Age and axial length on peripapillary retinal nerve fiber layer thickness measured by optical coherence tomography in nonglaucomatous Taiwanese participants

Pai Huei Peng¹, Sheng Yao Hsu², Wei Shin Wang³, Mei Lan Ko⁴,⁵ *

¹ Department of Ophthalmology, Shin-Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan, ² Department of Ophthalmology, China Medical University Hospital- An Nan Branch, Tainan, Taiwan, ³ Antibody Engineering Technology Department, Biomedical Technology and Device Research Laboratories, Industrial Technology Research Institute, Chutung, Hsinchu, Taiwan, ⁴ Department of Ophthalmology, National Taiwan University Hospital, Hsin Chu Branch, Hsinchu City, Taiwan, ⁵ Department of Biomedical Engineering and Environmental Science, National Tsing Hua University, Hsinchu City, Taiwan

* aaddch@gmail.com

Abstract

Purpose
This study investigates the influence of age and axial length (AL) on the peripapillary retinal nerve fiber layer (RNFL) thickness, as measured by optical coherence tomography (OCT).

Methods
Healthy patients visiting an eye clinic at a county hospital were recruited. All participants underwent comprehensive ophthalmologic examinations, and their retinas were scanned using 3D OCT-1000. In total, 223 patients with 446 eyes were included. The mean age and AL were 42.07 ± 13.16 (21–76) years and 25.38 ± 1.73 (21.19–30.37) mm, respectively.

Results
The average RNFL thickness decreased by 2.71 μm for every 10-year increase in age (P < 0.001). Age-related RNFL thinning was more significant in participants older than 41 years (-0.24 μm/year; P = 0.015). The earliest sector showing a significant decline in RNFL thickness was after 35 years of age (-0.70 μm/year; P = 0.011) at the superior quadrant and at the 1–2 o’clock hour (-1.42 μm/year; P = 0.009). Meanwhile, the maximal rate of age-associated RNFL decay was observed in these two regions as well. The reduction of RNFL with age progression did not differ in eyes with long AL (> 27 mm; -0.16 μm/year) or those with short AL (< 25 mm; -0.22 μm/year). For every 1-mm-greater AL, RNFL was thinner by 1.78 μm (P < 0.001). The inferior quadrant showed the greatest tendency of RNFL decline with longer AL (4.46 μm/mm; P < 0.001).
Conclusions

The factors of age and AL should be considered when interpreting the results. Significantly age-associated RNFL thinning was found in participants older than 41 years. Reduction of RNFL thickness with increasing age was not affected by AL. Topographic variations in RNFL thinning were observed in that the maximal decline of RNFL thickness with advancing age at the superior quadrant whereas with elongation of AL at the inferior quadrant.

Introduction

Glaucoma, a specific form of optic neuropathy with irreversible visual loss, affects millions of people worldwide. The progressive loss of the peripapillary retinal nerve fiber layer (RNFL) and the deeper and larger optic disk cup are recognized as pathological alterations of glaucoma. Therefore, the assessment of RNFL plays a major role in the diagnosis and follow-up of glaucoma[1, 2]. Compared with conventional red-free photography, optical coherence tomography (OCT), which measures RNFL thickness based on reflectivity changes between adjacent tissues, provides instant and quantitative information on RNFL thickness. However, the performance of OCT could be compromised by several factors such as image quality[3], accuracy of the centering of the scan circle [4], and the influence of myopia[5, 6].

The incidence of myopia in Asian countries is extremely high [7], which includes Taiwan [8]. The elongation of axial length (AL) occurs because increased negative refractive power and certain optic disk features of myopic eyes affect the performance accuracy of OCT[9–11]. The reported associations between AL and RNFL thickness vary with different study populations, OCT instruments, and whether ocular magnification is adjusted. Certain studies have shown that the average RNFL thickness inversely correlated with AL or negative refractive power[2, 12, 13]. By contrast, certain studies have reported a positive relationship between AL and RNFL thickness [14, 15].

Although most studies have been in agreement that RNFL thickness decreased with age [2, 13, 16, 17], distinguishing between age- or glaucoma-induced RNFL thinning is still a challenge at this point. A longitudinal study spanning for 4 years on 192 eyes found approximately 0.2% per year of age-related thinning in circumpapillary and macular RNFL [18]. The 3D OCT-1000 is a spectrum-domain OCT that uses high-resolution raster scan patterns, and is designed without correction for age and ocular magnification. Information regarding demographic and ocular parameters that affect RNFL measurement by 3D OCT-1000 are limited. Further knowledge regarding the factors contributing to misleading OCT findings is critical, because the determination of glaucomatous damage by OCT is to compare our findings with the normative database developed by manufacturers. The effects of age and refraction on the measurement of peripapillary RNFL thickness by 3D OCT-1000 were studied. In a similar manner, the topographic profile of RNFL thickness in myopic eyes was assessed.

Materials and methods

Healthy patients were invited to participate in the study when they visited an eye clinic at a county hospital from April to December of 2011. The IRB Number (HCGH99IRB-8) was specifically approved by the institution Review Board of Hsin-Chu General Hospital. Informed consent was obtained from each participant, and the tenets of the Declaration of Helsinki were followed. Detailed ophthalmic examinations, including refractive error measurement
conducted using the Autoref keratometer RC-5000 (Tomey Co. Nagoya, Japan), slit lamp examination, intraocular pressure (IOP) measurement using the Non-Contact Tonometer NT-530 (Nidex Co., Gamagori, Japan), fundoscopy, and a visual field (VF) test by using an Octopus Visual Field Analyzer (Interzeag AG, Berne, Switzerland), were performed. AL measurements were obtained using IOL Master (Carl Zeiss MEDITEC, Dublin, USA). Participants who were contraindicated for pupillary dilation or intolerable to topical anesthetics or mydriatics were excluded. Only paired eyes of participants were considered for analyses, unless any of the eyes exhibited any corneal, retinal, or optic nerve diseases, a best corrected visual acuity of less than 0.6, IOP ≥ 22 mmHg, or unreliable VF results (false-positive and false-negative rate > 15%, fixation losses > 20%). Retina scanning by 3D OCT-1000 (Topcon, Japan) with a 512 × 128-fast scan protocol was performed, which used a 3.4-mm diameter circle around the optic nerve head and covered a 6 × 6 mm² area. The image volume consists of 128 frames each with 512 A-lines. For data processing and analysis, the optic disc scans were segmented using the Topcon Advanced Boundary Segmentation (TABS) algorithm in FastMapTM 8.11. In brief, a circumpapillary annulus of 1.7 mm radius was extracted from the 3D volume data sets to generate retinal NFL thickness measurements corresponding to the overall circle as well as to the individual temporal, superior, nasal, and inferior quadrants. All optic disc scans were automatically centered for the circumpapillary analyses. To avoid centering errors, two experienced technicians checked and adjusted positions of the scan by placing a transparent plastic plate with multiple concentric rings on red free fundus images. Eyes were also excluded if image quality of OCT less than 45 or any algorithm line failures. The three-dimensional data setting to generate RNFLT measurements corresponding to the overall circle, the individual quadrants (temporal, superior, nasal, inferior) and 12 clock hours were presented.

To determine the break-point that the RNFL showed a significant decline with age, the rates of thinning before and after that age were compared (started from age 21 and up) until the significant difference was disclosed.

Statistical analyses were performed with R program software. The generalized estimating equation (GEE) linear model was used to examine the association between RNFL thickness and age, AL, and spherical equivalent (SE), and the inter-eye correlation was taken into account. A P value < 0.05 was considered statistically significant.

Results

The study population consisted of 223 healthy participants (446 eyes) aged 21–79 years. Of these participants, 104 (42.1%) were men. Table 1 shows the clinical characteristics of the study population. The right eyes are more myopic than the left eyes (p = 0.01).

In agreement with most previous studies, our results revealed that the average RNFL thickness decreased with age. Overall, for every 10-year increase in age, the average RNFL thickness decreased in the magnitude of 2.71 μm (P < 0.001). Age-related global RNFL thinning was more pronounced after 41 years of age (rate of thinning: 0.24 μm/year; 97.5% CI, 0.05 to 0.44; P = 0.015). The right eye showed earlier thinning than the left eye, however there is no significant difference of the rate of RNFL thickness in paired eyes under Dummy variable analysis (p = 0.121). Sectoral variations were noticed in age-related RNFL thinning (Table 2), with the superior quadrant displaying the earliest as well as the steepest decline in participants after 35 years of age (rate of thinning: 0.70 μm/year; 97.5% CI, 0.16 to 1.25; P = 0.011), followed by the temporal quadrant (age of 41 years; rate of thinning: 0.36 μm/year; 97.5% CI, 0.06 to 0.67; P = 0.020). RNFL thickness at the inferior and nasal quadrants was unaffected by age.

The study eyes were further divided into three groups according to the AL: short (< 25mm), medium (25 to 27 mm), and long (> 27 mm) AL group. The rates of age-related
The reduction of RNFL thickness in these three groups were -0.22 (short AL group), -0.19 (medium AL group), and -0.16 (long AL group) μm/year, respectively (Fig 1). The geepack are used for GEE models in R. There exists no significant differences among the following each two groups: long and short AL groups (P = 0.86), long and medium AL groups (P = 0.84) and short and medium AL groups (P = 0.53).

Table 3 shows the results regarding age when a significant correlation with clock hour RNFL thickness was noticed. For the right eye, the earliest age-related RNFL thinning was found after 35 years at 1–2 o’clock hour (1.89 μm/year; 97.5% CI, 0.67 to 3.11; P = 0.003). In addition, the maximal rate of age-associated RNFL thinning was located at this clock-hour. The other regions showing a significant age-related RNFL thinning were at 12–1 (after age 44 with a rate of thinning 0.49 μm/year; 97.5% CI, 0.01 to 0.96; P = 0.044), 8–9 (after age 40 with a rate of thinning 0.77 μm/year; 97.5% CI, 0.11 to 1.37, P = 0.021), respectively. For the left eye, the earlier age-related RNFL decline was found after 38 years at 12–1 o’clock (0.83 μm/year; 97.5% CI, 0.01 to 1.65; P = 0.048). The other regions showing a significant RNFL thinning as progression of age were at 1–2 (after age 41 with a rate of thinning 0.69 μm/year; 97.5% CI, 0.02 to 1.36; P = 0.044), 2–3 (after age 55 with a rate of thinning 0.29 μm/year; 97.5% CI, 0.02 to 0.57; P = 0.038), 4–5 (after age 48 with a rate of thinning 0.79 μm/year; 97.5% CI, 0.01 to 1.46; P = 0.011). The greatest rate of thinning was located at this clock-hour. The other regions showing a significant RNFL thinning as progression of age were at 1–2 (after age 41 with a rate of thinning 0.69 μm/year; 97.5% CI, 0.02 to 1.36; P = 0.044), 2–3 (after age 55 with a rate of thinning 0.29 μm/year; 97.5% CI, 0.02 to 0.57; P = 0.038), 4–5 (after age 48 with a rate of thinning 0.79 μm/year; 97.5% CI, 0.01 to 1.46; P = 0.011).

| Tour | Age (years) | Rate of thinning (μm/year) | 97.5% CI | P |
|------|-------------|-----------------------------|----------|---|
| Superior | 35          | 0.70                        | 0.16–1.25 | 0.011 |
| Nasal | 0.07        | -0.15–0.02                  | NS        |
| Inferior | 0.23       | 0.12–0.34                   | NS        |
| Temporal | 0.36       | 0.06–0.67                   | 0.020     |

Table 1. Age and biometric features of the study participants.

| Parameter | Age (years) | SEb (Diopter) | ALc (mm) |
|-----------|-------------|---------------|----------|
| OU        | 42.07 ± 13.16 | -4.64 ± 4.11 | 25.38 ± 1.73 |
| OD        | 21 – 76      | -17.50 –+4.25 | 21.19 – 30.37 |
| OS        | same         | -17.25–+4.25  | 21.19 – 29.91 |

Table 2. Age when thinning of mean and quadrant RNFL thickness was significantly different.

| Tour | Age of thinning (μm/year) | 97.5% CI | P |
|------|----------------------------|----------|---|
| Superior | 0.70      | 0.16–1.25 | 0.011 |
| Nasal | 0.07        | -0.15–0.02 | NS |
| Inferior | 0.23       | 0.12–0.34 | NS |
| Temporal | 0.36       | 0.06–0.67 | 0.020 |

aSD, standard deviation.
bSE, spherical equivalent.
cAL, axial length.

*SD, standard deviation.
*SE, spherical equivalent.
*AL, axial length.

https://doi.org/10.1371/journal.pone.0179320.t001

https://doi.org/10.1371/journal.pone.0179320.t002

https://doi.org/10.1371/journal.pone.0179320.0001

https://doi.org/10.1371/journal.pone.0179320.0002
The reduction of RNFL with ageing didn’t differ in eyes with long or short AL.

**Fig 1.** The rates of age-related RNFL thinning in different axial length groups. Linear model was applied to explore the relationship between AL and the rates of age-related RNFL thinning. (A) Short AL group with
The reduction in RNFL thickness with age was higher with longer AL as well as with advancing age, particularly after 46 years of age. The magnitude of reduction in RNFL thickness with increasing age was similar in eyes with longer or shorter AL. Meanwhile, RNFL thinning with AL and age did not occur in a uniform manner around the optic disc.

Table 3. Age when thinning of clock hour RNFL thickness was apparent.

| Clock hour | OD | Age | Rate of thinning (μm/yr) | 97.5% CI | P  | OS | Age | Rate of thinning (μm/yr) | 97.5% CI | P  |
|------------|----|-----|--------------------------|----------|----|----|-----|--------------------------|----------|----|
| 12–1       | 44 | 0.49| 0.01–0.96                | 0.044    |    |    | 38  | 0.83                     | 0.01–1.65 | 0.048|
| 1–2        | 35 | 1.89| 0.67–3.11                | 0.003    |    |    | 41  | 0.69                     | 0.02–1.36 | 0.044|
| 2–3        | -0.05| 0.26–0.14 | NS               |          |    |    | 55  | 0.29                     | 0.02–0.57 | 0.038|
| 3–4        | -0.08| 0.20–0.04 | NS               |          |    |    | 55  | 0.29                     | 0.02–0.57 | 0.038|
| 4–5        | 0.08 | 0.23–0.06 | NS               |          |    |    | 48  | 0.45                     | 0.04–0.87 | 0.034|
| 5–6        | 37  | 0.85 | 0.04–1.66               | 0.039    |    |    | 54  | 0.42                     | 0.09–0.75 | 0.014|
| 6–7        | 36  | 1.46 | 0.32–2.60               | 0.013    |    |    | 37  | 0.98                     | 0.01–1.95 | 0.047|
| 7–8        | 40  | 0.47 | 0.23–0.72               | NS       |    |    | 05  | -0.15–0.25               | NS       |    |
| 8–9        | 40  | 0.77 | 0.05–1.49               | 0.037    |    |    | 08  | -0.24–0.08               | NS       |    |
| 9–10       | 0.25| 0.09–0.40 | NS               |          |    |    | 05  | -0.17–0.07               | NS       |    |
| 10–11      | 0.31| 0.13–0.49 | NS               |          |    |    | -0.03| -0.20–0.13               | NS       |    |
| 11–12      | 39  | 0.74 | 0.11–1.37               | 0.021    |    |    | 49  | 0.45                     | 0.02–0.88 | 0.041|

https://doi.org/10.1371/journal.pone.0179320.t003
was selected for analysis) were divided by age into 4 groups: 5–20, 20–35, 35–50, and >50 years, and the authors reported that age-associated RNFL thinning was most prominent after the age of 50 years. Quigley et al. provided histological data that the RNFL thinning rate was faster after 50 years of age (approximately 2500 optic nerve fibers lost per year before the age of 50 years vs 7500 lost per year after the age of 50 years), although the authors examined only 5 human eyes[22]. The possible reasons why our results of significant age-related RNFL thinning is younger (41 years old) than the prior two studies might due to further detailed statistical analysis by each year and criteria for selecting of studied population (refractive error within ± 5 diopter of sphere and 3 Diopter cylinder by Parikh et al[16]. In clinical practice, Feuer et al. suggested that to confirm the loss of RNFL caused by glaucoma, the rate of change must be faster than the expected rate from the 95% confidence interval at a particular location[17].

In agreement with other studies, our results also showed a topographic variation in age-related RNFL thinning[13, 16, 17]. Studies have reported that the maximal rate of decay in RNFL was at the superior quadrant, whereas the inferior region appeared to be the most resistant sector to RNFL loss[16, 17]. The present study was in agreement in terms of the superior sector having had the maximal reduction of RNFL thickness, and that it was the earliest region exhibiting RNFL thinning (by the age of 35 years). The reason for a topographic difference in age-related RNFL thinning remains unknown. Jonas et al. found that age-associated axonal loss particularly affected small nerve fiber axons [20]. FitzGibbon and Taylor recently mentioned that retinal ganglion cell axons in the inferior and nasal quadrants were on average larger than those in the superior and/or temporal quadrants[23]. Additional evidence is required to confirm whether small nerve axons in the superior quadrant are more vulnerable to age-related thinning. The present study also showed aging difference on the average RNFL between both eyes. The differences between both eyes of the same individual are commonly noted in clinic, for instance, refractive error, cataract stage, intraocular pressure and blood flow. The dominant eye may consume more oxygen than another eye due to working harder and sending more visual messages to the brain. These various factors may influence the aging difference between both eyes. Further studies are needed to reconfirm and clarify the pathomechanisms.

A positive or negative correlation between the average RNFL thickness and AL measured by OCT was reported. The default AL in TOPCON 3D-OCT is 24.39 mm, and the average refractive error of Asian subjects for the normative database is -0.66 ± 1.70 D (range: -5.75 to 2.88 D). In this present study, the mean AL and refractive error is 25.36 mm and -4.68 ± 4.16 D (range: -17.5 to +4.25 D), respectively. Due to a considerable proportion of myopic eyes in our study population, the mean RNFL thickness (88.17 ± 10.61 μm) is lower than other studies on healthy Chinese eyes (107.02 μm in Hsu study and 96.04 μm in Qu study[15, 24]. As a result, to avoid over-diagnosis of glaucoma, knowledge of the effects of AL on RNFL is warranted, especially for high myopic eyes. Increased AL leading to a larger retinal surface, while with unchanged numbers of retinal ganglion cell axons could cause thinner RNFL measured by OCT related to increased AL. To date, no anatomical evidence has been presented showing that retinal ganglion cells/axons degeneration is due to the elongation of AL.

Although both age and AL factors affect the measurement of RNFL by OCT, eyes with longer AL did not show a faster rate of age-associated RNFL thinning than those with shorter AL. Another point is that the RNFL is rather thin in aged high myopic people; however, their VF results remain within normal range. Further studies of any impacts of the reduced RNFL thickness on visual functions are needed to determine.

In addition to the reduction in the average RNFL thickness in myopic eyes, a variation in the RNFL profile with increasing AL has been reported[5, 14, 15, 25]. A study included 115 eyes of 115 healthy participants (75 eyes with high myopia and 40 with low-to-moderate...
myopia), and reported that the most frequent abnormal sector of RNFL thickness was at the 2 o'clock position, which differed from our study, and thus, showed that the effect of AL on RNFL thickness was more pronounced in the inferior quadrant. In the Kim et al.'s study, of the 48 myopic patients, they reported thinner RNFL's in the higher myopia group than those in both lower and moderate myopia groups in the non-temporal quadrants; however, while in the temporal quadrant, thicker RNFL's are associated with the higher myopia group [25]. In the present study, although we did not find a significant correlation between AL and the RNFL at the temporal quadrant, the RNFL decreased with increasing AL at non-temporal quadrants. Variations in sample composition might be responsible for these discrepancies.

This study has a number of limitations, and thus, additional comprehensive research is warranted. First, the participants were recruited from a clinic; therefore, selection bias cannot be denied. Second, within the constraints of a cross-sectional design, our findings might be inaccurate in estimating the longitudinal changes of RNFL.

In conclusion, RNFL thickness measured by 3D OCT-1000 is reduced by 2.71 μm per decade with progression of age, and by 1.78 μm per 1-mm increase in AL. Decline of RNFL thickness is significantly beyond the age of 41 years. The superior quadrant shows the earliest as well as the maximal slope of age-related RNFL thinning. On the other hand, the most severely RNFL thinning with increasing AL is seen at the inferior quadrant. The rates of age-associated RNFL thinning are not different in eyes with long or short AL. Further studies are warranted to explore the reasons accounting for the regional variations of age- and AL-related decline in RNFL thickness.

Acknowledgments

This research (HcH -2-990001) was supported with the grant of National Taiwan University Hospital, Hsin Chu Branch. The IRB Number (HCGH99IRB-8) was approved by the institution Review Board of Hsin-Chu General Hospital. In line with the institutional change, Hsin Chu General Hospital of the Department of Health was renamed the Hsin-Chu Branch of National Taiwan University Hospital (NTUH) in July 2011. We appreciate Prof. Henry HS Lu for his invaluable advice and support on statistical analysis methods in this study.

Author Contributions

Conceptualization: MLK.
Data curation: MLK WSW.
Formal analysis: WSW.
Funding acquisition: MLK.
Investigation: MLK.
Methodology: SYH.
Project administration: MLK.
Resources: PHP.
Software: WSW.
Supervision: MLK.
Validation: MLK.
Visualization: MLK.
Writing – original draft: PHP.
Writing – review & editing: PHP.

References

1. Huang ML, Chen HY. Development and comparison of automated classifiers for glaucoma diagnosis using Stratus optical coherence tomography. Invest Ophthalmol Vis Sci. 2005; 46(11):4121–9. Epub 2005/10/27. https://doi.org/10.1167/iovs.05-0069 PMID: 16249489.

2. Budenz DL, Anderson DR, Varma R, Schuman J, Cantor L, Savell J, et al. Determinants of normal retinal nerve fiber layer thickness measured by Stratus OCT. Ophthalmology. 2007; 114(6):1046–52. Epub 2007/01/11. https://doi.org/10.1016/j.jophtha.2006.08.046 PMID: 17210181; PubMed Central PMCID: PMCPmc2916163.

3. Sung KR, Wollstein G, Schuman JS, Bilonick RA, Ishikawa H, Townsend KA, et al. Scan quality effect on glaucoma discrimination by glaucoma imaging devices. The British journal of ophthalmology. 2009; 93(12):1580–4. Epub 2009/08/21. https://doi.org/10.1136/bjo.2008.152223 PMID: 19692363; PubMed Central PMCID: PMCPmc2728289.

4. Gabriele ML, Ishikawa H, Wollstein G, Bilonick RA, Townsend KA, Kagemann L, et al. Optical coherence tomography scan circle location and mean retinal nerve fiber layer measurement variability. Invest Ophthalmol Vis Sci. 2008; 49(6):2315–21. Epub 2008/06/03. https://doi.org/10.1167/iovs.07-0873 PMID: 18515577; PubMed Central PMCID: PMCPmc2742764.

5. Leung CK, Mohamed S, Leung KS, Cheung CY, Chan SL, Cheng DK, et al. Retinal nerve fiber layer measurements in myopia: An optical coherence tomography study. Invest Ophthalmol Vis Sci. 2006; 47(12):5171–6. Epub 2006/11/24. https://doi.org/10.1167/iovs.06-0545 PMID: 17122099.

6. Rauscher FM, Sekhon N, Feuer WJ, Budenz DL. Myopia affects retinal nerve fiber layer measurements as determined by optical coherence tomography. J Glaucoma. 2009; 18(7):501–5. Epub 2009/09/12. https://doi.org/10.1097/IJG.0b013e318193c2be PMID: 19745664; PubMed Central PMCID: PMCPmc2728289.

7. Matsumura H, Hirai H. Prevalence of myopia and refractive changes in students from 3 to 17 years of age. Survey of ophthalmology. 1999; 44 Suppl 1:S109–15. Epub 1999/11/05. PMID: 10548123.

8. Lin LL, Shih YF, Hsiao CK, Chen CJ. Prevalence of myopia in Taiwanese schoolchildren: 1983 to 2000. Ann Acad Med Singapore. 2004; 33(1):27–33. Epub 2004/03/11. PMID: 15008558.

9. Vongphanit J, Mitchell P, Wang JJ. Population prevalence of tilted optic disks and the relationship of this sign to refractive error. Am J Ophthalmol. 2002; 133(5):679–85. Epub 2002/05/07. PMID: 11992666.

10. Melo GB, Libera RD, Barbosa AS, Pereira LM, Doi LM, Melo LA Jr. Comparison of optic disk and retinal nerve fiber layer thickness in nonglaucomatous and glaucomatous patients with high myopia. Am J Ophthalmol. 2006; 142(5):858–60. Epub 2006/10/24. https://doi.org/10.1016/j.ajo.2006.05.022 PMID: 17056370.

11. Hwang YH, Yoo C, Kim YY. Characteristics of peripapillary retinal nerve fiber layer thickness in eyes with myopic optic disc tilt and rotation. J Glaucoma. 2012; 21(6):394–400. Epub 2011/09/29. https://doi.org/10.1097/IJG.0b013e3182186567 PMID: 21946540.

12. Cheung CY, Li H, Lamoureux EL, Mitchell P, Wang JJ, Tan AG, et al. Validity of a new computer-aided diagnosis imaging program to quantify nuclear cataract from slit-lamp photographs. Invest Ophthalmol Vis Sci. 2011; 52(3):1314–9. Epub 2010/11/06. https://doi.org/10.1167/iovs.10-5427 PMID: 21051727.

13. Bendschneider D, Tornow RP, Horn FK, Laemmer R, Roessler CW, Juennemann AG, et al. Retinal nerve fiber layer thickness in normals measured by spectral domain OCT. J Glaucoma. 2010; 19(7):475–82. Epub 2010/01/07. https://doi.org/10.1097/IJG.0b013e318181c4b0c7 PMID: 20051888.

14. Kang SH, Hong SW, Im SK, Lee SH, Ahn MD. Effect of myopia on the thickness of the retinal nerve fiber layer measured by Cirrus HD optical coherence tomography. Invest Ophthalmol Vis Sci. 2010; 51(8):4075–83. Epub 2010/03/20. iovs.09-4737 [pii] https://doi.org/10.1167/iovs.09-4737 PMID: 20237247.

15. Hsu SY, Chang MS, Ko ML, Hamod T. Retinal nerve fibre layer thickness and optic nerve head size measured in high myopes by optical coherence tomography. Clinical & experimental ophthalmol. 2013; 96(4):373–8. Epub 2013/04/08. https://doi.org/10.1111/ceo.12052 PMID: 23561012.

16. Parikh RS, Parikh SR, Sekhar GC, Prabakaran S, Babu JG, Thomas R. Normal age-related decay of retinal nerve fiber layer thickness. Ophthalmology. 2007; 114(5):921–6. Epub 2007/05/01. https://doi.org/10.1016/j.jophtha.2007.01.023 PMID: 17467529.

17. Budenz DL, Anderson DR, Cantor L, Greenfield DS, Savell J, et al. Topographic differences in the age-related changes in the retinal nerve fiber layer of normal eyes measured by Stratus optical coherence tomography.
The reduction of RNFL with ageing didn’t differ in eyes with long or short AL.