Aspects of the Etiology of Myopic Axial Elongation with Respect to the Lamina Cribrosa and Cornea in Glaucomatous Eyes

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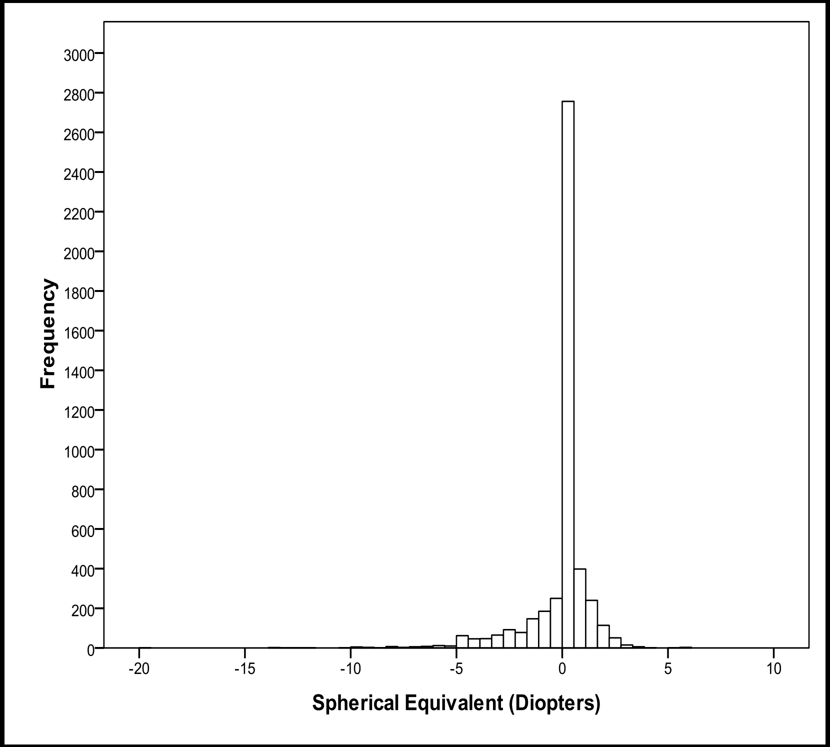
Financial Disclosures

- Patent holder with Biocompatibles UK Ltd. (Franham, Surrey, UK) (Title: Treatment of eye diseases using encapsulated cells encoding and secreting neuroprotective factor and / or anti-angiogenic factor; Patent number: 20120263794); and
- Patent application: Agents for use in the therapeutic or prophylactic treatment of myopia or hyperopia; European Patent Number: 3 070 101. (Amphiregulin and EGF)

Central India Eye and Medical Study (2006-2008)*

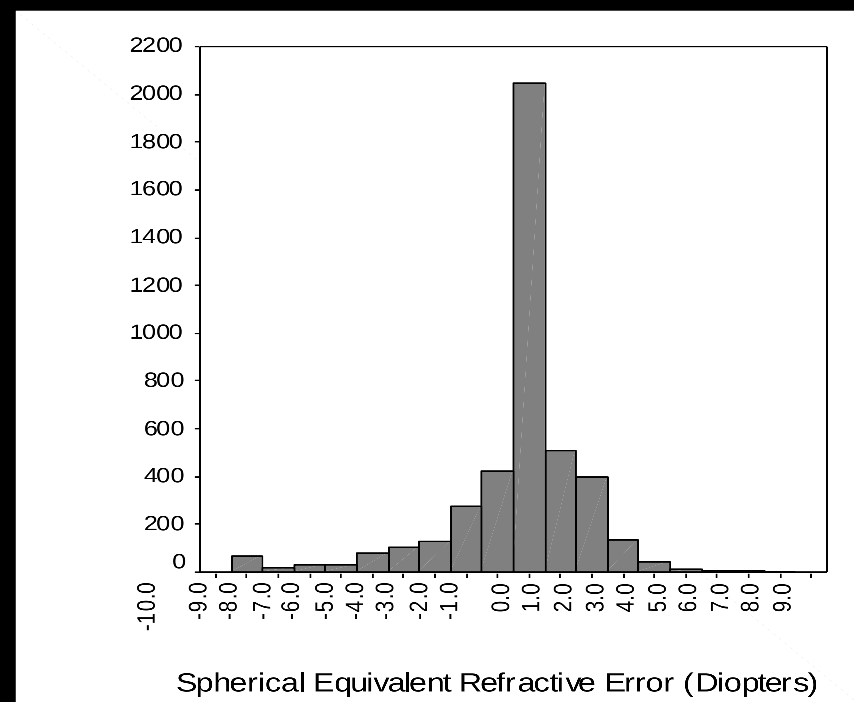
- Age: 49.5 ± 13.4 years (range: 30 - 100 years)
- Refractive error: –0.20 ± 1.51 diopters)
- Hyperopia (>0.5 D): 18.0 ± 0.6%
- **Myopia (>–1.0 D): 13.0 ± 0.5%**
- Myopia (> -6.0 D): 0.9 ± 1.4%
- **High myopia (>–8 D): 0.4 ± 0.1%**



Nangia V, Jonas JB, Sinha A, Matin A, Kulkarni M.Refractive error in Central India.The Central India Eye and Medical Study. Ophthalmology 2010;117:693-9.

Beijing Eye Study 2001: Refractive Error

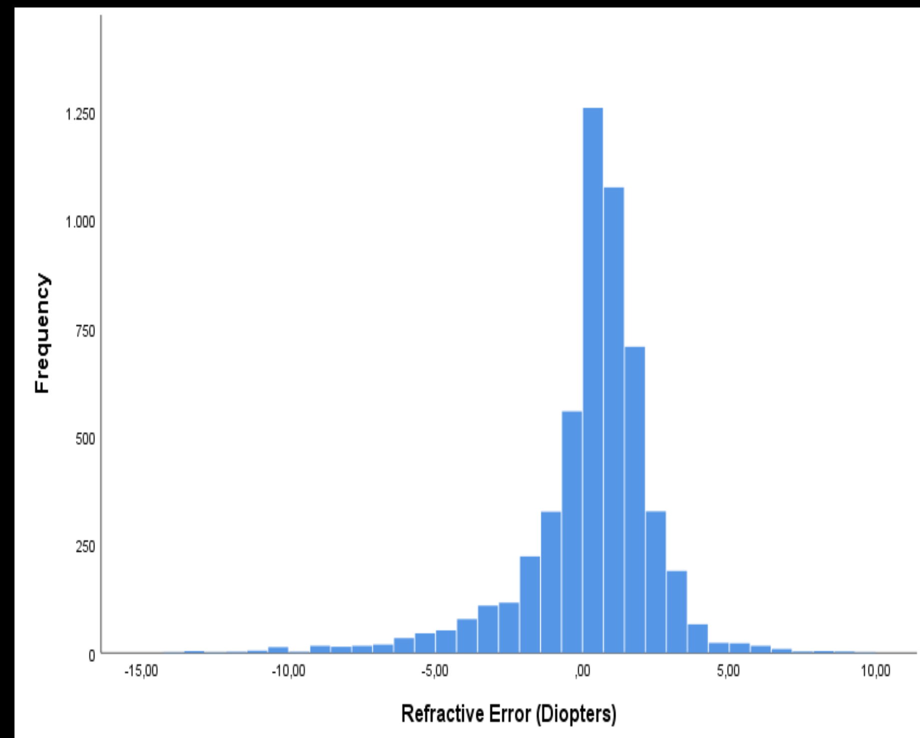
- Age: 55.9 ± 10.3 years (range: 40 – 90 years).
- Refractive error: -0.33 ± 2.07 dpt (-18.75 to +7.50 dpt)
- Myopia/hyperopia >0.50 dpt: - 22.9% myop; - 20.0% hyperop
- **Myopia > -1.0 dpt: 16.9%**
- Myopia > -6.0 dpt: 2.6%
- **Myopia > -8.0 dpt: 1.5%**



Xu L, Li J, Cui T, Hu A, Fan G, Zhang R, Yang H, Sun B, Jonas JB. Refractive error in urban and rural adult Chinese in Beijing. Ophthalmology 2005;112:1676-1683

Ural Eye and Medical Study (2015-2017)

- Age: 58.4 ± 10.3 years (range: 40 – 94 years)
- Refractive error: +0.26 ± 2.35 dpt (median: 0.26 dpt; range: -23.25 to +10.0 dpt)
- Hyperopia >0.50 dpt: 49.7%;
- Myopia >-0.50 dpt: 21.7%
- Myopia > -1.0 dpt: 16.9%
- Myopia > -6.0 dpt: 2.2%
- Myopia > -8.0 dpt: 1.1%

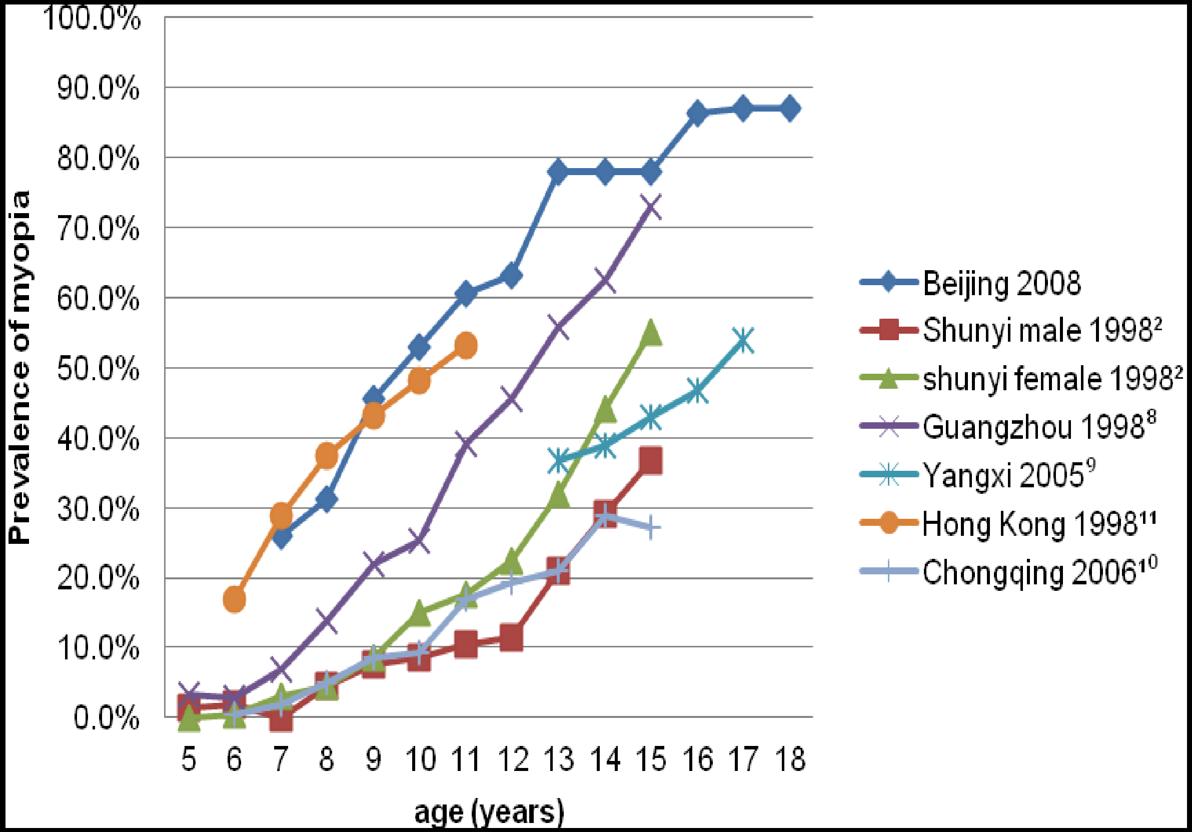


Bikbov MM, Kazakbaeva GM, Gilmanshin TR, Zainullin RM, Arslangareeva II, Salavatova VF, Bikbova GM, Panda-Jonas S, Nikitin NA, Zaynetdinov AF, Nuriev IF, Khikmatullin RI, Uzianbaeva YV, Yakupova DF, Aminev SK, Jonas JB. Axial length and its associations in a Russian population: The Ural Eye and Medical Study. PLoS One 2019;14:e0211186.

Beijing Pediatric Eye Study

Myopia associated with:

- higher age
- female gender
- key school type
- higher family income
- parental myopia
- dim reading illumination
- longer daily studying duration
- shorter duration of TV watching (or computer)



You QS, Wu LJ, Duan JL, Luo YX, Liu LJ, Li X, Gao Q, Wang W, Xu L, Jonas JB, Guo XH. Factors associated with myopia in school children in China. The Beijing Childhood Eye Study. PLoS One 2012;7:e52668

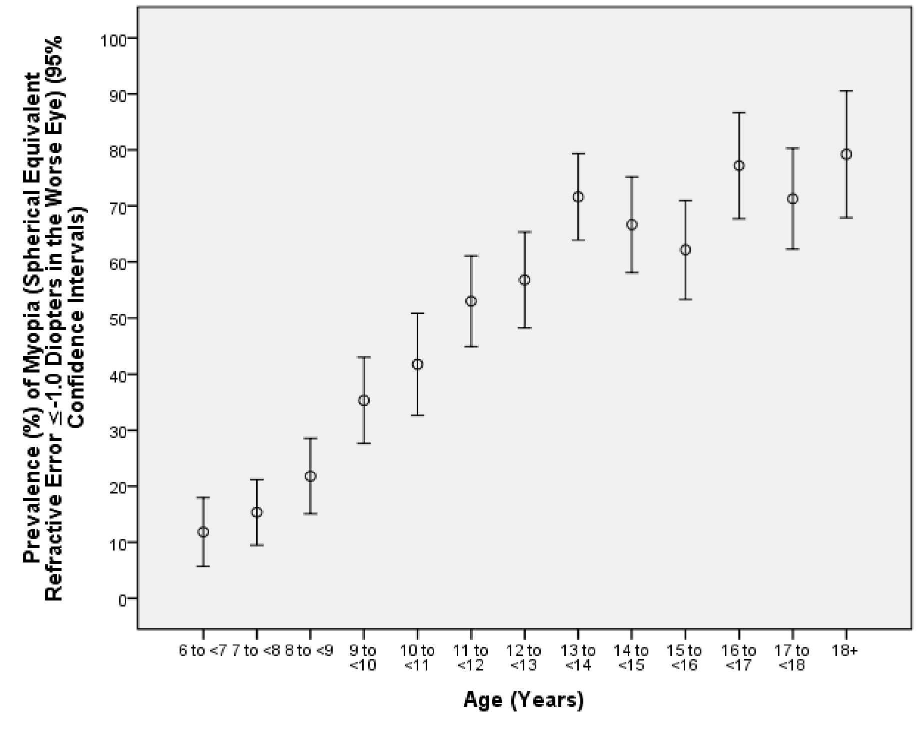
The Gobi Desert Children Eye Study (2013)*

- School-based observational cross-sectional study
- Cylcoplegic refractometry
- Out of 1911 eligible children, 1565 (81.9%) children with a mean age of 11.9±3.5 years (range:6-21 years) participated.
- Refractive error (worse eye): -1.38 ± 2.04 D (median-0.88D; range: -13.00D to +6.50D).

Guo K, Yang DY, Wang Y, Yang XR, Jing XX, Guo YY, Zhu D, You QS, Tao Y, Jonas JB. Prevalence of Myopia in School Children in Ejina. The Gobi Desert Children Eye Study. Invest Ophthalmol Vis Sci. 2015; 56:1769-1774

The Gobi Desert Children Eye Study (2013)*

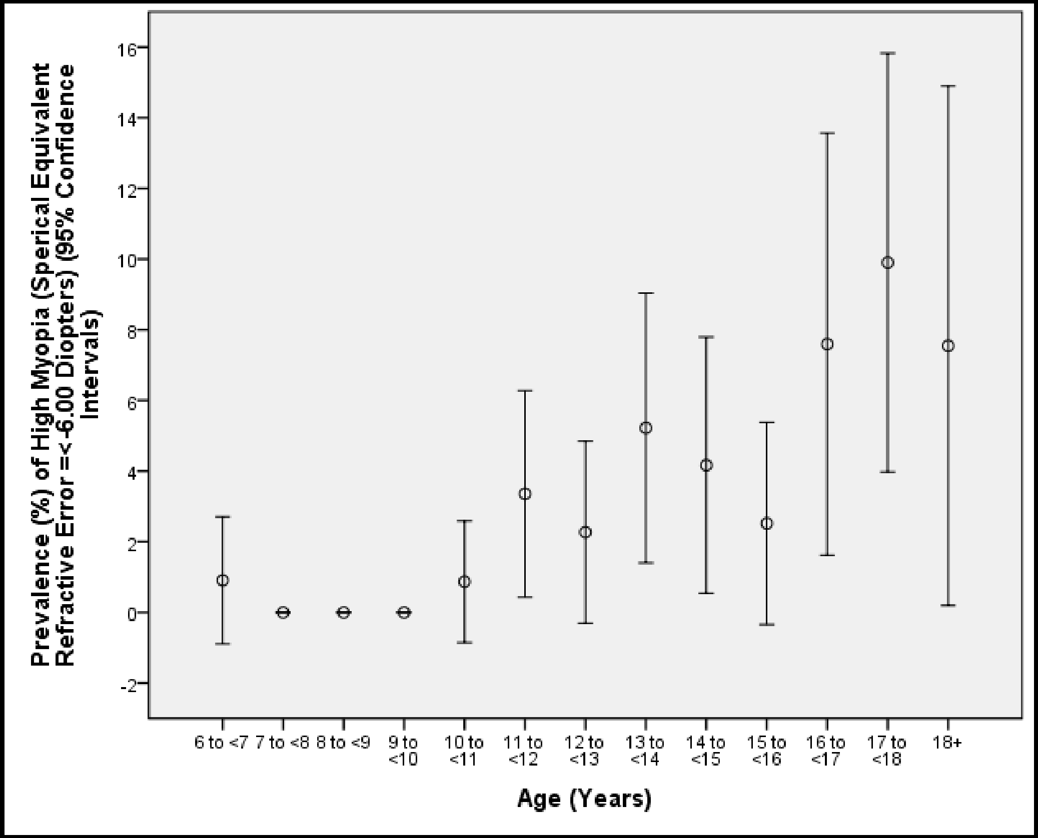
- The prevalence of myopia, defined as refractive errors (spherical equivalent) of ≤-0.50D, ≤-1.00D, and ≤-6.00D in the worse eye, was 60.0±1.2%, 48.0±1.3%, and 2.9±0.4%, respectively.



Guo K, Yang DY, Wang Y, Yang XR, Jing XX, Guo YY, Zhu D, You QS, Tao Y, Jonas JB. Prevalence of Myopia in School Children in Ejina. The Gobi Desert Children Eye Study. Invest Ophthalmol Vis Sci. 2015; 56:1769-1774

The Gobi Desert Children Eye Study (2013)*

- The prevalence of high myopia (≤-6.00D) was 2.9±0.4% in the whole study population, and it was 9.9±3.0% in 17-year-olds.



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Meta-Analysis

Recent meta-analysis: In 2000:

- - 1406 million people with myopia (22.9% of the world population; 95% CI: 932-1932 million [15.2%-31.5%]),
- 163 million people with high myopia (2.7% of the world population; 95% CI, 86-387 million [1.4%-6.3%]) in 2000.

Predicted for 2050:

- 4758 million people with myopia (49.8% of the world population; 3620-6056 million [95% CI, 43.4%-55.7%]),
- 938 million people with high myopia (9.8% of the world population; 479-2104 million [95% CI, 5.7%-19.4%]).

Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, Wong TY, Naduvilath TJ, Resnikoff S. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016;123:1036-42.

Beijing Eye Study 2001: Causes for Visual Impairment and Blindness

Visual Impairment (better eye: < 20/60 and >= 20/400)

	n	%
• Cataract	18	36.7
• Myopic maculopathy	16	32.7
• Glaucoma	7	14.3 (4xPOAG; 3x PACG)
• Corneal Opacity	3	6.1
• Optic nerve atrophy	1	2.0
• Age-related mac. Deg.	1	2.0
• Macular hole	1	2.0
• Central serous ret.pathy	1	2.0
• Undefined	1	2.0

Xu L, Wang Y, Li Y, Jing Li, Wang Y, Cui T, Li J, Jonas JB. Causes of blindness and visual impairment in an urban and rural area in Beijing: the Beijing Eye Study. Ophthalmology 2006;113:1141.e1-3

High-School Students in Beijing (2013)*

Higher prevalence of myopia was associated (multiple logistic regression analysis) with

- Female sex
- Attending key schools (OR=1.48; 95%CI:1.24,1.77)
- Higher socioeconomic background of the parents (family income, level of education
- Parental myopia
- Urban region of habitation
- More time spent indoors versus outdoors

You QS, Wu LJ, Duan JL, Luo YX, Liu LJ, Li X, Gao Q, Wang W, Xu L, Jonas JB, Guo XH. Factors associated with myopia in school children in China. The Beijing Childhood Eye Study. PLoS One 2012;7:e52668

Wu LJ, You QS, Duan JL, Luo YX, Liu LJ, Li X, Gao Q, Zhu HP, He Y, Xu L, Jonas JB, Wang W, Guo XH. Prevalence and associated factors of myopia in high-school students in Beijing. PLoS One. 2015;10:e0120764.

Literature: Outdoors Activity and Myopia

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- Mutti DO, Mitchell GL, Moeschberger ML, et al. Parental myopia, near work, school achievement, and children's refractive error. Invest Ophthalmol Vis Sci 2002;43:3633-40.
- Low W, Dirani M, Gazzard G, et al. Family history, near work, outdoor activity, and myopia in Singapore Chinese preschool children. Br J Ophthalmol 2010;94:1012-6.
- Saw SM, Wu HM, Seet B, et al. Academic achievement, close up work parameters, and myopia in Singapore military conscripts. Br J Ophthalmol 2001;85:855-60.
- Lu B, Congdon N, Liu X, et al. Associations between near work, outdoor activity, and myopia among adolescent students in rural China: the Xichang Pediatric Refractive Error Study report no. 2. Arch Ophthalmol 2009;127:769-75.
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- Sherwin JC, Hewitt AW, Coroneo MT, et al. The association between time spent outdoors and myopia using a novel biomarker of outdoor light exposure. Invest Ophthalmol Vis Sci 2012:53:4363-70.
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- Saw SM, Shankar A, Tan SB, et al. A cohort study of incident myopia in Singaporean children. Invest Ophthalmol Vis Sci 2006;47:1839-44
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- Parssinen O, Lyyar AL. Myopia and myopic progression among schoolchildren: a three-year follow-up study. Invest Ophthalmol Vis Sci 1993;34:2794-802.
- Saw SM, Nieto FJ, Katz J, et al. Factors related to the progression of myopia in Singaporean children. Optom Vis Sci 2000:77:549-54.
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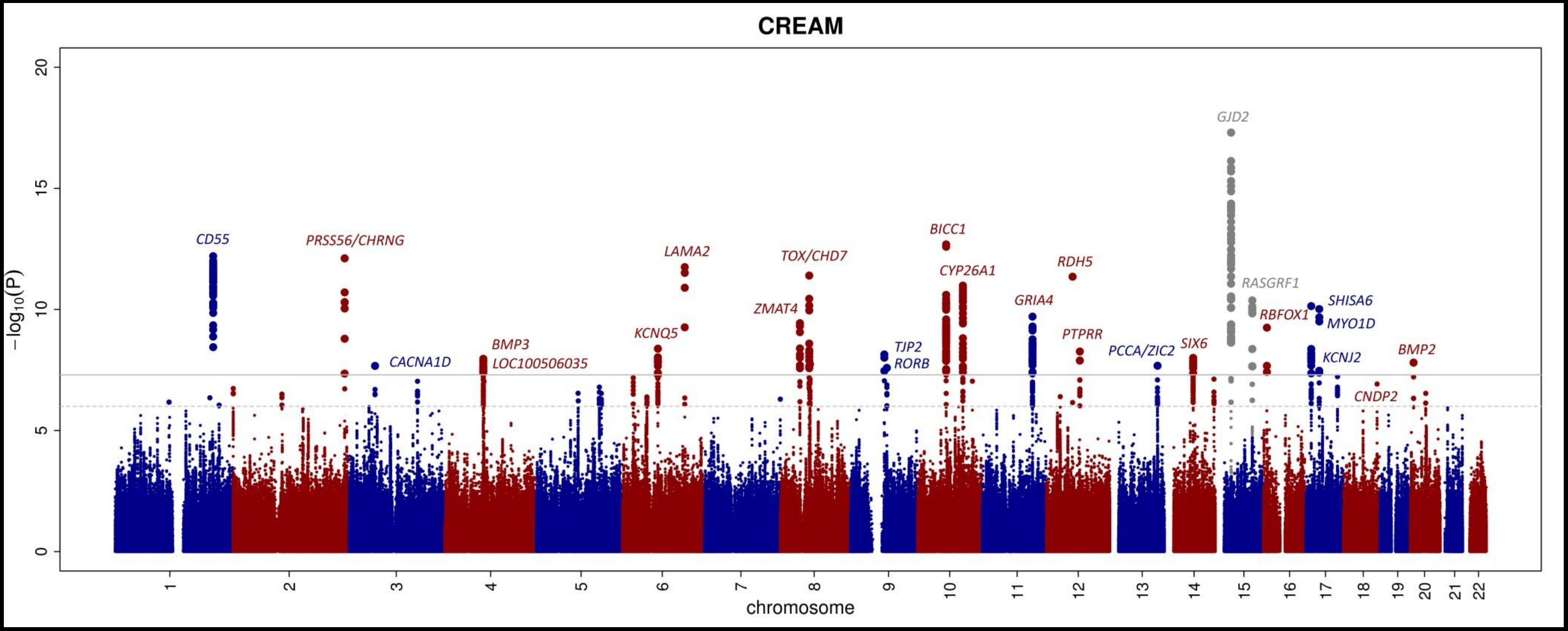
Genetic Aspects in Myopia



The genetic variants explained 3.4% of the phenotypic variation in refractive error in the Rotterdam Study.

Verhoeven VJ, et al. Genome-wide meta-analyses of multiancestry cohorts identify multiple new susceptibility loci for refractive error and myopia. Nat Genet. 2013;45(3):314-8.

Beijing Eye Study, Singapore Malay Eye Study, Central India Eye and Medical Study, Kailuan Study: Associated factors of AMD and diabetic retinopathy

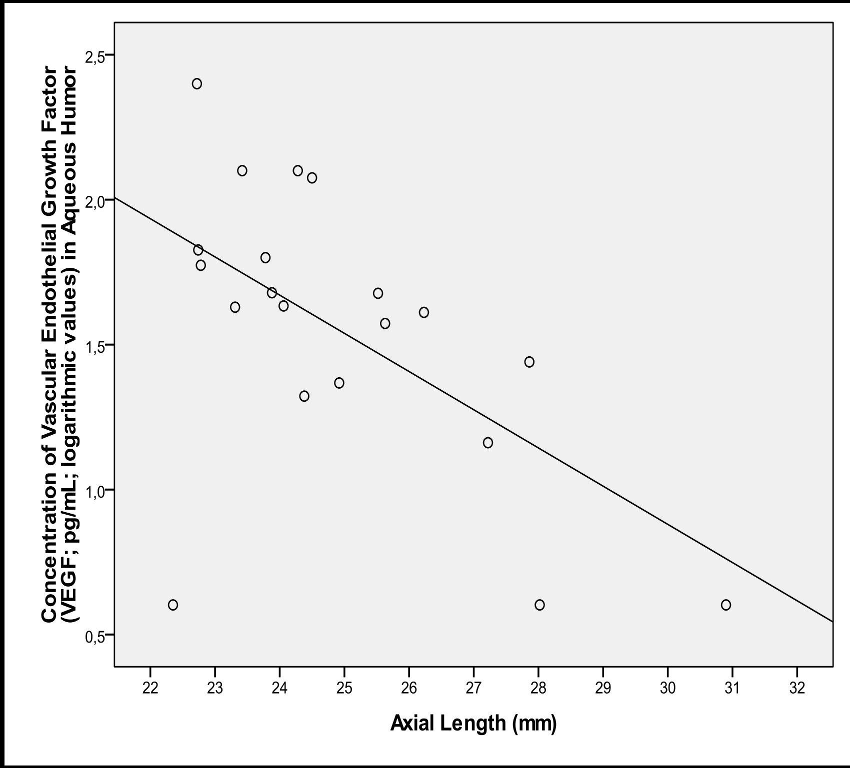
- In binary logistic regression analysis (BES), AMD (early stage) was associated with:

• Age	(P<0.001; 95% CI: 1.04; 1.08)
• **Hyperopia**	**(P=0.008; 95% CI: 1.04; 1.28)**
• Rural region	(P<0.001; 95% CI: 0.17; 0.49)
• Low level of education	(P=0.01; 95%CI: 1.07; 1.65)

In a similar manner, longer axial length was associated with a lower prevalence of diabetic retinopathy

Xu L, Wang S, Li Y, Jonas JB. Retinal vascular abnormalities and prevalence of age-related macular degeneration in adult Chinese. The Beijing Eye Study. Am J Ophthalmol 2006; 113:1752-1757.
Lavanya R, Kawasaki R, Tay WT, et al. Hyperopic refractive error and shorter axial length are associated with age related macular degeneration: The Singapore Malay Eye Study. Invest Ophthalmol Vis Sci. 2010;51:6247-52.
Wang Q, Wang YX, Wu SL, Chen SH, Yan YN, Yang MC, Yang JY, Zhou WJ, Chan SY, Zhang XH, Yang X, Lei YH, Qin SQ, Chen MX, Jonas JB, Wei WB. Ocular axial length and diabetic retinopathy: The Kailuan Eye Study. Invest Ophthalmol Vis Sci. 2019 Aug 1;60(10):3689-3695

Association between longer axial length (and myopic refractive error) and decreased intraocular concentration of VEGF in normal eyes*



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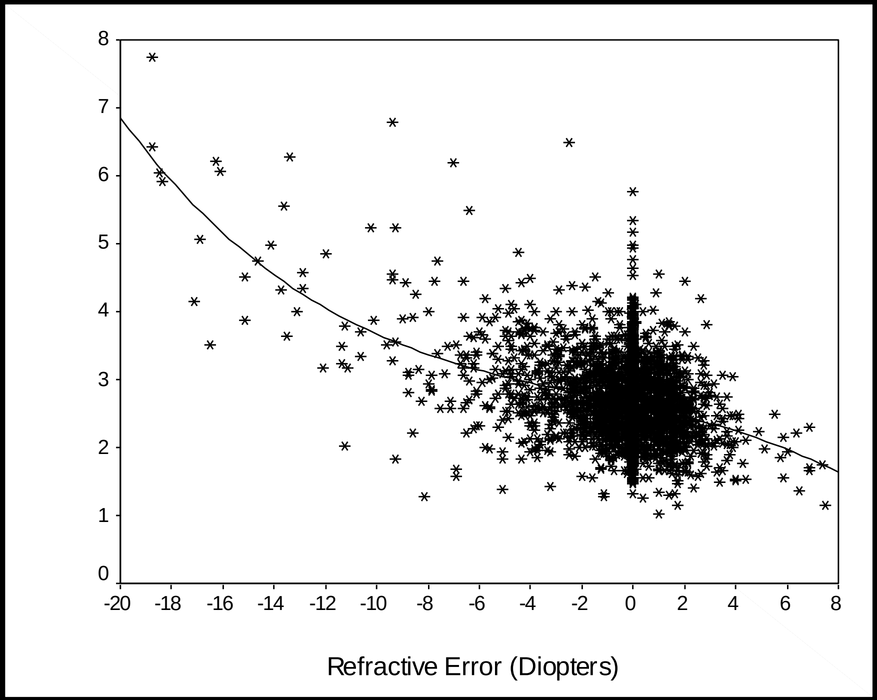
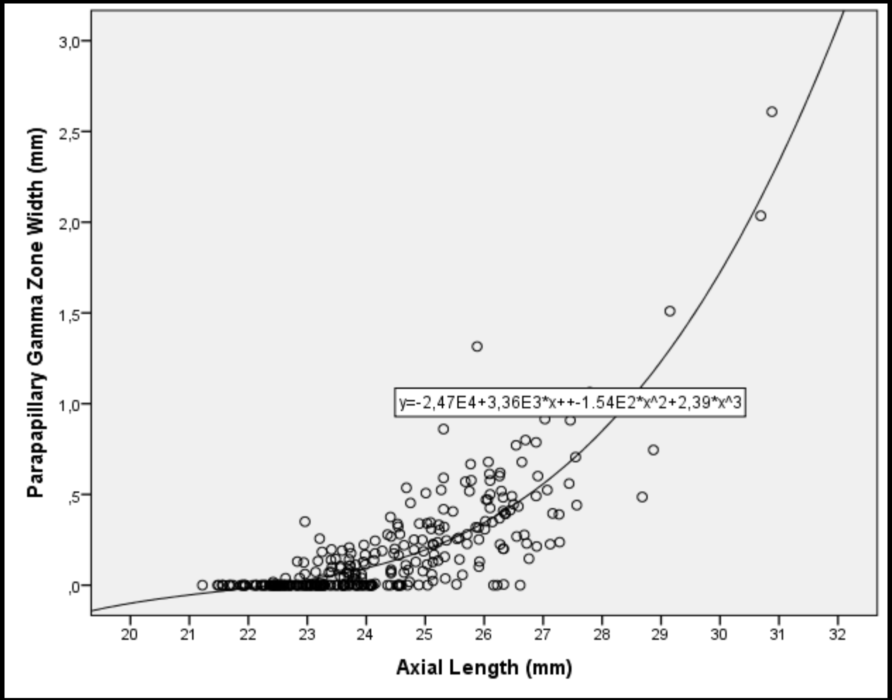
Definition of High Myopia

- High myopia defined as a refractive error associated increase in optic disc size and beta zone of PPA: Beijing Eye Study: Cut-Off at about -8 diopters





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- Jonas JB. Optic disc size correlated with refractive error. Am J Ophthalmol 2005;139:346-348.
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- Jonas JB, Jonas SB, Jonas RA, Holbach L, Dai Y, Sun X, Panda-Jonas S. Parapapillary atrophy: Histological gamma zone and delta zone. PLoS One. 2012;7(10):e47237.
- Jonas JB, Wang YX, Zhang Q, Liu Y, Xu L, Wei WB. Macular Bruch´s membrane length and axial length. The Beijing Eye Study. PloS One 2015;10(8):e0136833

Definition: Myopic Retinopathy*

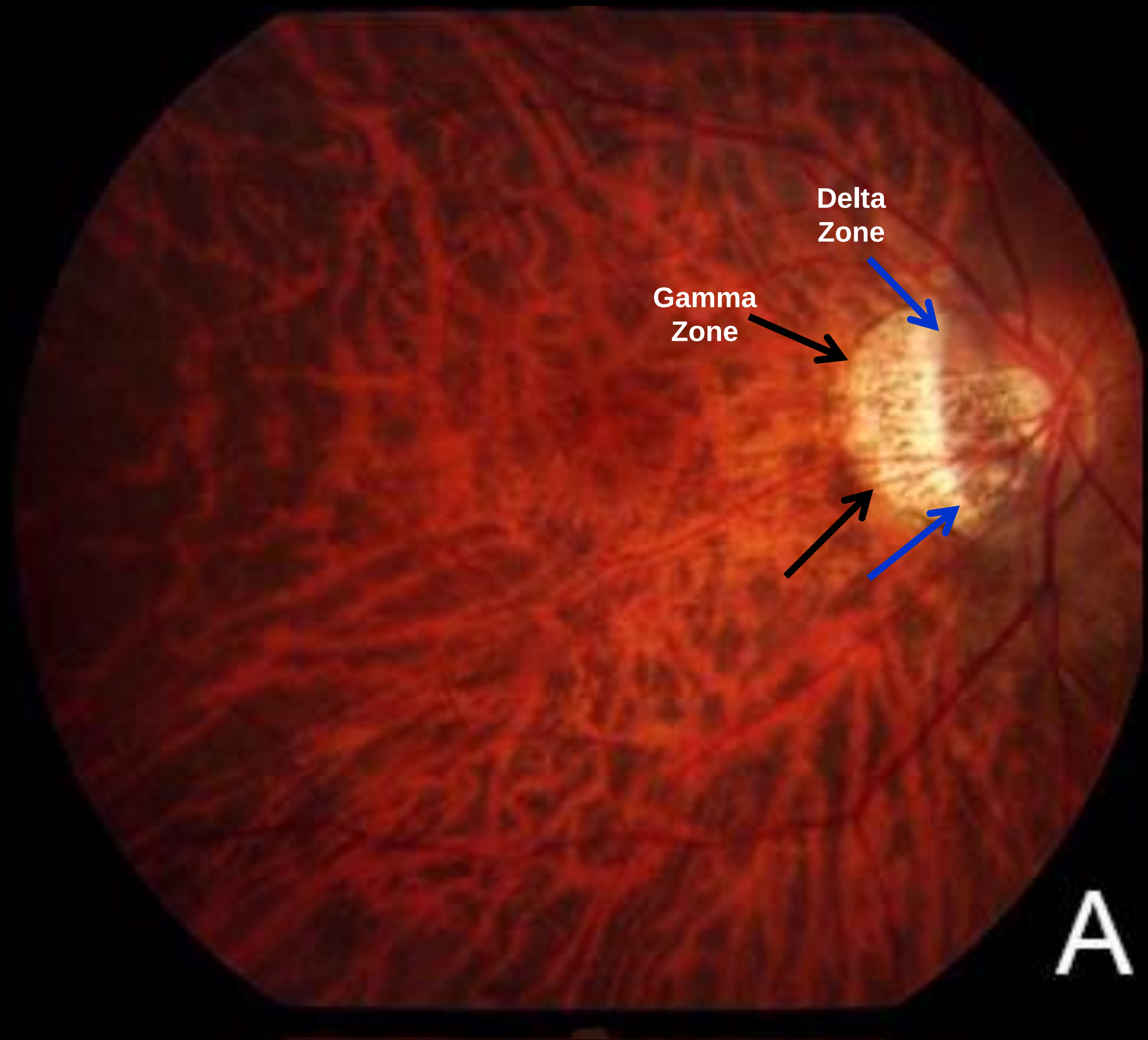
Category 0: No myopic retinal degenerative lesion
Category 1: Tessellated fundus
Category 2: Diffuse chorioretinal atrophy
Category 3: Patchy chorioretinal atrophy
Category 4: Macular atrophy

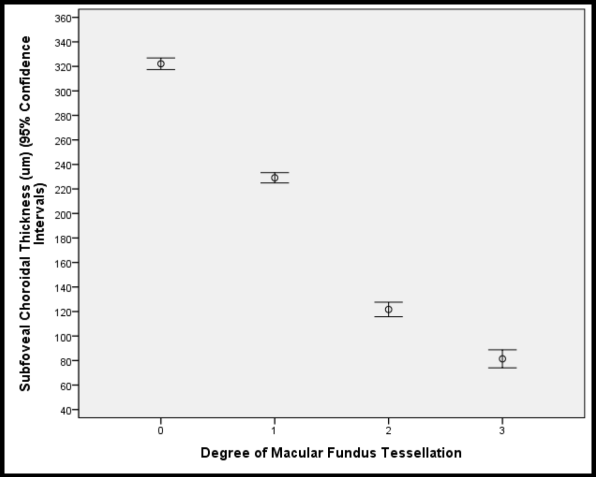
Plus lesions:

- Lacquer cracks,
- Myopic choroidal neovascularization
- Fuchs' spot
- (Posterior staphyloma)

*Ohno-Matsui K, Kawasaki R, Jonas JB, Gemmy-Cheung CM, Saw SM, Verhoeven V, Klaver C, Moriyama M, Shinohara K, Kawasaki Y, Yamazaki M, Meuer S, Ishibashi T, Yasuda M, Yamashita H, Sugano A, Wang JJ, Mitchell P, Wong TY, for the META-analysis for Pathologic Myopia (META-PM) Study Group. International classification and grading system for myopic maculopathy. Am J Ophthalmol. 2015;159:877-883.

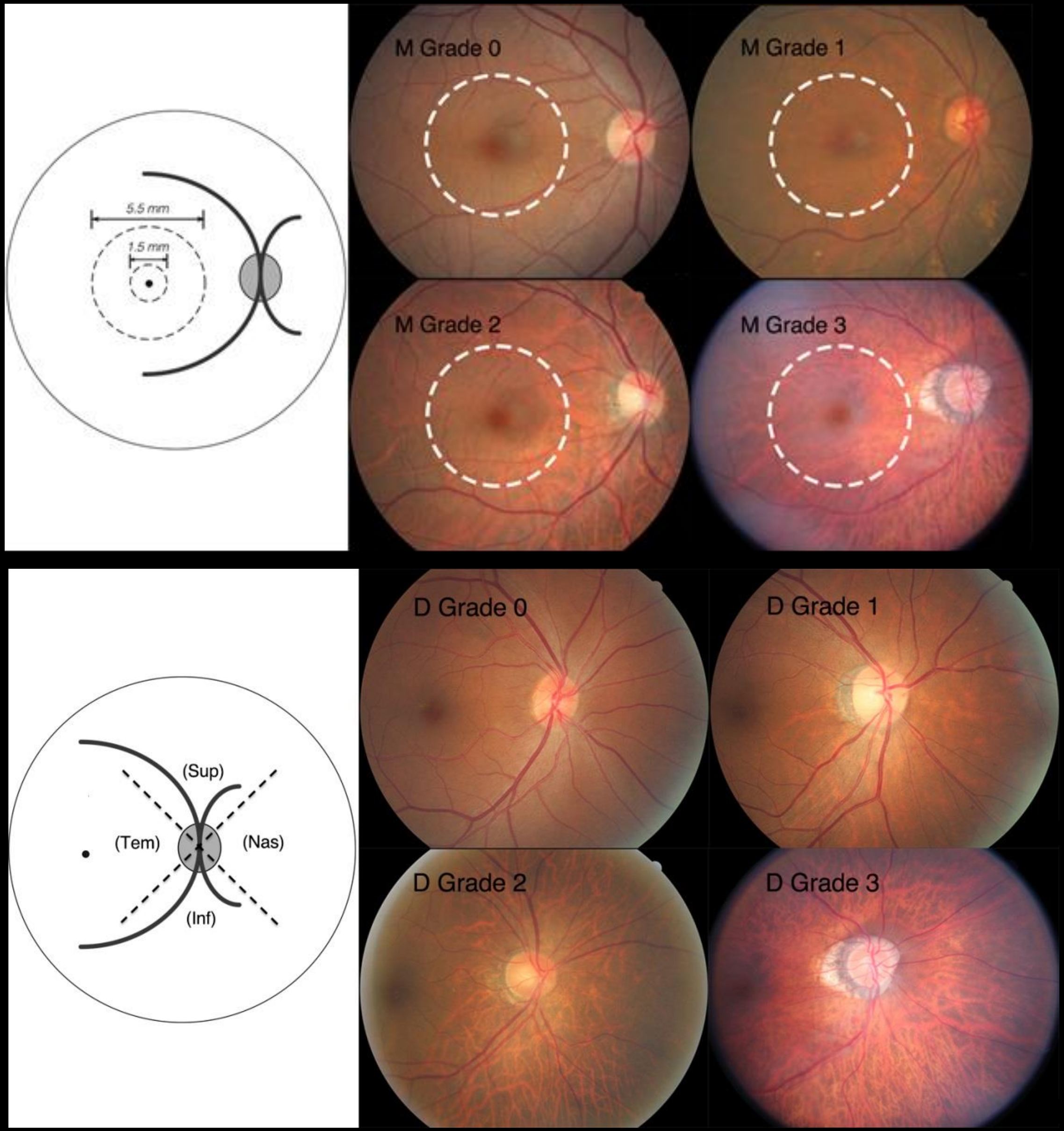
META-analysis for Pathologic Myopia (META-PM) Study Group, Myopic Retinopathy: Category 1: Tessellated Fundus





Ohno-Matsui K, Kawasaki R, Jonas JB, Gemmy-Cheung CM, Saw SM, Verhoeven V, Klaver C, Moriyama M, Shinohara K, Kawasaki Y, Yamazaki M, Meuer S, Ishibashi T, Yasuda M, Yamashita H, Sugano A, Wang JJ, Mitchell P, Wong TY, for the META-analysis for Pathologic Myopia (META-PM) Study Group. International classification and grading system for myopic maculopathy. Am J Ophthalmol. 2015;159:877-883.

Fundus Tessellation and Choroidal Thickness : The Beijing Eye Study 2011.



Yan YN, Wang YX, Xu L, Xu J, Wei WB, Jonas JB. Fundus tessellation: Prevalence and associated factors. The Beijing Eye Study 2011. Ophthalmology. 2015;122:1873-80

Fundus Tessellation and Choroidal Thickness : The Beijing Eye Study 2011.

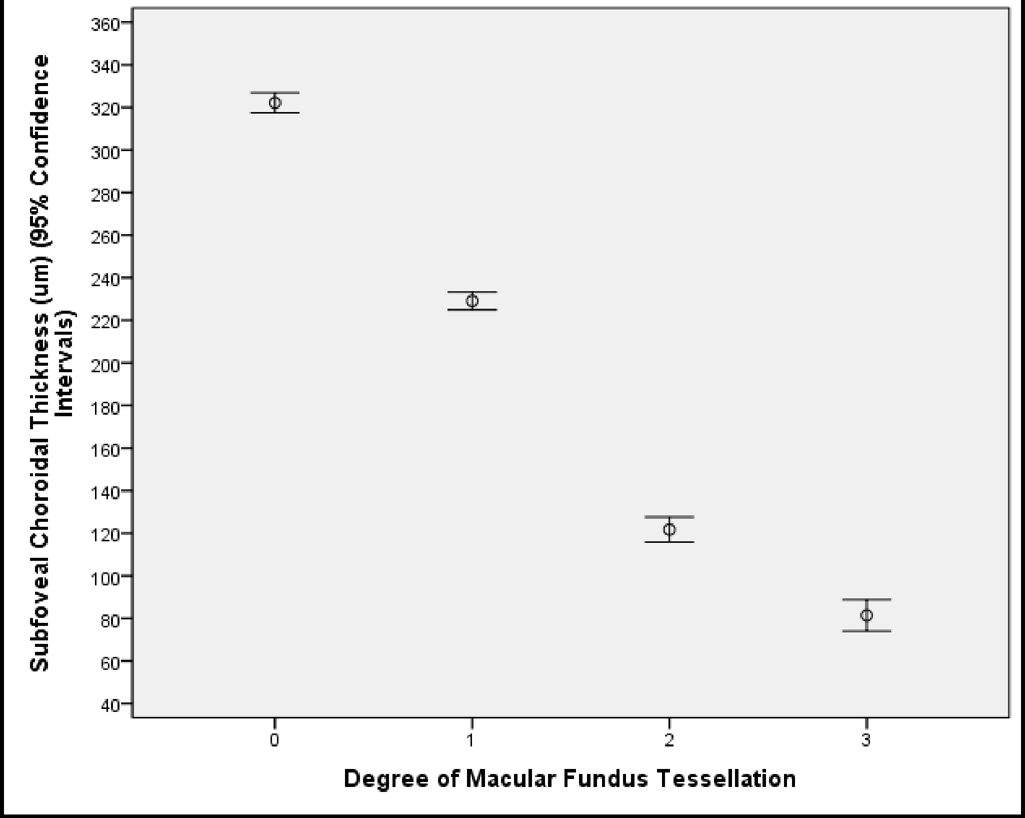
In multivariate analysis (r: 0.68), higher degree of fundus tessellation (mean: 0.84±0.79) was associated with

- older age (*P*<0.001; beta: 0.14),
- male sex (*P*<0.001; beta:-0.08),
- lower body mass index (*P*=0.03; beta:0.03),
- worse best corrected visual acuity (*P*<0.001; beta:0.05),
- **thinner subfoveal choroidal thickness (*P*<0.001; beta:-0.51),**
- longer axial length (*P*<0.001; beta:0.11),
- larger parapapillary beta zone (*P*<0.001; beta:0.08),
- lower prevalence of intermediate age-related macular degeneration (*P*=0.02; beta:-0.04), and lower prevalence of late age-related macular degeneration (*P*=0.007; beta:-0.04).

Yan YN, Wang YX, Xu L, Xu J, Wei WB, Jonas JB. Fundus tessellation: Prevalence and associated factors. The Beijing Eye Study 2011. Ophthalmology. 2015;122:1873-80

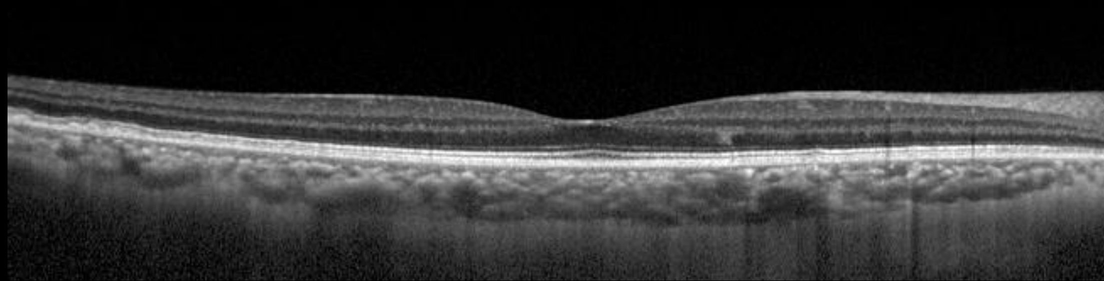
Fundus Tessellation and Choroidal Thickness : The Beijing Eye Study 2011.

In univariate analysis, subfoveal choroidal thickness decreased from 322±90μm in eyes without fundus tessellation to 229±80μm in eyes with grade 1 of fundus tessellation, to 122±52μm in eyes with grade 2, and to 81±37μm in eyes with grade 3 of macular fundus tessellation.

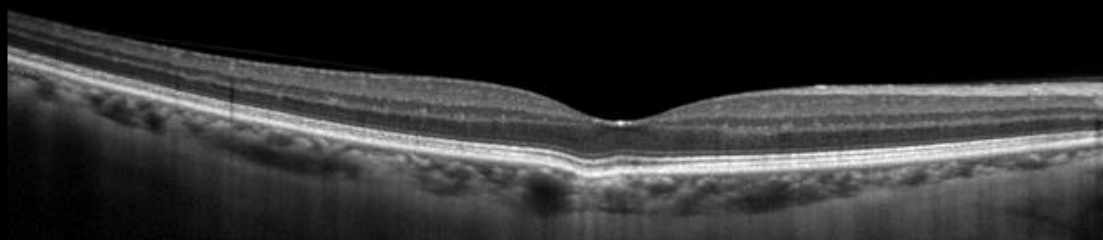


Yan YN, Wang YX, Xu L, Xu J, Wei WB, Jonas JB. Fundus tessellation: Prevalence and associated factors. The Beijing Eye Study 2011. Ophthalmology. 2015;122:1873-80

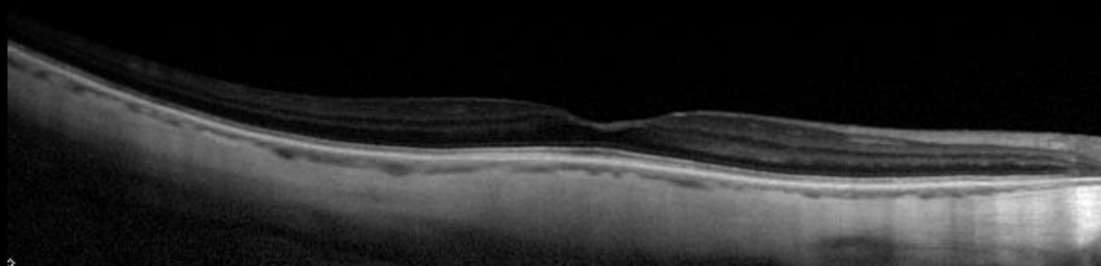
Beijing Eye Study: Choroidal Thickness



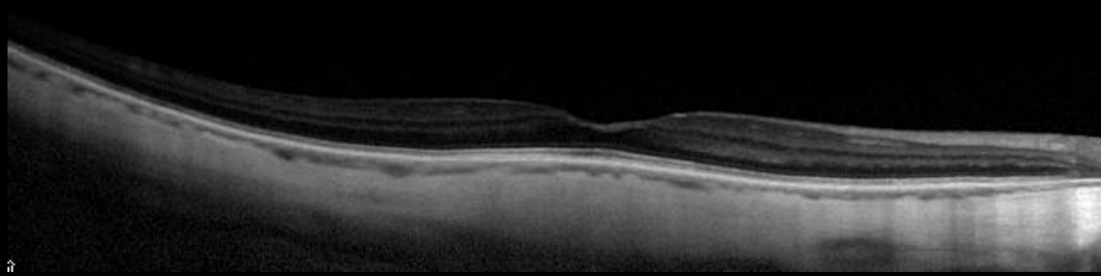
O dpt; 55 years; 244 µm



-6.0 dpt; 56 years; 179 µm

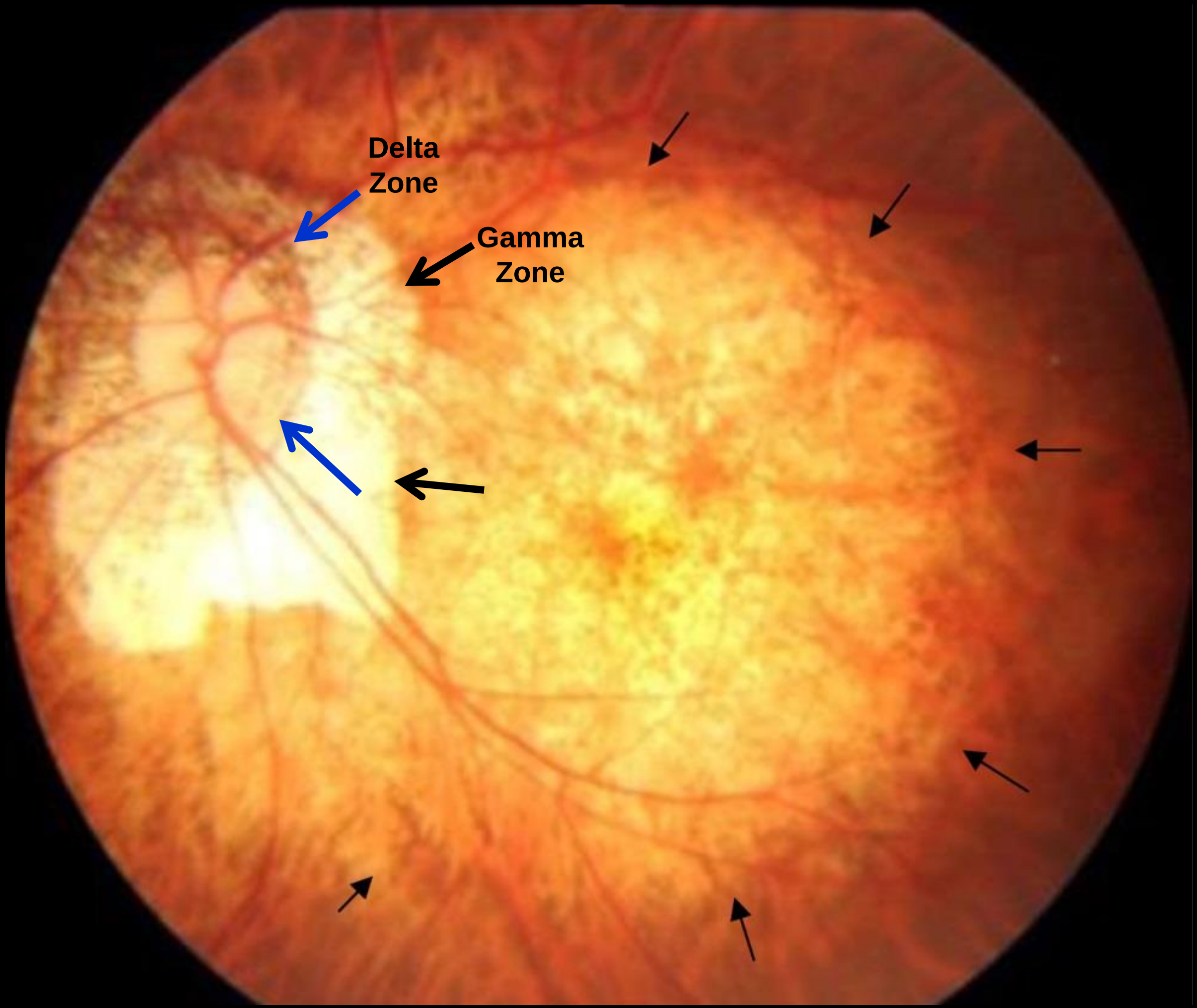


-9.5 dpt; 70 years; 57 µm



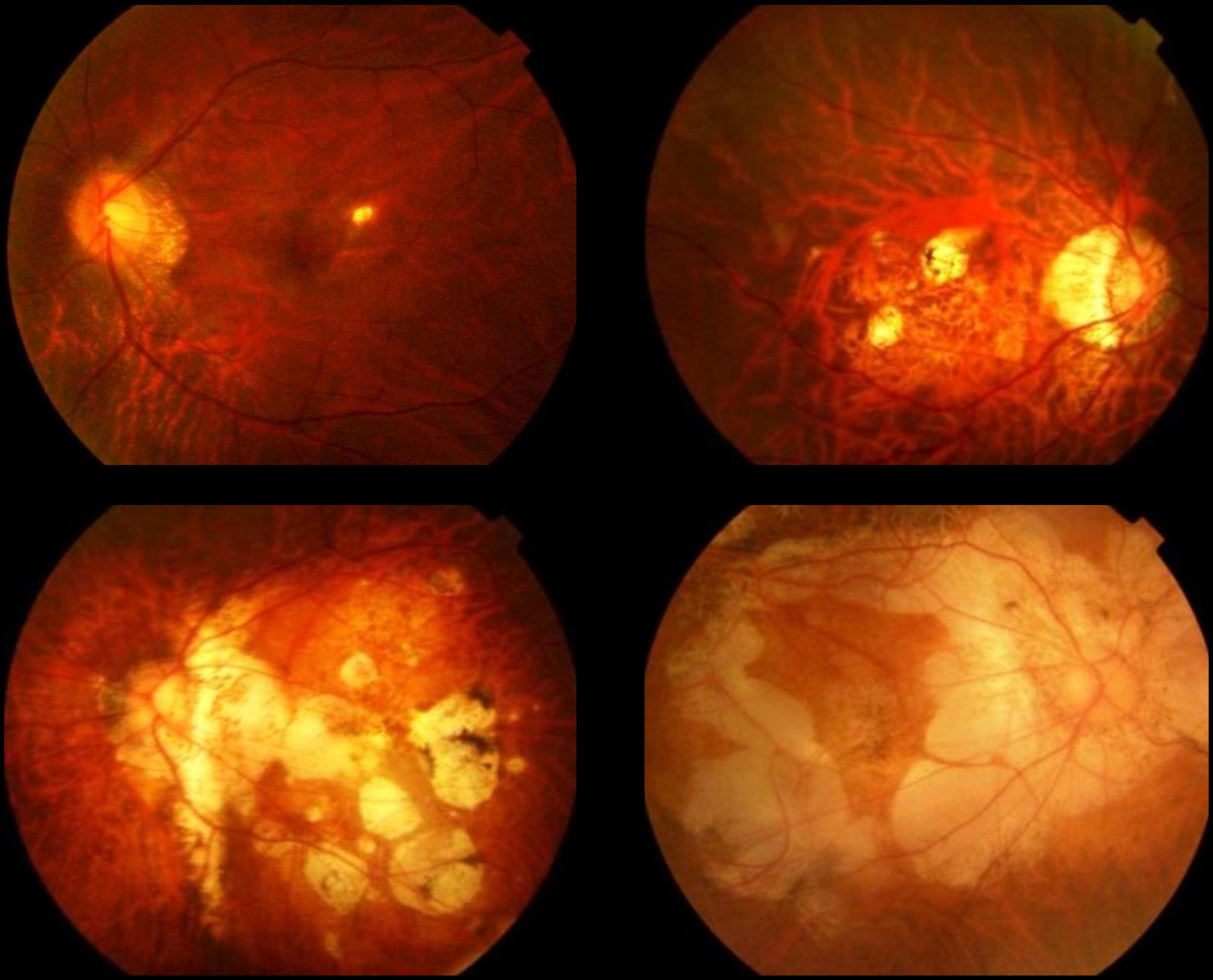
-19.0 dpt; 70 years; 8 µm

Myopic Retinopathy: Category 2: Diffuse Chorioretinal Atrophy

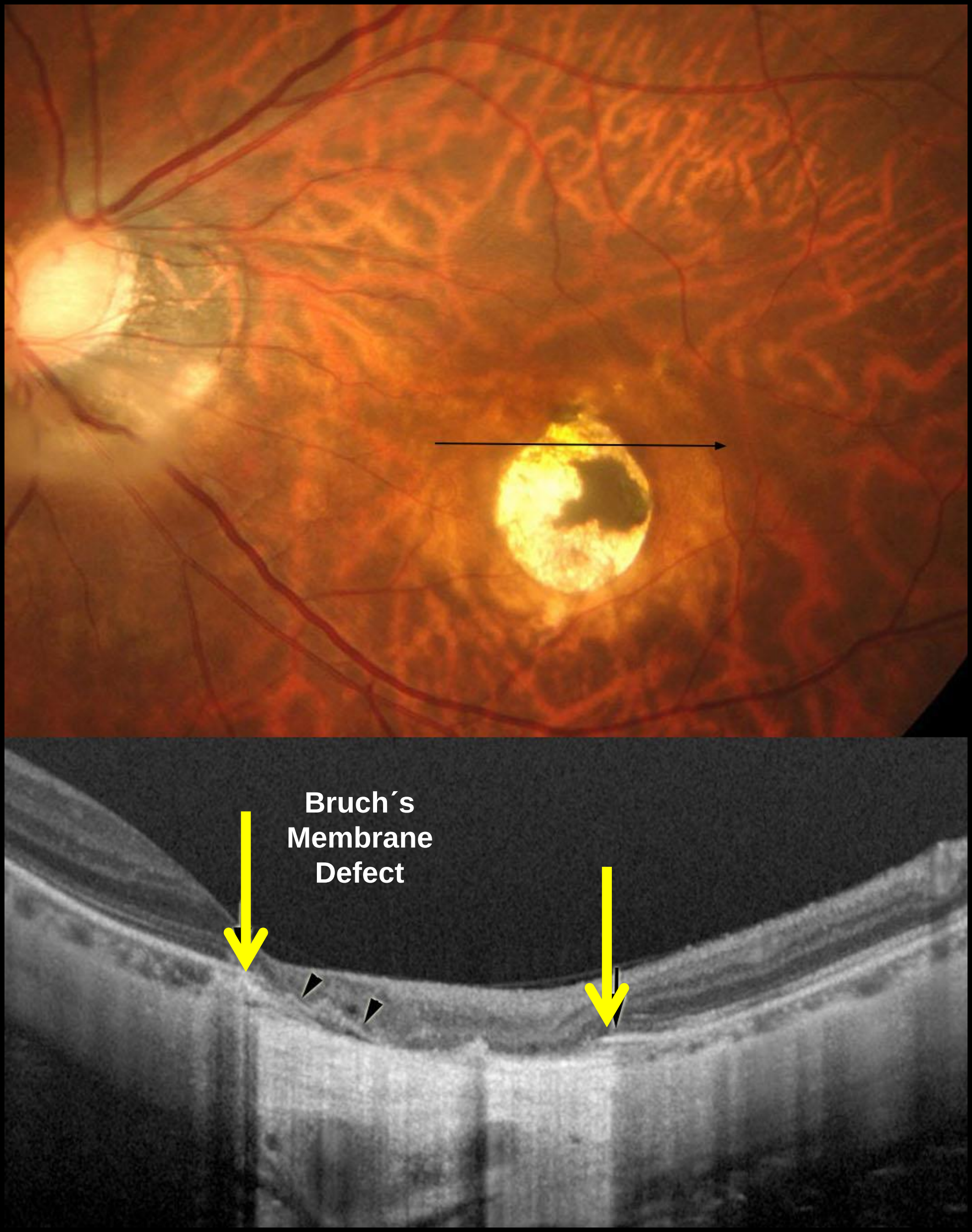


Ohno-Matsui K, Kawasaki R, Jonas JB, Gemmy-Cheung CM, Saw SM, Verhoeven V, Klaver C, Moriyama M, Shinohara K, Kawasaki Y, Yamazaki M, Meuer S, Ishibashi T, Yasuda M, Yamashita H, Sugano A, Wang JJ, Mitchell P, Wong TY, for the META-analysis for Pathologic Myopia (META-PM) Study Group. International classification and grading system for myopic maculopathy. Am J Ophthalmol. 2015;159:877-883.

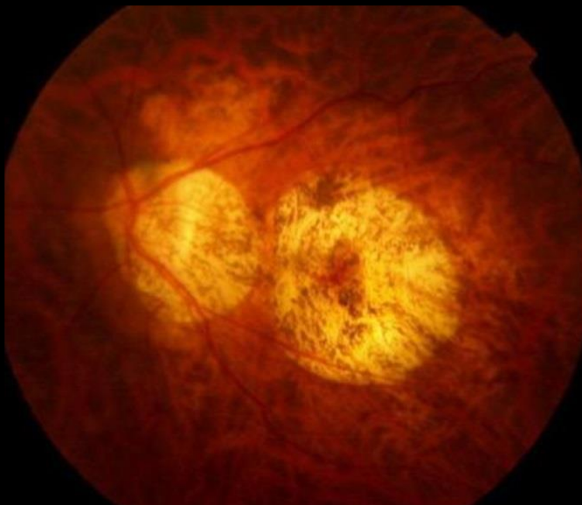
Myopic Retinopathy: Category 3: Patchy Chorioretinal Atrophy

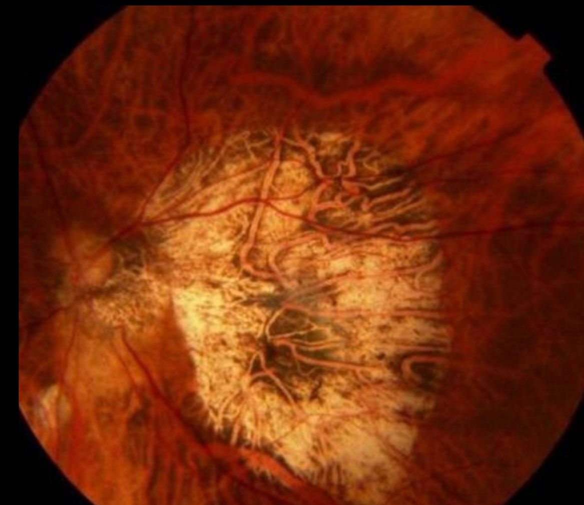


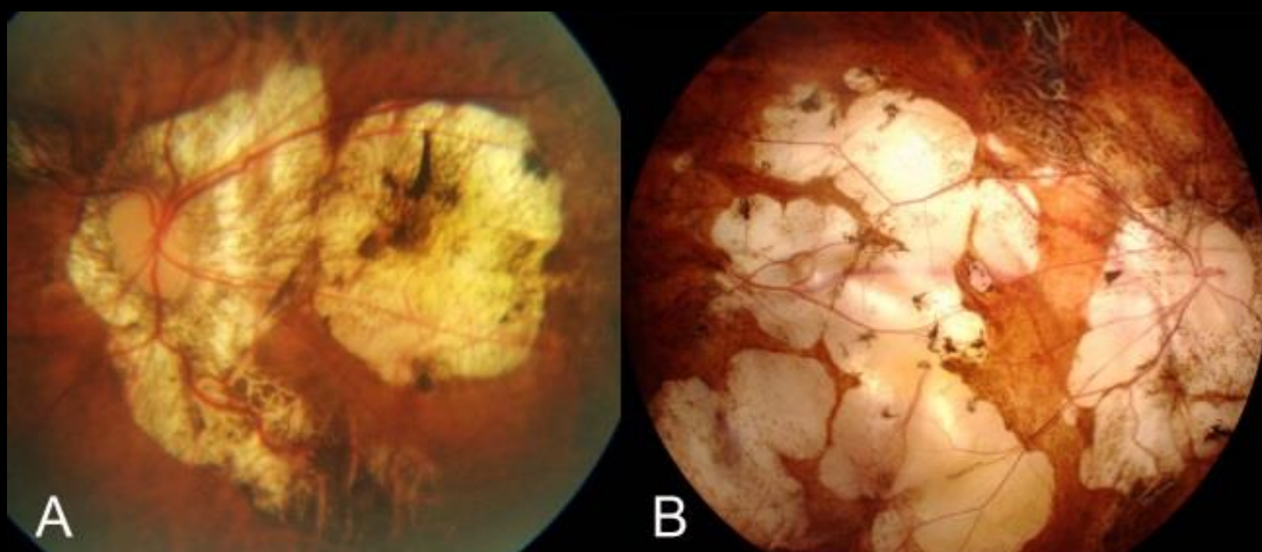
Myopic Retinopathy: Category 3: Patchy Chorioretinal Atrophy



Myopic Retinopathy: Category 4: Macular Atrophy







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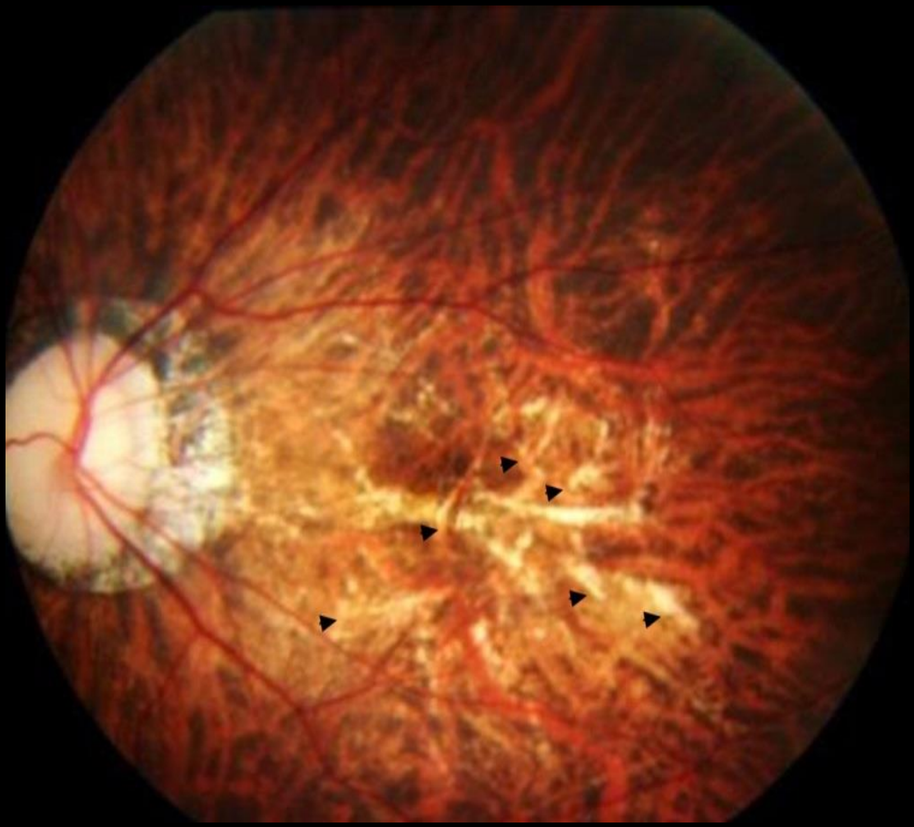
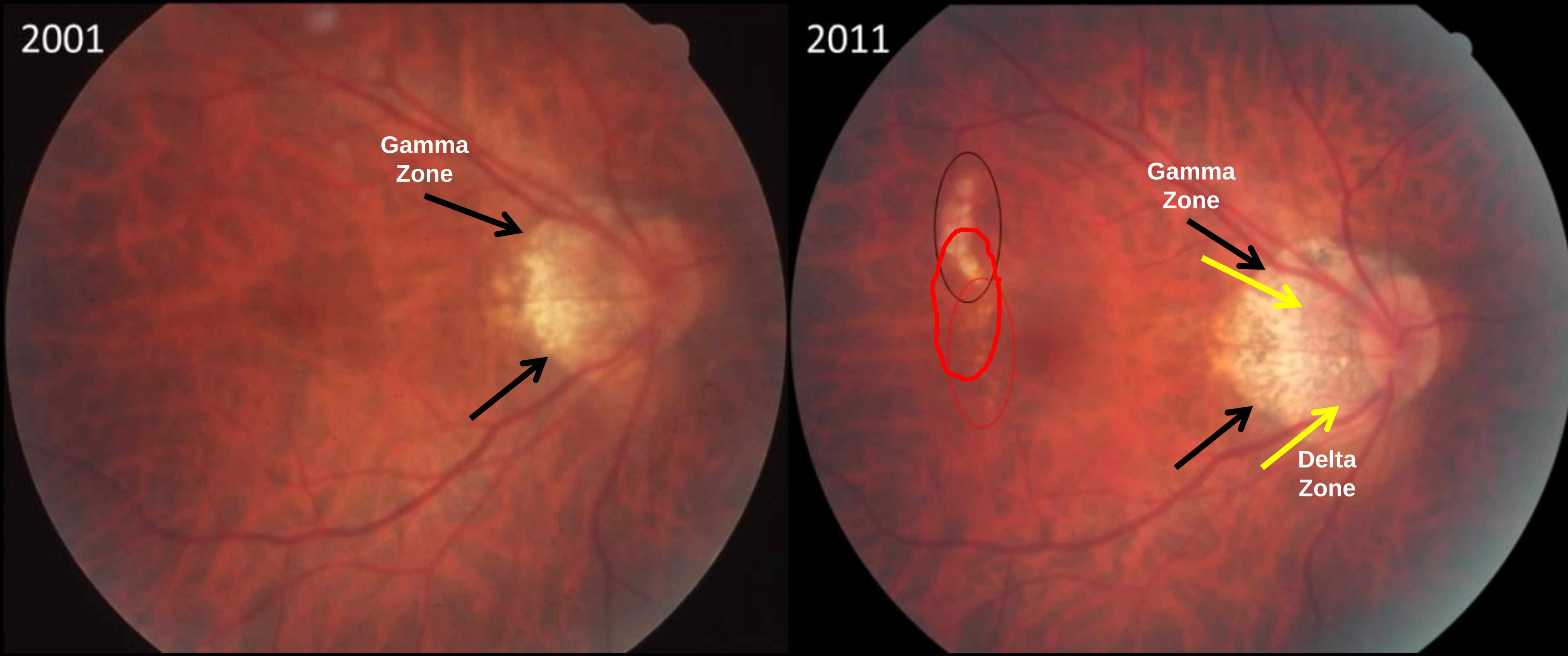
Category 5: Plus Lesions: Lacquer Cracks, CNV



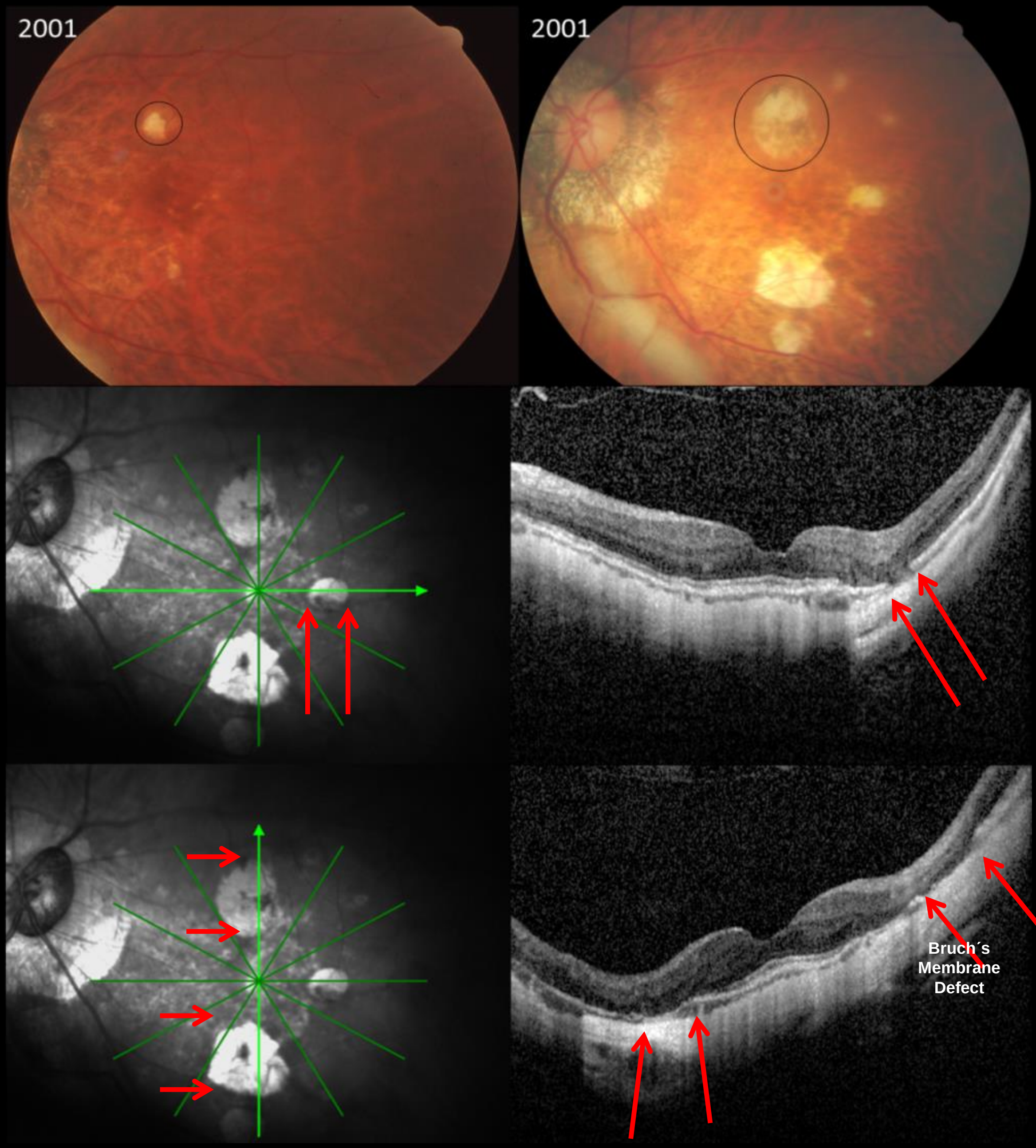
Ohno-Matsui K, Kawasaki R, Jonas JB, Gemmy-Cheung CM, Saw SM, Verhoeven V, Klaver C, Moriyama M, Shinohara K, Kawasaki Y, Yamazaki M, Meuer S, Ishibashi T, Yasuda M, Yamashita H, Sugano A, Wang JJ, Mitchell P, Wong TY, for the META-analysis for Pathologic Myopia (META-PM) Study Group. International classification and grading system for myopic maculopathy. Am J Ophthalmol. 2015;159:877-883.

Beijing Eye Study 2001 / 2011

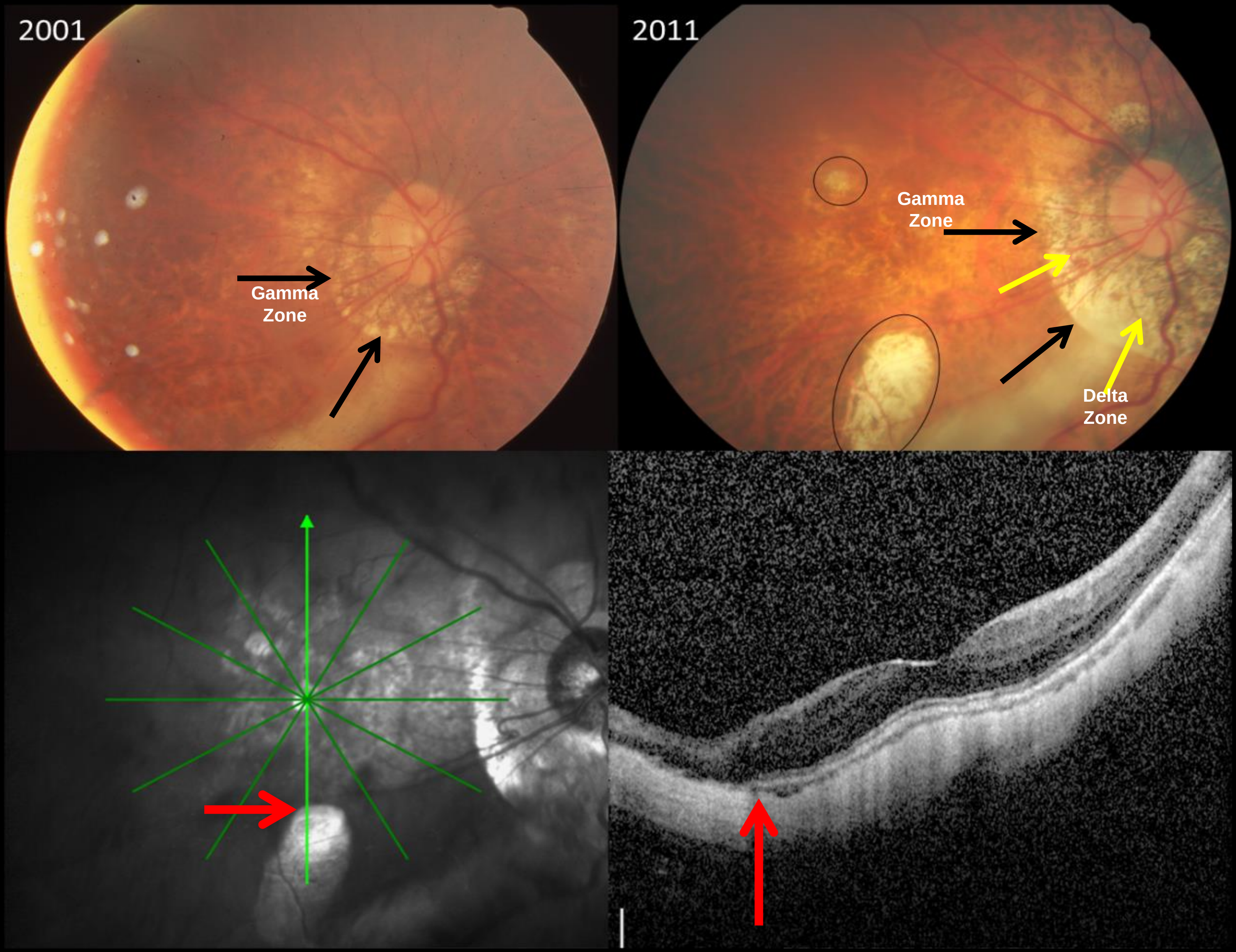


Yan YN, Wang YX, Yang Y, Xu L, Xu J, Wang Q, Yang JY, Yang X, Zhou WJ, Ohno-Matsui K, Wei WB, Jonas JB. Ten-year progression of myopic maculopathy. The Beijing Eye Study 2001-2011. Ophthalmology 2018;125(8):1253-1263

Beijing Eye Study 2001 / 2011



Beijing Eye Study 2001 / 2011



Beijing Eye Study 2001 / 2011

- Out 4439 subjects in 2001, 2695 (66.4%) participants in 2011
- Out of 110 highly myopic eyes at baseline, 39 (35.5%) eyes showed progression:
- <u>15 (19%) of 79 eyes with tessellated fundus at baseline</u>
- <u>17 (71%) of 24 eyes with diffuse chorioretinal atrophy</u>
- <u>All 6 (100%) eyes with patchy chorioretinal atrophy</u>
- The one eye with macular atrophy at baseline.
- Lacquer cracks in 2 eyes developed into a small patchy atrophy (1 eye) or widened (one eye).
- Five eyes developed new lacquer cracks.

Beijing Eye Study 2001 / 2011

Progression of myopic maculopathy was associated with:

- Longer axial length (*P*<0.001; OR: 7.13; 95% CI: 2.49, 20.4)
- Older age (*P*=0.001; OR: 1.25; 95%CI: 1.10, 1.42)
- Higher prevalence of staphylomas (*P*=0.03; OR: 24.3; 95%CI: 2.89, 204)
- Smaller parapapillary gamma zone in 2011 (*P*=0.01; OR: 0.61; 95%CI: 0.41, 0.91)
- Female gender (*P*=0.04; OR: 9.78; 95%CI: 1.06, 90.6)

Yan YN, Wang YX, Yang Y, Xu L, Xu J, Wang Q, Yang JY, Yang X, Zhou WJ, Ohno-Matsui K, Wei WB, Jonas JB. Ten-year progression of myopic maculopathy. The Beijing Eye Study 2001-2011. Ophthalmology 2018;125(8):1253-1263

Prof. Kyoko Ohno-Matsui, Tokyo: Progression of Myopic Maculopathy During 18-Year Follow-Up

810 eyes of 432 patients (age: 42.3±16.8 years; axial length: 28.8±1.9 mm; mean follow-up: 18.7±7.1 years).

Within the pathologic myopia (PM) group (n=521 eyes), progression of myopic maculopathy was associated with:

- Female gender (OR: 2.21; *P*=0.001),
- Older age (OR: 1.03; *P*=0.002),
- Longer axial length (OR: 1.20; *P*=0.007),
- Greater axial elongation (OR: 1.45; *P*=0.005), and
- Development or enlargement of parapapillary atrophy (OR: 3.14; *P*<0.001).

Fang Y, Yokoi T, Nagaoka N, Shinohara K, Onishi Y, Ishida T, Yoshida T, Xu X, Jonas JB, Ohno-Matsui K. Progression of myopic maculopathy during 18-year follow-up. Ophthalmology 2018;125:863-877

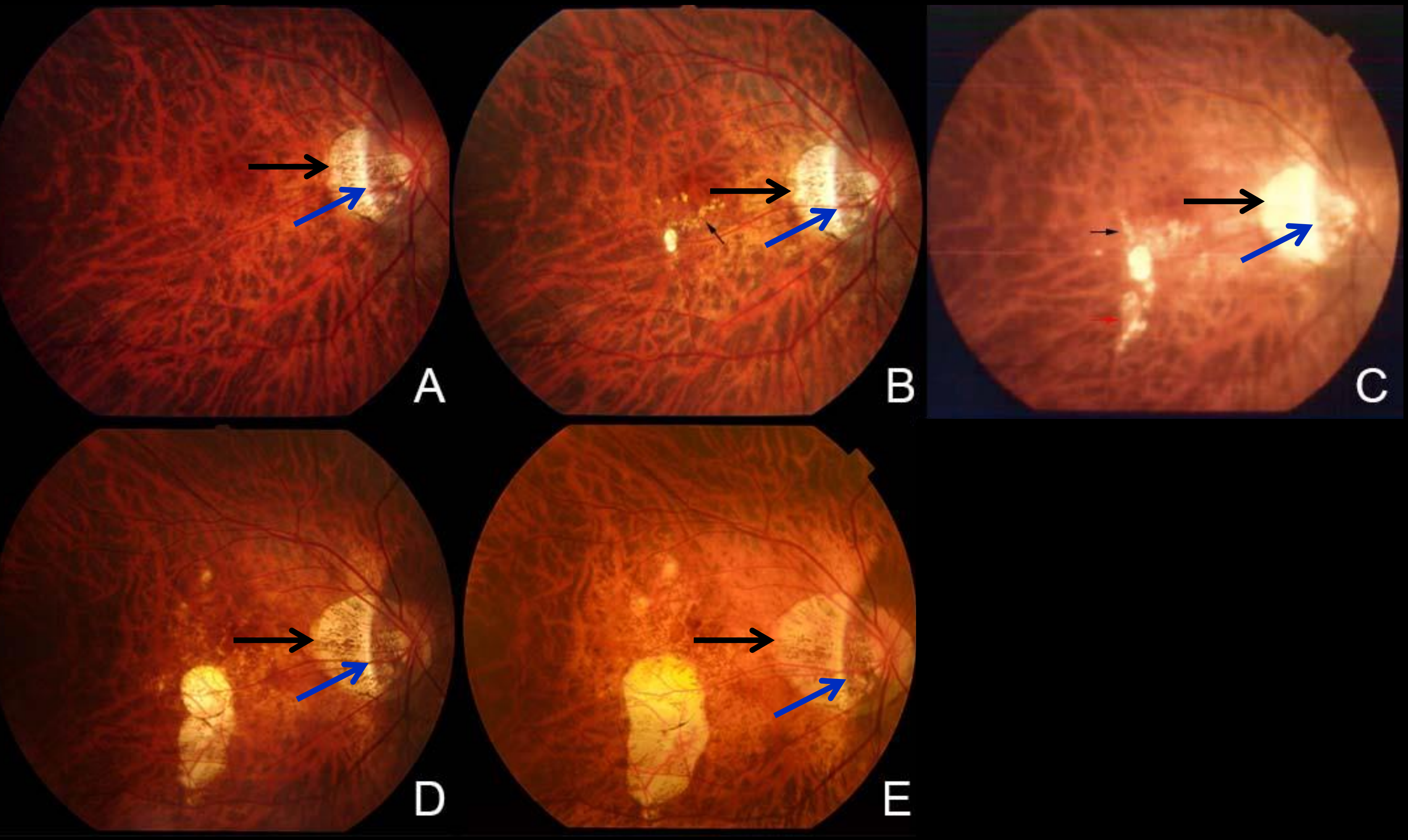
Progression of Myopic Maculopathy During 18-Year Follow-Up

- Diffuse chorioretinal atrophy (n=217 eyes) at baseline: Progression in 111 (51%) eyes (to macular diffuse atrophy (58%), patchy atrophy (n=59; 53%), myopic CNV (n=18; 16%), LCs (n=9; 5%) and patchy-related macular atrophy (n=3; 3%)).
- Patchy atrophy (n=63): Progression in 60 (95%) eyes (to enlargement of original patchy atrophy (n=59; 98%), new patchy atrophy (n=29; 48%), CNV-related macular atrophy (n=13; 22%) and patchy-related macular atrophy (n=5; 8%)).
- Out of 66 eyes with LCs at baseline, 43 (65%) eyes showed progression (to new patchy atrophy (n=38; 88%) and new LCs (n=7; 16%)).

- Reduction in visual acuity was mainly associated (all *P*<0.001) with the development of CNV or CNV-related macular atrophy and enlargement of macular atrophy.

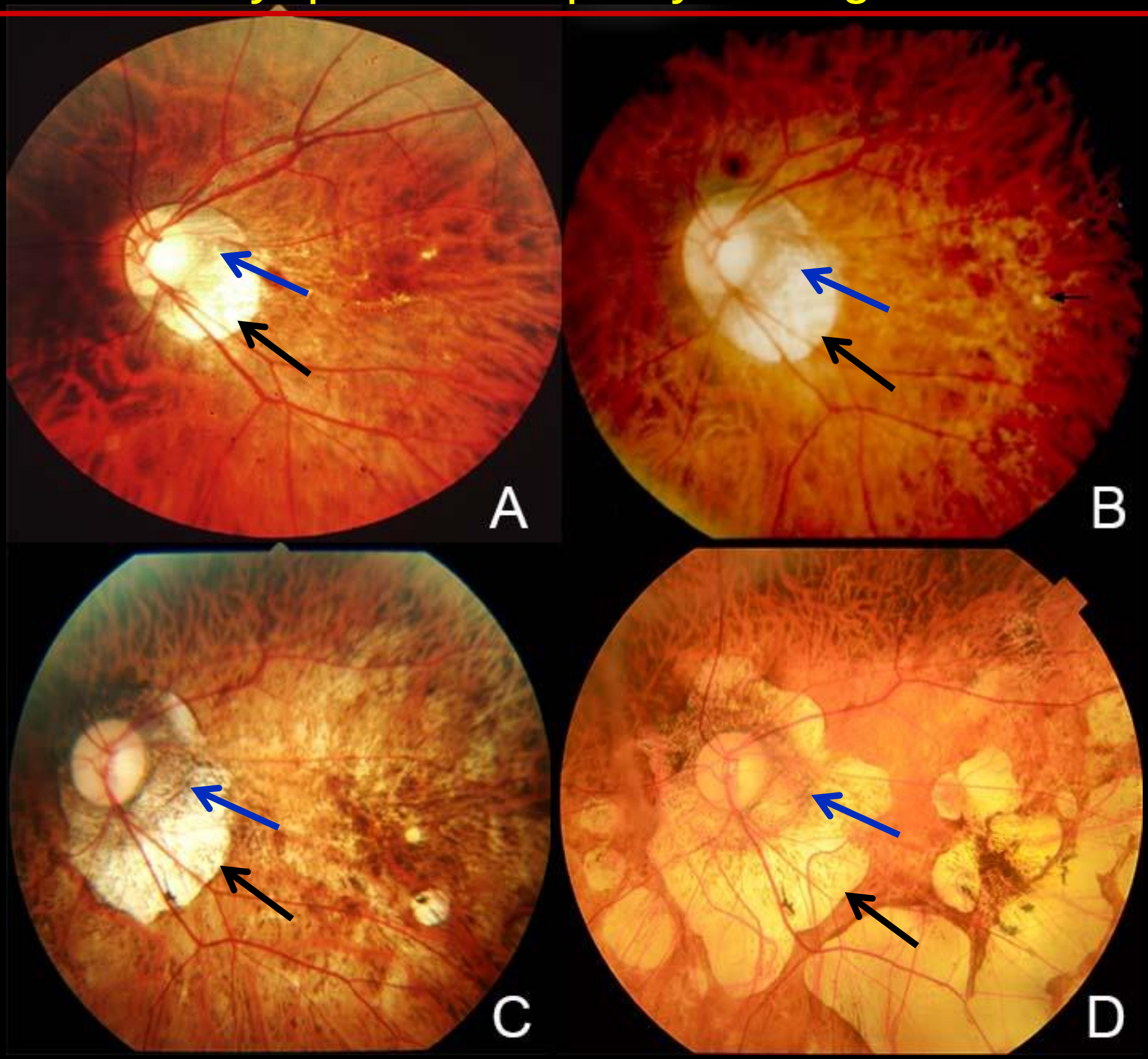
Fang Y, Yokoi T, Nagaoka N, Shinohara K, Onishi Y, Ishida T, Yoshida T, Xu X, Jonas JB, Ohno-Matsui K. Progression of myopic maculopathy during 18-year follow-up. Ophthalmology 2018;125:863-877

Progression of Myopic Maculopathy During 18-Year Follow-Up



Fang Y, Yokoi T, Nagaoka N, Shinohara K, Onishi Y, Ishida T, Yoshida T, Xu X, Jonas JB, Ohno-Matsui K. Progression of myopic maculopathy during 18-year follow-up. Ophthalmology. 2018 Jan 19. [Epub ahead of print]

Progression of Myopic Maculopathy During 18-Year Follow-Up

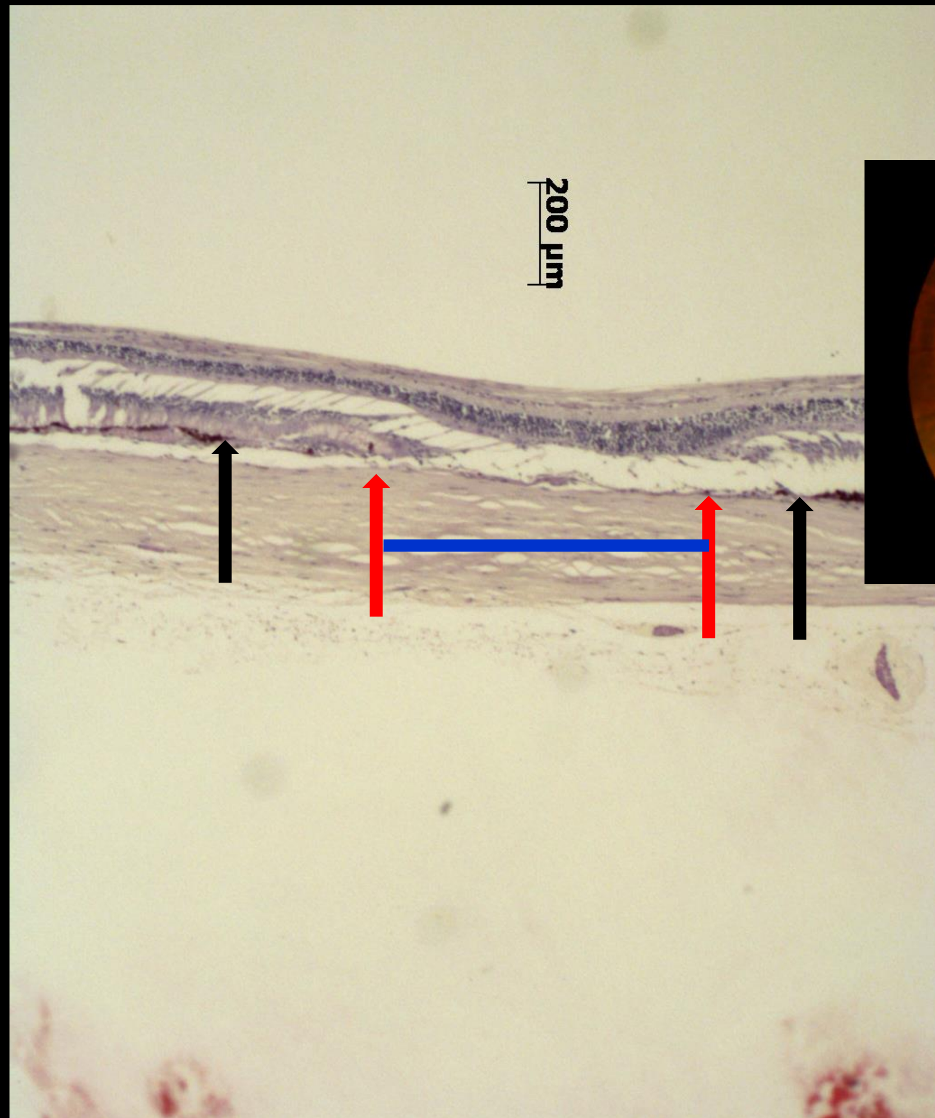


Fang Y, Yokoi T, Nagaoka N, Shinohara K, Onishi Y, Ishida T, Yoshida T, Xu X, Jonas JB, Ohno-Matsui K. Progression of myopic maculopathy during 18-year follow-up. Ophthalmology. 2018 Jan 19. [Epub ahead of print]

Myopic Maculopathy, Histology

Liu HH, Xu L, Wang YX, Wang S, You QS, Jonas JB. Prevalence and progression of myopic retinopathy in Chinese adults: The Beijing Eye Study. Ophthalmology 2010;117:1763-8.

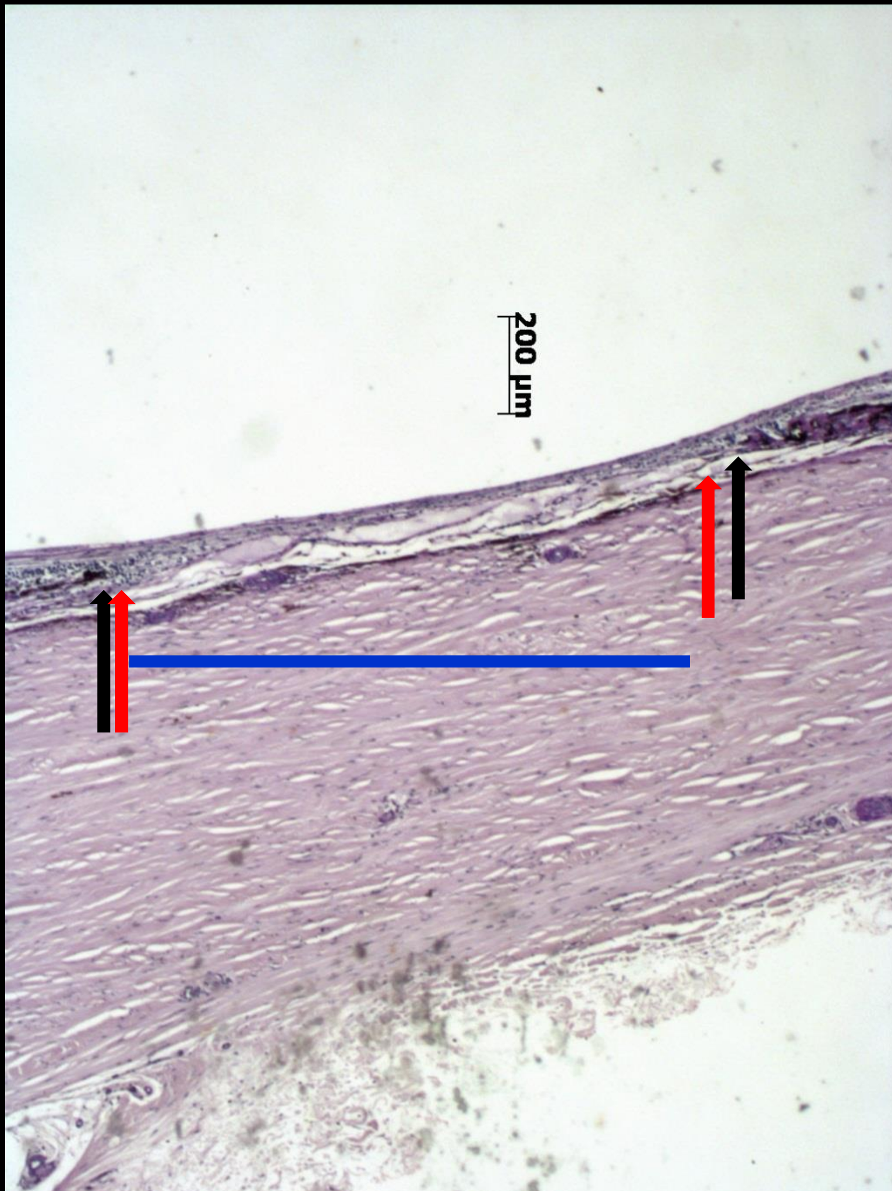
Bruch´s Membrane Defect in the Highly Myopic Macula

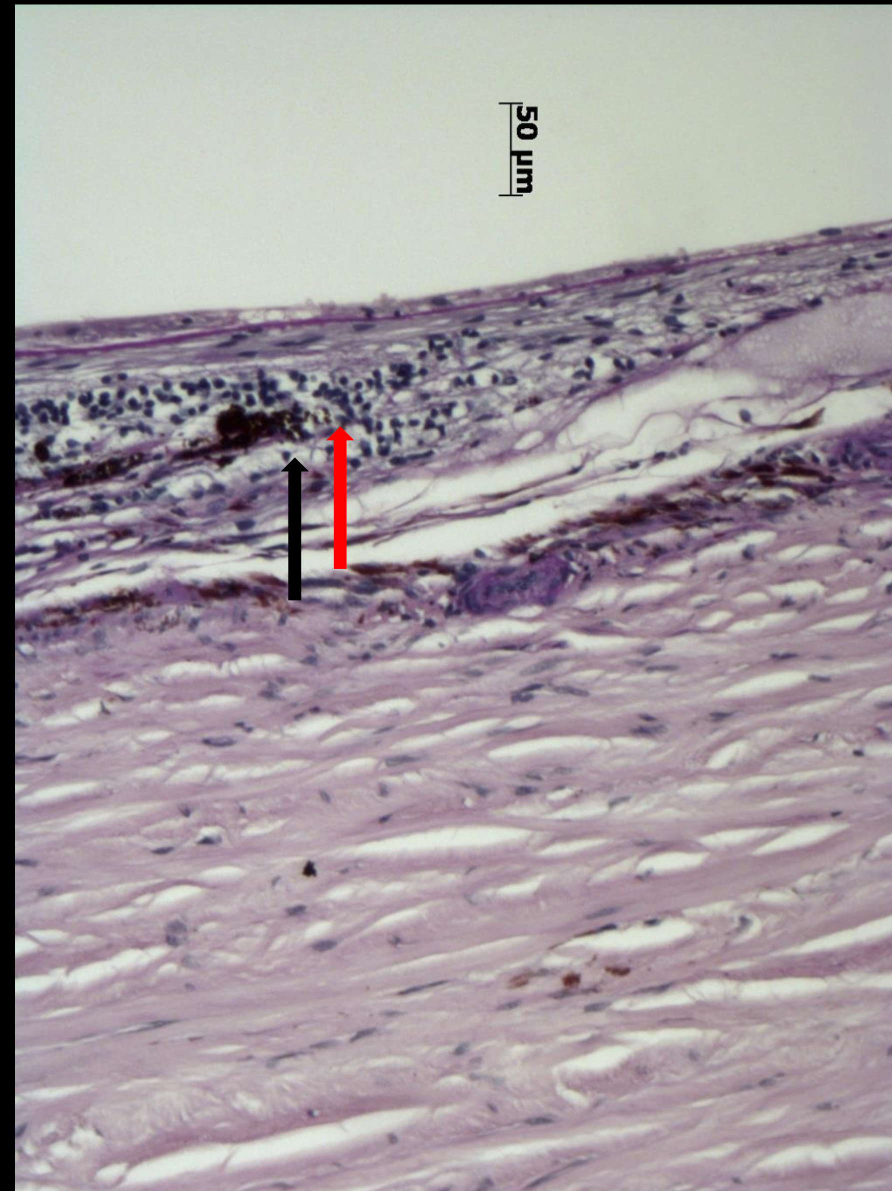


Black arrows: end of RPE; Red arrows: end of BM; Blue line: region without BM

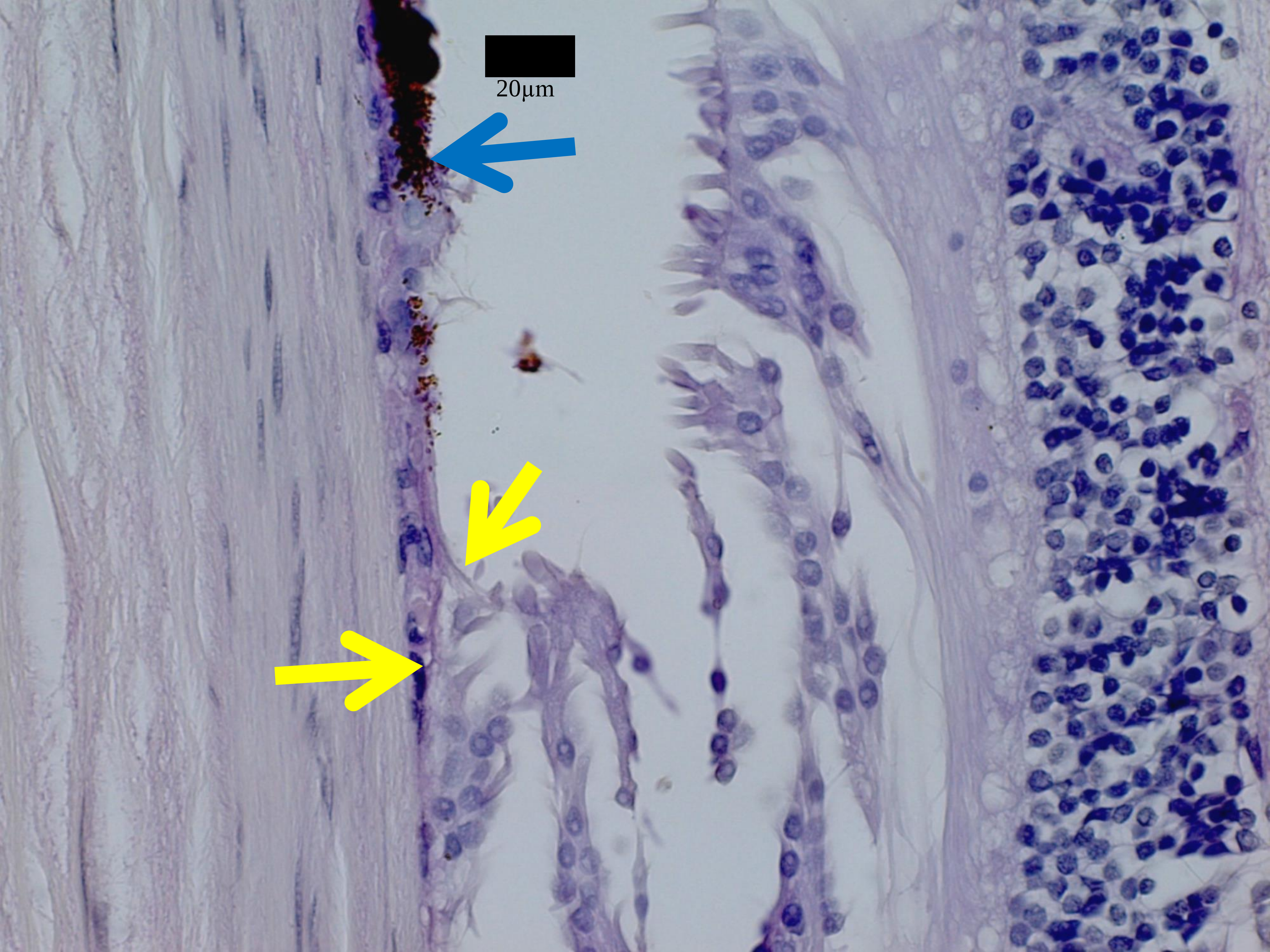
Jonas JB, Ohno-Matsui K, Spaide RF, Holbach L, Panda-Jonas S. Macular Bruch´s membrane holes in high myopia: Associated with gamma zon
and delta zone of parapapillary region. Invest Ophthalmol Vis Sci 2013;54:1295-30.

Histological Changes of the Macula in High Myopia

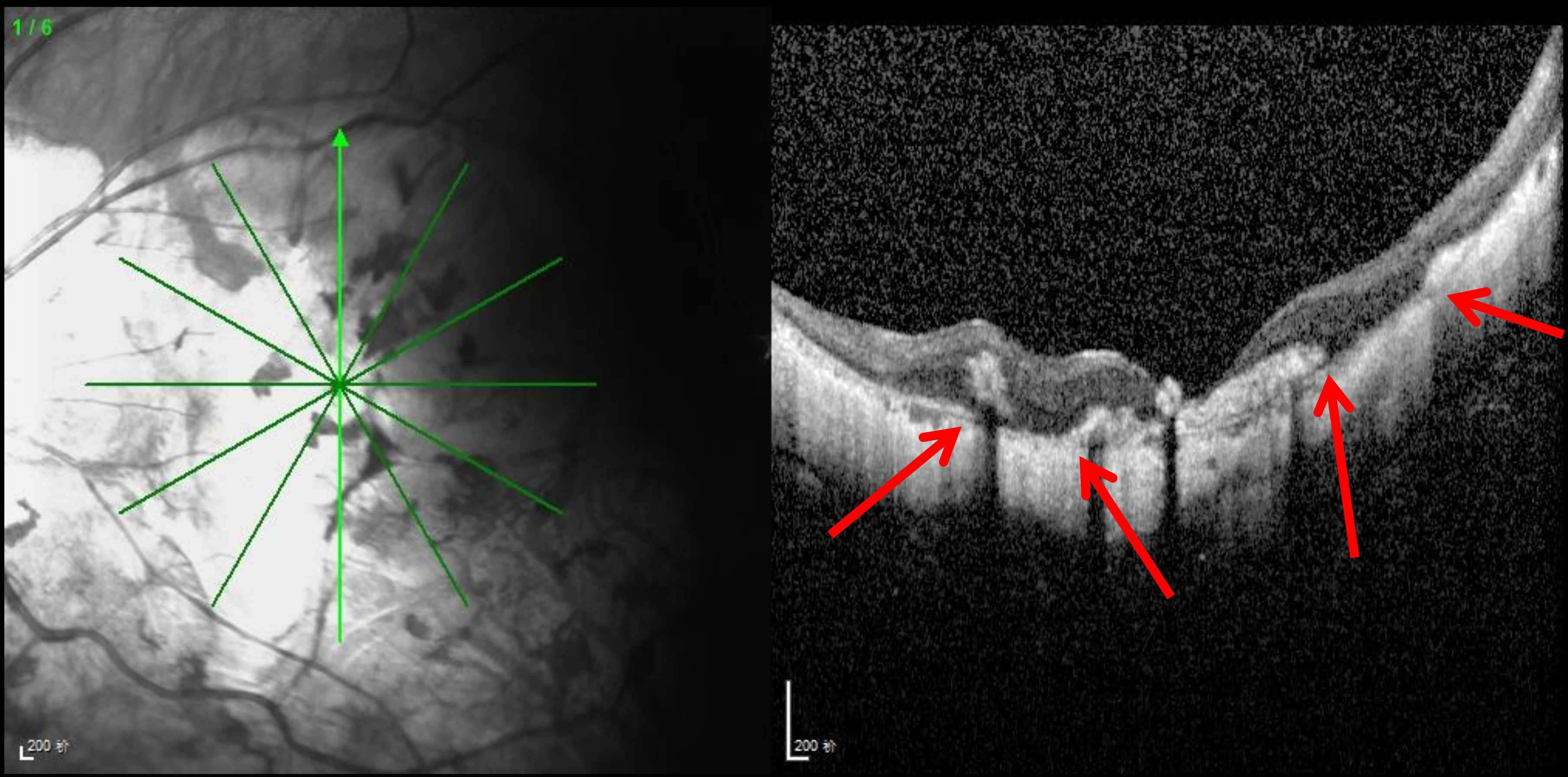




Black arrows: end of RPE; Red arrows: end of BM; Blue line: region without BM (right image magnification from left image)


20μm

Macular Bruch´s Membrane Defects



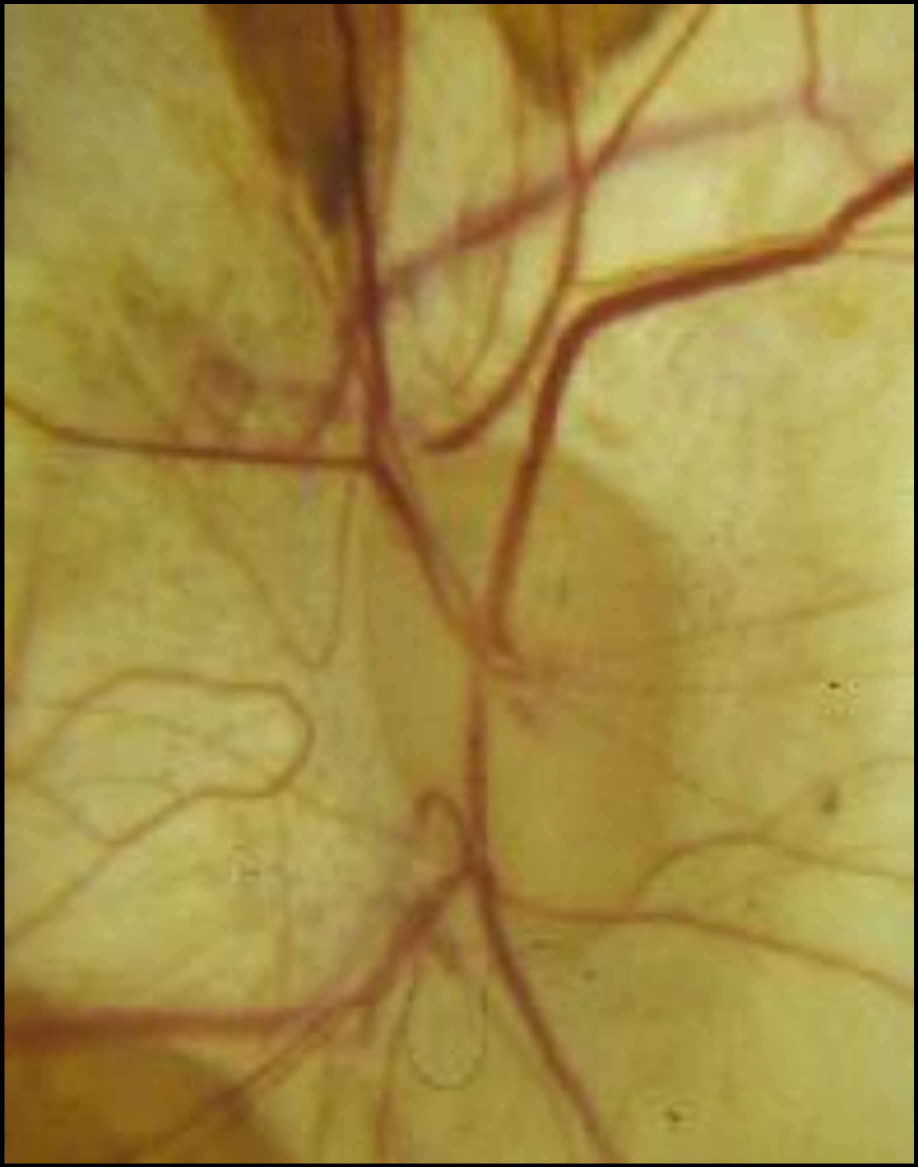
You QS, Peng XY, Xu L, Chen CX, Wang YX, Jonas JB. Myopic maculopathy imaged by optical coherence tomography. The Beijing Eye Study. Ophthalmology 2014;121:220-4.

Primary Macrodiscs Versus Secondary Macrodiscs

- Jonas JB, Gusek GC, Naumann GOH. Optic disk morphometry in high myopia. Graefes Arch Clin Exp Ophthalmol 1988; 226: 587-590
- Xu L, Li Y, Wang S, Wang Y, Wang Y, Jonas JB. Characteristics of highly myopic eyes. The Beijing Eye Study. Ophthalmology 2007;114:121-6.

Beijing Eye Study: High Myopia and Glaucoma*

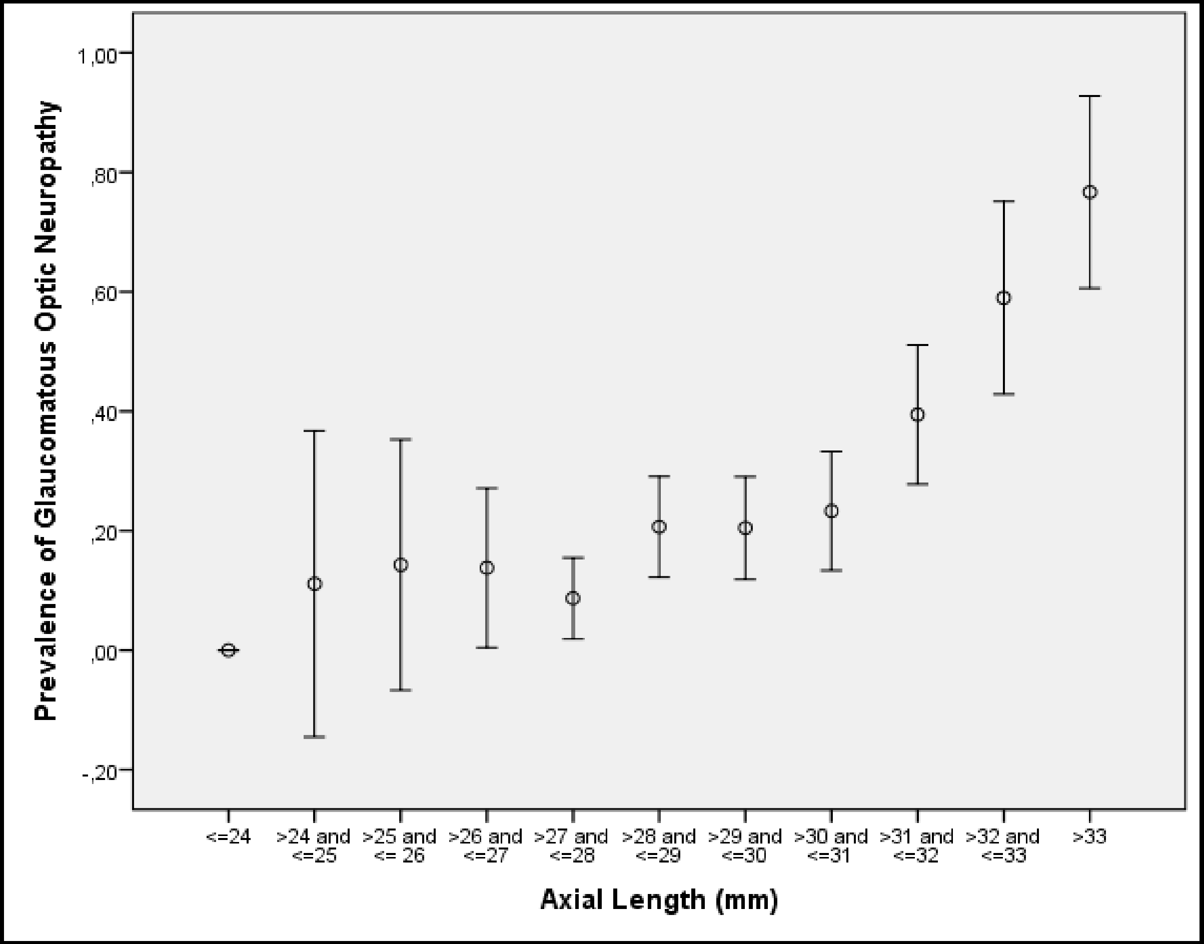
- Glaucoma prevalence higher (p=0.001) in marked or high myopia (>-6 dpt) than in moderate myopia, low myopia, emmetropia, and hyperopia



Xu L, Wang Y, Wang S, Wang Y, Jonas JB. High myopia and glaucoma susceptibility. The Beijing Eye Study. Ophthalmology 2007;114:216-20

High Myopia and Glaucoma

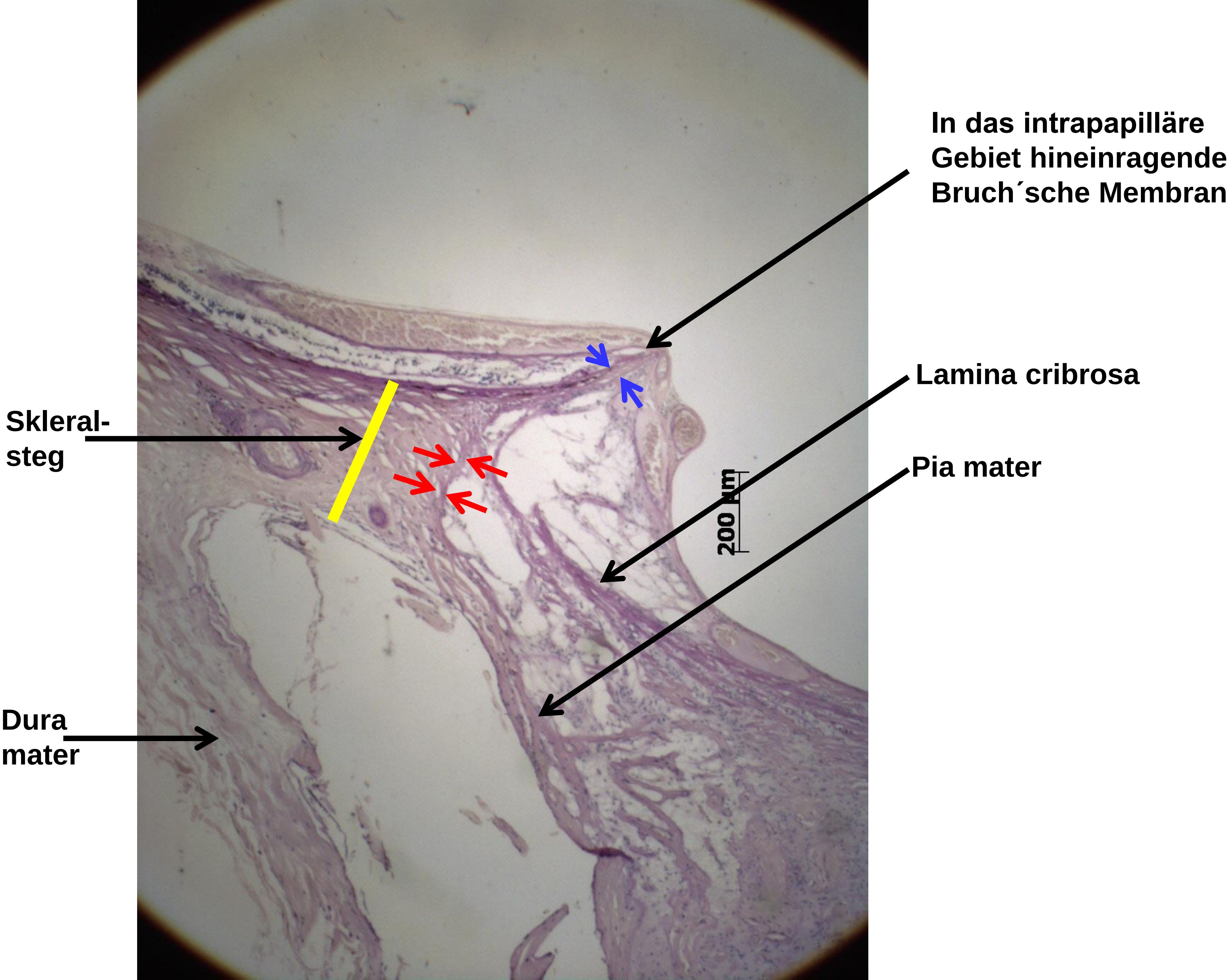
- Glaucomatous optic neuropathy was present in 141 (27.2%). increased from 12.2% in axial length <26.5mm to 42.1% in axial length ≥30mm



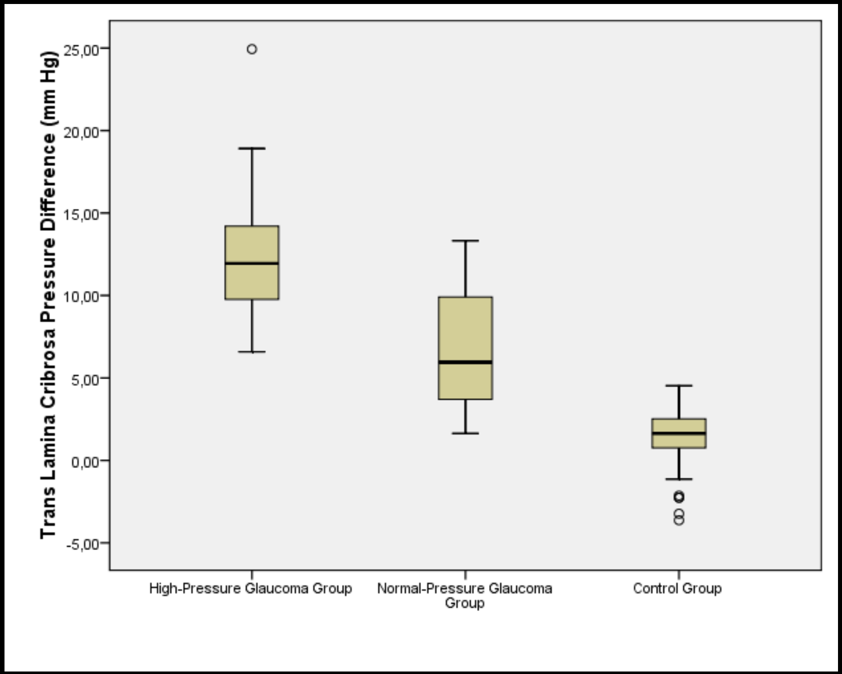
Jonas JB, Weber P, Nagaoka N, Ohno-Matsui K. Glaucoma in high myopia and parapapillary delta zone. PLoS One. 2017;12:e0175120

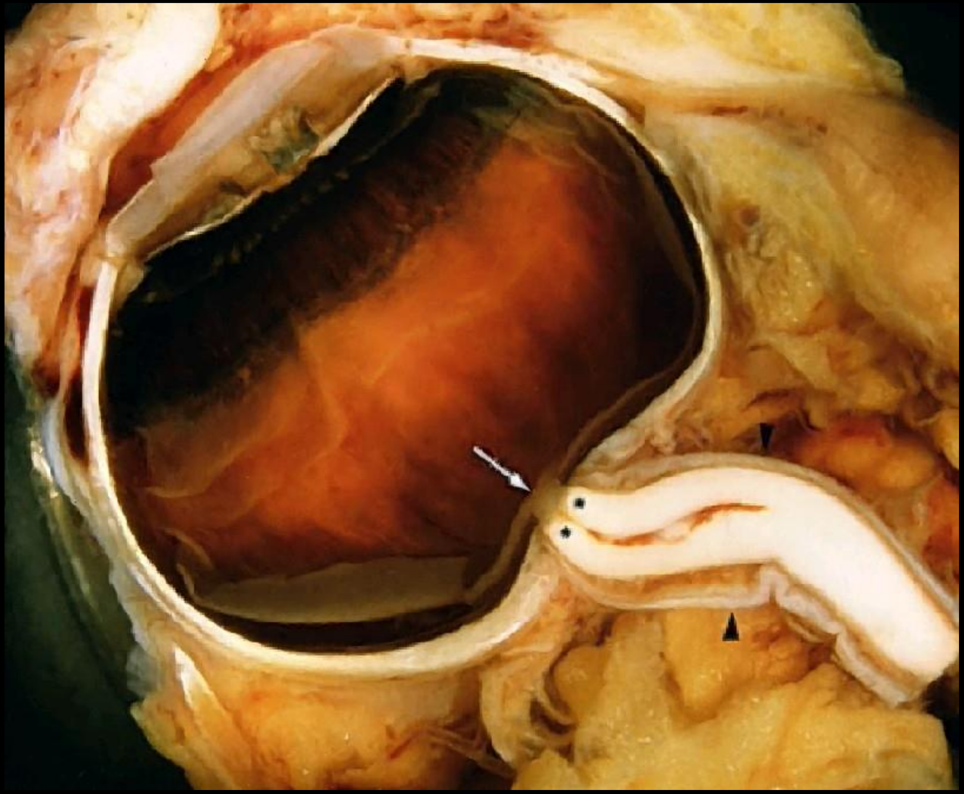
Histological Changes in the Optic Head in Highly Myopic Glaucoma

Jonas JB, Berenshtein E, Holbach L. Lamina cribrosa thickness and spatial relationships between intraocular space and cerebrospinal fluid space in highly myopic eyes. Invest Ophthalmol Vis Sci 2004; 45: 2660-2665


In das intrapapilläre Gebiet hineinragende Bruch´sche Membran
Lamina cribrosa
Pia mater
Skleral-steg
Dura mater
200 µm

Cerebrospinal Fluid Pressure: Component in Normal-Pressure Glaucoma?*





-Ren R, Jonas JB, Tian G, Zhen Y, Ma K, Li S, Wang H, Li B, Zhang X, Wang N. Cerebrospinal fluid pressure in glaucoma. A prospective study. Ophthalmology 2010;117:259-266

-Jonas JB. Role of cerebrospinal fluid pressure in the pathogenesis of glaucoma. Acta Ophthalmol 2011;89:505-514.

-Ren R, Zhang X, Wang N, Li B, Tian G, Jonas JB. Cerebrospinal fluid pressure in ocular hypertension. Acta Ophthalmol 2011;89;E142-E148

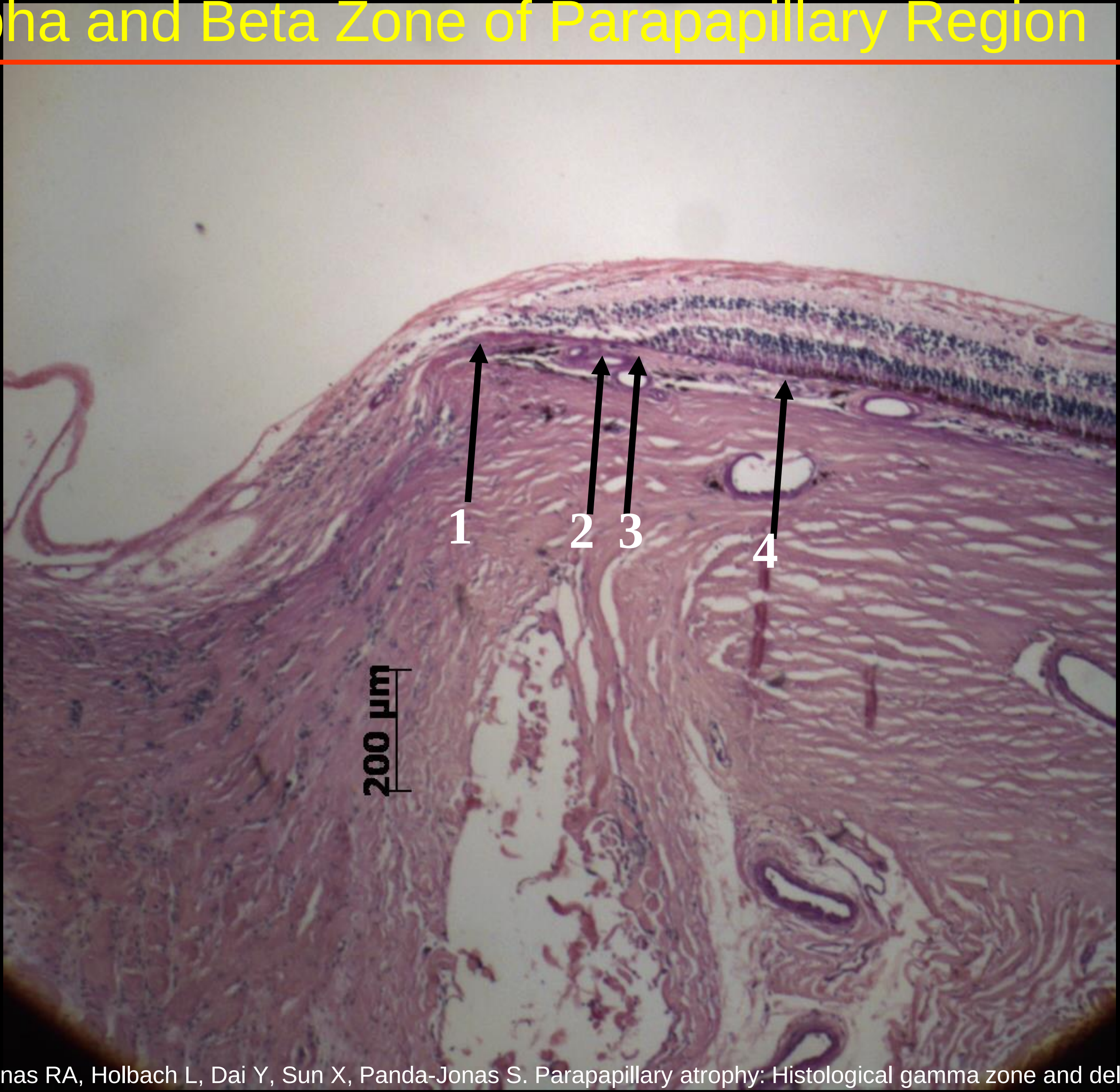
- Ren R, Wang NL, Zhang X, Tian G, Jonas JB. Cerebrospinal fluid pressure correlated with body mass index. Graefes Arch Clin Exp Ophthalmol 2012;250:445-446

- Jonas JB, Wang NL. Association between arterial blood pressure, cerebrospinal fluid pressure and intraocular pressure in the pathophysiology of optic nerve head diseases. Clin Exp Ophthalmol 2012;40:e233-234

- Xu L, Wang YX, Wang S, Jonas JB. Neuroretinal rim area and body mass index. PLoS One. 2012;7:e30104.

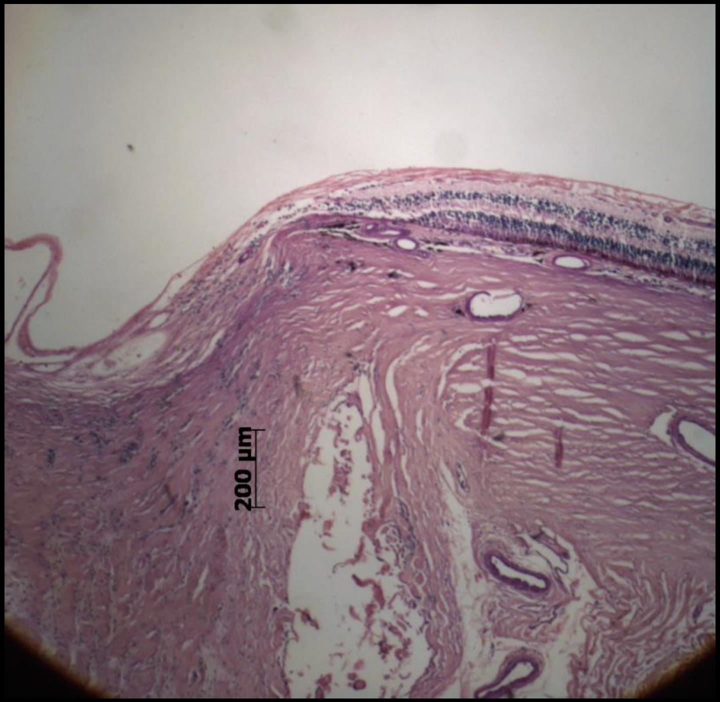
- Wang N, Xie X, Yang D, Xian J, Li Y, Ren R, Wang H, Zhang S, Kang Z, Peng X, Sang J, Zhang Z, Jonas JB, Weinreb RN. Orbital cerebrospinal fluid space in glaucoma. Ophthalmology. 2012 Oct;119(10):2065-2073.e1

Alpha and Beta Zone of Parapapillary Region



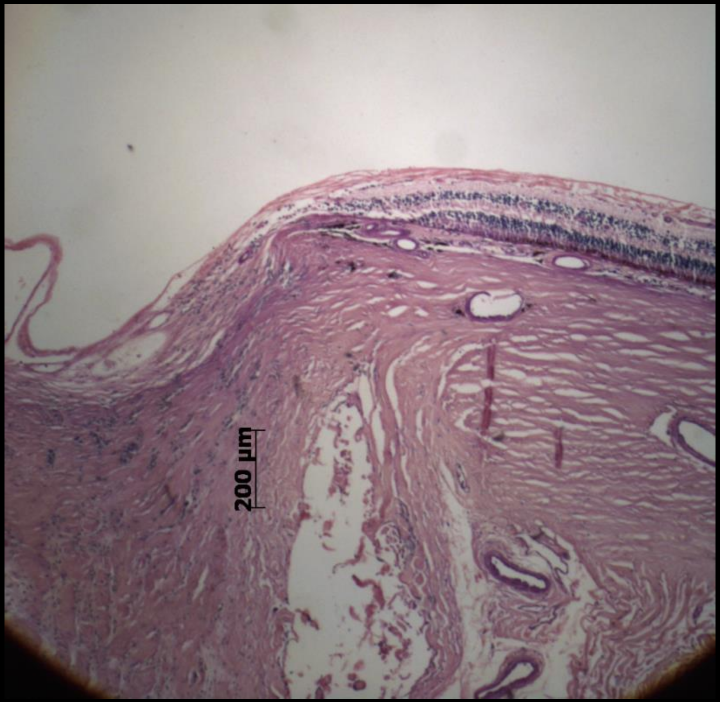
Jonas JB, Jonas SB, Jonas RA, Holbach L, Dai Y, Sun X, Panda-Jonas S. Parapapillary atrophy: Histological gamma zone and delta zone. PLoS One. 2012;7:e47237.

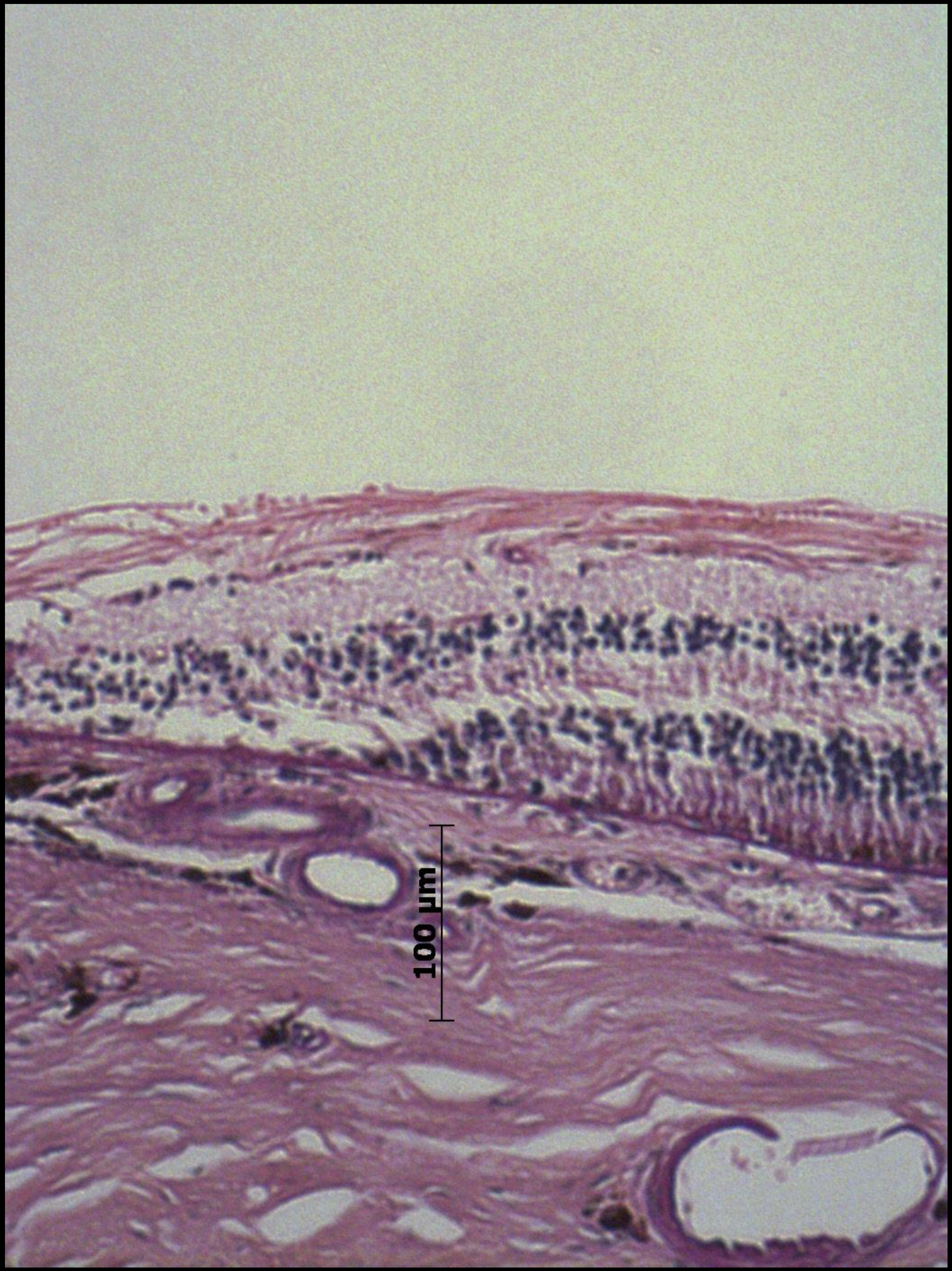
Alpha and Beta Zone of Parapapillary Region



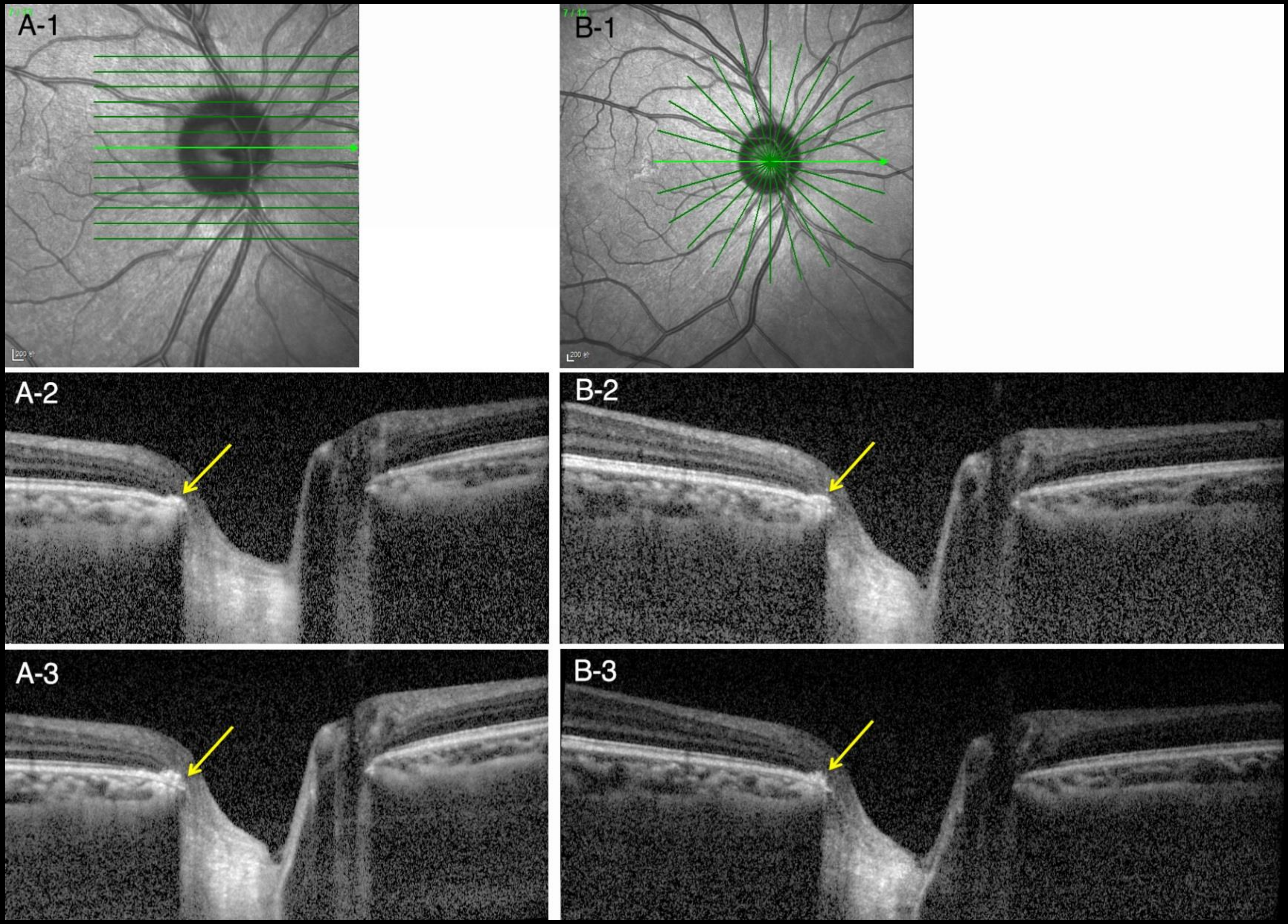
Jonas JB, Jonas SB, Jonas RA, Holbach L, Dai Y, Sun X, Panda-Jonas S. Parapapillary atrophy: Histological gamma zone and delta zone. PLoS One. 2012;7:e47237.

Alpha and Beta Zone of Parapapillary Region



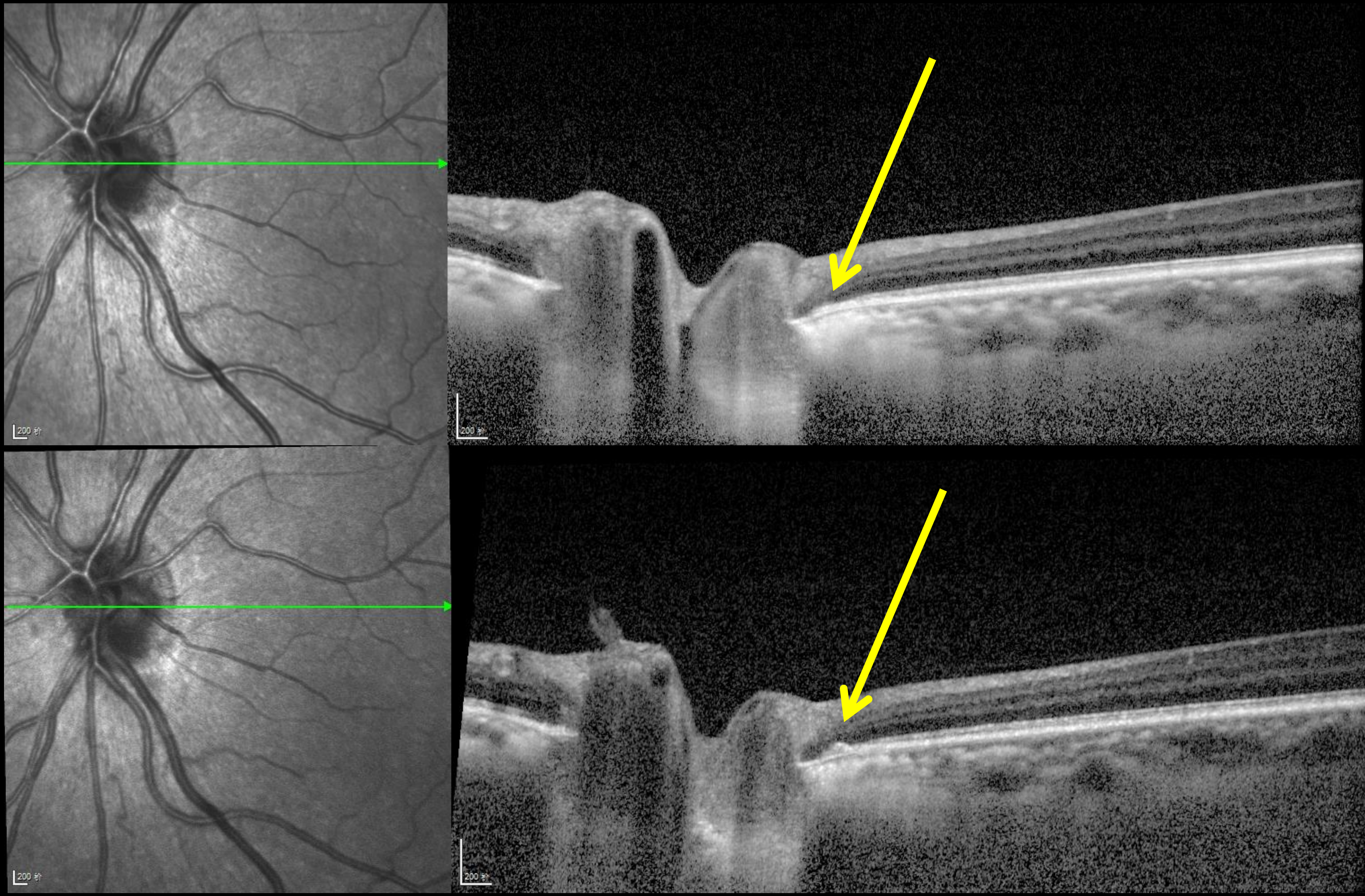


Dark Room Adaptation Test with IOP Rise from 22 mmHg to 50 mmHg



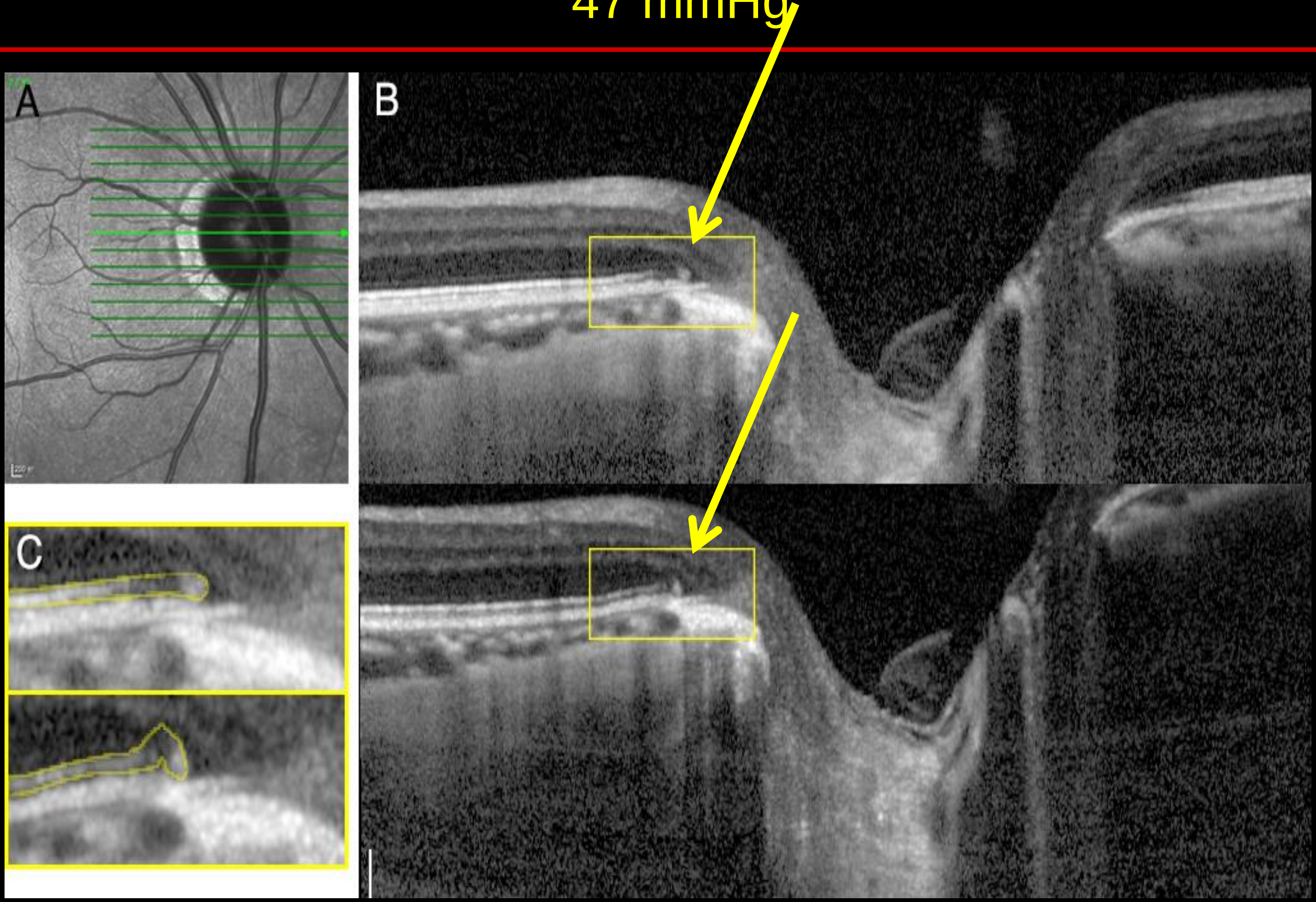
Wang YX, Jiang R, Wang NL, Xu L, Jonas JB. Acute peripapillary retinal pigment epithelium changes associated with acute intraocular pressure elevation. Ophthalmology 2015; In Print

Dark Room Adaptation Test with IOP Rise



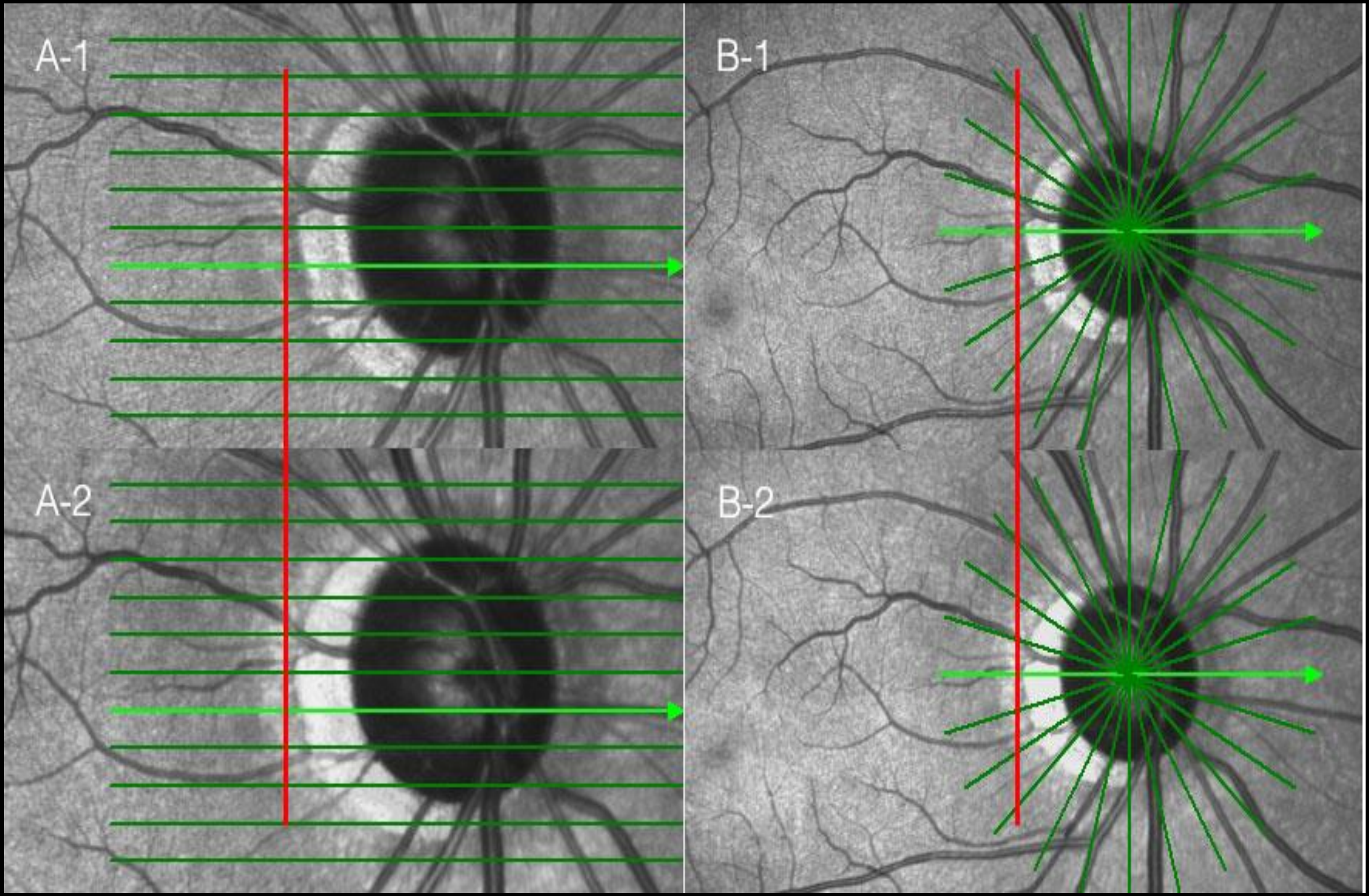
Wang YX, Jiang R, Wang NL, Xu L, Jonas JB. Acute peripapillary retinal pigment epithelium changes associated with acute intraocular pressure elevation. Ophthalmology 2015; In Print

Dark Room Adaptation Test with IOP Rise from 13 mmHg to 47 mmHg



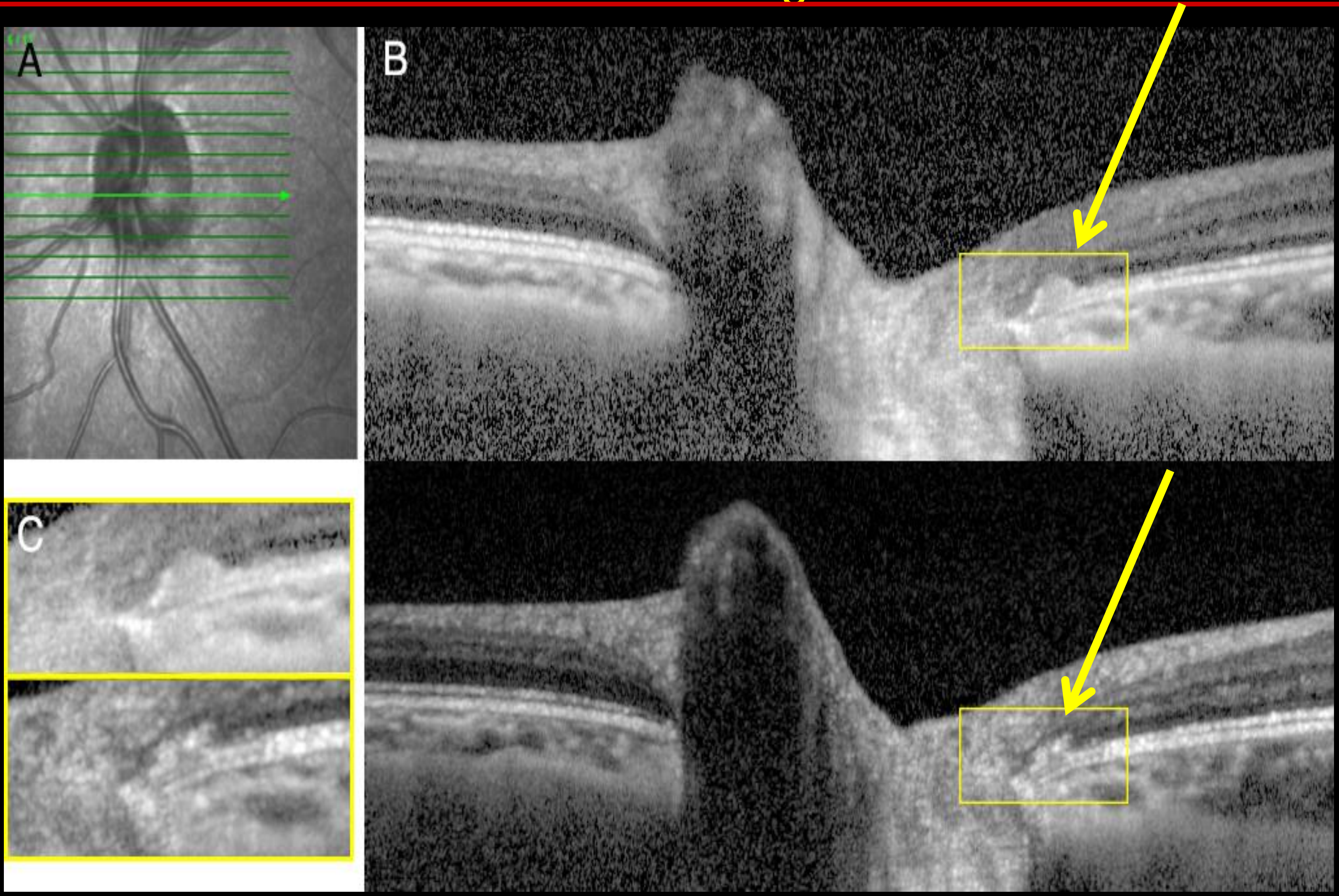
Wang YX, Jiang R, Wang NL, Xu L, Jonas JB. Acute peripapillary retinal pigment epithelium changes associated with acute intraocular pressure elevation. Ophthalmology 2015; In Print

Dark Room Adaptation Test with IOP Rise from 13 mmHg to 47 mmHg



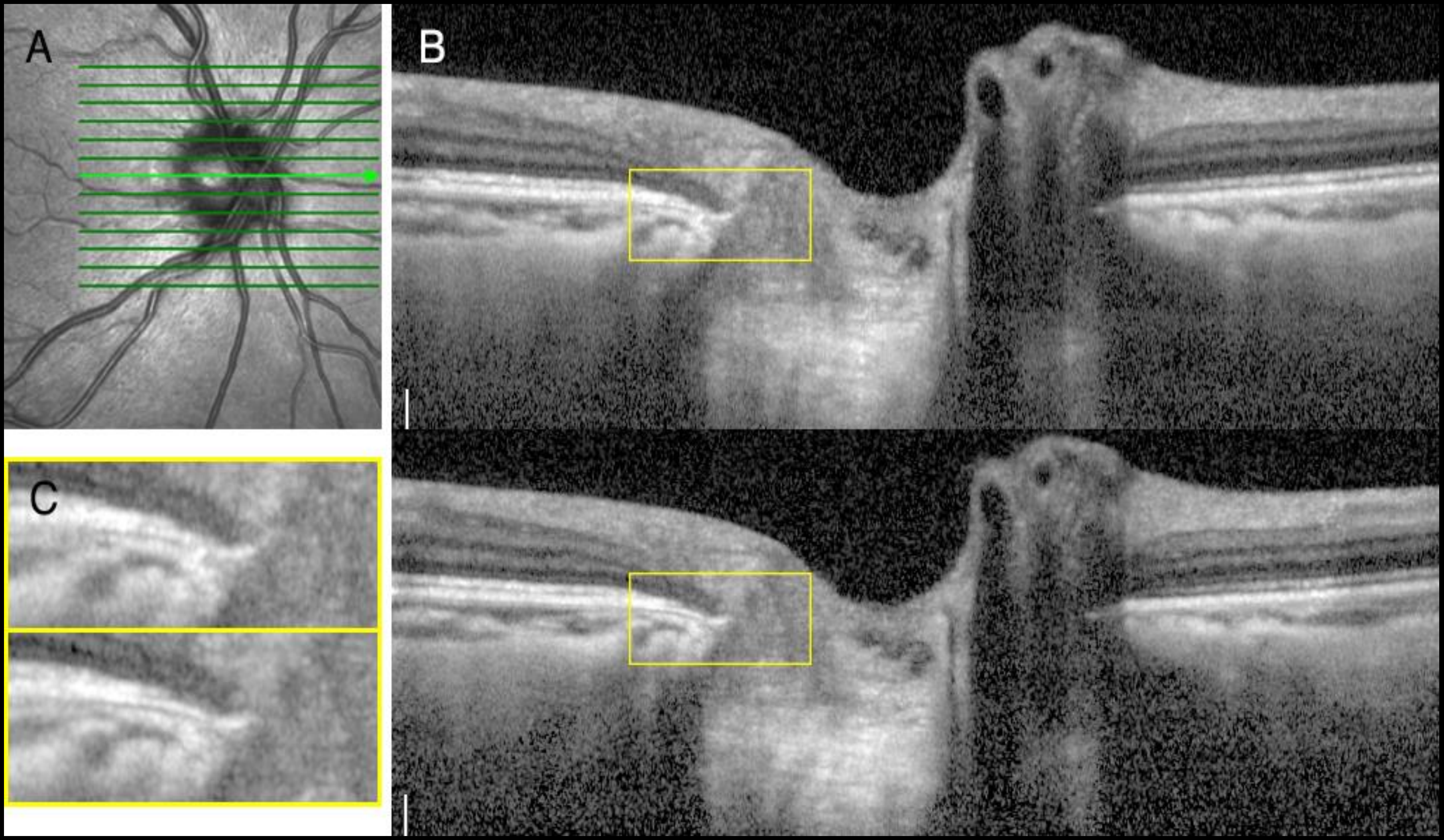
Wang YX, Jiang R, Wang NL, Xu L, Jonas JB. Acute peripapillary retinal pigment epithelium changes associated with acute intraocular pressure elevation. Ophthalmology 2015; In Print

Dark Room Adaptation Test with IOP Drop from 57 mmHg to 17 mmHg



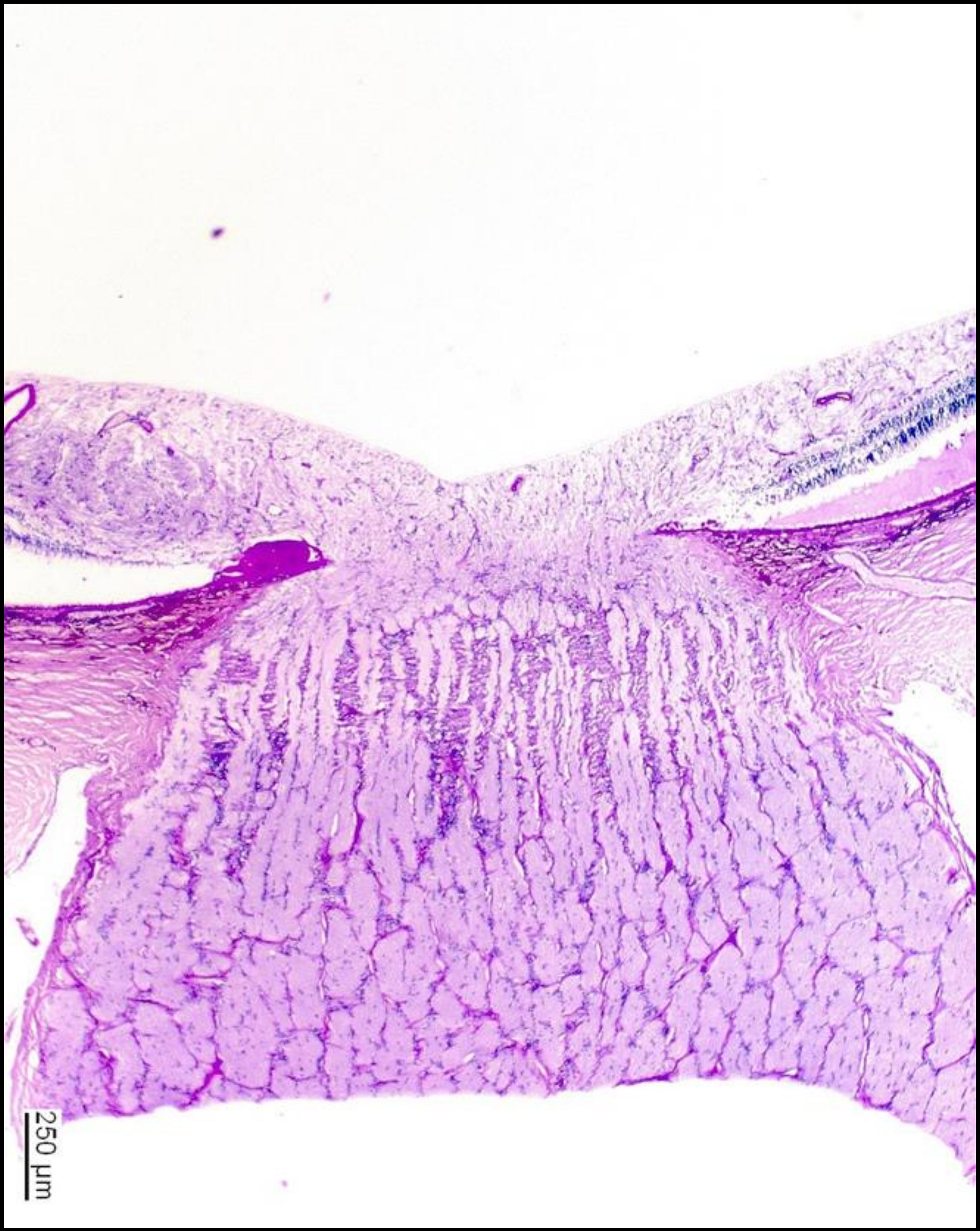
Wang YX, Jiang R, Wang NL, Xu L, Jonas JB. Acute peripapillary retinal pigment epithelium changes associated with acute intraocular pressure elevation. Ophthalmology 2015; In Print

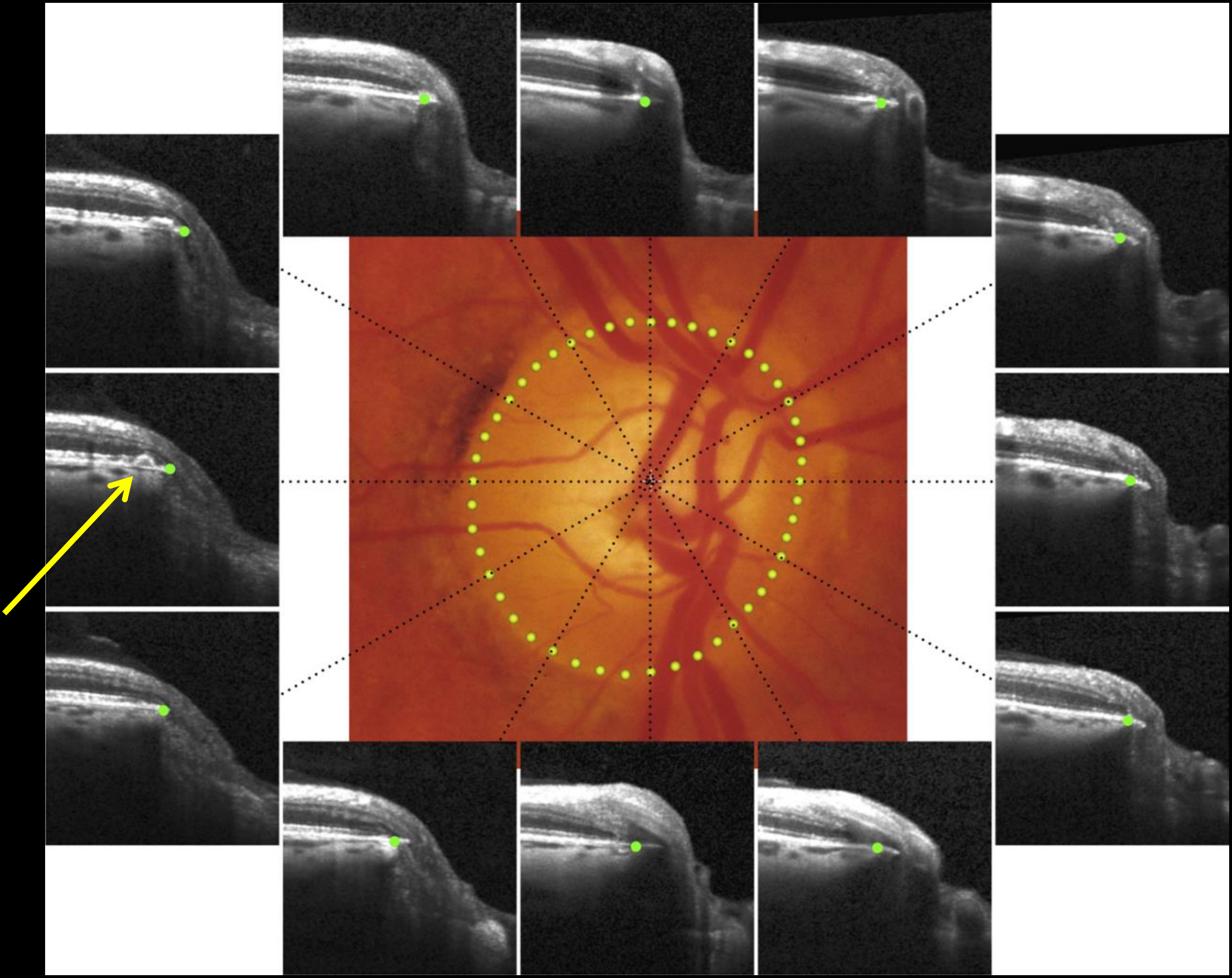
Dark Room Adaptation Test with IOP Rise from 16 mmHg to 36 mmHg without Change in RPE



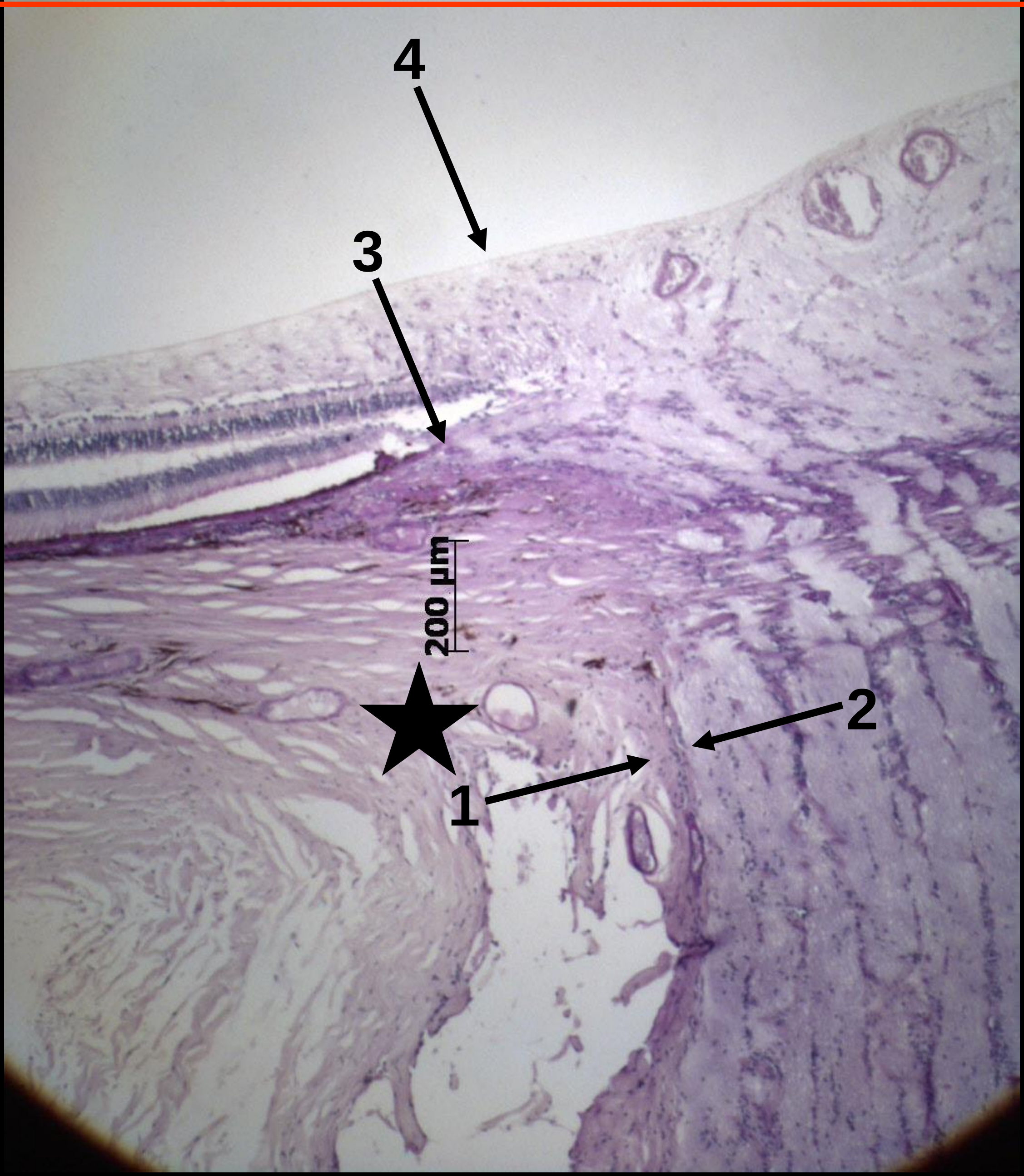
Wang YX, Jiang R, Wang NL, Xu L, Jonas JB. Acute peripapillary retinal pigment epithelium changes associated with acute intraocular pressure elevation. Ophthalmology 2015; In Print

Parapapillary Drusen of the RPE

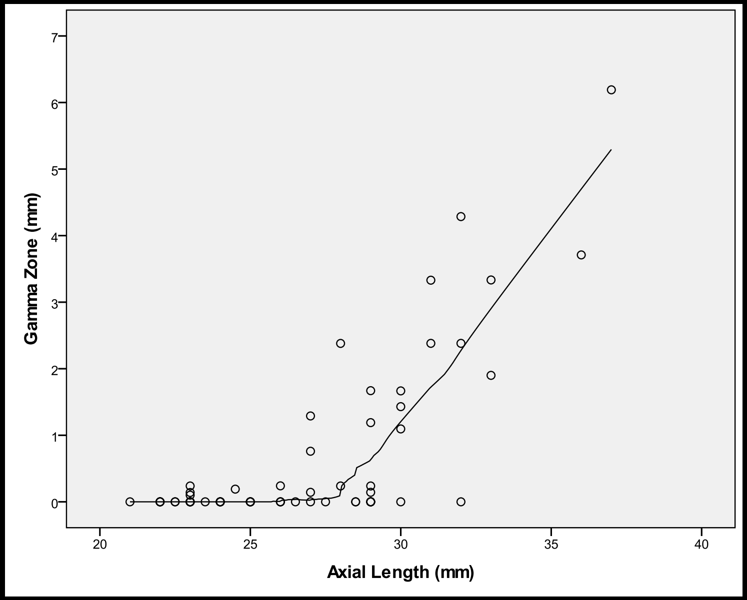


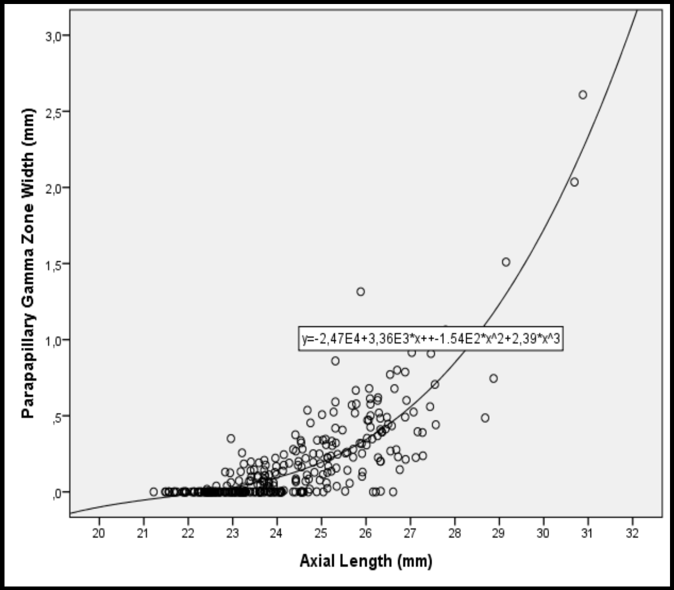


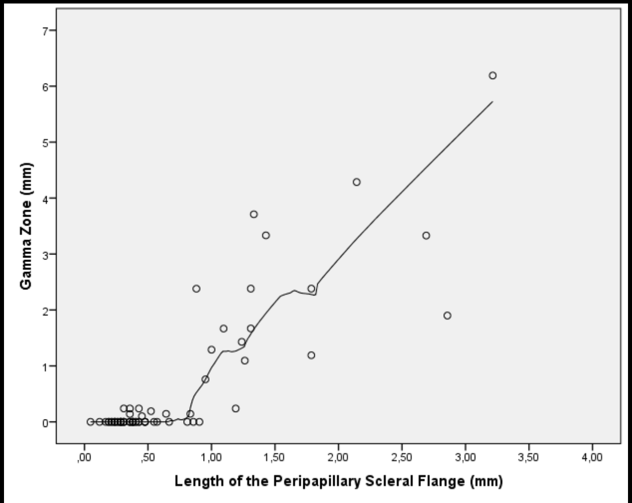
Gamma Zone of Parapapillary Region



Parapapillary Gamma Zone

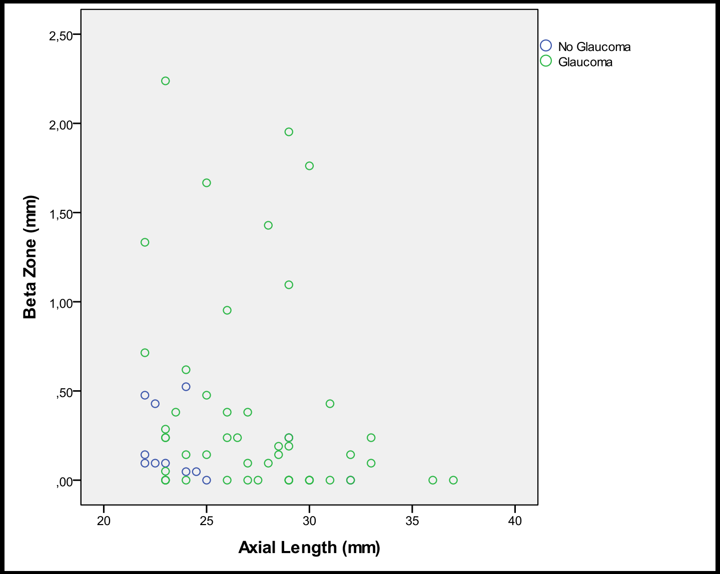


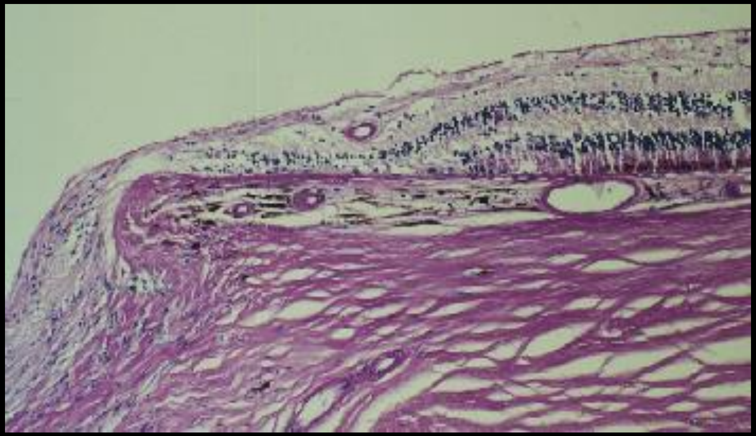


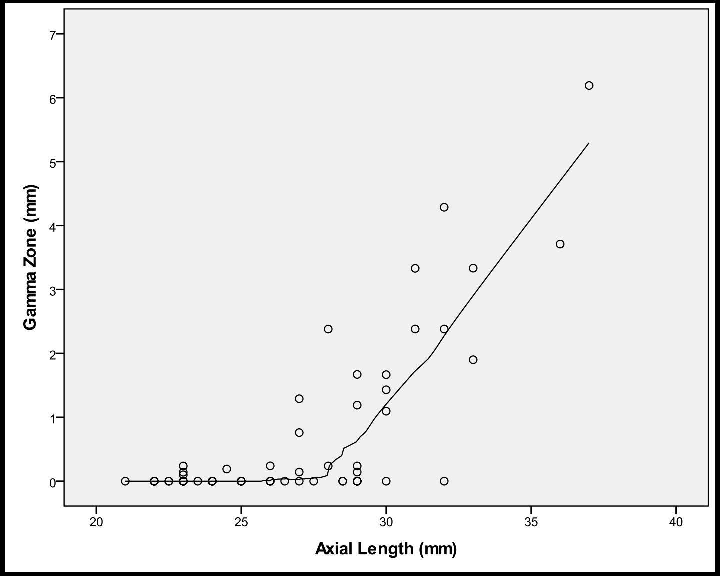


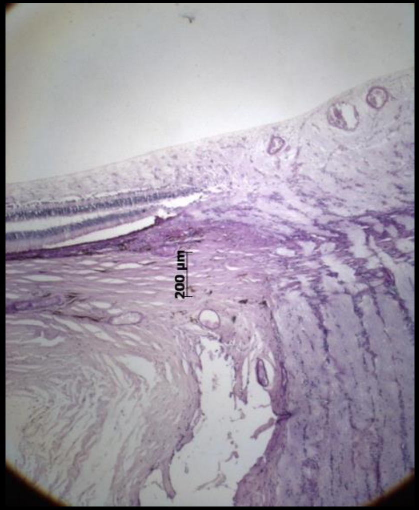
Jonas JB, Jonas SB,Jonas RA,Holbach L,Dai Y,Sun X,Panda-Jonas S.Parapapillary atrophy: Histological gamma zone and delta zone. PLoS One.2012;7:e47237
Jonas JB, Wang YX, Zhang Q, Liu Y, Xu L, Wei WB. Macular Bruch´s membrane length and axial length. The Beijing Eye Study. PloS One 2015;10:e0136833

Beta / Gamma Zone of Parapapillary Region



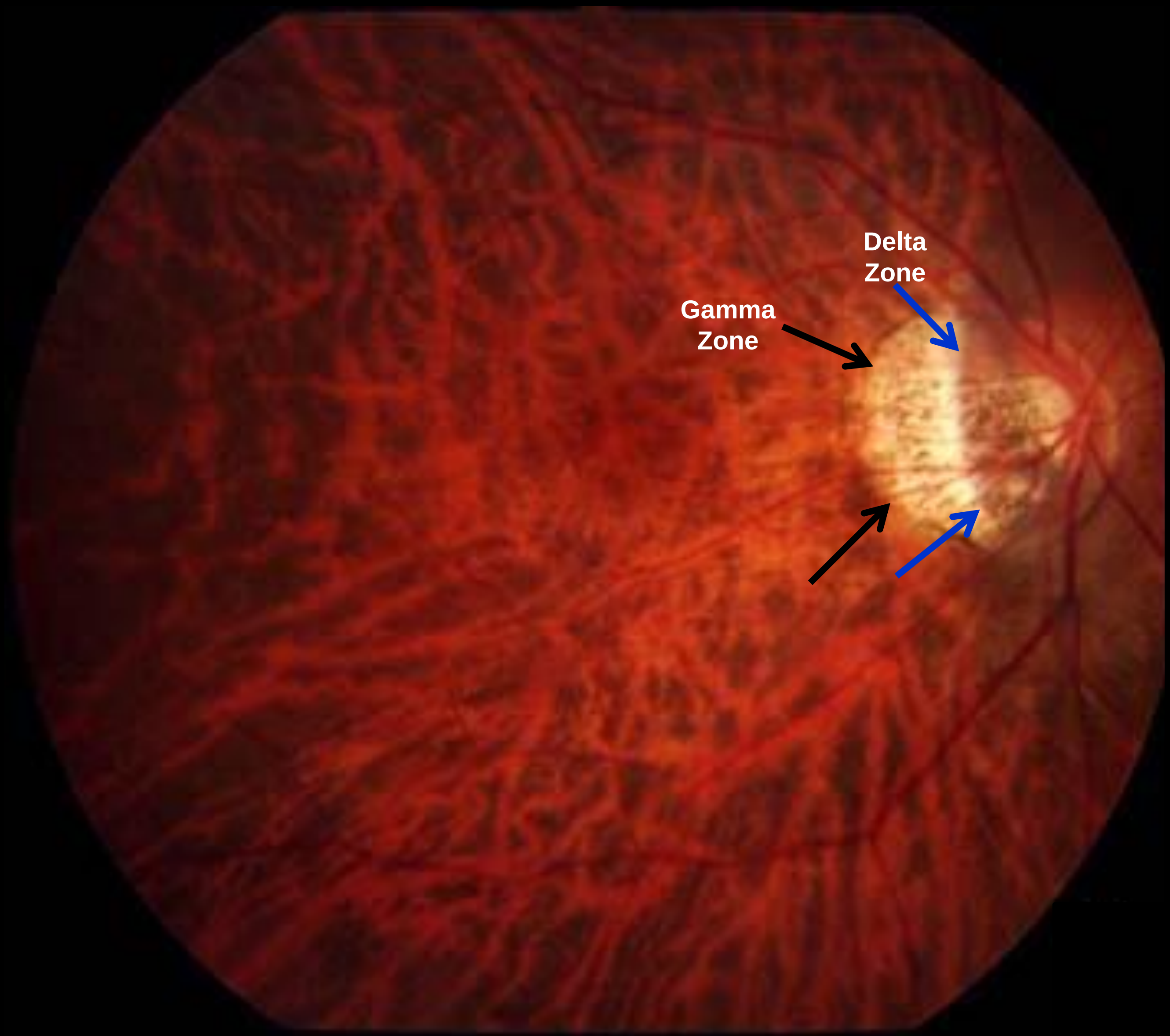




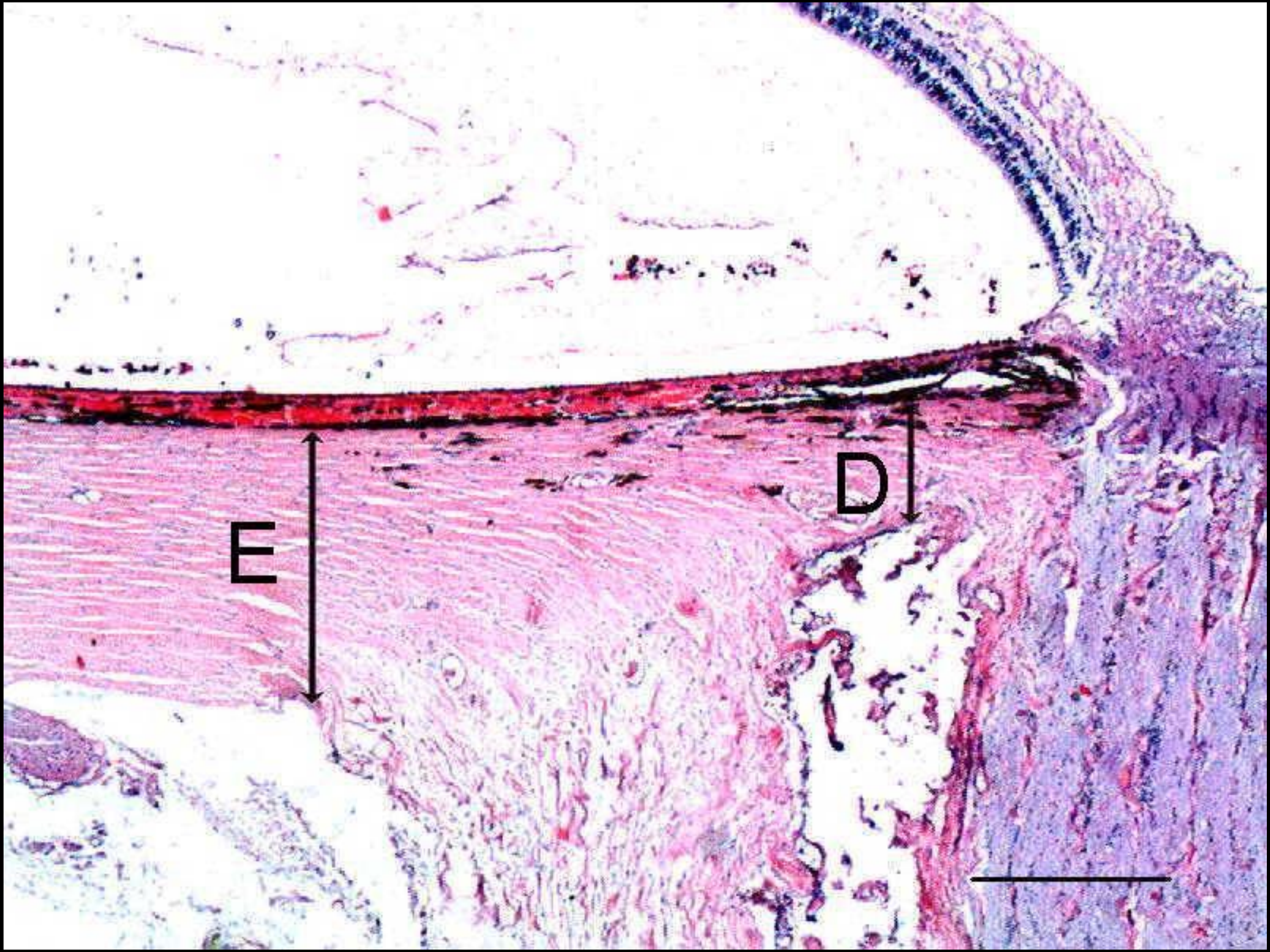


Jonas JB, Jonas SB, Jonas RA, Holbach L, Dai Y, Sun X, Panda-Jonas S. Parapapillary atrophy: Histological gamma zone and delta zone. PLoS One. 2012;7(10):e47237.

Parapapillary Gamma Zone and Delta Zone

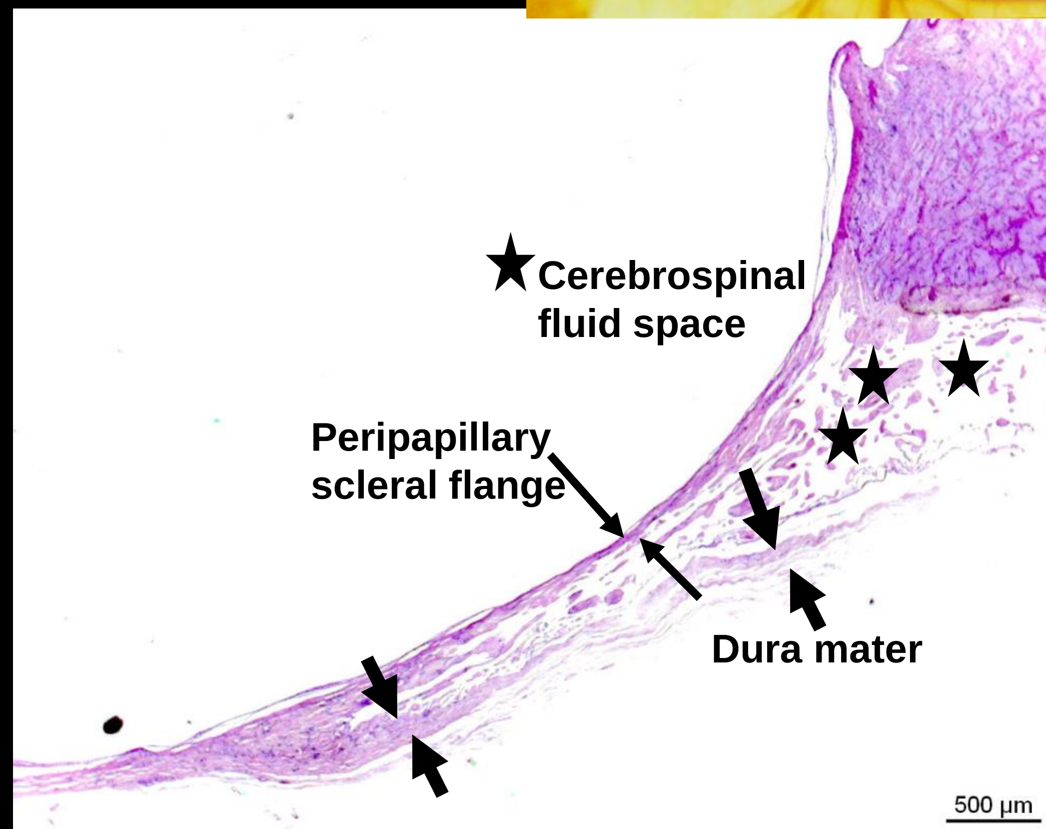


Peripapillary Scleral Flange = 50% of Posterior Sclera



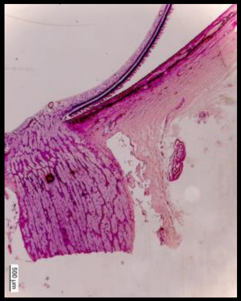
Ren R, Wang N, Li B, Li L, Gao F, Xu X, Jonas JB. Lamina cribrosa and peripapillary sclera histomorphometry in normal and advanced glaucomatous Chinese eyes with normal and elongated axial length. Invest Ophthalmol Vis Sci; 2009;50:2175-2184.

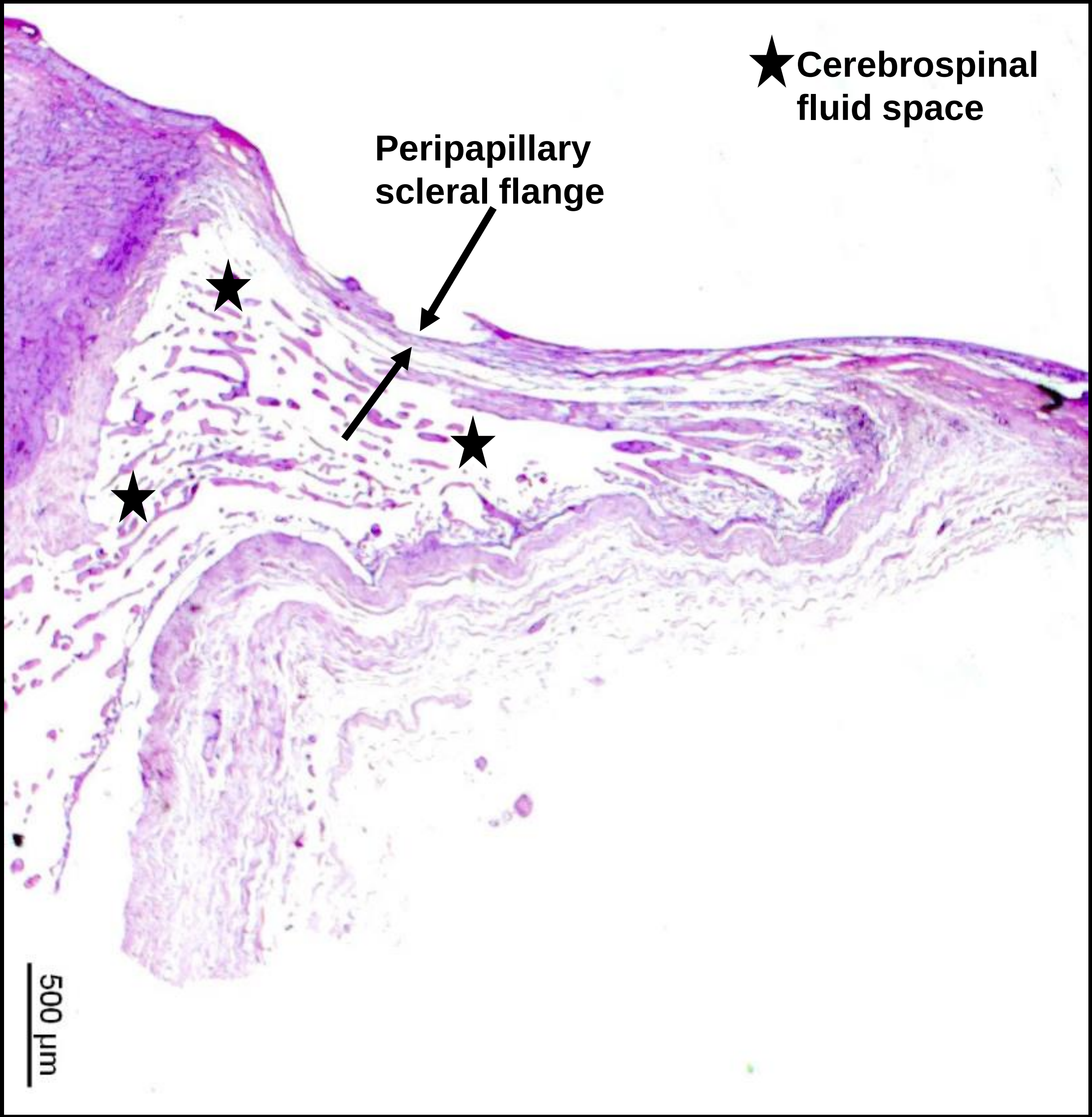
Thinning of the Peripapillary Sclera in Highly Myopic Eyes



Dichtl A, Jonas JB, Naumann GOH. Histomorphometry of the optic disc in highly myopic eyes with glaucoma. Br J Ophthalmol 1998;82:286-9.
Jonas JB, Jonas SB Jonas RA, Holbach L, Panda-Jonas S. Histology of the parapapillary region in high myopia. Am J Ophthalmol 2011;152:1021-9

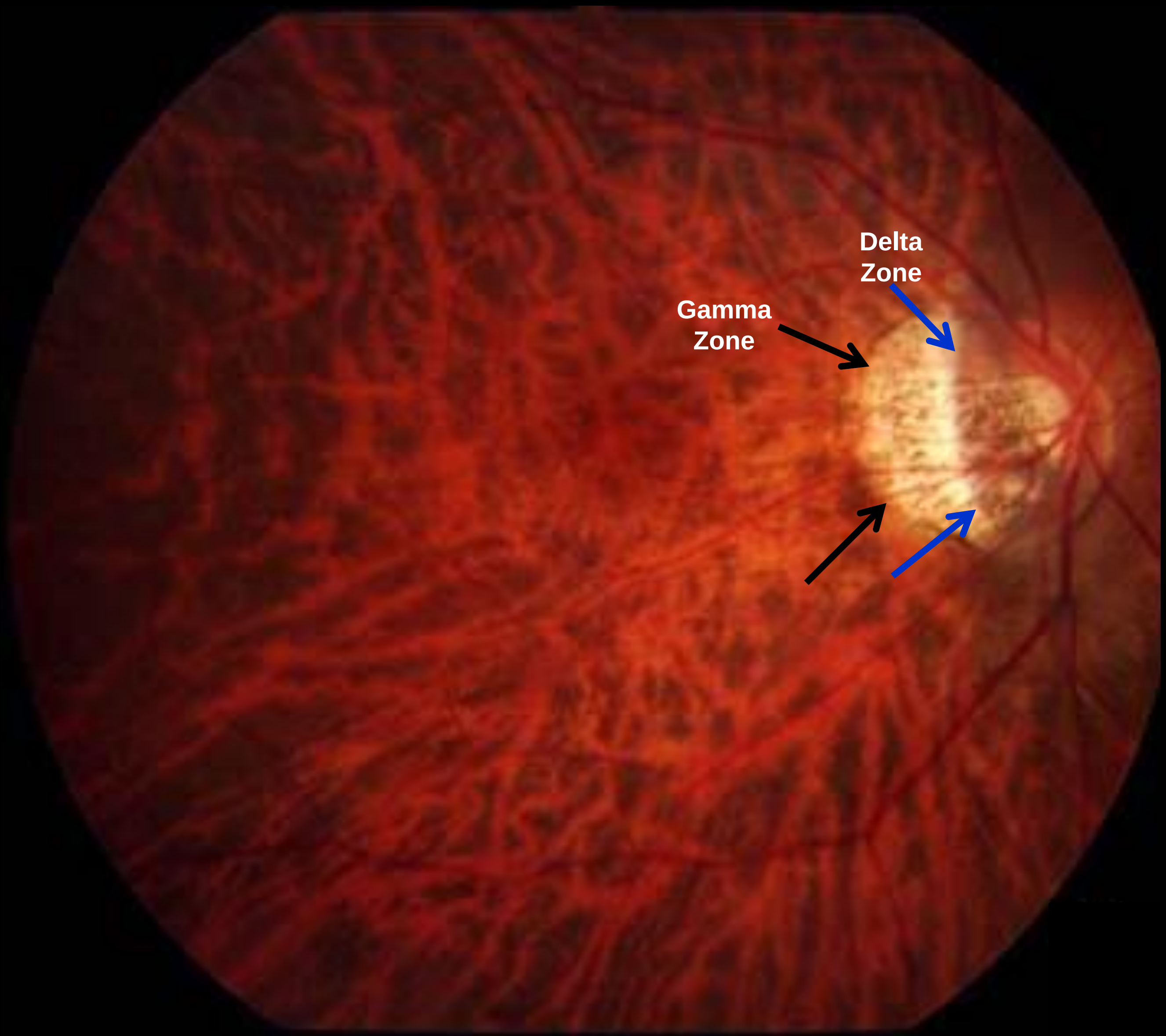
Parapapillary Delta Zone: Peripapillary Scleral Flange in High Myopia

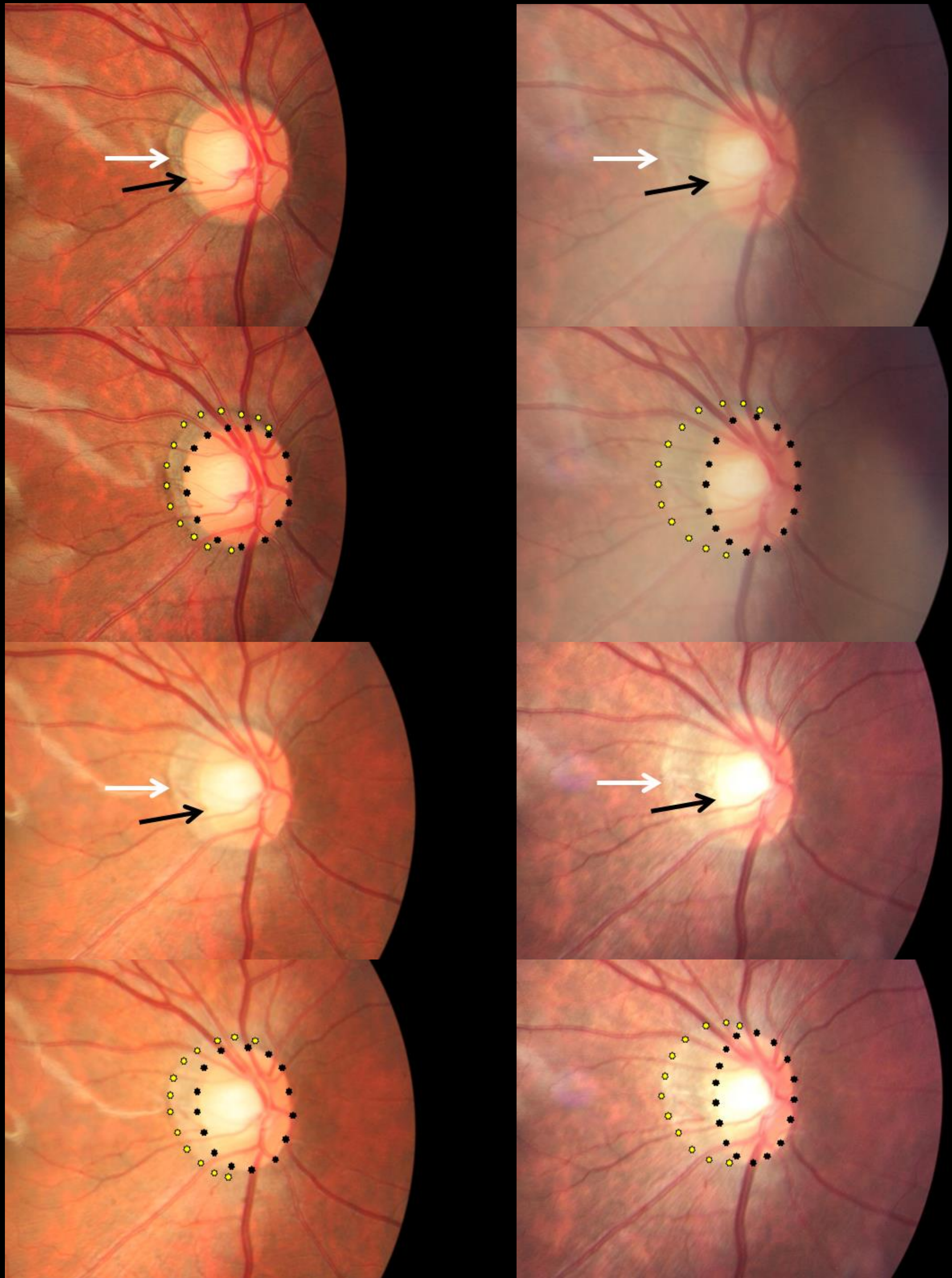


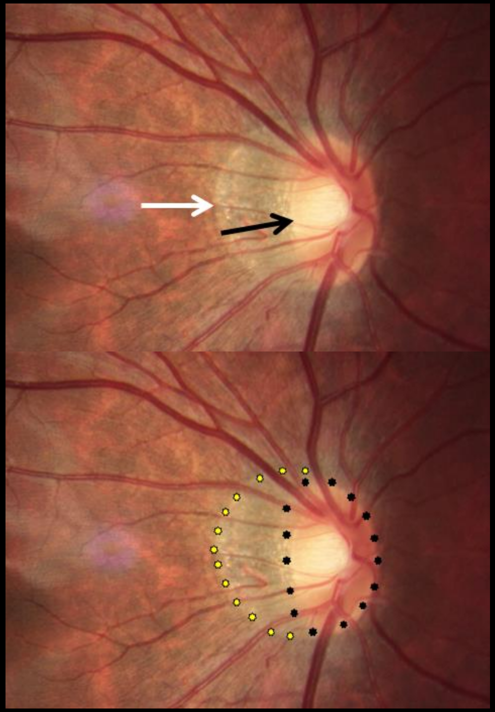


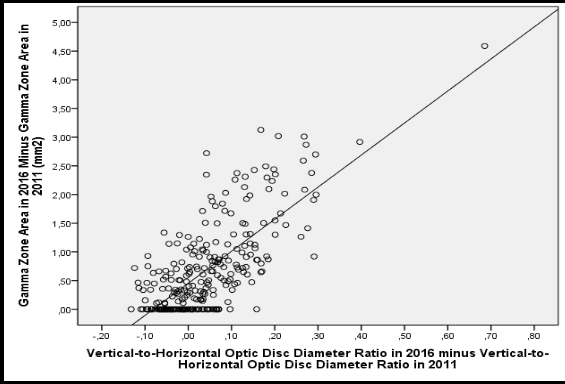
Jonas JB, Jonas SB Jonas RA, Holbach L, Panda-Jonas S. Histology of the parapapillary region in high myopia. *Am J Ophthalmol. 2011;152:1021-1029.*

Parapapillary Gamma Zone and Delta Zone





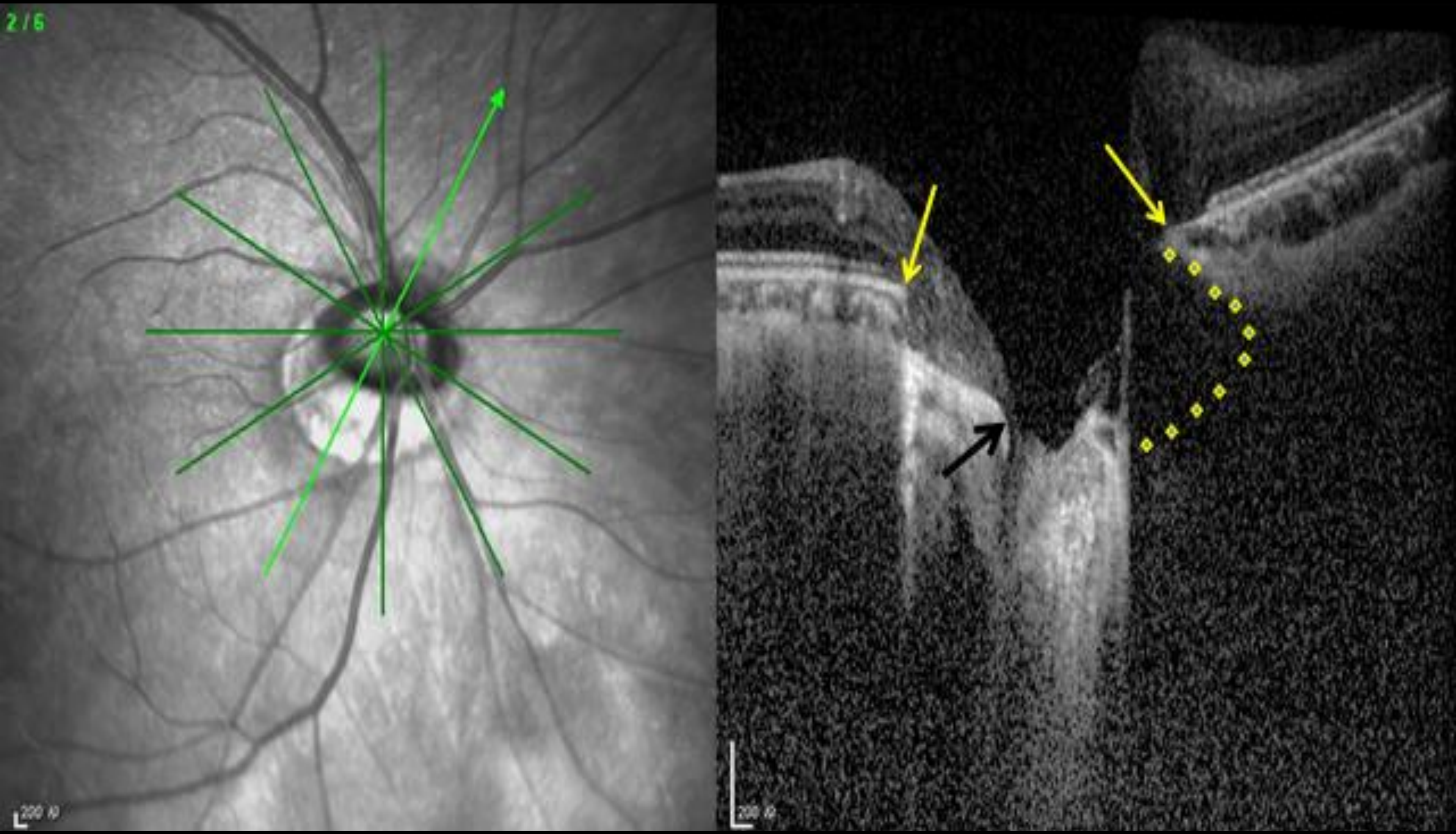




Guo Y, Liu LJ, Tang P, Feng Y, Lv YY, Wu M, Xu L, Jonas JB. Parapapillary gamma zone and progression of myopia in school children: The Beijing Children Eye Study. Invest Ophthalmol Vis Sci 2018;59:1609-1616

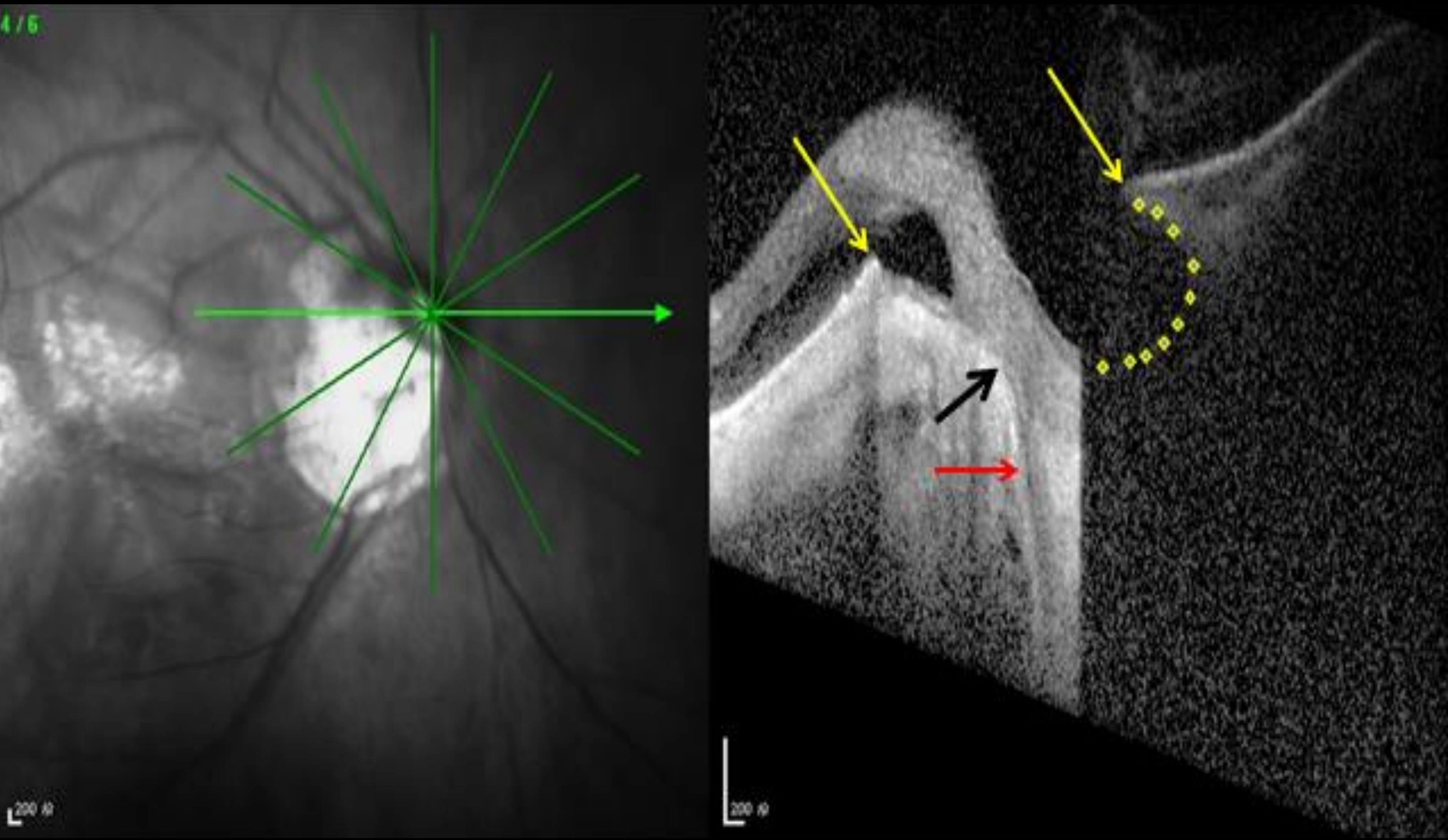

2006-12-25
2008-09-28
2011-09-01

Bruch´s Membrane Opening



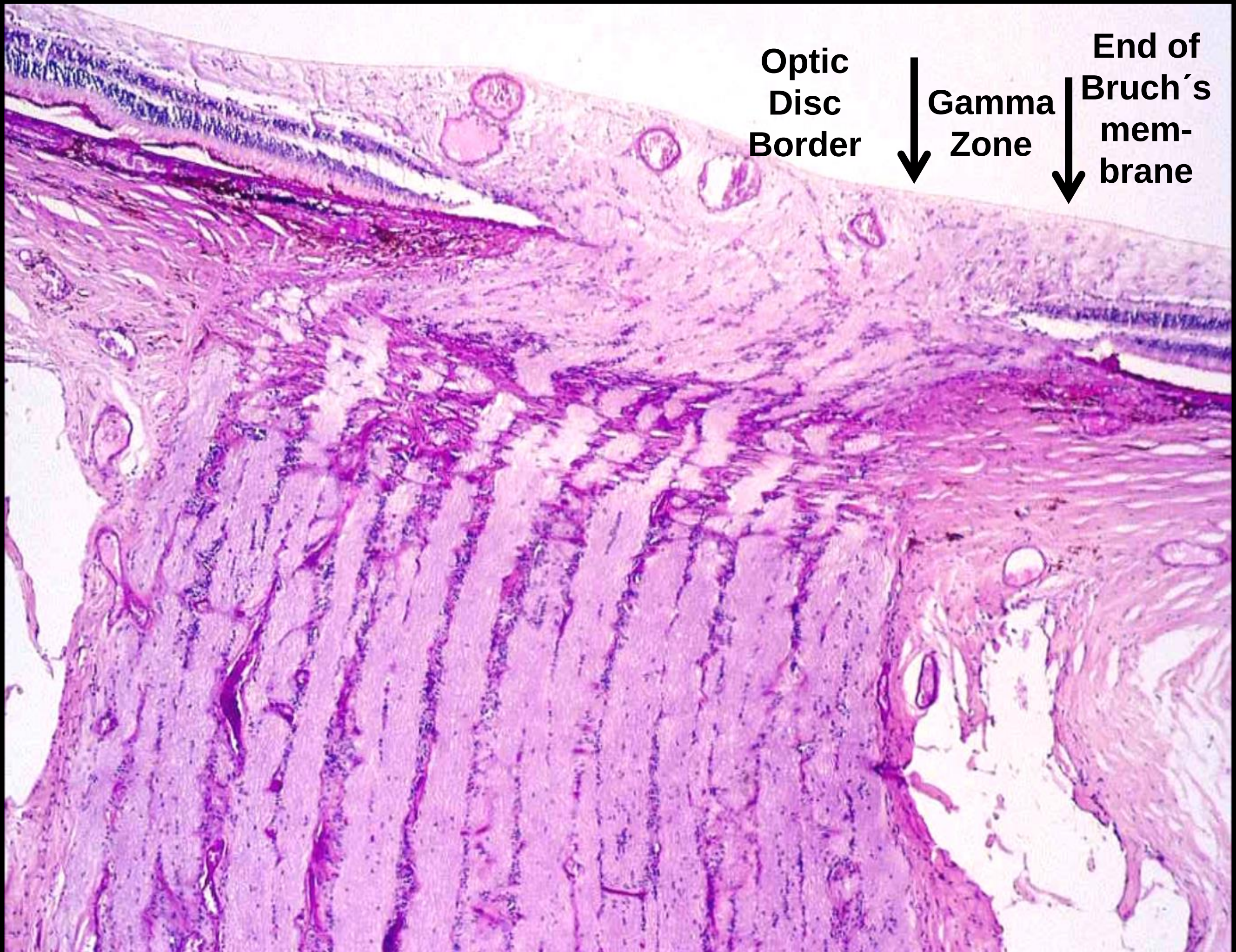
Zhang Q, Xu L, Wei WB, Wang YX, Jonas JB. Size and shape of Bruch´s membrane opening in relationship to axial length, gamma zone and macular Bruch´s membrane defects. Invest Ophthalmol Vis Sci 2019;;60:2591-8

Bruch s Membrane Opening

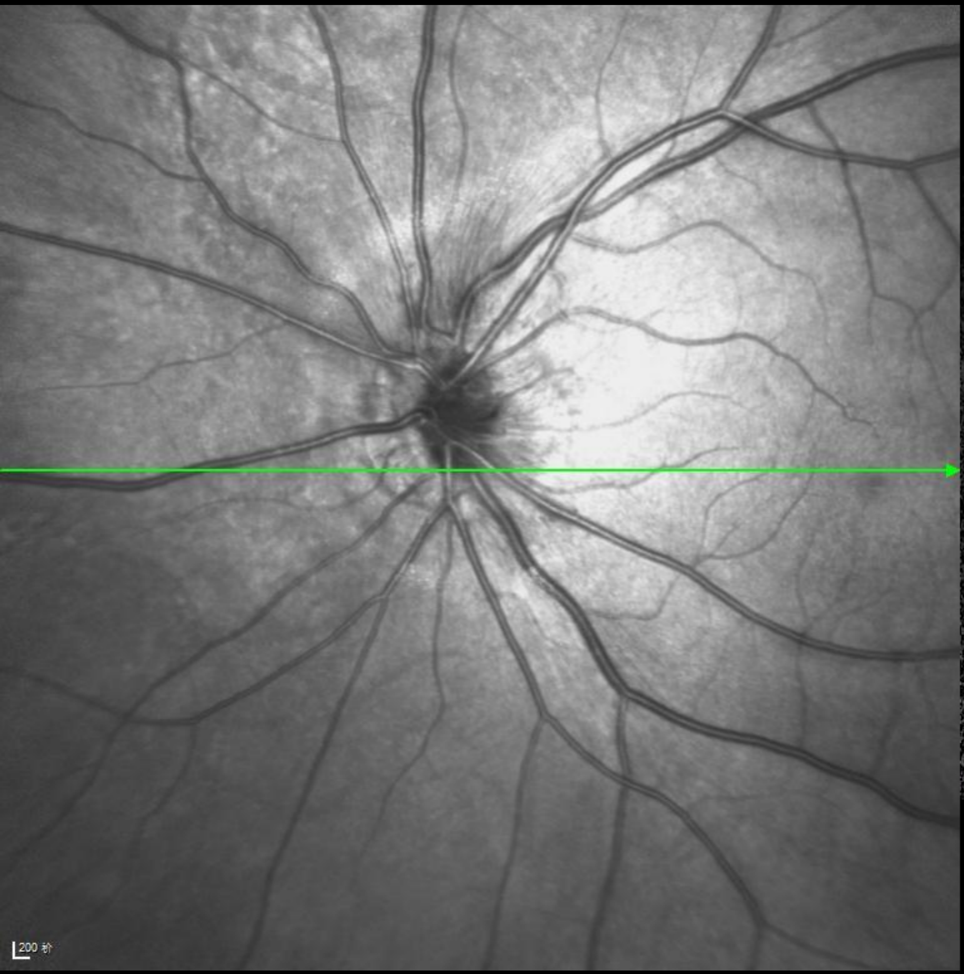


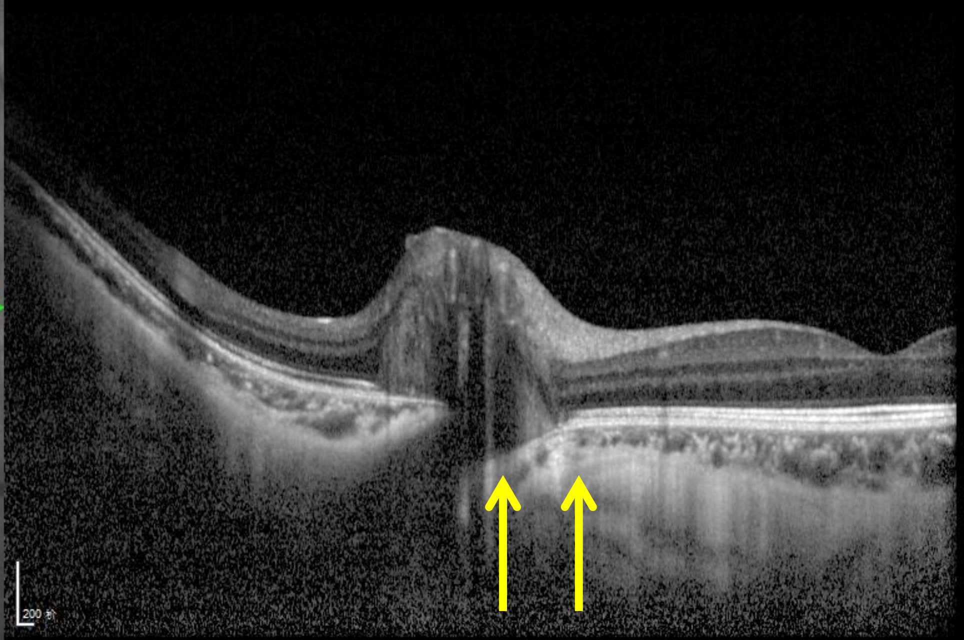
Zhang Q, Xu L, Wei WB, Wang YX, Jonas JB. Size and shape of Bruch´s membrane opening in relationship to axial length, gamma zone and macular Bruch´s membrane defects. Invest Ophthalmol Vis Sci 2019;;60:2591-8

Mechanism of Process of Emmetropization (Myopization)
Temporal Shift of BM-Opening and Oblique Orientation of the Optic Nerve Head

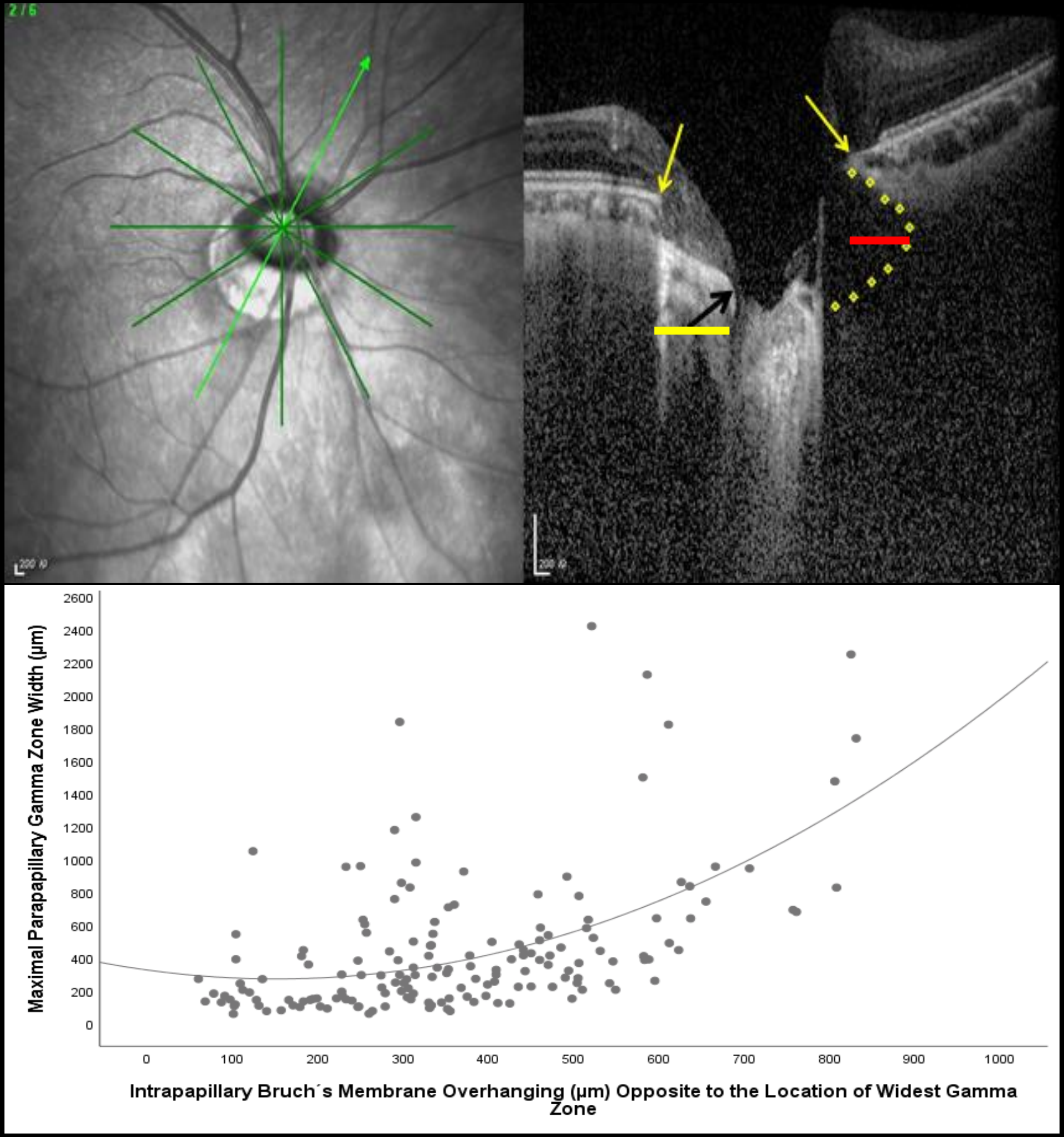


Oblique Opticnerve Head Channel



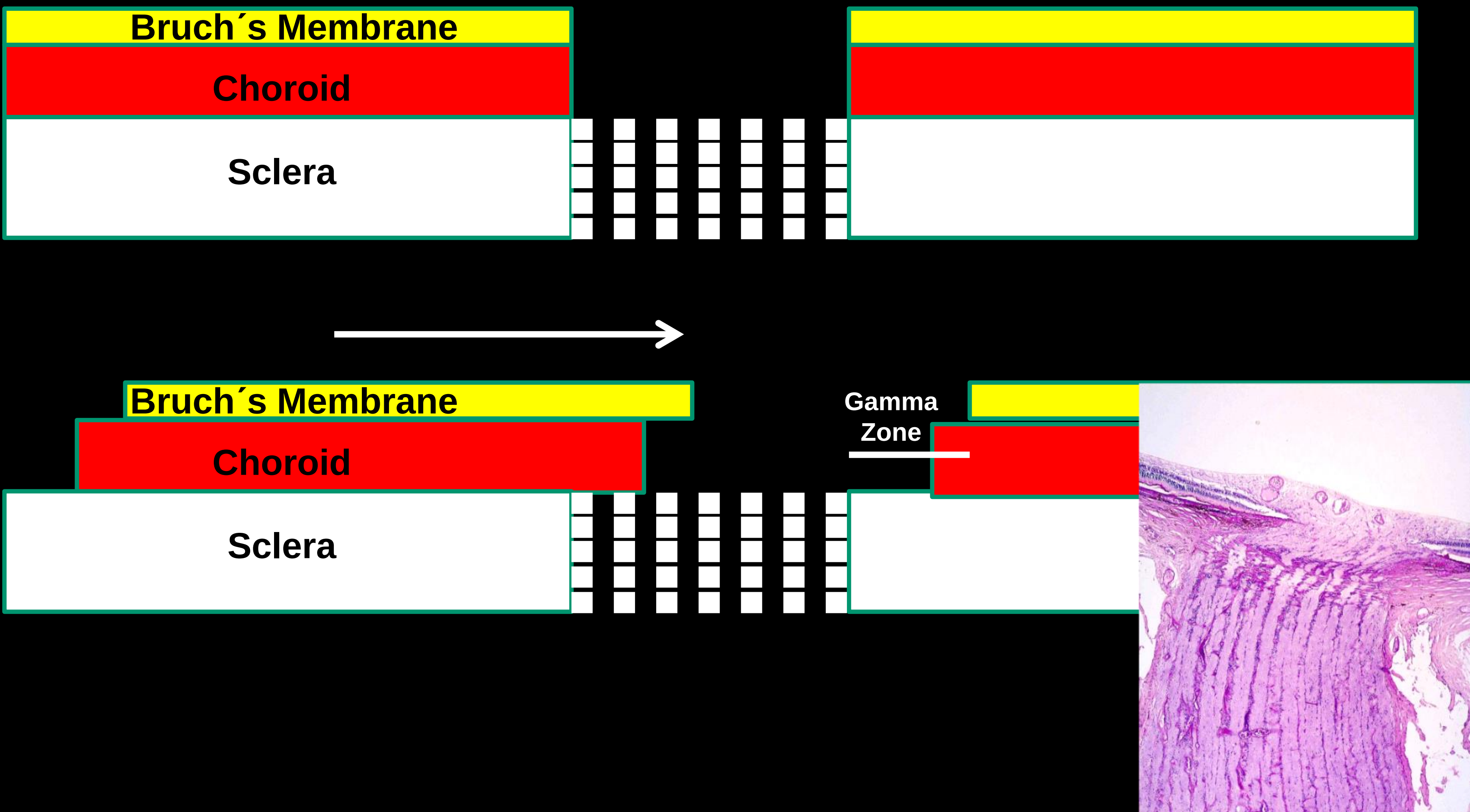


Bruch´s Membrane Opening

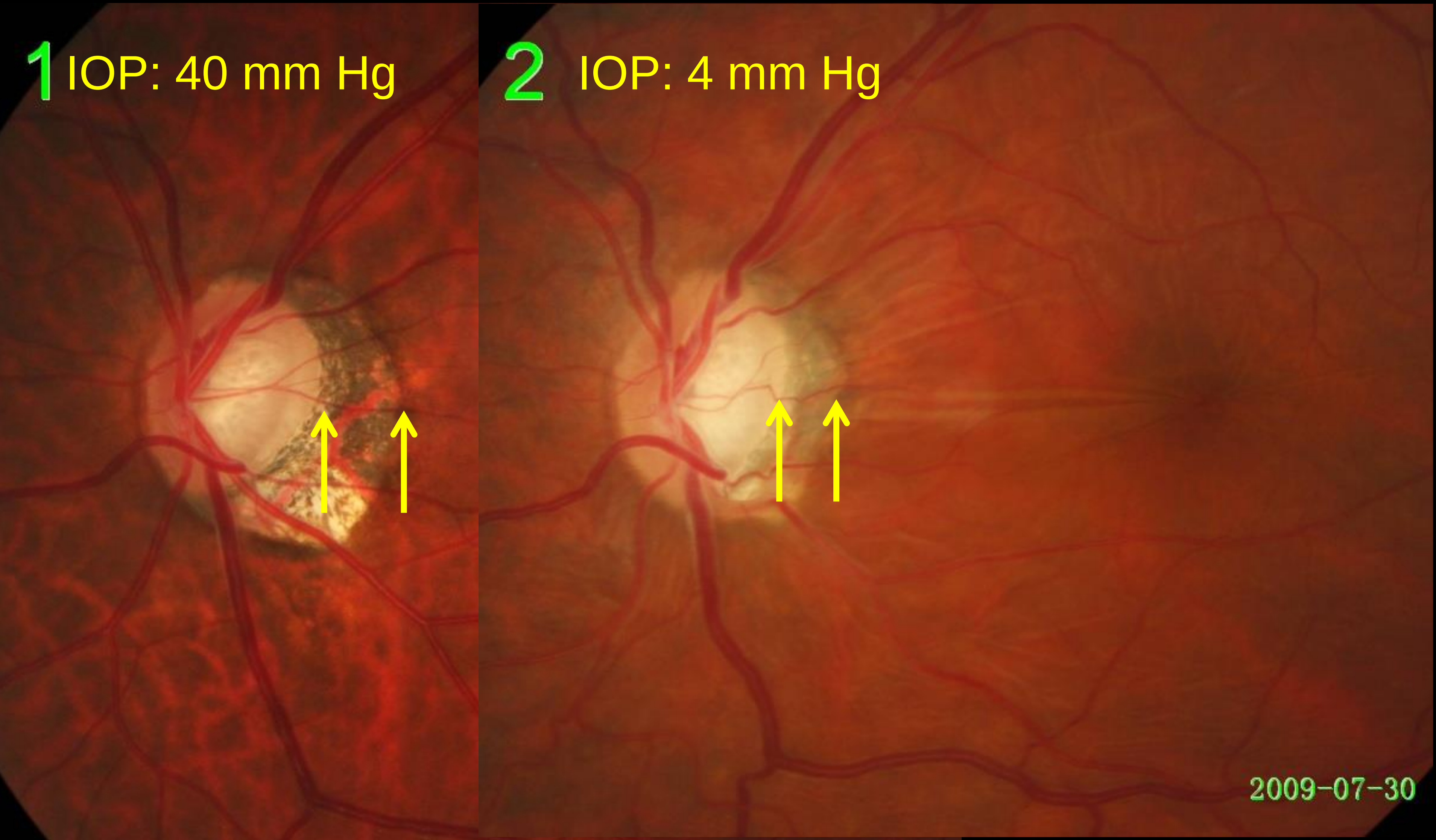


Zhang Q, Xu L, Wei WB, Wang YX, Jonas JB. Size and shape of Bruch´s membrane opening in relationship to axial length, gamma zone and macular Bruch´s membrane defects. The Beijing Eye Study. Submitted 2019

Parapapillary Gamma Zone and Bruch´s Membrane Opening: Optic Nerve Head as Three-Layered Hole

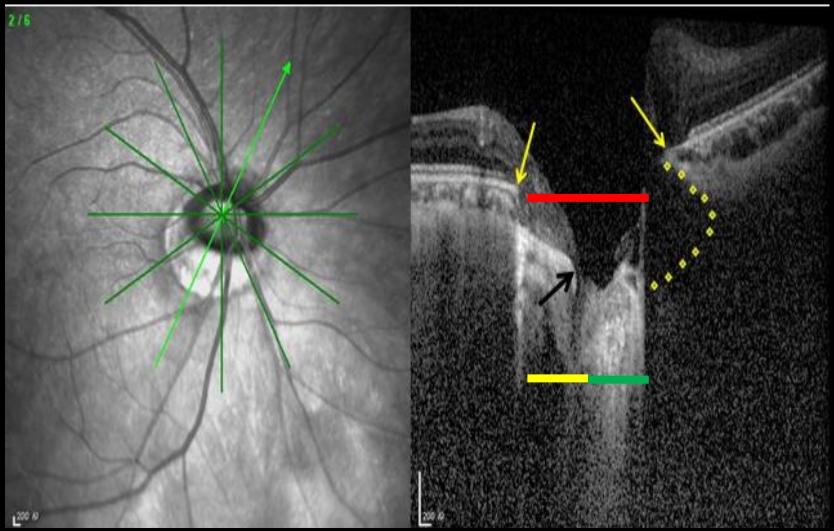


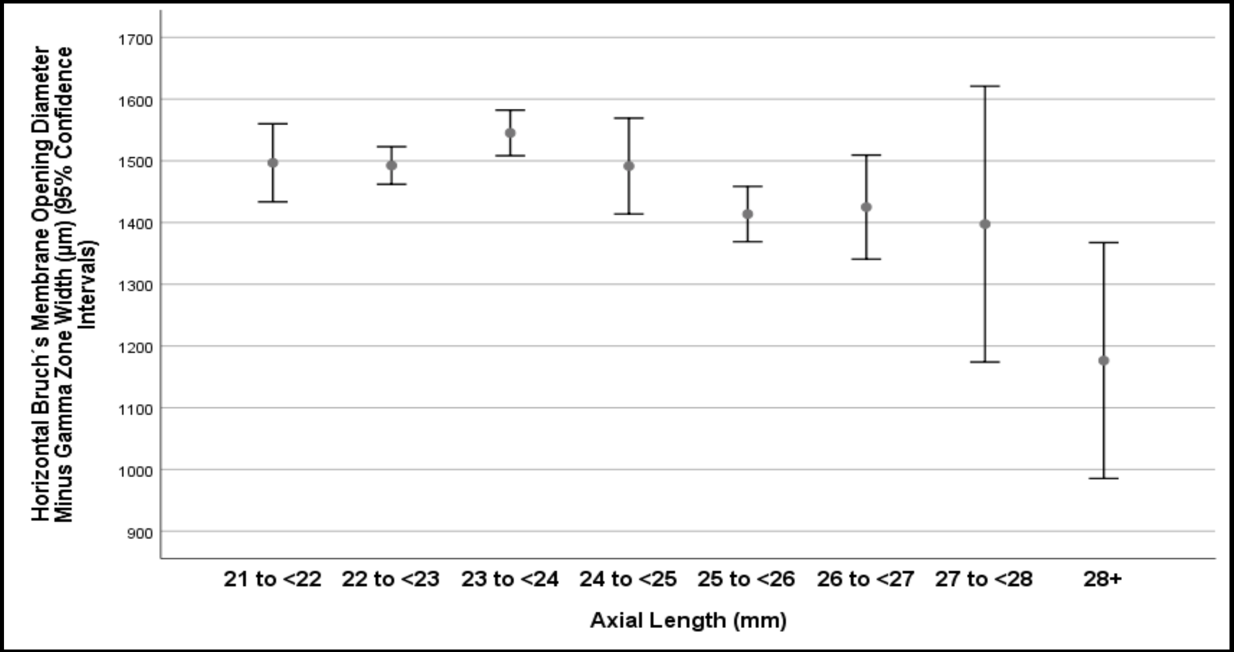
Etiology of Gamma Zone: Bruch´s Membrane Opening:
Sliding of Bruch´s Membrane



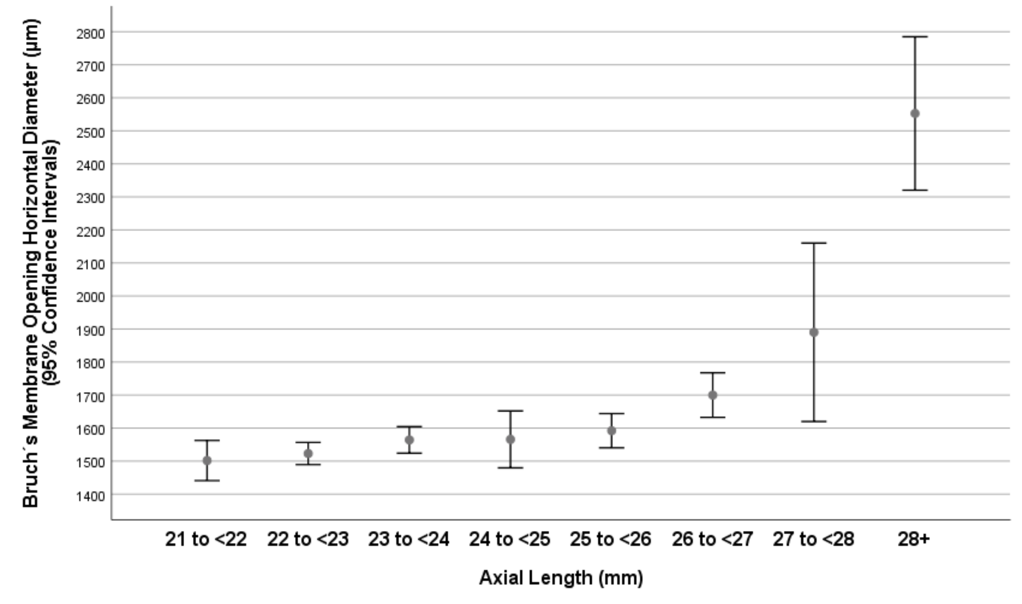
Panda-Jonas S, Xu L, Yang H, Wang YX, Jonas SB, Jonas JB. Optic disc morphology in young patients after antiglaucomatous filtering surgery. Acta Ophthalmol 2014;92:59-64.

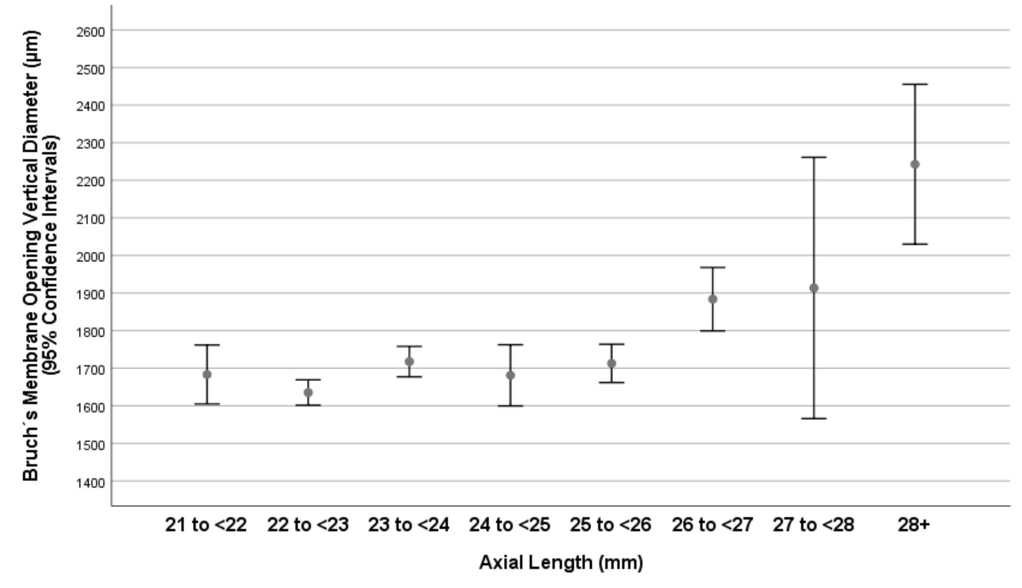
Bruch´s Membrane Opening





Bruch´s Membrane Opening





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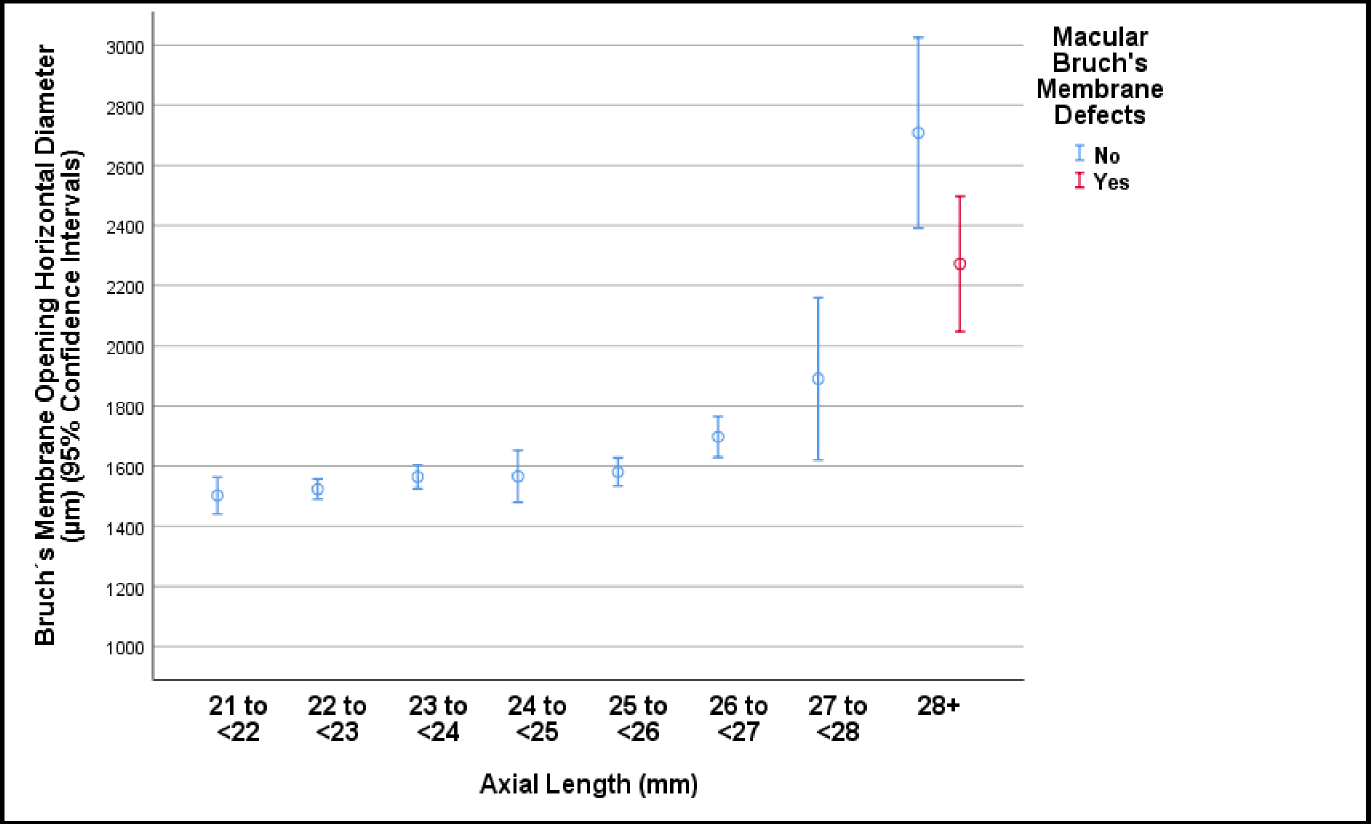
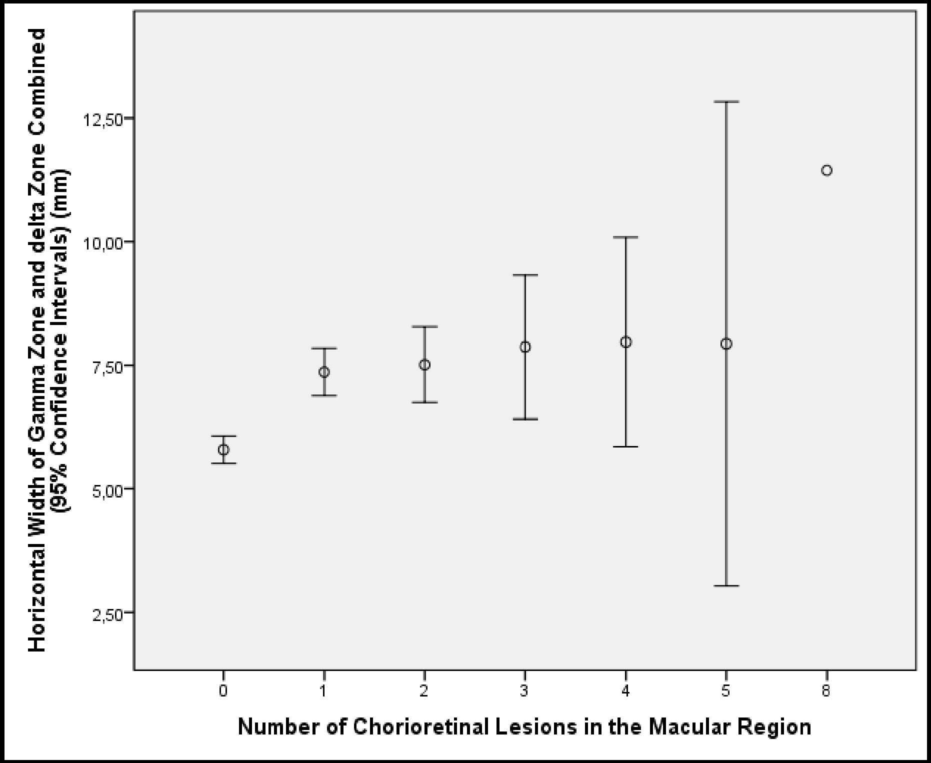
Bruch´s Membrane Opening



Zhang Q, Xu L, Wei WB, Wang YX, Jonas JB. Size and shape of Bruch´s membrane opening in relationship to axial length, gamma zone and macular Bruch´s membrane defects. The Beijing Eye Study. Submitted 2019

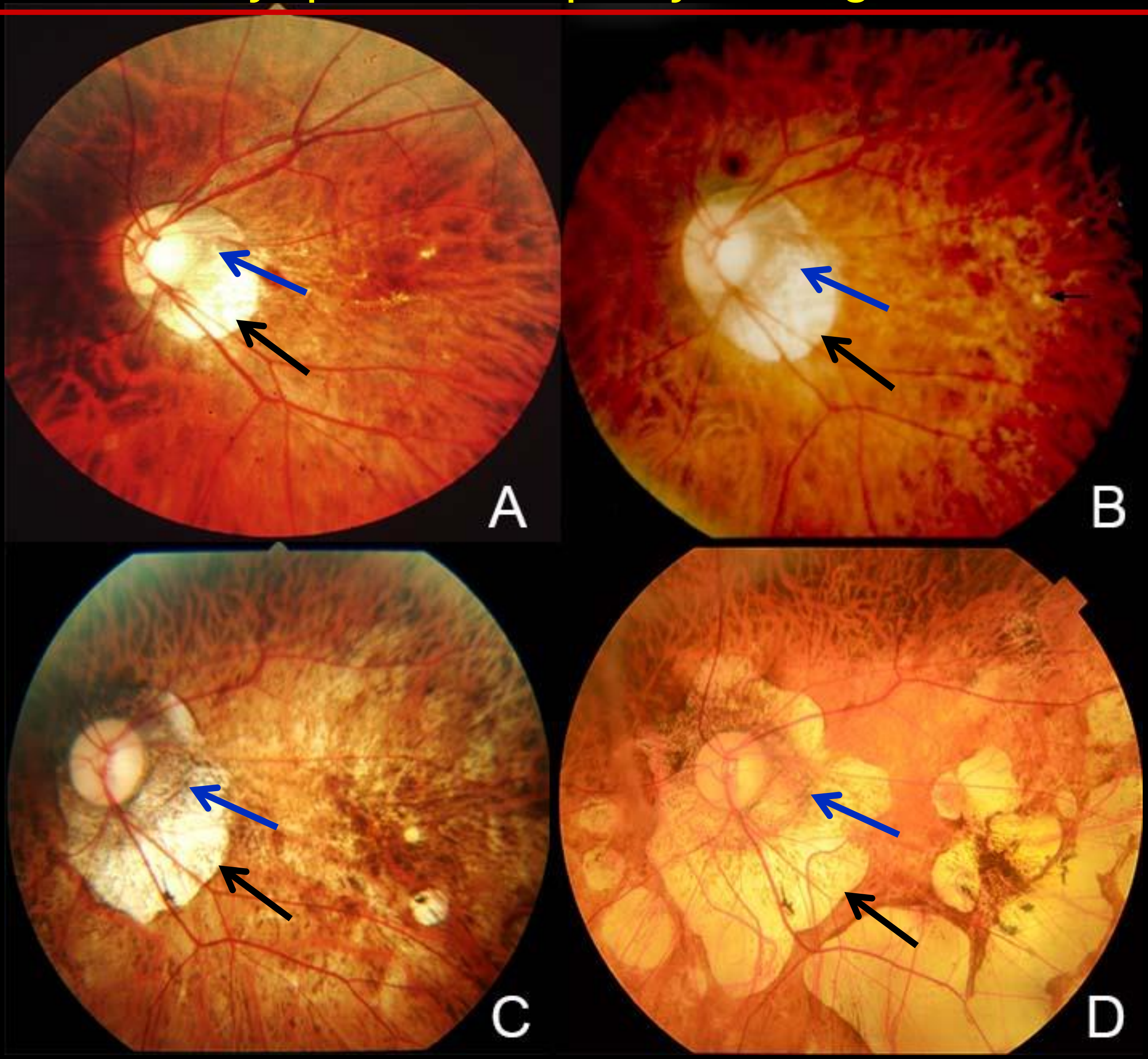
Parapapillary Gamma Zone and Delta Zone in High Myopia

- Longer width of gamma zone and of delta zone together was associated with higher number of chorioretinal lesions (P<0.001; beta:0.30), after adjusting for longer horizontal disc diameter (P<0.001; beta:0.31), higher ratio of vertical-to-horizontal disc diameter (P=0.001; beta:0.18), longer disc-fovea distance (P<0.001; beta:0.19), shorter fovea-outer gamma zone border distance (P<0.001; beta:-0.18), and longer vertical distance between the superior and inferior temporal arterial arcade (P=0.001; beta: 0.13).
- Parapapillary gamma und delta zones may develop before chorioretinal lesions develop and enlarge



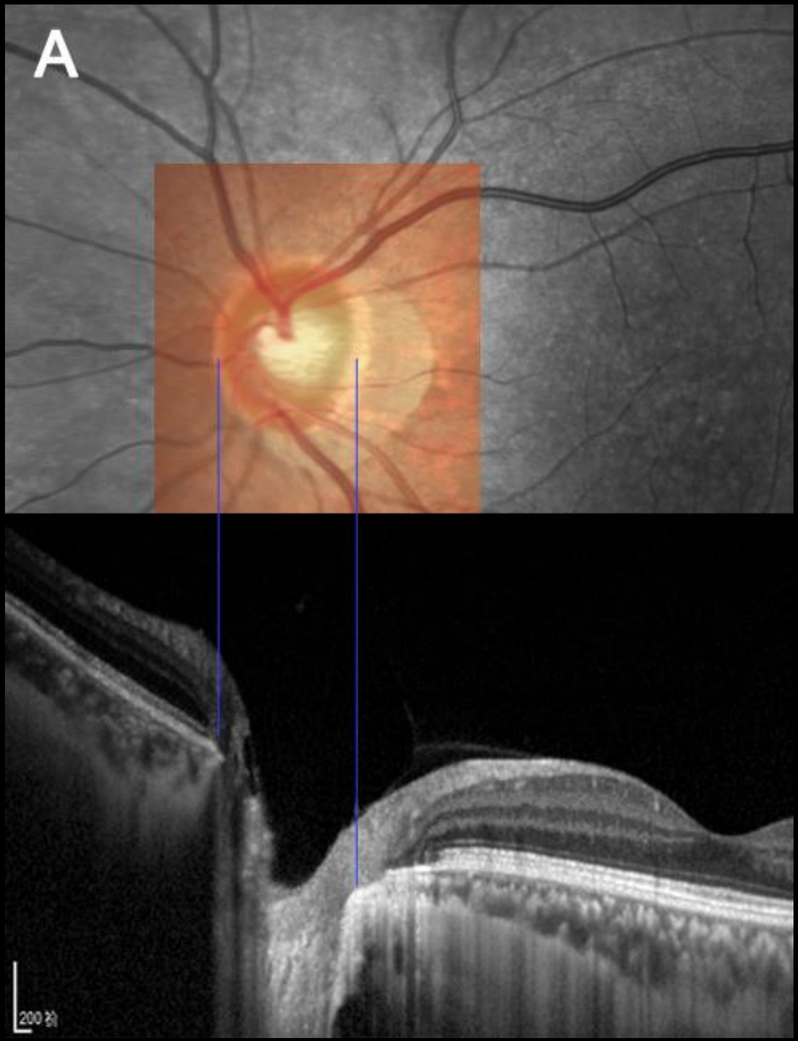
Jonas JB, Fang Y, Weber P, Ohno-Matsui K. Parapapillary gamma zone and delta zone in high myopia. Retina 2017; Zur Publikation angenommen

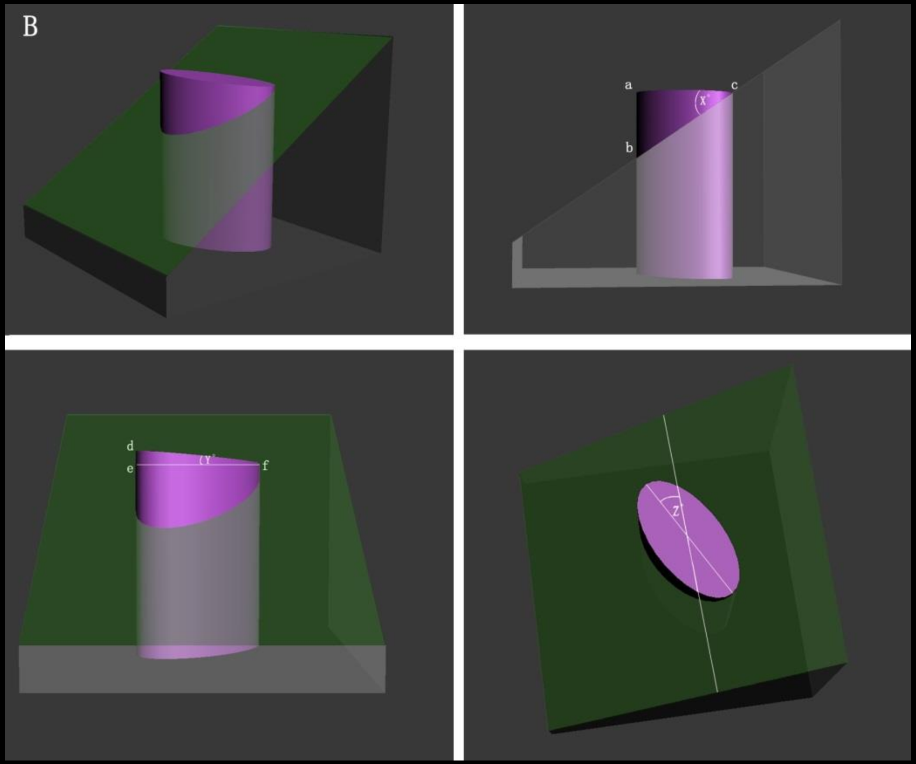
Progression of Myopic Maculopathy During 18-Year Follow-Up



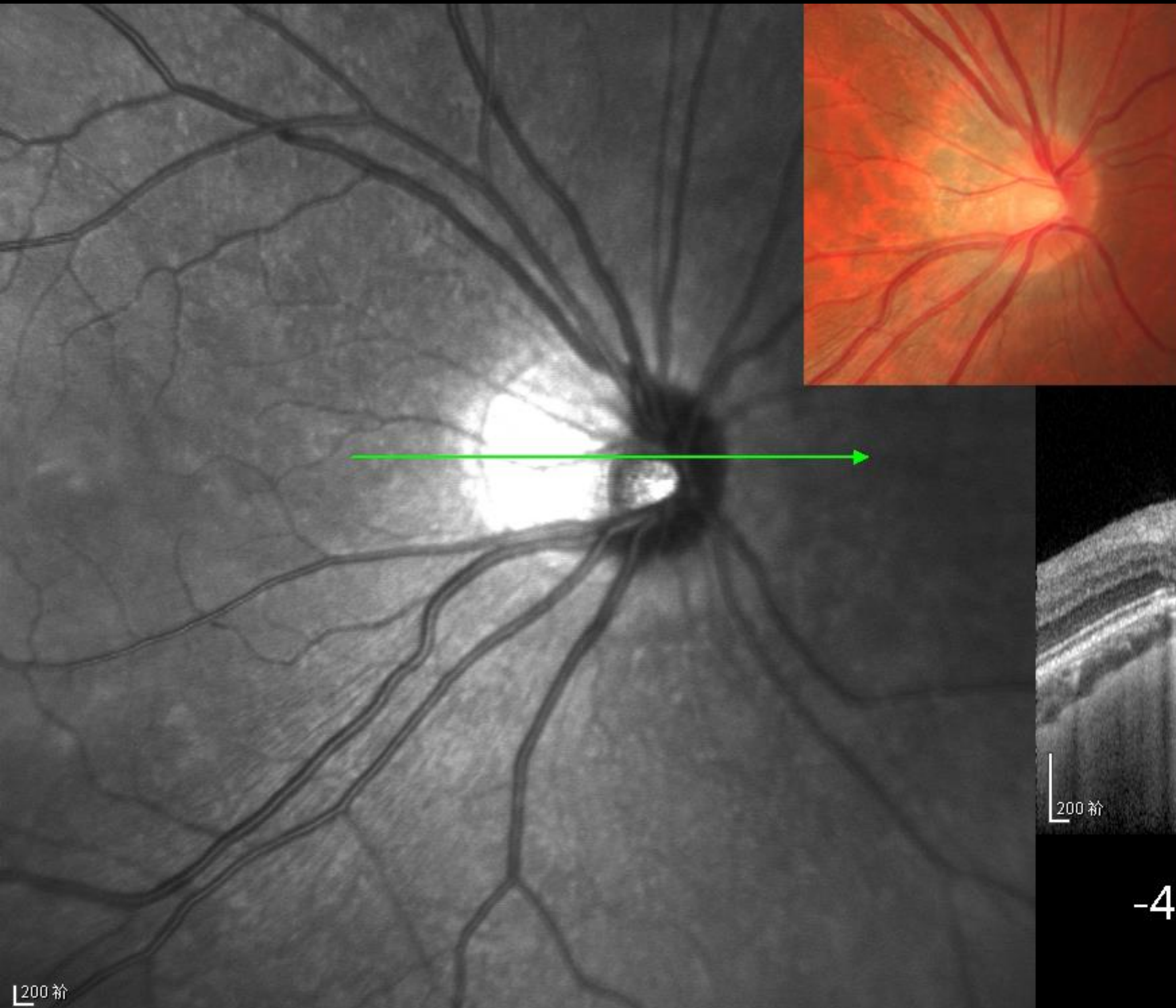
Fang Y, Yokoi T, Nagaoka N, Shinohara K, Onishi Y, Ishida T, Yoshida T, Xu X, Jonas JB, Ohno-Matsui K. Progression of myopic maculopathy during 18-year follow-up. Ophthalmology. 2018 Jan 19. [Epub ahead of print]

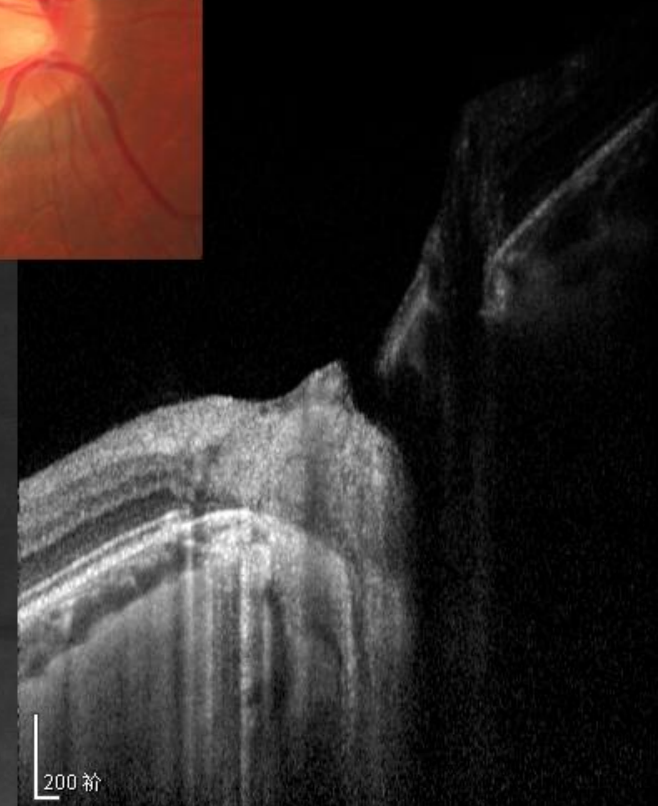
Ophthalmoscopic-Perspectively Distorted Optic Disc Diameters and Real Disc Diameters





Dai Y, Jonas JB, Ling Z, Sun X. Ophthalmoscopic-perspectively distorted optic disc diameters and real disc diameters

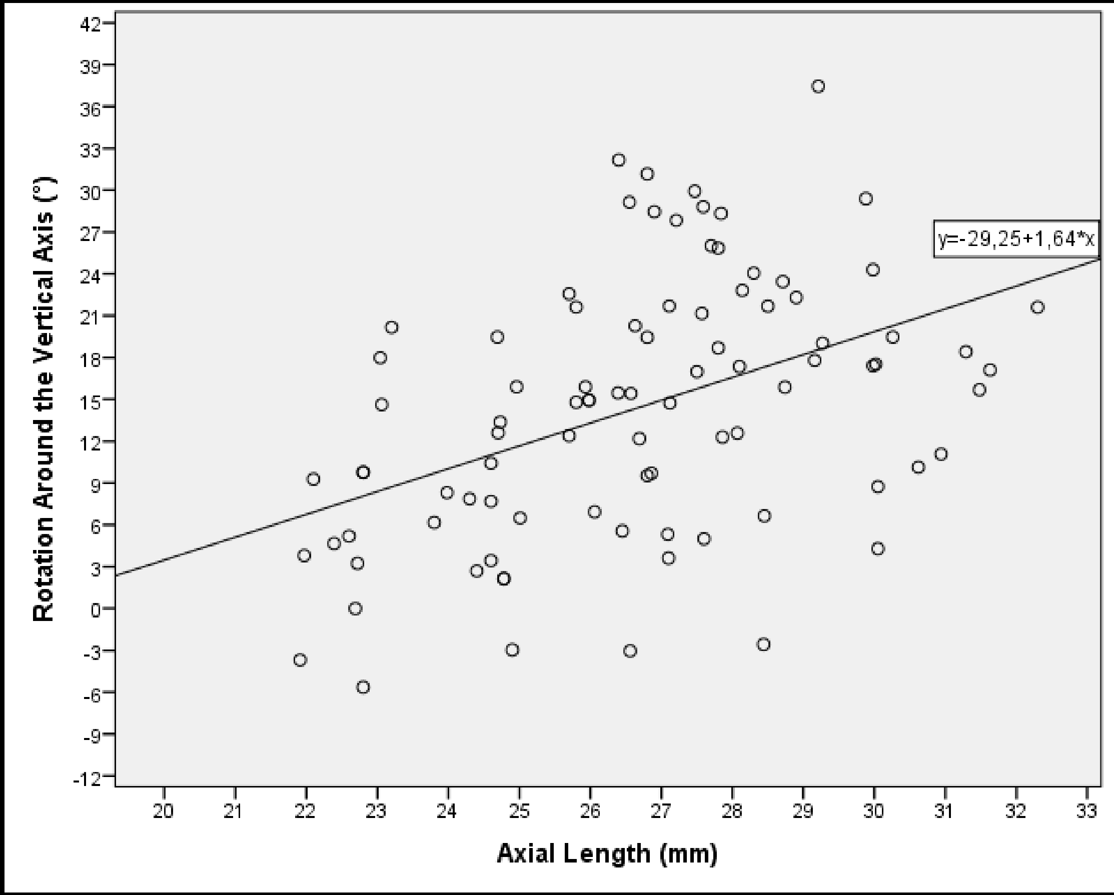




-4.5D

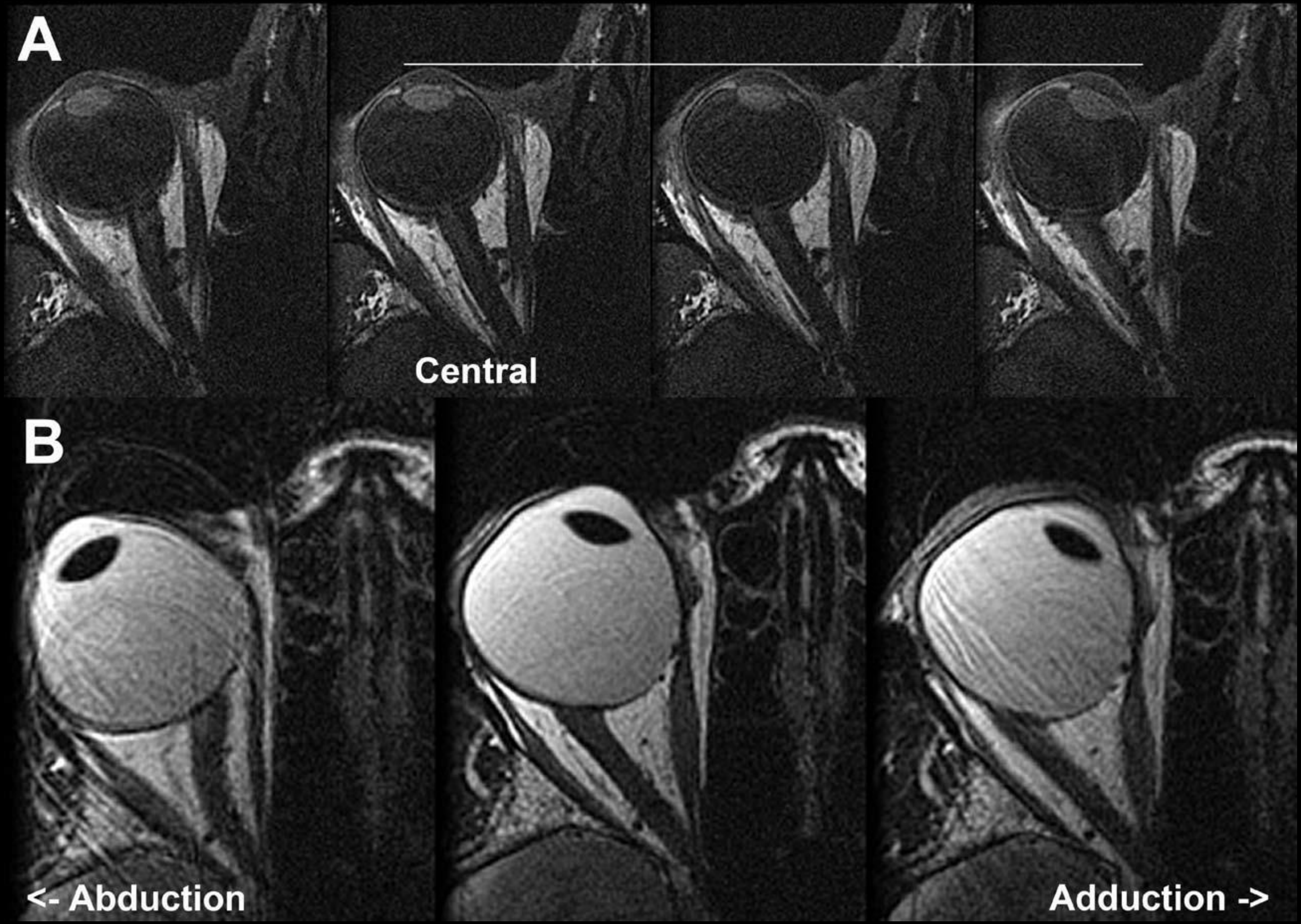
Ophthalmoscopic-Perspectively Distorted Optic Disc Diameters and Real Disc Diameters

- Mean optic disc rotation around vertical axis was 14.4±9.3°, rotation around sagittal axis was 23.0±21.3°, and rotation around horizontal axis was 4.7±6.6°.



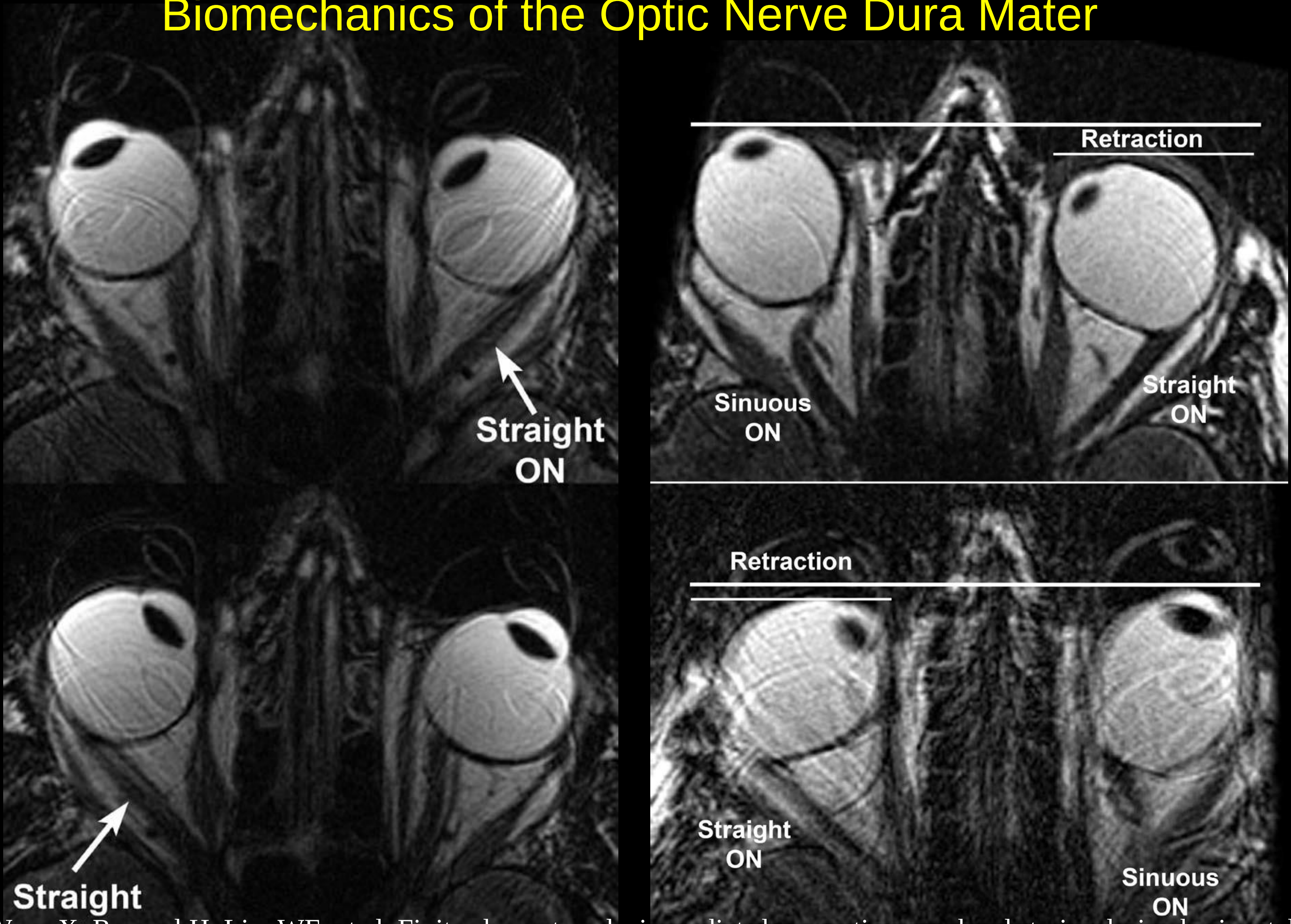
Dai Y, Jonas JB, Ling Z, Sun X. Ophthalmoscopic-perspectively distorted optic disc diameters and real disc diameters

Biomechanics of the Optic Nerve Dura Mater



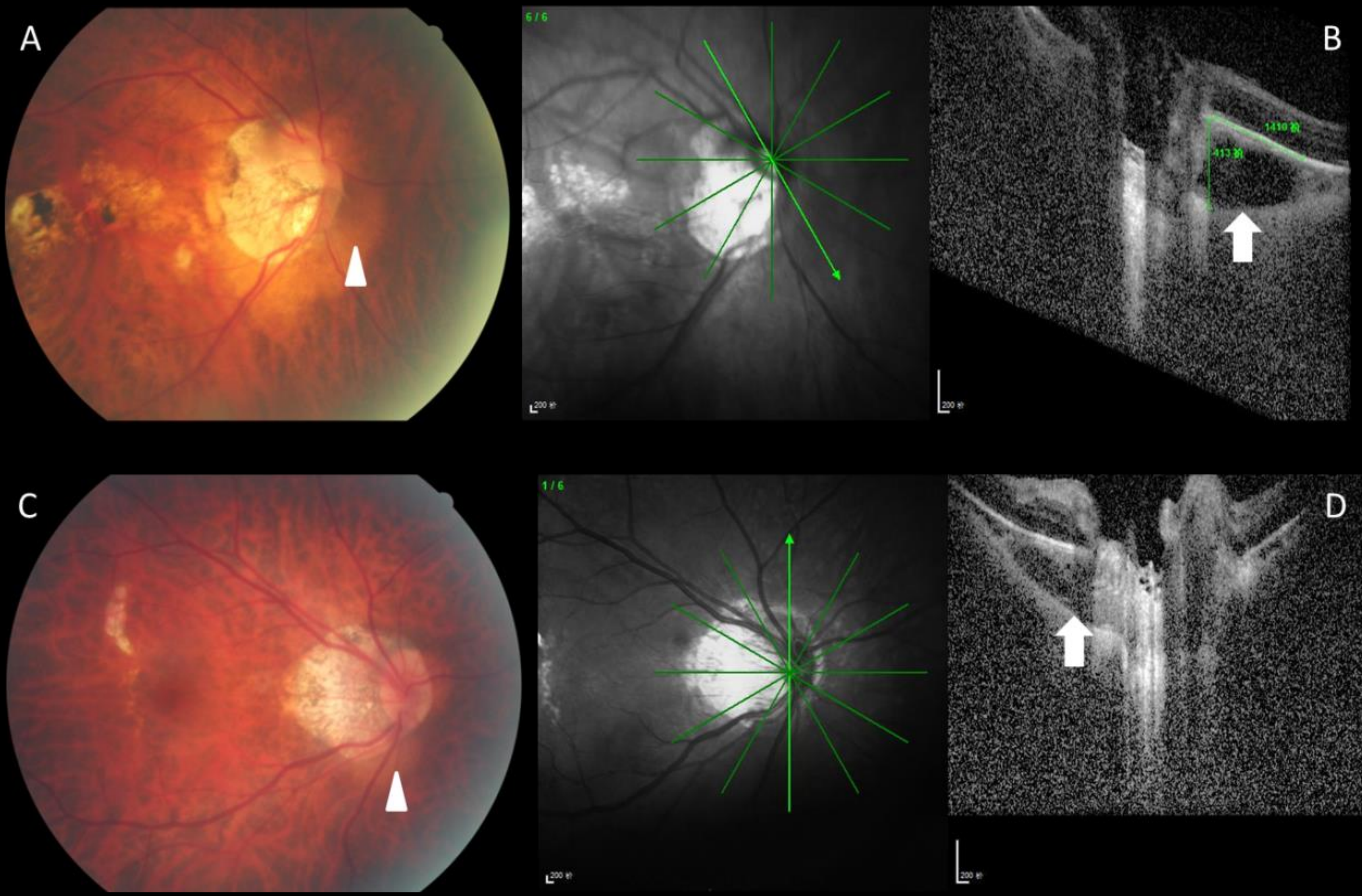
Wang X, Rumpel H, Lim WE, et al. Finite element analysis predicts large optic nerve head strains during horizontal eye movements. Invest Ophthalmol Vis Sci. 2016;57:2452-62.

Biomechanics of the Optic Nerve Dura Mater



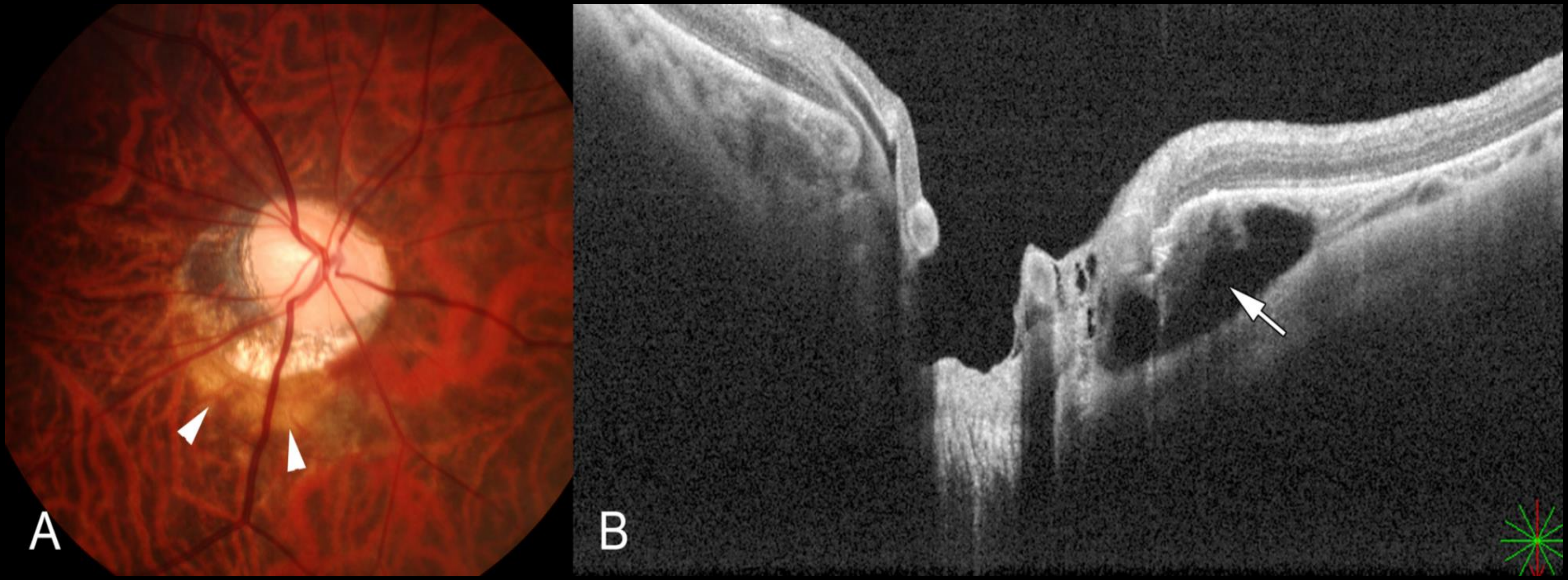
Wang X, Rumpel H, Lim WE, et al. Finite element analysis predicts large optic nerve head strains during horizontal eye movements. Invest Ophthalmol Vis Sci. 2016;57:2452-62.

Peripapillary Suprachoroidal Cavitations. The Beijing Eye Study



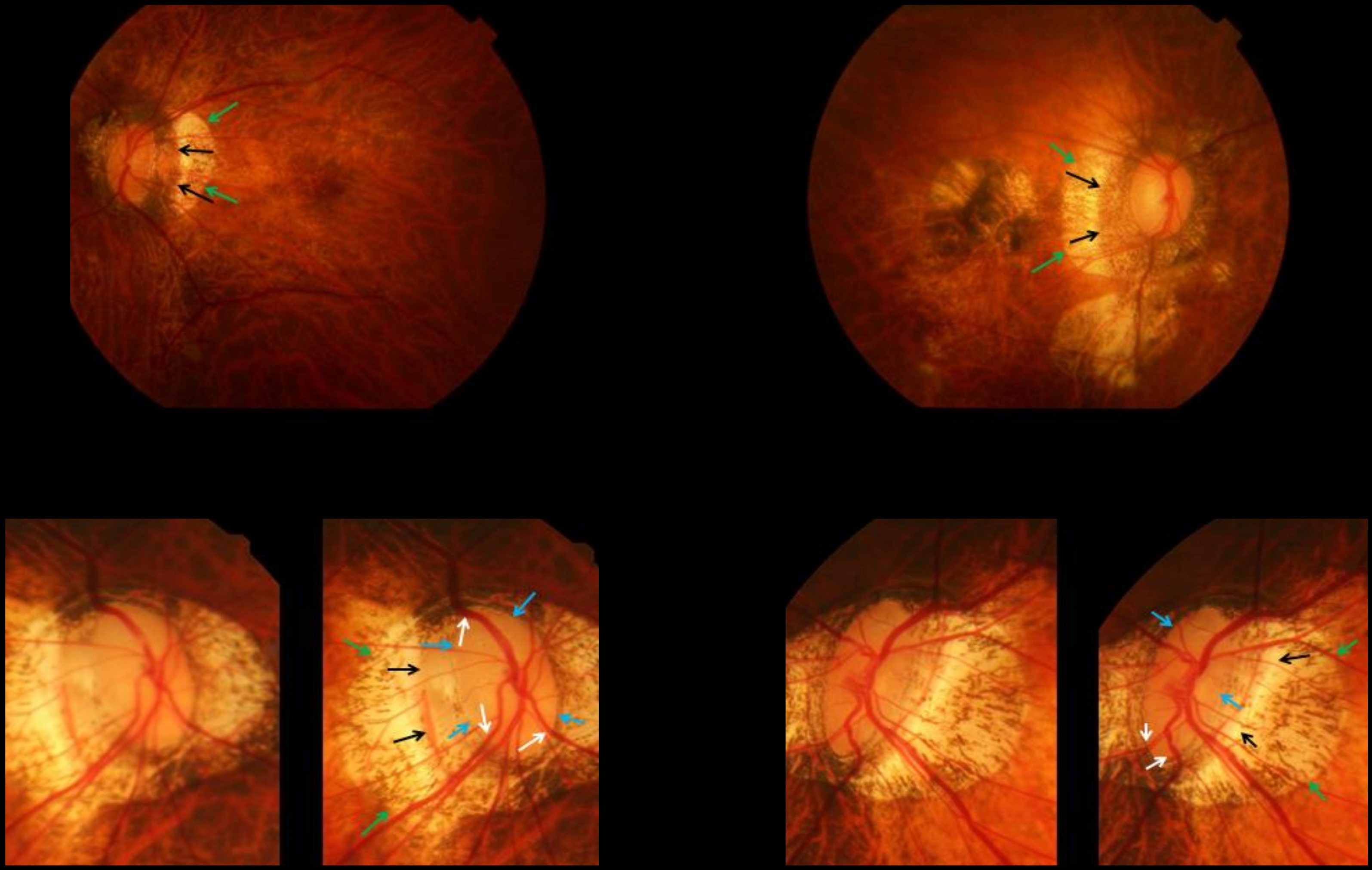
You QS, Peng XY, Chen CX, Xu L, Jonas JB. Peripapillary intrachoroidal cavitations. The Beijing Eye Study. PLoS One. 2013;8:e78743

Peripapillary Suprachoroidal Cavitations. The Beijing Eye Study



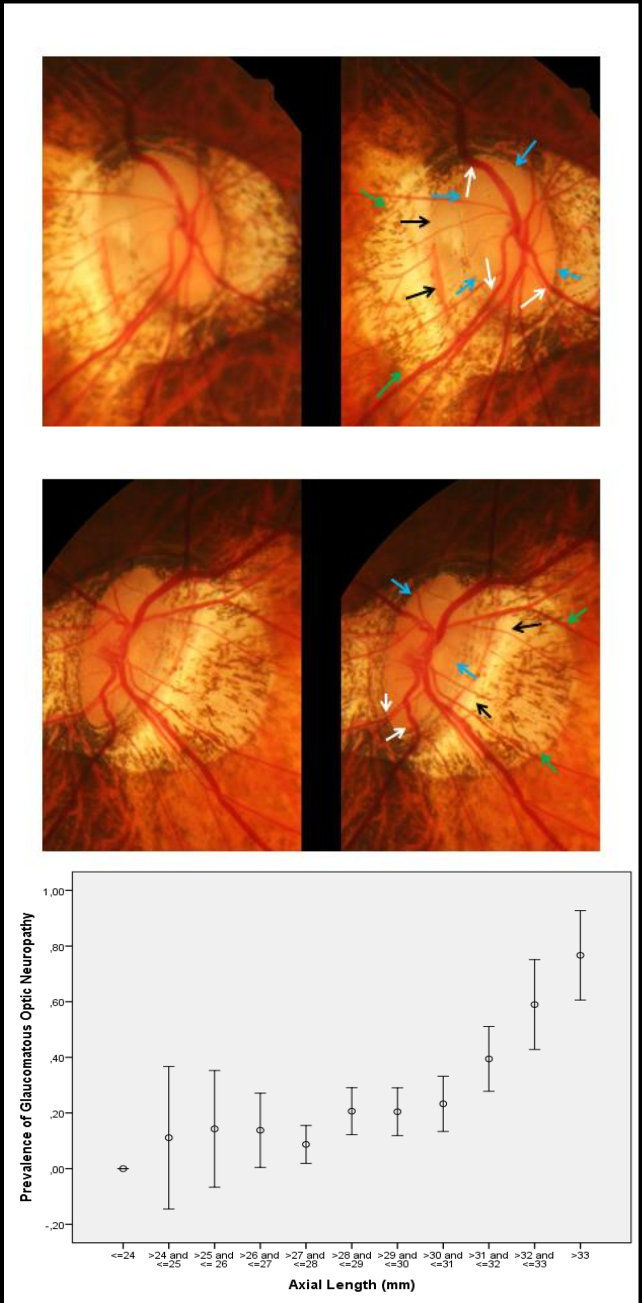
High Myopia and Glaucoma

- 519 eyes (mean axial length: 29.5±2.2 mm; range:23.2-35.3mm)



Jonas JB, Weber P, Nagaoka N, Ohno-Matsui K. Glaucoma in high myopia and parapapillary delta zone. PLoS One. 2017;12:e0175120

Glaucoma in High Myopia and Parapapillary Delta Zone



- 519 eyes (axial length: 29.5±2.2 mm); GON present in 141 (27.2%) eyes.
- Prevalence of GON increased from 12.2% (1.7, 22.7) in eyes with an axial length of <26.5mm to 42.1% (35.5, 48.8) in eyes with an axial length of ≥30mm.

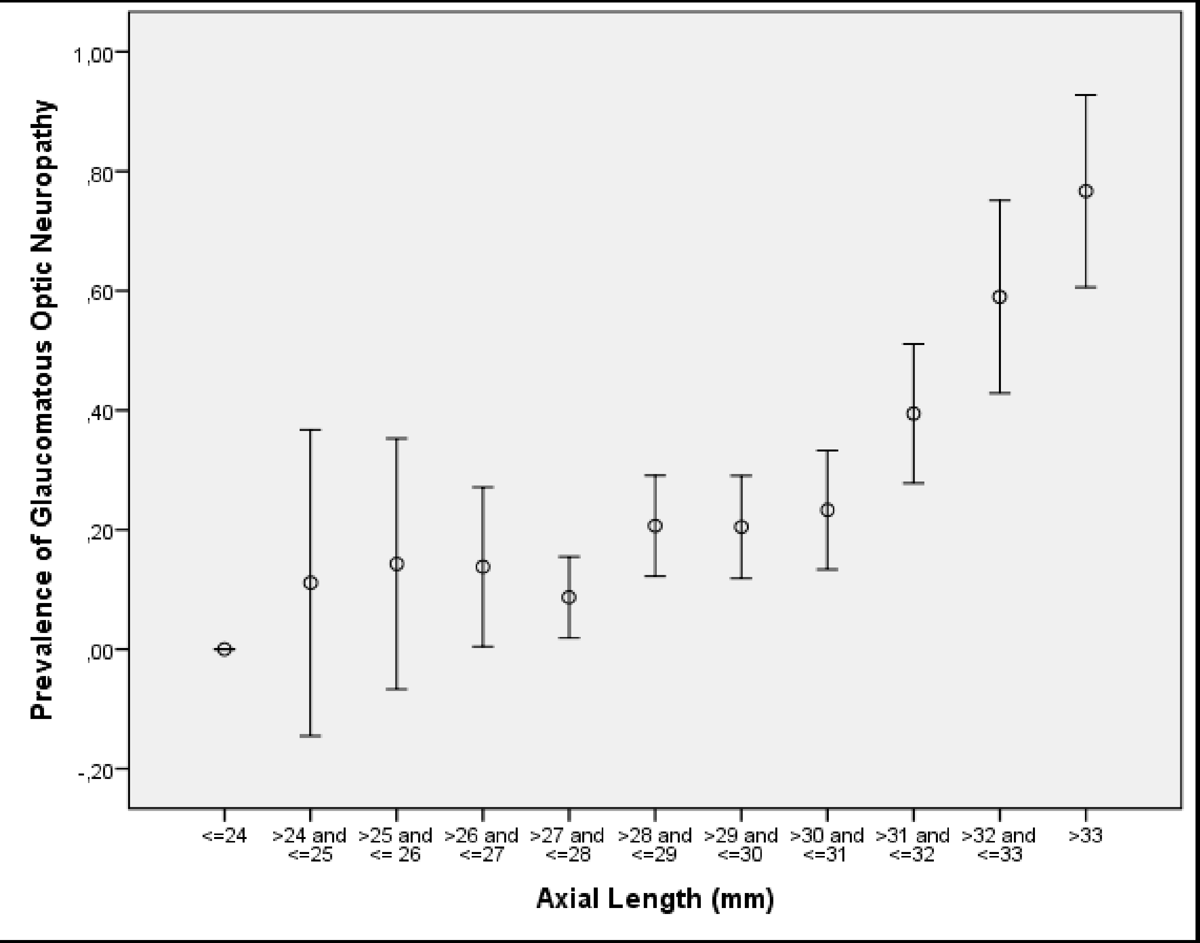
- In multivariate analysis, higher GON prevalence was associated (Nagelkerke r2: 0.28) with **larger parapapillary delta zone** diameter (P<0.001; OR:1.86), **longer axial length** (P<0.001; OR:1.45;7) and **older age** (P=0.01).

- If parapapillary delta zone width was replaced by the **vertical disc diameter**, higher GON prevalence was associated with larger vertical optic disc diameter (P=0.04; OR:1.70)

Jonas JB, Weber P, Nagaoka N, Ohno-Matsui K. Glaucoma in high myopia and parapapillary delta zone. PLoS One. 2017 Apr 5;12(4):e0175120.

High Myopia and Glaucoma

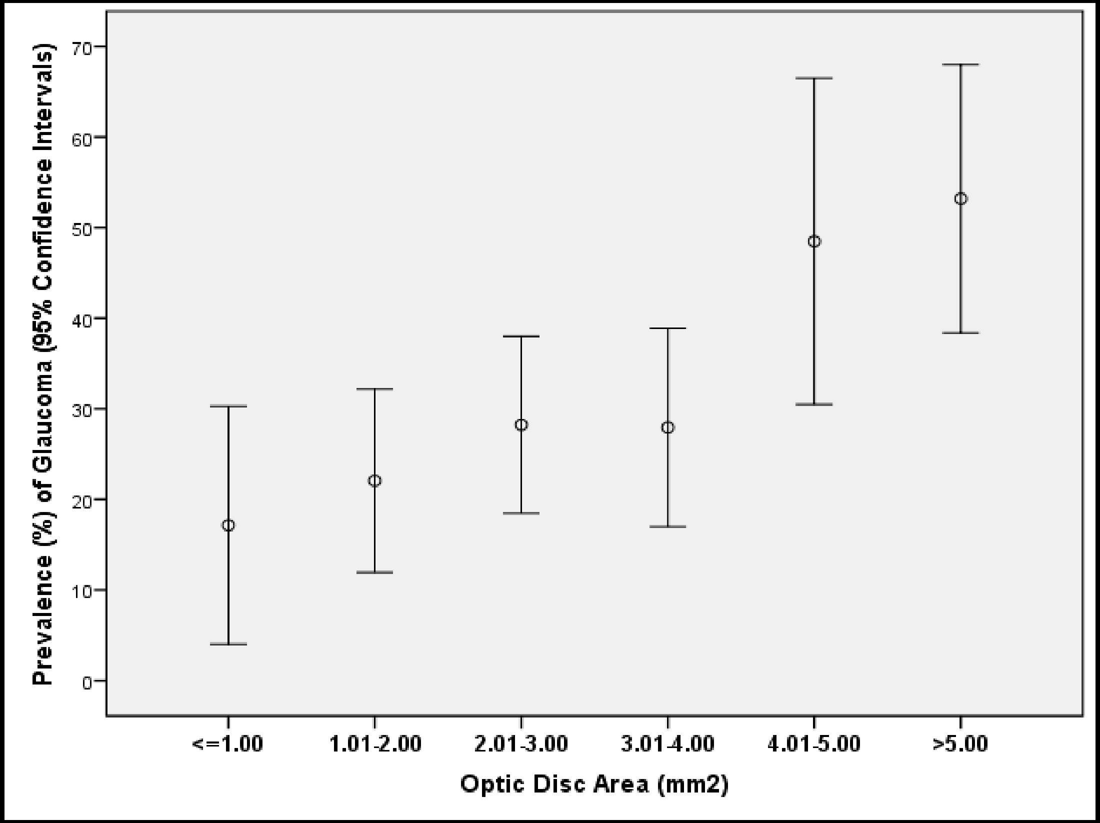
- Glaucomatous optic neuropathy was present in 141 (27.2%). increased from 12.2% in axial length <26.5mm to 42.1% in axial length ≥30mm



Jonas JB, Weber P, Nagaoka N, Ohno-Matsui K. Glaucoma in high myopia and parapapillary delta zone. PLoS One. 2017;12:e0175120

High Myopia and Glaucoma

- In multivariate analysis, glaucoma prevalence was 3.2 times higher (*P*<*0.001*) in megalodiscs (>3.79 mm^2) than in normal-sized discs or small discs (<1.51 mm^2) after adjusting for older age.



Nagaoka N, Jonas JB, Morohoshi K, Moriyama M, Tanaka Y, Shimada N, Yoshida T, Ohno-Matsui K. Glaucomatous-type optic discs in high myopia. PLoS One. 2015;10:e0138825

High Myopia and Glaucoma

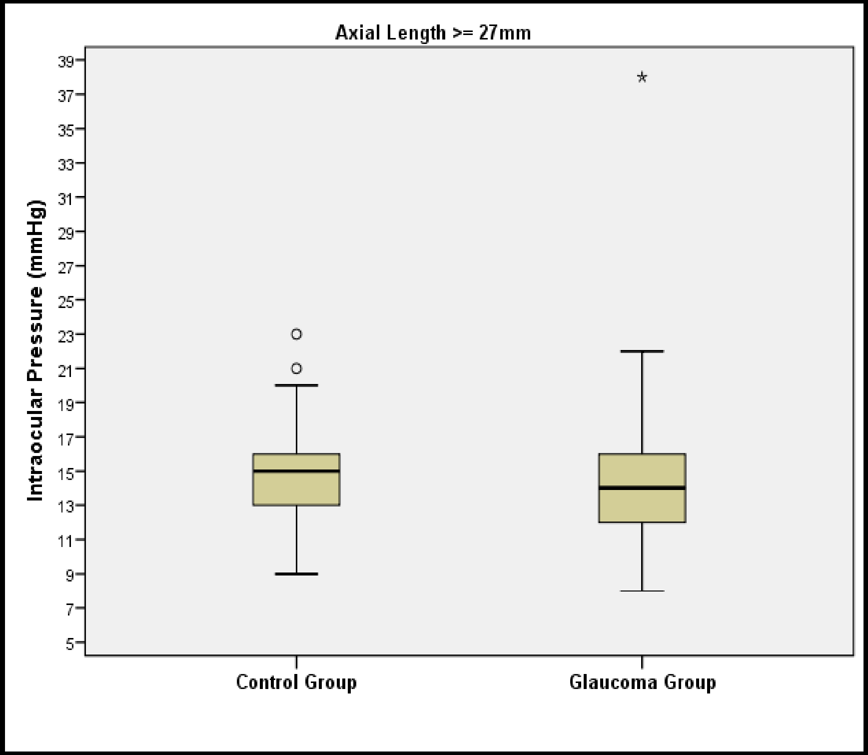
Higher GON prevalence was associated (multivariate analysis) with

- larger parapapillary delta zone diameter (*P*<0.001; OR: 1.86),
- (or alternatively, vertical disc diameter (*P*=0.04; OR:1.70)),
- longer axial length (*P*<0.001; OR:1.45) and
- older age (*P*=0.01; OR:1.03).

Jonas JB, Weber P, Nagaoka N, Ohno-Matsui K. Glaucoma in high myopia and parapapillary delta zone. PLoS One. 2017;12:e0175120

Intraocular Pressure and Glaucomatous Optic Neuropathy in High Myopia:

517 eyes (axial length: 29.5±2.2mm) GON was present in 141 (27.3%) eyes

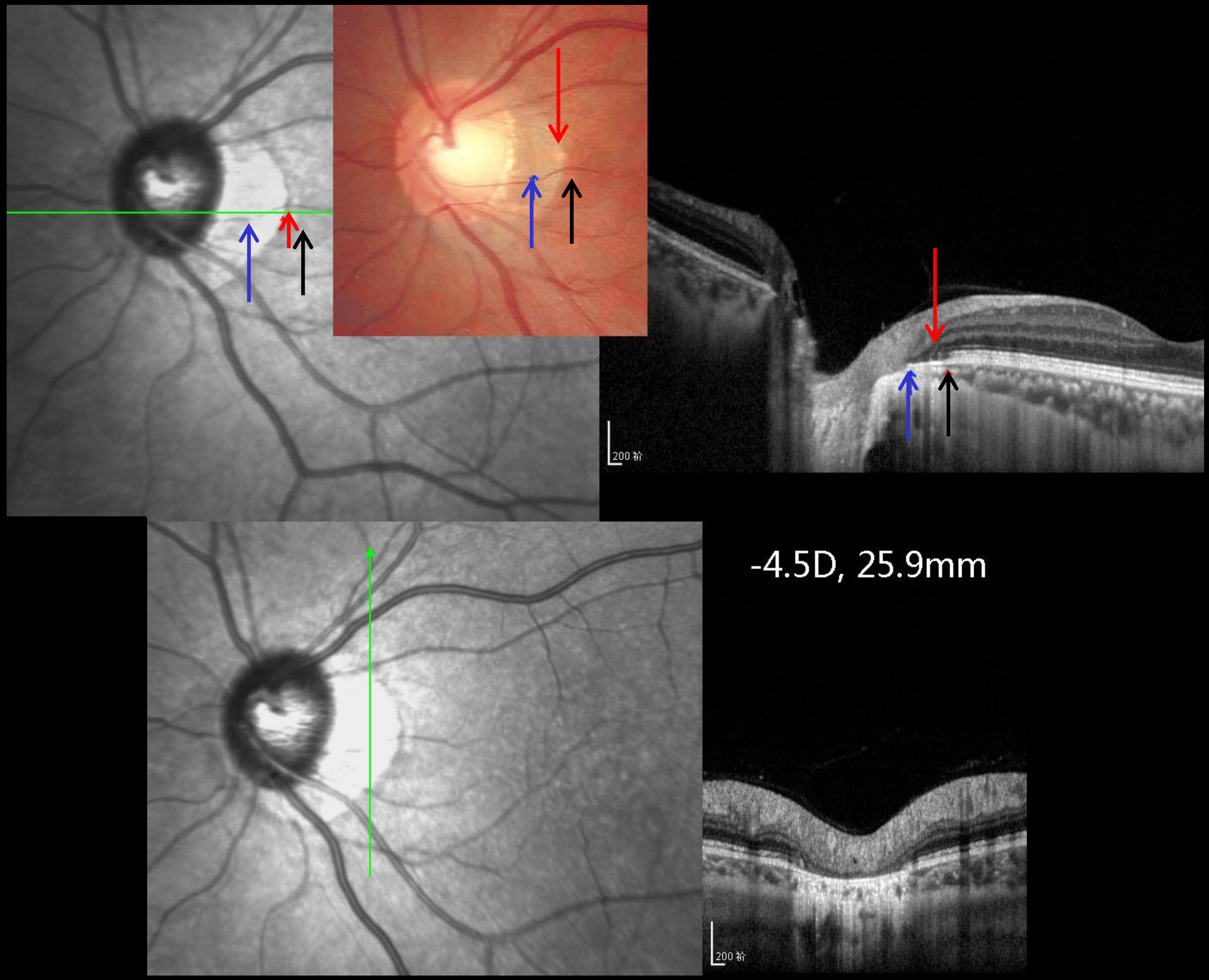


Jonas JB, Nagaoka N, Fang YX, Weber P, Ohno-Matsui K. Intraocular pressure and glaucomatous optic neuropathy in high myopia. Invest Ophthalmol Vis Sci 2017;58(13):5897-5906.

Alpha, Beta, Gamma, Delta Zone

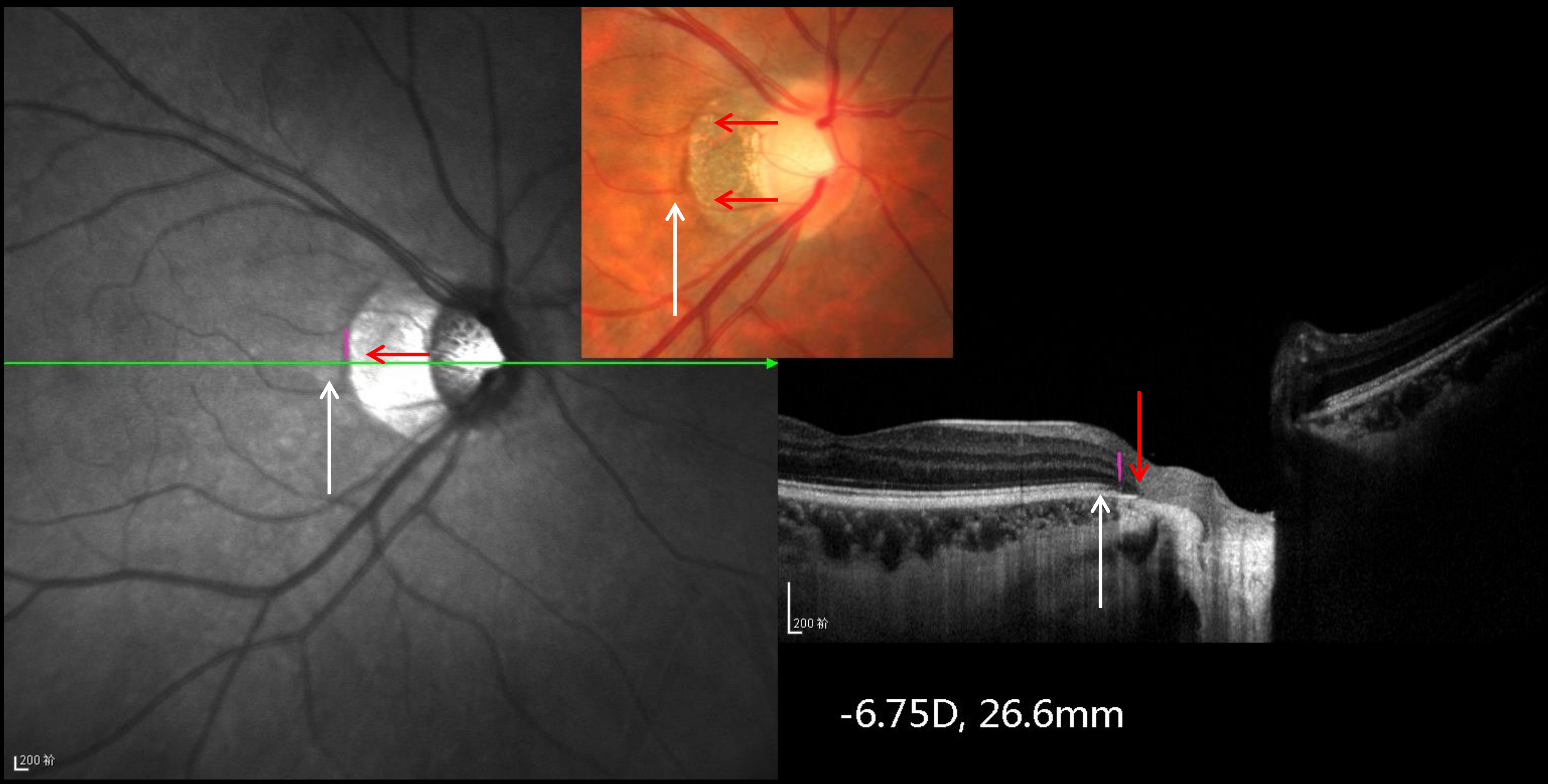
- Alpha Zone: Bruch´s membrane present, RPE> irregualrly structured
- Beta Zone: Bruch´s membrane present, no RPE, no photoreceptors (plus choriocapillaris occluded); associated with glaucoma; not associated with myopia
- Gamma Zone: No Bruch´s membrane, therefore no photoreceptors, no RPE, no choriocapillaris; associated with myopia; not associated with glaucoma
- Delta Zone: elongated (and thinned) peripapillary scleral flange in highly myopic eyes; bordering the orbital cerebrospinal fluid space

OCT Correlate of Parapapillary Region



Dai Y, Jonas JB, Huang H, Wang M, Sun X. Microstructure of parapapillary atrophy: Beta zone and gamma zone. Invest Ophthalmol Vis Sci 2013;54(3):2013-8

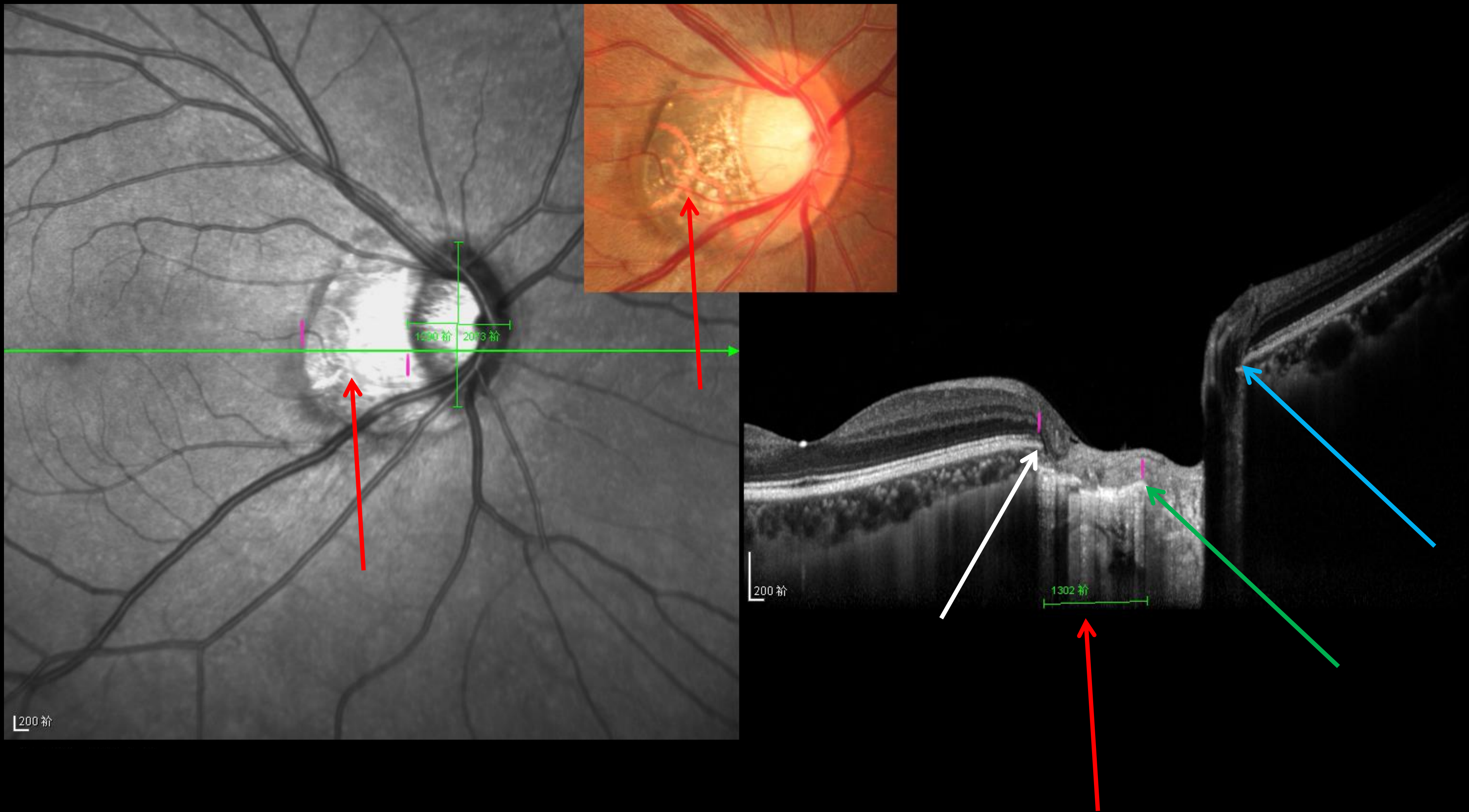
OCT Correlate of Parapapillary Region



-6.75D, 26.6mm

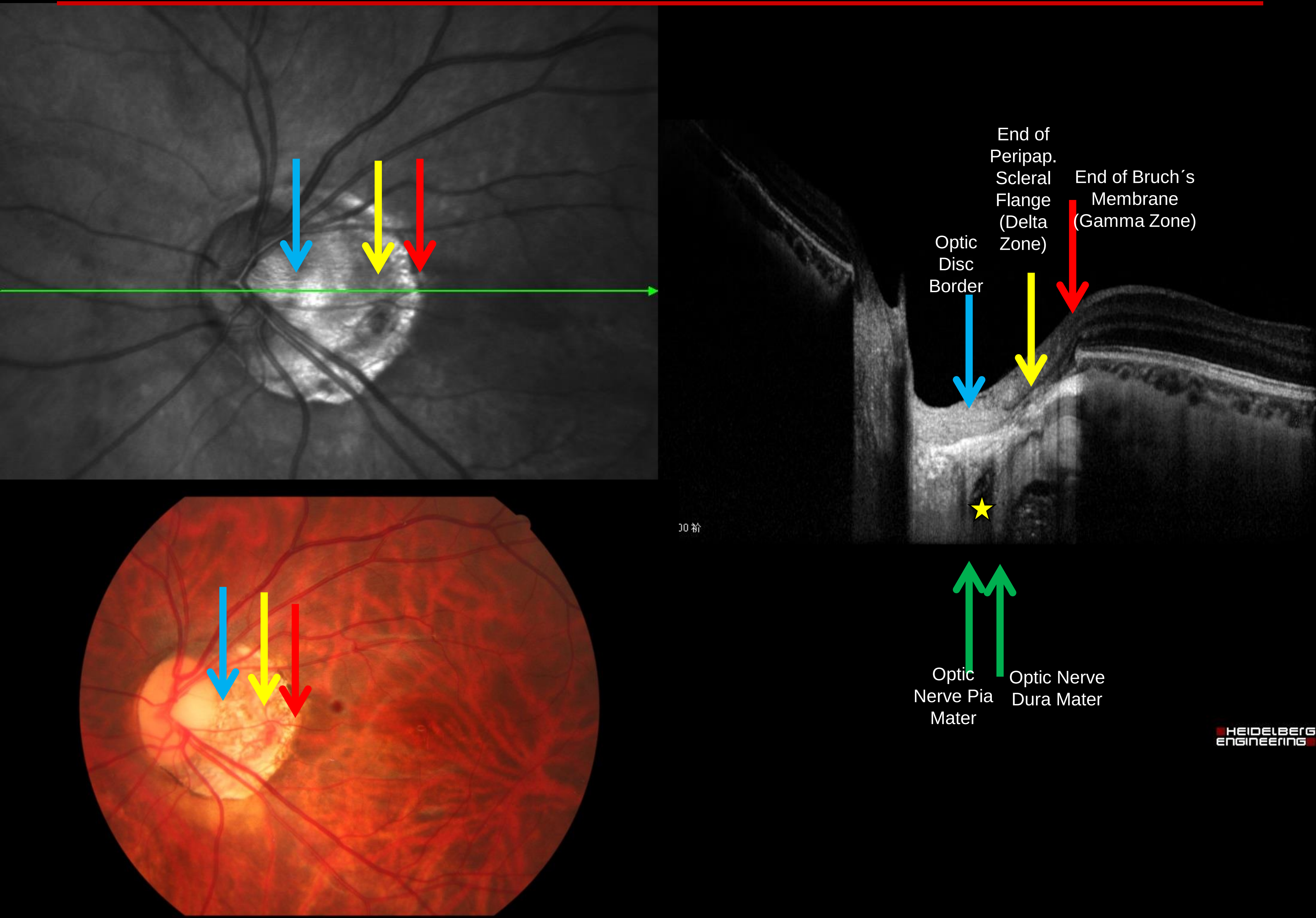
Dai Y, Jonas JB, Huang H, Wang M, Sun X. Microstructure of parapapillary atrophy: Beta zone and gamma zone. Invest Ophthalmol Vis Sci 2013;54(3):2013-8

OCT Correlate of Parapapillary Region

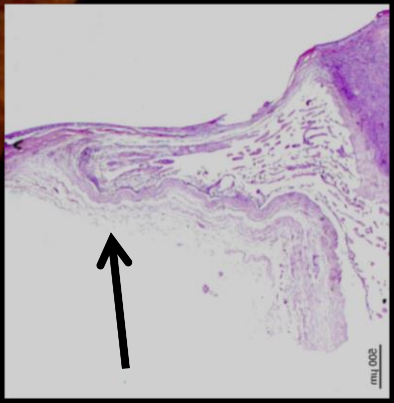


Dai Y, Jonas JB, Huang H, Wang M, Sun X. Microstructure of parapapillary atrophy: Beta zone and gamma zone. Invest Ophthalmol Vis Sci 2013;54:2013-8

Parapapillary Delta Zone: Peripapillary Scleral Flange in High Myopia



Parapapillary Delta Zone: Peripapillary Scleral Flange in High Myopia



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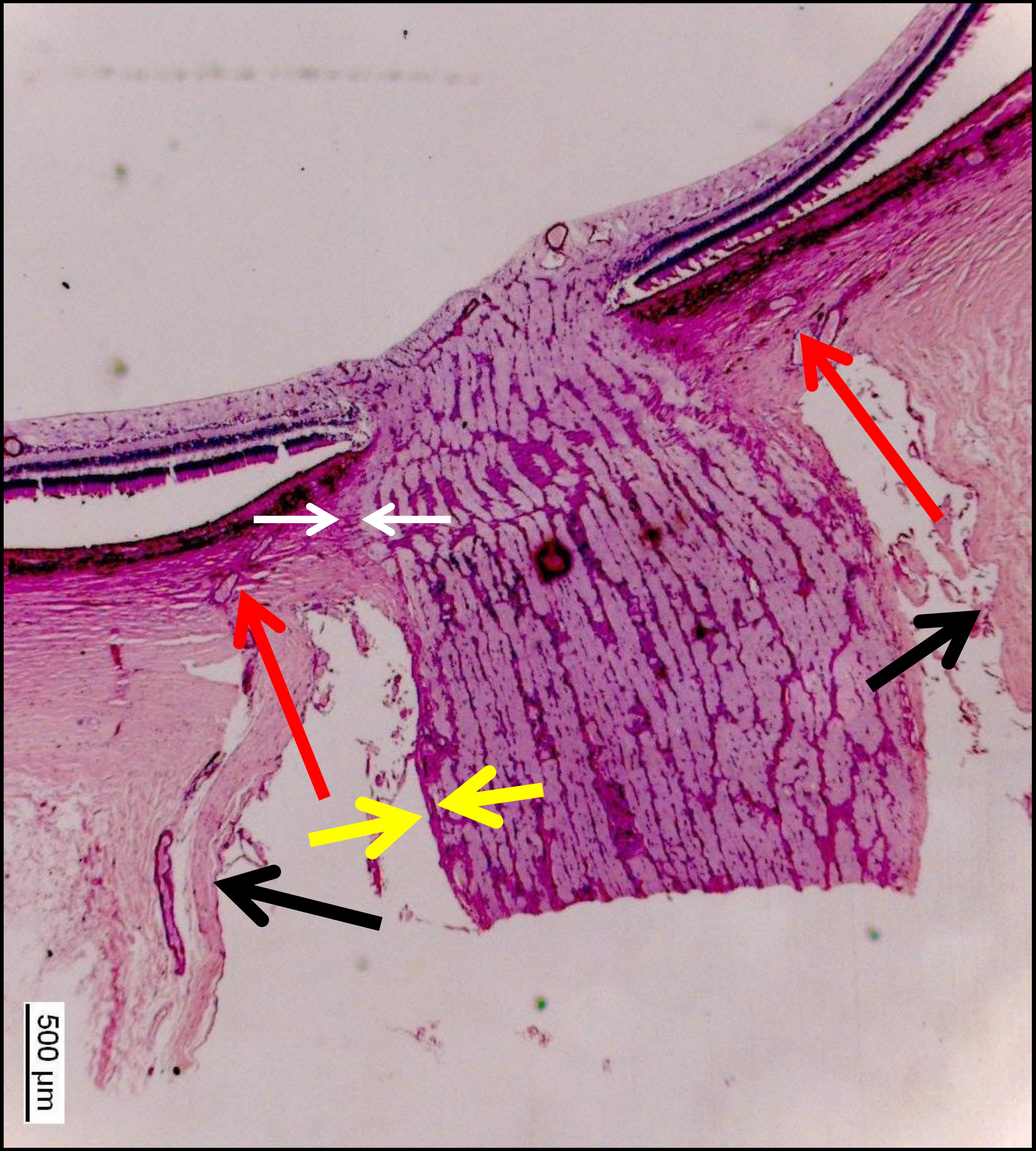
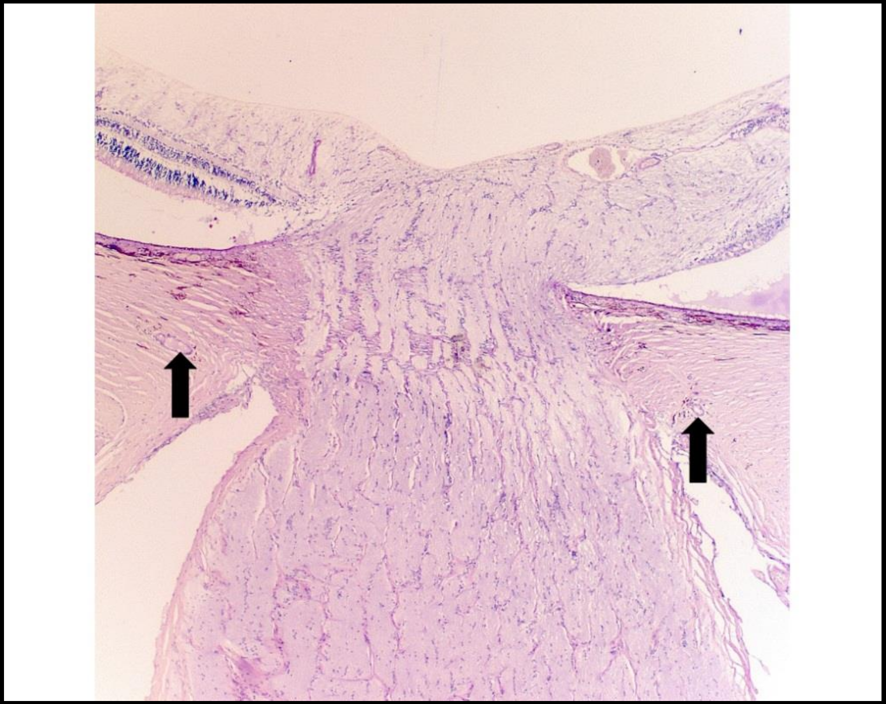
Parapapillary Delta Zone: Peripapillary Scleral Flange in High Myopia

Circular Peripapillary Arterial Ring of Zinn-Haller



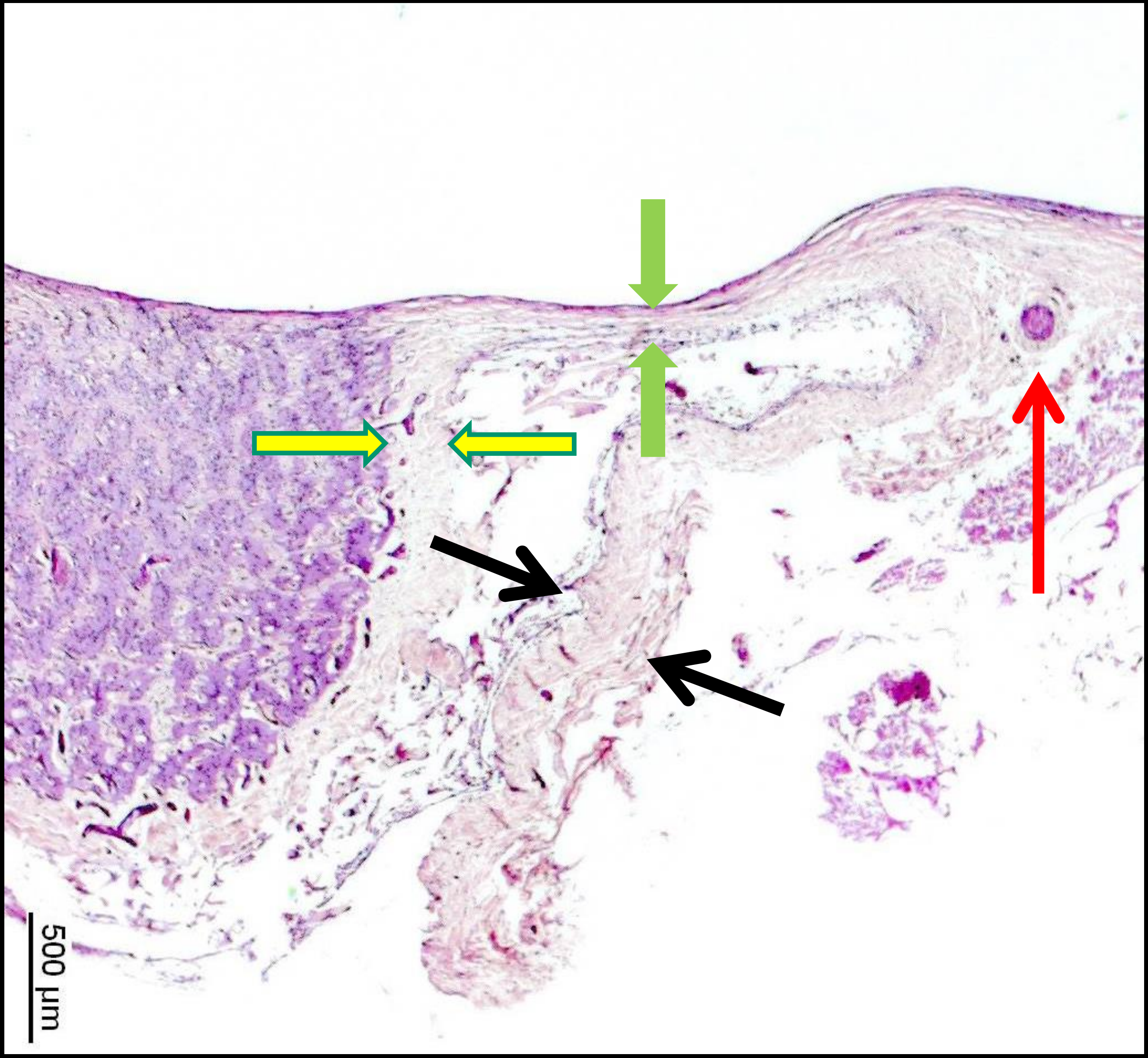
Circular Peripapillary Arterial Ring of Zinn-Haller



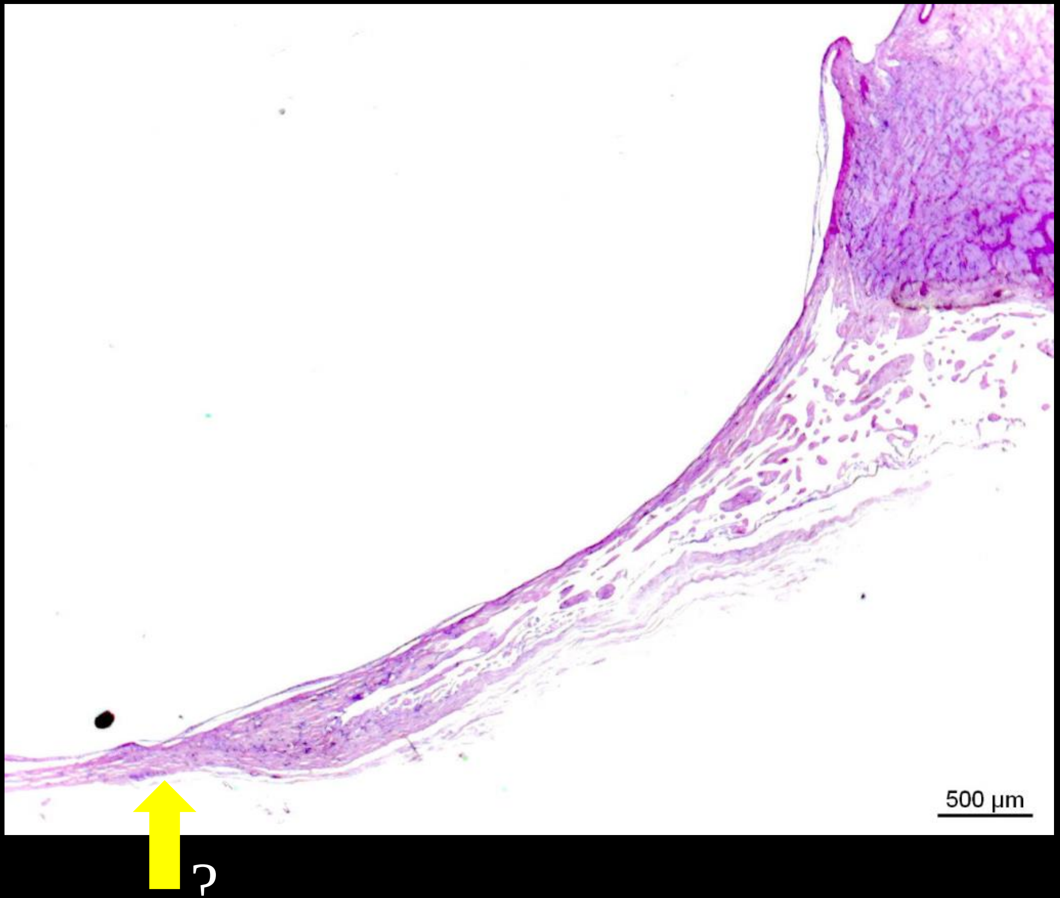
The peripapillary arterial circle of Zinn-Haller was present in all human eyes examined and did not vary significantly in location and diameter between eyes with secondary angle-closure glaucoma and non-glaucomatous eyes, nor between non-highly myopic versus hyperopic eyes

Jonas JB, Jonas SB. Histomorphometry of the circular arterial ring of Zinn-Haller in normal and glaucomatous eyes. Acta Ophthalmol 2010;88:e317-e322

Circular Peripapillary Arterial Ring of Zinn-Haller

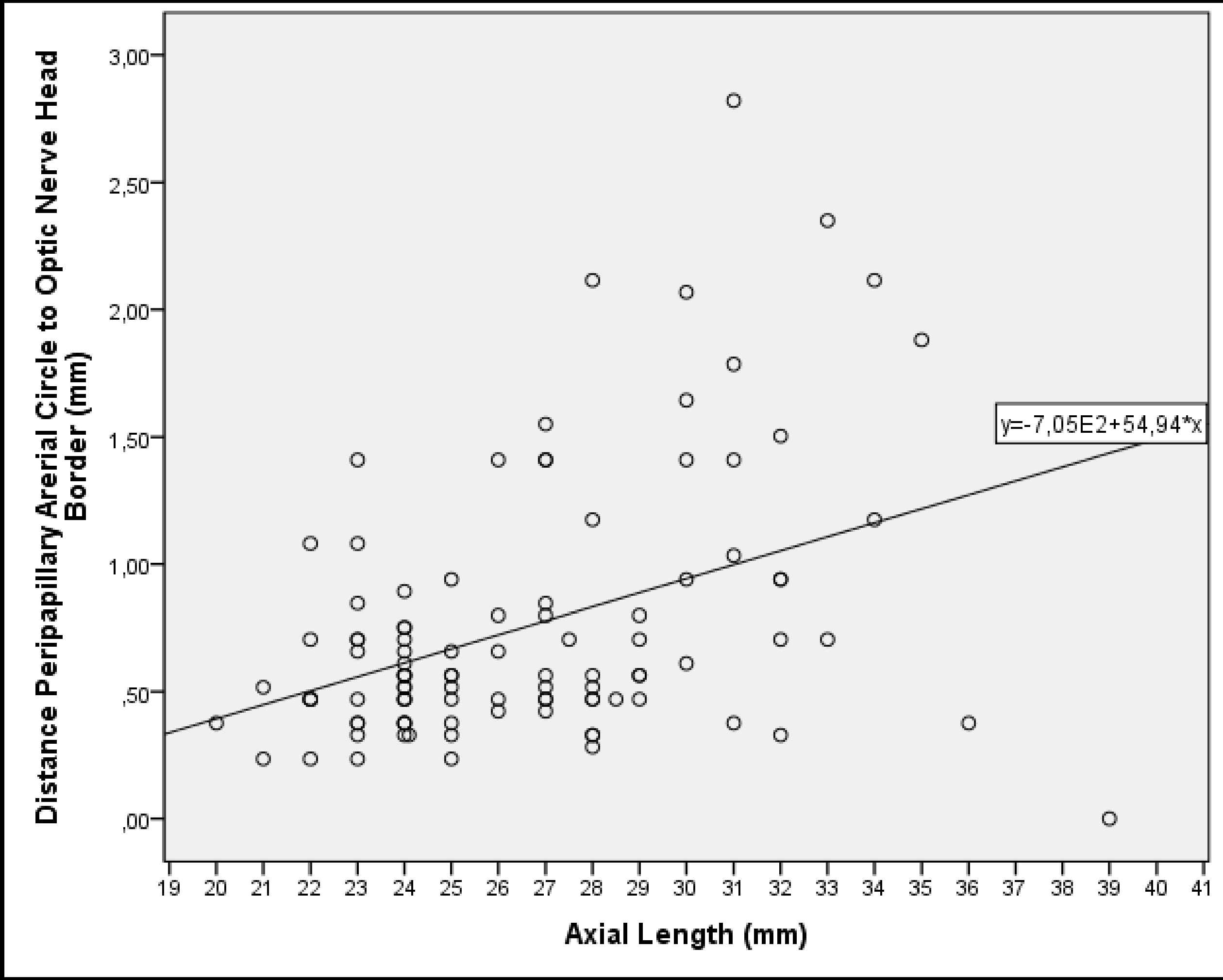


Circular Peripapillary Arterial Ring of Zinn-Haller



The distance between the peripapillary arterial circle Zinn-Haller and optic nerve border was longer in highly myopic eyes

Circular Peripapillary Arterial Ring of Zinn-Haller



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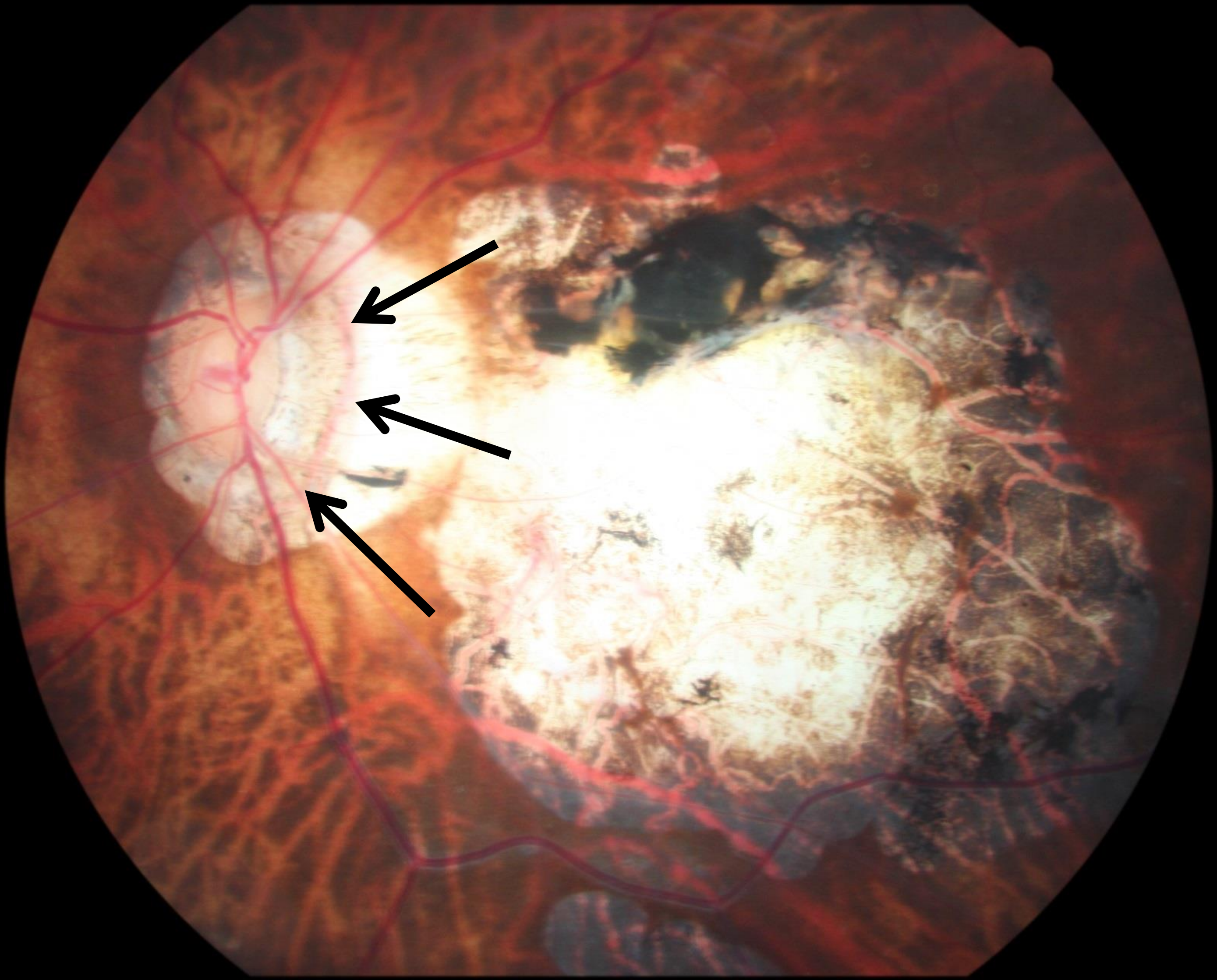
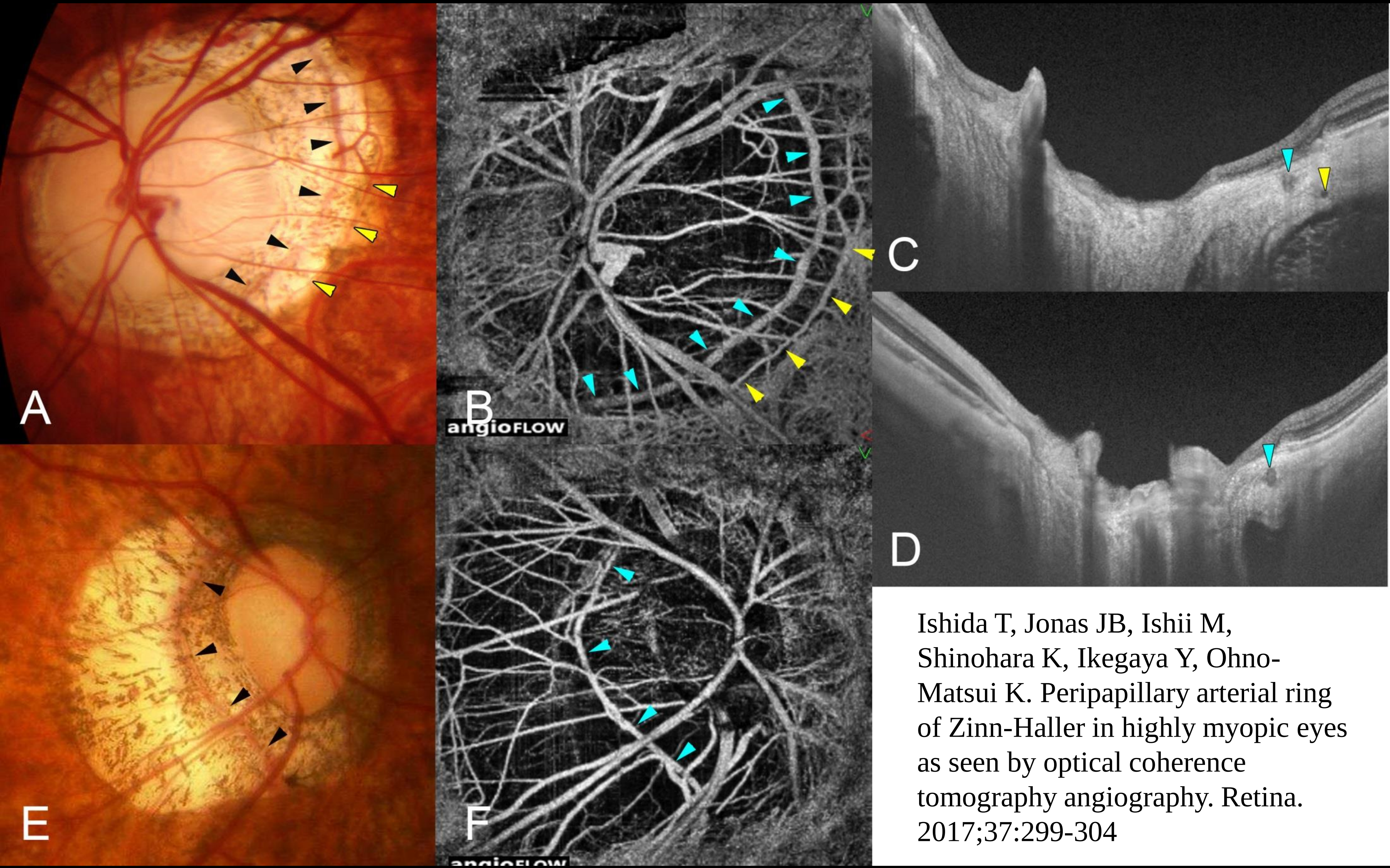
Circular Peripapillary Arterial Ring of Zinn-Haller



Peripapillary Arterial Ring of Zinn-Haller in Highly Myopic Eyes As Detected by Optical Coherence Tomography Angiography

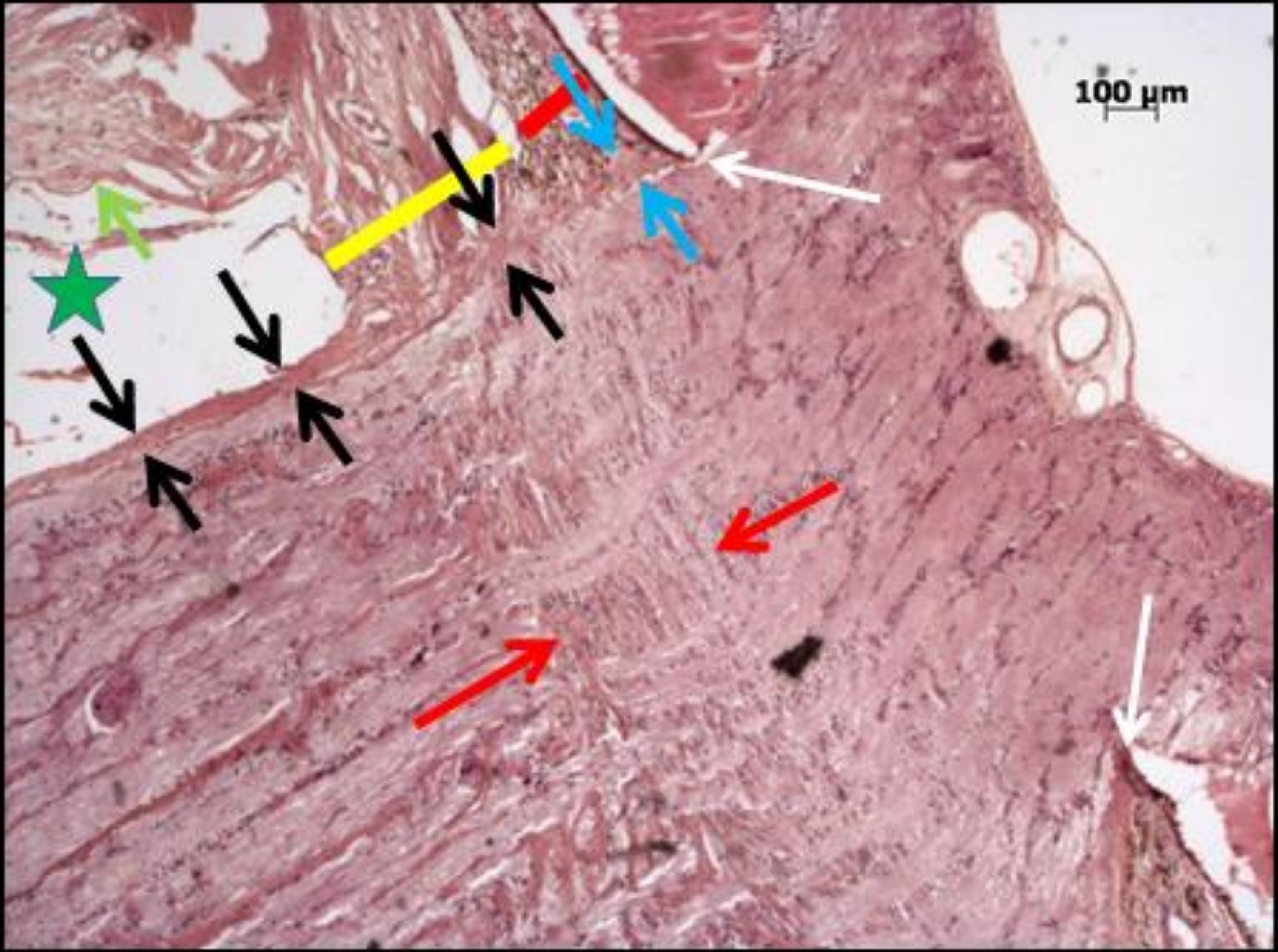


Ishida T, Jonas JB, Ishii M, Shinohara K, Ikegaya Y, Ohno-Matsui K. Peripapillary arterial ring of Zinn-Haller in highly myopic eyes as seen by optical coherence tomography angiography. Retina. 2017;37:299-304

Peripapillary Ring

Jonas JB, Holbach L, Panda-Jonas S. Peripapillary ring: Histology and correlations. Acta Ophthalmol 2014;92:e273-9

Peripapillary Ring



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Peripapillary Ring

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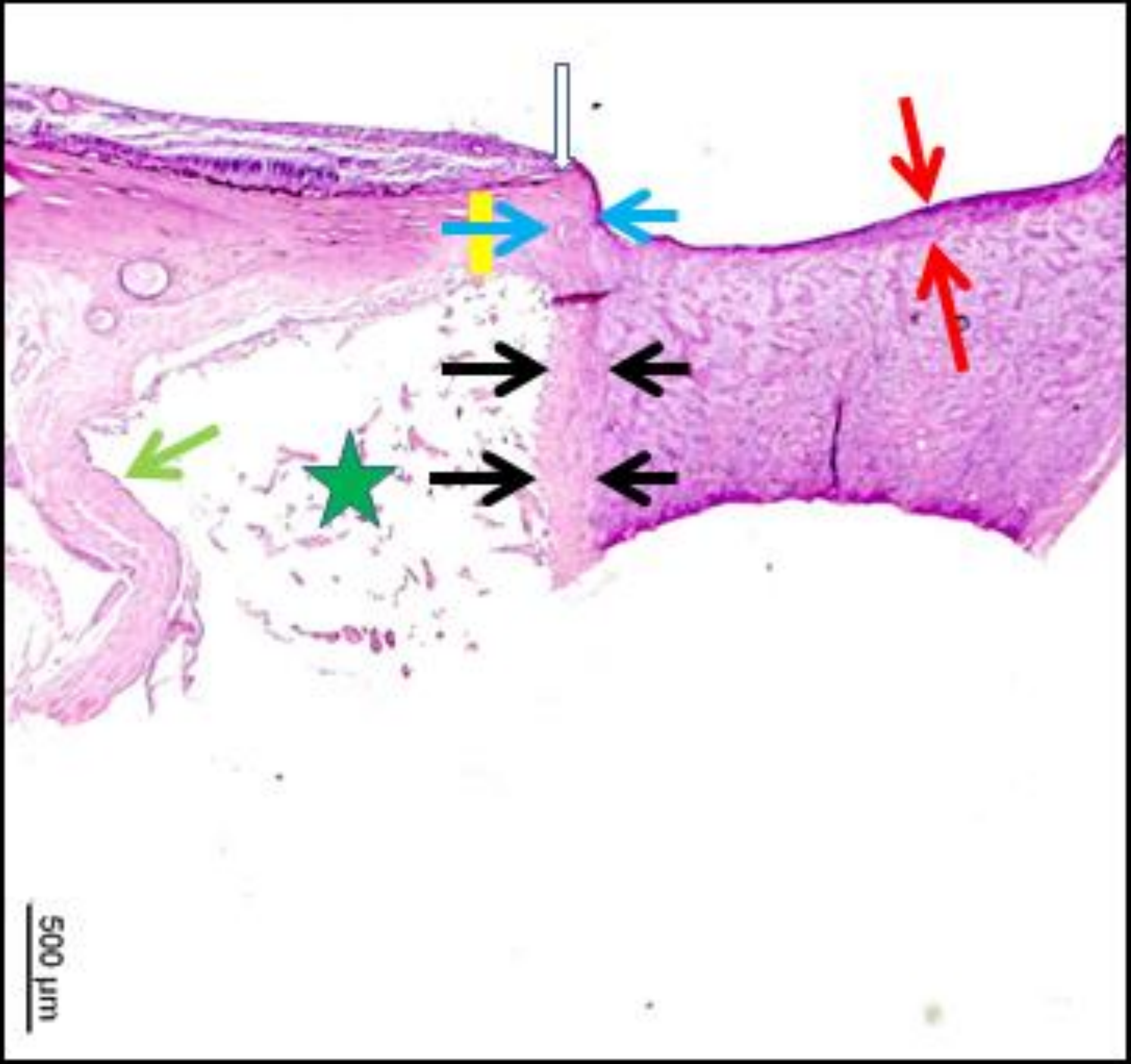
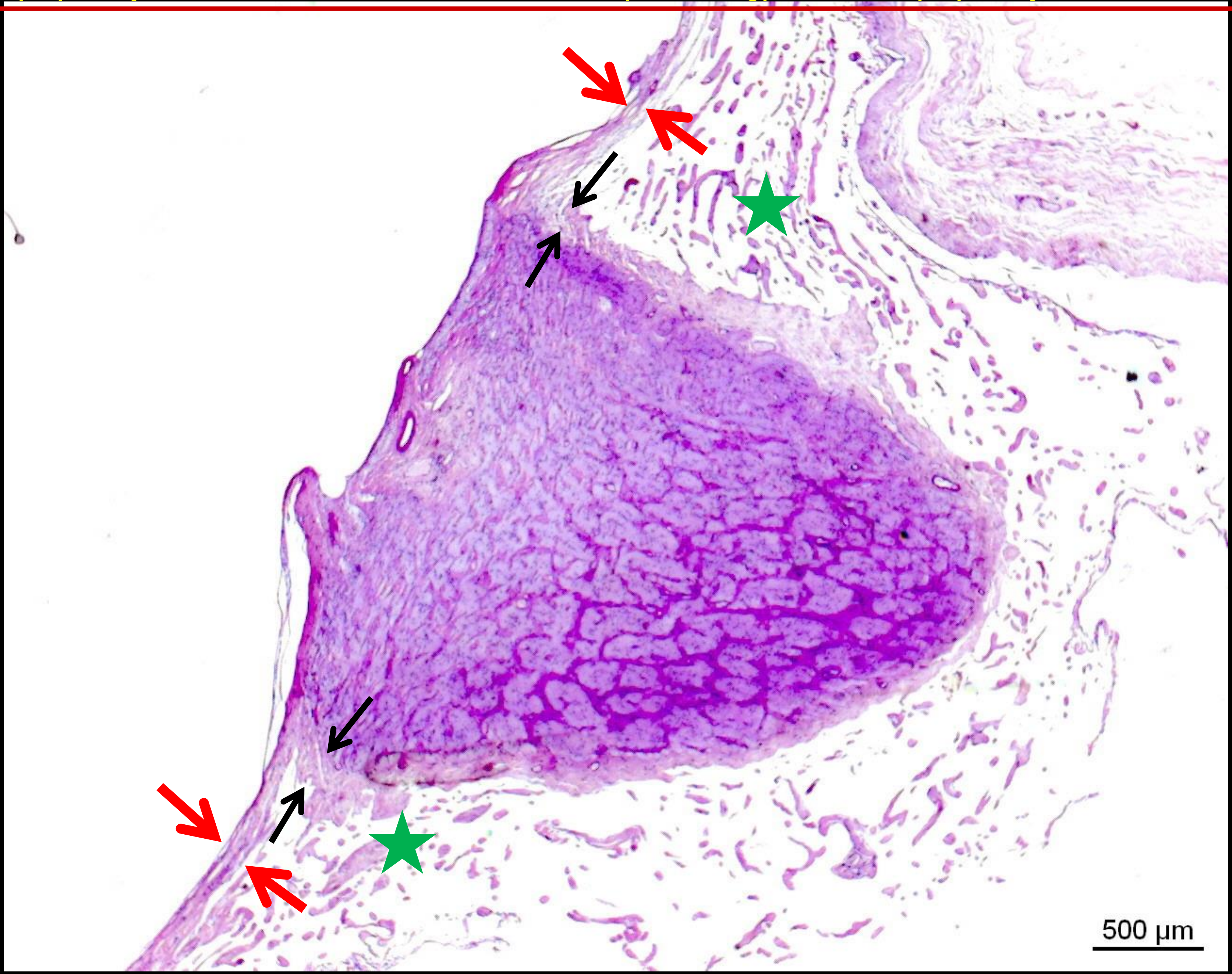
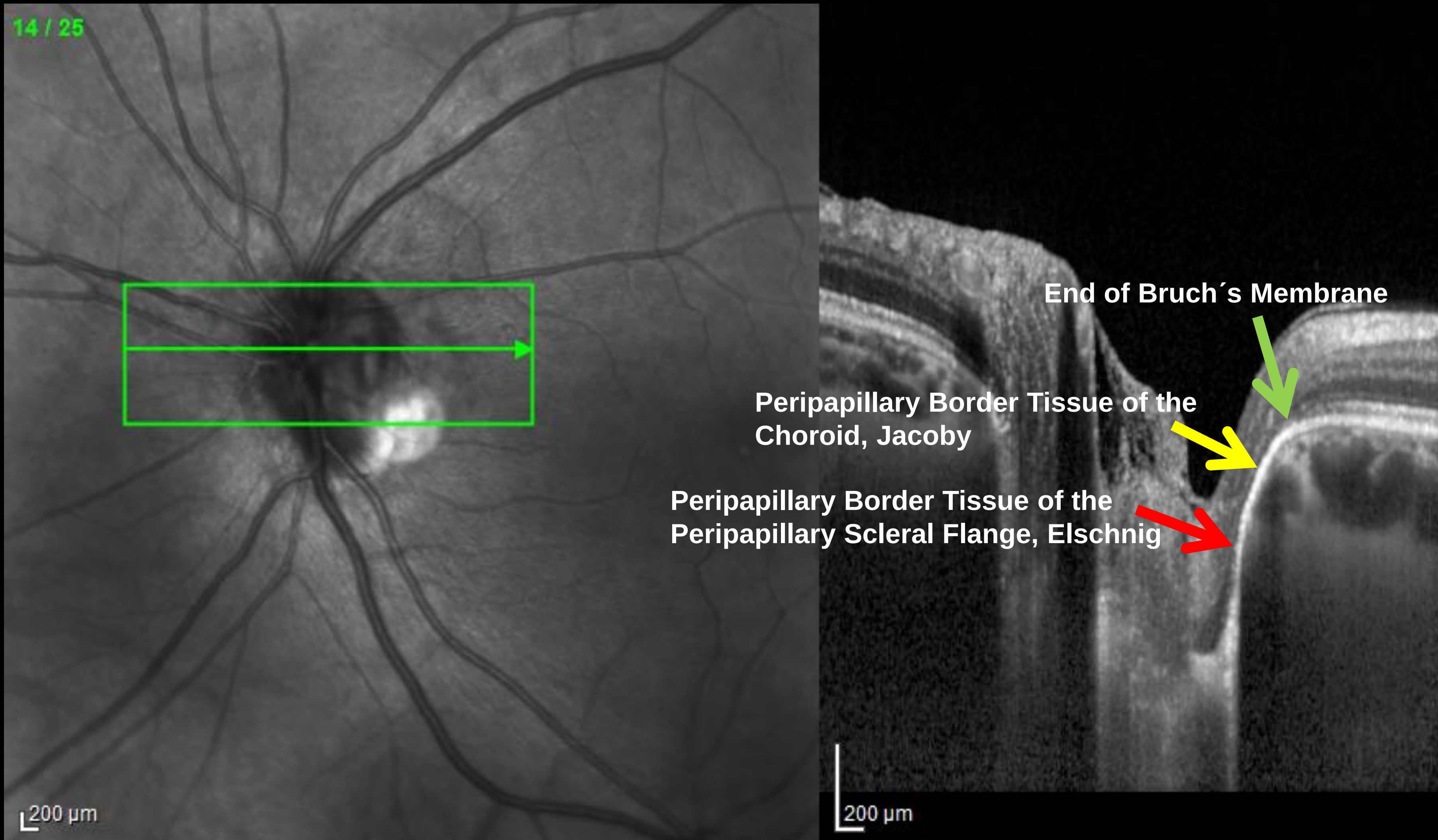
Peripapillary Ring

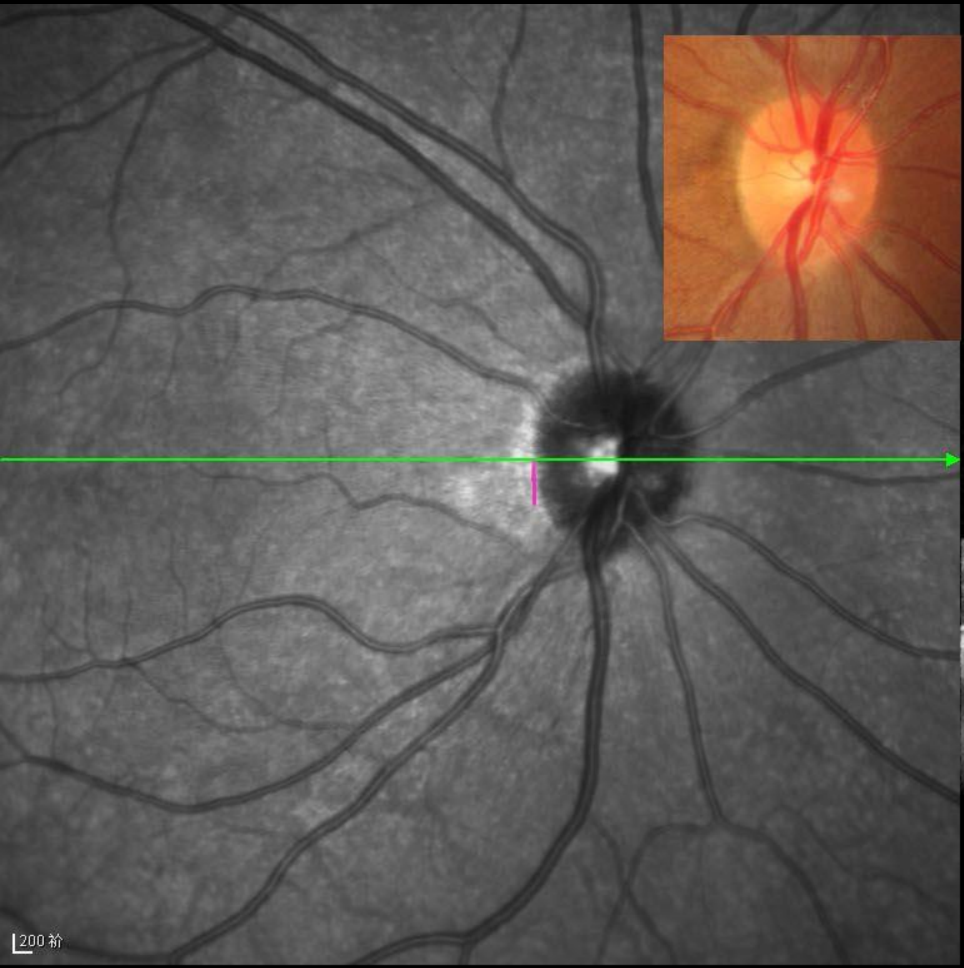


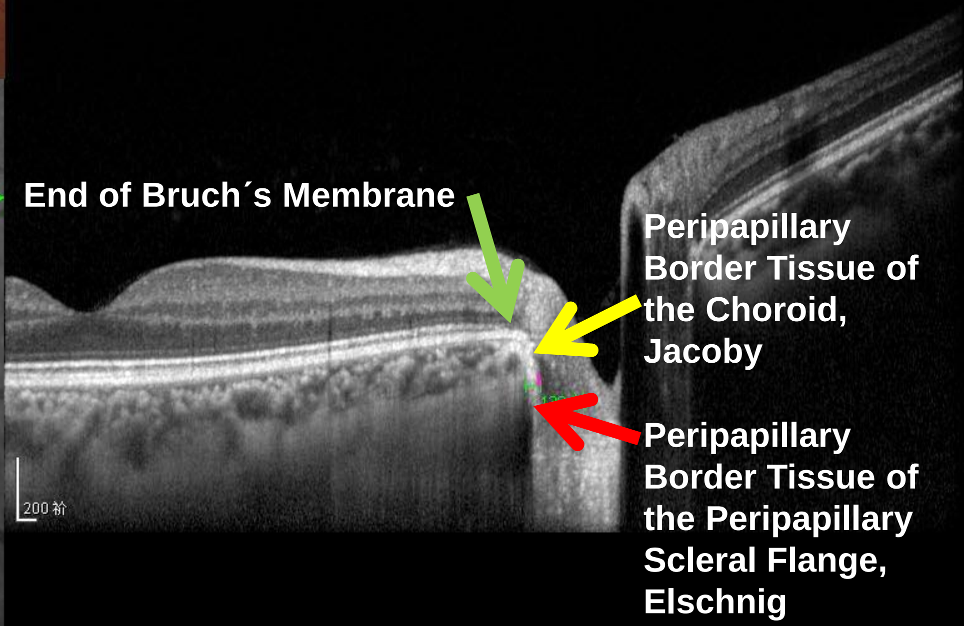
Jonas JB, Holbach L, Panda-Jonas S. Peripapillary ring: Histology and correlations. Acta Ophthalmol 2014;92:e273-9

Peripapillary Border Tissue of the Choroid (Elschnig) and Peripapillary Scleral Tissue




14 / 25
200 µm
End of Bruch´s Membrane
Peripapillary Border Tissue of the
Choroid, Jacoby
Peripapillary Border Tissue of the
Peripapillary Scleral Flange, Elschnig
200 µm





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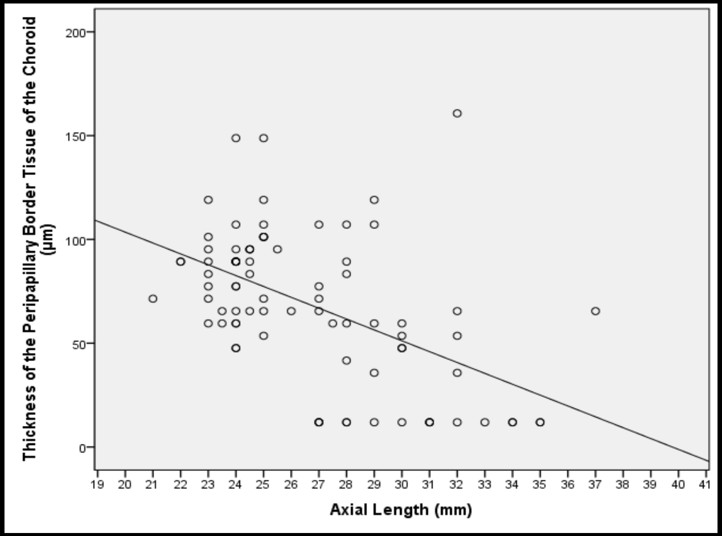
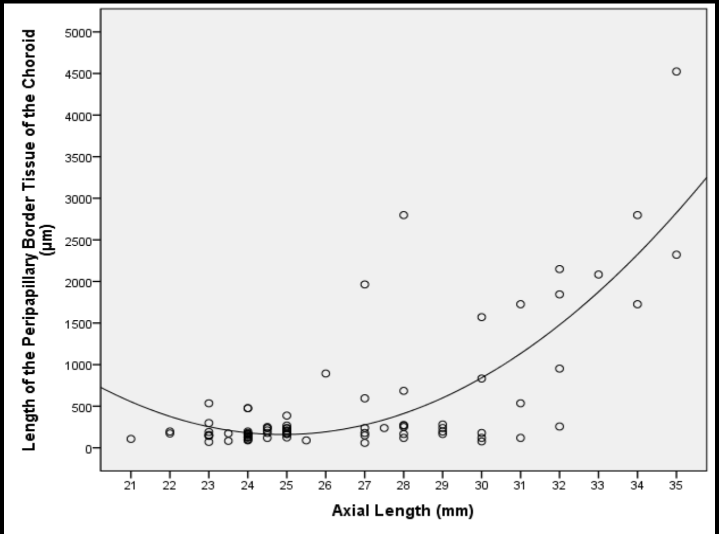
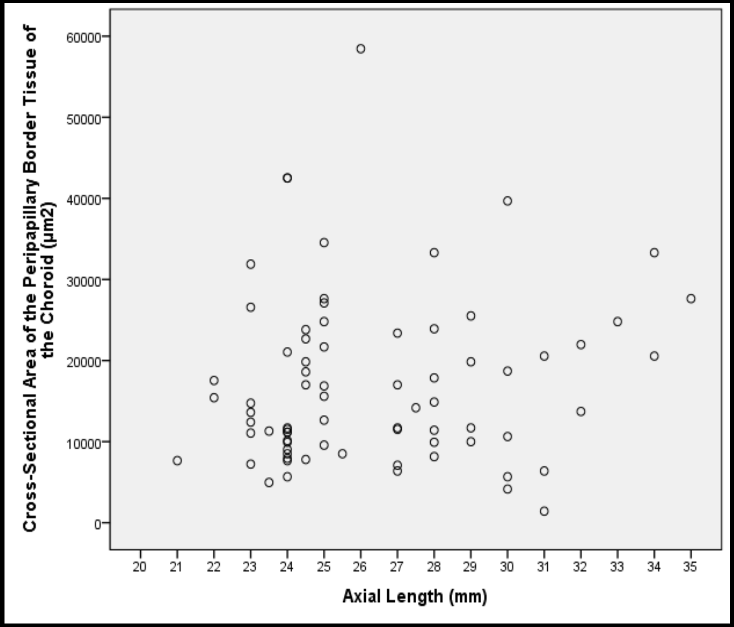
Peripapillary Border Tissue of the Choroid (Elschnig) and Peripapillary Scleral Tissue

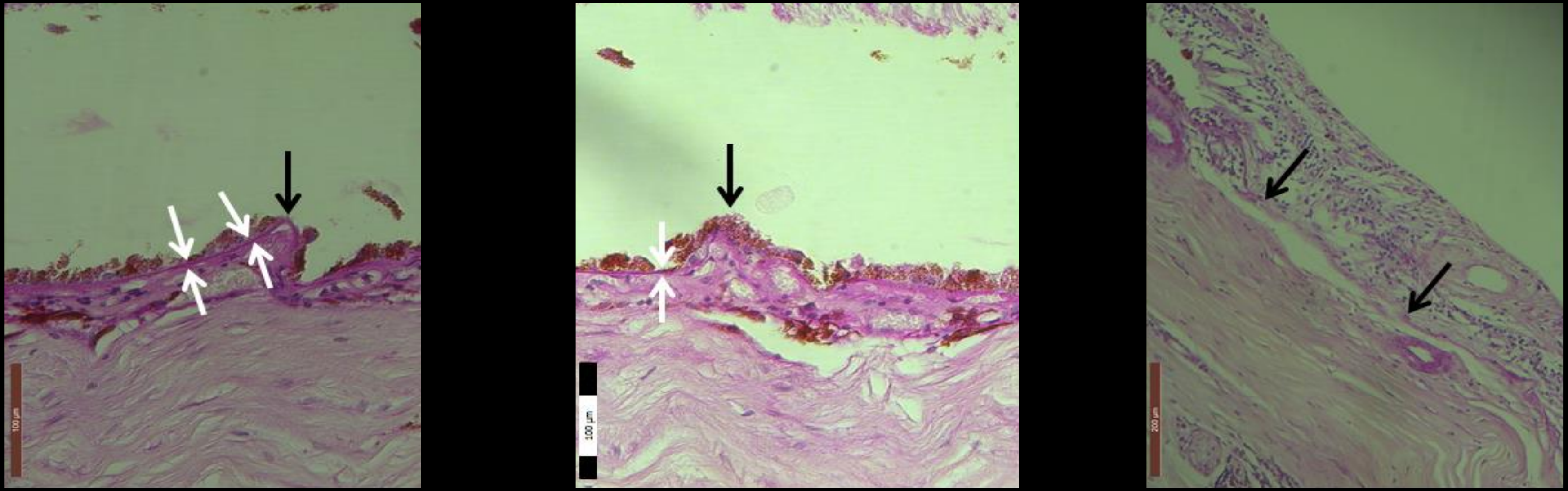






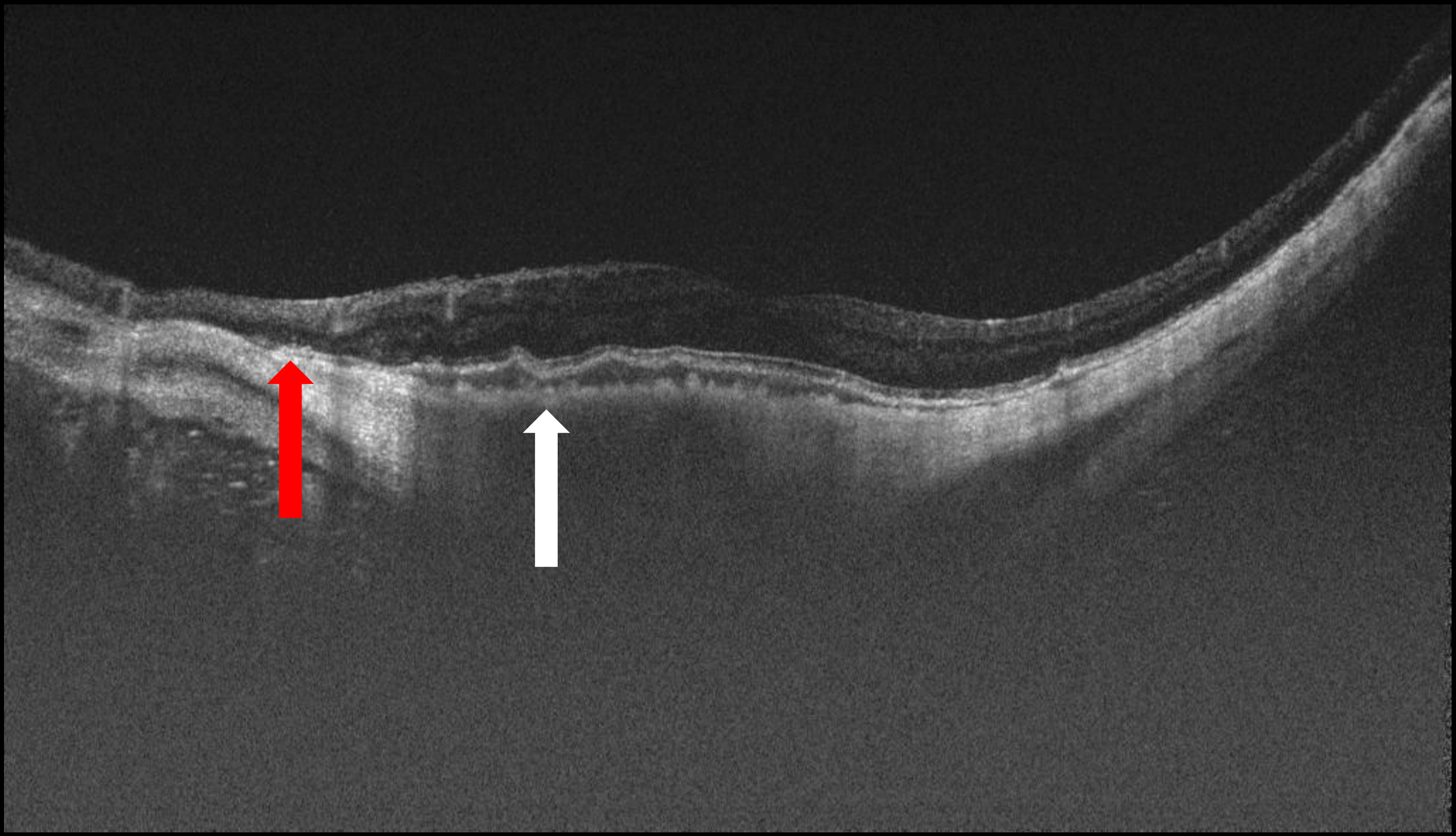
Corrugated Bruch´s Membrane in High Myopia

- 85 eyes (axial length:26.7±3.5 mm).
- BM corrugation was detected in 7 (54%) out of 13 eyes with macular BM defects.
- The single eye with BM corrugation and without macular BM defect showed the corrugated BM located in the parapapillary region at the peripheral end of a large parapapillary gamma zone.



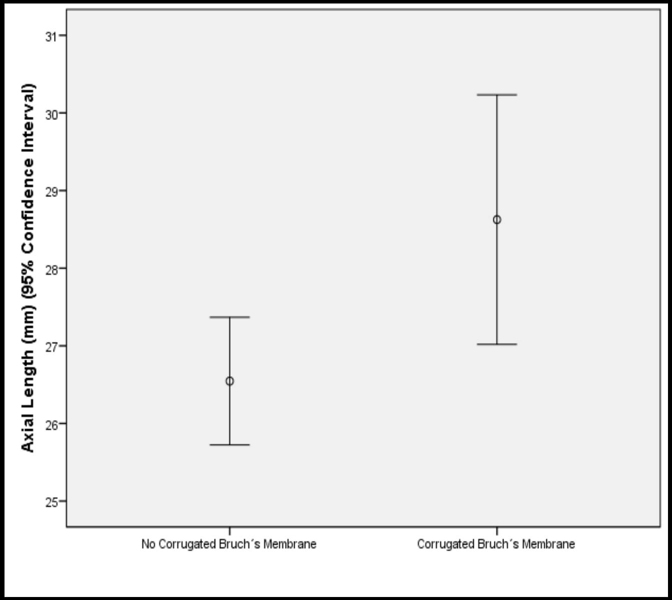
Jonas JB, Jonas RA, Ohno-Matsui K, Holbach L, Panda-Jonas S. Corrugated Bruch's membrane in high myopia. Acta Ophthalmol. 2017 Dec 13. doi: 10.1111/aos.13537. [Epub ahead of print]

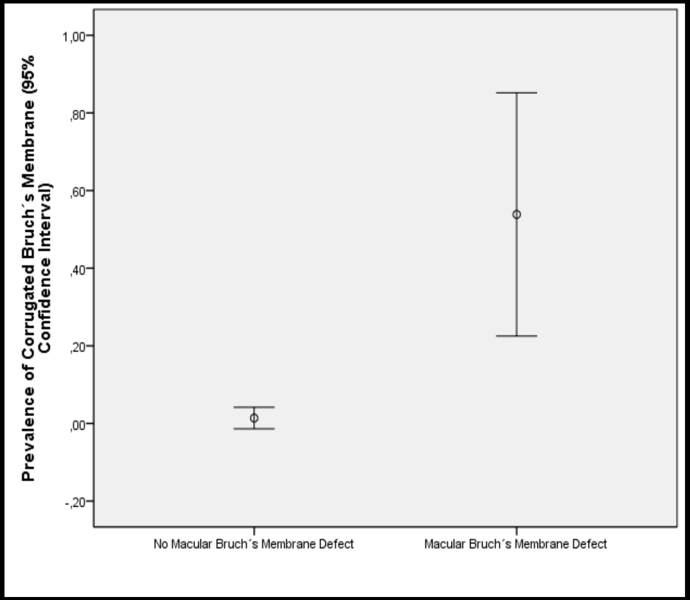
Corrugated Bruch´s Membrane in High Myopia (Courtesy Prof. K. Ohno-Matsui)



Corrugated Bruch´s Membrane in High Myopia

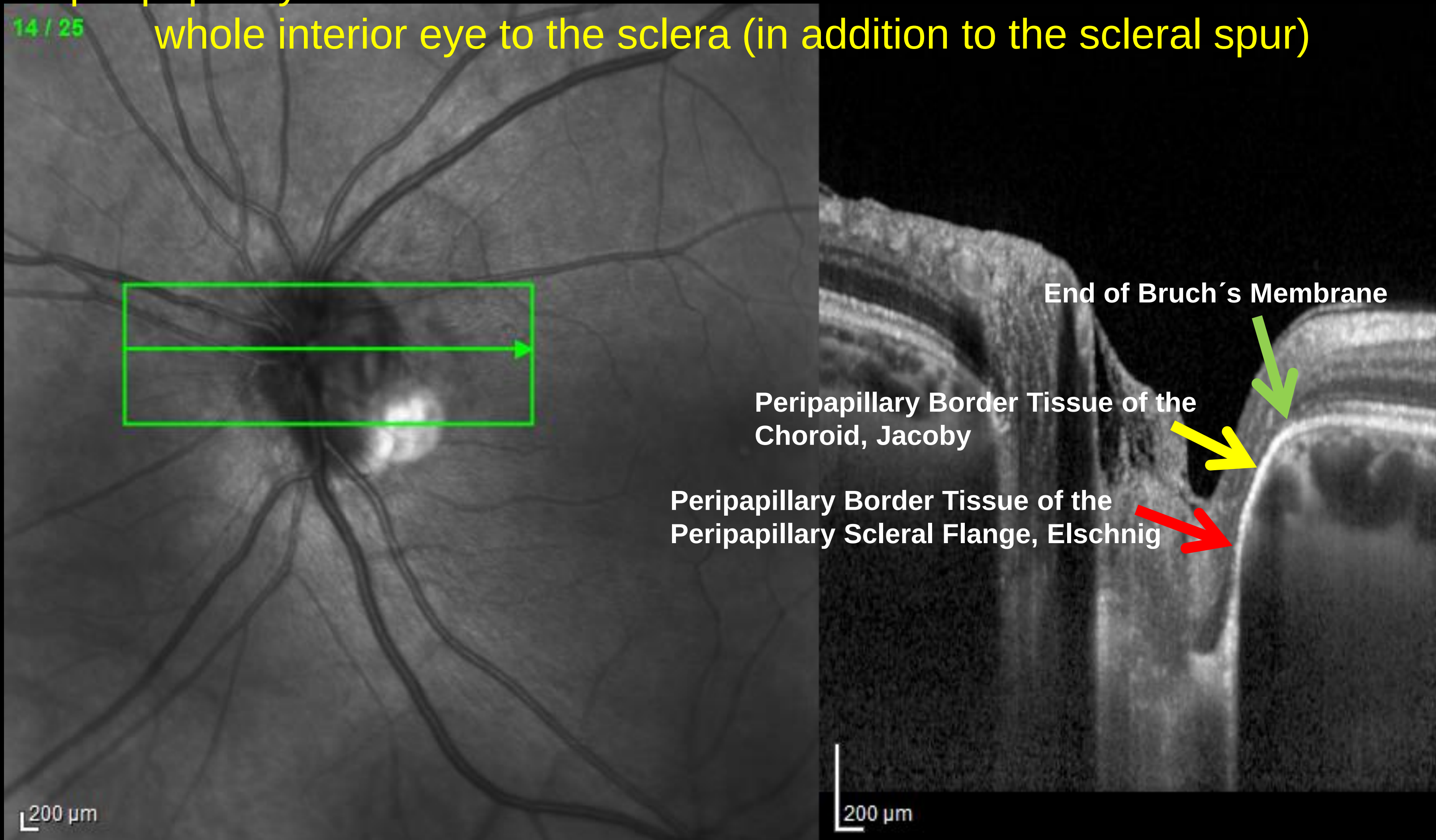
- In multivariate analysis, presence of a corrugated BM, detected in 8 (9.4%) eyes, was strongly associated with the presence of macular BM defects (P=0.001; OR: 4.18), but not with axial length (P=0.54).
- Conclusions: BM corrugation can be present in the vicinity of macular BM defects in highly myopic eyes, perhaps due to differences in the tension within BM in various regions at the margin of the BM defect. BM corrugation may also develop at the papillary end of BM in eyes with a large parapapillary gamma zone, potentially due to a disinsertion of BM at the end of the peripapillary choroidal border tissue of Jacoby.



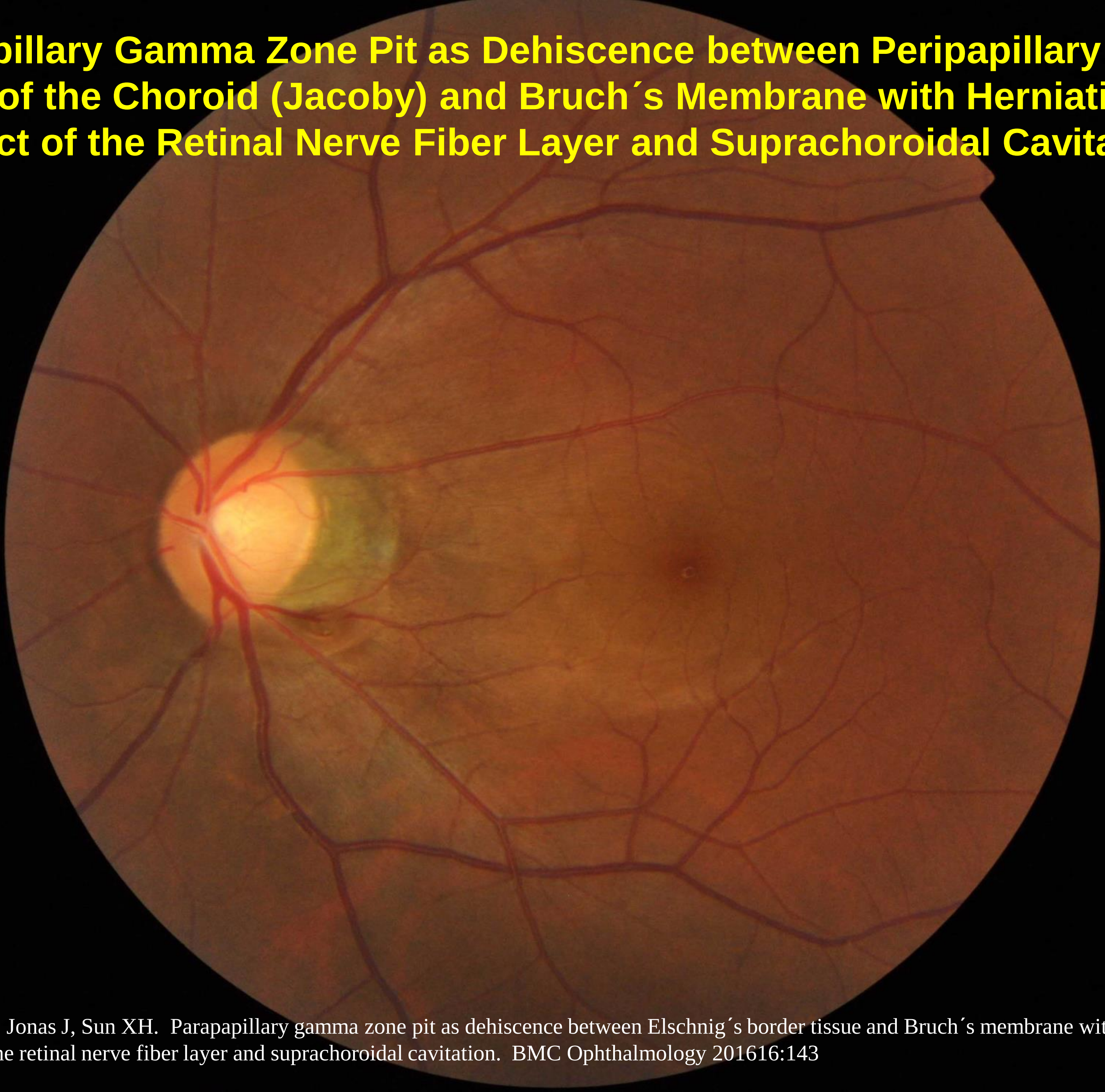


Jonas JB, Jonas RA, Ohno-Matsui K, Holbach L, Panda-Jonas S. Corrugated Bruch's membrane in high myopia. Acta Ophthalmol. 2017 Dec 13. doi: 10.1111/aos.13537. [Epub ahead of print]

The peripapillary border tissue of the choroid is the biomechanical anchor of the whole interior eye to the sclera (in addition to the scleral spur)

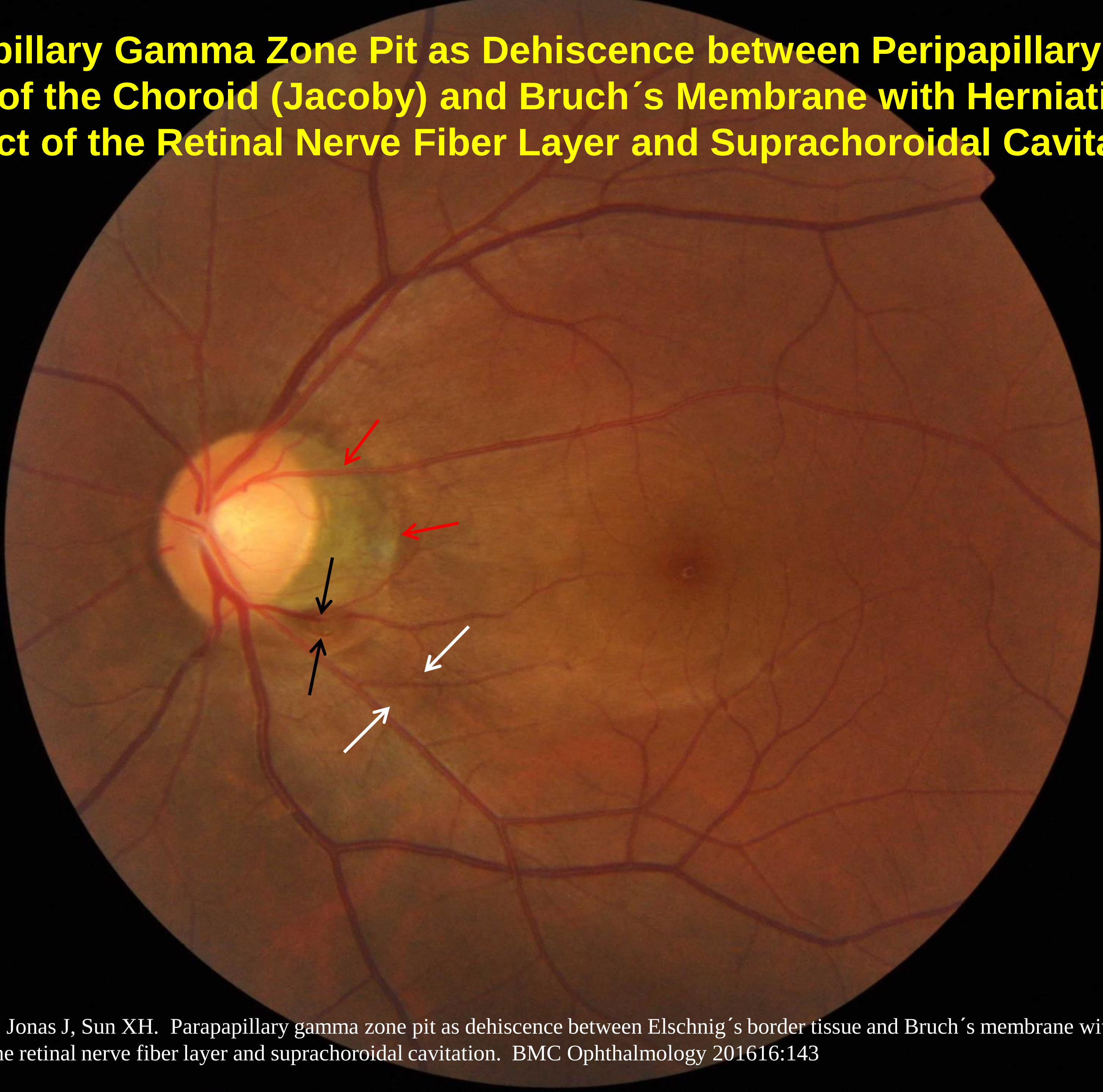


Parapapillary Gamma Zone Pit as Dehiscence between Peripapillary Border Tissue of the Choroid (Jacoby) and Bruch´s Membrane with Herniation and Defect of the Retinal Nerve Fiber Layer and Suprachoroidal Cavitation



Hu XX, Dai Y, Jonas J, Sun XH. Parapapillary gamma zone pit as dehiscence between Elschnig´s border tissue and Bruch´s membrane with herniation and defect of the retinal nerve fiber layer and suprachoroidal cavitation. BMC Ophthalmology 201616:143

Parapapillary Gamma Zone Pit as Dehiscence between Peripapillary Border Tissue of the Choroid (Jacoby) and Bruch´s Membrane with Herniation and Defect of the Retinal Nerve Fiber Layer and Suprachoroidal Cavitation



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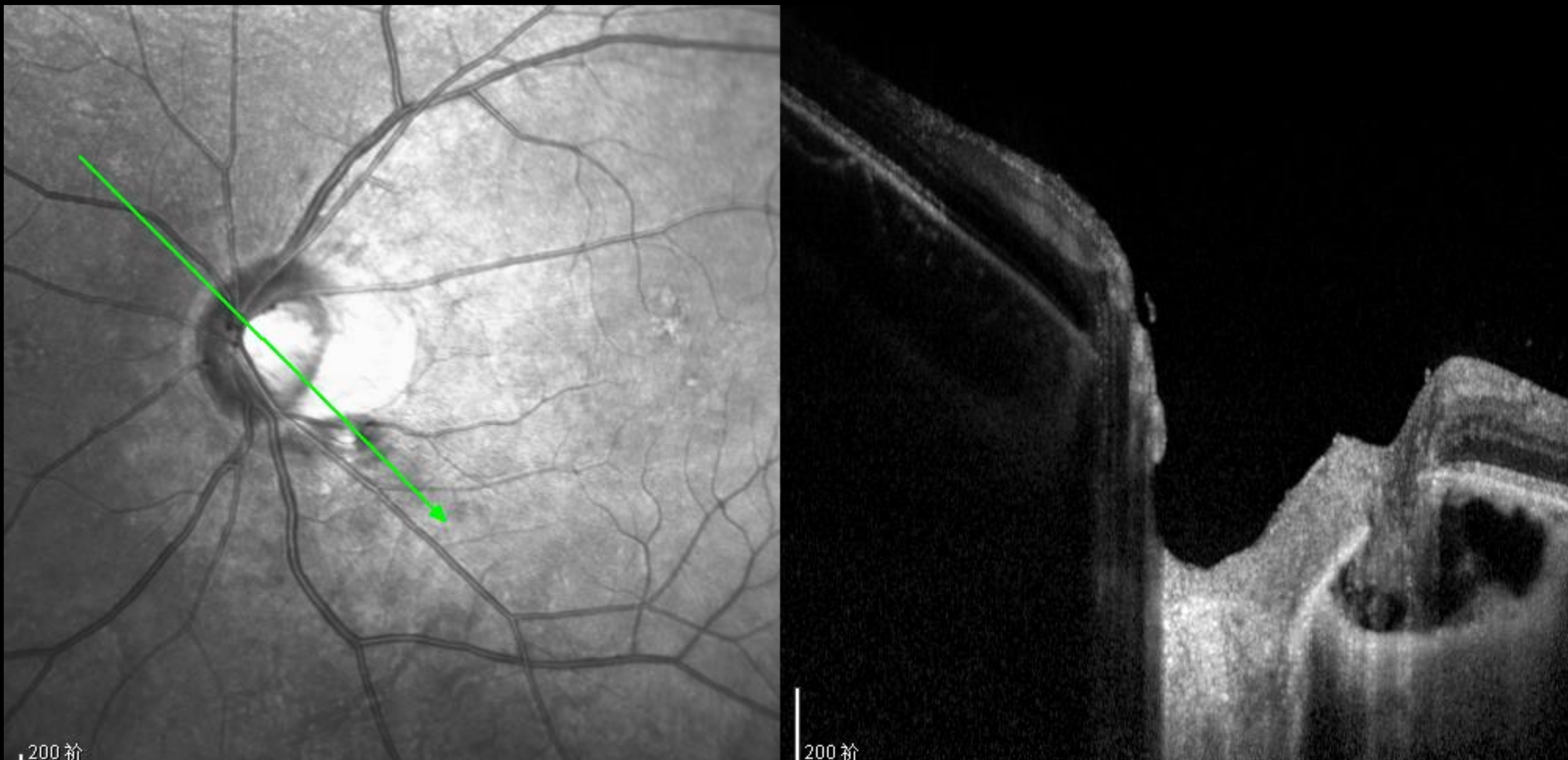

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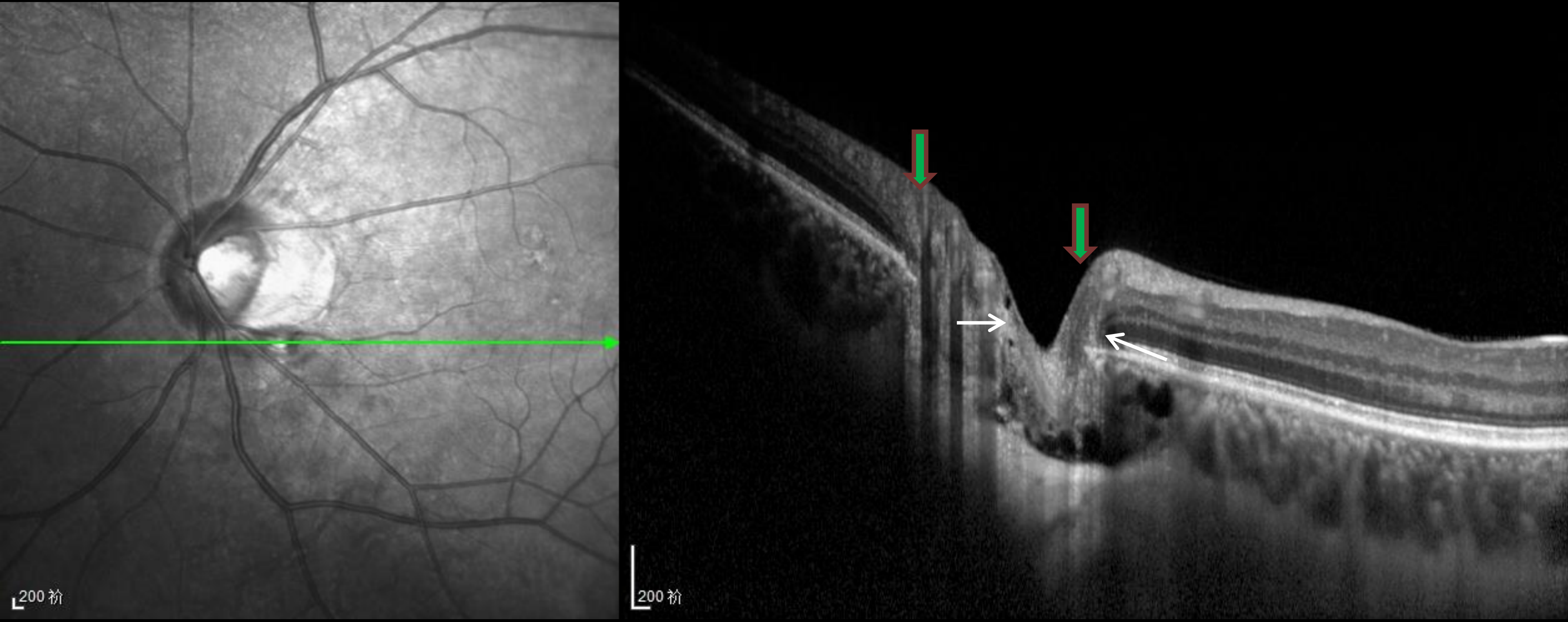
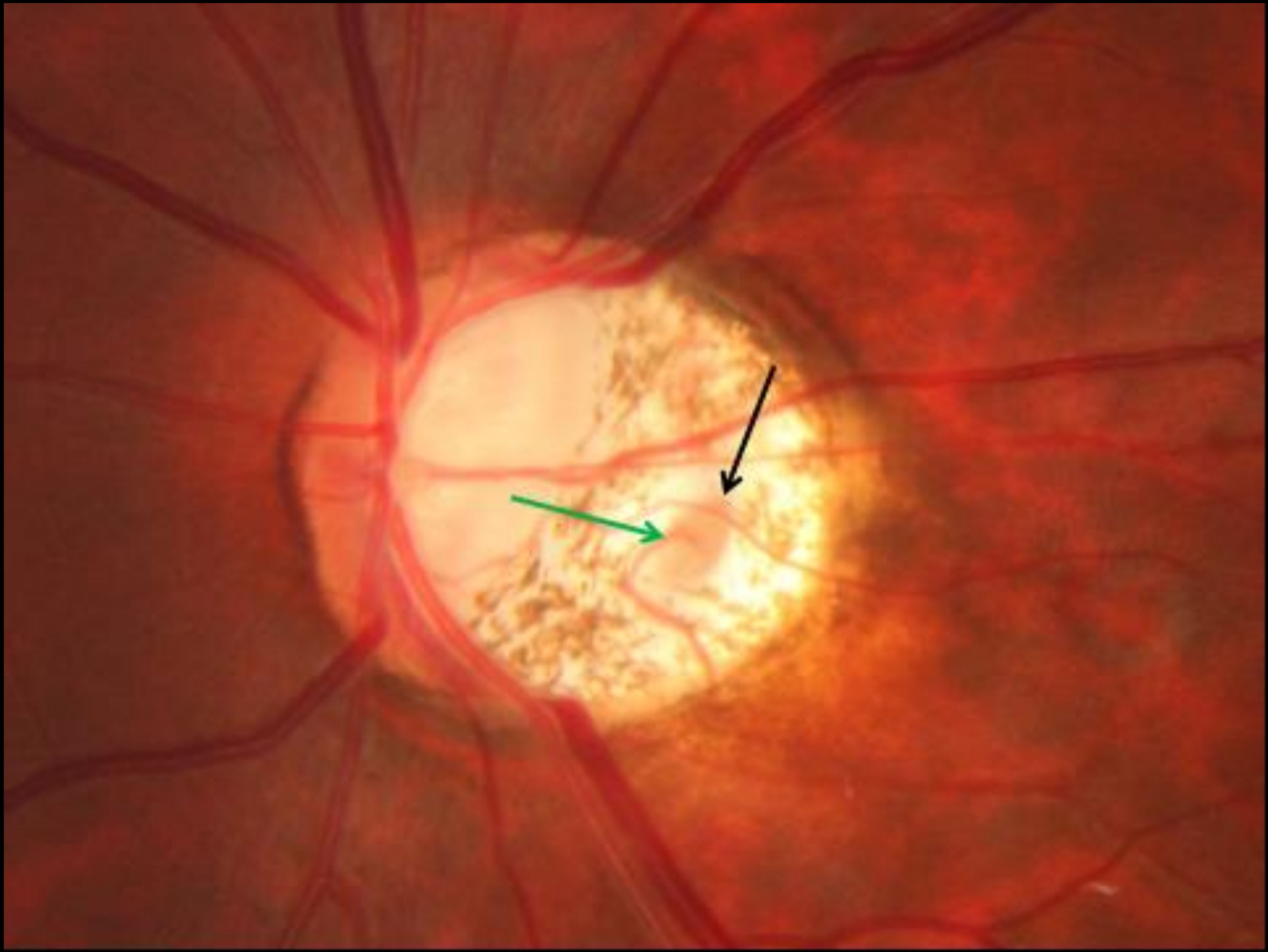
Parapapillary Gamma Zone Pit as Dehiscence between Peripapillary Border Tissue of the Choroid (Jacoby) and Bruch´s Membrane with Herniation and Defect of the Retinal Nerve Fiber Layer and Suprachoroidal Cavitation



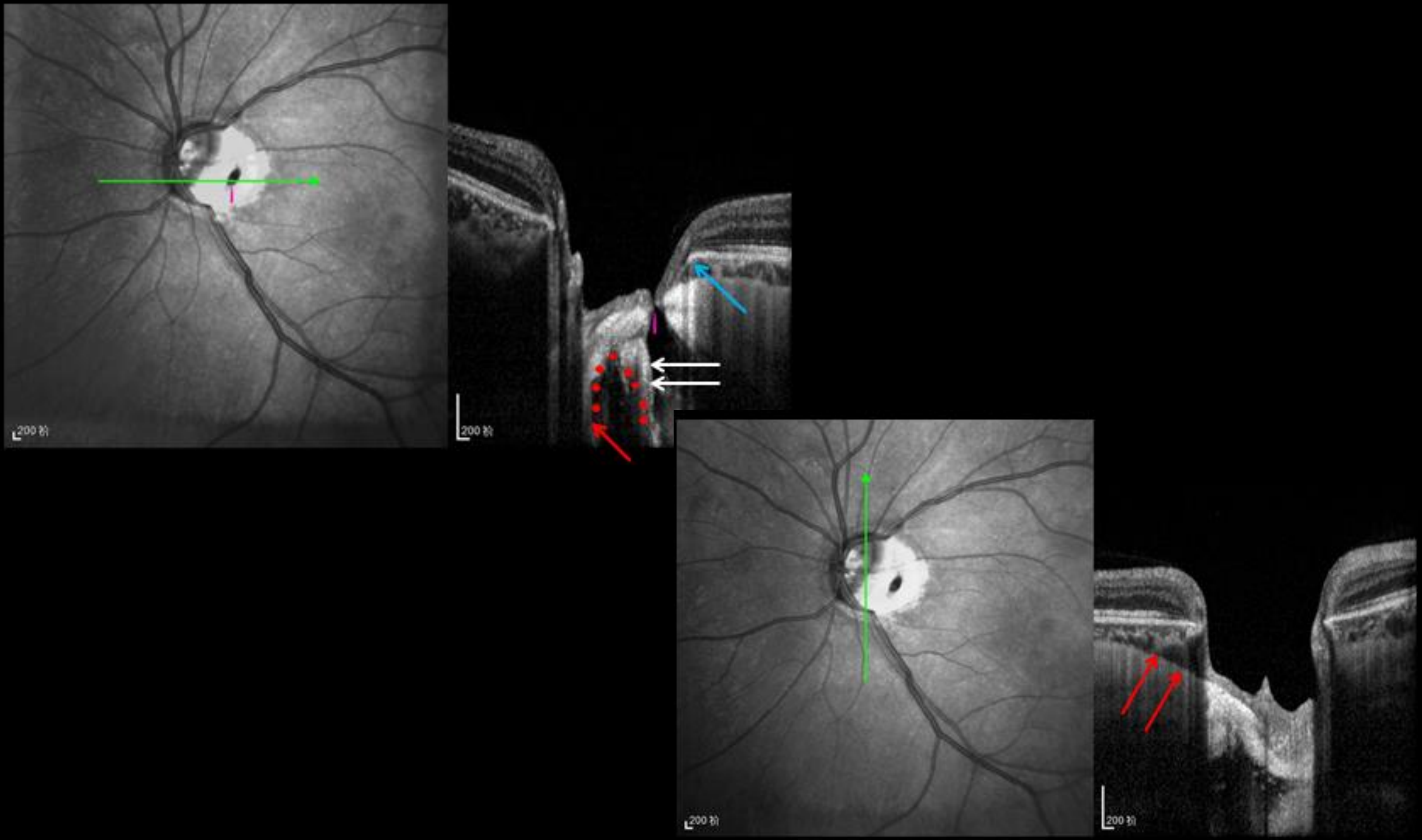
Hu XX, Dai Y, Jonas J, Sun XH. Parapapillary gamma zone pit as dehiscence between Elschnig´s border tissue and Bruch´s membrane with herniation and defect of the retinal nerve fiber layer and suprachoroidal cavitation. BMC Ophthalmology 201616:143

Peripapillary Hole in Gamma Zone



Dai Y, Jonas JB, Ling Z, Sun X. Parapapillary gamma zone hole. J Glaucoma 2013;22:e33-5

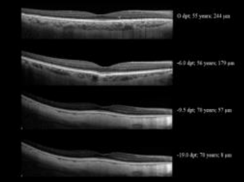
Peripapillary Hole in Gamma Zone as Dehiscence in Peripapillary Border Tissue of the Scleral Flange (Elschnig)



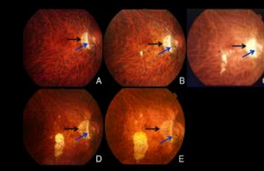
Dai Y, Jonas JB, Ling Z, Sun X. Parapapillary gamma zone hole. J Glaucoma 2013;22:e33-5

Ophthalmoscopical Features of Axial Myopia

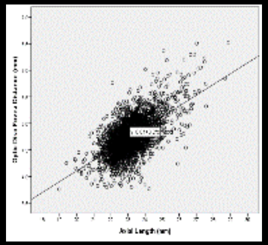
Macula:

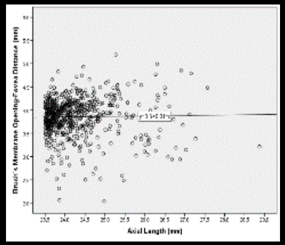


- Fundus tessellation with thinning of the posterior choroid (leptochoroid)
- Lacquer cracks

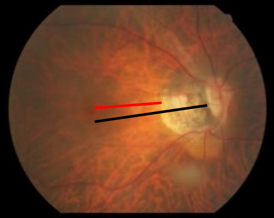


- Patchy atrophies (Bruch´s membrane defects)
- Macular atrophy (Bruch´s membrane defects)
- Choroidal neovascularization
- Retinoschisis

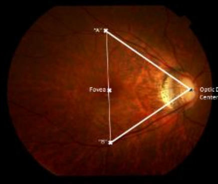


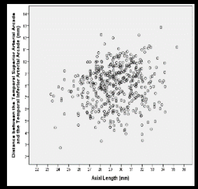


- Macula ridge
- Dome-Shaped macula
- Scleral staphyloma
- Disc-Fovea distance increases with longer axial length



- Length of (horizontal) macular Bruch´s membrane (Disc-fovea distance minus parapapillary gamma zone width) is not related with axial length (if > 24 mm)
- Length of (vertical) macular Bruch´s membrane (distance temp. arterial arcade) is not significantly related with axial length, so that the angle kappa decreases in myopia

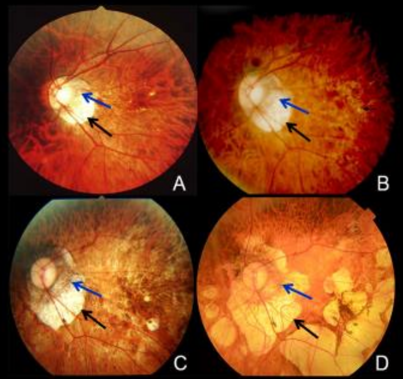


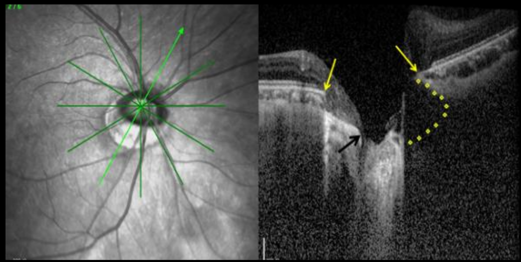


Ophthalmoscopical Features of Axial Myopia

<u>Optic nerve head:</u>

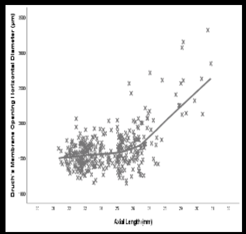
- Parapapillary gamma zone enlargement temporal by a temporal shift of the Bruch´s membrane opening
- Gamma Zone enlargement circular
- Delta zone enlargement (elongation of peripapillary scleral flange)
- Optic disc (lamina cribrosa) enlargement

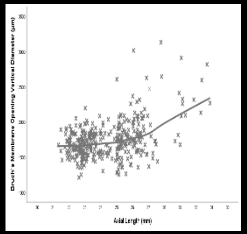


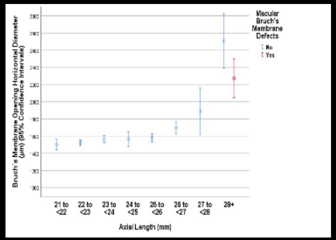


Histology:

- Shift of Bruch´s membrane in temporal direction leading to BM overhanging nasally and lack of BM temporally (gamma zone)
- Elongation and thinning of the lamina cribrosa (decrease in distance between intravitreal cabity and retrobulbar compartment)
- BM-free zone temporally (gamma zone) and eventually circularly
- Elongation and thinning of the peripapillary scleral flange (delta zone)





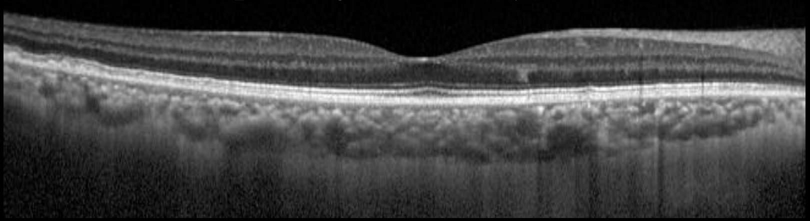


Mechanism of Process of Emmetropization (Myopization)

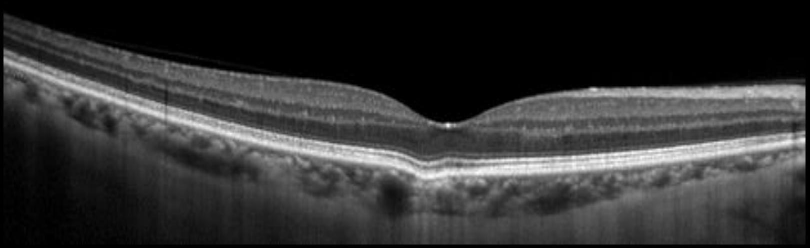
Addressing the question about the driving force to elongate the eye in myopia, one may, in contrast to the common belief, not consider the sclera but Bruch´s membrane (BM) as the primary driver elongating the globe, since:

- If the sclera was the primary moving structure in axial elongation, the choroidal space would widen.

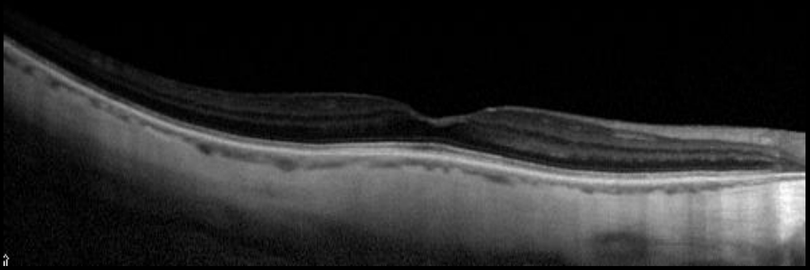
O dpt; 55 years; 244 µm



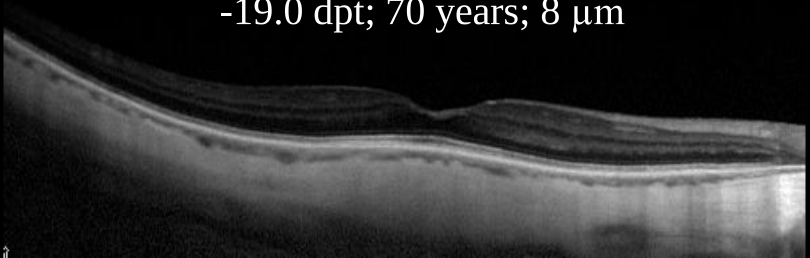
-6.0 dpt; 56 years; 179 µm



-9.5 dpt; 70 years; 57 µm



-19.0 dpt; 70 years; 8 µm

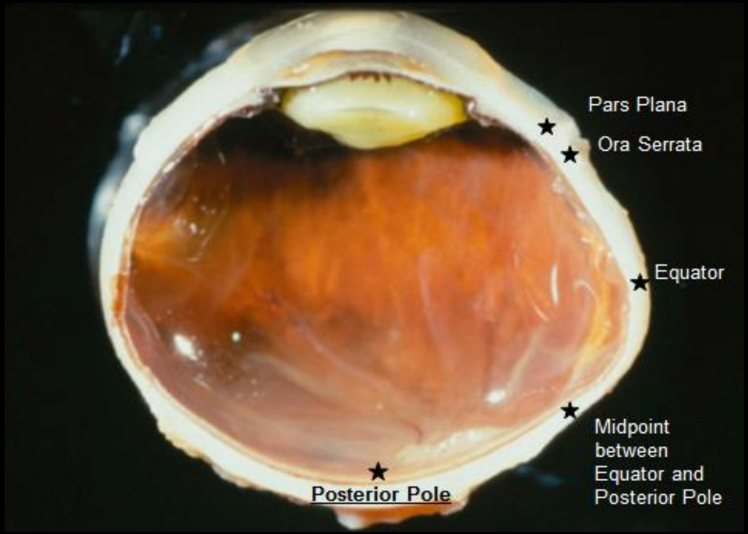


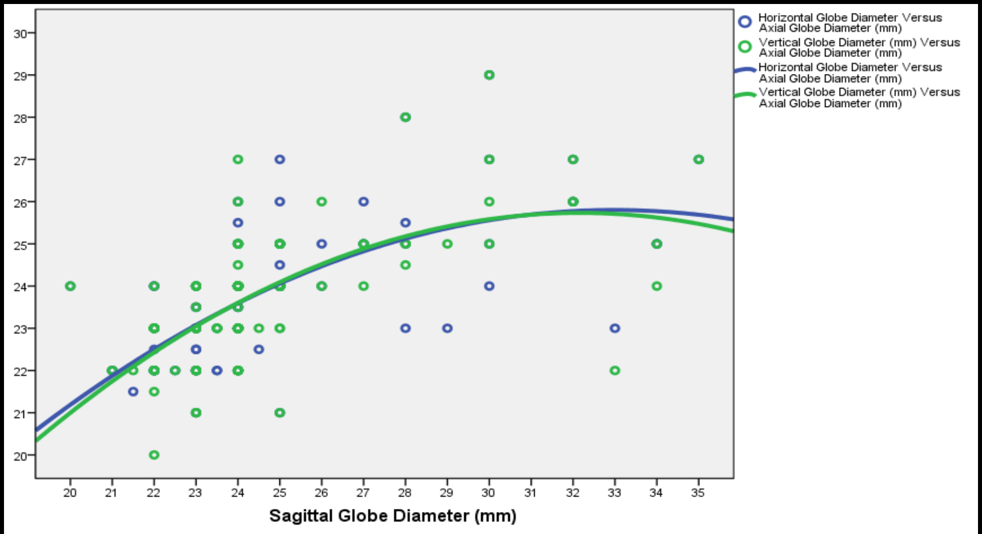
Mechanism of Process of Emmetropization (Myopization)
Bruch´s Membrane as Biomechanically Supporting Structure

- Globe Diameters:

- Axial length >24 mm, the horizontal and vertical globe diameter increases by 0.19mm and 0.21mm, respectively, for each mm increase in axial diameter

- It suggests an elongation of the eye walls in regions close to the equator.



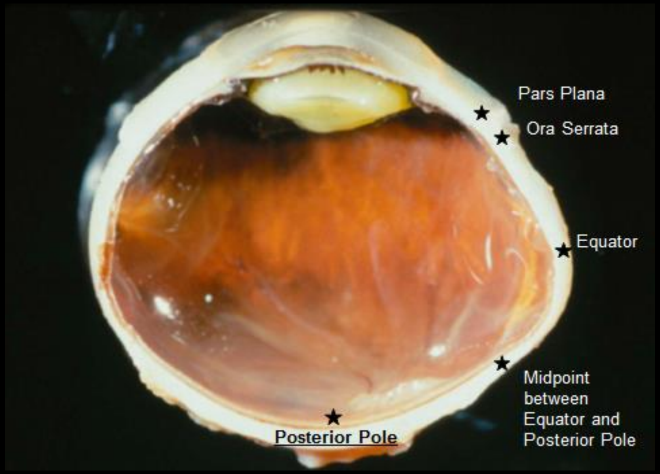


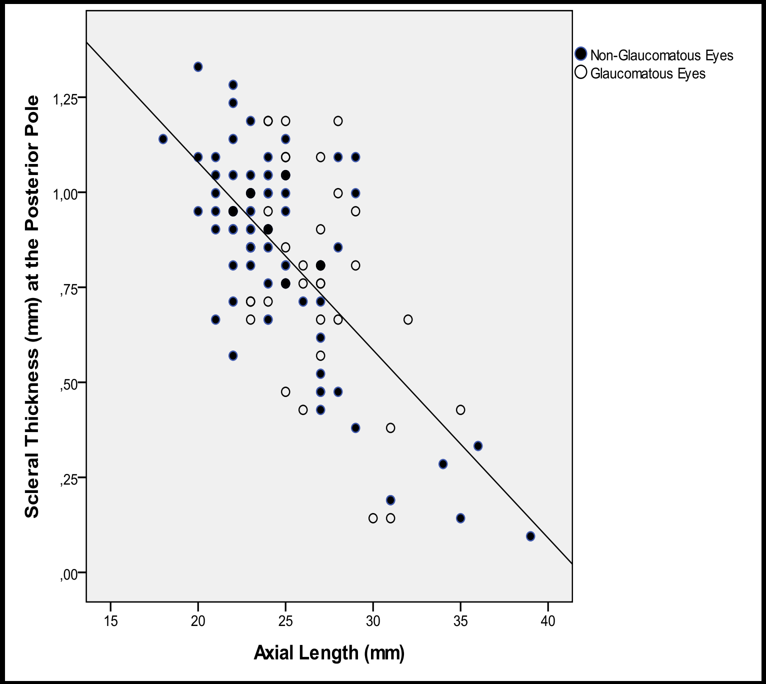
Jonas JB, Ohno-Matsui K, Holbach L, Panda-Jonas S. Association between axial length and horizontal and vertical globe diameters. Graefes Arch Clin Exp Ophthalmol 2017;255:237-42

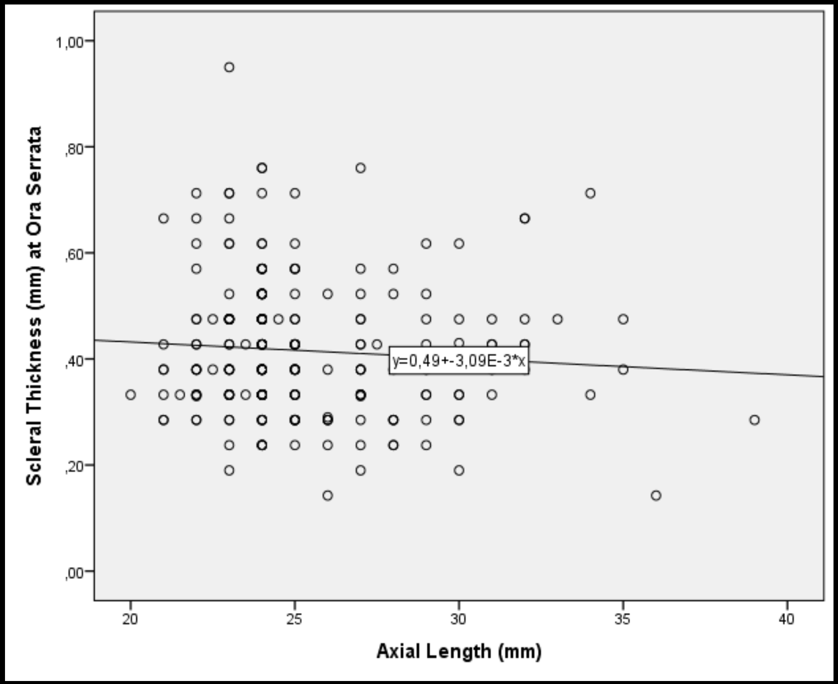
Mechanism of Process of Emmetropization (Myopization)
Bruch´s Membrane as Biomechanically Supporting Structure

- Scleral thickness:

- Decreases with longer axial length, most marked at the posterior pole, least marked in pars plana region







Heine L. Beiträge zur Anatomie des myopischen Auges. Arch Augenheilkd 1899;38:277-90
Vurgese S, Panda-Jonas S, Jonas JB. Scleral thickness in human eyes. PLoS One 2012;7:e29692.

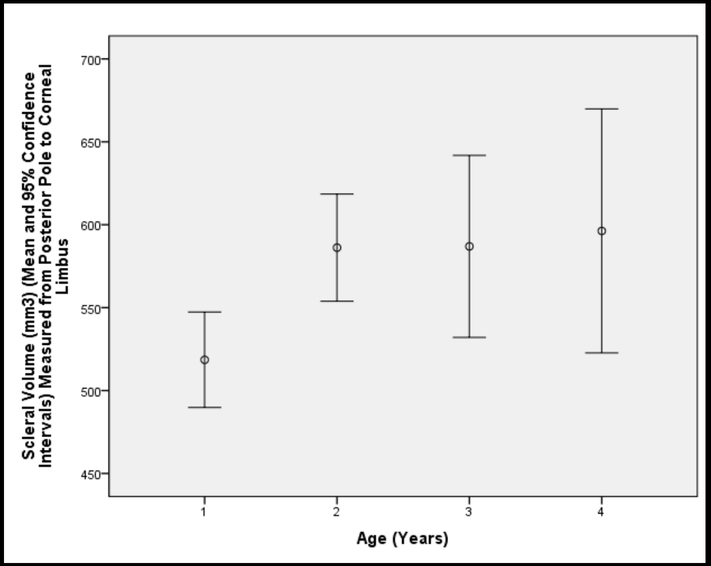
Mechanism of Process of Emmetropization (Myopization)
Bruch´s Membrane as Biomechanically Supporting Structure

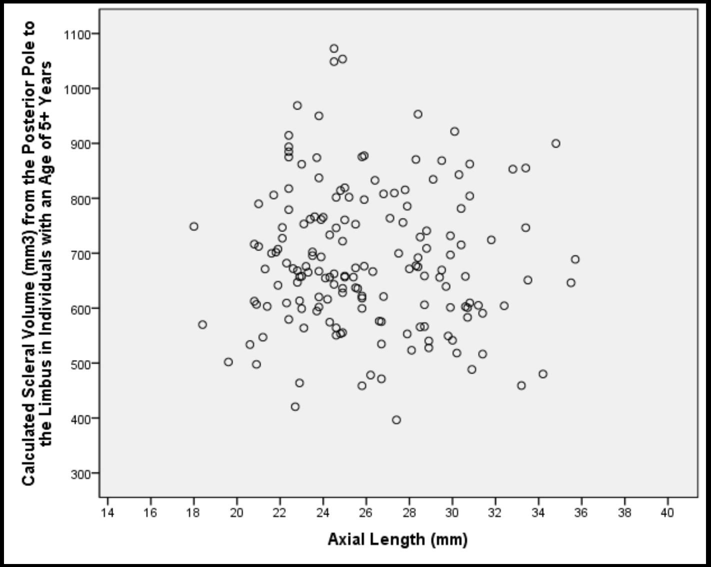
- Scleral Volume:

- Increases up to the end of the second year of life, and remaines then constant

- In individuals aged ≥5years, scleral volume is not significantly associated with axial length (*P*=0.70)

- There is no active scleral growth





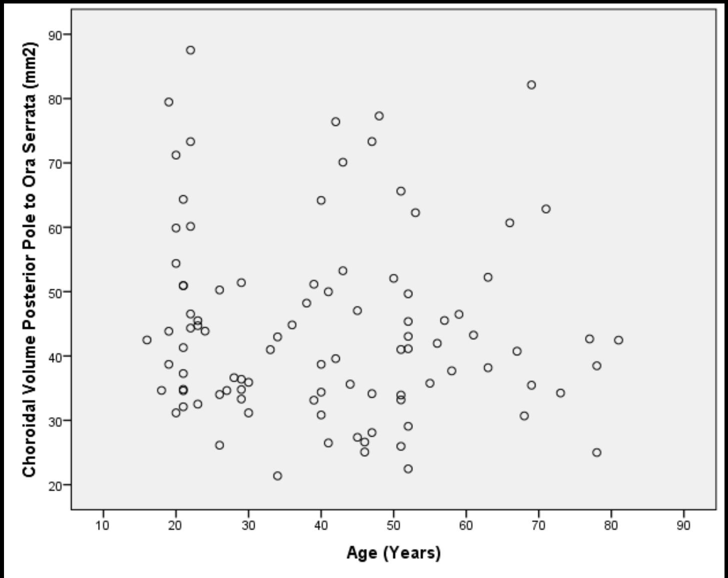
Jonas JB, Holbach L, Panda-Jonas S. Scleral cross section area and volume and axial length. PLoS One. 2014 Mar 28;9(3):e93551.
Shen L, Xu X, You QS, Gao F, Zhang Z, Li B, Jonas JB. Scleral thickness in Chinese eyes. Invest Ophthalmol Vis Sci 2015;56:2720-7

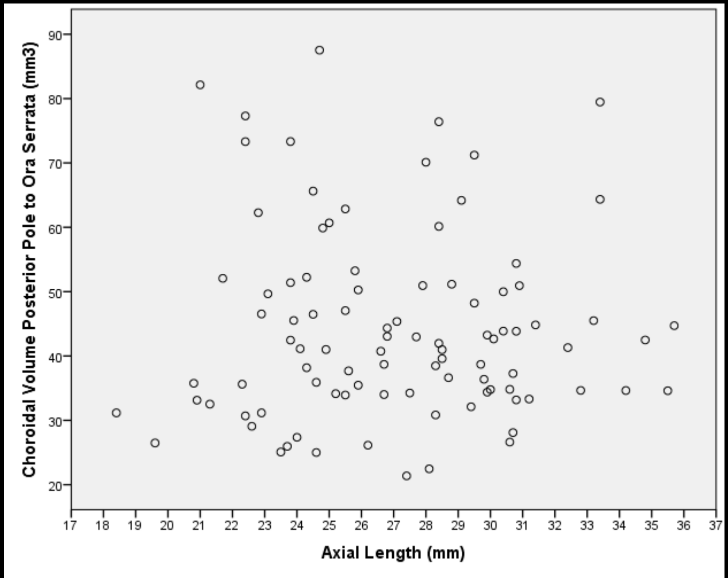
Mechanism of Process of Emmetropization (Myopization)
Bruch´s Membrane as Biomechanically Supporting Structure

- Choroidal Volume:

- Not significantly associated with age (*P*=0.47) or axial length (*P*=0.83) in individuals aged 16+ years.

- There is no active choroidal growth





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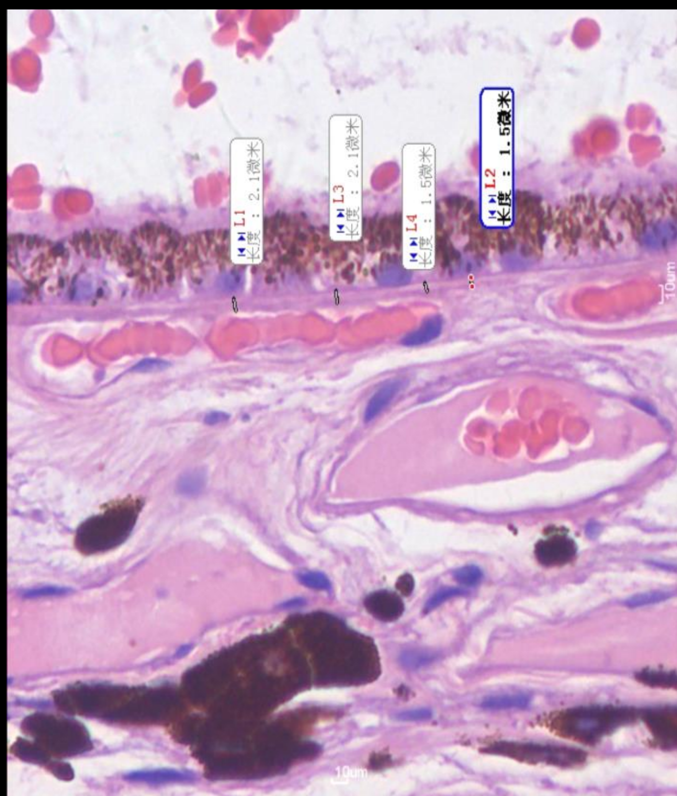
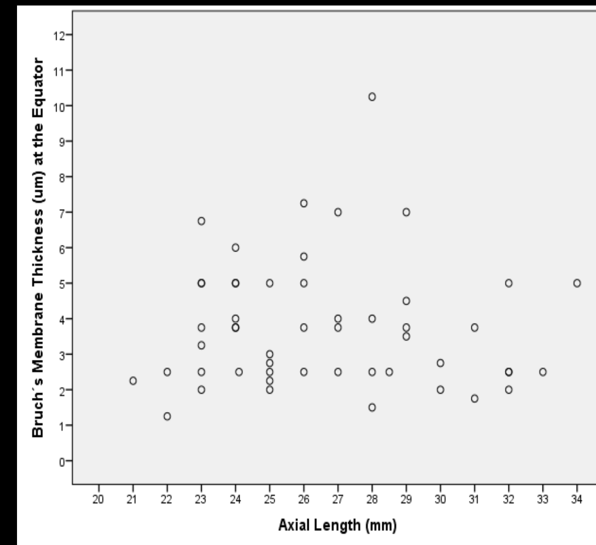
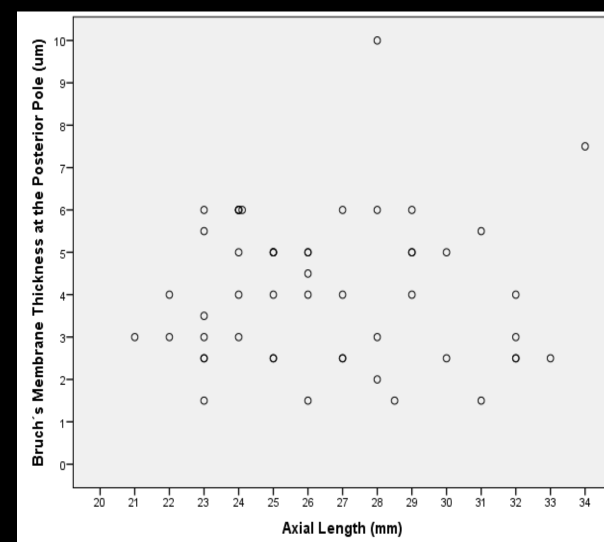
Mechanism of Process of Emmetropization (Myopization)
Bruch´s Membrane as Biomechanically Supporting Structure

- In contrast to sclera and choroid, BM thickness at any location is not (all P>0.45) related with axial length.
- BM increases in volume with axial length



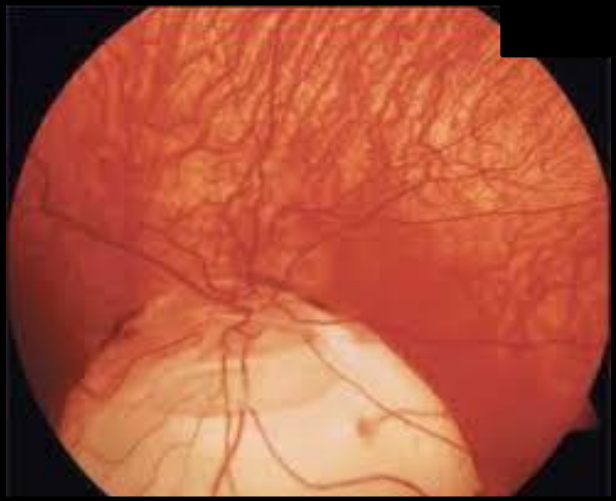


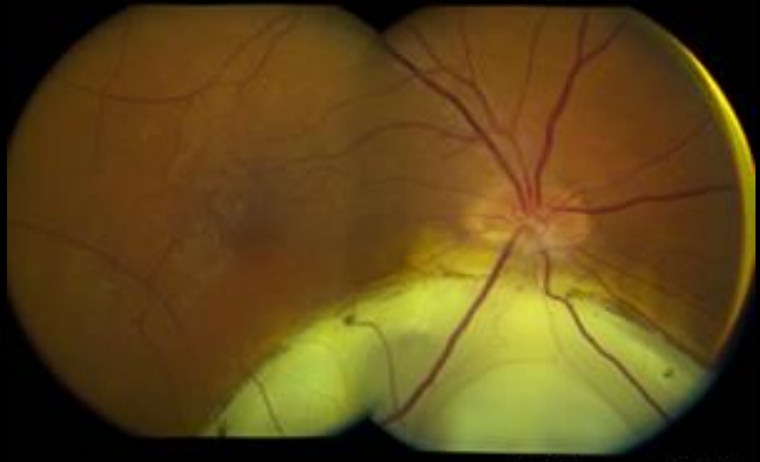


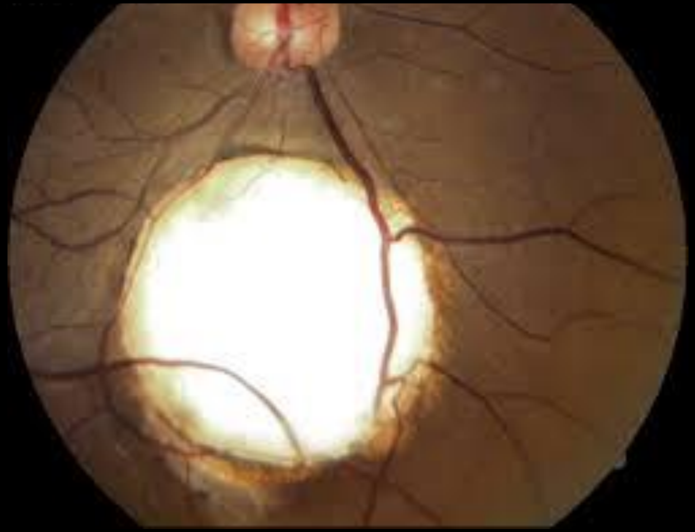
Jonas JB, Holbach L, Panda-Jonas S. Bruch´s membrane thickness in high myopia. Acta Ophthalmol 2014;92:e470-4
Bai HX, Mao Y, Shen L, Xu XL, Gao F, Zhang ZB, Li B, Jonas JB. Bruch´s membrane thickness in relationship to axial length. PLoS One. 2017; 12:e0182080

Mechanism of Process of Emmetropization (Myopization)
Bruch´s Membrane as Biomechanically Supporting Structure

- Primary Bruch´s membrane defects in congenital colobomata are associated with scleral staphyloma

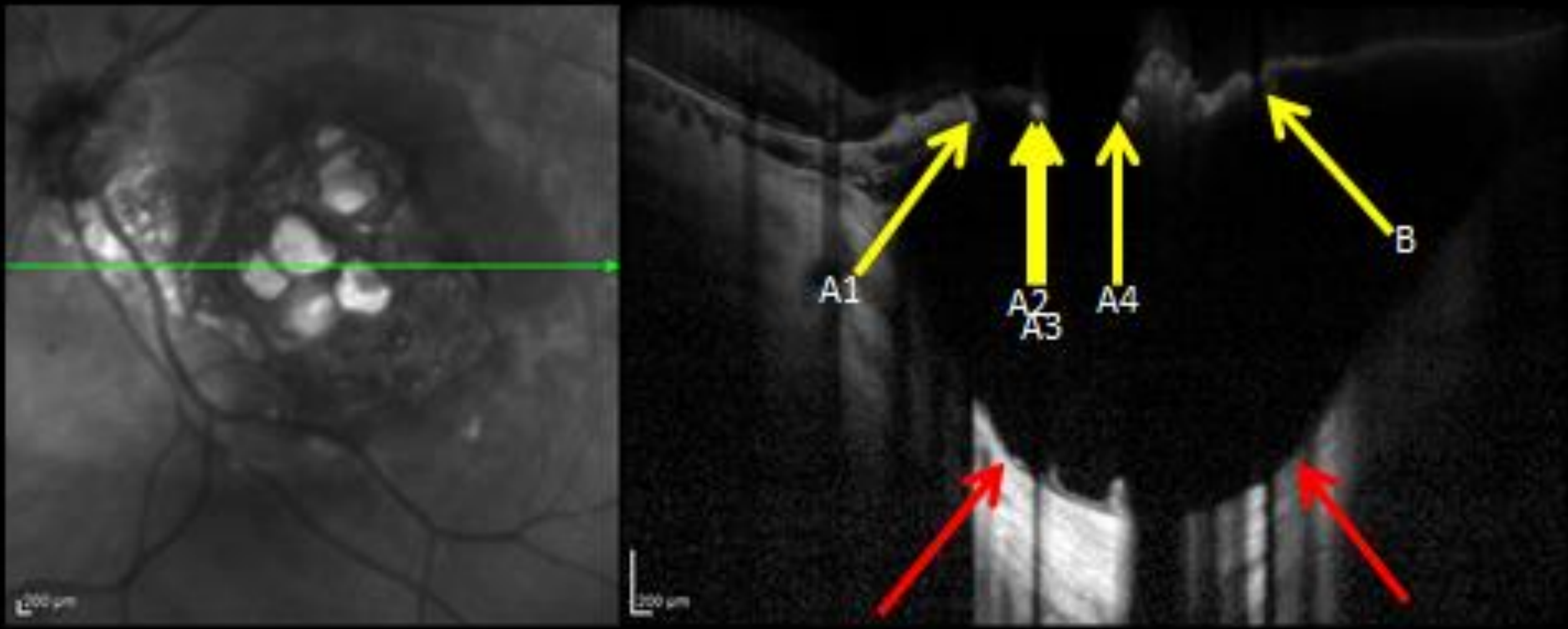






Mechanism of Process of Emmetropization (Myopization)
Bruch´s Membrane as Biomechanically Supporting Structure

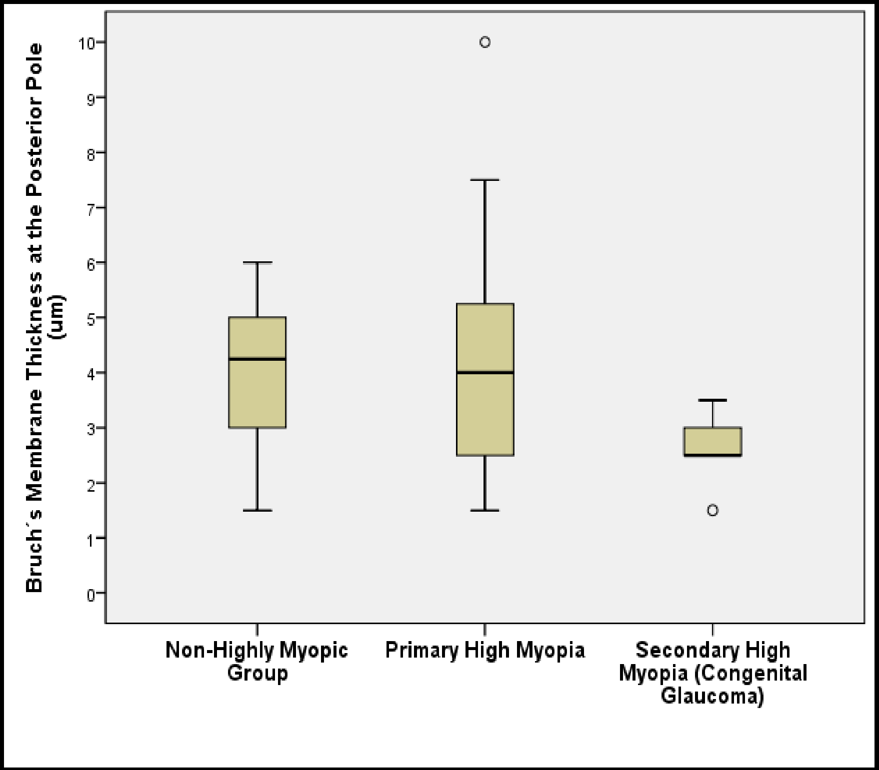
- Secondary Bruch´s Membrane defects are associated with collateral scleral staphyloma (toxoplasmotic scars)

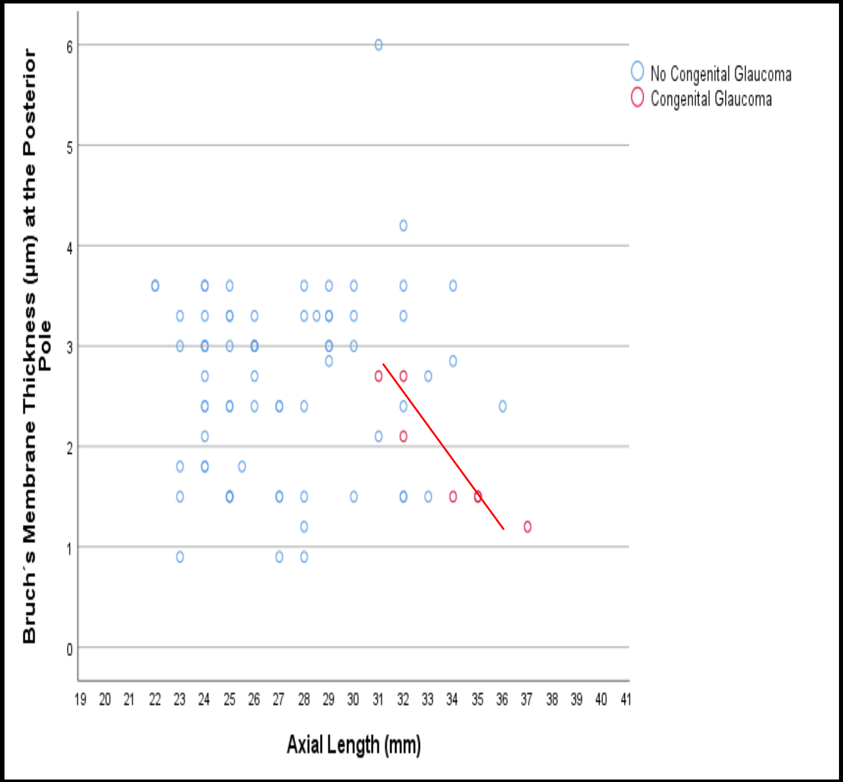


Jonas JB, Panda-Jonas S. Secondary Bruch´s membrane defects and scleral staphyloma in toxoplasmosis. Acta Ophthalmol. 2016;94(7):e664-e666

Mechanism of Process of Emmetropization (Myopization) Bruch´s Membrane as Biomechanically Supporting Structure

- In secondary high myopia due to congenital glaucoma, Bruch´s membrane is thinner than in primary high myopia or emmetropia, and decreases with longer axial length



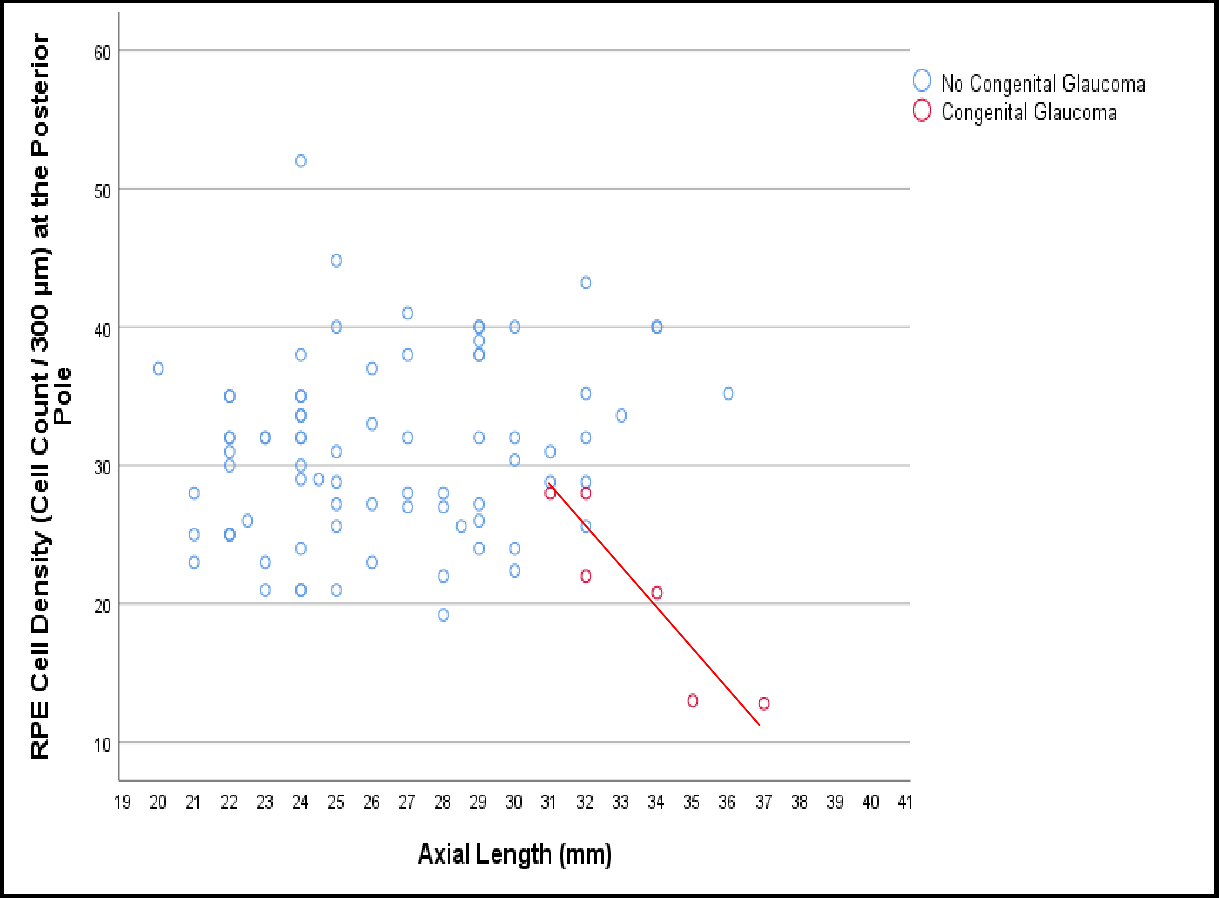


Jonas JB, Holbach L, Panda-Jonas S. Histologic differences between primary high myopia and secondary high myopia due to congenital glaucoma. Acta Ophthalmol 2016;94:147-153

Jonas JB, Dong L, Holbach L, Panda-Jonas S. Retinal pigment epithelium cell density and Bruch´s membrane thickness in secondary versus primary high myopia and emmetropia. Submitted

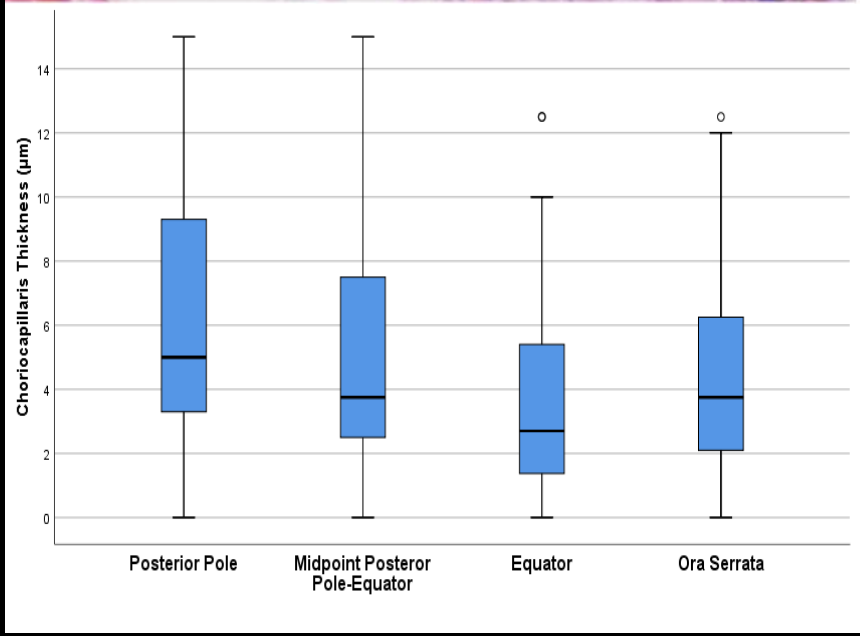
Mechanism of Process of Emmetropization (Myopization)
Bruch´s Membrane as Biomechanically Supporting Structure

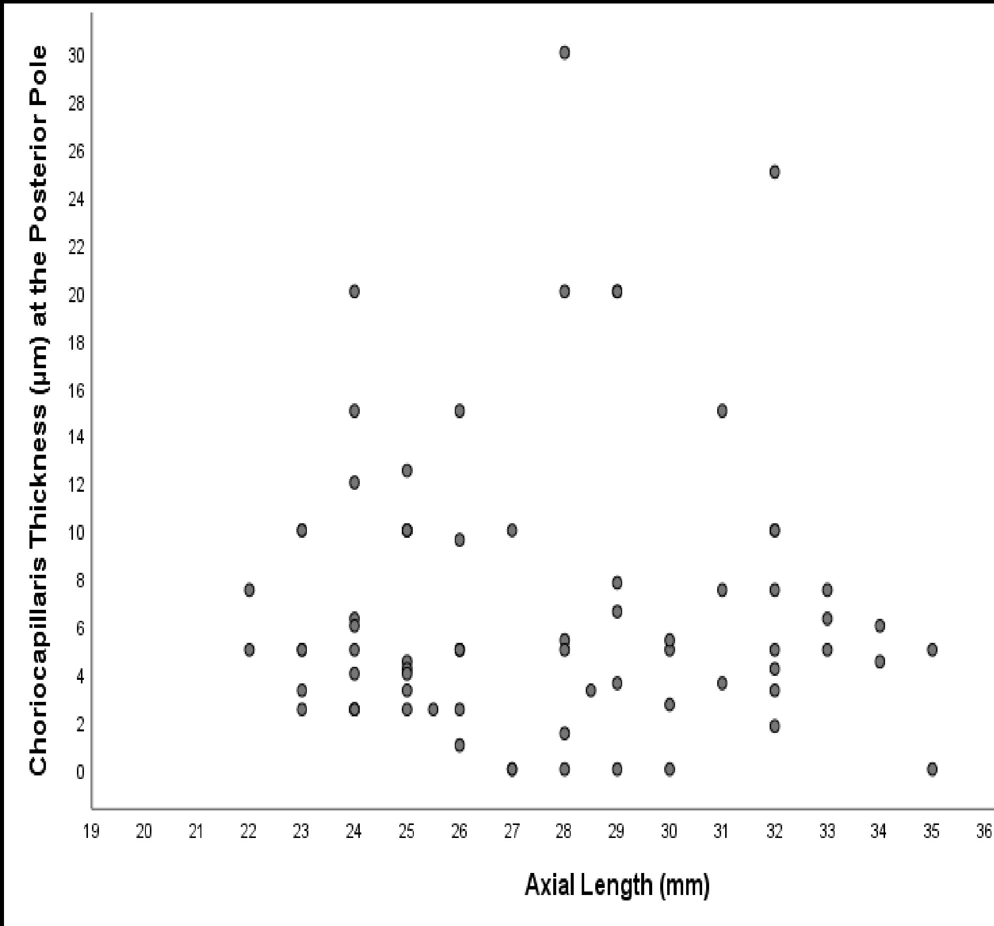
- In secondary, but not in primary, high myopia, RPE cell density decreases with longer axial length at the posterior pole and ora serrata



Jonas JB, Dong L, Holbach L, Panda-Jonas S. Retinal pigment epithelium cell density and Bruch´s membrane thickness in secondary versus primary high myopia and emmetropia. Submitted

Choriocapillaris Thickness and Density in High Myopia





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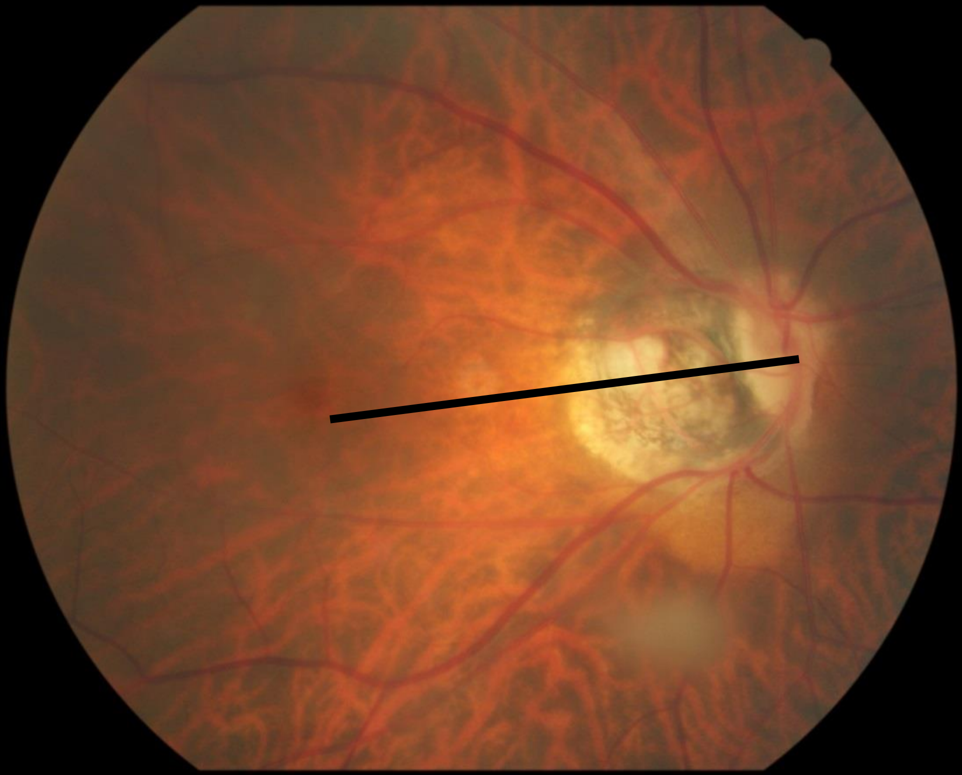
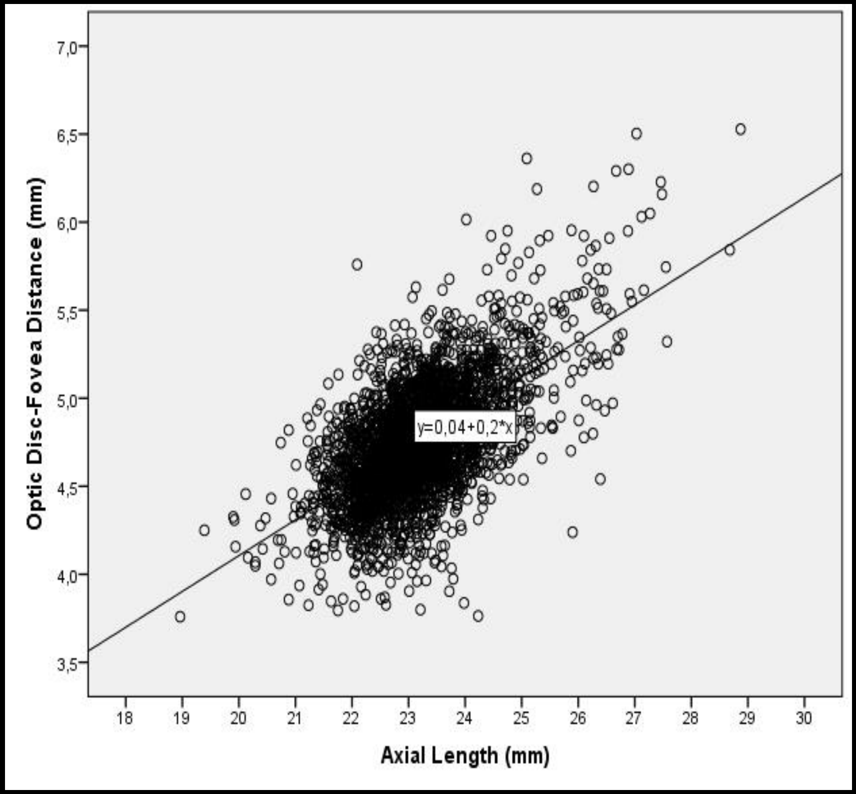
Mechanism of Process of Emmetropization (Myopization)
Bruch´s Membrane as Biomechanically Supporting Structure

- Optic disc-fovea distance increased with longer axial length

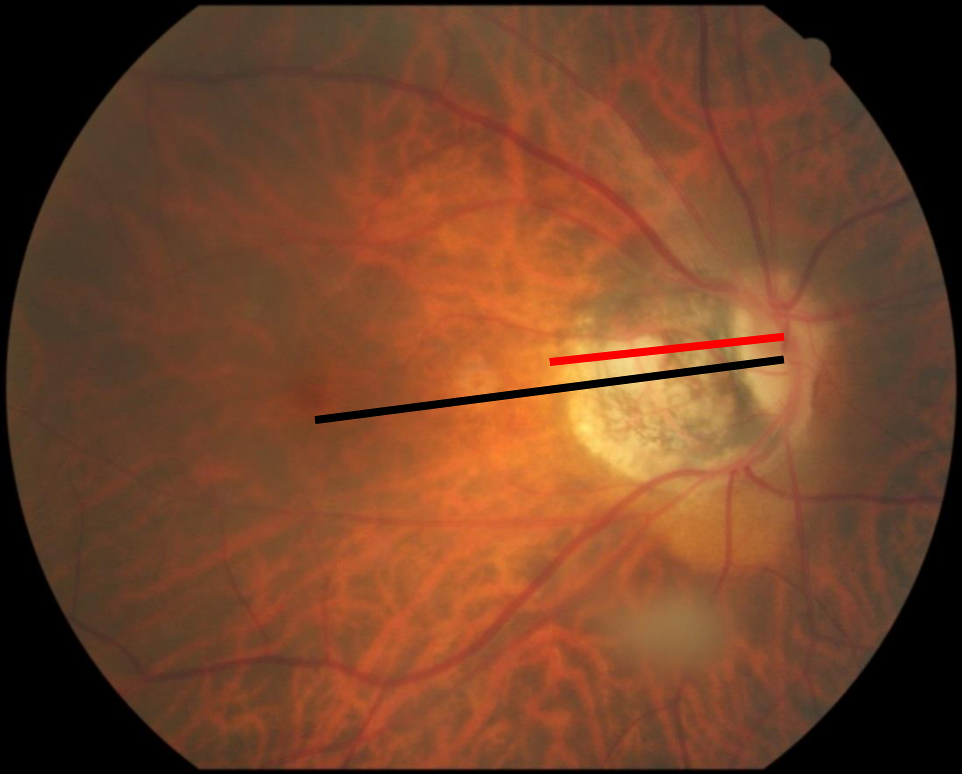


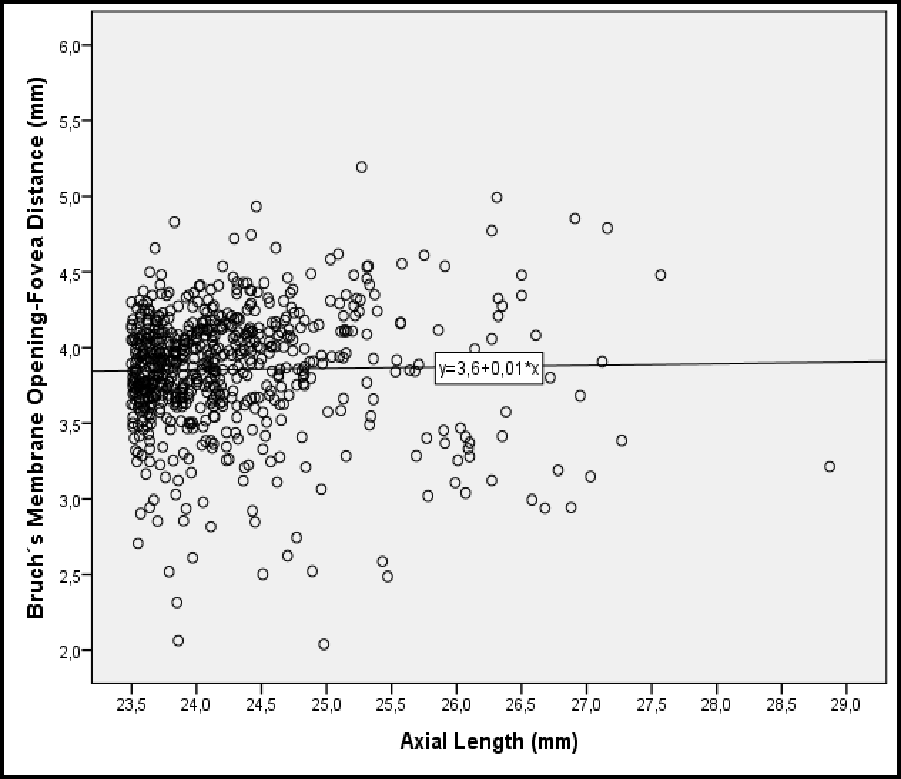


Jonas RA, Wang YX, Yang H, Li JJ, Xu L, Panda-Jonas S, Jonas JB. Optic disc - fovea distance, axial length and parapapillary zones. The Beijing Eye Study 2011. PloS One 2015;10(9):e0138701

Mechanism of Process of Emmetropization (Myopization)
Bruch´s Membrane Biomechanically Supporting Structure

- Length of (horizontal) macular Bruch´s membrane (Disc-fovea distance minus parapapillary gamma zone width) is not related with axial length (if > 24 mm)

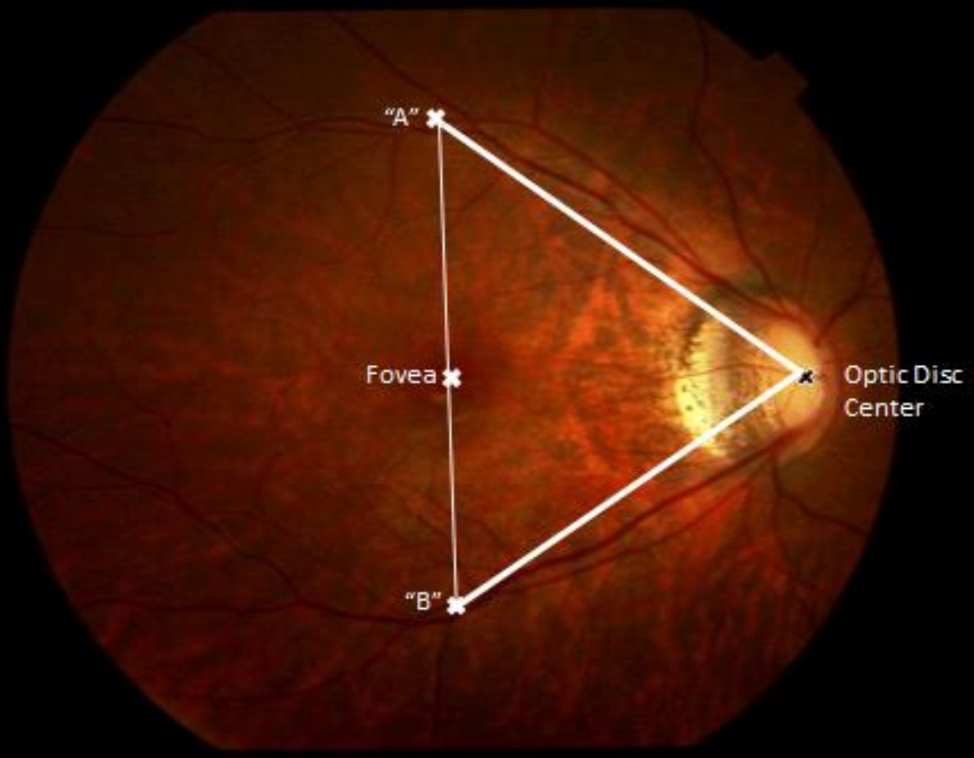


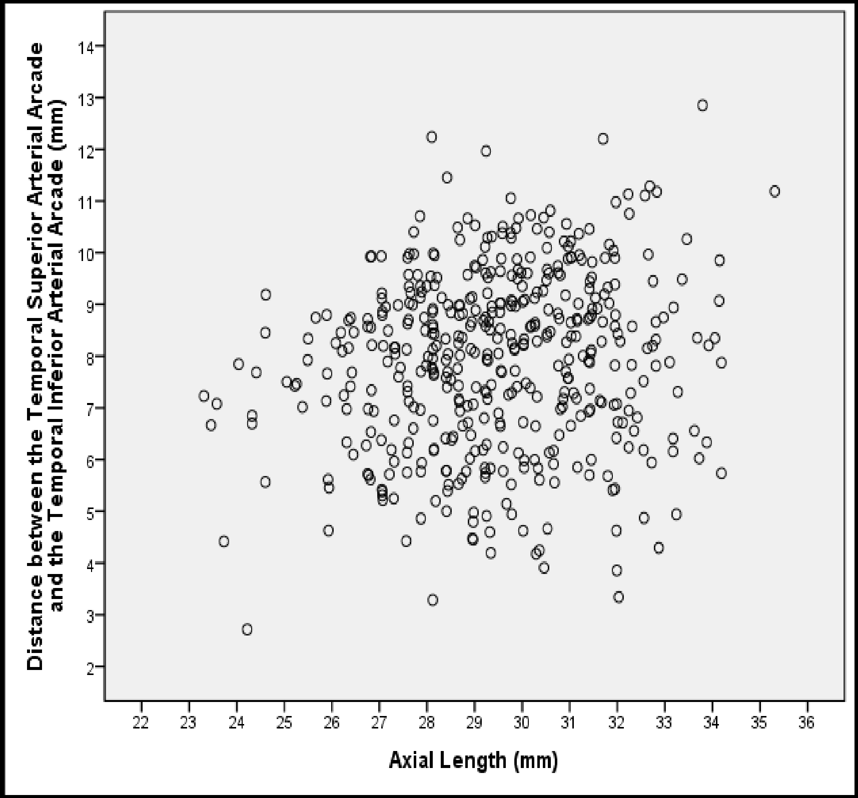


Jonas JB, Wang YX, Zhang Q, Liu Y, Xu L, Wei WB. Macular Bruch´s membrane length and axial length. The Beijing Eye Study. PloS ONE 2015;10:e0136833

Mechanism of Process of Emmetropization (Myopization) Bruch´s Membrane as Biomechanically Supporting Structure

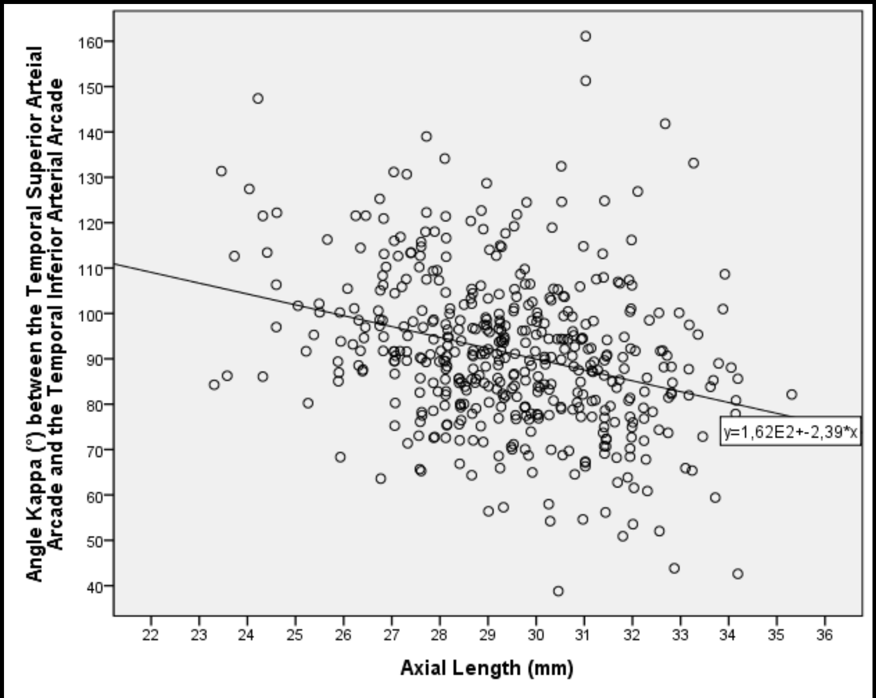
- Length of (vertical) macular Bruch´s membrane (distance temp. arterial arcade) is not significantly related with axial length, so that the angle kappa decreases in myopia





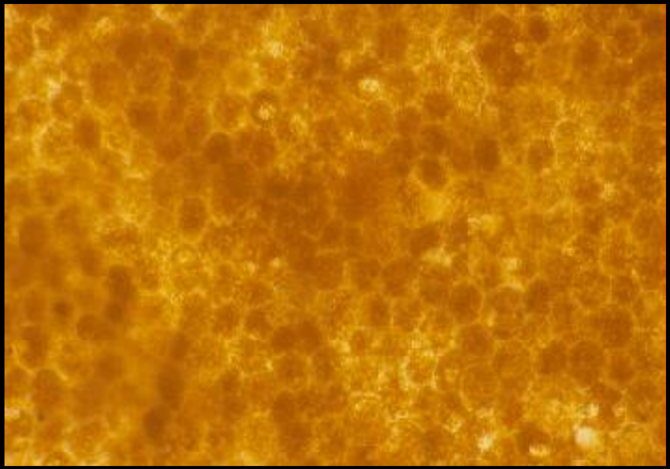
Jonas JB, Weber P, Nagaoka N, Ohno-Matsui K. Temporal vascular arcade width and angle in high axial myopia. Retina. 2017 Aug 1. doi: 10.1097/IAE.0000000000001786. [Epub ahead of print]

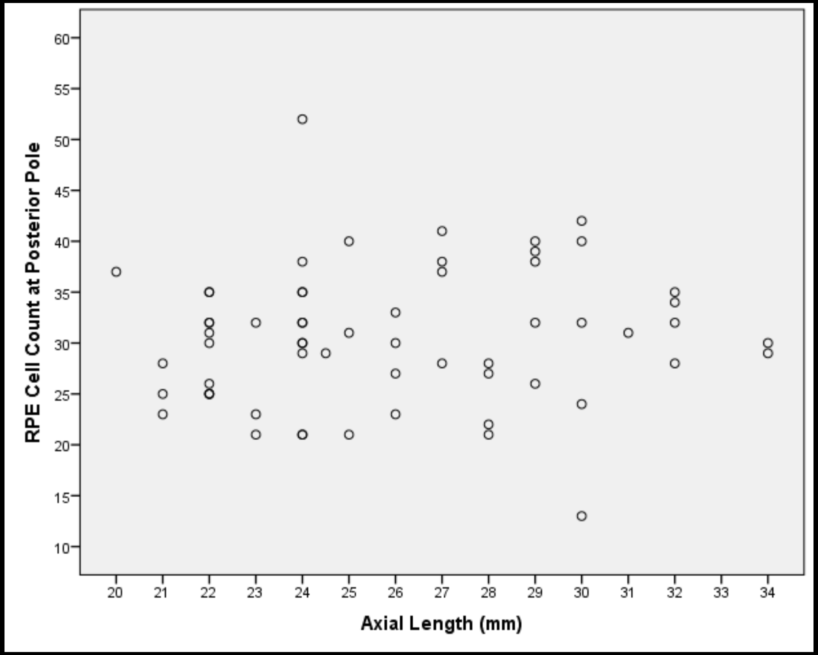
Mechanism of Process of Emmetropization (Myopization)
Bruch´s Membrane as Biomechanically Supporting Structure

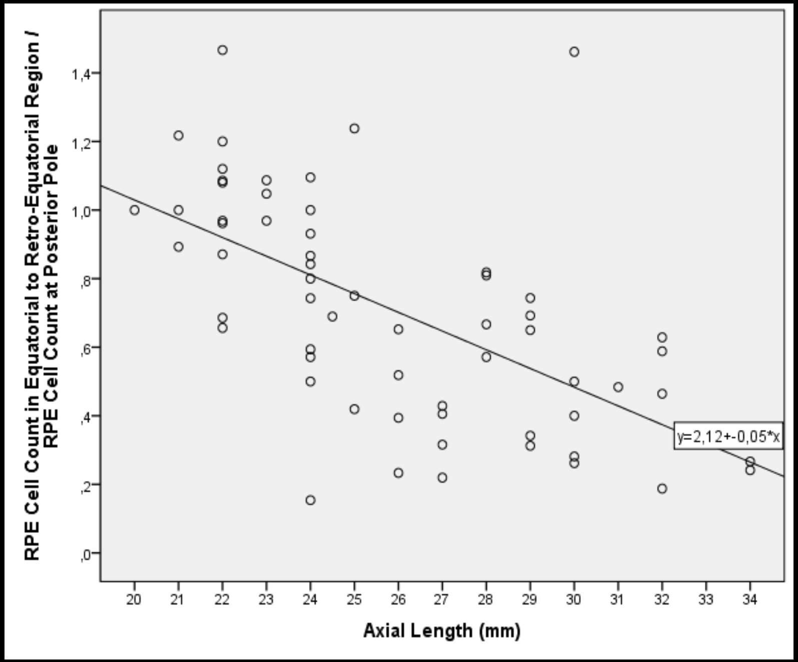


Mechanism of Process of Emmetropization (Myopization) Bruch´s Membrane as Biomechanically Supporting Structure

- Retinal pigment epithelium cell density is independent of axial length at the posterior pole and ora serrata, while
- It decreases with longer axial length in the equatorial to retro-equatorial region, where presumable the feedback mechanism of emmetropization is located.



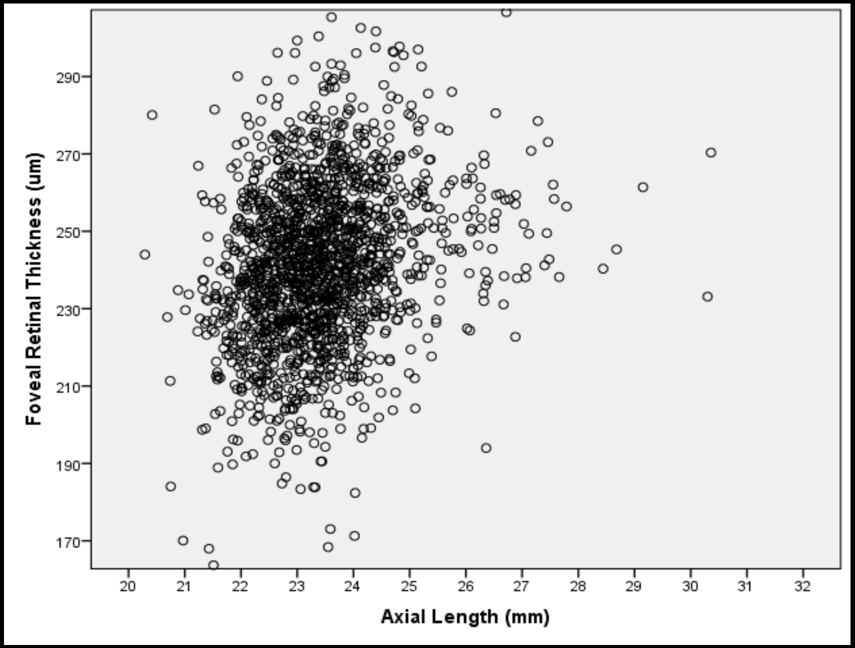


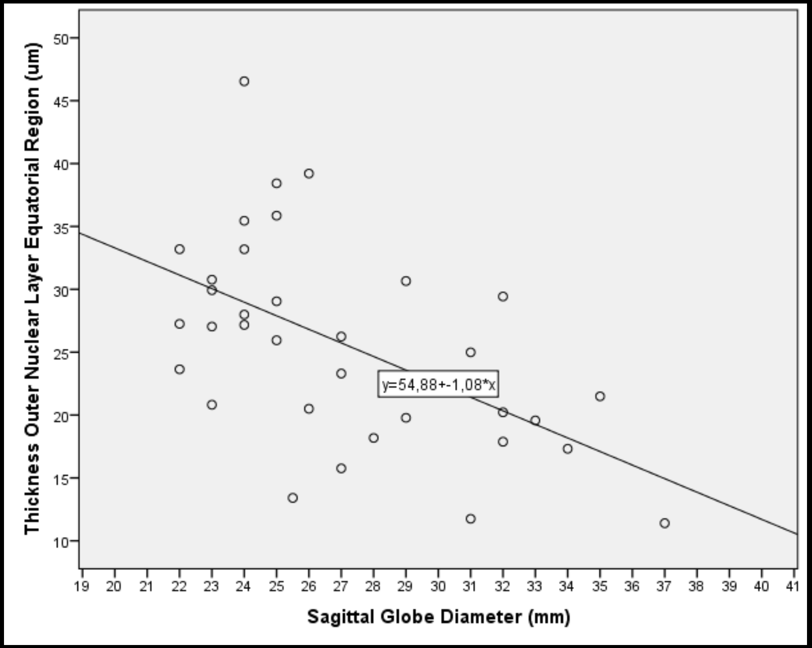


Jonas JB, Xu L, Wei WB, Pan Z, Yang H, Holbach L, Panda-Jonas S, Wang YX. Macular retinal thickness and axial length. Invest Ophthalmol Vis Sci 2016;57:1791-7

Mechanism of Process of Emmetropization (Myopization)
Bruch´s Membrane as Biomechanically Supporting Structure

- Retinal thickness is independent of axial length in the macula, while
- It decreases with longer axial length in the equatorial to retro-equatorial region.
- Correspondingly, best corrected visual acuity is independent of axial length





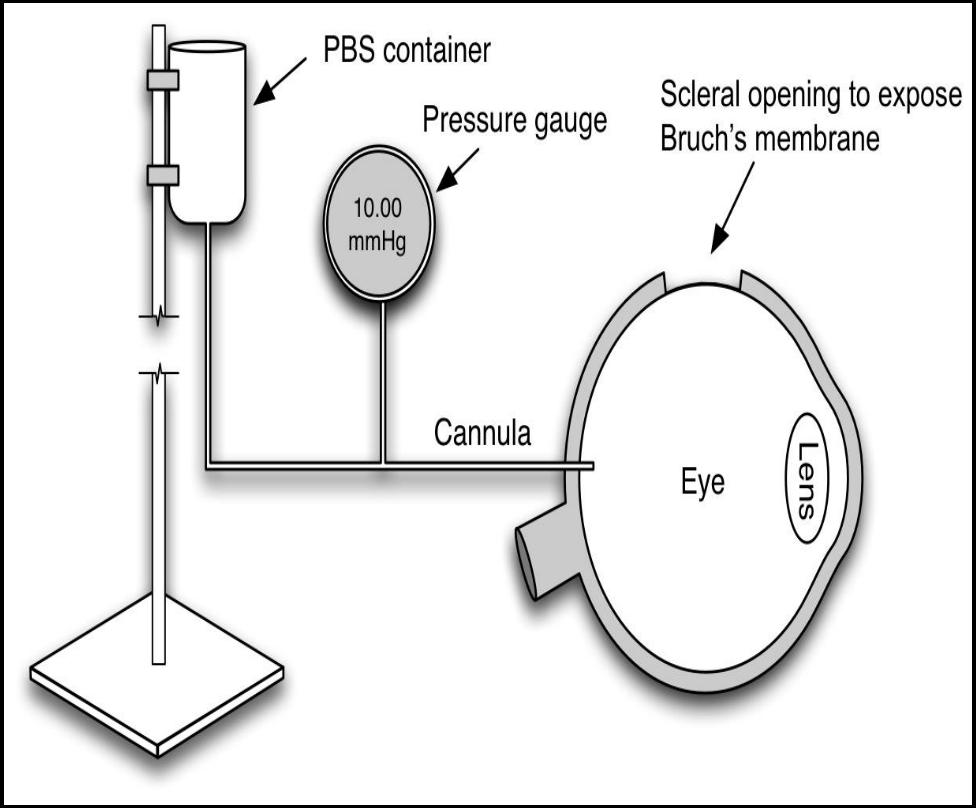
Jonas JB, Xu L, Wei WB, Pan Z, Yang H, Holbach L, Panda-Jonas S, Wang YX. Macular retinal thickness and axial length. Invest Ophthalmol Vis Sci 2016;57:1791-7

Potential Mechanism of Process of Emmetropization (Myopization)

- Up to second year of life, globe increases spherically with increase in scleral volume
- Beyond that age, process of emmetropization: Fine-tuning of optical axis length to the optical characteristics of lens and cornea
- Axial elongation by production and elongation of Bruch´s membrane in the equatorial region: Sagittal enlargement (1 mm in length to 0.2 mm in vertical / horizontal direction)
- Explains decrease in RPE density and retinal thinning at the equator
- Fovea primarily unaffected: Retinal thickness, RPE density, choriocapillaris thickness and best corrected visual acuity normal
- Increase in disc-fovea distance due to parapapillary gamma zone
- Enlargement of Bruch´s membrane opening and development of macular BM defects due to tension in BM in coronal direction
- BM as primary driver of axial elongation leads to choroidal compression (thinning)
- Also: The optical axis ends at the photoreceptor outer segments in close proximity to the RPE and BM
- The sclera is separated from the photoreceptor puter segments by the spongy and variable choroid.

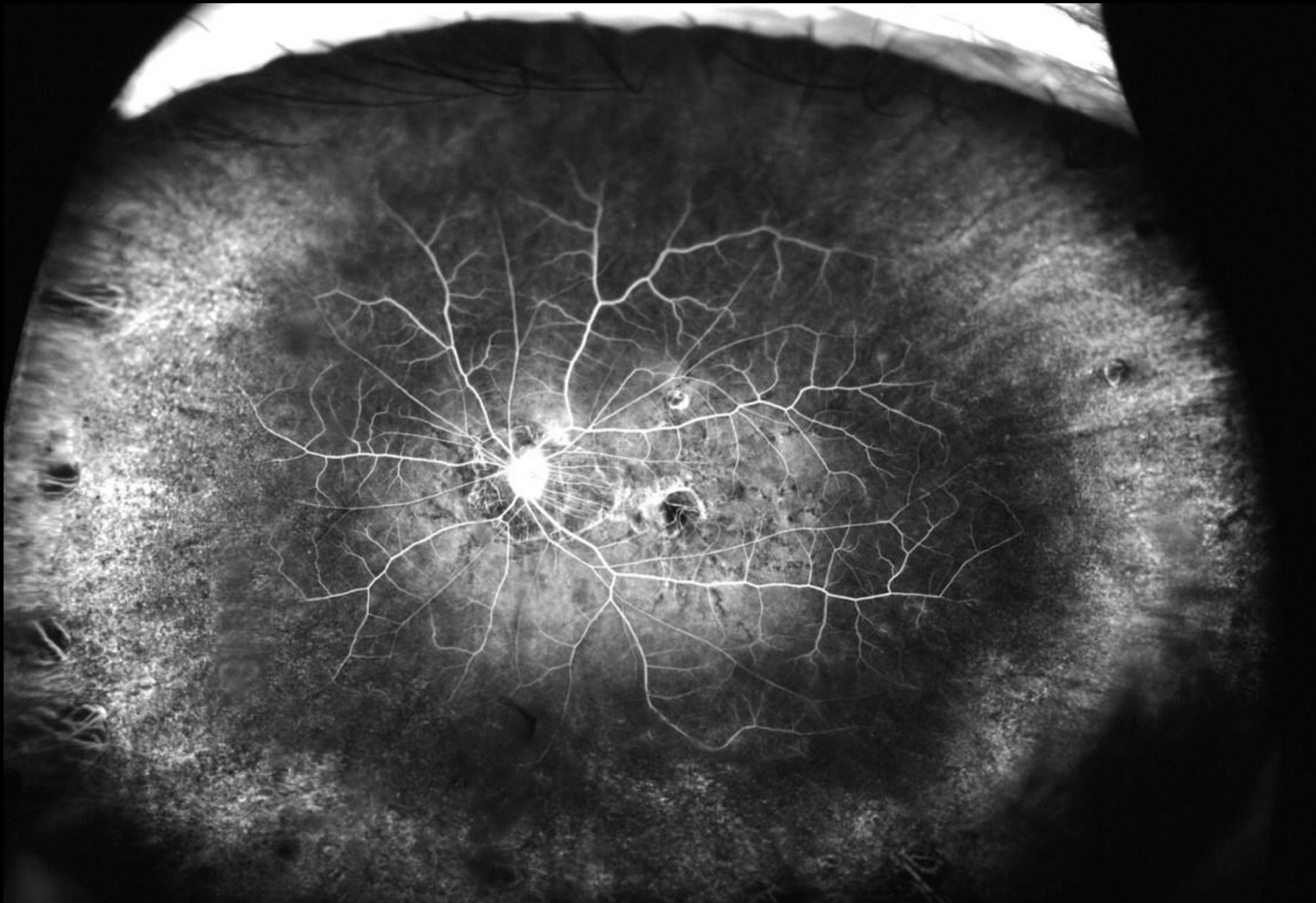
Mechanism of Process of Emmetropization (Myopization)
Bruch´s Membrane as Biomechanically Supporting Structure

- Biomechanical strength of Bruch´s membrane: Pressure required to burst BM: 82 mmHg (range: 39-147 mmHg)



Wang X, Teoh CKG, Chan ASY, Thangarajoo S, Jonas JB, Girard MJA. Biomechanical properties of Bruch's membrane-choroid complex and their influence on optic nerve head biomechanics. Invest Ophthalmol Vis Sci 2018 In Print

Bruch´s Enlargementoin the Fundus Periphery in Axial Elongation



Courtesy: Prof. Kyoko Ohno-Matsui, Department of Ophthalmology and Visual Science, Tokyo Medical and Dental University, Tokyo, Japan

Dependence of the angle between light rays, traveling from the end of the retinal vascular region through the pupil, on axial length: Concentric visual field constriction?