

DISCUSSION

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Optical Coherence Tomography (OCT) is a non-invasive non-contact, trans-pupillary imaging method that performs objective high-resolution cross-sectional images of retinal tissue. The recently introduced SD-OCT provides measurements of the RNFL and macula with greatly improved image acquisition speed and image resolution up to 5 μm .⁽⁹⁰⁾ This is particularly helpful when applying this technology in uncooperative children. Several studies have proved the feasibility of OCT in the pediatric population.⁽⁹¹⁻⁹⁸⁾ Nevertheless, all OCT devices have an integrated normative database only for adult subjects 18 years of age and older.

The present study aimed at establishing a normative pediatric data base for macular thickness in healthy Egyptian children aged 6-16 years using Spectralis SD-OCT.

In the present study, the mean CSF thickness of healthy Egyptian children was $259.9 \pm 22.8 \mu\text{m}$. Several similar studies were previously performed aimed to reach pediatric normative data base. Among those studies, Yanni et al reported the mean CSF thickness in North American children aged 5-15 years. The study included non-Hispanic white, African American, Hispanic, and Asian using Spectralis SD-OCT, Yanni et al reported CSF thickness of $271.2 \pm 2 \mu\text{m}$ for those children. This value is higher than reported for CSF thickness in the present study.⁽⁹⁹⁾ Turkish study by Yilmaz et al reported that the mean CSF thickness in Turkish children aged 6-15 years using Spectralis SD-OCT was $261 \pm 27 \mu\text{m}$ ⁽¹⁰⁰⁾, this result is comparable to the present study. Chopovska et al reported the mean CSF thickness in German children aged 6-17 years using Spectralis SD-OCT to be $269 \pm 20.1 \mu\text{m}$ ⁽¹⁰¹⁾, which is higher than the present study.

The difference in CSF thickness between the present study and the others could be explained by racial differences. The cause of racial difference in retinal thickness measurements are still not known. It has been hypothesized that attenuation of incident optical radiation by the increased pigment in the apical portion of the RPE cells, leading to a decreased signal of posterior retinal segments and concomitant under assessment of retinal thickness in darkly pigmented persons.⁽¹⁰²⁾ Further research is necessary to elucidate the precise nature of the posterior retinal surface on OCT measurements and the cause of racial variation in retinal thickness. The techniques of segmentation and thickness mapping of individual retinal layers by SD-OCT have been proposed as ways to elucidate them.⁽¹⁰³⁾ This is in agreement with the study of Asefzadah et al that stated that retinal thickness as measured by stratus OCT in the fovea and macula is significantly thinner in blacks compared with age-matched whites.⁽¹⁰⁴⁾

Wagner-Shuman et al stated that race-associated differences are more likely due to differences in foveal pit morphology⁽¹⁰⁵⁾ as they developed an automated technique to quantify the morphology of the foveal pit (depth, diameter, and slope) and observed significant variation in all three parameters between Africans, African Americans and Caucasians and found that African, African Americans had significantly deeper and broader foveal pits than the Caucasians. This is consistent with the finding of Nolan et al as they stated that whites had significantly narrower foveal width measurements than did nonwhites.⁽¹⁰⁶⁾ As they observed about a $100 \mu\text{m}$ difference in foveal diameter between whites and non-whites which is half the magnitude of the difference reported in Wagner-Shuman et al.

Al-Hadad et al reported that the CSF thickness in Middle Eastern children 6 to 17 years of age using Cirrus OCT was $249.1 \pm 20.2 \mu\text{m}$. This value is less than the CSF thickness in the present study by Spectralis OCT.⁽¹⁰⁷⁾ Barrio-Barrio et al reported that the CSF thickness in Caucasian children 4-17 years using Cirrus OCT was $253.85 \pm 19.7 \mu\text{m}$, which is also less than the present study with Spectralis SD-OCT.⁽¹⁰⁸⁾

This could be explained by difference in segmentation algorithm between Cirrus and Spectralis OCT. Cirrus segmentation algorithm placed the PRE boundary line just below the front edge of the hyper-reflective band interpreted as the anatomic RPE. The Spectralis OCT typically segments the back edge of the same hyper-reflective band, leading to somewhat thicker retinal thickness measurements.⁽⁵⁵⁾ Considering this factor, the CSF thickness in the present study is very comparable to Al-Hadad et al and Barrio-Barrio et al.^(107,108)

Read et al reported the mean CSF thickness in Australian children aged 4-12 years using Copernicus SD-OCT. The majority of participating children were of white ethnic origin, while the remaining children having East Asian, Middle Eastern, South American and Indian ethnic origins. Scott et al reported CSF thickness of $255 \pm 16 \mu\text{m}$ for those children.⁽¹⁰⁹⁾ This result is comparable to the present study. Considering the difference in segmentation algorithm between Copernicus and Spectralis OCT. As the boundaries for macular thickness in Copernicus OCT is defined as the distance from internal limiting membrane to the outer segment of the photoreceptor, and the boundaries for macular thickness in Spectralis OCT is defined as the distance from the internal limiting membrane to the outer RPE/Bruch Membrane.⁽¹¹⁰⁾

In the present study, topographically the foveal center was the thinnest, macular thickness increased gradually to reach its maximum in the inner ring then decreased again. In the inner ring, there were no statistically significant differences between the different inner ring subfields except for the temporal subfield ($330.4 \pm 16.8 \mu\text{m}$) being statistically thinner than the superior, nasal and inferior subfields (343.7 ± 18.1 , 341.2 ± 16.9 and $340 \pm 17.6 \mu\text{m}$ respectively). This is consistent with previous OCT studies in adults.⁽¹¹¹⁻¹¹⁷⁾

This could be explained anatomically by that, the ETDRS inner ring corresponds to regions with the thickest total retina and ganglion cell layer and a relatively thin RNFL. The relatively symmetric macular configuration in the inner ring may reflect the symmetric nature of the anatomic configuration of the retinal layers beneath the RNFL.⁽¹¹⁷⁾ In the outer ring, the temporal subfield ($290.3 \pm 20.1 \mu\text{m}$) was the thinnest followed by inferior, superior and nasal subfields (294.1 ± 17.9 , 302.4 ± 24.9 and $315.5 \pm 19.5 \mu\text{m}$ respectively) and this difference was statistically significant. Greater asymmetry of the macular thickness of the outer ring compared with that of the inner ring may be due to the vertically symmetric, but horizontally asymmetric anatomic nature of the RNFL, in which retinal nerve fibers from the superior and inferior arcuate bundles and the papillomacular bundle converge towards the optic disc.⁽¹¹⁷⁾

In the present study, males had thicker CSF thickness (264.3 ± 18.8) compared to females ($255.8 \pm 25.4 \mu\text{m}$) but this was not statistically significant. In spite of this the mean retinal thickness in the inner ETDRS sub-fields and the average of inner ring were significantly thicker in males ($343.4 \pm 17.3 \mu\text{m}$) than female ($334.6 \pm 14.4 \mu\text{m}$), but there is no statistically significant difference in the outer ETDRS sub-fields and the average outer ring between males and females. Chopovska et al reported that, the CSF and all inner ETDRS subfields were significantly thicker in males than in females.⁽¹⁰¹⁾

Al-Hadad et al, Barrio-Barrio et al and Huynh et al reported that gender differences applied only in CSF measurements which were significantly increased in males.^(97,107,108)

Turk et al and Yanni et al and found that no intersex difference in macular thickness using spectralis SD-OCT in pediatric populations.^(87,99)

Read et al reported that no intersex difference in macular thickness using Copernicus SD-OCT in pediatric population.⁽¹⁰⁹⁾

Other studies showed that the mean retinal thicknesses in all regions of the ETDRS grid were significantly thicker in males than in females in adults.^(110,117-122)

The layer responsible for the intersex difference in retinal thickness is yet unknown.⁽¹¹⁷⁾ As the minimum thickness of nerve fiber layers and maximum thickness of photoreceptor outer segments occur in the CSF and inner macular regions, the retinal layers responsible for intersex differences may be located underneath the nerve fiber layer. In addition, most previous studies reported no intersex difference in mean circumpapillary RNFL thickness.^(123,124) Another study by Abou Shousha et al using Cirrus OCT reported that RNFL thickness is higher in males than in females.⁽¹²⁵⁾ A recent study by Ooto et al.⁽¹²⁶⁾ using a 3D SD-OCT (Topcon) with the new automated retinal layer segmentation algorithm⁽¹²⁷⁾ to measure the thickness of individual retinal layers found that the INL and OPLwith ONL were significantly thicker in males than females.

In the current study the mean retinal thickness in all regions of the ETDRS grid found no significant difference between the right and left eye. This is in accordance with previous studies of Appukuttan et al and Wagner –Schuman et al.^(105, 128)

The current study included three different age groups (6-<10,10-<14,14-16).Therefore a generalized relationship with age is obtained. The present study showed increase in the CSF thickness between ages 6-16years, with CSF averaging 10 μ m less in children aged 6-<10 years than in children aged 10-16 years but these results were not statistically significant. Yanni et al found that a significant increase in CSF thickness between ages 5-15 years, with CSF thickness averaging 10 μ m less in children aged 5-7 years than in children aged 11-15 years.⁽⁹⁹⁾ This trend is consistent with anatomic studies suggesting continued development of the fovea beyond the age of 5 years.^(129,130) In the present study the inner ring EDTRS subfields had a statistically significant increase in thickness with age. This is consistent with the previous studies of Al-Haddad et al and Chopovska et al^(107,101) Several other studies using the stratus OCT found no relationship of central subfield thickness with age.^(93,131-134) This could be explained by increasing length of the OS of the photoreceptor cells at the fovea with age,⁽¹³⁰⁾ as no such association was found for stratus OCT, where OS are not included into the measurement of the retinal thickness.^(135,136) A Positive correlation between central subfield thickness and age was found in children by Huynh et al⁽⁹⁷⁾.

Similar to the present study, Read et al found that a significant increase in CSF and MIM thickness with age, as they found increase in retinal thickness of about 1.7-1.8 μ m per year.⁽¹⁰⁹⁾

Elkayal et al reported that the CSF thickness of the adult Egyptians with Spectralis OCT was 262.7 \pm 19.64 μ m.⁽¹³⁷⁾ In comparison of the present study with Elkayal et al there is no significant difference in CSF and inner ring values between children and adults, As

CSF thickness in children was $259.9 \pm 22.8 \mu\text{m}$ and in adults was $262.7 \pm 19.6 \mu\text{m}$, and MIM thickness in children was $338.8 \pm 16.4 \mu\text{m}$ and in adults was $338.14 \pm 14.7 \mu\text{m}$. but there is significant difference in the mean outer ring thickness in children ($300.6 \pm 17.4 \mu\text{m}$) and adult ($293.9 \pm 11.5 \mu\text{m}$).

Abou Shousha et al reported that the CSF thickness in adult Egyptians using Cirrus OCT was $242 \pm 18 \mu\text{m}$. This value is less than CSF thickness in Egyptian Children.⁽¹²⁵⁾ Considering the difference in segmentation algorithm between Cirrus and Spectralis, this could explain the lower value of normal CSF reported by Abou Shousha et al compared to the present study.

SUMMARY

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Spectral domain optical coherence tomography (SD-OCT) is a non-invasive, cross-sectional and highly reproducible imaging technique that can measure macular thickness. OCT rapidly has become a popular technique for diagnosis and determining progression of retinal diseases. Macular thickness may be affected by many ocular and systemic diseases and normative database is needed to distinguish normal macular thickness measurements from abnormal measurements. Macular thickness measurements via OCT and their reproducibility have been studied extensively in the past. A normative data base is not available for pediatric population.

The present study was conducted to determine the normative data of macular thickness in the Egyptian children and to assess the effect of age, gender, and laterality of the eye on it. Fifty healthy Egyptian children underwent a comprehensive ophthalmic examination, including Spectralis SD-OCT scanning, in the Alexandria Main University Hospital. The images were obtained over maculae, using the fast volume scan protocol. Macular thickness was calculated based on center thickness and nine areas that corresponded to the ETDRS map by OCT mapping software. The relationships between macular thickness and sex, age, laterality of the eye were analyzed in this cross-sectional study.

There were 24 (48%) males and 26 (52%) females. The range of age was 6-16 years, the mean age of the subjects was 10.2 ± 2.7 years. The mean central subfield thickness was 259.9 ± 22.8 μm . Mean macular thickness values in the Egyptian children was found to be less than those seen in the Spectralis SD-OCT studies published previously on American and German children but it was near to the studies on Turkish children.

The mean macular thickness values in all inner ETDRS subfields were significantly greater in males than in females. There was no significant difference in CSF and outer ETDR subfields between males and females. There was no significant difference in macular thickness values between right and left eye in the studied children. The inner macular thickness increase significantly in the all inner ETDRS subfields with age. There is no significant difference in CSF and outer ETDR subfields between age groups.

CONCLUSIONS

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- Normal central subfield thickness in Egyptian children is $259.9 \pm 22.8 \mu\text{m}$.
- Normal mean inner macular thickness in Egyptian children is $338.8 \pm 16.4 \mu\text{m}$.
- Normal mean outer macular thickness in Egyptian children is $300.6 \pm 17.4 \mu\text{m}$.
- Males have thicker mean inner macula than females.
- There is no effect for sex on the central subfield and the mean outer macular thickness.
- There is no difference between the right and left eye in the all nine early treatment diabetic retinopathy subfields.
- Mean inner macular thickness increase significantly with age.