Chapter 4
High Myopia and Myopic Glaucoma: Findings in the Peripapillary Retina and Choroid in Highly Myopic Eyes

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Abstract Because increasing evidence indicates that there is a close relationship between glaucoma and myopia, we hypothesized that conformational changes around the optic disc and axial elongation may biomechanically stress the optic nerve and increase the susceptibility of the lamina cribrosa to intraocular pressure. The area has a unique appearance, including the shape of the disc, an enlarged area of peripapillary atrophy, and nasal elevation with temporal flattening of the disc. These signs potentiality result from stretching of the posterior ocular wall and oblique insertion of the optic nerve, and investigators are expecting to find the key to the pathogenesis of glaucoma. Moreover, recent advances in imaging technologies are enabling visualization of the deep structural characteristics. This chapter reviews the morphologic and histologic changes in the peripapillary area in highly myopic eyes and addresses the underlying mechanism of glaucoma.

Keywords Myopia • Optic nerve head • Optic disc tilting • Optical coherence tomography • Choroid • Peripapillary atrophy

4.1 Introduction

Recent investigations have shed light on a relationship between myopia and glaucoma. The detailed mechanism is not fully understood; however, it is believed to result from increased susceptibility to intraocular pressure (IOP) in highly myopic eyes due to deformation of the eye wall at or around the optic disc area resulting from axial length elongation. The details of this relationship remain unclear because of difficulties observing the deep structures around the myopic disc *in vivo*. Recent advances in imaging modalities have enabled visualization of these tissues and fostered an understanding of the underlying pathologies stemming from deformity of the posterior wall. This chapter reviews the currently recognized

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optic nerve and peripapillary tissue changes in high myopia and discusses a possible relationship with glaucoma.

4.2 General Morphology of the Myopic Optic Disc

4.2.1 Ophthalmoscopic Appearance

The myopic nerve head is often vertically ovoid along the long axis and appears oblique, i.e., the so-called tilted disc (Fig. 4.1). In non-myopic eyes, the nerve running into the eye usually courses at almost a right angle to the ocular surface. However, in myopic eyes, the course of the nerve axis is more oblique toward the temporal side as a result of posterior ocular wall protrusion (Fig. 4.2). This causes conformational changes in the disc surface that flatten the temporal side and elevate the nasal side [1]. Other characteristics are a secondary enlarged macrodisc, shallow disc cupping, and decreased contrast between the color of the neuroretinal rim and the color of the optic cup (Fig. 4.3). These features result from stretching of the posterior ocular structures because of the myopic shift.

A histomorphometric study reported that high myopic disc is about 1.5 times larger than non-myopic in absolute glaucoma [2], and fundus photographs show a substantially larger, and shallower disc in primary open-angle glaucoma with high myopia [3]. A large population study of Asian individuals reported that the disc area in myopic eyes is about 2–3 times larger than in emmetropic eyes and that the disc area is associated significantly with the degree of myopia. Interestingly, a graph of disc sizes showed a steep curve in high myopia, but the curve was relatively

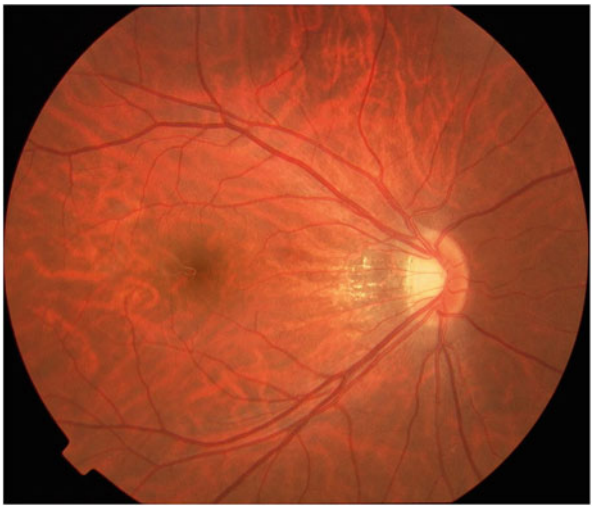

Fig. 4.1 Typical myopic disc with tilting on fundus photograph. The disc appears oval with the maximal diameter along the vertical axis

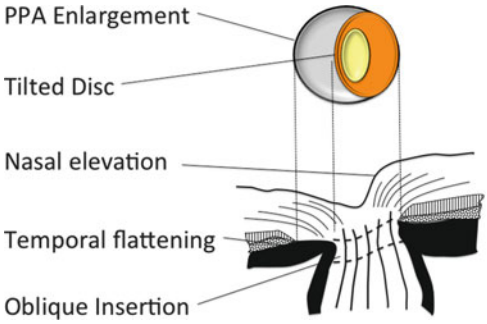

Fig. 4.2 The schema of oblique insertion and disc tilting in high myopia. The optic nerve runs oblique to the eye wall, resulting in flattening of the temporal side and elevating of the nasal side

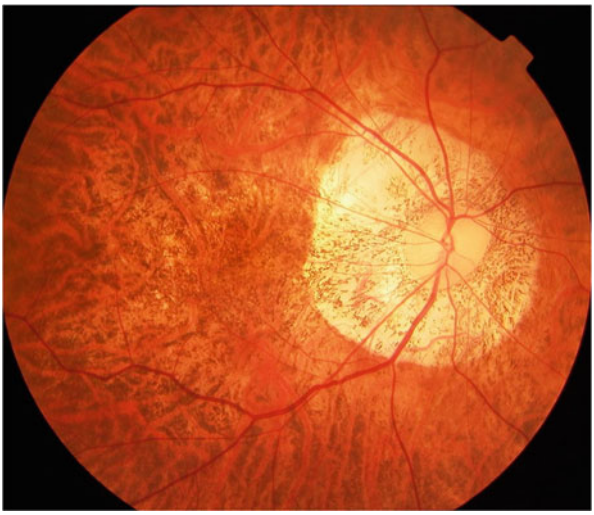

Fig. 4.3 A typical myopic macrodisc. The disc is not tilted, and unlike that in Fig. 4.1, this disc is flat with shallow cupping

horizontal in moderate myopia, suggesting that the highly myopic disc has specific features among the different degrees of myopia [4].

4.3 Peripapillary Atrophy

4.3.1 Definition

The myopic temporal crescent, sometimes referred to as beta-zone peripapillary atrophy (PPA) and conus myopicus (myopic conus), is a white, sharply defined area on the temporal side of the optic disc where the inner scleral surface is directly observable (Fig. 4.4). The myopic temporal crescent results from displacement of the choroid and retinal pigment epithelium (RPE) because of protrusion of the posterior pole [1]. A larger area of PPA and a higher refractive error are highly

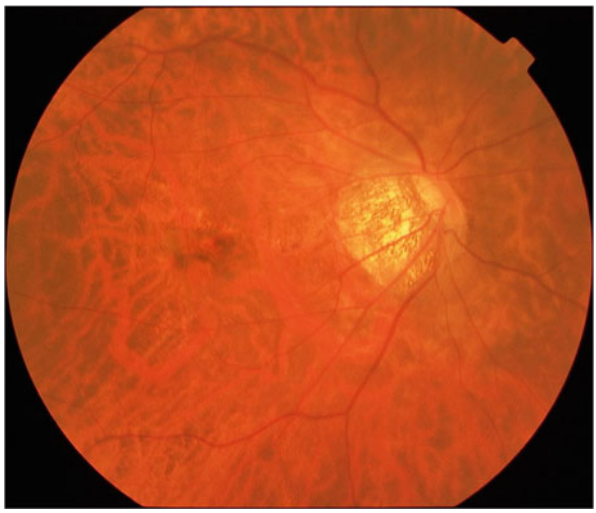

Fig. 4.4 The typical appearance of beta-peripapillary atrophy in high myopia. A whitish lesion with a well-defined border is seen that normally develops inferotemporal or temporal to the optic disc

correlated, and steep myopic increases exceeding −7 to −8 diopters have been reported [5], indicating that a large area of PPA is a hallmark of high myopia. There are two types of PPA. The first is a peripheral zone (alpha zone) characterized by irregular hypopigmentation and hyperpigmentation by fundus observation that is adjacent to the retina on the outer side; the second is the beta zone on the inner side, which is characterized by visible sclera and large choroidal vessels [6]. The myopic crescent normally presents temporal or inferotemporal to the disc and must be differentiated from the congenital tilted disc, which normally occurs inferiorly [7].

4.3.2 Histological Observation

Histologically, the alpha zone corresponds to irregularities in the RPE, while the beta zones is characterized by complete loss of RPE cells and almost complete loss of photoreceptors and closure of the choriocapillaris [8].

Recently, gamma and delta zones also have been proposed based on the results of a histologic study of myopic eyes [9]. The gamma zone is between the end of Bruch's membrane and the edge of the optic nerve head and was found predominantly in eyes with an axial length exceeding 26.5 mm, suggesting that the zone is specific to high myopia. The delta zone is part of the gamma zone in which blood vessels were not present. Interestingly, the length of the beta zone was not associated with high myopia but with glaucoma, while the lengths of the gamma and delta zones were associated with high myopia but not with glaucoma. We hypothesized that these proportional changes in the PPA zone may be associated with the susceptibility of the IOP in highly myopic eyes and may be why glaucoma develops in certain highly myopic eyes.

4.3.3 Optical Coherence Tomographic Findings

Some unique features within the area of PPA are specific to myopia or glaucoma. Spectral-domain optic coherence tomography (OCT) has shown that Bruch's membrane is often absent within the beta-PPA area in highly myopic eyes. The scleral bed configurations within the PPA can be classified into three types based on OCT findings: straight, a downward curving Bruch's membrane, or a downward bending slope without Bruch's membrane. Only the last is associated significantly with the myopic refractive error, and interestingly, the second is associated significantly with glaucoma [10]. This fact suggests that the configuration of the scleral bed within the PPA is related closely to myopic glaucoma, which partly agrees with histologic observations [9].

New imaging modalities including SD-OCT provide detailed information about the anatomic relationships among the disc edge, Bruch's membrane, and RPE. Observation using these new modalities has resulted in an argument that the beta-PPA should be redefined based on the findings using the latest generation of imaging tools. SD-OCT studies have found that the RPE was within the beta-PPA area in many cases, which is contrary to the initial definition based on histologic studies without RPE cells [11, 12].

4.3.4 Progression

The area of PPA enlarges over time with myopic progression (Fig. 4.5). The congenital crescent that normally does not enlarge must be ruled out. The myopic disc shifts nasally with axial length elongation, which induces myopic crescent development temporally. A follow-up study found a significant correlation between optic disc deviation and myopic progression [13].

Serial disc photographs also showed progressive tilting of the optic nerve head with development or enlargement of the area of PPA in myopic children. In the group with changes in the optic nerve head and area of PPA, the mean horizontal-to-vertical disc diameter ratio decreased from 0.92 to 0.86, and the mean maximal PPA width-to-vertical disc diameter ratio increased from 0.08 to 0.20 during a mean follow-up period of 38.1 months. These changes were most marked in children between 7 and 9 years of age and were associated with a greater myopic shift [14]. Thus, a myopic shift induces disc tilting and consequent PPA enlargement in myopic eyes.

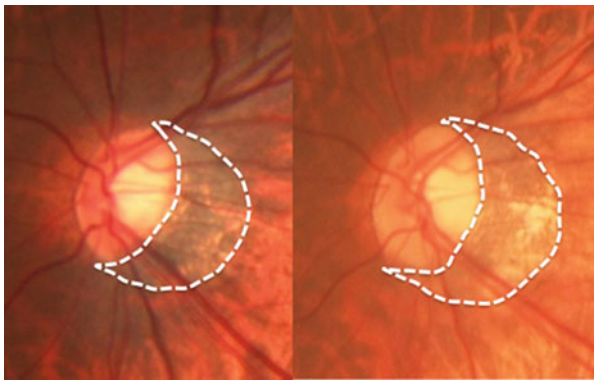

Fig. 4.5 Enlargement of peripapillary atrophy (PPA) over years. The same patient at baseline (*left*) and 10 years later (*right*); enlargement of PPA and increased disc tilting are seen (*white dashed lines*). The axial length has elongated from 28.67 mm to 29.03 mm

4.4 Tilted Disc

4.4.1 Ophthalmoscopic Appearance

Tilting is one of the most common features of a myopic disc; the nasal margin typically becomes elevated relative to the temporal margin. Angulation of the optic cup axis inferonasally is also common. Myopic discs with acquired crescents and congenital tilted discs can be difficult to distinguish because both have a severely attenuated RPE, Bruch's membrane, and choroid close to the disc.

4.4.2 Relation to Myopia

Several studies have reported a positive association between tilted discs and long axial lengths. One study found that 55 of 150 myopic eyes had markedly tilted optic discs, with a cut-off value of the disc index less than 0.8. In addition, smaller disc ovality was observed in more highly myopic eyes with a longer axial length [15]. The relationship between optic disc tilt and myopia also has been reported in pediatric patients. Schoolchildren with tilted discs have significantly longer axial lengths and greater myopic refractive errors [16].

4.4.3 Conventional Indices for Tilted Discs

Because the maximal angle of the disc tilting cannot be measured directly, it is estimated by the degree of disc ovality (Fig. 4.6). When viewed along the visual axis, the less perpendicular the optic nerve is when it enters the globe, the greater the elliptical appearance is. The papillary index, defined by the shortest axis/longest

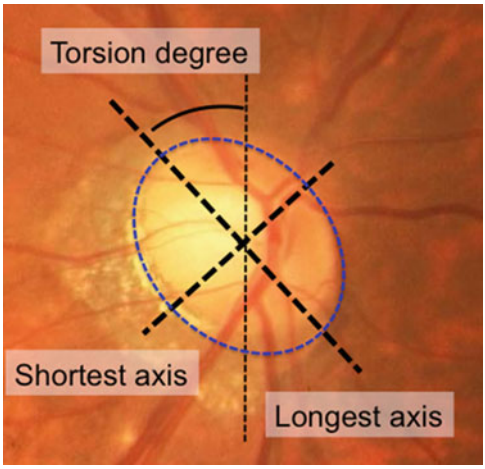

Fig. 4.6 Measurement of disc tilting. The disc is regarded as an ellipsoid and the maximal and minimal diameters crossing perpendicularly at the center of the optic nerve head are obtained. The index is the ratio of the minimal/maximal diameters. The angle between the maximal diameter and the vertical line is expressed as the degree of torsion

axis on fundus photographs, has been used as the gold standard to represent the degree of disc tilting [17]. The threshold to define the tilted disc often is lower than 0.8–0.75. Non-myopic discs are minimally oval with the vertical diameter slightly longer than the horizontal, and the index is close to 1.0.

The second geometric variable in tilted discs is rotation around the sagittal axis of the optic nerve (Fig. 4.6), which is referred to optic disc torsion. The longest diameter usually falls within 15° of the vertical meridian; axes beyond 15° are commonly defined as "torted."

4.4.4 Peripapillary Tilting Index

Because tilted discs associated with myopia occur as a result of posterior conformational changes from axial elongation, the morphologic changes at the peripapillary area are supposed to be related closely to the direction and degree of disc tilting. Measuring the disparity between the maximal and minimal surface elevations of the disc is an indirect way to measure the angle of the optic nerve as it enters the eye. The greater the elevation is in surface levels against the opposite side, the greater the tilting is assumed to be.

We developed a new system to measure this disparity in the 360° of the disc. We use a circular peripapillary scan with the average RPE height as the reference plane. The RPE line is divided into 24 sectors and the heights in all sectors is averaged. The difference in height from the average value is referred to as the peripapillary tilting index (PTI) (Fig. 4.7). This value does not exactly represent the degree of disc oblique insertion, but the degree of tilting in each direction around the disc. Another advantage of this system is that it identifies the direction in which the disc is most tilted. The minimal PTI value agreed well with the disc ovality index. We

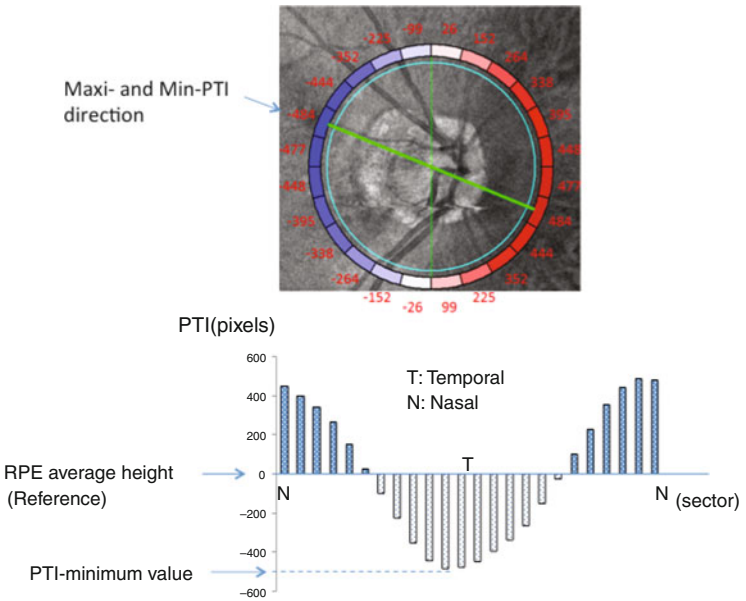

Fig. 4.7 Measurement of the peripapillary tilting index. The average position of the retinal pigment epithelium in 24 sectors in a peripapillary circular scan is obtained, and the difference from the average value is measured in each sector. This shows the degree of tilting in a particular direction

found that the minimal PTI was in the inferotemporal direction in myopic discs, indicating that myopic discs predominantly tilt in that direction. We currently are investigating the relationship with myopic normal tension glaucoma (NTG).

4.5 Peripapillary Choroidal Thickness

4.5.1 Choroidal Thickness in Normal Eyes

There is wide interindividual variability in choroidal thickness with age, refractive error, and axial length. The choroid in myopic eyes is thinner because of stretching of the posterior eye. For example, the mean subfoveal choroidal thickness ranges from 250 to 350 μm in emmetropic eyes, while in high myopia it is about 100 μm, depending on the degree of myopia [18, 19]. A histologic study reported that the loss of capillaries and fibrous tissue replacement are evident in highly myopic eyes [20].

Choroidal thinning is disproportional at the macula [18, 19]. In highly myopic eyes, the inferior and nasal sectors are thinner, and the temporal and superior sectors are relatively thicker. The subfovea is the thickest in non-myopic eyes.

Thus, the stretching affects each locations differently in highly myopic eyes. In the peripapillary area, the inferior sector is significantly thinner than other sectors in the peripapillary lesions of non-myopic normal eyes [21].

4.5.2 Glaucoma and Choroidal Thickness

The mechanism of NTG in myopic eyes is puzzling. We hypothesized that this might depend on the posterior eye wall configuration and conducted a study to measure the choroidal thickness in eyes with myopic glaucoma. The study included 12 eyes of eight patients under 45 years of age who had NTG with refractive errors between −6 and −12 diopters and axial lengths exceeding 26.5 mm and 12 eyes of matched healthy volunteers with a similar degree of myopia. The mean choroidal thickness in the NTG group was significantly thinner at the fovea and superior, superotemporal, temporal, and inferotemporal to the optic nerve head (Fig. 4.8).

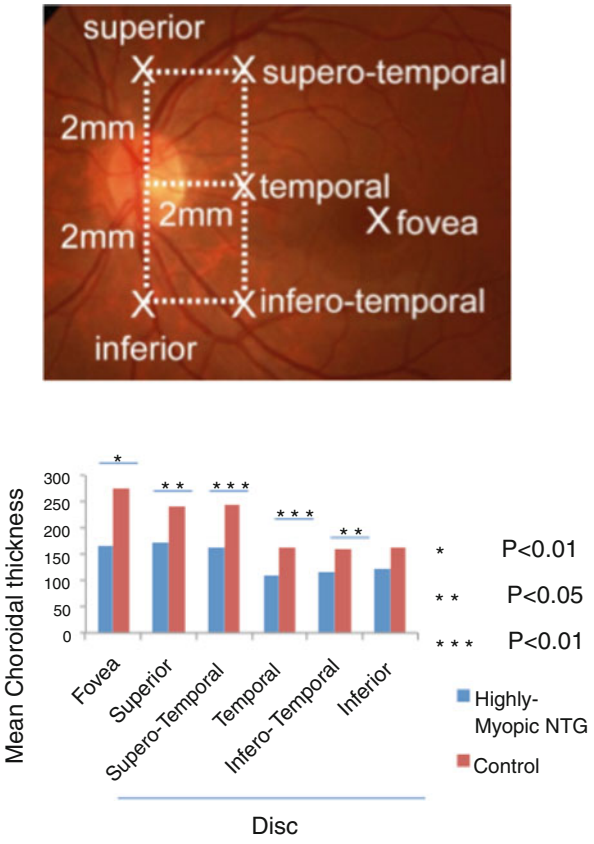

Fig. 4.8 The mean choroidal thickness in highly myopic eyes with or without normal tension glaucoma (NTG). The thickness is significantly smaller around the disc and at the macula in NTG

This suggested that choroidal thinning is related to highly myopic NTG and the indices may be a useful diagnostic parameter for myopic NTG.

4.5.3 Controversies in Glaucoma and Choroidal Thicknesses

However, a controversy remains. Many studies have reported that there is no significant difference in the choroidal thickness between normal and glaucomatous eyes, such as those with primary open angle glaucoma [22]. However, others have reported that NTG is associated with significant thinning inferonasal, inferior, and inferotemporal to the optic nerve head [23]. Interestingly, the choroidal thickness varies based on the damage to the optic nerve, and the sclerotic type was associated with a significantly thinner choroid than compared with the diffuse and focal types and even healthy controls [24]. Thus, the choroidal thickness may not differ in most types of glaucoma but may differ in some specific conditions such as high myopia or in eyes with peripapillary thinning.

4.6 Summary

High myopia is a disease of morphologic changes of the posterior ocular wall that causes mechanical stress on the deep structures, such as the optic nerve, peripapillary choroid or sclera, and the lamina cribrosa. The peripapillary region in highly myopic eyes is markedly deformed due to axial length elongation and seems to contribute greatly to the high glaucoma risk. However, its relationship is not totally understood. Modern imaging technologies such as OCT may reveal the underlying mechanism of the stress around the disc area. This field has come under intense scrutiny in the last 10 years, and hopefully the predictive factors and risks will be determined in the near future.

References

1. Apple DJ et al (1982) Congenital anomalies of the optic disc. Surv Ophthalmol 27(1):3–41
2. Dichtl A et al (1998) Histomorphometry of the optic disc in highly myopic eyes with absolute secondary angle closure glaucoma. Br J Ophthalmol 82(3):286–289
3. Jonas J, Dichtl A (1997) Optic disc morphology in myopic primary open-angle glaucoma. Graefes Arch Clin Exp Ophthalmol 235(10):627–633
4. Wu R-Y et al (2011) Relationship of central corneal thickness with optic disc parameters: the Singapore Malay Eye Study. Invest Ophthalmol Vis Sci 52(3):1320–1324
5. Xu L et al (2010) Definition of high myopia by parapapillary atrophy. The Beijing Eye Study. Acta Ophthalmol 88(8):e350–e351

6. Jonas J (2005) Clinical implications of peripapillary atrophy in glaucoma. Curr Opin Ophthalmol 16(2):84–88
7. Vongphanit J et al (2002) Population prevalence of tilted optic disks and the relationship of this sign to refractive error. Am J Ophthalmol 133(5):679–685
8. Jonas J, Nguyen X (1989) Parapapillary chorioretinal atrophy in normal and glaucoma eyes. I. Morphometric data. Invest Ophthalmol Vis Sci 30(5):908–918
9. Jonas J et al (2012) Parapapillary atrophy: histological gamma zone and delta zone. PLoS One 7(10):e47237
10. Hayashi K et al (2012) Spectral-domain optical coherence tomography of β-zone peripapillary atrophy: influence of myopia and glaucoma. Invest Ophthalmol Vis Sci 53(3):1499–1505
11. Park SC et al (2010) In-vivo microstructural anatomy of beta-zone parapapillary atrophy in glaucoma. Invest Ophthalmol Vis Sci 51(12):6408–6413
12. Lee K et al (2010) Cross-sectional anatomic configurations of peripapillary atrophy evaluated with spectral domain-optical coherence tomography. Invest Ophthalmol Vis Sci 51 (2):666–671
13. Nakazawa M et al (2008) Longterm findings in peripapillary crescent formation in eyes with mild or moderate myopia. Acta Ophthalmol 86(6):626–629
14. Kim T-W et al (2012) Optic disc change with incipient myopia of childhood. Ophthalmology 119(1):21–26
15. Tay E et al (2005) Optic disk ovality as an index of tilt and its relationship to myopia and perimetry. Am J Ophthalmol 139(2):247–252
16. Samarawickrama C et al (2011) Myopia-related optic disc and retinal changes in adolescent children from Singapore. Ophthalmology 118(10):2050–2057
17. Giuffrè G (1991) Chorioretinal degenerative changes in the tilted disc syndrome. Int Ophthalmol 15(1):1–7
18. Ikuno Y et al (2010) Choroidal thickness in healthy Japanese subjects. Invest Ophthalmol Vis Sci 51(4):2173–2176
19. Ikuno Y, Tano Y (2009) Retinal and choroidal biometry in highly myopic eyes with spectral-domain optical coherence tomography. Invest Ophthalmol Vis Sci 50(8):3876–3880
20. Ohno H (1983) Electron microscopic studies of myopic retinochoroidal atrophies 1. Choroidal changes (in Japanese). Folia Ophthalmol Jpn 43:1244–1253
21. Ho J et al (2011) Analysis of normal peripapillary choroidal thickness via spectral domain optical coherence tomography. Ophthalmology 118(10):2001–2007
22. Banitt M (2013) The choroid in glaucoma. Curr Opin Ophthalmol 24(2):125–129
23. Hirooka K et al (2012) Evaluation of peripapillary choroidal thickness in patients with normal-tension glaucoma. BMC Ophthalmol 12(1):29
24. Roberts KF et al (2012) Peripapillary choroidal thickness in healthy controls and patients with focal, diffuse, and sclerotic glaucomatous optic disc damage peripapillary choroidal thickness in glaucoma. Arch Ophthalmol 130(8):980–986