KJO
pISSN: 1011-8942 eISSN: 2092-9382

Korean J Ophthalmol 2012;26(4):271-276
http://dx.doi.org/10.3341/kjo.2012.26.4.271

Original Article

# The Effect of Axial Length on the Variability of Stratus Optical Coherence Tomography

Jeong Hun Bae[1], So Young Han[1], Hyunjoong Kim[2], Joon Mo Kim[1], Ki Ho Park[3], Jung Gon Cho[4]

[1]*Department of Ophthalmology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea*
[2]*Department of Applied Statistics, Yonsei University, Seoul, Korea*
[3]*Department of Ophthalmology, Seoul National University College of Medicine, Seoul, Korea*
[4]*Yebon Eye Clinic, Seoul, Korea*

**Purpose:** To evaluate the effect of axial length on the variability of retinal nerve fiber layer (RNFL) thickness measurements using the Stratus optical coherence tomography (OCT) in normal and glaucomatous eyes.

**Methods:** We measured the RNFL thickness in 474 subjects using the Stratus OCT twice during the same day. Axial length was measured with the IOLMaster, and refractive error was the absolute value of the spherical equivalent measured with an auto ref-keratometer. Standard deviation in overall mean RNFL thickness was used as the dependent variable to identify significant correlations.

**Results:** Long axial length affected the variability in the RNFL thickness value by stratus OCT at the temporal quadrant ($p$ = 0.006) and clock-hour sector 9 ($p$ = 0.001). Refractive error also affected the variability of the RNFL thickness value by stratus OCT at the temporal quadrant ($p$ = 0.025) and clock-hour sector 9 ($p$ = 0.024).

**Conclusions:** It is clinically significant that longer axial length demonstrates greater variability in temporal area as detected by OCT, a measurement which correlates with the preferably damaged position in the myopic glaucoma eye.

**Key Words:** Axial eye length, Glaucoma, Optical coherence tomography, Variability

Glaucoma is an optic neuropathy characterized by progressive injury to the optic nerve and retinal nerve fiber. Since injury due to glaucoma is largely irreversible, early detection and prevention of glaucomatous damage is critical. Examination of the optic nerve head and retinal nerve fiber layer (RNFL), as well as the visual field test, are considered essential for detecting glaucoma. Optical coherence tomography (OCT) allows for cross-sectional imaging and quantitative analysis of the peripapillary RNFL thickness, which may be useful in detecting patients with glaucoma. Within the last several years, OCT has become an important tool contributing to earlier and more accurate diagnosis of glaucoma. Currently, OCT is the most common monitoring modality, while spectral domain OCT (SD OCT) is an emerging technology. Considering the price and compatibility of OCT data with that of SD OCT, OCT is expected to be used commonly in the near future [1].

In East Asian countries, the prevalence of myopia is high, with increases in the number of new cases and the severity of the condition [2,3]. The association between myopia and glaucoma is well recognized, and there is an increased prevalence of myopia in patients with ocular hypertension, primary open-angle glaucoma, and normal-tension glaucoma [4-10]. However, optic disc appearances in myopic patients are often difficult to interpret and may mask early glaucomatous damage. Few studies have used RNFL photography in myopic eyes. This may be due to the fact that accurate RNFL measurements can be obscured by relatively small amounts of pigment in the retinal pigment epithelium in patients with myopia. The visual field test also has limitations in detecting glaucoma; it is less sensitive for early glaucoma, and abnormal results occur frequently in patients with high myopia due to myopic

*Received*: June 20, 2011 *Accepted*: September 2, 2011

Corresponding Author: Joon Mo Kim, MD. Department of Ophthalmology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, #29 Saemunan-ro, Jongno-gu, Seoul 110-746, Korea. Tel: 82-2-2001-2257, Fax: 82-2-2001-2262, E-mail: kjoonmo@dreamwiz.com

degeneration. OCT is commonly used to measure RNFL thickness in a non-invasive manner; therefore, concern has been raised regarding the accuracy and reliability of OCT in myopic eyes. Despite this, OCT is rarely revised by measuring axial length in myopic patients, though it is not clear how this may influence clinical diagnosis. Previous studies in myopic patients have focused on peripapillary RNFL thickness distribution with OCT. The results have been conflicting; in some studies, the degree of myopia was correlated with the mean RNFL thickness measurements [11,12]. On the other hand, some studies have found that there is no significant correlation between level of myopia or axial length and RNFL thickness measurement [13]. In this present study, we investigated the effects of refractive error and axial length on the variability of stratus OCT measurements.

## Materials and Methods

Subjects were recruited from the outpatient glaucoma service of the Department of Ophthalmology, Kangbuk Samsung Hospital. This prospective study looked at 668 eyes in 668 participants. Informed consent was obtained from each subject. This study was performed after approval from the institutional review board and ethics committee of the Kangbuk Samsung Hospital in Seoul, Korea.

All subjects underwent a full medical and ocular history and a detailed ocular examination including measurements of visual acuity, intraocular pressure using the Goldman applanation tonometer, and slit lamp and fundus examinations. Axial length was measured using the IOLMaster (Carl Zeiss Meditec, Dublin, CA, USA) as the mean of three measurements. Refractive error was defined as the absolute value of the spherical equivalent measured with an auto ref-keratometer (RK-F1; Canon, Tokyo, Japan).

Normal participants were included if they had a bilateral highest documented intraocular pressure of 20 mmHg, bilateral normal eye examination findings (including those from dilated fundus examinations), and bilateral normal visual field results, defined as pattern standard deviation within 95% of normal limits and a glaucoma hemi-field test result within 99% of normal limits. Subjects with glaucoma included those with diagnosis of open angle glaucoma, defined as optic disc abnormalities consistent with glaucomatous optic neuropathy with or without visual field loss. Other inclusion criteria for both normal and glaucomatous subjects were age of 18 years or older, best-corrected visual acuity of 20 / 40 or better, no history of ocular or neurologic disease or surgery that may produce test results or visual changes that might confound recognition of a test result due solely to glaucoma, and no history of amblyopia.

### Optical coherence tomography technique

Subjects were scanned twice with a Stratus OCT (software ver. 4.0.1, Carl Zeiss Meditec) during the same day with short breaks between each measurement. The OCT scan was performed by a single technician through a dilated pupil. Fast RNFL thickness protocols were performed with internal fixation. The operator applied artificial tears (Hyalein; Santen Pharmaceuticals, Osaka, Japan) before the subsequent scan.

The selected fundus image was sufficiently visible to distinguish the optic disc and the scanning circle. Images with poor scan quality, decentration, poor focus, low analysis confidence, or low signal strength (less than 6) were excluded. For subjects who had both eyes scanned, one eye was randomly chosen for analysis. The analysis algorithm reported 17 RNFL thickness values: mean RNFL thickness around the entire circumference, average thickness within the four quadrants (temporal, superior, nasal, and inferior), and average thickness in each of 12 clock-hour sectors provided, where clock-hours one to five represented the nasal clock hours and clock-hours seven to 12 represented the temporal ones. Left optic disc areas were considered to be mirror images of the right ones. In all tables, the measured areas of the nasal region were named clockwise from 12 to 6, and those of the temporal region from 6 to 12.

We used standard deviation (SD) to determine the reproducibility of RNFL thickness. The SD is a measure of the variability of a data set or a probability distribution. Each patient's SD values were based on two measurements of RNFL thickness. A low SD indicated that the data points tended to be very close to the same value, while a high SD indicated that the data were spread out over a large range of values. We analyzed the reliability between measurements using the intraclass correlation coefficient (ICC), a ICC is commonly used statistic for assessing the reliability between two or more quantitative measures or ratings using the ratio of the intrasubject components of the variance (the sum of intravisit variance components referred to as the intrasubject standard deviation) to the total variance.

**Table 1.** Demographic and ophthalmic characteristics of the study participants

| | Normal (103) | Glaucoma (371) |
|---|---|---|
| Mean age (yr) | 58.77 ± 10.53 (34-77) | 58.83 ± 12.04 (25-87) |
| Sex (male / female) | 59 / 53 | 189 / 181 |
| SE mean (diopters) | -0.92 ± 2.16 | -1.00 ± 2.54 |
| AL mean (mm) | 23.99 ± 1.25 | 24.65 ± 1.85 |
| Average RNFL thickness (μm) | 95.77 ± 11.21 | 76.32 ± 17.37 |

SE = spherical equivalent; AL = axial length; RNFL = retinal nerve fiber layer.

We analyzed the correlation between parameters using SPSS ver. 17.0 (SPSS Inc., Chicago, IL, USA).

## Results

Six hundred sixty-eight subjects were initially enrolled in the study. We excluded 184 subjects because of poor quality analysis (signal strength [SS] <6, low analysis confidence, or a difference between two SS figures) in one of the metrics. We included a group of 474 subjects comprised of 103 normal subjects and 371 glaucoma patients in the final analysis. Participant demographic and ophthalmic characteristics are shown in Table 1. ICC and coefficients of variation of all 474 subjects are shown in Table 2. Correlations between variability (SD) in overall mean RNFL, quadrant RNFL, clock-hour RNFL, and spherical equivalent (SE) are shown in Table 3. Significant correlations were found between the SD in RNFL thickness in the temporal quadrant and SE. Significant correlations were also observed between the SD in RNFL thickness at clock-hour 9 and SE. The statistically significant variable portions (temporal area, clock-hour 9) were plotted against SE (Fig. 1).

Correlations between the variability (SD) in overall mean RNFL, quadrant RNFL, clock-hour RNFL, and axial length (AL) are shown in Table 3. Significant correlations were observed between the SD in RNFL thickness in the temporal quadrant and AL. Significant correlations were observed between the SD in RNFL thickness at clock-hour nine and AL. The statistically significant variable portions (temporal area, clock-hour 9) were plotted against AL (Fig. 2).

**Table 2.** ICC and CV for all 474 subjects

| Location of RNFL | ICC (lower 95% CI) | CV (%) |
|---|---|---|
| Overall mean | 0.989 (0.987) | 2.3 |
| Temporal quadrant | 0.968 (0.962) | 4.8 |
| Superior quadrant | 0.977 (0.973) | 4.0 |
| Nasal quadrant | 0.910 (0.893) | 6.7 |
| Inferior quadrant | 0.987 (0.985) | 3.5 |
| Clock-hour 1 | 0.951 (0.942) | 6.1 |
| Clock-hour 2 | 0.907 (0.889) | 8.2 |
| Clock-hour 3 | 0.854 (0.828) | 9.6 |
| Clock-hour 4 | 0.886 (0.865) | 8.3 |
| Clock-hour 5 | 0.958 (0.950) | 5.7 |
| Clock-hour 6 | 0.979 (0.974) | 5.1 |
| Clock-hour 7 | 0.982 (0.978) | 5.4 |
| Clock-hour 8 | 0.956 (0.947) | 6.7 |
| Clock-hour 9 | 0.944 (0.933) | 6.3 |
| Clock-hour 10 | 0.969 (0.963) | 5.4 |
| Clock-hour 11 | 0.972 (0.967) | 5.3 |
| Clock-hour 12 | 0.966 (0.960) | 5.5 |

ICC = intraclass correlation coefficient; CV = coefficients of variation; RNFL = retinal nerve fiber layer; CI = confidence interval.

## Discussion

Myopia is one of the greatest risk factors for glaucoma. Myopic eyes have a 2- to 3-fold greater risk of developing glaucoma than emmetropic eyes. This increased risk is

**Table 3.** Reproducibility correlations with SE, AL and clock-hour measurements

| Location of RNFL | SE in RNFL thickness | | | AL in RNFL thickness | | |
|---|---|---|---|---|---|---|
| | Regression | $r^2$ | Coefficient | Regression | $r^2$ | Coefficient |
| Overall mean | 0.025 | 0.011 | 0.069 | 0.046 | 0.011 | -0.122 |
| Temporal quadrant | 0.026 | 0.011 | -0.125 | 0.006 | 0.022 | 0.288 |
| Superior quadrant | 0.648 | 0 | 0.029 | 0.581 | 0.001 | -0.069 |
| Nasal quadrant | 0.823 | 0 | 0.017 | 0.534 | 0.001 | 0.093 |
| Inferior quadrant | 0.276 | 0.003 | 0.065 | 0.184 | 0.005 | -0.15 |
| Clock-hour 1 | 0.876 | 0 | -0.015 | 0.485 | 0.001 | 0.125 |
| Clock-hour 2 | 0.09 | 0.006 | 0.181 | 0.451 | 0.002 | -0.157 |
| Clock-hour 3 | 0.819 | 0 | -0.023 | 0.464 | 0.002 | 0.137 |
| Clock-hour 4 | 0.352 | 0.002 | -0.09 | 0.236 | 0.004 | 0.223 |
| Clock-hour 5 | 0.942 | 0 | 0.006 | 0.629 | 0.001 | 0.08 |
| Clock-hour 6 | 0.3 | 0.002 | 0.098 | 0.384 | 0.002 | -0.154 |
| Clock-hour 7 | 0.623 | 0.001 | -0.048 | 0.677 | 0 | -0.078 |
| Clock-hour 8 | 0.19 | 0.004 | -0.102 | 0.077 | 0.009 | 0.267 |
| Clock-hour 9 | 0.011 | 0.014 | -0.161 | 0.001 | 0.032 | 0.405 |
| Clock-hour 10 | 0.389 | 0.002 | -0.059 | 0.837 | 0 | 0.026 |
| Clock-hour 11 | 0.912 | 0 | 0.01 | 0.2 | 0.005 | -0.223 |
| Clock-hour 12 | 0.187 | 0.004 | 0.119 | 0.194 | 0.005 | -0.23 |

SE = spherical equivalent; AL = axial length; RNFL = retinal nerve fiber layer.

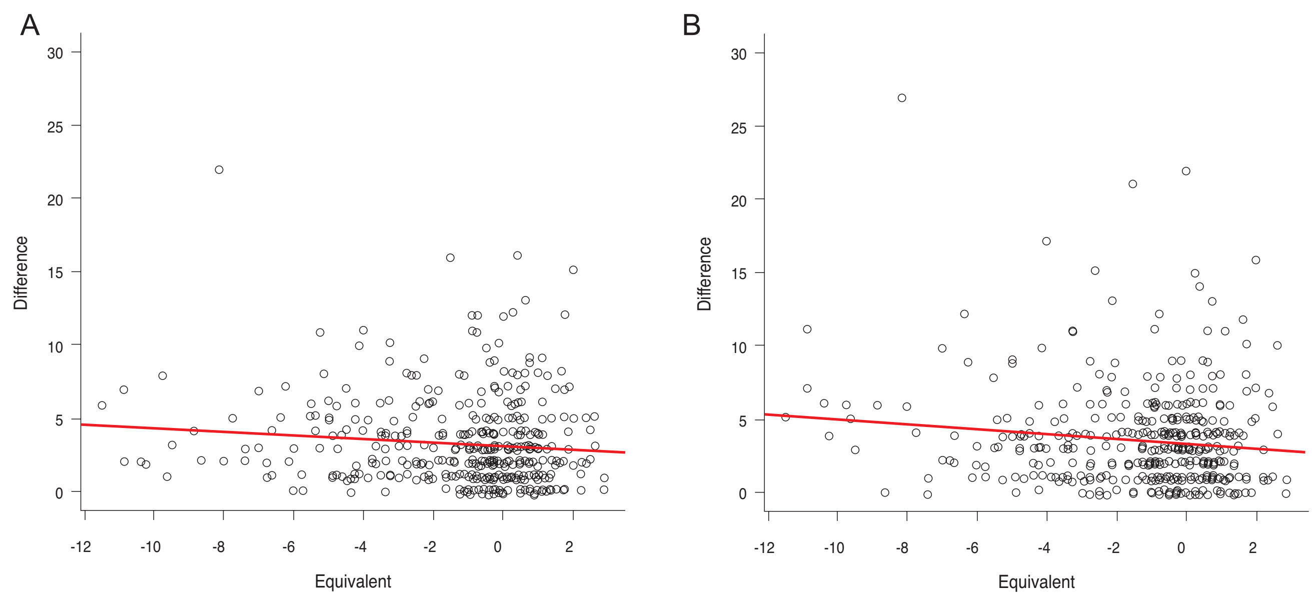


**Fig. 1.** Plot diagrams of temporal (A) and clock-hour 9 (B) with spherical equivalent. Positive correlations between the standard deviation in retinal nerve fiber layer thickness at clock-hour 9 and spherical equivalent.

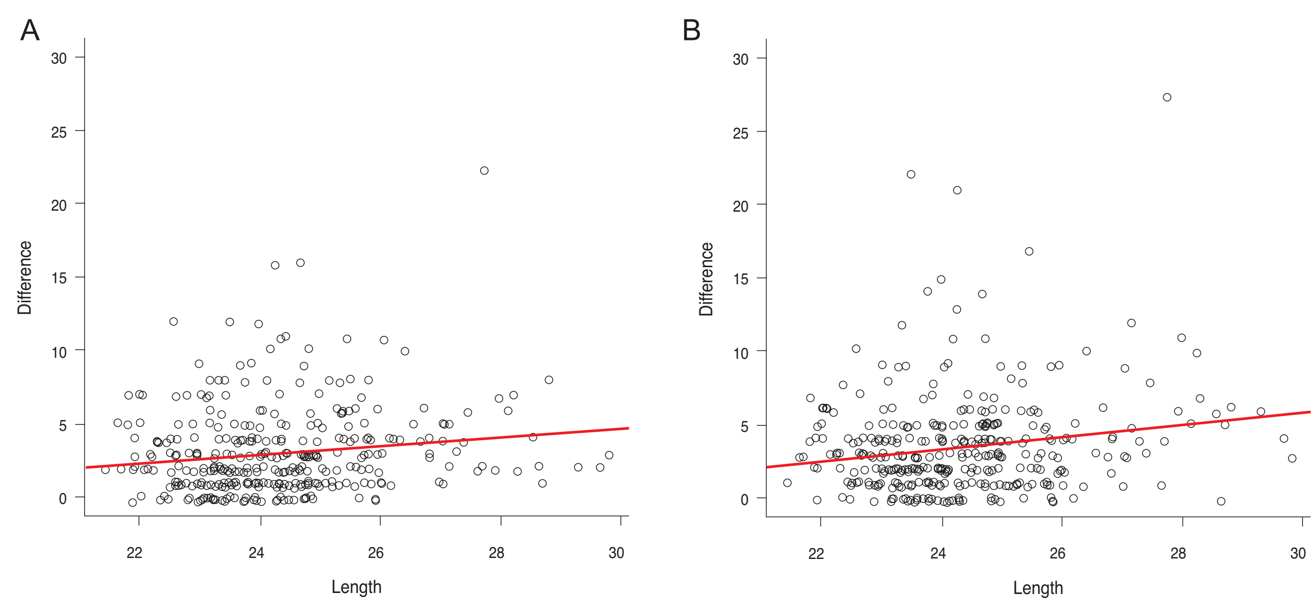


**Fig. 2.** Plot diagrams of temporal (A) and clock-hour 9 (B) with axial length. Positive correlations were observed between the standard deviation in retinal nerve fiber layer thickness at clock-hour 9 and axial length.

independent of other risk factors such as high intraocular pressure [13]. Currently, the number of young myopic adults is increasing, with fundus examination for refractive surgery or routine check-up allowing for early detection of glaucoma. In high myopia, RNFL thinning appears to occur, and the higher visual field indicates deviation compared with emmetropia. The optic discs seen in myopic patients may appear large, with greater cut-to-disc ratios than emmetropic patients [11]. Also, in myopic patients, myopic visual field defects interfere with the diagnosis of glaucoma by visual field tests. These similarities can complicate the diagnosis and monitoring of glaucoma in myopic eyes. Imaging modalities such as OCT may be effective in these cases.

Our results may be an important finding as the correlation of axial length and refractive error has an influence on the temporal area. Previous studies [14,15] have found that variability increases in the nasal area, while some have reported temporal peripapillary RNFL remains unaffected by increasing myopia [11]. Clinically, the nasal area of the optic disc is not significant in glaucoma. Conversely, the temporal side is of considerable importance in the progression of the disease and in identifying subjective symptoms. In the early- to moderately-advanced stages of open angle glaucoma, myopia is positively associated with changes in the cecocentral visual field [16-18]. Large variability in the temporal area, especially at clock-hour nine, is an important concern. Several studies have demonstrated that RNFL thickness may vary with the refractive status [11,13]. While some investigators hold that the average RNFL thickness decreases with negative refractive power and increasing axial length [11], others assert that the mean peripapillary RNFL thickness does not vary with myopic SE or axial length [13]. In our previous study, an increase in the axial length of Korean patients was correlated with thin RNFL thickness [19]. Also, in our present study, we demonstrated a positive correlation between refractive error and the variability of the temporal side (Table 2), which is a similar to results obtained in other studies.

Various factors can impair the efficacy of the OCT and result in poor-quality scans, thus greatly affecting the accuracy of the measurements [20-22]. In this study, we obtained repeated measurements of RNFL thickness using the Stratus OCT with the same operator on the same day. We believe that this is the most useful method to maximize the reproducibility of OCT, as it lowers the coefficient of variation to confirm accuracy of the variability of the value of RNFL thickness.

Similar to the results in this study, Budenz et al. [14] reported that the nasal quadrant appears to have the lowest reproducibility, which translates into the highest variability. The cases with long axial lengths also demonstrated the poorest reproducibility in the nasal segment. However, the temporal quadrant is an important area in glaucoma, so one should take care in analyzing this area in the highly myopic eye where variability increases with axial length, though it demonstrates the highest reproducibility in the normal eye.

The default value of axial length in OCT scanning is 24.46 mm, and the scanning radius for the fast/standard RNFL scanning protocol is fixed at 1.7 mm. Therefore, the real scanning radius in a myopic eye may be longer than 1.7 mm due to the magnification effect. This may be one of the causes of variability in the myopic eye. Also, the scanning procedure is based on the assumption that the optic disc exists in one plane; this may be other contributing factors as the eyeball is a roughly spherical three-dimensional shape. Abnormal disc figure or size by myopic stretching may influence variability; however, the exact reasons for this variability are not known.

In summary, AL variation produces a significant difference in the temporal area and average RNFL thickness. There was a positive correlation between axial length and the variability of the temporal area. This finding indicates that clinicians should consider the temporal quadrant variability in a high myopic patient, even if another RNFL thickness portion shows a stationary state. Variability is very important as it is an essential factor for detecting the progression of glaucoma and may lead to false-positive or false-negative results. It is clinically significant that myopia and advanced myopia demonstrate greater variability in the temporal area as detected by OCT, especially at the clock-hour 9 position, which correlates with the cecocentral visual field. Therefore, myopia should be considered when interpreting OCT scans of RNFL thickness, especially in the temporal area, in order to avoid misdiagnosis.

## Conflict of Interest

No potential conflict of interest relevant to this article was reported.

## Acknowledgements

This study was supported by Medical Research Funds from Kangbuk Samsung Hospital.

## References


1. Vizzeri G, Weinreb RN, Gonzalez-Garcia AO, et al. Agreement between spectral-domain and time-domain OCT for measuring RNFL thickness. *Br J Ophthalmol* 2009;93:775-81.
2. Seet B, Wong TY, Tan DT, et al. Myopia in Singapore: taking a public health approach. *Br J Ophthalmol* 2001;85:521-6.
3. Lin LL, Shih YF, Hsiao CK, et al. Epidemiologic study of the prevalence and severity of myopia among schoolchildren in Taiwan in 2000. *J Formos Med Assoc* 2001;100:684-91.
4. Suzuki Y, Iwase A, Araie M, et al. Risk factors for open-angle glaucoma in a Japanese population: the Tajimi Study. *Ophthalmology* 2006;113:1613-7.
5. Perkins ES, Phelps CD. Open angle glaucoma, ocular hypertension, low-tension glaucoma, and refraction. *Arch Ophthalmol* 1982;100:1464-7.
6. Grodum K, Heijl A, Bengtsson B. Refractive error and glaucoma. *Acta Ophthalmol Scand* 2001;79:560-6.
7. Fong DS, Epstein DL, Allingham RR. Glaucoma and myopia: are they related? *Int Ophthalmol Clin* 1990;30:215-8.
8. Seddon JM, Schwartz B, Flowerdew G. Case-control study of ocular hypertension. *Arch Ophthalmol* 1983;101:891-4.
9. Leung CK, Chan WM, Yung WH, et al. Comparison of macular and peripapillary measurements for the detection of glaucoma: an optical coherence tomography study. *Ophthalmology* 2005;112:391-400.
10. Hoffmann EM, Medeiros FA, Sample PA, et al. Relationship between patterns of visual field loss and retinal nerve fiber layer thickness measurements. *Am J Ophthalmol*

2006;141:463-71.
11. Leung CK, Mohamed S, Leung KS, et al. Retinal nerve fiber layer measurements in myopia: an optical coherence tomography study. *Invest Ophthalmol Vis Sci* 2006;47:5171-6.
12. Choi SW, Lee SJ. Thickness changes in the fovea and peripapillary retinal nerve fiber layer depend on the degree of myopia. *Korean J Ophthalmol* 2006;20:215-9.
13. Hoh ST, Lim MC, Seah SK, et al. Peripapillary retinal nerve fiber layer thickness variations with myopia. *Ophthalmology* 2006;113:773-7.
14. Budenz DL, Chang RT, Huang X, et al. Reproducibility of retinal nerve fiber thickness measurements using the stratus OCT in normal and glaucomatous eyes. *Invest Ophthalmol Vis Sci* 2005;46:2440-3.
15. Budenz DL, Fredette MJ, Feuer WJ, Anderson DR. Reproducibility of peripapillary retinal nerve fiber thickness measurements with stratus OCT in glaucomatous eyes. *Ophthalmology* 2008;115:661-6.e4.
16. Mayama C, Suzuki Y, Araie M, et al. Myopia and advanced-stage open-angle glaucoma. *Ophthalmology* 2002;109:2072-7.
17. Araie M, Arai M, Koseki N, Suzuki Y. Influence of myopic refraction on visual field defects in normal tension and primary open angle glaucoma. *Jpn J Ophthalmol* 1995;39:60-4.
18. Greve EL, Furuno F. Myopia and glaucoma. *Albrecht Von Graefes Arch Klin Exp Ophthalmol* 1980;213:33-41.
19. Park SH, Park KH, Kim JM, Choi CY. Relation between axial length and ocular parameters. *Ophthalmologica* 2010;224:188-93.
20. Ray R, Stinnett SS, Jaffe GJ. Evaluation of image artifact produced by optical coherence tomography of retinal pathology. *Am J Ophthalmol* 2005;139:18-29.
21. El-Ashry M, Appaswamy S, Deokule S, Pagliarini S. The effect of phacoemulsification cataract surgery on the measurement of retinal nerve fiber layer thickness using optical coherence tomography. *Curr Eye Res* 2006;31:409-13.
22. Youm DJ, Kim JM, Park KH, Choi CY. The effect of soft contact lenses during the measurement of retinal nerve fiber layer thickness using optical coherence tomography. *Curr Eye Res* 2009;34:78-83.