

MACULAR THICKNESS MEASUREMENTS IN HEALTHY EYES USING SPECTRAL OPTICAL COHERENCE TOMOGRAPHY

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ABSTRACT

AIM: The aim of the present study was to measure macular thickness in healthy eyes and find whether it changes with age.

MATERIAL AND METHODS: We examined 163 healthy eyes of 84 healthy volunteers. In order to measure their macular thickness the patients were examined using spectral-domain optical coherent tomography (SD-OCT – iVue, Optovue). They were allocated into 6 age groups.

RESULTS: The mean central macular thickness (inner circle - fovea centralis) was $248.9 \pm 17.9 \mu\text{m}$ (mean $\pm$ SD), and the mean total macular thickness (an area including 9 subfields as defined by ETDRS) was $286.2 \pm 13.9 \mu\text{m}$ (mean $\pm$ SD). We found that it correlated negatively with age ($r = -0.18$; $p = 0.03$; Pearson correlation).

CONCLUSION: We found a statistically significant decrease of mean macular thickness as age increased.

Key words: optical coherence tomography (OCT), macular thickness, healthy eyes

INTRODUCTION

Macular thickness and the macular region changes correlate with the changes of the visual function.¹ Macular edema results in increased retinal thickness and often causes vision loss. This process can be found in patients with diabetic retinopathy, retinal vein occlusion, uveitis and other ocular disorders.^{2,3} Good knowledge of retinal parameters can help in diagnosing various pathological processes and in the follow-up study after therapy.⁴

Optical coherence tomography (OCT) is a method used for macular thickness measurement and quantitative assessment of the retina.^{4,5} It is a modern non-contact, non-invasive 3-D imaging technique to perform diagnostics of the retina and the optic nerve.^{7,8} OCT works in a way very similar to B-scan ultrasound, but instead of ultrasound the OCT instruments use a beam of light emitted from a low-frequency laser source with 840 nm wave-length, which makes the OCT resolution much higher than the B-ultrasound.^{11,12} This method is harmless, repeatable and allows saving of the obtained information which enables clinicians to make comparative assessment of various methods of examination.¹³

AIM

The aim of the present prospective study was to measure the macular thickness in healthy eyes and

find if it changes with age.

MATERIAL AND METHODS

A total of 163 healthy eyes in 84 volunteers were included in the study (mean age of patients was 54.3 ± 13.3 years, a range of 20-78 years) examined at the University Clinic of Ophthalmology, Medical University-Plovdiv between January 17 and January 28, 2011. Female patients were predominant. Of all 84 volunteers 23 (27.4%) were males (44 eyes) and 61 (72.6%) were females (119 eyes). The patients were allocated into six age groups as follows: 20-29, 30-39, 40-49, 50-59, 60-69 and 70-79 years. All participants were Caucasian.

Exclusion criteria included any history of and/or evidence of retinal disorder, diabetes mellitus (with/without eye pathology – some studies have reported a greater macular thickness in patients with sub-clinical manifestation of diabetes mellitus⁴) or other systemic disease that could affect the eye, visual acuity < 0.5 (20/40), refractive spherical abnormalities $> \pm 5.0$ dioptres and astigmatism $> \pm 2$ dioptres, glaucoma, intraocular surgery (including cataract extraction) or laser therapy, and opacities in the vitreous body that may compromise the quality of the results.

In order to measure their macular thickness the patients were examined with the help of spectral-domain optical coherence tomography (SD-OCT

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- iVue, Optovue 100, 26 000 scans/sec., 5 μ resolution). Two strategies were used for scanning of the macular region: Retinal Map and High Resolution Cross Line. Retinal Map is a scan of 13 horizontal lines scanning an area of 6 mm in length and 5 additional horizontal lines scanning the central 2-mm zone. Scanning was performed on an area 6 x 6 mm (Fig. 1).

The parameters used to analyse retinal thickness were plotted on the chart with nine subfields as defined by Early Treatment Diabetic Retinopathy Study (ETDRS). The chart includes one central circle 1 mm in diameter in which the measured thickness is defined as central foveal thickness (CFT) and two peripheral rings divided into four quadrants (nasal, superior, temporal and interior). The inner ring has a radius of 1.0-3.0 mm and covers the para-macular zone. The outer ring has a radius of 3 to 6 mm and corresponds to the peri-macular zone. The thickness of the nine sectors is calculated automatically yielding digitally coded data. Mean total macular thickness (TMT) is calculated on the basis of all measurements in the nine quadrants using the following formula: $1/36$ (CFT) + $1/18$ (the sum of the inner four quadrants) + $1/16$ (the sum of the outer four quadrants).^{4,14}

SPSS 17.0 was used in the statistical analysis of the results. Descriptive analysis was used to determine the mean values (means) and the standard deviation (SD); analysis of correlation (the Pearson correlation) was used to find the correlation between two continuous quantities (the results were considered to be statistically significant at

$p < 0.05$); comparative analysis was used for statistical comparison of results obtained for the different age groups (one-way ANOVA, Bonferroni).

RESULTS

The mean CFT (central circle-fovea centralis) was found to be $248.9 \pm 17.9 \mu\text{m}$ (mean $\pm$ SD) and TMT (a region including 9 subfields as defined by ETDRS) was $286.2 \pm 13.9 \mu\text{m}$ (mean $\pm$ SD). The macular centre in the foveola region was the thinnest ($p < 0.001$, one-way ANOVA, Bonferroni), followed by the outer ring ($p < 0.001$, one-way ANOVA, Bonferroni). Maximal retinal thickness was found in the region of the inner ring ($p < 0.001$, one-way ANOVA, Bonferroni). Within the inner ring the temporal quadrant was the thinnest ($p < 0.001$, one-way ANOVA, Bonferroni), and the superior quadrant was not statistically significantly different from the nasal and interior quadrants. In the outer ring the nasal quadrant was the thickest ($p < 0.001$, one-way ANOVA, Bonferroni), followed by the superior quadrant ($p < 0.001$, one-way ANOVA, Bonferroni) and the difference in absolute values between the interior and the temporal quadrants was not significant (Fig. 2). Macular thickness of all 9 quadrants as defined by ETDRS is shown in Table 1 by age groups.

The statistical analysis of the results showed that mean CFT did not decrease significantly with age ($r = 0.04$; $p = 0.64$) (Table 2). We established an age-dependent decrease of TMT ($p = 0.003$; one-way ANOVA, Bonferroni) ($r = -0.18$; $p = 0.03$; Pearson correlation) (Fig. 3).

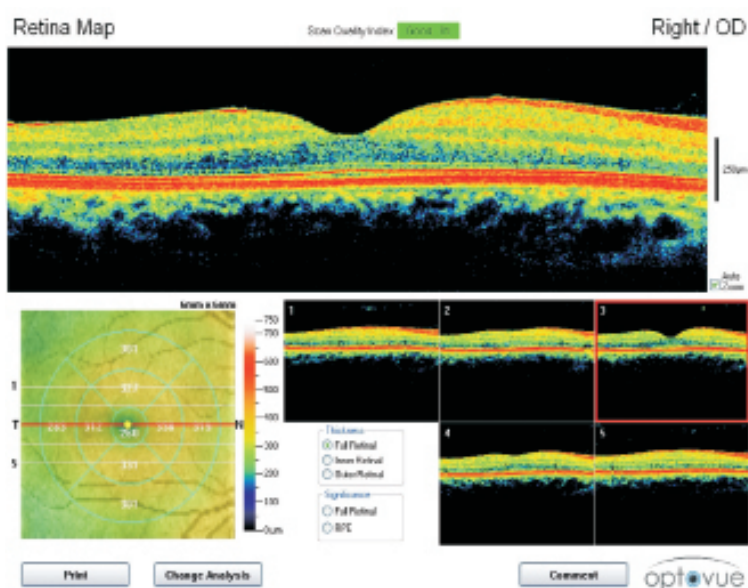


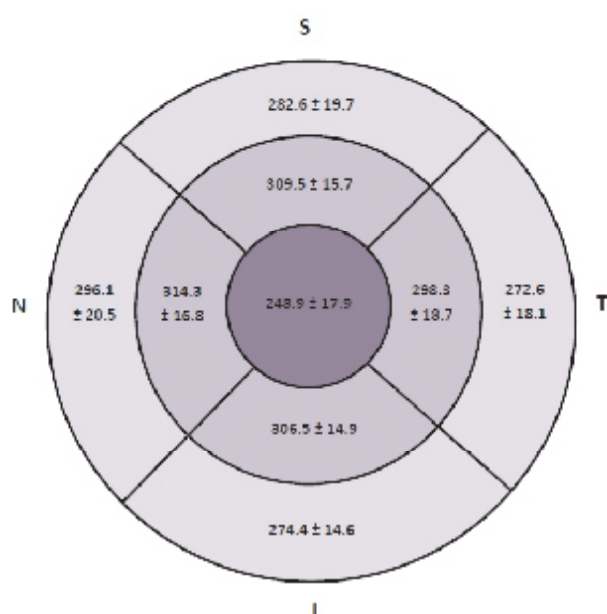
Figure 1. Retinal thickness mapping.

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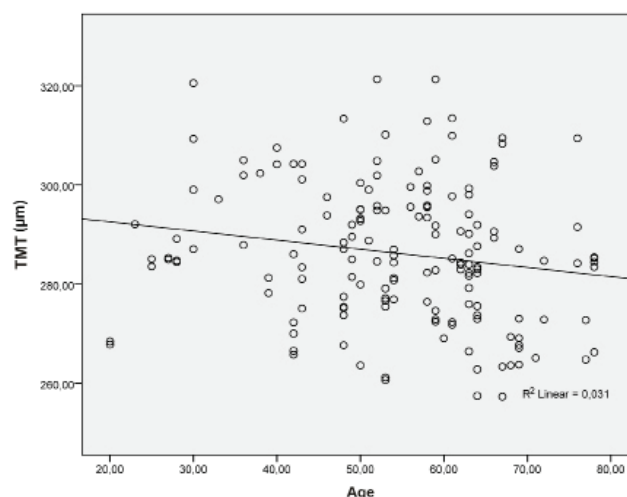
Table 1. Macular thickness (μm) (mean $\pm$ SD) of the examined healthy eyes by age groups

Age (years)	20-29	30-39	40-49	50-59	60-69	70-79
Number of eyes	11	11	28	51	49	13
Center	245.3 $\pm$ 8.4	253.6 $\pm$ 7	245.5 $\pm$ 16.8	251.9 $\pm$ 20.9	250.4 $\pm$ 18.1	238 $\pm$ 15.3
Nasal inner	311.4 $\pm$ 8.8	327.9 $\pm$ 13.1*	313.8 $\pm$ 14.1	315.6 $\pm$ 18.8	313 $\pm$ 17.3	305.8 $\pm$ 15.7*
Superior inner	305.6 $\pm$ 13	322.5 $\pm$ 12.5**	311.7 $\pm$ 14	311.3 $\pm$ 16.3	307.6 $\pm$ 15.9	297.6 $\pm$ 11.1**
Temporal inner	287.1 $\pm$ 16.6	307.6 $\pm$ 13.3	301 $\pm$ 15.3	302.6 $\pm$ 21.2	295.4 $\pm$ 17.2	288.4 $\pm$ 17.8
Inferior inner	303.3 $\pm$ 8.5	318 $\pm$ 13.8	305.8 $\pm$ 14.7	308.1 $\pm$ 14.6	304.8 $\pm$ 16.4	300.9 $\pm$ 12.1
Nasal outer	294 $\pm$ 9.7	305.1 $\pm$ 12.7	295.3 $\pm$ 22.6	302.2 $\pm$ 24.6*	290.1 $\pm$ 17.2*	290.7 $\pm$ 12.8
Superior outer	281.8 $\pm$ 10.3	298.9 $\pm$ 30.3**	280.1 $\pm$ 12.8	286.7 $\pm$ 18.9	276 $\pm$ 15**	283.1 $\pm$ 33.1
Temporal outer	270 $\pm$ 7.6	283.4 $\pm$ 28.4	274.4 $\pm$ 16.4	275.9 $\pm$ 20.8	268 $\pm$ 14.3	266.6 $\pm$ 13
Inferior outer	268 $\pm$ 9.4	282.3 $\pm$ 9.9	274.4 $\pm$ 15.6	277.6 $\pm$ 14.4	272.4 $\pm$ 16	268.4 $\pm$ 8.9
Overall	282.7 $\pm$ 7.6	297.2 $\pm$ 12.7*	286.1 $\pm$ 13.5	290 $\pm$ 13.5	282.2 $\pm$ 14.4*	280.8 $\pm$ 12.5*

* - at $p < 0.05$; ** - at $p < 0.01$; one-way ANOVA, Bonferroni analysis.

**Figure 2.** Macular thickness (μm) of the examined eyes in 9 subfields as defined by ETDRS (mean $\pm$ SD).**Table 2.** Correlation between mean macular thickness and age in 163 healthy eyes examined by OCT.

Correlations	r	p
Central	- 0.04	0.64
N - inner ring	- 0.15	0.06
S - inner ring	- 0.20	0.01
T - inner ring	- 0.10	0.20
I - inner ring	- 0.14	0.07
N - outer ring	- 0.12	0.13
S - outer ring	- 0.17	0.04
T - outer ring	- 0.17	0.03
I - outer ring	- 0.24	0.09
Overall	- 0.18	0.03

**Figure 3.** Correlation between total macular thickness (μm) and age in 163 healthy eyes under examination.

We found a significant thinning with age (though of low correlation) in the superior ($p = 0.003$), the temporal ($p = 0.009$) and the nasal ($p = 0.04$) quadrants of the inner ring and in the superior ($p = 0.006$), the nasal ($p = 0.032$) and the inferior ($p = 0.048$) quadrants of the outer ring (one-way ANOVA, Bonferroni) (Table 1).

CFT and TMT in the male subjects were $253.4 \pm 17.5 \mu\text{m}$ and $288.8 \pm 14.9 \mu\text{m}$, respectively; in the female subjects these were $247.3 \pm 17.9 \mu\text{m}$ and 285.3 ± 13.5 . Accordingly to gender the difference for CFT was marginally significant ($p = 0.053$; $r = - 0.15$; Pearson correlation), and for TMT it failed to reach significance ($p = 0.15$; $r = - 0.11$; Pearson correlation) for sex (Fig. 4).

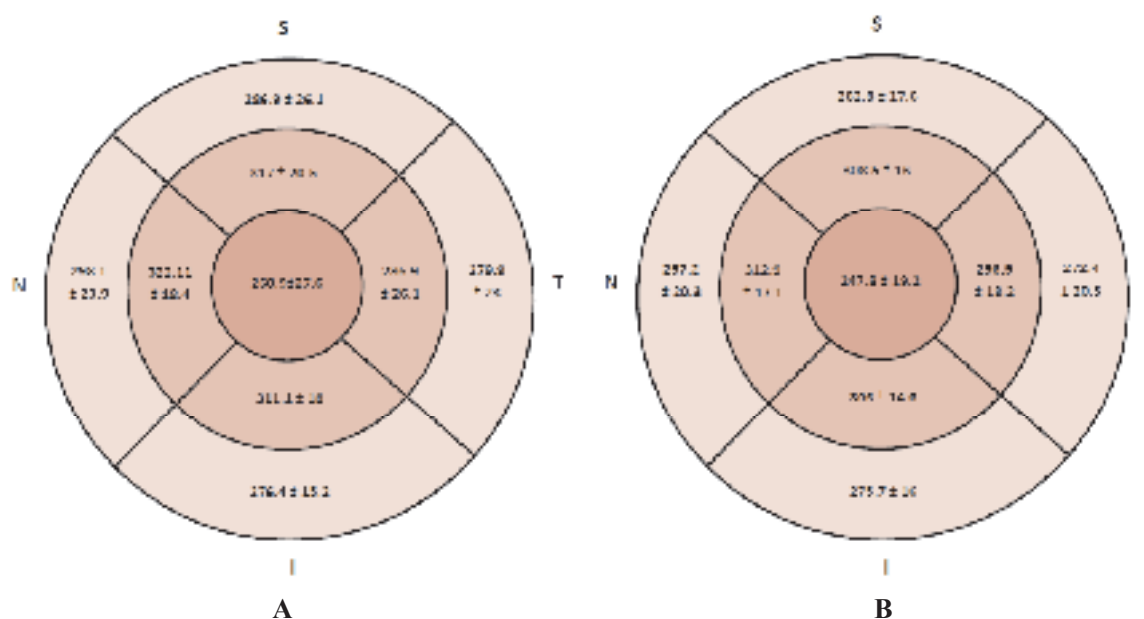


Figure 4. Macular thickness (μm) in males (A) and females (B) in the 9 subfields as defined by ETDRS.

DISCUSSION

The data entered in the instrument give a mean foveal thickness of $247 \pm 26.3 \mu\text{m}$, which is very close to the results we obtained herein – $248.9 \pm 17.9 \mu\text{m}$ for CFT. Wolf-Schnurbusch et al.¹⁵ examined each study patient using six different OCT instruments (1 time-domain system and 5 spectral-domain systems) and compared their central macular thickness; the results were in the range of $212 \pm 19 \mu\text{m}$ to $289 \pm 16 \mu\text{m}$. According to RTVue 100 (Optovue, Meditec) in the present study the mean CFT was $247 \pm 26 \mu\text{m}$.¹⁵ Menke et al. studied healthy volunteers and found a mean CFT of $231 \pm 23 \mu\text{m}$ and TMT – $265 \pm 27.7 \mu\text{m}$ when measured with RTVue; when measured with Cirrus OCT the mean CFT was $266 \pm 20 \mu\text{m}$ and TMT was $300 \pm 27.7 \mu\text{m}$, respectively.¹⁶ These results are consistent with those obtained by Sull et al. with healthy volunteers who were examined with RTVue: $267 \pm 15 \mu\text{m}$ (MM5) and $256 \pm 15 \mu\text{m}$ (MM6).¹⁷ In earlier studies of Hee et al.¹⁸ the mean CFT was much thinner ($174 \pm 18 \mu\text{m}$) in comparison with the results of the present study. The difference in retinal thickness when measured by different OCT apparatuses is caused by the different patterns of delineation of the outer boundary. When retinal thickness is measured (retinal thickness is the boundary between the internal limiting membrane (ILM) and the retinal pigment epithelium (RPE), all OCT instruments define ILM as the inner boundary. Stratus OCT defines the outer retinal boundary above the junction between the inner and the outer

segments (OS/IS) of the photoreceptors.¹⁹⁻²¹ Cirrus HD-OCT and RTVue 100 include the outer segment as well and measure nearer to the RPE. 3D OCT-1000 measures even nearer to RPE. The distance between the RPE/Bruch's membrane and IS/OS is from $60 \mu\text{m}$ to $80 \mu\text{m}$, which explains also the differences for one and the same retinal thickness measured by different OCT instruments.^{16,17} The differences in the parameters may also be due to the different direction of the scans applied.¹ The greater retinal thickness, which is reported in some recent studies, is probably due to the higher resolution of the OCT systems and the shorter time of scanning which minimizes the risk of sight deviation from the fixation point during examination. Even the smallest deviation of patient's sight from the fixation point may result in increased retinal thickness as the central region is a rather small area to measure and is most sensible during micro-movements of the eyes. It is obvious that TMT has greater practical application than CFT has and is a more reliable indicator in assessing macular changes.³

We found herein that the mean CFT does not decrease significantly with age, while other studies on healthy volunteers have found that it tends to increase.^{1,4} The increase of CFT in older patients is a result of the internal limiting membrane thickening and the centripetal forces of the vitreous body resulting in elevation of the fovea with age.^{4,14}

The mean TMT of healthy volunteers in the present study seems to decrease with age. Retinal thinning outside of the central macula is a result

of loss of photoreceptors, pigment epithelial cells and ganglion cells. The density of photoreceptors outside fovea centralis decreases significantly with age. That loss was more tangible for the rods than for the cones and was better expressed in the zone of 5-8 mm from the centre compared with that in the more peripheral zones - 14-20 mm from the centre. It is estimated, on the basis of literature data, that the cell loss per year is about 0.2% – 0.4% and it is similar to the loss of pigmented epithelial cells and ganglion cells.^{21,22} The loss of ganglion cells results in the thinning of the nerve-fiber-layer (a process which is associated with aging and does not affect the central foveal zone because of absence of a nerve-fiber-layer there).⁴

The topographic data we obtained in the present study showed that the nasal quadrant is the thickest in the outer ring, which may be accounted for by the anatomical distribution of the nerve fibres in the papillo-macular region. Similar results were obtained by Chan et al.²¹ Duan et al. found that in the region of the inner ring the superior quadrant was the thickest, and in the outer ring – it was again the nasal quadrant.⁴ We observed statistically more significant thinning in the superior and temporal quadrants of the inner ring and the superior quadrant of the outer ring. Further studies on which zone would change the most might lead to the identification of a selective region that is more susceptible to neural loss.¹³

Macular thickness is sex-dependent according to some studies^{4,23,24}, while others do not find such correlation^{1,17,25,26}. We found a marginal statistically significant difference in CFT according to gender: CFT was found to be greater in male than in female subjects. The female subjects in the present study were more than twice as many as men, which may potentially confound the correct interpretation of the results.

All participants in the present study are Caucasian. A statistically significant difference in macular thickness has been reported in literature between African Americans and the Caucasians: the macula is thinner in African-Americans than in Caucasian. This should be taken into consideration in patients with initial macular edema.^{2,4}

CONCLUSIONS

We have found a statistically significant decrease of the mean total macular thickness with age.

Our results may be used to build up a database which may be useful for the diagnosis, interpretation and treatment of a number of pathological processes

(glaucoma, diabetic retinopathy, vascular retinal disorders and uveitis) all resulting in changes of the retinal architectonics and poor visual response.

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ОЦЕНКА ТОЛЩИНЫ МАКУЛЫ ЗДОРОВЫХ ГЛАЗ С ПОМОЩЬЮ ОПТИЧЕСКОЙ КОХЕРЕНТНОЙ ТОМОГРАФИИ

В. Миткова-Христова, М. Конарева-Костянева

РЕЗЮМЕ

ЦЕЛЬ: Установить толщину макулы здоровых глаз и возможность ее изменения с возрастом.

МАТЕРИАЛ И МЕТОДЫ: Исследовано 163 здоровых глаза (84 пациента-добровольца). В целях верифицирования толщины макулы пациентов исследовали спектраль-домейн оптическим кохерентным томографом (SD-

OCT – iVue, Optovue). Пациенты разделены на 6 возрастные группы.

РЕЗУЛЬТАТЫ: Средняя центральная толщина макулы (внутренний круг-фовеа централис) – $248.9 \pm 17.9 \mu\text{m}$ (mean $\pm$ SD), а средняя тотальная толщина макулы (область, включающая 9 полетов по ET-DRS) – $286.2 \pm 13.9 \mu\text{m}$ (mean $\pm$ SD). Наблюдается отрицательная корреляционная связь с нарастанием возраста ($r = -0.18$; $p = 0.03$; Pearson Correlation).

ВЫВОДЫ: Полученные результаты показывают статистически значимое уменьшение средней толщины макулы с нарастанием возраста.