Effect of Pupil Size on the Measurements Obtained by Optical Coherence Thomography in Children

Çocuklarda Pupil Büyüklüğünün Optik Koherens Tomografi ile Elde Edilen Ölçümlere Etkisi

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ABSTARCT

Purpose: To evaluate the effect of pupil size on macular and RNFL thickness, and optic disc measurements obtained by Stratus OCT in healthy preschoolers.

Material and Methods: One hundred and eleven healthy children aged between 3 and 6 years were examined in this study. The children were measured by optical coherence thomography (OCT) before and after pupil dilation for macula and RNFL thickness, and optic disc parameters. The pupil sizes of the children were determined by the Scheimpflug camera before and after pupil dilation. The measurements taken before and after pupil dilation were compared statistically.

Results: One hundred and forty seven eyes of ninety four children were included in our study. The mean age of the children was 58.56±11.24 months (range: 34-78 months). The pupil size of the children before and after dilation was 2.76±0.50 mm (range: 1.5 mm- 4.57 mm) and 7.27±1.02 mm (range: 3.08 mm- 9.70 mm), respectively. There was a statistically significant difference between the values obtained before and after pupil dilation in the nasal inner, superior inner, and nasal outer macular segments (p<0.001; p<0.001 and p=0.046, respectively). The values before dilation were significantly different from those after dilation in the parameters of cup area, cup area/disc area ratio, vertical cup/disc ratio, and signal strength of optic disc scan (p=0.034; p= 0.036; p=0.005 and p=0.001, respectively). There was no statistically significant difference between the values before and after pupil dilation for all RNFL parameters.

Conclusion: In preschoolers, pupil size may partially affect the measurements of the macula and optic disc obtained by OCT-3 whereas the RNFL measurements are not influenced by pupil size.

Key Words: Optical coherence tomography, pupil size, children.

ÖZ

Amaç: Okul öncesi yaş grubundaki sağlıklı çocuklarda pupil büyüklüğünün; Stratus OKT ile elde edilen makula, RSLT kalınlık ve optik disk ölçümlerine etkisini incelemek.

Gereç ve Yöntem: Çalışmada, yaşları 3 ile 6 arasında değişen 111 sağlıklı çocuk incelendi. Çocuklar, dilatasyon öncesi ve sonrası makula, RSLT kalınlığı ve optik disk parametreleri için OKT ile ölçüldü. Çocukların pupil boyutları, Scheimpflug kamera ile dilatasyon öncesi ve sonrasında belirlendi. Pupil dilatasyonu öncesi ve sonrasında elde edilen veriler istatistiksel olarak karşılaştırıldı.

Bulgular: Çalışmamıza 94 çocuğun 147 gözü dahil edildi. Çocukların ortalama yaşı 58.56±11.24 ay (aralık:34-78 ay). Çocukların dilatasyon öncesi ve sonrası pupil çapı sırasıyla 2.76±0.50 mm (aralık:1.5 mm-4.57 mm) ve 7.27±1.02 mm (aralık:3.08 mm-9.70 mm) idi. Pupil dilatasyonu öncesi ve sonrası elde edilen ölçüm değerleri arasında istatistiksel olarak anlamlı farklılık sadece nazal-iç, superior-iç ve nazal-dış makula segmentlerinde elde edildi (sırasıyla, p<0.001; p<0.001 ve p=0.046). Dilatasyon öncesi elde edilen cup alanı, cup alanı/disk alanı oranı, vertikal cup/disk alan oranı ve optik disk sinyal gücü parametre değerleri, dilatasyon sonrası elde edilen değerlerden belirgin olarak farklıdır (sırasıyla, p=0.034; p=0.036; p=0.005 ve p=0.001). Tüm RSLT kalınlık parametrelerinin dilatasyon öncesi ve sonrası elde edilen değerleri arasında istatistiksel olarak anlamlı bir fark tespit edilmedi.

Sonuç: Okul öncesi yaş grubundaki çocuklarda pupil büyüklüğü, OKT-3 ile elde edilen makula ve optik disk ölçümlerini kısmen etkilerken; RSLT ölçümleri pupil boyutlarından etkilenmemektedir.

Anahtar Kelimeler: Optik koherens tomografi, pupil boyutu, çocuk.

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INTRODUCTION

Optical coherence tomography (OCT) is a widely used clinical device for the diagnosis and monitorization of several macular and optic nerve diseases.[1] OCT is a non-contact, rapid, and non-invasive imaging method, and it provides reliable and reproducible quantitative data obtained from the macula and optic disc; topographic or cross sectional images can also be created for the clinical evaluation.[2] Hence, it is ideally suitable for imaging in the pediatric population.[3]

A number of studies have used OCT for measurement in children and it has been shown to be a helpful tool for imaging some retinal and optic nerve disease in children such as macular hole[4] and edema,[5] foveal hypoplasia,[6] retinopathy of prematurity,[7] retinoschisis,[8] retinitis pigmentosa and related disease,[9] some intraocular tumors,[10-13] ocular infections and inflammations,[14-16] hereditary vitreoretinal syndromes,[17] glaucoma,[18,19] optic disc swelling,[20] optic atrophy,[21] and congenital optic disc abnormalities.[22]

Recently, Fourier (spectral) domain OCT (FD-OCT) has been introduced for clinical practice and it improves the image resolution of the retina and shortens the duration of scanning.[23] However, Stratus OCT, the latest version of time domain OCT (TD-OCT), is cost effective and technically mature; nonetheless, Stratus OCT is widely used type of OCT in the clinics of many developing countries and even in some clinics of developed countries.[24]

While scanning with Fourier (spectral) domain OCT, pupil dilation may not be necessary, but dilation is usually performed as general rule before the scanning for time-domain OCT. Although it was found that axial resolution was not impaired when scanning with TD-OCT through a non-dilated or poor dilated pupil,[25] the optic plane is affected and the imaging area get narrowed.[26] There are a few studies evaluating the effects of pupil dilation on the measurements of OCT.[26-30] These studies were generally performed in adults and controversy remains regarding the effect of pupil dilation on the measurements obtained by TD-OCT.

In our study, we evaluated the influence of pupil dilation on the measurements of the macula, retinal nerve fiber layer (RNFL), and optic disc obtained by Stratus OCT in preschool age children.

MATERIAL AND METHODS

One hundred eleven healthy children aged between 3 and 6, who were brought to our clinic for their routine eye examination by their parents between January 2011 and March 2011 were evaluated in the study.

All parents were informed that all the measurements would be performed for investigative purposes only and written informed consent was obtained from both parents of all the children. The study was approved by the Human Research Ethics Committee and it was conducted in accordance with the tenets of the Declaration of Helsinki.

After taking a broad history and birth properties of these children from their parents, we performed a whole ophthalmologic examination including autorefractometry (using the Topcon KR-3500 autokeratorefractometer, Tokio, Japan before and after pupil dilation), visual acuity test, digital intraocular pressure measurement, slit-lamp biomicroscopy, and funduscopy in all subjects.

Inclusion criteria in our study were: Age between 3 and 6 years; no history of systemic or ocular disease and no history of previous ocular surgery, no medicine intake, no retinal or optic disc abnormalities on fundoscopy, a cup\disc ratio under 0.4.

The children, who were assumed to be systemically and ophthalmologically 'healthy', were scanned with the Stratus OCT (Stratus OCT, Version 4.0.5 (0076), Carl Zeiss Meditech, Dublin, CA, USA) at least once by the same technician for each measurement of macular, retinal nerve fiber layer and optic disc parameters. Cycloplegia was carried out by cyclopentolate (Sikloplejin, Cyclopentolate 1%, Abdi İbrahim, Turkey) for both eyes of all children.

OCT scanning was performed before and after cycloplegia for all children. When taking measurements of the macula, we used the parameters of 'Fast Macular Thickness Map' including macular volume, and the thicknesses of the fovea, central macula, and inner and outer macular segments (superior, inferior, nasal, and temporal segments).

For the measurements of the retinal nerve fiber layer, we used the parameters of 'Fast RNFL Thickness (3.4)' including superior, temporal, inferior, nasal, and average RNFL thicknesses; and for the optic disc, the parameters of 'Fast Optic Disc' including disc area (DA), rim area (RA), cup area (CA), cup/disc area ratio (C/D-A), horizontal cup/disc ratio (C/D-H) and vertical cup/disc ratio (C/D-V) were used.

The scans obtained by OCT before and after pupil dilation, which had a signal strength of at least 5, were accepted as reliable and included in the study. For the pupil diameter, all eyes were measured before and after pupil dilation by the Galilei Dual-Scheimpflug Analyzer (Ziemer Ophthalmic Systems AG, Port, Switzerland) at a room with dimmed light in which OCT scans were performed in order to obtain similar illumination.

Table 1: Comparison of the macular measurements before and after dilation is shown.

Macular Parameters	Before Dilation (Mean±SD)	After Dilation (Mean±SD)	P
Macular Volume (mm^3)	6.81±0.35 (5.77- 7.72)	6.80±0.38 (5.05-7.67)	0.985
Foveal (µm)	146.08±23.80 (109- 228)	149.78±27.36 (107-255)	0.340
Central (µm)	178.64±19.20 (131- 239)	181.22±20.72 (131-252)	0.134
Superior Inner (µm)	269.26±13.47 (221- 301)	267.60±15.48 (203–297)	0.48
Temporal Inner (µm)	252.85±13.11 (219- 280)	251.96±15.06 (178-283)	0.845
Inferior Inner (µm)	258.75±13.72 (218- 288)	259.12±16.18 (195-289)	0.83
Nasal Inner (µm)	258.43±16.27 (195- 292)	260.33±17.93 (171-292)	<0.001
Superior Outer (µm)	236.44±13.19 (206- 270)	234.15±14.38 (188-268)	<0.001
Temporal Outer (µm)	221.33±12.85 (188- 253)	221.57±14.78 (152-259)	0.219
Inferior Outer (µm)	234.61±14.64 (199- 274)	235.81±15.92 (179-281)	0.062
Nasal Outer (µm)	256.49±14.85 (218- 299)	254.64±16.78 (158-294)	0.046
Signal Strength	7.14±1.21 (5- 10)	7.27±1.22 (5-10)	0.272

**Wilcoxon Signed Rank Test, **Mean±SD: Mean±Standard Deviation.*

Statistical Analysis

The data about the demographic properties of the children and the measurements taken before and after the pupil dilation were recorded and statistical analysis was performed by SPSS 16 (SPSS Inc, Chicago, Illinois, USA) for Windows and MedCalc version 11.2. All values were analyzed by the Kolmogorov-Smirnov test for the distribution of the measurements. The values displayed non-parametric distribution, and the Wilcoxon Signed Rank test and Spearman correlation test were therefore used to evaluate the comparison and correlation of the measurements obtained before and after the pupil dilation. For the statistical tests, a P-value of less than 0.05 indicated statistical significance. The agreement between the measurements of RNFL thicknesses measured before and after pupil dilation was also investigated by the Bland-Altman and Mountain plot.

RESULTS

One hundred and forty seven eyes of ninety four healthy children were included in the study. 50 of the subjects were male and the rest of them (n=44) were female. The mean age of the children was 58.56±11.24 months (range: 34-78 months).

Seventeen children were excluded from the study because they were not compatible for OCT scanning after pupil dilation. The mean diameter of the pupil before and after the dilation was 2.76±0.50 mm (range: 1.5 mm-4.57 mm) and 7.27±1.02 mm (range: 3.08 mm-9.70 mm), respectively.

There were statistically significant differences between the values before and those after dilation in only three parameters of the macula. These were the nasal inner, superior inner, and nasal outer macular segments ($p<0.001$; $p<0.001$ and $p=0.046$, respectively).

Table 2: Comparison of the optic disc measurements before and after dilation is shown.

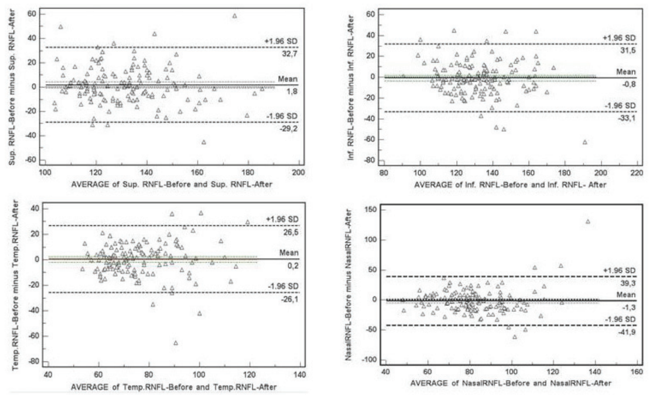
Optic Disc Parameters	Before Dilation (Mean±SD)	After Dilation (Mean±SD)	P
Disc Area (mm^2)	2.66±0.54 (1.59-4.50)	2.63±0.53 (1.68-4.19)	0.504
Cup Area (mm^2)	0.41±0.30 (0-1.66)	0.39±0.29 (0-2.00)	0.034
Rim Area (mm^2)	2.25±0.62 (0.84-4.50)	2.25±0.60 (1.08-3.86)	0.965
Cup Area/Disc Area Ratio	0.16±0.11 (0-0.56)	0.15±0.10 (0-0.46)	0.036
Horizontal Cup/Disc Ratio	0.38±0.19 (0-0.79)	0.38±0.18 (0-0.82)	0.352
Vertical Cup/Disc Ratio	0.33±0.17 (0-0.79)	0.32±0.15 (0-0.66)	0.005
Signal Strength	7.78±1.26 (5-10)	8.23±1.28 (5-10)	0.001

**Wilcoxon Signed Rank Test, **Mean±SD: Mean±Standard Deviation.*

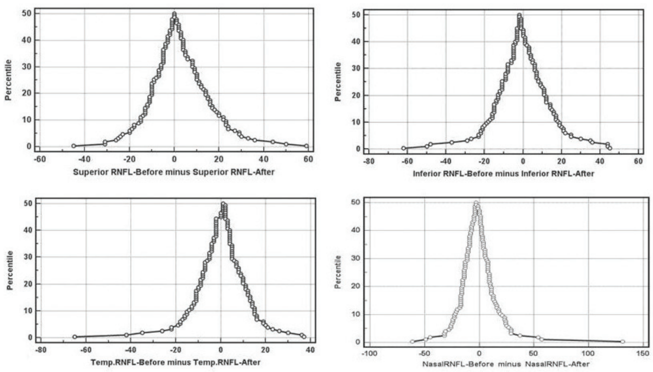
Table 3: *Comparison of the RNFL measurements before and after dilation is shown.*

RNFL Thicknesses	Before Dilation (Mean±SD)	After Dilation (Mean±SD)	P
Avg-RNFL (µm)	105.58±11.12 (85.57-148.91)	105.43±11.58 (82.30-146.62)	0.728
Superior RNFL (µm)	132.62±17.86 (95-204)	130.99±19.19 (81-191)	0.485
Inferior RNFL (µm)	132.00±18.34 (91-186)	132.27±20.22 (82-222)	0.480
Temporal RNFL (µm)	76.02±15.19 (50-134)	75.97±14.98 (48-123)	0.576
Nasal RNFL (µm)	81.70±19.59 (40-202)	82.74±17.85 (48-132)	0.100
Signal Strength	7.96±1.33 (5-10)	8.23±1.45 (5-10)	0.104

Wilcoxon Signed Rank Test, **Avg.: Average, * Mean± SD: Mean±Standard Deviation.*

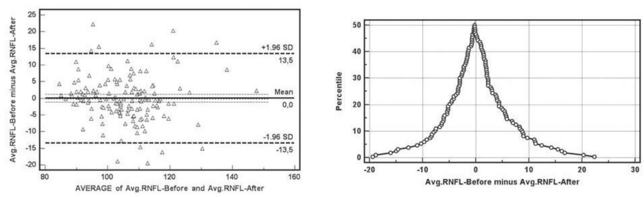


Graphic 1: *In a Bland-Altman plot, the distributions of the differences (RNFL-Before minus RNFL-After) between the measurements of superior, inferior, temporal, and nasal RNFL before and after pupil dilation are shown.*



Graphic 2: *Mountain plots demonstrating the percentiles of differences in the distributions of RNFL-Before minus RNFL-After values for superior, inferior, temporal, and nasal RNFL measurements are displayed.*

The mean signal strength of macular scans did not show a statistical difference before and after dilation (p=0.272). The macular measurements before and after dilation are compared in table 1. The values before dilation were significantly different from those after dilation in the parameters of cup area, cup area / disc area ratio, vertical cup/disc ratio, and signal strength (p=0.034; p=0.036; p=0.005 and p=0.001, respectively), (Table 2). There was no statistically significant difference between the values before and after pupil dilation for all RNFL parameters (Table 3). In the Bland-Altman plots, RNFL thicknesses obtained before and after dilation were investigated (Graphic 1-3). The difference between the measurements before and after pupil dilation was close to zero for all RNFL parameters and nearly all of them were within the 95% limit of agreement. There were moderate correlations between the measurements of superior, inferior, temporal, and nasal RNFL thicknesses before and after dilation (r=0.63, p<0.001; r=0,65, p<0.001; r=0.64, p<0.001; and r=0.50, p<0.001; respectively) while average RNFL measurements before and after pupil dilation showed good correlation (r=0.80; p<0.001).



Graphic 3: *The distribution and the percentiles of the difference (Average RNFL-Before minus Average RNFL-After) between the measurements of average RNFL before and after pupil dilation are shown in Bland-Altman and Mountain plots.*

DISCUSSION

Pupil dilation is usually performed in order to improve the quality of images as a general rule when scanning with Stratus OCT (OCT-3). Pupil dilation cannot be induced in adults with angle closure glaucoma, exfoliation syndrome or long-standing diabetes and elderly subjects and they may be scanned by OCT-3 without pupil dilation. After administration of any eye drops to children, it can be observed that most children and especially preschoolers become uncooperative for ocular examination.

Fifteen percent of the preschoolers (n=17) could not be scanned by OCT after pupil dilation in our study, although all of them were easily scanned before the dilation. Fast ocular scanning without eye drops may therefore be more suitable for some children. We also need to know whether there is a difference between the measurements obtained by OCT in the dilated and undilated states when measuring children.

It was found that reliable measurements can be obtained by OCT-1 without pupil dilation in adults.[31,32] However, Paunescu et al.[27] reported a significant effect of pupil size on the measurements taken by OCT-3. When performing macular scan by OCT-3 without pupil dilation, the scanning cursor of the device must be located on the foveal pit and the patient should maintain the fixation of his or her eye on the target of the device for nearly 2 seconds in order to get precise macular measurement.

Wang et al.[33] found that there was no significant difference in the retinal thickness measurements taken by OCT-1 between the undilated and dilated states. Hee et al.[25] showed that it is possible to measure by OCT-1 through an undilated or poorly dilated pupil and axial resolution is not affected by limited pupil size. However, they noticed that the optical alignment was sensitive to the pupillary aperture and a reduction of viewing field occurred.

Although we found a significant difference between the undilated and dilated states for only the parameters of the superior outer, nasal inner and outer segments, the mean difference between the measurements before and after pupil dilation for these macular parameters was about 2 µm and it may be assumed to be clinically insignificant as the coefficient of repeatability for macular thickness measurements was previously found to be 6-8 µm.[34]

It is known that RNFL thickness shows significant difference between glaucomatous and healthy eyes in children.[18,19] Recently, Chen et al.[35] reported that fourier- domain and time-domain OCTs showed equal diagnostic power in early glaucoma, ocular hypertension, glaucoma-suspect, primary open angle glaucoma, and primary angle closure glaucoma eyes. TD-OCTs may therefore continue to detect glaucomatous change in clinical practice for some time. Most of the studies previously performed for the evaluation of the effect of pupil size on OCT measurements generally used only the RNFL measurements.[26,28-30]

Savini et al.[30] found a marginal effect of pupil size on the RNFL thickness measurements obtained by OCT-3. However, Hsu and Tsai[28] reported that the measurements of all RNFL thicknesses (superior, inferior, temporal, nasal, and average RNFL thicknesses) obtained with OCT-3 before and after pupil dilation showed no significant difference in healthy Taiwanese people. Cheng et al.[37] recently reported that pupil dilation had a variable and non-statistically significant effect on the RNFL measurements obtained through clear media by both FD-OCT and TD-OCT. Zafar et al.[26] similarly found that there was no significant difference between the RNFL measurements before and after pupil dilation. In their study, they found a trend showing increased RNFL thickness after dilation was also demonstrated with scanning laser polarimetry.[36] In our study, this phenomenon was not seen in all RNFL parameters (Table 3) and we found no significant difference between the RNFL measurements before and after pupil dilation in preschoolers and there was a good correlation between the measurements of average RNFL before and after dilation (Table 3; Graphic 1-3).

As occurred in some macular parameters, the measurements obtained in dilated states were statistically different from those taken in undilated states for some parameters of the optic disc (Table 1,2).

Increasing signal strength after pupil dilation occurred only in optic disc scans and no significant difference was found in the signal strength of the macula and RNFL scans between the before and after pupil dilation states. This may result in significantly different measurements before and after dilation in optic disc scans. For macular and optic disc scans, a wider pupillary aperture may be needed because the diameters of scan planes in these scan options are larger than in the RNFL scan. Even so, the differences in macular and optic disc measurements between the before and after dilation states may be assumed as clinically insignificant.

FD-OCT has recently become commercially available for clinical practice and it can take images with high quality in a very short time, and it requires a 2 mm pupil size for scanning whereas OCT-3 requires a 4 mm pupil diameter.[38] OCT-3 needs a wider pupil than FD-OCT to take data across the retina because OCT-3 uses an off-axis CCD camera whereas FD-OCT uses an on-axis line camera for scanning the fundus.

In some studies performed by FD-OCT, it was shown that pupil size did not influence the RNFL measurements.[38,39] Similar findings were obtained in other studies[26,28] in which RNFL measurements taken by TD-OCT were also not affected by pupil size.

However, Cheng et al.[37] found that OCT-3 had excellent reproducibility for the RNFL measurements in both dilated and undilated states after cataract surgery but poor reproducibility before cataract surgery whereas excellent reproducibility was achieved by FD-OCT before and after cataract removal but with poor reproducibility in the undilated state.

They noticed that pupil dilation was necessary for getting excellent reproducibility with FD-OCT and lens clarity was required for OCT-3. To the best of our knowledge, this is the first study to investigate the influence of pupil dilation on macular, RNFL, and optic disc measurements obtained by OCT-3 in children. Nonetheless, this study also provides normative data of OCT measurements for healthy preschool age children. Objective, reproducible, and quantitative measurements can be obtained by OCT in clinical practice and it is advantageous for the diagnosis and follow-up of glaucoma in the pediatric population when comparing with conventional methods such as visual field test and optic disc analysis.[18,19] OCT is also a useful clinical tool for monitoring pseudotumor cerebri in children.[20] It may be thought that there is no need to dilate the pupil for the measurements of RNFL thickness in children with such diseases during the monitorization but cooperation of the child and his or her fixation on the target of the device are important factors to get reliable and precise measurements while scanning by OCT-3 through an undilated pupil.

In our study, we evaluated healthy preschoolers with good visual acuity, so further studies are needed to evaluate children with ocular disease such as glaucoma or pseudotumor cerebri. Smith et al.[29] reported that the quality and reproducibility of RNFL measurements obtained in the undilated condition were not satisfactory in 25% of glaucoma patients. However, they scanned glaucoma patients with lens opacity and more advanced age in their study.

OCT-3 is a technically mature and non-invasive device, and very suitable for the pediatric population.[3,24] It may provide reliable clinical data about the macula, RNFL thickness and optic disc morphology in a few seconds for the pediatric group, even in the undilated condition. During the follow-up, children should be measured in the same condition, i.e., with or without pupil dilation and more than one scan should be taken when scanning children by OCT-3 in the undilated state so that the more reliable one can be used for clinical practice.

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