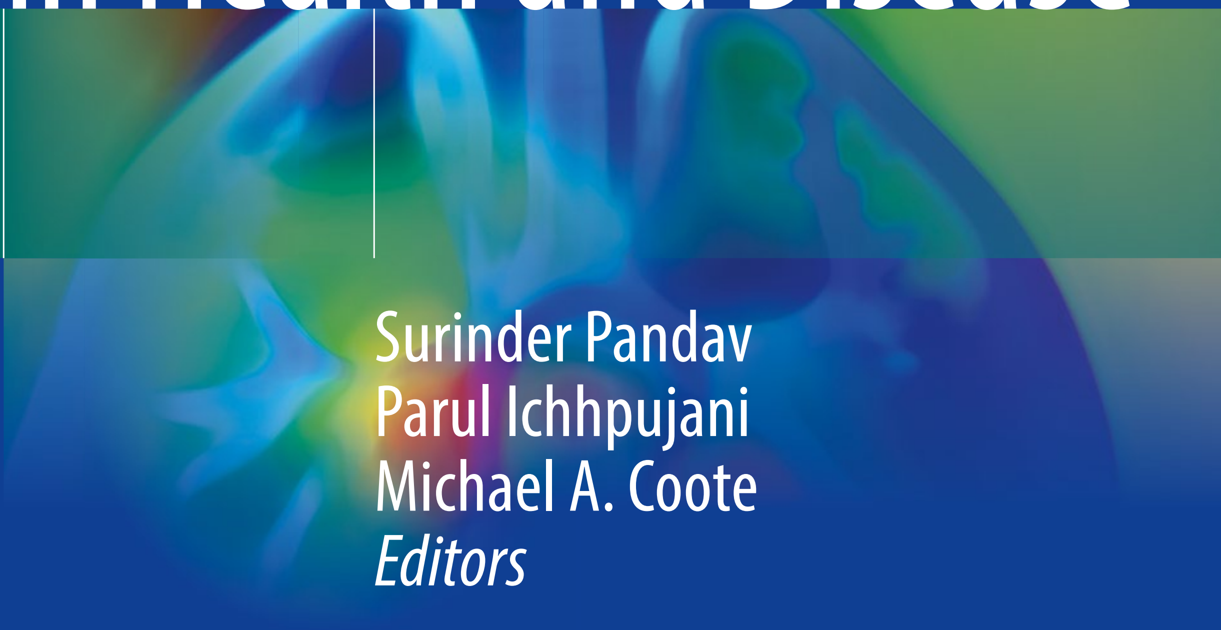
The Optic Nerve Head in Health and Disease



Surinder Pandav
Parul Ichhpujani
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Editors

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Foreword

You see only what you look for.
You look for only what you know.

"What do you see there? Is that nerve damaged by glaucoma?" The teacher asks the student looking at the optic nerve. Some students see the damage; others do not. When examining patients, some doctors look but do not see. So, they miss things important to the health of patients. Rather than learn to see, many say to themselves, "ophthalmoscopy does not work," and turn to another method, such as optical coherence tomography (OCT). But the major issue is not with ophthalmoscopy or tomography, but rather with the learning. Those not able to see ophthalmoscopically are not likely to see using other methods. For example, they look at the printout of the OCT but do not understand what it means. At which point they either blindly follow an algorithm, without the thinking that is needed to give good care (and not as an aside, makes life worthwhile) or they say "OCT is not reliable" and switch to yet another method. To help patients, one has to learn what to look for. One also has to learn how to see. This book will help people learn those things.

Those with glaucoma— whether newborn infant, stressed young mother, hardworking farmer, busy bank president, or demented old man—are best cared for by a knowledgeable, skilled, wise person doing only what is necessary: taking a probing, empathetic, pertinent, honest, revealing history, carefully assessing visual function and pupillary responses, validly characterizing the anterior chamber angle and the optic nerve and retina. Yes, a rough idea of the intraocular pressure can give some guidance, but not much.

In a person being considered for glaucoma, the caregiver needs to determine if the person **already** has troublesome symptoms, and, if so, why; the answers to that question are likely to come most reliably from the history and the nature of the optic nerve. The caregiver and the patient will want to know whether troublesome symptoms *are likely to develop*: the history, the nature of the anterior chamber angle, and the nature of the optic nerve help address that issue. Risk factors for the development of open-angle glaucoma, such as age, central corneal thickness, and family history, provide guidance related to the frequency of follow-up but are of little help in diagnosing or deciding the treatment, because they were developed by considering groups with certain characteristics and are not applicable to all individuals. Consider two patients: one is an 85-year-old man with an intraocular pressure of 30 mm Hg, central cornea thickness of 450 microns, a positive family history, and a cup/disc ratio of 0.6; the other patient is a 25-year-old woman with an intraocular pressure of 15mm Hg, central corneal thickness of 550 microns, a negative family history, and a cup/disc ratio of 0.4. Of these two people who is more likely to be helped with treatment? The answer is, we do *NOT* know. Both have the same likelihood of becoming disabled from glaucoma: either 100% or 0% but on the basis of the data given no one can predict accurately which will remain stable and which will get worse; people can have all the findings of the old man and remain stable or all the findings of the young woman and go blind from glaucoma. So, the information provided is *not* the essential information. Now, add the fact that the 85-year-old man has a disc damage likelihood score (DDLS) of 4 and the 25-year-old woman a DDLS of 6, and suddenly we know what to do! The 85-year-old man does not need any treatment, while the 25-year-old woman already has glaucoma with field loss that was missed earlier.

Having said that, however, a further comment is necessary, for it is not the assessment of the optic nerve and retina that is needed and helpful. It is the *accurate* assessment that is needed and helpful. Wrong data are worse than no data! This book importantly addresses this issue.

We need to recall that in 1976, Lichter found that glaucoma specialists agreed poorly with each other when evaluating photographs of optic discs [1]. But in 1992, in a similar study, Varma and colleagues found the agreement excellent [2]; in 1994, Abrams and colleagues reported concurrence was sometimes good and sometimes bad [3], while in 1917 Haslett and colleagues found excellent agreement among specialists regarding the character of the optic nerve when examined with a high + lens [4]. Which is correct? All are correct relative to the study performed. None can be generalized to answer "can clinicians evaluate the optic disc validly." The correct answer to that is not a "yes" or a "no." The correct answer is "some can and some cannot." The differences in the results were partly due to the different quality with which the assessments of the optic nerve were performed. Few physicians seem to understand that the value of a test is usually more related to *how well* a test is performed and interpreted, rather than *the type of test* performed. For example, ophthalmoscopy is helpful or not depending on how well it is performed and interpreted. OCT is helpful or not depending on how well it is performed and interpreted. Perhaps artificial intelligence can help. Perhaps. Will it further decrease clinical skills? Or enhance them?

A noted glaucoma specialist once said to me, "Why do you keep stressing looking at the nerve when you know few can look at it well?" His comment is right and it is wrong. (1) (right) few look at the nerve well, but (2) he is wrong in thinking that doctors *cannot* look at it well. Accurate ophthalmoscopic assessment of the optic nerve *is* possible. Seeing well demands correct examination skills, cognitive knowledge about the strengths and weaknesses of various examination methods, recognizing discs that are likely to mislead or are too atypical to categorize validly with one or more methods, but likely to be better understood by using another method.

The quality of the clinical examination seems to be getting even worse. As practitioners substitute technology for clinical examination, their examining skills plummet. Even the most renowned pianists practice daily; honest surgeons know that they will not be as sharp in the operating room after missing surgery for two weeks, so they start the day with cases that should not be challenging.

Maintaining a skill takes constant practice but the goal should not be just maintenance—it is improvement. Improving skills requires effort, will, and discipline- and practice, whether playing the piano, writing poetry, or examining the optic disc. And the quality of the practice is instrumental in affecting whether it is associated with improvement. For example, the disc must be examined and drawn *prior* to looking at the previous drawing; then the two are compared so the examiner can compare the two, not just to consider whether the patient's disc has worsened, but importantly to evaluate the validity of the drawing: how could it be done better?! Without masking oneself, one simply copies the prior drawing and learns nothing. By evaluating one’s skills constantly, one can become better and better and better. These comments apply to all technologies; learning to determine whether the test was performed properly and how to tease meaning out of the seemingly objective but actually, subjective printouts take constant practice, designed to improve skills. The OCT’s mechanics are relatively objective, the choice of subject and how the technician operates the machine are subjective. The printer prints objectively, but the content on the paper is subjective. However, it is not whether the test is objective or subjective that matters: it is whether the results are *valid, relevant, and important,* and those considerations are unrelated to objective or subjective.

All technologies, such as optical coherence tomography, ophthalmoscopy, or angiography, yield information not possible to obtain with other technologies, and no technology provides complete information. Before a test is done, expending the time and effort of the patient, the technician, and the doctor, and increasing the costs of care, the person ordering the test needs to consider whether the information intended to be gained will be *valid, relevant, and important***.** If not, why do the test?

New technologies may help the brain do its job. The technologies are not aware that there is never a perfectly correct answer in medical care. The wise clinician knows this and is constantly considering whether the data are valid enough, are truly relevant, and are necessary; if they are not valid enough, relevant, and important, they must be discarded, and the person ordering the test should say either “why did I get that test?” or “why were those test results not satisfactory?”

The present text will help clinicians obtain evidence that is valid, determine its relevance, and use it appropriately in making decisions, so that patients may be better able to celebrate their lives.

You see only what you look for.
You look for only what you know.

Truth lies within these lines. So also does inadequacy. Learning so that one can look better and see more is a good start. But more challenging, and also important to betterment of the world, is seeing what you do not know and then finding out what you have seen. The thoughtful reader of *The Optic*

Nerve in Health and Disease will learn much, and be stimulated to see even more, that which has still not been understood.

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He is the developer of the Glaucomatous Optic Neuropathy Evaluation (GONE) project, the largest online evaluation and teaching system for ONH evaluation ever created. He is the co-author of the World Glaucoma Association Teaching module for ONH evaluation (https://wga.one/wga/basic-course-in-glaucoma/). His subspecialty interests include glaucoma management and glaucoma surgery, complex and failed glaucoma surgery, minimally invasive glaucoma surgery, anterior segment repair, cataract, and complex cataract surgery.

1 What Is the Range of Normal Variations in the Optic Nerve Head Appearance?

Sahil Thakur and Suresh Kumar

The art of examining the optic nerve head (ONH) begins before you even look at the patient's eye. It is imperative to keep in mind the patient history, vision status, and systemic abnormalities before you can examine and classify a suspicious ONH. A wide array of presentations are possible as different pathological processes affect different parts of the ONH. While the presentation may differ, the examination of the ONH remains a systematic process. It entails evaluation of the disc morphology, cup characteristics, and finally the neuroretinal rim features that help in flagging the abnormal. Usually clinching a diagnosis will require ancillary testing, like visual field evaluation for glaucoma or a MRI for an intracranial space occupying lesion/demyelination disorder like multiple sclerosis; it is the initial ONH appearance that may be the only sign apparent in a potentially life threatening condition. However, a majority of the eyes examined by an ophthalmologist are normal or physiologically normal variants. Normal ONH morphology can be affected by factors like age, gender, ethnicity, spherical equivalent, axial length, and even by the examination/assessment modality used. This chapter will present the readers with a wide variety of 'normal' ONH variants and help them develop a method to evaluate the ONH with reliable accuracy and confidence. In this chapter we will however limit ourselves to evaluation of the ONH using slit lamp biomicroscopy and stereoscopic or conventional fundus photographs. Many of the entities discussed are elaborated or discussed with a different perspective in other chapters as well.

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1.1 Normal ONH

A normal ONH is pink in colour, usually round or oval in shape, mildly elevated, with a central depression called as the cup (Fig. 1.1).

The optic disc represents the point of exit of the retinal nerve fibres and point of entry for the vascular supply of the eye. Thus, it is the connection between the eye and the brain. The horizontal diameter of the typical ONH is ~1500 μm or 1.5 mm but population-based studies have shown significant variation across the normal population (Table 1.1). It is always imperative to evaluate the normal ONH in conjunction with other ocular parameters like visual acuity, colour vision, contrast sensitivity, and visual fields as structural findings need to be correlated with functional parameters for making a reasonably sound diagnosis.

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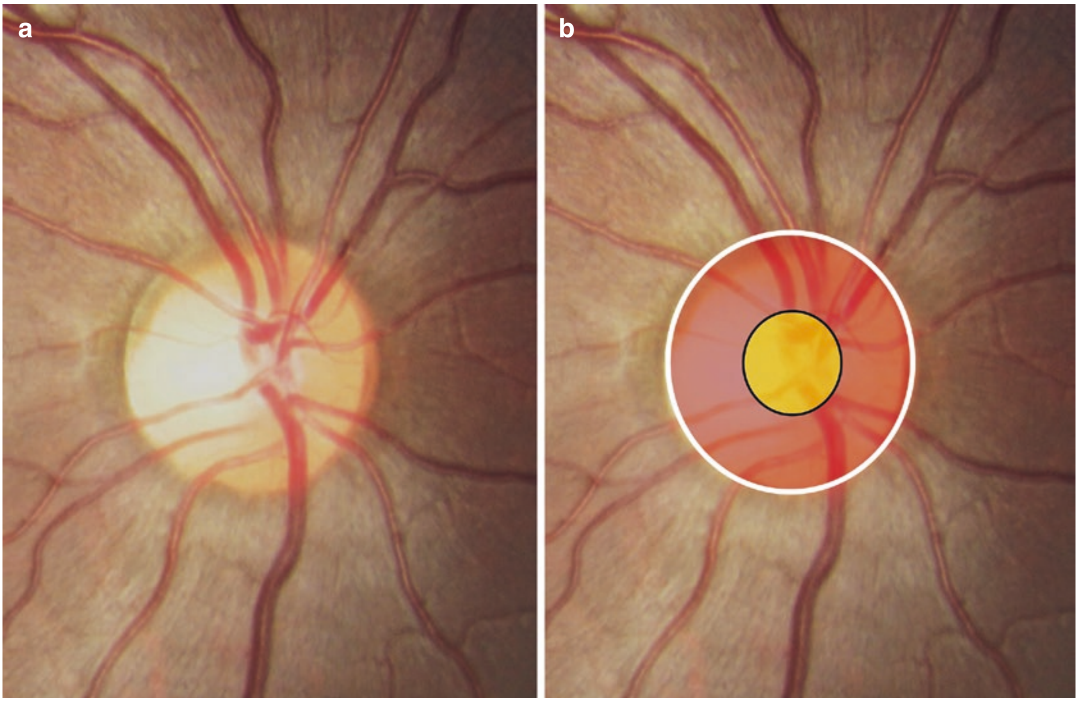

Fig. 1.1 (**a**) Normal ONH and (**b**) the schematic overlay of ONH features like the central cup (yellow), neuroretinal rim (red), and the peripapillary scleral ring of Elschnig (white ring)

Table 1.1 Normative disc diameter from selected population-based studies

Year	Study	Horizontal disc diameter (mm)	Vertical disc diameter (mm)
2001	Andhra Pradesh Eye Study [1]	1.97 ± 0.19	2.12 ± 0.23
2004	Blue Mountain Eye Study [2]		1.50 (50th percentile)
2008	Tanjong Pagar Eye Study [3]	1.58 ± 0.18	1.73 ± 0.19
2011	Chennai Glaucoma Study [4]	1.81 ± 0.19	1.94 ± 0.2

1.2 Evaluating the ONH

A wide variety of techniques and imaging modalities can be used to evaluate the ONH that are covered subsequently in the book. From the humble ophthalmoscope to optical coherence tomography angiography (OCTA) assisted evaluation, the features that define the normal ONH remain fairly consistent. Despite having a plethora of published literature, available textbooks and guides, observation of the ONH has remained a difficult art. In order to assist ophthalmologists in examining the optic nerve several online web-based platforms are now available that can help sharpen the observation skills for all clinicians. These offer educational features that are convenient and suitable for the learning needs of today's ophthalmologists. The glaucoma courses by the World Glaucoma Association [5] and the optic nerve examination course by the Glaucomatous Optic Neuropathy Evaluation [6] (GONE) project are two such excellent resources that can help readers develop good ONH observation skills at their own comfort and convenience. However, for those readers who prefer to have a conventional textbook approach, this chapter can serve as a primer for developing a systematic method of examining features of the ONH.

For clarity of presentation and also for aid in the systematic evaluation of the ONH, we have divided the ONH features into:

1. Disc morphology.
2. Cup characteristics.
3. Neuroretinal rim (NRR) and peripapillary retinal nerve fibre layer (RNFL) features.

In the subsequent sections of this chapter these features will be discussed in more detail.

1.2.1 Note on Magnification/ Correction Factors

As different lenses are available for assessment of the ONH using slit lamp biomicroscopy it is imperative to know the correction factor for measurements made on the slit lamp (Table 1.2).

1.2.2 Disc Morphology

The morphological features that define the outer limits of the ONH are often the ones that provide the most information about the underlying physiological state of the eye. Usually these morphological features show considerable range of normal findings in population-based studies (Table 1.3). These features are the peripapillary atrophy (PPA), disc size, disc shape, and the disc tilt (Fig. 1.2). This has been addressed in detail in Chap. 5.

1.2.2.1 Peripapillary Atrophy (PPA)

The PPA is the surrounding area that marks the boundary of the ONH and the peripheral retina. Classically two types of PPA have been described: the α (alpha) and the β (beta) PPA

Table 1.2 Correction factors for common fundus examination lenses

Lens	Magnification	Correction factor [7]	Working distance	Field of view (static/dynamic)
60D (Volk-Nikon)	1.15X	0.94–1.03	13 mm	$68^0/81^0$
78D (Volk)	0.93X	1.13	8 mm	$81^0/97^0$
90D (Volk-Nikon)	0.76X	1.36–1.59	7 mm	$74^0/89^0$
Super field® (Volk)	0.76X	1.50	7 mm	$95^0/116^0$

Table 1.3 Normative disc morphology parameters from selected population-based studies

Year	Study	Disc area (mm^2)	Neuroretinal rim area (mm^2)
1999	Rotterdam Eye Study [8]	2.42 ± 0.47	1.85 ± 0.39
2001	Andhra Pradesh Eye Study [1]	3.36 ± 0.68	2.79 ± 0.52
2003	Vellore Eye Study [9]	2.58 ± 0.65	1.60 ± 0.37
2003	Beijing Eye Study [10, 11]	2.65 ± 0.57	1.70 ± 0.30
2008	Tanjong Pagar Eye Study [3]	2.17 ± 0.46	1.43 ± 0.29
2011	Chennai Glaucoma Study [4, 12]	2.82 ± 0.52	2.29 ± 0.39

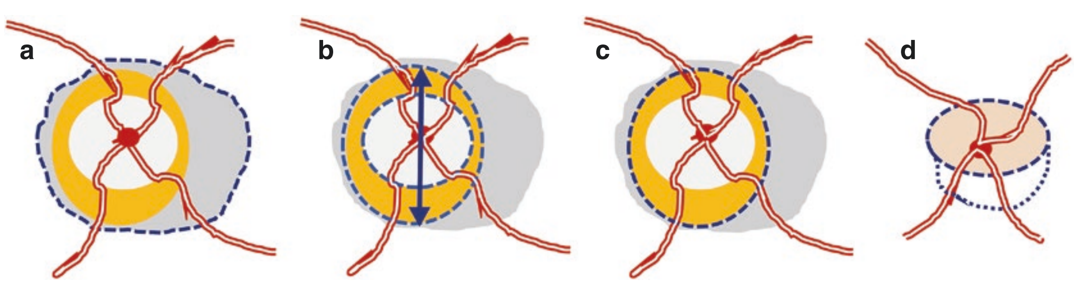

Fig. 1.2 Disc morphology features: (**a**) peripapillary atrophy (blue dotted line), (**b**) disc size, (**c**) disc shape, and (**d**) disc tilt/tort (adapted from the GONE [6, 13] project)

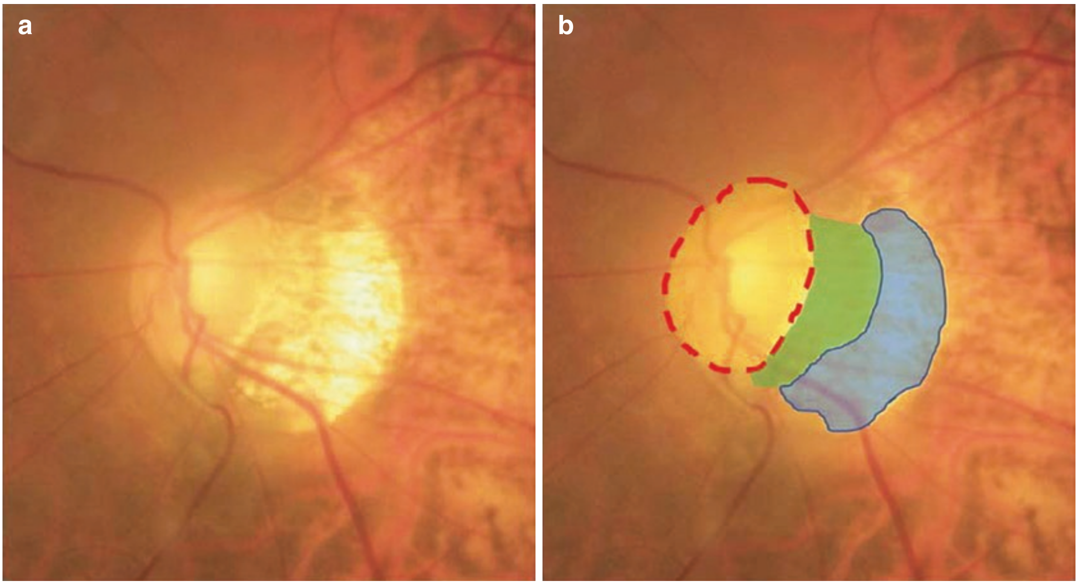

Fig. 1.3 (**a**) Tilted disc with extensive peripapillary atrophy and (**b**) classical α (alpha) zone: blue and the β (beta)zone: green peripapillary atrophy along with peripapillary scleral rim (red dotted line)

(Fig. 1.3a). The outer α zone is defined as the outermost/peripheral zone that occurs due to areas of hypo- and hyperpigmentation of the retinal pigment epithelium (RPE) layer, while the inner β zone is due to atrophy of the RPE leading to baring of the underneath choroidal and scleral tissue (Fig. 1.3b) [8]. Table 1.4 shows the normative PPA parameters from population-based studies. PPA is an important indicator of how much mechanical stretch the eye is under. Typically, in highly myopic eyes, PPA is larger and more apparent [14]. It is important to differentiate between the types of PPA and features of myopic degeneration in eyes with high myopia before starting anti-glaucoma therapy as these eyes may show fixed visual field defects due to morphological factors that can mimic glaucomatous damage [15–17].

Recently types of PPA have been expanded based upon the histological and OCT imaging-based data in highly myopic eyes [20–23]. Now there are 4 distinct types/zones of PPA: α, β, γ (gamma), and δ (delta). Fig. 1.4 shows a highly simplified scheme for understanding these four types of PPA. The δ zone corresponds to the peripapillary scleral flange which is the biomechanical anchor of the lamina cribrosa. It has been shown to be associated with increased risk of glaucoma in myopic eyes [23]. The γ zone corresponds to the peripapillary sclera without overlying choroid, Bruch's membrane, and deep retinal layers (details in Chap. 3). To differentiate between γ and δ zones, the blood vessels are an indicator. If vessels of at least 50 μm diameter and a minimal length of 300 μm are not detected, it is classified as δ zone [21, 22]. Typically, the arterial circle of Zinn–Haller lies in the γ zone [21].

1.2.2.2 Disc Size

Disc size is one of the most important morphological determinants of the ONH [24]. It is vital to classify the disc into small, normal, or large as it significantly affects evaluation of other ONH parameters like the cup–disc ratio (CDR) and the NRR. The discs can be classified on the basis of the disc diameter as: small (1.1–1.3 mm), medium (1.4–1.7 mm), and large (1.8–2 mm). Crowston et al. have shown that when compared for a small (1.2 mm) and large (1.9 mm) size optic disc, the 97.5th percentile CDR increased from 0.6 for small optic discs to 0.75 for large optic discs and from 0.62 to 0.83 for the 99th percentile [2]. This

Table 1.4 Peripapillary atrophy parameters from selected population-based studies

Year	Study	Sample	Prevalence/Progression		Area (mm^2)		Remarks
			α	β	α	β	
1999	Rotterdam Eye Study [8]	1672 eyes, 894 subjects	58%	13%			α zone prevalence decreased 0.4% per decade (P = 0.035), β zone prevalence increased 1.3% per 1D myopia (P < 0.001)
2003	Vellore Eye Study [9]	70 subjects	98.6%	11.4%	0.84 ± 0.29	0.13 ± 0.38	α PPA usually temporal, correlates with disc and rim area
2007	Beijing Eye Study [18]	4003 subjects, 93 glaucoma				1.21 ± 1.92 mm^2 (glaucoma) versus 0.32 ± 0.99 mm^2 (normals); P < 0.001	β zone area increases with age (P < 0.001), myopia (P < 0.001), and glaucoma (P < 0.001)
2008	Beijing Eye Study [14]	4439 subjects	71.2%	19.9%	0.52 ± 0.64	0.46 ± 1.82	α and β usually temporal, size correlates with disc size (P < 0.001), age (P < 0.001), myopia (P < 0.001), and reduced visual acuity (P < 0.001)
2012	Beijing Eye Study (5 year follow up) [19]	3251 subjects	0.6 ± 0.1% progression	8.2 ± 0.5% progression			β progression associated with higher age, higher intraocular pressure, myopia, glaucoma, co-progression of α (all P < 0.001), rural region of habitation (P = 0.002), thicker central corneal thickness (P = 0.02), and absence of arterial hypertension (P = 0.03)

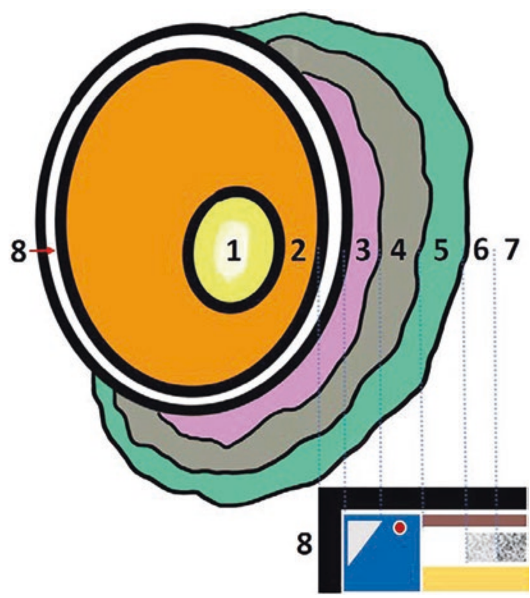

Fig. 1.4 Different types of peripapillary atrophy (PPA) in highly myopic eyes and the structures that define them. 1: optic cup, 2: neuroretinal rim, 3: δ (delta) zone, 4: γ (gamma) zone, 5: β (beta) zone, 6: α (alpha) zone, 7: peripheral retina, 8: parapapillary scleral ring of Elschnig (histologically: pia mater), blue box: peripapillary sclera without overlying choroid, Bruch's membrane, and deep retinal layers, white triangle: parapapillary scleral flange, red dot: arterial circle of Zinn–Haller, brown line: Bruch's membrane, black/white dotted box: retinal pigment epithelium, yellow box: choroid

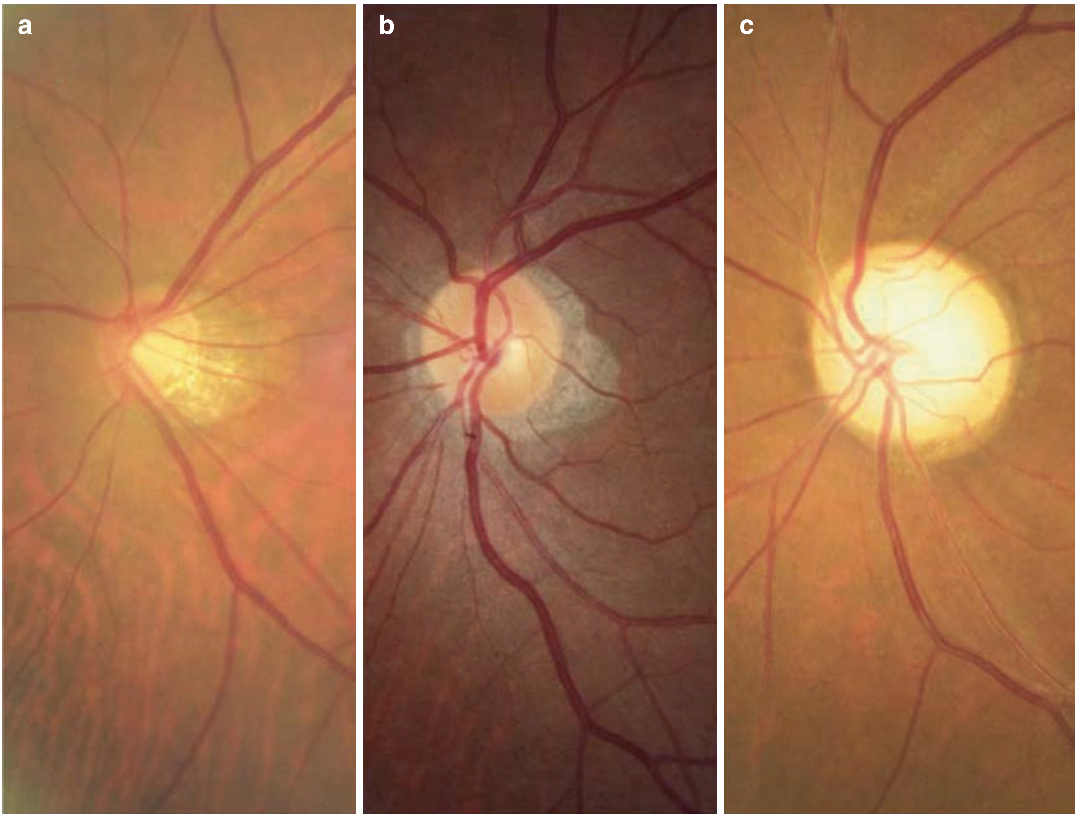

Fig. 1.5 Range of optic nerve head (ONH) size: (**a**) small, (**b**) medium, and (**c**) large

shows how the traditional CDR based diagnostic criteria can change significantly based on the disc size [25, 26]. If this is overlooked it can lead to overdiagnosis of glaucoma suspects and subsequently unnecessary visits for visual field and imaging tests. Thus, in order to classify a normal disc, it is vital to evaluate its features by corresponding them with the disc size (Fig. 1.5).

1.2.2.3 Disc Shape

The disc shape is another morphological parameter that can help identify the underlying physiological state and may get altered in pathological conditions. The disc shape also helps in defining the shape of the NRR and thus is vital in studies that evaluate structure function correlation. Garway-Heath et al. have previously described how visual field areas correspond to the ONH [27]. This map is now being incorporated in the OCT machines and is being increasingly used for structure function correlation studies [28, 29]. However, it is important to keep in mind that disc shape can significantly alter the representation areas in such analysis (Fig. 1.6).

1.2.2.4 Disc Tilt

The disc tilt helps in identifying the direction of the ONH as it enters the sclera. It can be traditionally classified as horizontally or vertically tilted (Fig. 1.7). Disc tilt is a vital parameter to record while disc evaluation, as conventional OCT machines cannot account for the impact of the disc tilt on automated measurements and thus may lead to incorrect observations about the pathological nature of the findings. Disc tilts can also lead to persistent scotomas on the visual field that can be misinterpreted as glaucomatous damage [15] (Fig. 1.6).

Disc tilt has also been defined based on the index of tilt and the angle of tilt which defines how torted the disc is (Fig. 1.8). Optic disc ovality is assessed using the ratio of minimum