Choriocapillaris thickness and density in axially elongated eyes

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ABSTRACT.
Purpose: Axial myopia is characterized by a thinning of the choroid. We examined whether the myopic choroidal thinning also includes a thinning of the choriocapillaris.
Methods: Using light microscopy, we measured thickness and density of the choriocapillaris at the posterior pole, posterior pole–equator midpoint (PPEMP), equator and close to the ora serrata on histological sections of 58 enucleated human globes (mean age: 62.4 ± 17.8 years; range: 24–88 years; mean axial length: 27.8 ± 4.0 mm; range: 22.0–37.0 mm).
Results: Choriocapillaris thickness decreased \((p < 0.001)\) from the posterior pole (median: 3.9 \(\mu m\); interquartile range (IQR): 3.3–6.0) to the equator (median: 2.7 \(\mu m\); IQR: 1.5, 4.2). It was not significantly associated with axial length, neither at the posterior pole \((p = 0.25)\), the PPEMP \((p = 0.81)\), equator \((p = 0.80)\) or ora serrata \((p = 0.50)\). Mean choriocapillaris density decreased from the posterior pole to the equator \((198 \mu m/300 \mu m; IQR: 152/300, 246/300; p < 0.001)\). Choriocapillaris density was not significantly associated with axial length \((\text{posterior pole}: p = 0.07; \text{PPEMP}: p = 0.33; \text{equator}: p = 0.22; \text{ora serrata}: p = 0.36)\).
Conclusions: The choriocapillaris thickness and density, decreasing from the posterior pole to the fundus periphery, were not significantly associated with axial length. These findings may be of interest for the understanding of high myopia and pathologic myopia.

Key words: choriocapillaris – myopia – Bruch’s membrane – myopic maculopathy – Scleral staphyloma

Introduction
Choroidal thinning at the posterior pole is a hallmark of myopic axial elongation (Spaide et al. 2008). Clinical and population-based studies have shown a reduction in subfoveal choroidal thickness by approximately 46 \(\mu m\) for each millimetre increase in axial length, after adjusting for parameters such as age and gender (Spaide et al. 2008; Fujiwara et al. 2009; Wei et al. 2013). Choroidal thinning in axially myopic eyes was most marked at the posterior pole, while the effect of an axial elongation-associated reduction in choroidal thickness decreased towards the periphery of the fundus (Hoseini-Yazdi et al. 2019). A recent population-based study suggested that the subfoveal choroidal thinning in myopic eyes mainly affected Haller’s layer of the large choroidal vessels and Sattler’s layer of the medium-sized choroidal vessels, while the optical coherence tomography (OCT)-based assessment of the small-vessel choroidal layer was less affected (Zhao et al. 2018). Due to limitations in the spatial resolution of imaging by OCT, it was not possible to specifically examine the thickness of the choriocapillaris (Ramrattan et al. 1994; Esmaeelpour et al. 2014). The choriocapillaris is a dense mono-layered capillary network the basal membrane of which forms the outer layer of Bruch’s membrane (BM) and which covers the posterior surface of BM (Jonas et al. 2011; Schachat et al. 2017). Since the choriocapillaris is of utmost importance for the physiology of the retinal photoreceptors and since it could not be examined upon OCT imaging, we conducted this histomorphometric study to measure the thickness and density of the choriocapillaris in enucleated human globes, and to gain information about relationships between the choriocapillaris thickness and density, and axial length. We measured both parameters, thickness and density of the choriocapillaris, to get, by using the two-dimensional histological slides, as much information as possible about the dimensions of the choriocapillaris.

Methods
The study consisted of patients of European descent whose globes had...
been enucleated because of the diagnosis of an end-stage painful glaucoma or of a malignant melanoma of the choroid. None of the eyes included into the study were hypotonic or phthisical. According to the Declaration of Helsinki guidelines, the Medical Ethics Committee II of the Medical Faculty Mannheim of the Heidelberg University approved the study. The ethics committee waived the necessity of an informed written consent signed by the study participants, since the enucleations had been carried out up to 50 years before we initiated the study. The eyes were part of the ophthalmological-pathological archives of the Department of Erlangen. Some of the eyes had already been assessed in previous studies on different topics (Jonas et al. 2011, 2018). All the eyes had been fixated, measured and prepared for the histological examination at the time of enucleation, that is up to 50 years ago. Since most of the eyes were prepared in the same laboratory, they had undergone the same preparatory steps.

Immediately after enucleation, the globes were fixed in a solution of 4% formaldehyde and 1% glutaraldehyde for one week at room temperature (Curcio et al. 1998; Edwards et al. 2017; Seddon et al. 2016). Before fixation, the globes had not been opened nor had the preservative agent been injected intravitreally. We determined the globe diameters in the sagittal, horizontal and vertical direction, and then removed the middle part out of the fixed globes. This segment had a thickness of approximately 8 mm and went through the optic nerve head, the pupil and the macular region, except for eyes which contained a choroidal tumour. In these eyes, the middle segment ran in an anterior–posterior direction through the tumour and the optic nerve head. We dehydrated the middle segment in alcohol, imbedded it in paraffin and sectioned it for light microscopy. We used the periodic acid–Schiff method or haematoxylin–eosin to stain the tissue. For all eyes, we took one section with a thickness of approximately 5–8 μm and which ran through the central part of the pupil and optic nerve head.

Using the in-built millimetre scale in the objective of the microscope, we measured histomorphometrically the thickness of the choriocapillaris, sclera, BM and retinal pigment epithelium (RPE), the density of the RPE cells and the cumulative or running length of the choriocapillaris for a distance of 300 μm (Figs 1–3). The measurements were performed at the posterior pole, the midpoint between the posterior pole and the equator, the equator, and just posterior to the ora serrata. The choriocapillaris was defined as the capillary layer just posterior to BM. Care was taken not including vessels of Haller’s or Sattler’s layer into the measurements. The height of the RPE was defined as the distance between the inner surface of BM and the inner surface of the RPE cell layer. We determined the RPE cell density as the number of RPE cells per 300 μm. We measured the density of the choriocapillaris as cumulative or running length of open choriocapillaris vessels per 300 μm (Figs 1–3). Due to postenucleation changes causing artefacts such as a choroidal detachment from the sclera, we did not measure the total choroidal thickness. We defined high axial elongation by an axial length of ≥26.0 mm. For all measurements, areas within or close to choroidal tumours and areas with histological features of category 3 or category 4 of myopic maculopathy, such as BM defects, were excluded (Jonas et al. 2013; Ohno-Matsui et al. 2015). All measurements were performed by one grader (JBJ). To assess the intra-observer variability, the choriocapillaris parameters of ten eyes were re-measured, and the coefficient of variability was calculated as the mean of the standard deviations divided by the mean of the means.

Using a statistical software program (SPSS for Windows, version 25.0; IBM-SPSS, Chicago, Illinois, USA), we assessed the mean values, standard deviations and 95% confidence intervals (CI) of the parameters with a normal distribution, or the medians and interquartile ranges of the non-parametric parameters. We determined the significance of regional differences in the measurements of the choriocapillaris using the Wilcoxon signed-rank test. We tested associations between the choriocapillaris thickness or choriocapillaris density with axial length and other parameters applying a linear regression analysis. We calculated the standardized regression coefficient beta and the non-standardized regression coefficient B and its 95% CI. The level of significance was 0.05 (two-sided) in all statistical tests.

**Results**

The study consisted of 58 eyes of 58 patients (29 (50%) men) with a mean age of 62.4 ± 17.8 years (median:
66.5 years; range: 24–88 years) and a mean axial length of 27.8 ± 4.0 mm (median: 26.5 mm; range: 22.0–37.0 mm). The study population consisted of 34 highly axially elongated globes (mean axial length: 30.4 ± 3.1 mm) and 24 non-highly axially elongated eyes (24.1 ± 0.9 mm). There were 41 (71%) glaucomatous eyes.

The choriocapillaris was slightly, however not significantly (Wilcoxon signed-rank test) (p = 0.28) thicker at the fovea (median: 3.9 µm; interquartile range [IQR]: 3.3–6.0) than at the posterior pole–equator midpoint (median: 3.6 µm; IQR: 2.7, 4.2), where it was significantly (p = 0.004) thinner than at the ora serrata (median: 3.6 µm; IQR: 1.5, 5.4) (Fig. 4).

The choriocapillaris thickness was not significantly associated with axial length, neither at the posterior pole (B: 0.09; 95% CI: −0.07, 0.25; p = 0.25) (Fig. 5), at the posterior pole–equator midpoint (B: 0.02; 95% CI: −0.17, 0.22; p = 0.81), at the equator (B: −0.02; 95% CI: −0.17, 0.13; p = 0.80) or at the ora serrata (B: −0.08; 95% CI: −0.30, 0.15; p = 0.50). Similar results were obtained if the presence of glaucoma or the presence of a malignant choroidal melanoma as independent variables were added in a multivariable analysis, in which both, axial length and glaucoma (axial length, p = 0.56; glaucoma, p = 0.50), and in which both, axial length and presence of choroidal melanoma (axial length, p = 0.74; choroidal melanoma, p = 0.43), were not significantly associated with choriocapillaris thickness at the posterior pole. Also in a univariate analysis, the choriocapillaris thickness was not significantly associated with the presence of glaucoma (posterior pole: p = 0.48; posterior pole–equator midpoint: p = 0.66; equator: p = 0.31; ora serrata: p = 0.44). Choriocapillaris thickness was neither associated with the presence of malignant choroidal melanoma in univariate analysis (posterior pole: p = 0.48; posterior pole–equator midpoint: p = 0.26; equator: p = 0.18; ora serrata: p = 0.32).

Adjusting the analyses for sex and age did not alter the result of a lack of an significant association between choriocapillaris thickness and axial length (posterior pole p = 0.24; posterior pole–equator midpoint p = 0.58; equator p = 0.34; close to the ora serrata p = 0.23).

In univariate analysis, choriocapillaris thickness was not significantly associated with age and gender when measured at the posterior pole (p = 0.53 and p = 0.71, respectively), at the equator (p = 0.75 and p = 0.39, respectively) and close to the ora serrata (p = 0.67 and p = 0.93, respectively). Choriocapillaris thickness...
measured at the posterior pole–equator midpoint was significantly and negatively associated with age in univariate analysis \( (p = 0.02, r = -0.45) \). In the multivariate analysis with age and axial length as the independent variables, the association between choriocapillaris thickness at the posterior pole–equator midpoint and age remained to be statistically significant \( (p = 0.02, \text{beta: } -0.45; \text{B: } -0.06; 95\% \text{ CI: } -0.12, -0.01) \), while the association with axial length was not significant \( (p = 0.57, \text{beta: } -0.11; \text{B: } 0.06; 95\% \text{ CI: } -0.29, 0.16) \).

The median of the choriocapillaris density was at the posterior pole 198 \( \mu m/300 \mu m \) (IQR: 152/300, 246/300), at the posterior pole–equator midpoint 186 \( \mu m/300 \mu m \) (IQR: 141/300, 240/300), at the equator 156 \( \mu m/300 \mu m \) (IQR: 123/300, 216/300) and close to the ora serrata 183 \( \mu m/300 \mu m \) (IQR: 96/300, 245/300). The difference in choriocapillaris density between the posterior pole and the equator \( (p < 0.001) \) and between the equator and the ora serrata \( (p = 0.049) \) was significant (Wilcoxon signed-rank test).

The choriocapillaris thickness was not significantly associated with axial length, neither at the posterior pole \( (B: 4.77; 95\% \text{ CI: } -0.48, 10.0; p = 0.07) \) (Fig. 6), at the posterior pole–equator midpoint \( (B: 3.04; 95\% \text{ CI: } -3.13, 9.20; p = 0.33) \), at the equator \( (B: 4.06; 95\% \text{ CI: } -2.49, 10.6; p = 0.22) \) or at the ora serrata \( (B: 3.20; 95\% \text{ CI: } -3.76, 10.2; p = 0.36) \). Similar results were obtained if the presence of glaucoma or the presence of a malignant choroidal melanoma were added to axial length in the list of independent variables in a multivariable analysis, in which the presence of glaucoma \( (p = 0.31) \) or the presence of the choroidal melanoma \( (p = 0.11) \) was not significantly associated with choriocapillaris density at the posterior pole. Also in a univariate analysis, the choriocapillaris density was not significantly correlated with the presence of glaucoma (posterior pole: \( p = 0.49 \); posterior pole–equator midpoint: \( p = 0.12 \); equator: \( p = 0.19 \); ora serrata: \( p = 0.96 \)). Choriocapillaris thickness was neither associated with the presence of malignant choroidal melanoma in univariate analysis (posterior pole: \( p = 0.48 \); posterior pole–equator midpoint: \( p = 0.43 \); equator: \( p = 0.27 \); ora serrata: \( p = 0.78 \)). Adjusting the analyses for sex and age did not alter the result of a lack of a significant association between choriocapillaris density and axial length (posterior pole \( p = 0.31 \); posterior pole–equator midpoint \( p = 0.94 \); equator \( p = 0.53 \); close to the ora serrata \( p = 0.81 \)).

The choriocapillaris thickness was not significantly associated with the thickness and height of the RPE cells, neither at the posterior pole \( (p = 0.16 \) and \( p = 0.16 \), respectively), at the posterior pole–equator midpoint \( (p = 0.85 \) and \( p = 0.69 \), resp.) at the equator \( (p = 0.93 \) and \( p = 0.87 \), resp.) or at the ora serrata \( (p = 0.26 \) and \( p = 0.50 \), resp.). In a similar manner, the choriocapillaris density was not significantly associated with the thickness and height of the RPE cells, neither at the posterior pole \( (p = 0.09 \) and \( p = 0.10 \), respectively), at the posterior pole–equator midpoint \( (p = 0.71 \) and \( p = 0.98 \), resp.), at the equator \( (p = 0.57 \) and \( p = 0.32 \), resp.) or at the ora serrata \( (p = 0.94 \) and \( p = 0.11 \), resp.).

The RPE height and RPE cell density measured at the posterior pole 6.8 \( \pm 2.4 \mu m \) and 29.0 \( \pm 7.8 \) cells/480 \( \mu m \), respectively, at the posterior pole–equator midpoint 5.5 \( \pm 2.2 \mu m \) and 21.5 \( \pm 8.1 \) cells/480 \( \mu m \), respectively, at the equator 5.4 \( \pm 2.2 \mu m \) and 17.9 \( \pm 8.0 \) cells/480 \( \mu m \), respectively, and close to the ora serrata 5.8 \( \pm 2.6 \mu m \) and 24.2 \( \pm 8.8 \) cells/480 \( \mu m \), respectively.

The coefficient of variability of the re-measurements of the choriocapillaris thickness was 7%, and of the choriocapillaris density, it was 14%.
Discussion

Our histomorphometric study did not detect a significant association between the choriocapillaris thickness measured at any point and axial length nor between the choriocapillaris density and axial length. It suggested that both, choriocapillaris thickness and density, might not be related with axial length. The choriocapillaris thickness showed a tendency to decrease from the posterior pole to the ora serrata, while the choriocapillaris density showed a tendency to decrease from the posterior pole towards the equator.

The observation that the choriocapillaris thickness was not significantly associated with axial length agrees with clinical measurements of the choroidal thickness and its various layers in a recent population-based study in which the ratio of the small-vessel layer thickness to total choroidal thickness increased with longer axial length, while the ratios of the thickness of Sattler’s layer and Haller’s layer to the total choroidal thickness decreased with longer axial length (Zhao et al. 2018). It also concurs with the findings made in a recent OCT-angiographic study in which myopic eyes and non-myopic eyes did not differ significantly (p = 0.55) in the choriocapillaris perfusion area (1.9 ± 0.07 mm² versus 1.9 ± 0.05 mm²) (Al-Sheikh et al. 2017). In a study conducted by Mo and colleagues, OCT-angiographic patterns of the choriocapillaris did not differ between emmetropic eyes and highly myopic eyes with pathological myopia (Mo et al. 2017). As a corollary, Scherm and colleagues found that the subfoveal pattern of the choriocapillaris was not associated with axial length (p = 0.80) or choroidal thickness (p = 0.27) (Scherm et al. 2019). In another OCT-angiographic clinical study, Al-Sheikh and associates reported that the total number of signal voids in the choriocapillaris was lower, while the total and average flow void area was significantly higher in a myopic study group than in a non-myopic control group (Al-Sheikh et al. 2017). The myopia-associated decrease in total choroidal thickness was not significantly associated with quantitative parameters of the choriocapillaris (Al-Sheikh et al. 2017). In contrast, angiographic studies examining the choriocapillaris in eyes with myopic maculopathy have revealed that regions of patchy atrophy as category 3 or 4 of the spectrum of myopic maculopathy showed a complete loss of the choriocapillaris structure as well as a loss of the large choroidal vessels (Sayanagi et al. 2017). Eyes with a diffuse atrophy (category 2 of myopic maculopathy) demonstrated a low-density pattern of the choriocapillaris. In another clinical investigation, a lower choriocapillaris flow was detected in myopic eyes with diffuse and patchy atrophy (category 2 and 3 of myopic maculopathy), and in some eyes with tessellated fundus (Wong et al. 2019).

A reason for the partially diverging results of the OCT-angiographic-based investigations and our histomorphometric findings may be the partial inclusion of eyes with pathological myopia into the study populations of the previous investigations. Macular BM defects in eyes with category 3+ of myopic maculopathy do not have a choriocapillaris in the region of the patchy atrophy. If areas with BM defects were included into the measurements, the mean thickness and density of the choriocapillaris as averaged across the total examination area would be lower as if the patchy atrophy regions were excluded as in our investigation.

Our observation of a lack of a statistically significant relationship between thickness and density of the choriocapillaris on one side and axial length on the other side fits with observations made in other studies. Previous histologic studies have shown that the thickness of BM was not related to axial length so that extremely axially elongated eyes had a similar BM thickness as eyes did with a normal axial length (Jonas et al. 2014). The length of BM in the macular region was neither dependent on axial length (Jonas et al. 2015a). The increased distance between the optic disc and the fovea in axially elongated eyes was due to the development and enlargement of BM-free parapapillary gamma zone (Jonas et al. 2015b). As a corollary to the unchanged length of BM in the macular region of axially elongated eyes, the density of RPE cells in the macular region and the thickness of the retina in the macular region were independent of axial length (Jonas et al. 2017a, Jonas et al., 2017b). If BM in the macular region is not enlarged in myopic eyes, and considering that the choriocapillaris is firmly attached to BM since the basal membrane of the choriocapillaris forms the outer layer of BM, one may infer that also the density of the choriocapillaris may be independent of axial length as was found in the present study.

Interestingly, choriocapillaris thickness at the posterior pole-equator midpoint decreased significantly with older age in univariate analysis (p = 0.02) and in multivariate analysis (p = 0.02) with axial length as additional independent variable, while the association between choriocapillaris thickness with axial length was not statistically significant (p = 0.57) in that model. Although the association between choriocapillaris thickness at
the posterior pole-equator midpoint and age lost its statistical significance if a Bonferroni correction for performing multiple statistical comparisons was conducted, the observation fits with findings made in previous studies, that the thickness of the total choroid decreased with age by approximately 4 μm per year of age (Wei et al. 2013). The finding that the association between thinner choriocapillaris thickness and older age was not observed in other ocular regions fits with the observation made in a clinical study that ageing-associated (and axial elongation-associated) choroidal thinning affected predominantly the large and medium-sized vessel layers of the choroid (Haller’s layer and Sattler’s layer) as compared to the small-vessel choroidal layer comprising the choriocapillaris (Zhao et al. 2018).

Besides the choriocapillaris density, the thickness of the choriocapillaris was independent of axial length. Although the size of a vessel is not the single parameter determining the blood flow within the vessel, one may infer that the findings of the present study do not give reason to assume a decreased choriocapillaris blood perfusion in myopic eyes. Since the choriocapillaris is the major blood source for the retinal photoreceptor, the findings made in the present study concur with clinical data that the best corrected visual acuity was independent of axial length in eyes without myopic maculopathy (Shao et al. 2014). Correspondingly, Gupta and colleagues reported that highly myopic eyes had a low total subfoveal choroidal thickness, but total choroidal thickness was not an independent predictor of visual acuity (Gupta et al. 2016). In a similar manner, Fang and colleagues found in a study on 1487 eyes that the subfoveal choroidal thickness was not a significant predictive factor of visual acuity after adjusting for age, gender, axial length and presence of myopic maculopathy (Fang et al. 2019). If these assumptions are valid, the observations point against a notion that a decreased perfusion of the choriocapillaris may primarily be involved in the aetiology of myopic axial elongation.

Limitations of our study should be taken into account when its findings are discussed. First, morphologic vessel measurements give only an indirect hint on blood flow, so that the results of our postenucleation histomorphometric study cannot be taken to make firm conclusions on the blood flow of the choriocapillaris. Second, tissue swelling due to the ischaemia occurring after enucleation and before fixation and fixation-related shrinkage of the tissue is unavoidable postenucleation changes which might have influenced the dimensions of the ocular tissues in our study. Also, mechanically induced changes during the histological processing of the globes may have altered the tissues. In addition, rapid blood loss out of the choroid shortly after enucleation before fixation may have decreased the volume of the choroid and of the choriocapillaris. These changes might however have affected the globes independently of their axial length so that these procedure-related tissue changes may not have markedly influenced the analysis of associations between the tissue parameters and axial length. Third, the study material of our investigation might have had a marked selection bias since it was based on human globes enucleated for clinical reasons. The findings of our study may therefore not directly be transferred to eyes without these diseases. Fourth, serial sections of the globes were not available. Fifth, the study population consisted of enucleated eyes because of malignant choroidal melanomas and end-stage painful glaucoma. These underlying disorders might have influenced choroidal blood perfusion and thickness of the choriocapillaris (Kwon et al. 2018; Wen et al. 2018; Rao et al. 2019). Thickness and density of the choriocapillaris were however not associated with any of these disorders in the statistical analysis, and ocular regions affected by the tumours were excluded from the analysis. In addition, eyes with a choroidal malignant melanoma as compared to tumour-free eyes were significantly shorter (24.6 ± 1.6 mm versus 28.6 ± 3.7 mm; p < 0.001) so that in case of falsely large choriocapillaris thickness measurements in the tumour group the axially elongated group as compared to the group with normal axial length would indirectly have had thinner choriocapillaris thickness measurements. That was not the case.

In conclusion, thickness and density of the choriocapillaris as measured histomorphometrically decreased from the posterior pole to the fundus periphery and did not show significant associations with axial length, neither at the posterior pole nor at the posterior pole-equator midpoint or equator. These findings may be of interest for the understanding of pathologic myopia.

References

Al-Sheikh M, Phasukkijwatana N, Dolz-Marco R, Rahimi M, Iafe NA, Freund KB, Sadda SR & Sarraf D (2017): Quantitative OCT angiography of the retinal microvasculature and the choriocapillaris in myopic eyes. Invest Ophthalmol Vis Sci 58: 2063–2069.

Cuccio CA, Medeiros NE & Millican CL (1998): The Alabama age-related macular degeneration grading system for donor eyes. Invest Ophthalmol Vis Sci 39: 1085–1096.

Edwards MM, McLeod DS, Bhutto IA, Grebe R, Duffy M & Lutty GA (2017): Subretinal glial membranes in eyes with geographic atrophy. Invest Ophthalmol Vis Sci 58: 1352–1367.

Esmaeelpour M, Kajic V, Zabihian B et al. (2014): Chorioidal Haller’s and Sattler’s layer thickness measurement using 3-dimensional 1060-nm optical coherence tomography. PLoS One 9:e99690.

Fang Y, Du R, Nagaoka N et al. (2019): OCT-based diagnostic criteria for different stages of myopic maculopathy. Ophthalmology 126: 1018–1032.

Fujiwara T, Imamura Y, Margolis R, Slakter JS & Spaide RF (2009): Enhanced depth imaging optical coherence tomography of the chorioid in highly myopic eyes. Am J Ophthalmol 148: 445–450.

Gupta P, Cheung CY, Saw SM et al. (2016): Chorioidal thickness does not predict visual acuity in young high myopes. Acta Ophthalmol 94: e709–e715.

Hoseini-Yazdi H, Vincent SJ, Collins MJ, Read SA & Alonso-Caneiro D (2019): Wide-field choroidal thickness in myopes and emmetropes. Sci Rep 9: 3474.

Jonas JB, Jonas RA, Holbach L & Panda-Jonas S (2011): Histology of the parapapillary region in high myopia. Am J Ophthalmol 152: 1021–1029.

Jonas JB, Ohno-Matsui K, Spaide RF, Holbach L & Panda-Jonas S (2013): Macular Bruch’s membrane defects and axial length: association with gamma zone and delta zone in peripapillary region. Invest Ophthalmol Vis Sci 54: 1295–1302.

Jonas JB, Holbach L & Panda-Jonas S (2014): Bruch’s membrane thickness in high myopia. Acta Ophthalmol 92: e470–e474.

Jonas JB, Wang YX, Zhang Q, Liu Y, Xu L & Wei WB (2015a): Macular Bruch’s membrane length and axial Length. The Beijing eye study. PLoS One 10: e0136833.

Jonas RA, Wang YX, Yang H, Li JJ, Xu L, Panda-Jonas S & Jonas JB. (2015b). Optic
disc-fovea distance, axial length and parapapillary zones. The Beijing Eye Study 2011. PLoS One 10: e0138701.
Jonas JB, Ohno-Matsui K, Holbach L & Panda-Jonas S (2017a): Retinal pigment epithelium cell density in relationship to axial length in human eyes. Acta Ophthalmol 95: e22-e28.
Jonas JB, Ohno-Matsui K, Jiang WJ & Panda-Jonas S (2017b): Bruch’s membrane and the mechanism of myopization. A new theory. Retina 37: 1428–1440.
Jonas JB, Jonas RA, Ohno-Matsui K, Holbach L & Panda-Jonas S (2018): Corrugated Bruch’s membrane in high myopia. Acta Ophthalmol 96: e147–e151.
Kwon J, Shin JW, Lee J & Kook MS (2018): Choroidal microvasculature dropout is associated with parafoveal visual field defects in glaucoma. Am J Ophthalmol 188: 141–154.
Mo J, Duan A, Chan S, Wang X & Wei W (2017): Vascular flow density in pathological myopia: an optical coherence tomography angiography study. BMJ Open 7: e013571.
Ohno-Matsui K, Kawasaki R, Jonas JB et al. (2015): International classification and grading system for myopic maculopathy. Am J Ophthalmol 159: 877–883.e7.
Ramrattan RS, van der Schaft TL, Mooy CM, de Bruijn WC, Mulder PG & de Jong PT (1994): Morphometric analysis of Bruch’s membrane, the chorio capillaris, and the choroid in aging. Invest Ophthalmol Vis Sci 35: 2857–2864.
Rao HL, Sreenivasiah S, Riazuddin M et al. (2019): Choroidal microvascular dropout in primary angle closure glaucoma. Am J Ophthalmol 199: 184–192.
Sayanagi K, Ikuno Y, Uematsu S & Nishida K (2017): Features of the choriocapillaris in myopic maculopathy identified by optical coherence tomography angiography. Br J Ophthalmol 101: 1524–1529.
Schachat AP, Wilkinson CP & Hinton DR, Sadda SR & Wiedemann P (2017): Ryan’s Retina. 6ed. Amsterdam, The Netherlands: Elsevier Health Sciences.
Scherm P, Pettenkofer M, Maier M, Lohmann CP & Feucht N (2019): Choriocapillary blood flow in myopic subjects measured with OCT angiography. Ophthalmic Surg Lasers Imaging Retina 50: e133–e139.
Seddon JM, McLeod DS, Bhutto IA, Villalonga MB, Silver RE, Wenick AS, Edwards MM & Lutty GA (2016): Histopathological insights into choroidal vascular loss in clinically documented cases of age-related macular degeneration. JAMA Ophthalmol 134: 1272–1280.
Shao L, Xu L, Wei WB et al. (2014): Visual acuity and subfoveal choroidal thickness: the Beijing Eye Study. Am J Ophthalmol 158: 702–709.e1.
Spaide RF, Koizumi H & Pozzoni MC (2008): Enhanced depth imaging spectral-domain optical coherence tomography. Am J Ophthalmol 146: 496–500.
Wan KH, Lam AKN & Leung CK (2018): Optical coherence tomography angiography compared with optical coherence tomography macular measurements for detection of glaucoma. JAMA Ophthalmol 136: 866–874.
Wei WB, Xu L, Jonas JB et al. (2013): Subfoveal choroidal thickness: the Beijing Eye Study. Ophthalmology 120: 175–180.
Wong CW, Teo YCK, Tsai STA et al. (2019): Characterization of the choroidal vasculature in myopic maculopathy with optical coherence tomographic angiography. Retina 39: 1742–1750.
Zhao J, Wang YX, Zhang Q, Wei WB, Xu L & Jonas JB (2018): Macular choroidal small-vessel layer, Sattler’s layer and Haller’s layer thicknesses. The Beijing Eye Study. Sci Rep 8: 4411.