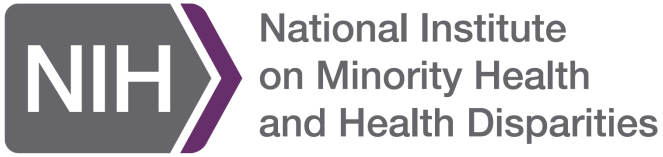
Washington University

Mae Gordon, Ph.D. (PI)

Michael A. Kass, M.D. (PI & Chair)

Julia Huecker, M.S.

OHTS Funding



OHTS Funding

NIH National Eye Institute

OHTS 3 OCT Funding

NIH National Institute on Minority Health and Health Disparities

Research to Prevent Blindness

HEIDELBERG ENGINEERING

Pfizer

MERCK Research Laboratories

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33 OHTS Clinical Centers 1994 – 2019

- Bascom Palmer Eye Institute
- Baylor Eye Clinic
- Charles R. Drew University
- Columbia University Medical Center
- Devers Eye Institute
- Drew University
- Emory University Eye Center
- Eye Associates of Washington, DC
- Eye Consultants of Atlanta
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- University of Louisville
- University Suburban Health Center
- Washington Eye Physicians & Surgeons
- Washington University, St. Louis

OHTS 3 Specific Aims: (2015-2020): OCT was included!

Main OHTS 3

1. To determine the cumulative incidence and severity of POAG after 20 years of follow-up among participants in the OHTS.

2. To determine the frequency and severity of self-reported functional limitations associated with POAG.

3. To develop a 20-year prediction model for stratifying OHT patients by their risk of developing POAG and, among those who developed POAG, a prediction model for the rate of visual field loss.

OCT OHTS 3

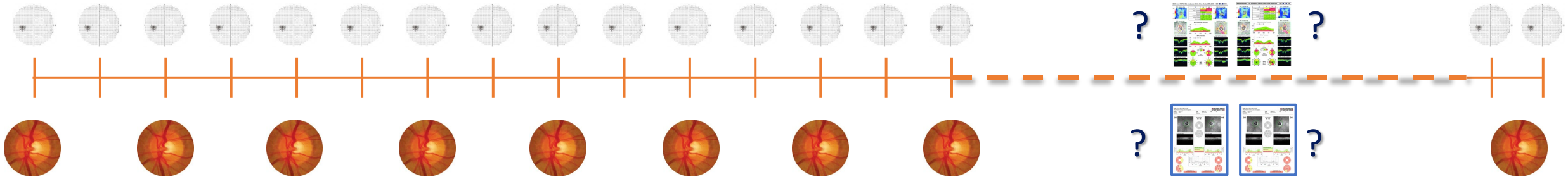
1. Does review of OCT ONH and macular scans improve detection of the OHTS POAG endpoint? **(Zangwill IPS 2022)**

2. What is association between OCT structural damage and functional limitations?

3. **How does structural damage before and after POAG onset differ from normal aging (eyes that never developed POAG)?**

   (Walker IPS 2022)

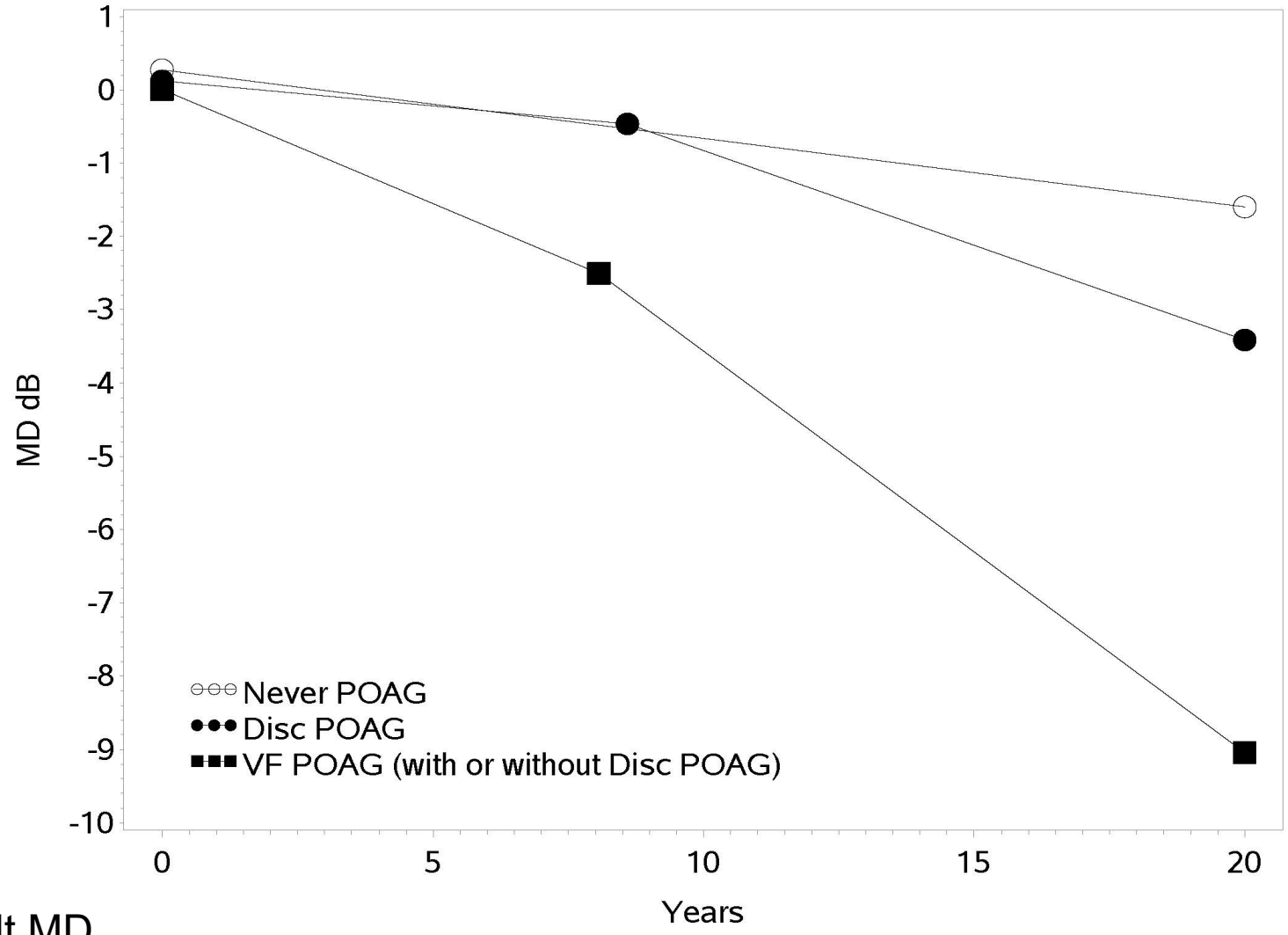
OHTS Timeline (1994 – 2019)



OHTS 1 1994 - 2002	OHTS 2 2002 – 2009		OHTS 3 2016 – 2019
N = 819	672		533
Observation	All patients offered medication	Community care	≈ 70% of all subjects remained on medications
Medication			
N = 817	694		545

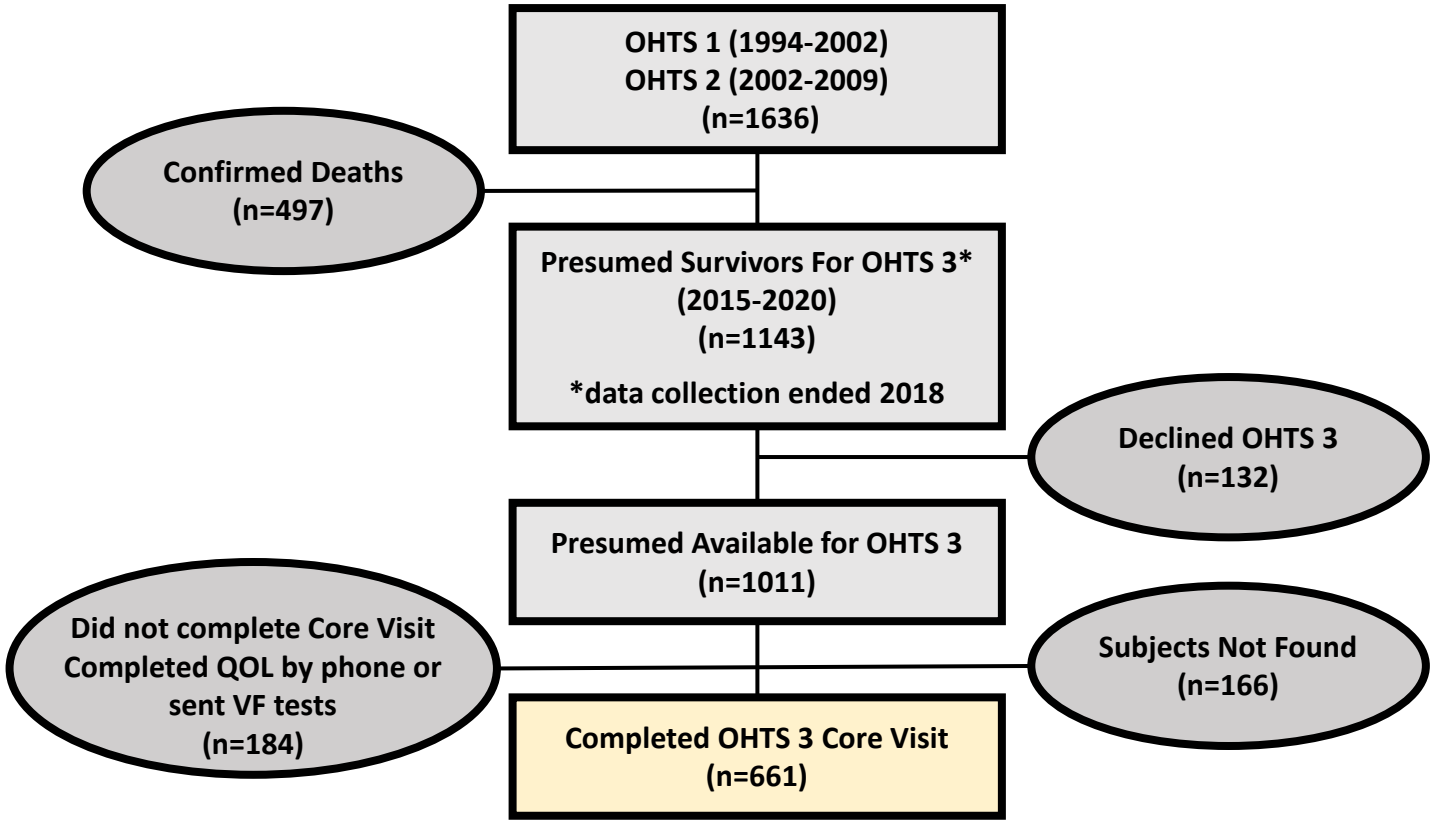
Courtesy of Jamie Brandt MD

Visual Field Mean MD slopes before and after POAG projected over 20 years

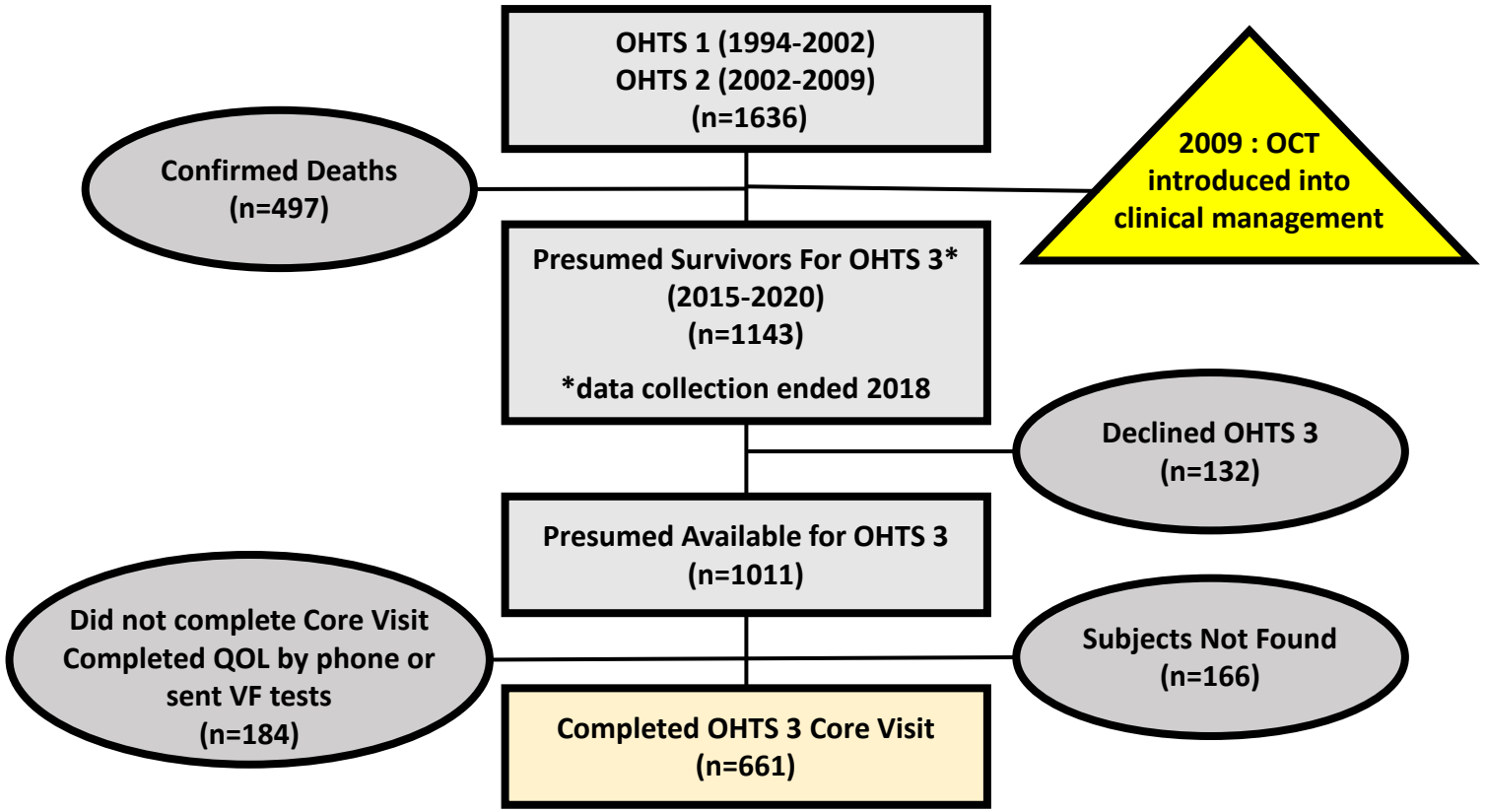


Courtesy of Jamie Brandt MD

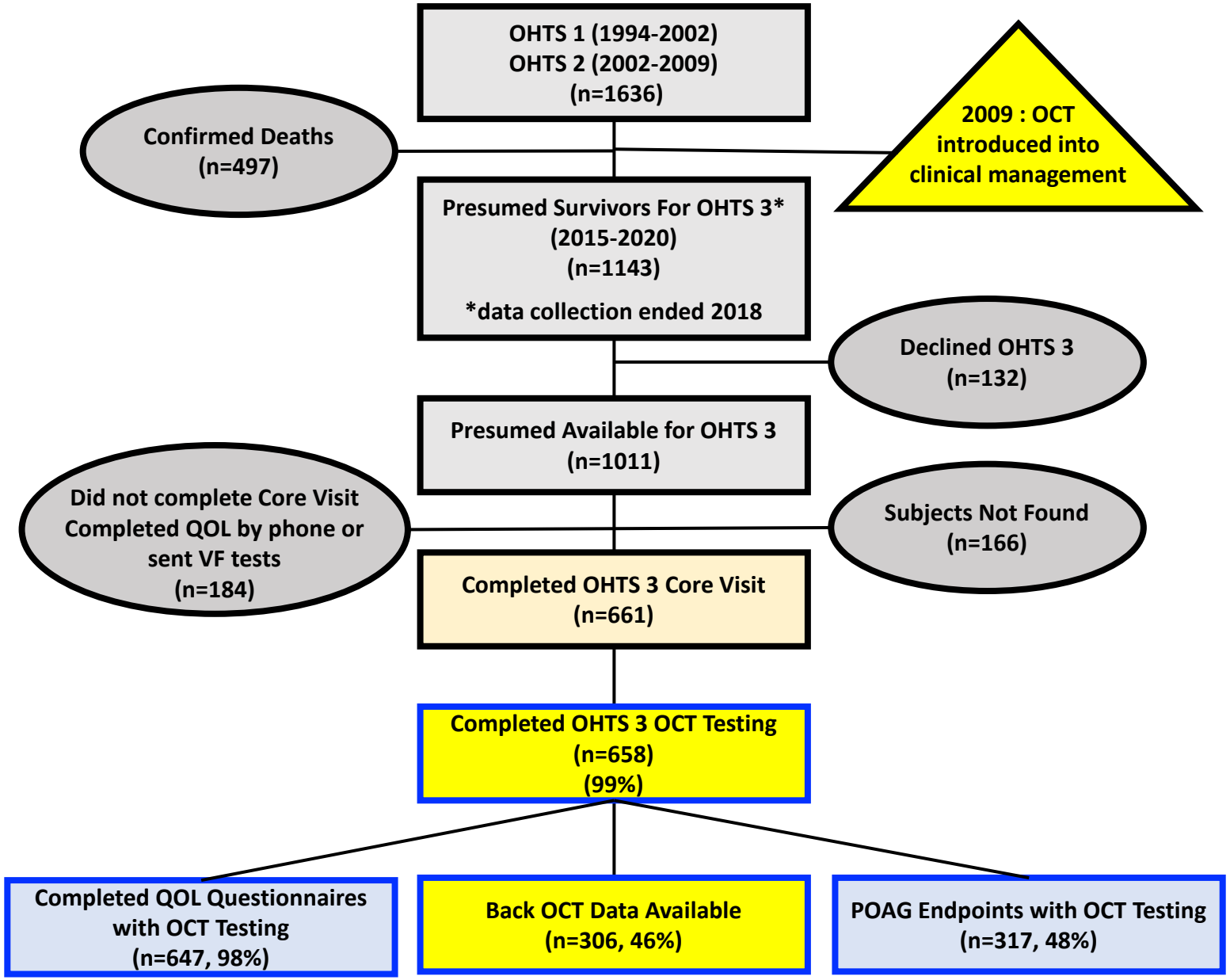
OHTS 3 20-year Follow-up: Flow Chart and Sample Sizes Including OCT



OHTS 3 20-year Follow-up: Flow Chart and Sample Sizes Including OCT



OHTS 3 20-year Follow-up: Flow Chart and Sample Sizes Including OCT



OCT Data Collection

- During OHTS visit, acquire scans on either
  - Cirrus or Spectralis instrument

- Include in OHTS OCT data transfer to OCTRC:

  - OCT scans acquired as part of OHTS visit

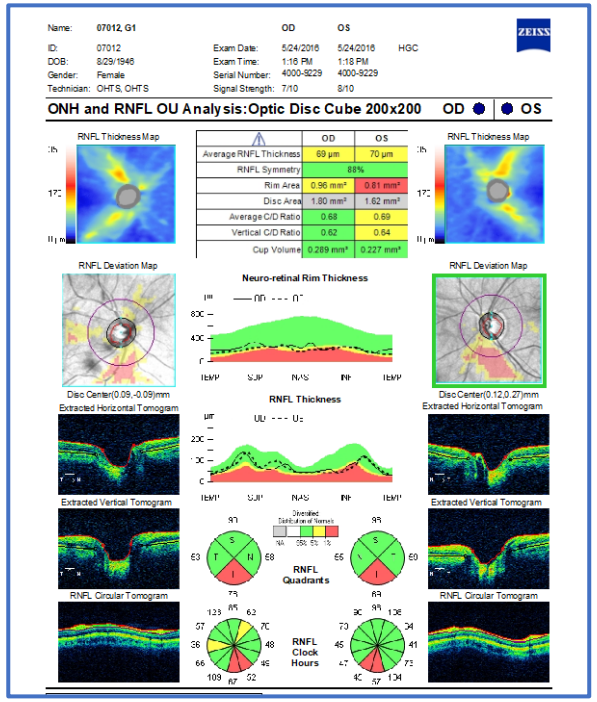
  AND

  - All OCT scans that were previously acquired as part of regular clinical care

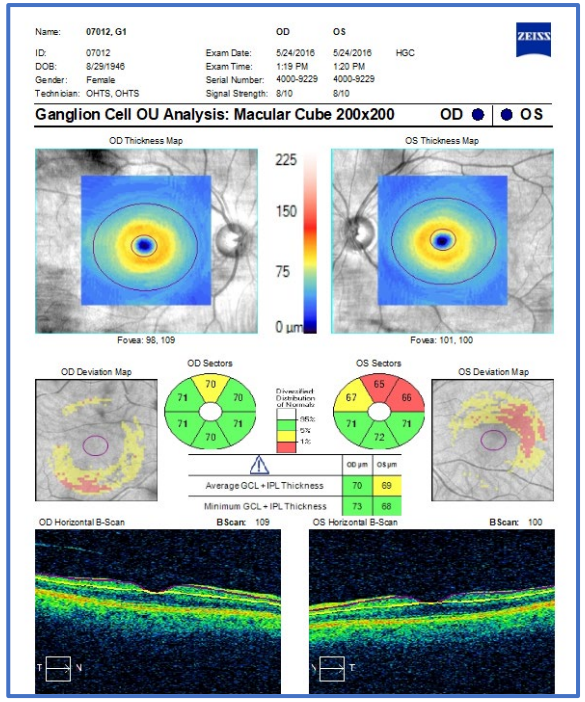
OHTS OCT Protocol: Optic Nerve Head and Macula Scans (Cirrus or Spectralis)

Cirrus

Optic Disc Cube 200x200

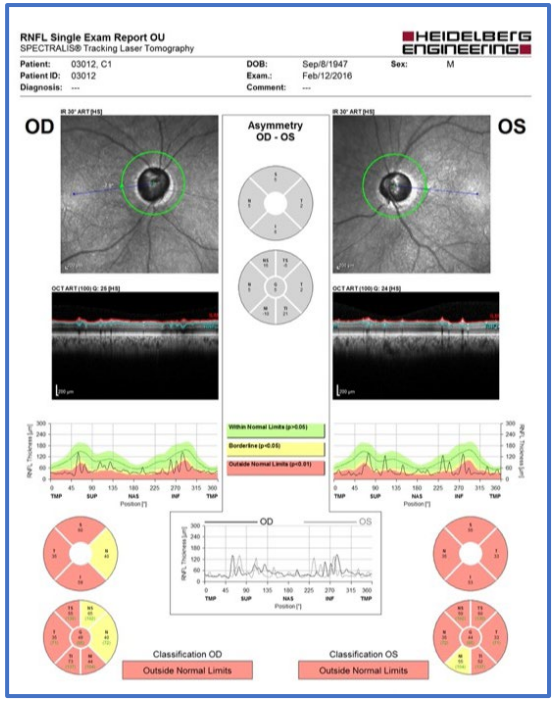


Macula Cube 512x128

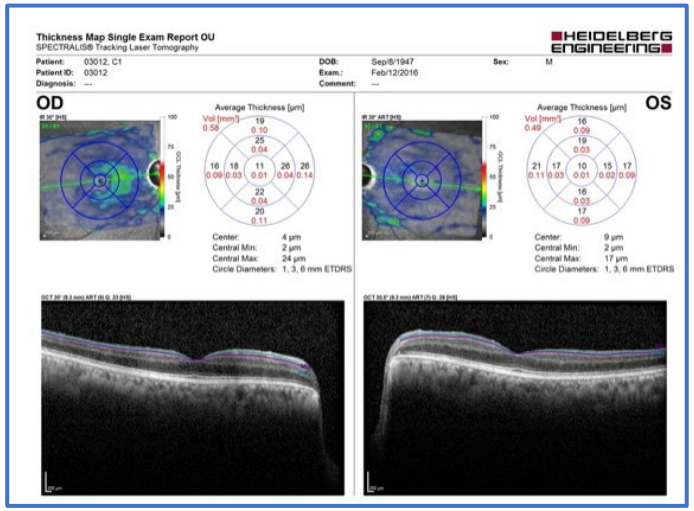


Spectralis

RNFL Circle Scan



Macula Posterior Pole Scan



OHTS 3 OCT Scan Data Received – including OCTs from clinical care during gap in OHTS (2009+)

OHTS OCT Study Data Received	Cirrus	Spectralis	Total
# of study participants	448*	215*	658
# of sites that have sent OCT scans	25	14	39
# of participants with back data received	213	93	306
Average # of back data visits received	3.7	7.9	5.8 (mean)
Maximum length of follow-up	7.5 yrs	9.6 yrs	8.4 yrs (mean)
OCT optic disc scans received (n=11,903)			
- OCT optic disc scans from OHTS 3 visit only	2,310	1,091	3,401
- OCT optic disc scans from OHTS 3 visit and back data	3,653	4,849	8,502
OCT macula scans received (n=8133)			
- OCT macula scans from OHTS 3 visit only	1,877	1,103	2,980
- Scans from OHTS 3 visit and back data	3,092	2,061	5,153

* some participants provided both Cirrus and Spectralis scans

OHTS 3 Visit Scans Were of Significantly Better Quality than OHTS 3 Clinical Scans (p<0.001)

	OHTS 3 Visit Cirrus Scans			OHTS 3 Back Clinic Visit Cirrus Scans		
	ALL	Optic Disc	Macula	ALL	ONH	Macula
n	1,642	799	843	3,882	2175	1707
% good quality	**92.1%**	**90.1%**	**93.7%**	**86.5%**	**88.1%**	**84.4%**

Objective: Compare RNFL thickness and Ganglion Cell/ Inner Plexiform Layer (GCIPL) and change over time in eyes that developed POAG and those that never developed POAG

- Disc (only) POAG
- VF POAG (with and without Disc POAG)
- Never POAG

Participants:

- No evidence of glaucoma related VF defect based on HFA and no evidence of GON based on fundus photograph assessment.
- IOP between 21 and 32 mmHg at OHTS study enrollment.
- Participants with good quality Cirrus (n= 478) optic nerve head (ONH) and macula
- Study Groups:
  - POAG by disc assessment
  - POAG by VF (with or without POAG by disc)
  - Never POAG

Clinical characteristics of Participants by POAG Type:

	Never POAG (n = 260 eyes)	Disc Only POAG (n = 126 eyes)	VF POAG (With or Without Disc) (n = 114 eyes)	p-value
Mean Age (years)	73.4 (72.5, 74.4)	73.2 (71.7, 74.6)	76.7 (75.2, 78.1)	< 0.001
Sex (% Female)	160 (61.5%)	75 (59.5%)	59 (51.8%)	0.038
Race				0.044
Black, Non-Hispanic	61 (23.5%)	35 (27.8%)	38 (33.3%)	
White, Non-Hispanic	185 (71.2%)	81 (64.3%)	69 (60.5%)	
Other	14 (5.4%)	10 (7.9%)	7 (6.1%)	
Global RNFL Thickness (um)	n = 462 eyes 84.7 (83.7, 85.7)	n = 148 76.3 (74.5, 78.1)	n = 146 67.66 (65.8, 69.5)	< 0.001
Global GCIPL Thickness (um)	n = 472 eyes 74.1 (73.4, 74.9)	n = 157 69.2 (67.7, 70.7)	n = 142 63.91 (62.4, 65.5)	< 0.001

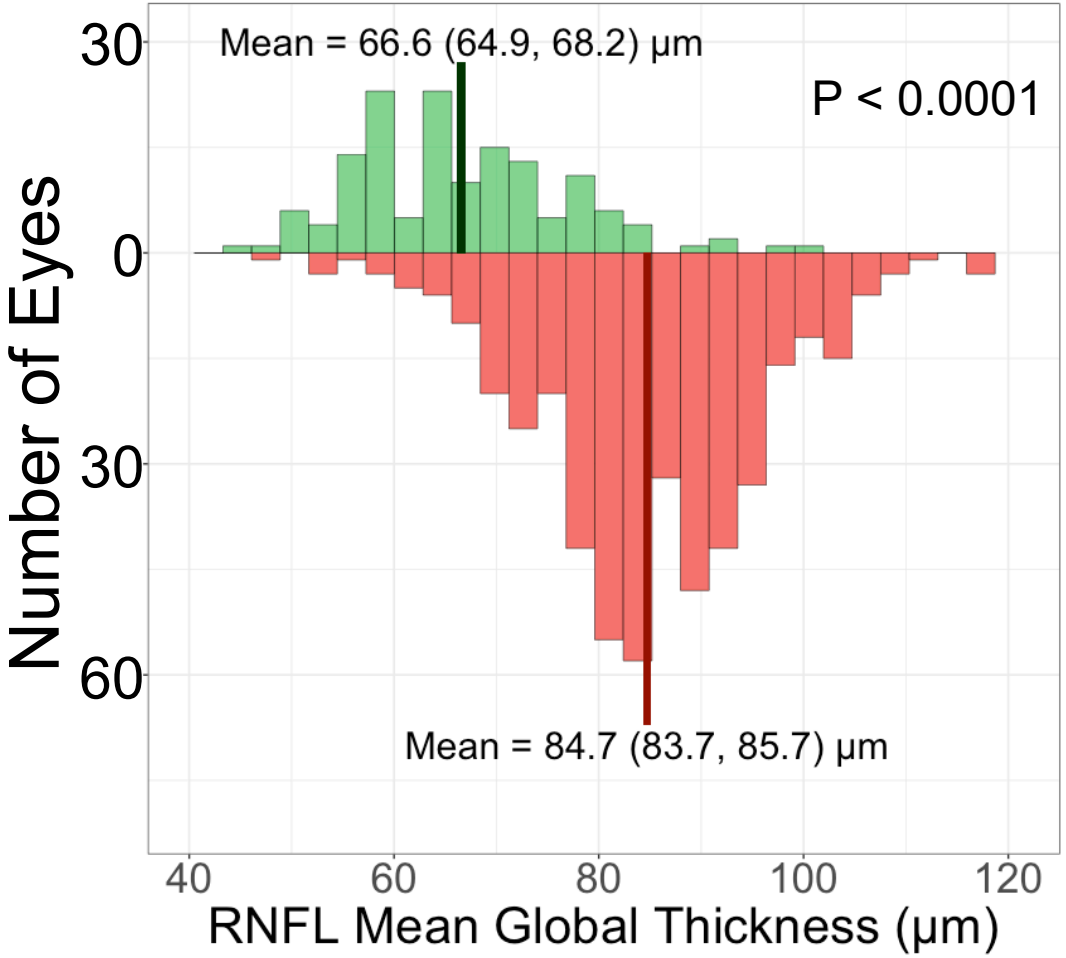
Cross-Sectional Analysis:

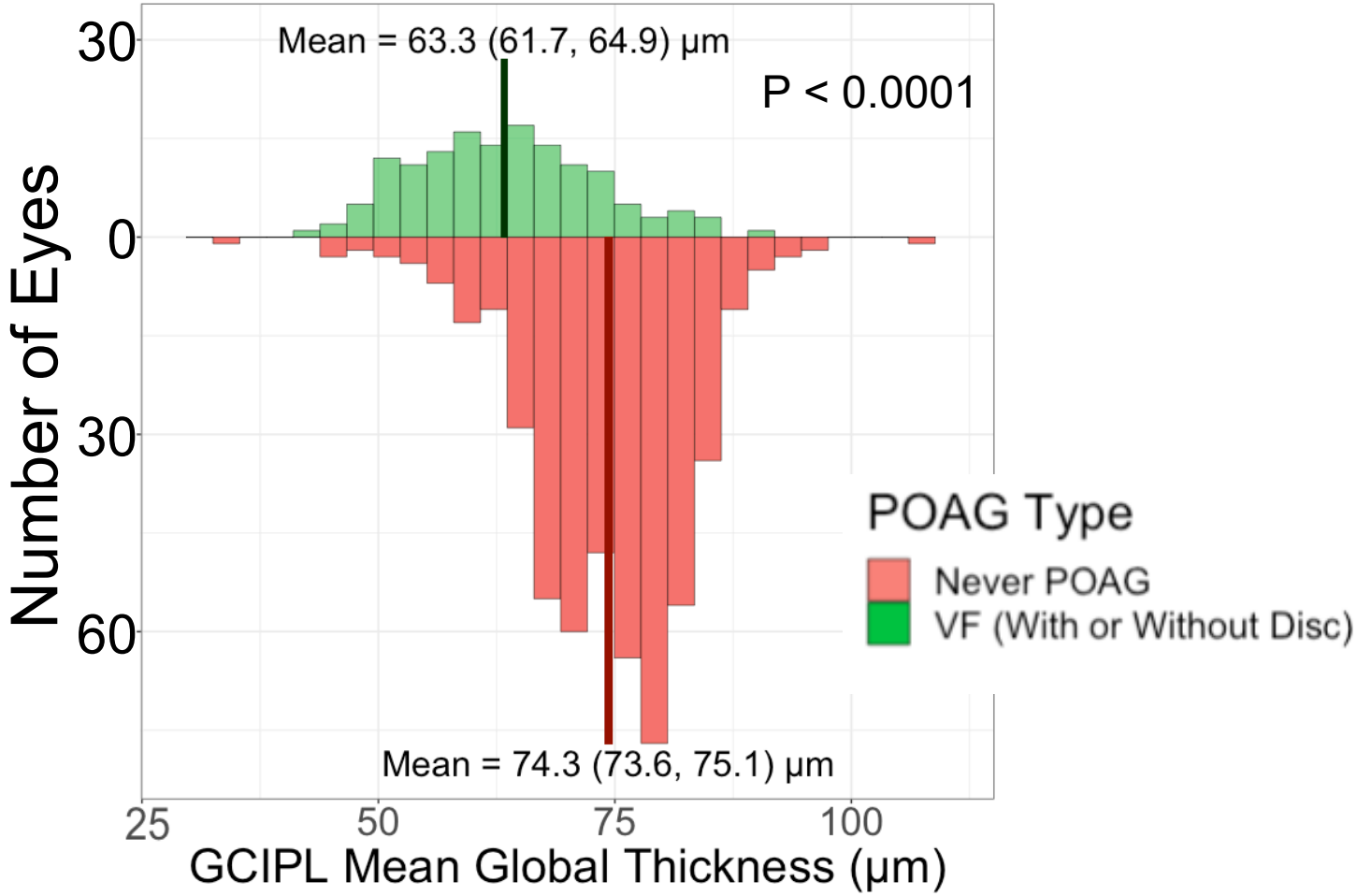
- RNFL and GCIPL were compared between Study Groups using Linear Mixed-Effects models to account for within-subject variability.
- Subject-level demographic information compared between Study Groups using Fisher's Exact Test, and T-tests.
- Eye-level clinical measurements were compared between Study Groups using Linear Mixed-Effects models to account for within-subject variability.

Study Group	# subjects* (eyes)
Never POAG	260 (493)
Disc (only) POAG	126 (165)
VF POAG (with or without Disc POAG)	114 (156)

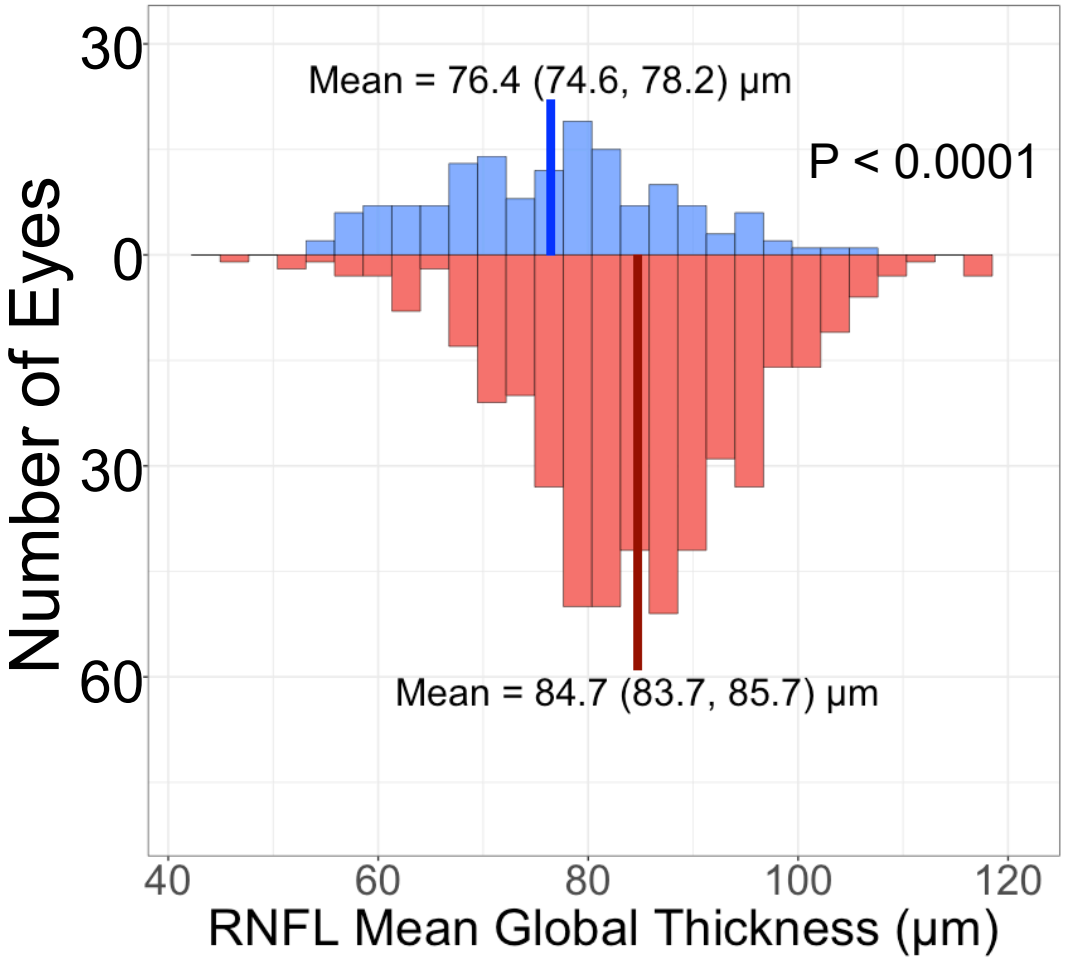
Note: 22 subjects had one eye with Disc POAG and a fellow eye with VF POAG

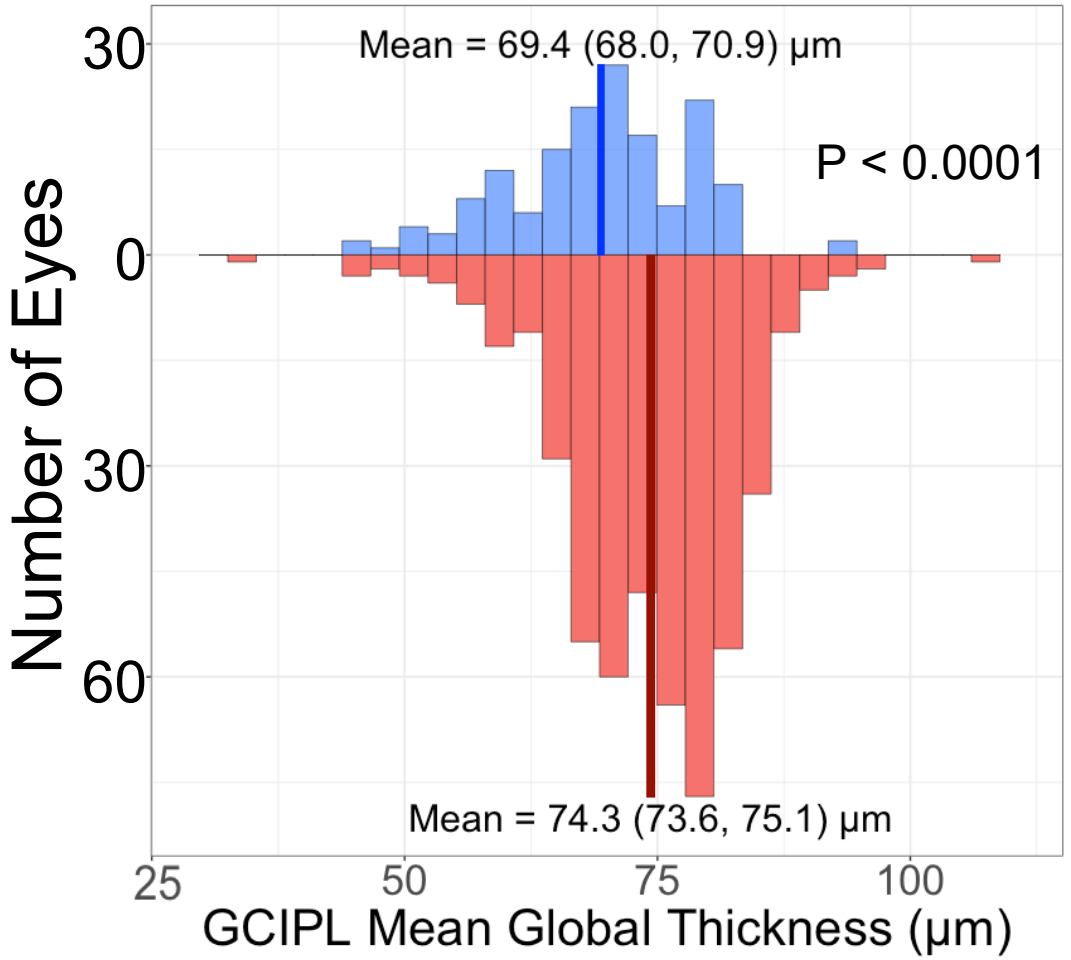
Mean (95% CI) Global RNFL and GCIPL Thickness: Significantly Thinner in VF POAG versus Never POAG Eyes





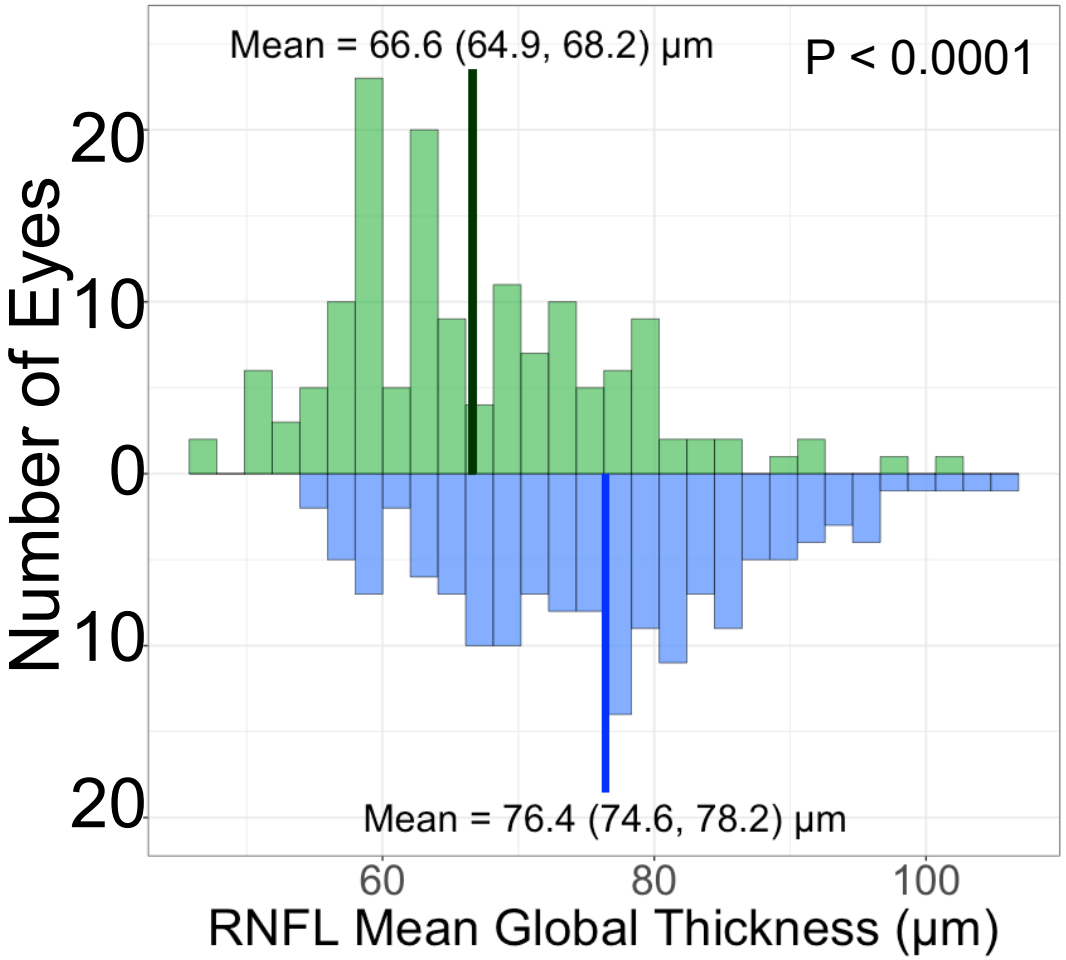
Mean (95% CI) Global RNFL and GCIPL Thickness: Significantly Thinner in Optic Disc POAG versus Never POAG Eyes

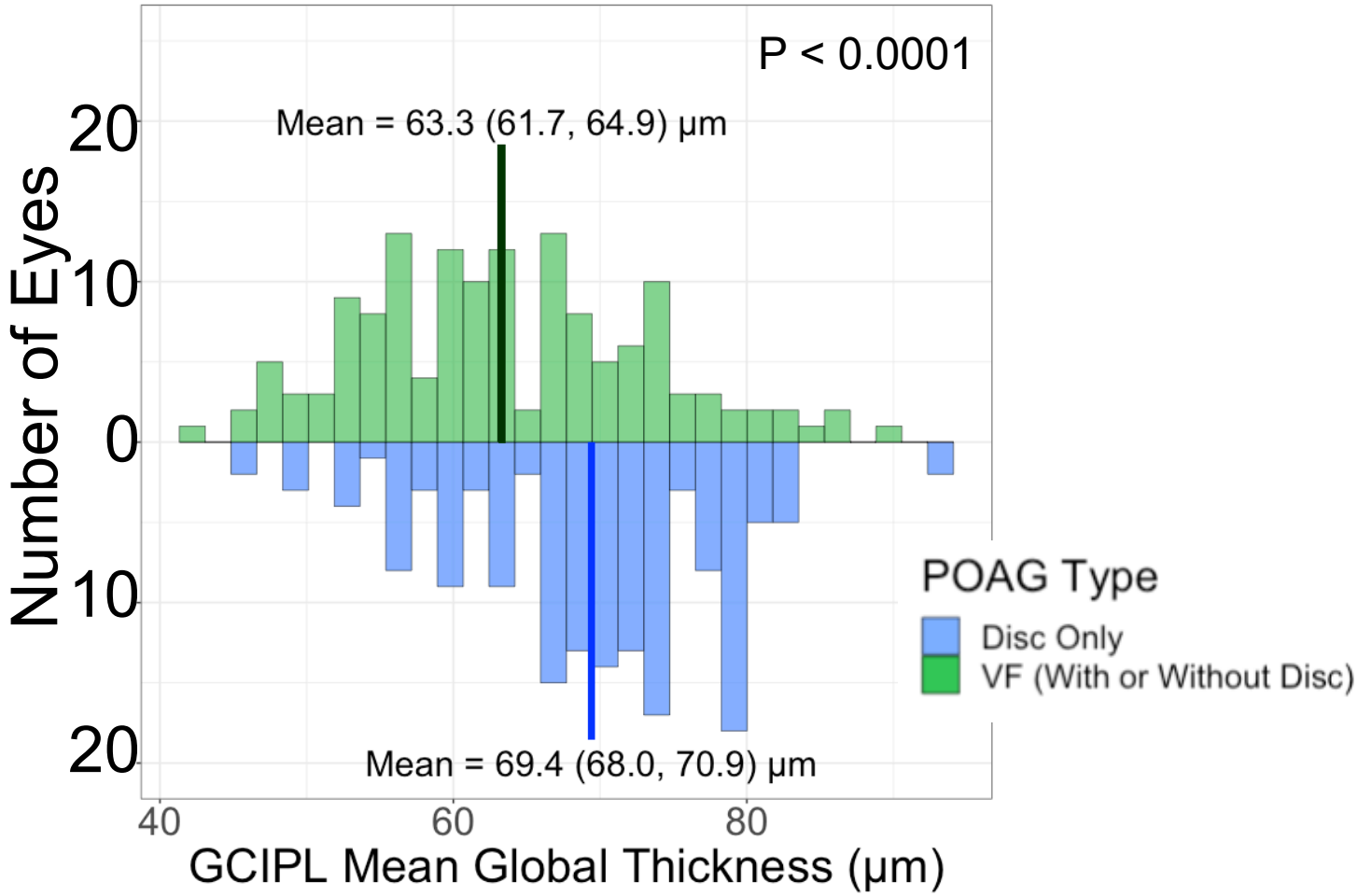




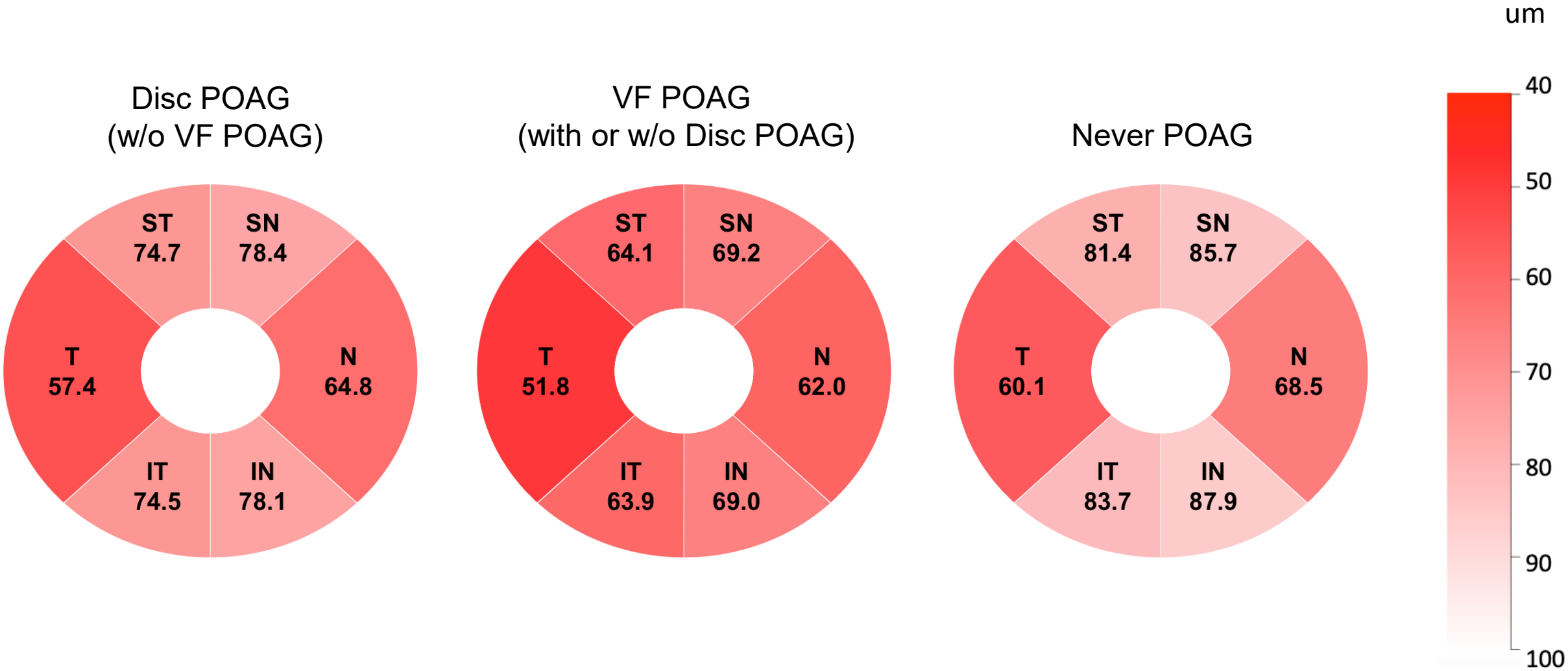
POAG Type
Disc Only
Never POAG

Mean (95% CI) Global RNFL and GCIPL Thickness: Significantly Thinner in VF POAG versus Optic Disc POAG Eyes

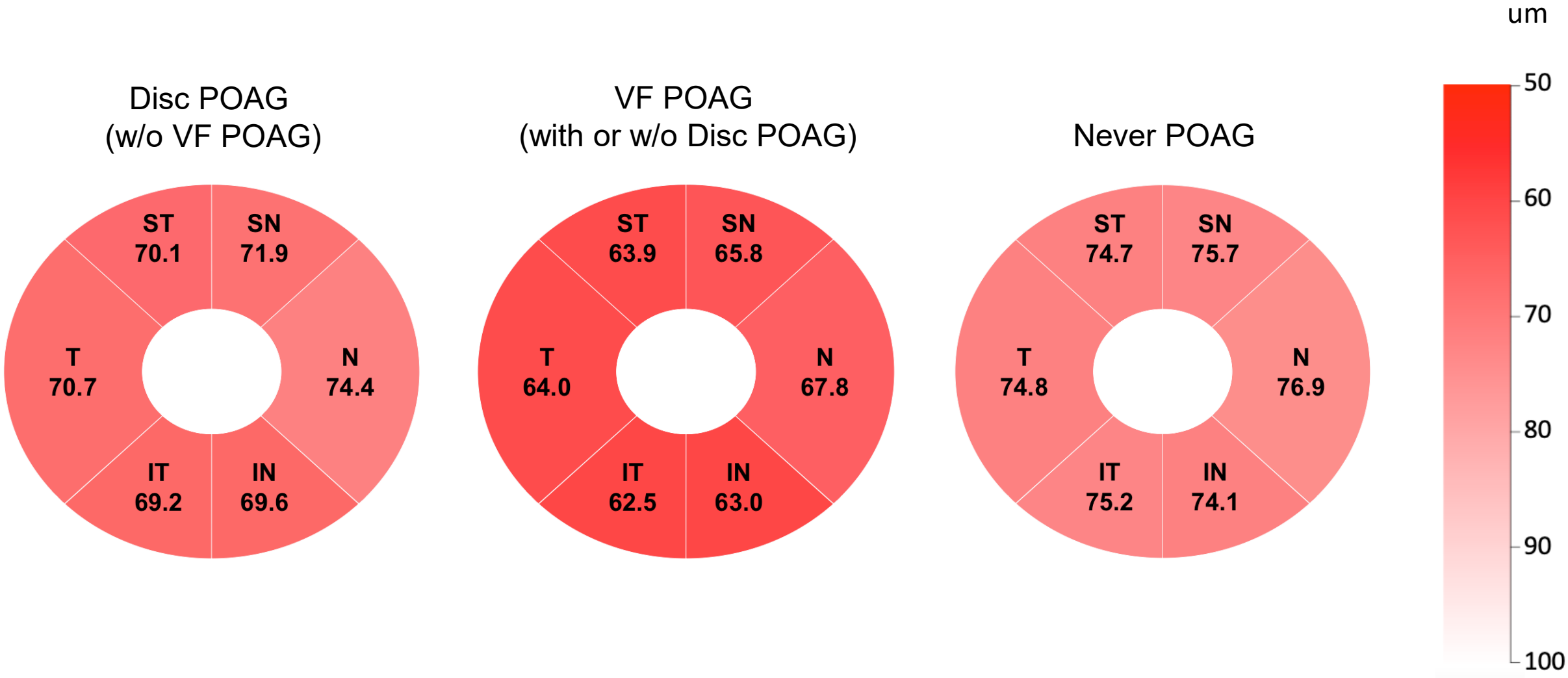




OHTS 3 OCT RNFL Thickness: Sectoral RNFL Thinnest in VF POAG Eyes in inferior temporal and superior temporal sectors



OHTS 3 OCT GCIPL Thickness:
Sectoral GCIPL Thinnest in VF POAG eyes in inferior temporal and superior temporal and inferior nasal sectors

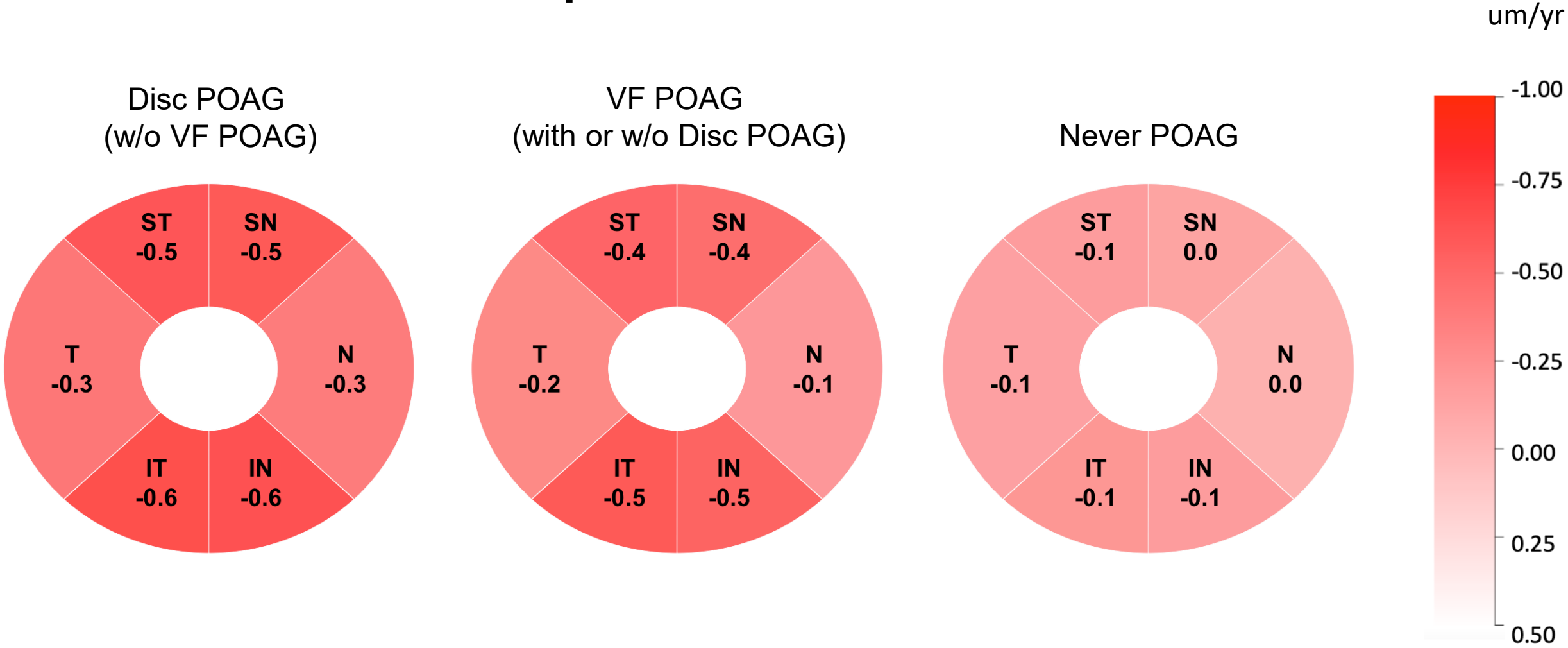


Longitudinal Analysis:

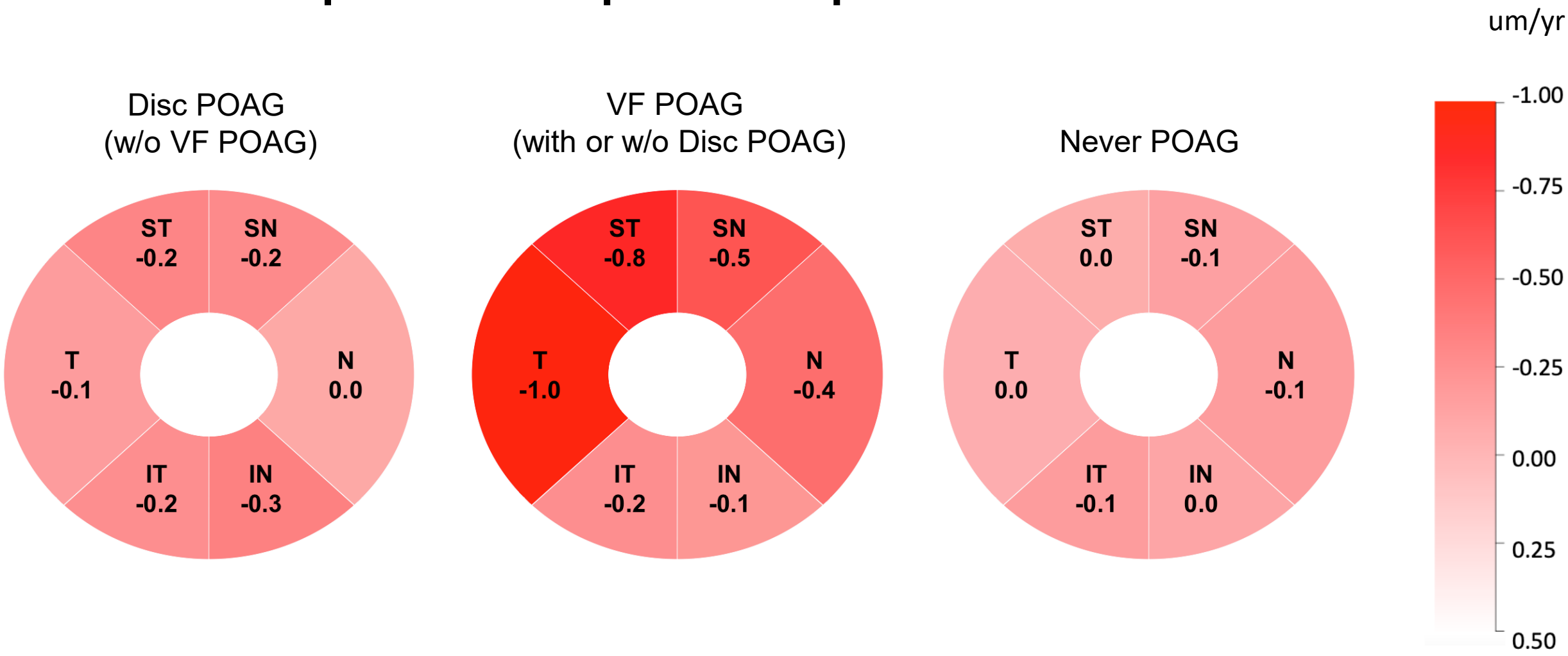
- Rate of RNFLT and GCIPLT change over time was calculated for participants with a minimum of 3 Cirrus OCT scans.
- Linear mixed-effects models were used to compare RNFLT and GCIPLT change over time between the three study groups.

Study Group	# subject (eyes) with longitudinal data	# of OCT Visits Mean (Range)	Years of OCT Follow Up Mean (Range)
Disc (only) POAG	38 (45)	7.0 (3, 28)	4.8 (0.8, 7.5)
VF POAG (with or without Disc POAG)	61 (84)	6.3 (3, 20)	3.9 (0.6, 7.5)
Never POAG	99 (173)	4.9 (3, 17)	3.9 (0.8, 7.5)

Sectoral RNFL Slopes:
Similar rate of RNFL thinning in Disc POAG and VF POAG; fastest in inferior and superior sectors

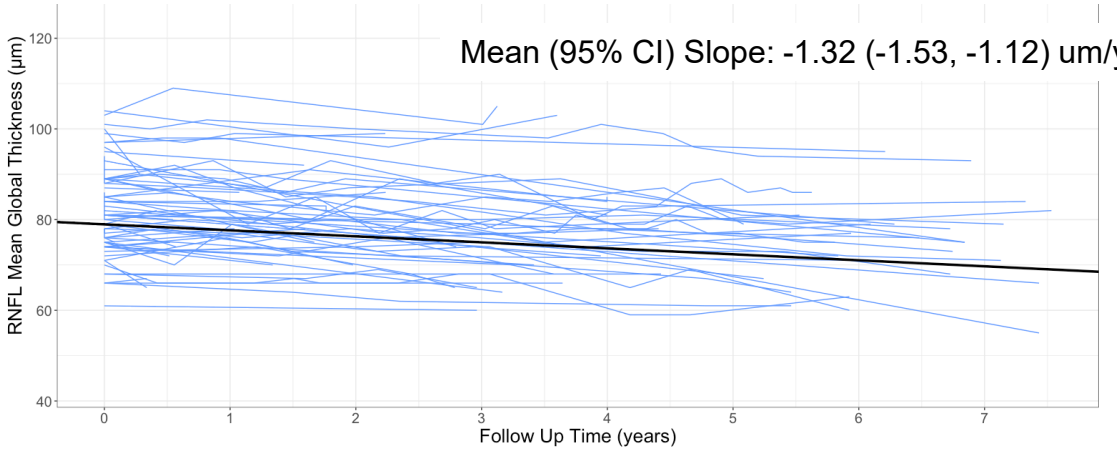


Sectoral GCIPL Slopes:
GCIPL thinning is faster in VF POAG than in Disc POAG;
Fastest in temporal and superior temporal sectors

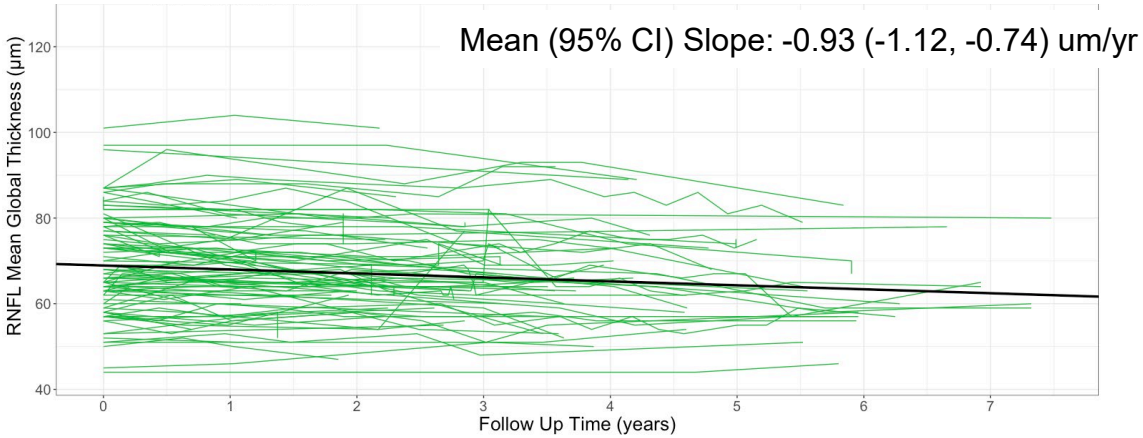


Cirrus OCT Global RNFL Slope:
POAG Eyes Significantly Faster than Never POAG Eyes (p < 0.001)
Disc POAG Significantly Faster than VF POAG Eyes (p = 0.007)

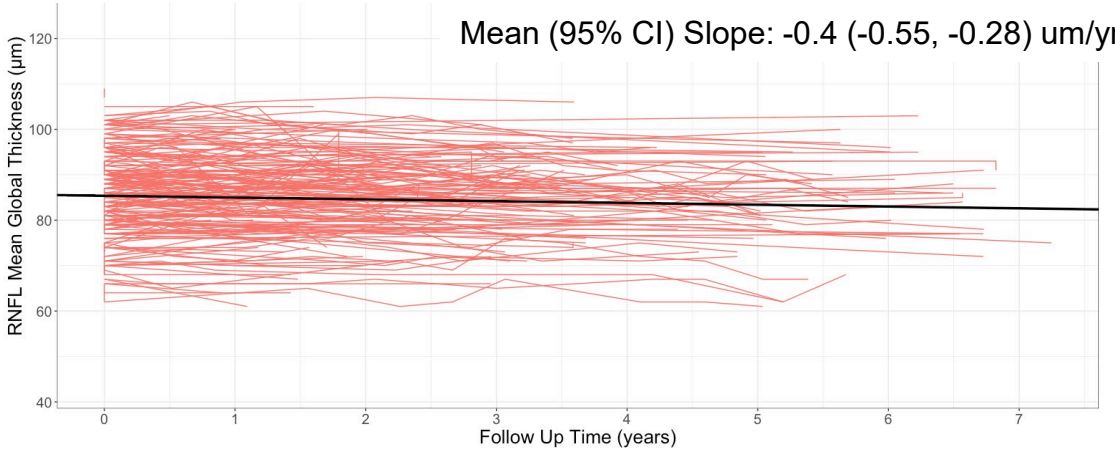
Disc POAG (n=127 participants, 160 eyes)



VF POAG (n=120 participants, 165 eyes)

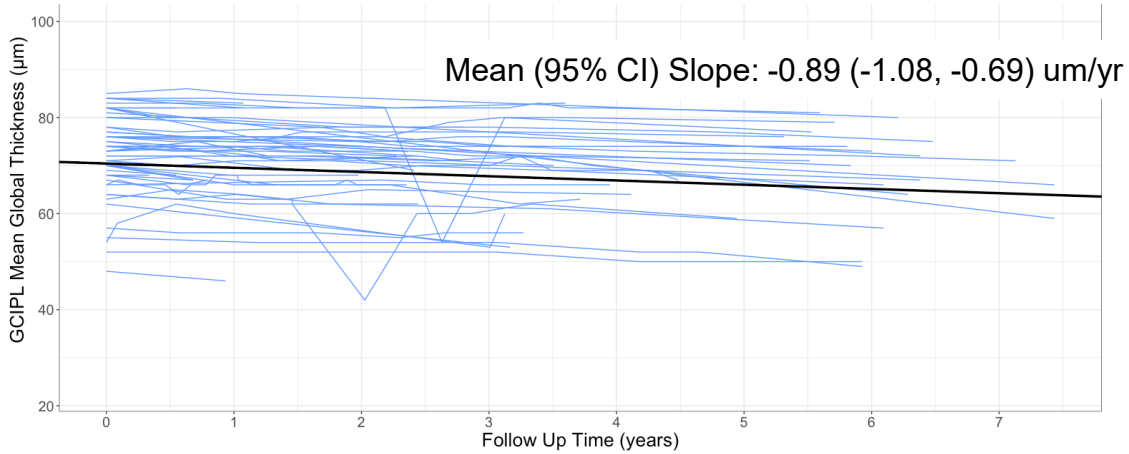


Never POAG (n=351 participants, 573 eyes)



Cirrus OCT Global GCIPL Slope:
POAG Eyes Significantly Faster than Never POAG Eyes (p = 0.006)
Disc POAG Not Significantly Faster than VF POAG (p = 0.543)

Disc POAG (n=127 participants, 160 eyes)



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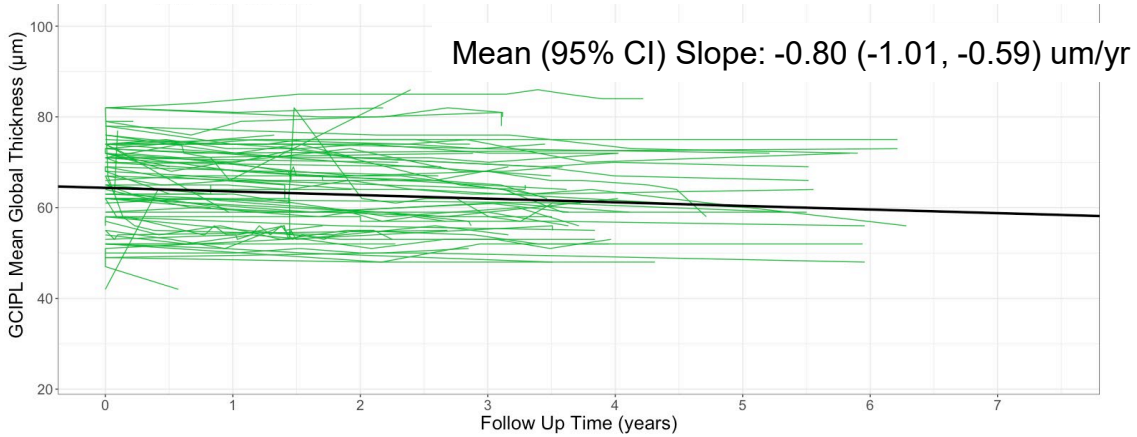

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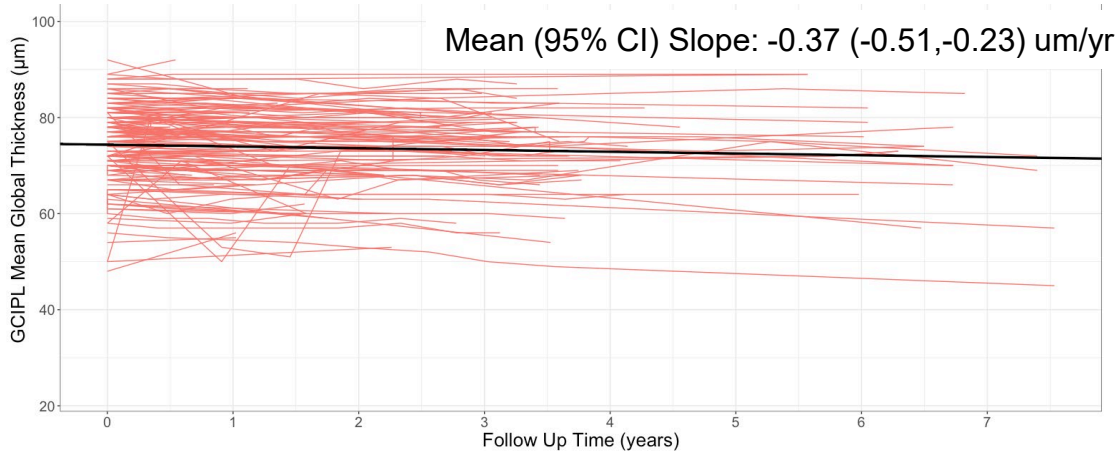


OHTS Never POAG rates of change are similar to other estimates of age-related RNFL and GCIPL thinning

	N (eyes)	Median Age (yrs)	Median Follow-up (yrs)	RNFL	GCIPL
				um /yr	um /yr
OHTS Never POAG	**260**	**51**	**3.4**	**-0.40**	**-0.37**
Leung (2013)	72	58	3.8	**−0.52**	**-0.32**
Hammel (2017)	56	47	1.7	**-0.48**	**-0.14**
Vianna (2015)	37	65	4.5	**-0.44**	**-**
Beijing Eye Study				**-0.21**	

Strengths and Limitations

Strengths:

- Large diverse sample
- Standardized protocol
- Standardized endpoint determination with date of POAG
- Longitudinal OCT scans obtained through one OHTS 3 visit

Limitations:

- Date of POAG for OHTS 3 not precisely determined due to gap in testing
- Variable number of tests and follow up time after POAG assessment by Disc and/or VF
- missing data on participants (particularly between the OHTS 2 and the OHTS 3)
- Lack of OCT measurements until the OHTS 3

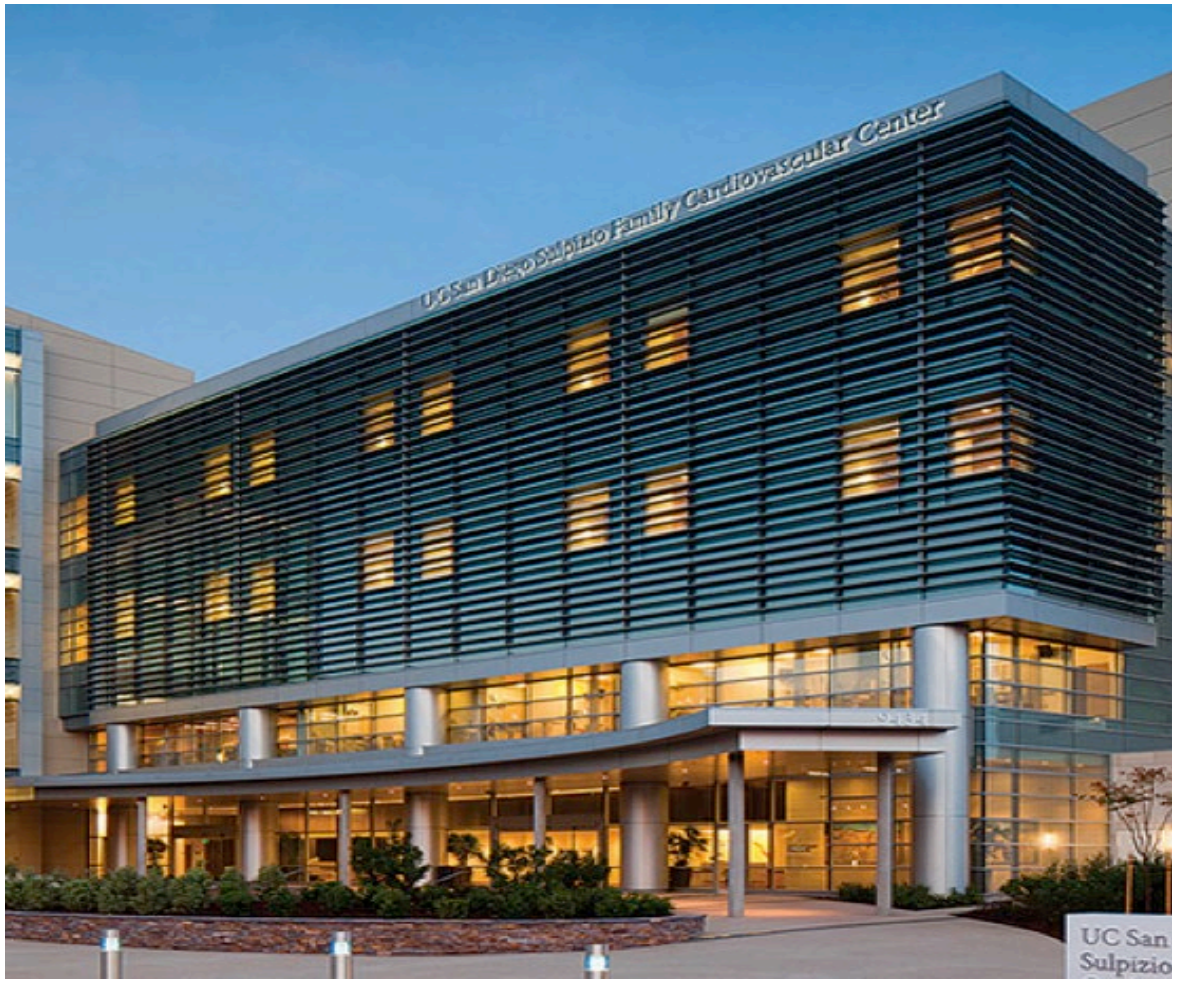
Kass MA, et al. Assessment of Cumulative Incidence and Severity of Primary Open-Angle Glaucoma Among Participants in the Ocular Hypertension Treatment Study After 20 Years of Follow-up. JAMA Ophthalmol. 2021

Conclusion

- Among eyes that developed POAG:
  - The RNFL and GCIPL was thinner than eyes that never developed POAG
  - The rate of RNFL and GCIPL thinning was faster than in eyes that never developed POAG according to longitudinal back data

- Optic Disc Only versus VF POAG (With or Without Disc):
  - The RNFL and GCIPL was thinner in eyes that developed VF POAG than eyes with Optic Disc POAG Only
  - Longitudinal analysis suggests eyes with Optic Disc POAG have a faster rate of thinning in RNFL than eyes with VF POAG

Thank you



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The Viterbi Family
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