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# Analysis of choroidal thickness, macular thickness, peripapillary retinal nerve fiber layer thickness, and macular vascular density in children with unilateral amblyopia using swept-source optical coherence tomography and their changes following occlusion therapy

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**Abstract:**

**PURPOSE:** The purpose of this study was to analyze choroidal thickness (CT), along with macular thickness (MT), peripapillary retinal nerve fiber layer thickness (RNFLT), and macular vascular density (MVD) using swept-source optical coherence tomography (SS-OCT) in children with unilateral amblyopia, and compare the same with normal fellow eyes and normal eyes of normal children before and following occlusion therapy.

**MATERIALS AND METHODS:** This was a prospective, longitudinal study of 60 children (4-18 years); 30 children had unilateral amblyopia and remaining 30 were normal. Group 1 consisted of 30 amblyopic eyes of children with unilateral amblyopia; Group 2 consisted of 30 fellow normal eyes of Group 1; Group 3 consisted of normal eyes of normal children. Best-corrected visual acuity (BCVA) using logarithmic minimum angle of resolution (LogMAR) chart, detailed ophthalmic examination, SS-OCT for CT, MT, RNFLT, and MVD at the level of superficial, deep, and choriocapillary plexus in both eyes were assessed at presentation, third, sixth and 12$^{th}$ month follow-up. In Group 1, spectacles (at presentation) and occlusion therapy (1 month) were advised.

**RESULTS:** In Group 1, the mean CT and MT were higher whereas LogMAR BCVA and MVD were lower than Groups 2 and 3 at presentation. In Group 1, post occlusion therapy, the mean CT and MT decreased whereas LogMAR BCVA and MVD increased. There was no significant change in RNFLT in Group 1 as compared to Groups 2 and 3, pre- and post occlusion therapy.

**CONCLUSION:** CT and MT in amblyopic eyes were significantly higher. Following occlusion therapy, CT decreased in each follow-up but was not significant whereas MT decreased significantly at the last follow-up visit. There was no difference in RNFLT in amblyopic eyes as compared with normal fellow eyes and control eyes before and after occlusion therapy. MVD was lower in amblyopic eyes and increased during follow-up visits but was not significant.

**Keywords:**

Amblyopia, choroidal thickness, occlusion therapy, swept-source optical coherence tomography, vascular density

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## Introduction

With the advent of optical coherence tomography (OCT), etiopathology of amblyopia is being better understood.[1] Occlusion therapy has been the mainstay of amblyopia treatment.[2] Various studies are available documenting changes in choroidal thickness (CT), macular thickness (MT), retinal nerve fiber layer thickness (RNFLT), and macular vascular density (MVD) in amblyopic eyes.[3-11] Hence, the purpose of our study was not only to analyze changes in CT, MT, peripapillary RNFLT, and MVD in unilateral amblyopic eyes and compare the same with normal fellow eye and normal eyes of normal children but also to understand the same following occlusion therapy.

## Materials and Methods

This prospective, interventional, longitudinal, comparative study was carried out at a tertiary care eye hospital in South India from September 2020 to February 2022. The study was approved by the Institutional Review Board (Sankara Eye Hospital, Shimoga Registration Number ECR/1296/Inst/KA/2019. IRB approval date: August 28, 2020) and adhered to all the principles mentioned in the Declaration of Helsinki 2000. The study was registered under the Clinical Trials Registry-India (CTRI) (Registration Number CTRI/2020/09/028092, registered on September 28, 2020). Based on previous literature with 80% statistical power and 95% confidence interval, the estimated sample size was 60 children (30 unilateral amblyopic children and 30 normal children). The eyes were divided into three groups: Group 1 – 30 amblyopic eyes, Group 2 – 30 normal fellow eyes of amblyopic children, and Group 3 – 60 normal eyes of 30 normal age- and sex-matched children (average of right eye [RE] and left eye [LE] measurements were considered to get a final measurement – 30 values).

Inclusion criteria: Children of either sex aged between 4 and 18 years with unilateral strabismic and/or anisometropic amblyopia with best-corrected visual acuity (BCVA) of logarithmic minimum angle of resolution (LogMAR) <0.2 (6/9) were included in Group 1; uncorrected visual acuity (UCVA) of LogMAR 0.00 in both eyes was included in Group 3; children with normal neurological, ocular, and systemic examination and those who were willing for follow-up were included in the study. Children with (1) previous history of spectacle wear and / or occlusion therapy and / or ocular surgery, (2) refractive error correction >6D spherical power and >3D cylindrical power, (3) presence of nystagmus/hearing impairment /developmental delay, (4) non-compliance for spectacle wear and/or occlusion therapy, (5) poor fixation and uncooperative for swept-source OCT (SS-OCT) test (due to poor vision or lower age), (6) only one follow-up visit were excluded from the study. After satisfying the inclusion and exclusion criteria, informed consent from the child's parent was obtained after counseling them regarding the nature of the study. Detailed history regarding any ocular and systemic conditions as per inclusion and exclusion criteria was noted. UCVA and BCVA for distance using a LogMAR three-meter chart (English letters or Symbols chart) and near using Snellen's chart were recorded. Other visual function tests such as color vision (Ishihara pseudoisochromatic plates), contrast sensitivity (Pelli-Robson contrast sensitivity chart), visual fields (Humphrey field analysis/confrontation test/Amsler chart), and electrophysiological tests were recorded wherever possible and required. Tests for strabismus were done using Hirschberg test, cover test, alternate cover test, and alternate prism bar cover test at 6 m and 40 cm fixation distances using an accommodative target with and without optical correction (if already used), and the type of strabismus was noted down. Intraocular pressure was measured using noncontact tonometry wherever possible. Detailed anterior segment examination was carried out using slit lamp wherever possible. Cycloplegic refraction using appropriate drug according to age was carried out in all children. Fundus examination was carried out after dilatation with slit-lamp biomicroscopy using +90D lens wherever possible and/or with indirect ophthalmoscopy using +20D condensing lens. The type of refractive error and amblyopia, if present, was noted. Following OCT scans of the retina and choroid were performed after dilatation of pupils by a single examiner: (1) Radial diameter 6.0 mm overlap 16 scan was used to measure CT and MT, (2) 3D disc 6 mm × 6 mm scan was used to measure peripapillary RNFLT, (3) OCT angiography (OCTA) 4.5 mm × 4.5 mm scan was used to measure MVD. CT, MT, peripapillary RNFLT, and MVD (at the level of superficial capillary plexus [SCP], deep capillary plexus [DCP], and choriocapillary plexus [CCP]) were measured using Topcon DRI OCT Triton Plus (Topcon Medical Systems, Tokyo, Japan) in both the eyes. All findings observed were recorded. Measurement of parameters was done as (a) CT: automated choroidal scleral interface (CSI) was verified for proper alignment. In cases with misalignment, CSI was modified manually in 12 radial scans. Then, the automated software was used to measure the CT in the Early Treatment Diabetic Retinopathy Study (ETDRS) grid. (b) MT: MT within the central 3 mm of the fovea was measured by automated software in ETDRS grid. (c) Peripapillary RNFLT: 3D disc protocol was used to measure peripapillary RNFLT by automated software in six sectors. (d) MVD: 4.5 mm × 4.5 mm OCTA was used to measure vascular density within central 3 mm of ETDRS grid. Density within

SCP was measured by automated software in superficial capillary slab identified by automated segmentation. The reference limit in SC slab was manually modified to display deep capillary slab and choriocapillary slab. Then, automated software was used to measure DCP and CCP. Following scans, spectacles were prescribed to children with refractive error according to the American Academy of Ophthalmology guidelines. One month after the first visit (postspectacle wear-refractive adaptation phase), the normal fellow eye of amblyopic children was patched for 4–6 h/day and was advised to perform near activities such as reading, writing, drawing, mobile games, and computer work. Parents were insisted upon maintaining a diary regarding the same to check for compliance. All amblyopic children were followed up at 3 months, 6 months, and 12 months. Children who had come for less than one follow-up were excluded from the study. At each follow-up visit, compliance for spectacle wear and occlusion therapy was analyzed. In addition, UCVA, BCVA, and OCT scans were done to measure the CT, MT, peripapillary RNFLT, and MVD. Those who were not compliant for spectacle wear and occlusion therapy were excluded. At the end of the study, data were analyzed using SPSS Software version 23.0 (IBM, Illinois, Chicago, United states) and using paired *t*-test. All precautions were followed with respect to COVID-19 while performing investigations.

### Statistical methods

CT, MT, RNFLT, and MVD were considered outcome variables. Amblyopia was considered an explanatory variable. Descriptive analysis was carried out by mean and standard deviation for quantitative variables and frequency and proportion for categorical variables. Data were also represented using appropriate tables and diagrams such as bar diagram. Initially, the outcome parameters were compared between Group 1, Group 2, and Group 3 using independent sample *t*-test. The mean values of all the outcome variables between Group 1 and Group 2 were compared at each follow-up interval separately using paired *t*-test.

## Results

Sixty children aged between 4 and 18 years were included in the analysis: 30 children had unilateral amblyopia; amblyopic eyes were included in Group 1 and normal fellow eyes in Group 2. The remaining 30 children were categorized as normal and to form the control group (Group 3). They were matched for age and sex with unilateral amblyopic children.

The mean age was 12.13 ± 3.17 years. Fourteen (46.70%) were females and 16 (53.30%) were males in each group. In Group 1, 13 (43.30%) children had amblyopia in RE and the remaining 17 (56.70%) in LE. Three children had strabismic amblyopia (astigmatism – 2 and hyperopia – 1) whereas 27 had anisometropic unilateral amblyopia (astigmatism – 22, hyperopia – 3, and myopia – 2).

At the time of presentation, the mean LogMAR BCVA of Group 1 was 1.01 whereas it was 0.0 in Group 2 and Group 3, and this difference was statistically significant ($P < 0.001$).

The mean CT (μm), MT (μm), RNFLT (μm), and MVD (%) at the level of SCP, DCP, and CCP in Group 1 were 326.50 ± 39.35, 241.50 ± 27.78, 105.60 ± 19.02, 12.57 ± 4.26, 4.99 ± 3.46, 33.19 ± 6.48, respectively; in Group 2 were 284.40 ± 39.54, 228.60 ± 20.13, 108.40 ± 15.27, 14.33 ± 4.12, 5.34 ± 4.63, 34.26 ± 4.06, respectively; and in Group 3 were 278.40 ± 38.52, 227.80 ± 18.26, 110.29 ± 14.15, 14.58 ± 4.23, 5.20 ± 2.66 and 34.15 ± 4.58 respectively. This difference was statistically significant with respect to CT and MT ($P < 0.001$), but it was not significant with respect to RNFLT and MVD ($P > 0.001$). The comparison of these parameters between the three groups at the time of presentation is depicted in Table 1.

All children had come for two follow-up visits. Fourteen out of 30 children had come for the first follow-up visit (3 months). Twenty-four children had come for the second follow-up visit (6 months). Twenty-two children had come for the third follow-up visit (12 months).

At the first follow-up visit (3 months), the mean LogMAR BCVA in Group 1 was 0.94 ± 0.32 whereas it was 0.0 in Group 2. This difference was statistically significant ($P < 0.001$). Mean CT (μm), MT (μm), RNFLT (μm), and MVD (%) at the level of SCP, DCP, and CCP in Group 1 were 321.57 ± 40.50, 235.64 ± 28.41, 101.05 ± 22.73, 13.98 ± 3.62, 5.91 ± 3.89 and 34.51 ± 4.84, respectively, and in Group 2 were 283.57 ± 43.31, 216.40 ± 17.55, 103.00 ± 17.99, 15.82 ± 3.50 7.35 ± 5.97 and 32.59 ± 3.60, respectively. This difference was statistically significant with respect to CT and MT ($P = 0.02$ and $P = 0.04$, respectively), but it was not significant with respect to RNFLT and MVD ($P > 0.001$).

At the second follow-up visit (6 months), the mean LogMAR BCVA in Group 1 was 1.02 ± 0.35 whereas it was 0.0 in Group 2. This difference was statistically significant ($P < 0.001$). Mean CT (μm), MT (μm), RNFLT (μm) and MVD (%) at the level of SCP, DCP and CCP in Group 1 were 315.16 ± 38.46, 229.79 ± 32.53, 101.40 ± 20.17, 13.39 ± 4.60, 5.95 ± 3.65 and 34.67 ± 6.41, respectively, and in Group 2 were 278.70 ± 36.95, 212.91 ± 21.93, 103.90 ± 16.29, 15.51 ± 4.01, 5.57 ± 5.09 and 34.84 ± 3.88, respectively. This difference was statistically significant with respect to CT and MT ($P < 0.001$ and

**Table 1: Comparison of various ocular parameters between Group 1, Group 2, and Group 3 at the time of presentation**

| Parameters | Group 1 | Group 2 (*P*) | Group 3 (*P*) |
|---|---|---|---|
| Mean LogMAR BCVA | 1.01±0.38 | 0.00 (<0.001) | 0.00 (<0.001) |
| Range of LogMAR BCVA | 1.77–0.47 | | |
| CT (μm) | 326.50±39.35 | 284.40±39.54 (0.001) | 278.40±38.52 (<0.001) |
| MT (μm) | 241.50±27.78 | 228.60±20.13 (0.04) | 227.80±18.26 (0.03) |
| RNFLT (μm) | 105.60±19.02 | 108.40±15.27 (0.49) | 110.29±14.15 (0.56) |
| SCP (%) | 12.57±4.26 | 14.33±4.12 (0.10) | 14.58±4.23 (0.07) |
| DCP (%) | 4.99±3.46 | 5.34±4.63 (0.97) | 5.20±2.66 (0.93) |
| CCP (%) | 33.19±6.48 | 34.26±4.06 (0.45) | 34.15±4.58 (0.51) |

BCVA=Best-corrected visual acuity, CT=Choroidal thickness, MT=Macular thickness, RNFLT=Retinal nerve fiber layer thickness, SCP=Superficial capillary plexus, DCP=Deep capillary plexus, CCP=Choriocapillary plexus, LogMAR=Logarithm of the minimum angle of resolution

*P* = 0.04, respectively), but it was not significant with respect to RNFLT and MVD (*P* > 0.001).

At the the follow-up visit (12 months), the mean LogMAR BCVA in Group 1 was 0.77 ± 0.34 whereas it was 0.00 in Group 2. This difference was statistically significant (*P* < 0.018). Mean CT (μm), MT (μm), RNFLT (μm) and MVD (%) at the level of SCP, DCP and CCP in Group 1 were 305.09 ± 41.78, 224.27 ± 18.86, 103.70 ± 17.78, 13.54 ± 3.85, 6.12 ± 3.34 and 34.79 ± 5.92, respectively, and in Group 2 were 277.31 ± 39.55, 210.36 ± 25.10, 105.80 ± 18.79, 15.60 ± 3.57, 5.73 ± 5.27 and 34.70 ± 4.29, respectively. This difference was statistically significant with respect to CT and MT (*P* = 0.02 and *P* = 0.043, respectively), but it was not significant with respect to RNFLT and MVD (*P* > 0.001). The comparison of various ocular parameters between Groups 1 and Group 2 at 3-month, 6-month, and 12-month follow-up is shown in Tables 2-4, respectively.

As compared to presentation visit, on subsequent follow-up visits in Group 1, we found that visual acuity was increasing (1.01 ± 0.38, 0.94 ± 0.32, 1.02 ± 0.35, and 0.77 ± 0.34), and this difference was statistically significant on the third follow-up visit when compared with presentation visit (*P* < 0.05). The mean CT (μm) started decreasing (326.50 ± 39.35, 321.57 ± 40.50, 315.16 ± 38.46, and 305.09 ± 41.78), but this decrease was not statistically significant (*P* > 0.05). Furthermore, the mean MT (μm) started decreasing on subsequent visits (241.50 ± 27.78, 235.64 ± 28.41, 229.79 ± 32.53, and 224.27 ± 18.86), and this decrease was statistically significant on the third follow-up visit as compared to presentation visit (*P* < 0.05). No statistically significant change in RNFLT (μm) was found (105.60 ± 19.02, 101.00 ± 22.73, 101.40 ± 20.17, and 103.70 ± 17.78) (*P* > 0.05) during follow up visits. MVD (%) at the level of SCP (12.57 ± 4.26, 13.98 ± 3.62, 13.39 ± 4.60, and 13.54 ± 3.85), DCP (4.99 ± 3.46, 5.91 ± 3.89, 5.95 ± 3.65, and 6.12 ± 3.34) and CCP (33.19 ± 6.48, 34.51 ± 4.84, 34.67 ± 6.41 and 34.79 ± 5.92) was found to be increasing during follow up visits though the difference was not statistically significant (*P* > 0.05). The analysis of various ocular parameters in the amblyopic eyes (Group 1) at various visits following occlusion therapy is shown in Table 5.

**Table 2: Comparison of various ocular parameters between Group 1 and Group 2 at the first follow-up visit (3 months)**

| Parameters | Group 1 | Group 2 | *P* |
|---|---|---|---|
| Mean LogMAR BCVA | 0.94±0.32 | 0.00 | <0.001 |
| Range of LogMAR BCVA | 1.30–0.47 | | |
| CT (μm) | 321.57±40.50 | 283.57±43.31 | 0.02 |
| MT (μm) | 235.64±28.41 | 216.40±17.55 | 0.04 |
| RNFLT (μm) | 101.05±22.73 | 103.00±17.99 | 0.84 |
| SCP (%) | 13.98±3.62 | 15.82±3.50 | 0.18 |
| DCP (%) | 5.91±3.89 | 7.35±5.97 | 0.45 |
| CCP (%) | 34.51±4.84 | 32.59±3.60 | 0.24 |

BCVA=Best-corrected visual acuity, CT=Choroidal thickness, MT=Macular thickness, RNFLT=Retinal nerve fiber layer thickness, SCP=Superficial capillary plexus, DCP=Deep capillary plexus, CCP=Choriocapillary plexus, LogMAR=Logarithm of the minimum angle of resolution

**Table 3: Comparison of various ocular parameters between Group 1 and Group 2 at the second follow-up visit (6 months)**

| Parameters | Group 1 | Group 2 | *P* |
|---|---|---|---|
| Mean LogMAR BCVA | 1.02±0.35 | 0.00 | <0.001 |
| Range of LogMAR BCVA | 1.30–0.47 | | |
| CT (μm) | 315.16±38.46 | 278.70±36.95 | 0.001 |
| MT (μm) | 229.79±32.53 | 212.91±21.93 | 0.04 |
| RNFLT (μm) | 101.40±20.17 | 103.90±16.29 | 0.62 |
| SCP (%) | 13.39±4.60 | 15.51±4.01 | 0.09 |
| DCP (%) | 5.95±3.65 | 5.57±5.09 | 0.76 |
| CCP (%) | 34.67±6.41 | 34.84±3.88 | 0.91 |

BCVA=Best-corrected visual acuity, CT=Choroidal thickness, MT=Macular thickness, RNFLT=Retinal nerve fiber layer thickness, SCP=Superficial capillary plexus, DCP=Deep capillary plexus, CCP=Choriocapillary plexus, LogMAR=Logarithm of the minimum angle of resolution

## Discussion

Amblyopia is defined as reduced BCVA in one or both eyes caused by abnormal visual experience during the development of a visual system without any organic abnormality of the eye.[12] Amblyopia was thought to be a disease associated with an abnormality of the retina.[13] However, amblyopia-induced cerebral changes were

later shown to mainly occur in the visual cortex and the lateral geniculate body.[14] With the advent of OCT, and desire to understand etiopathogenesis, there are various studies in the recent past documenting changes in the retina and choroid. Therefore, in our study, we intended to analyze changes in CT, MT, peripapillary RNFLT, and MVD in unilateral amblyopic eyes and compare the same with normal fellow eyes and normal eyes of normal children and also to understand the same following occlusion therapy.

## Choroidal thickness

It is well known that the major role of the choroid is nutrition and thermoregulation of the retina. However, a new function of the choroid has become popular in recent years – "emmetropization." The emmetropization may possibly be achieved by the changes in position of the retina through modulation of the thickness of the choroid.[15]

In our research, we observed that the CT (μm) in amblyopic eyes (326.5 ± 39.35) was notably greater than that in fellow normal eyes (284.4 ± 39.54) [Figure 1] and control eyes (278.4 ± 38.52) ($P < 0.05$), which aligns with findings from previous studies.[3,4,16,17] On the other hand, Kurt *et al*.[18] found no statistically significant difference between CT of amblyopic and normal fellow eyes whereas CT of amblyopic eyes was lower than control eyes. Nishi *et al*. hypothesized that in young children, hyperopic defocus causes choroidal thinning in fellow and healthy eyes; however, this does not occur in amblyopic eyes resulting in thicker choroid.[19]

There was no significant change ($P > 0.05$) in CT (μm) in amblyopic eyes (305.09 ± 41.78) following occlusion therapy similar to few studies.[20,21] On the other hand, Aslan Beyhan *et al*.[22] and Hashimoto *et al*.[23] found a significant reduction which was more at the last follow-up, although it did not equalize with the fellow normal eyes. Based on our findings, we are proposing that the increase in CT may not have a direct correlation with visual impairment.

Furthermore, the improvement in BCVA following successful amblyopia treatment does not seem to have a substantial impact on CT.[20]

## Macular thickness

We observed that MT (μm) in amblyopic eyes (241.5 ± 27.78) was significantly higher than fellow normal eyes (228.6 ± 20.13) [Figure 1] similar to few

**Table 4: Comparison of various ocular parameters between Group 1 and Group 2 at the third follow-up visit (12 months)**

| Parameters | Group 1 | Group 2 | *P* |
|---|---|---|---|
| Mean LogMAR BCVA | 0.77±0.34 | 0.00 | <0.01 |
| Range of LogMAR BCVA | 1.17–0.47 | | |
| CT (μm) | 305.09±41.78 | 277.31±39.55 | 0.02 |
| MT (μm) | 224.27±18.86 | 210.36±25.10 | 0.04 |
| RNFLT (μm) | 103.70±17.78 | 105.80±18.79 | 0.59 |
| SCP (%) | 13.54±3.85 | 15.60±3.57 | 0.07 |
| DCP (%) | 6.12±3.34 | 5.73±5.27 | 0.77 |
| CCP (%) | 34.79±5.92 | 34.70±4.29 | 0.95 |

BCVA=Best-corrected visual acuity, CT=Choroidal thickness, MT=Macular thickness, RNFLT=Retinal nerve fiber layer thickness, SCP=Superficial capillary plexus, DCP=Deep capillary plexus, CCP=Choriocapillary plexus, LogMAR=Logarithm of the minimum angle of resolution

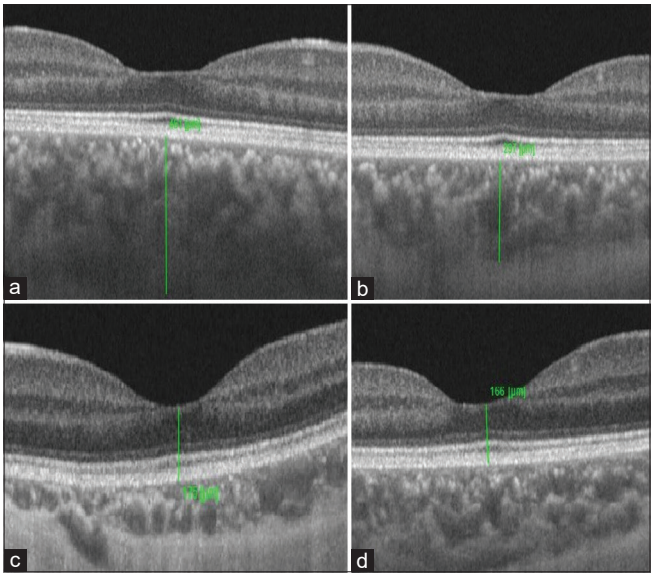


**Figure 1:** Comparison of choroidal thickness (CT) and macular thickness (MT) between amblyopic and fellow normal eyes at the time of presentation. (a and b) CT of amblyopic and fellow normal eyes, respectively, (c and d) MT of amblyopic and fellow normal eyes, respectively

**Table 5: Comparison of various parameters in Group 1 at various visits**

| Parameters | Presentation visit | First follow-up visit (*P*) | Second follow-up visit (*P*) | Third follow-up visit (*P*) |
|---|---|---|---|---|
| Mean LogMAR BCVA | 1.01±0.38 | 0.94±0.32 (0.15) | 1.02±0.35 (0.13) | 0.77±0.34 (0.03) |
| CT (μm) | 326.50±39.35 | 321.57±40.50 (0.70) | 315.16±38.46 (0.29) | 305.09±41.78 (0.06) |
| MT (μm) | 241.50±27.78 | 235.64±28.41 (0.51) | 229.79±32.53 (0.15) | 224.27±18.86 (0.01) |
| RNFLT (μm) | 105.60±19.02 | 101.00±22.73 (0.50) | 101.40±20.17 (0.11) | 103.70±17.78 (0.88) |
| SCP (%) | 12.57±4.26 | 13.98±3.62 (0.44) | 13.39±4.60 (0.33) | 13.54±3.85 (0.25) |
| DCP (%) | 4.99±3.46 | 5.91±3.89 (0.44) | 5.95±3.65 (0.33) | 6.12±3.34 (0.25) |
| CCP (%) | 33.19±6.48 | 34.51±4.84 (0.50) | 34.67±6.41 (0.40) | 34.79±5.92 (0.36) |

BCVA=Best-corrected visual acuity, CT=Choroidal thickness, MT=Macular thickness, RNFLT=Retinal nerve fiber layer thickness, SCP=Superficial capillary plexus, DCP=Deep capillary plexus, CCP=Choriocapillary plexus, LogMAR=Logarithm of the minimum angle of resolution

studies.[8,9,24,25] However, no significant difference was seen in studies done by Kurt *et al*.[18] and Wu *et al*.[26]

MT (μm) in amblyopic eyes (241.5 ± 27.78) was found to be significantly higher than control eyes (227.8 ± 18.26) similar to a study done by Kavitha *et al*.[9] However, few other studies[18,27,28] found no significant difference.

We noted a significant reduction ($P < 0.05$) in MT (μm) in amblyopic eyes (224.27 ± 18.86) following occlusion therapy similar to few studies.[5,9] However, there was no significant difference noted by Zhang *et al*.[27] and Zakaria Eid *et al*.[29] Yen *et al*. hypothesized that in amblyopia, normal maturation of the macula, which includes movement of Henle's fibers away from the foveola, is affected. This leads to increased MT.[30] With occlusion therapy, this process is reversed resulting in decreased MT.

## Retinal nerve fiber layer thickness

Yen *et al*. hypothesized that the normal postnatal reduction (apoptosis) of retinal ganglion cells is arrested in amblyopia because of the absence of normal vision stimulation. This would cause increased RNFLT.[30]

We did not find any significant difference in RNFLT (μm) in amblyopic eyes (105.6 ± 19.02) as compared to fellow normal eyes (108.4 ± 15.27), aligned to few studies.[8,9,20,24,25] However, Wu *et al*.[26] found a significant difference between these two groups, and this variation from other studies could be because of the type of refractive error considered in amblyopic eyes – hyperopic anisometropia. Peripapillary RNFLT decreases as the distance from the optic disc increases. Hence, a constant diameter circle on OCT scan protocol would be smaller on the retina of hyperopic or shorter eyes, which results in scan being closer to the disc margin and a thicker measured retinal nerve fiber layer. The converse would be true for myopic eyes.[25] It can also be attributed to other factors such as the use of different types of OCT machines, scanning protocols used, period of occlusion therapy, sample size, and type of amblyopia considered in the study.

There was no significant difference in RNFLT (μm) among amblyopic eyes (105.6 ± 19.02) and control eyes (110.29 ± 14.15) in our study similar to Kavitha *et al*.[20], but Alotaibi *et al*.[28] found a significant difference. Post occlusion therapy, there was no significant difference in RNFLT (103.7 ± 17.78 μm) in our study similar to few studies.[9,27] We could not find any literature showing a significant difference in RNFLT post occlusion therapy. This implies that the presence of amblyopia and improvement in BCVA after successful amblyopia treatment may not have an impact on RNFLT.

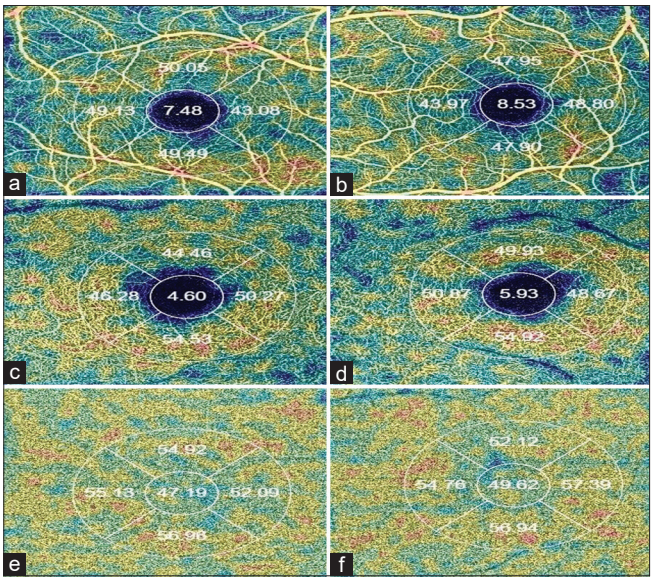


**Figure 2:** Comparison of macular vascular density (MVD) between amblyopic and fellow normal eyes at the time of presentation. MVD at the level of superficial capillary plexus (a and b), deep capillary plexus (c and d), and choriocapillary plexus (e and f) of amblyopic and fellow normal eyes, respectively

## Macular vascular density

We observed that MVD (%) at the level of SCP and DCP in amblyopic eyes (12.57 ± 4.26 and 4.99 ± 3.46, respectively) was lesser than that of fellow normal eyes (14.33 ± 4.12 and 5.34 ± 4.63, respectively) ($P > 0.05$) [Figure 2] similar to the results seen in a study done by Chen *et al*.[31] whereas Yilmaz *et al*.[11] found this difference to be statistically significant ($P < 0.05$).

MVD (%) at the level of SCP and DCP in amblyopic eyes (12.57 ± 4.26 and 4.99 ± 3.46, respectively) was lesser than that of control eyes (14.58 ± 4.23 and 5.2 ± 2.66, respectively) in our study ($P > 0.05$) as seen in few studies,[19,27,31] but Yilmaz *et al*.[11] and Lonngi *et al*.[32] found a significant difference between the two groups.

Post occlusion therapy, we found an increase in MVD (%) at the level of SCP and DCP (13.54 ± 3.85 and 6.12 ± 3.34, respectively) ($P > 0.05$) similar to Chen *et al*.[31] whereas Zhang *et al*.[27] found no significant difference. This difference probably could be due to factors such as age, ethnicity, type of refractive error, type of amblyopia, occlusion therapy compliance, and the scan protocol used.

We observed that MVD (%) at the level of CCP in amblyopic eyes (33.19 ± 6.48) is lower than that of fellow normal (34.26 ± 4.06) [Figure 2] and control eyes (34.15 ± 4.58). Post occlusion therapy, it increased in amblyopic eyes (34.79 ± 5.92) ($P > 0.05$). However, to our best knowledge, there are no studies available in the literature about MVD at the level of CCP in amblyopic eyes and effect of occlusion therapy on it. Lonngi *et al*. hypothesized that this abnormal development of

retinal vasculature may be related to lack of a normal visual experience in the early developmental period.[32] Demirayak *et al*. hypothesized that decreased MVD in amblyopic eyes may be secondary to retinal or choroid microvasculature alterations, which are secondary to underuse.[33]

### Best-corrected visual acuity

We found a significant improvement in BCVA ($P < 0.05$) in amblyopic eyes at the last follow-up visit after refractive error correction and successful occlusion therapy when compared with presentation visit [Tables 1-4] apart from binocular vision.[34,35] This indicates that amblyopic eyes with higher CT, MT, and lower MVD can improve and achieve values as that of healthy eyes.

The comparison of our study with various other studies is given in Table 6.

## Conclusion

CT and MT in amblyopic eyes were significantly higher. Following occlusion therapy, CT decreased in each follow-up but was not significant whereas MT decreased significantly at the last follow-up. There was no difference in RNFLT in amblyopic eyes when compared with normal fellow eyes and control eyes before and after occlusion therapy. MVD at the level of SCP, DCP, and CCP was lower in amblyopic eyes. Although it increased during each follow-up visit, the difference was not significant. In amblyopic eyes, changes that occurred at the cellular level were detected with the help of OCT, though fundus examination was normal. Therefore, from our study, it can be inferred that OCT has a role in helping us in the diagnosis of amblyopia and understanding the future course of various OCT parameters following occlusion therapy.

**Table 6: Comparison of our study with other similar studies available**

| Parameter | Comparison | Study (author) | Results | Comparison with our study/studies |
|---|---|---|---|---|
| 1. CT | Between amblyopic, normal fellow, and control eyes | Karaca *et al*.,[3] Tenlik *et al*.,[4] Aygit *et al*.,[16] Zha *et al*.[17] | Higher in amblyopic eye than fellow normal eye and control eye | Consistent |
| | | Kurt *et al*.[18] | No significant difference among three groups | Contrary |
| | Following occlusion therapy | Araki *et al*.,[20] Öner *et al*.[21] | No significant difference post occlusion therapy | Consistent |
| | | Aslan Bayhan and Bayhan,[22] Hashimoto *et al*.[23] | Significant decrease post occlusion therapy | Contrary |
| 2. MT | Between amblyopic and fellow normal eyes | Al-Haddad *et al*.,[8] Kavitha *et al*.,[9] Andalib *et al*.[24] and Huynh *et al*.[25] | Significantly higher in amblyopic eyes than normal fellow eyes ($P$<0.05) | Consistent |
| | | Kurt *et al*.,[18] Wu *et al*.[26] | Lesser in amblyopic eyes than fellow normal eyes | Contrary |
| | Between amblyopic and control eyes | Kavitha *et al*.[9] | Significantly higher in amblyopic eyes than normal fellow eyes ($P$<0.05) | Consistent |
| | | Kurt *et al*.,[18] Zhang *et al*.[27] and Alotaibi and Al Enazi[28] | No significant difference between two groups | Contrary |
| | Following occlusion therapy | Pang *et al*.[5] and Kavitha *et al*.[9] | Significant reduction in MT in amblyopic eyes | Consistent |
| | | Zhang *et al*.[27] and Zakaria Eid *et al*.[29] | No significant difference after occlusion therapy | Contrary |
| 3. RNFLT | Between amblyopic eyes and normal fellow eyes | Al-Haddad *et al*.,[8] Kavitha *et al*.,[9] Araki *et al*.,[20] Andalib *et al*.[24] and Huynh *et al*.[25] | No significant difference | Consistent |
| | | Wu *et al*.[26] | Significant difference between two groups | Contrary |
| | Between amblyopic eyes and control eyes | Kavitha *et al*.[9] and Araki *et al*.[20] | No significant difference among two groups | Consistent |
| | | Alotaibi and Al Enazi[28] | Significant difference found between two groups | Contrary |
| | Following occlusion therapy | Kavitha *et al*.,[9] Zhang *et al*.[27] | No significant reduction in RNFLT in amblyopic eyes | Consistent |
| 4. MVD at the level of SCP and DCP | Between amblyopic and normal fellow eyes | Chen *et al*.[31] | Lesser in amblyopic eyes than fellow normal eyes | Consistent |
| | | Yilmaz *et al*.[11] | Significant difference between two groups | Contrary |
| | Between amblyopic and control eyes | Demirayak *et al*.,[33] Zhang *et al*.[27] and Chen *et al*.[31] | Lesser in amblyopic eyes than fellow normal eyes | Consistent |
| | | Yilmaz *et al*.[11] and Lonngi *et al*.[32] | Significant difference found between two groups | Contrary |
| | Following occlusion therapy | Chen *et al*.[31] | Increase in MVD at the level of SCP and DCP | Consistent |
| | | Zhang *et al*.[27] | No significant difference | Contrary |

CT=Choroidal thickness, MT=Macular thickness, RNFLT=Retinal nerve fiber layer thickness, SCP=Superficial capillary plexus, DCP=Deep capillary plexus, CCP=Choriocapillary plexus, MVD=Macular vascular density

## Limitation

The sample size was smaller as compared to the other studies. The follow-up period was shorter. Bilateral refractive and visual deprivation amblyopia were not included in the study. The sustainability of the improved visual acuity and hence the status of other parameters following the discontinuation of occlusion therapy could not be assessed.


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| Name | Role |
|---|---|
| Administrators, staff, and colleagues of Sankara Eye Hospital Shimoga, Karnataka | Helped in carrying out the study, approval of the study by hospital scientific and ethics committee, patient recruitment, examination, data collection, counseling, and patient care. |
| Sankara Academy of Vision, Bangalore | Encouragement and support |
| Statistician – Mr. Shashidhar Kotian and team | Data analysis |


## Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.


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Nil.


## Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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