· Original article ·

Diurnal variation in choroidal thickness and body temperature

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脉络膜厚度与体温日间变化的研究

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摘要

目的:通过深度增强成像光断层扫描(EDI-OCT)技术以探究体温如何影响脉络膜厚度。

方法:前瞻性研究。通过 EDI-OCT 检测 9:00~17:00 中心凹(SF-CT),中心凹鼻侧 500μm(N-CT)和中心凹颞侧 500μm(T-CT)正常人(41 例)的脉络膜厚度(CT)。使用非接触式红外测温仪逐时检测体温(BT),以评估 CT 和 BT 日间变化的相关性。

结果:SF-CT 值在 9:00 和 13:00($P=0.021$),9:00 和 14:00($P=0.012$),9:00 和 16:00($P=0.048$),及 9:00 和 17:00($P=0.002$)之间存在显著性差异。N-CT 值在 8h 内(均 $P>0.05$)无显著性变化,9:00 和 13:00($P=0.004$)则存在明显差异。

结论:CT 与 BT 从 9:00~17:00 之间逐时变化无显著性差异。

关键词:体温;脉络膜厚度;日间变化

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Abstract

• AIM: To investigate how body temperature (BT) affects choroidal thickness (CT) according to measurements taken with enhanced depth imaging optical coherence tomography (EDI-OCT).

• METHODS: In this prospective study, the CT of 41 healthy patients was measured hourly from 9:00 to 17:00 at the fovea (SF-CT), 500 μm nasal to the fovea (N-CT), and 500 μm temporal to the fovea (T-CT) using EDI-OCT. BT was also measured hourly from 9:00 to 17:00 using a non-contact infrared thermometer. Possible correlations between diurnal variations of CT and BT were evaluated.

• RESULTS: SF-CT values significantly differed between measurements at 9:00 and 13:00 ($P=0.021$), 9:00 and 14:00 ($P=0.012$), 9:00 and 16:00 ($P=0.048$), and 9:00 and 17:00 ($P=0.002$). N-CT values also significantly differed between measurements at 9:00 and 13:00 ($P=0.004$), though T-CT did not significantly vary during the 8h period ($P>0.05$ for all).

• CONCLUSION: CT is not significantly associated with hourly changes in BT from 9:00 to 17:00.

• KEYWORDS: body temperature; choroidal thickness; diurnal variation

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INTRODUCTION

The choroid is an extensively vascularized, pigmented connective tissue that, with a thicker posterior than anterior, widens from the ora serrata to the optic nerve. The choroid bears one of the body's greatest tracts of blood flow, which supplies oxygen and nutrients to the retinal pigment epithelium and retina itself, at least to its inner nuclear layer, as well as calibrates temperature and transports waste[1].

The structural and functional health of the choroid's vasculature is also vital to retinal function. In fact, an abnormal blood volume in the choroidal tissue and/or compromised blood flow there may precipitate photoreceptor dysfunction and even death[2]. Different methods are available for measuring choroidal thickness (CT), including histology and ultrasonography, though the overall precision of these approaches remains poor. By contrast, new and improved methods, especially those involving spectral-domain optical coherence tomography (SD-OCT), can facilitate the *in vivo* assessment of choroidal pathology. For example, Spaide *et al*[3] have described an enhancing depth imaging (EDI) technique to optimize the properties of OCT acquisition in order to permit imaging CT in full. Detecting CT by using SD-OCT aids in investigating pathological changes related to

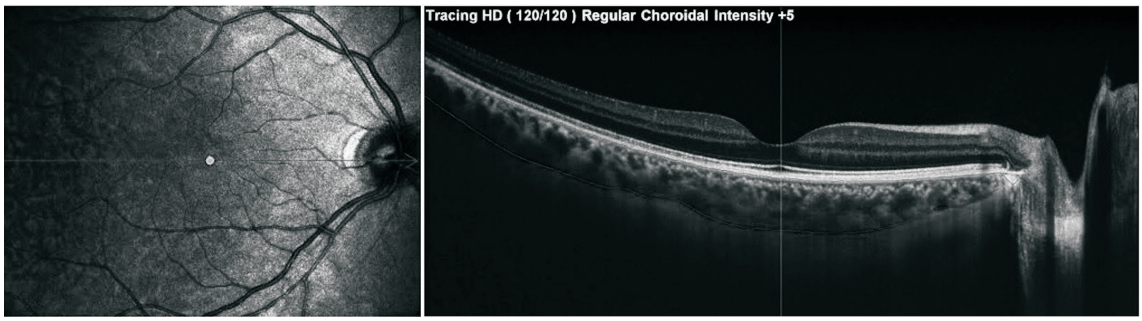

Figure 1 Optical coherence tomogram (enhanced depth imaging mode) of subfoveal choroid.

many ocular diseases, including degenerative myopia, age-related macular degeneration, central serous chorioretinopathy, diabetic retinopathy, polypoidal choroidal vasculopathy, Vogt-Koyanagi-Harada disease, and retinitis pigmentosa[4-8].

As choroidal vessels dilatate and vascular hyperpermeability develops, hydrostatic pressure within the choroidal tissue conclusively increases, thereby inducing choroidal thickening[8]. Several studies have determined that CT is influenced by an array of factors, including axial length (AL), age, refraction, central corneal thickness (CCT), intraocular pressure (IOP), ocular perfusion pressure, drinking coffee, and smoking[4,9-10]. At the same time, a few studies have found that CT exhibits diurnal variation[11-12].

Body temperature (BT) affects the blood flow either by active vasodilatation or by releasing the vessels' vasoconstrictor tone[13]. It was reported that BT varies day by day, suggesting that diurnal changes in CT may be associated with diurnal changes in BT[14]. To our knowledge, however, no study has demonstrated how, if at all, BT impacts CT and CT diurnal variation. With this study, we thus aimed to determine and describe how the BT of healthy subjects influences CT according to measurements gathered with enhanced depth imaging optical coherence tomography (EDI-OCT).

SUBJECTS AND METHODS

The right eyes of 41 (15 males, 26 females) healthy volunteers from the staff of the Department of Ophthalmology at Fatih University were included in the analysis. Data were evaluated prospectively. No participant smoked or consumed any caffeine for at least 12h prior to measurement. The study was conducted according to Declaration of Helsinki.

The inclusion criteria for all participants consisted of a best-corrected visual acuity of 20/20 or better, spherical refraction between +2.00 and -2.00 diopters (D), an AL of less than 25 mm, normal optic nerves without any abnormality in the neuroretinal rim, and a normal anterior chamber with an open angle. By contrast, exclusion criteria included any ocular disease, a history of ocular hypertension or glaucoma, tilted disc syndrome, refractive error greater than ±2.00 D, history of ocular surgery, AL greater than 25 mm, and systemic disease such as diabetes mellitus and hypertension.

All participants received a full ophthalmological examination including the measurement of corrected visual acuity. The refraction, axial measurements, age, gender, and BT of participants were also recorded. Objective refraction was evaluated with an autorefractometer (NIDEK ARK-1, serial No. 430087, Gamagori, Japan) and best corrected visual acuity was measured using Snellen charts. Biomicroscopic and fundoscopic examinations were conducted, and IOP was measured with a Goldmann applanation tonometer. Ocular AL was measured using biometrics (NIDEK US-4000 echo scan, serial No. 40811, Gamagori, Japan).

Meanwhile, BT was measured using a non-contact infrared thermometer (Microlife NC100, Widnau, Switzerland). Temperature measurements were taken by holding the thermometer approximately 3 cm from the body surface (forehead). All measurements were performed three times and average measurements obtained. The non-contact thermometer was first calibrated to the air-conditioned room temperature of 23.5℃ and then held perpendicular to the mid-forehead, thereby converging the thermometer's two range-finding, red-light-emitting diodes into one luminous point. The device was held in this position until a reliable reading was confirmed.

Measuring CT was performed by following the standard screening procedure with a retinal scanner (RS-3000 OCT Retina Scan, NIDEK, Gamagori, Japan), a high-speed SD-OCT/confocal ophthalmoscopic system. The retinal scanner supplies 53 000 A-scans/s and a 4-micron OCT axial resolution, which during acquisition by tracing improves the accuracy, as well as two additional higher-sensitivity scanning modes, which allow tracing that facilitates imaging *via* media opacities. The choroidal mode permits the exhaustive evaluation of the choroid with an extensive area scan of 9×9 mm showing the separate retinal layers. This mode also provides an accurate alignment of up to 120 macular line scanned images for expanded image averaging.

All SD-OCT and BT measurements were obtained by the same investigator from 9:00 to 17:00 hourly for both eyes. CT was measured using the SD-OCT software (NAVIS-EX Image Filing Software, RS-3000 OCT) and determined as the vertical distance between the hyperreflective pigment epithelial layer automatically detected by the instrument and the choroid-sclera junction, which was marked manually marked. CT was measured at the fovea (SF-CT), 500 μm nasal to the fovea (N-CT), and 500 μm temporal to the fovea (T-CT) (Figure 1). Only the CT of the right eye of each participant was determined.

Table 1 The distributions of defining characteristics

Parameters	Mean±SD[1] (Min/Max)[2]
Age (a)	31.9±9.2 (20.0/53.0)
Refraction, Diopter	0.5±1.3 (−2/2.5)
Axial length (mm)	23.1±0.8 (20.5/24.9)
Gender(F/M)(%)	26/15(63.4/36.6)

[1]SD: Standart deviation; [2]Min/max: minimum/ maximum.

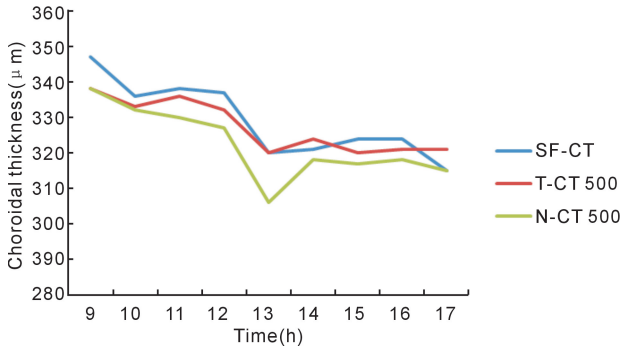

Figure 2 The mean choroidal thickness values at different measurement times.

Data Analysis All statistical analyses were performed using the Statistical Package for the Social Sciences version 16 (SPSS Inc. Chicago, IL, USA). The normality of data was confirmed using the Kolmogorov-Smirnov test, and an independent Student's *t*-test was applied to compare variables between groups. Pearson's correlation was implemented to examine the relationships among measured variables. Variation in CT was assessed using general linear models with repeated-measures analysis of variance. A $P<0.05$ was considered to be significant.

RESULTS

Forty-one healthy patients without any systemic or ocular diseases were included in the study sample. Twenty-six patients (63.4%) were female and 15 (36.6%) were male. The age of patients ranged from 20-53y with a mean age of 31.9±9.17y.

All eyes exhibited a best corrected visual acuity of 0.00 logMAR units, while refraction values ranged from −2 to 1.50 D with a mean of 0.50±1.25 D. The AL of participants ranged from 20.55 to 24.95 mm with a mean of 23.10±0.85 mm, while mean IOP was 14.3±2.3 mmHg. Table 1 shows the sample's demographic data.

All parts of the choroid were found to be thickest at 9:00 in the morning, when SF-CT, T-CT, and N-CT were found to be 347±80 μm, 338±68 μm, and 338±84 μm, respectively. SF-CT declined to 320±78 μm at 13:00, 321±78 μm at 14:00, 324±84 μm at 16:00, and 315±84 μm at 17:00. N-CT became thinner at 13:00, when it was found to be 306±80 μm. T-CT showed no alteration during these hours. The diurnal pattern of CT is reported in Figure 2 and Table 2 and 3.

Subfoveal CT values differed significantly between measurements taken at 9:00 and 13:00 ($P=0.021$), 9:00 and 14:00 ($P=0.012$), 9:00 and 16:00 ($P=0.048$), and 9:00 and 17:00 ($P=0.002$). The N-CT value also differed significantly between measurements taken at 9:00 and 13:00 ($P=0.004$), though T-CT showed no statistically difference during 9:00-17:00 ($P>0.05$ for all).

A correlation analysis was performed for changes between each pair of sequential time points for CT values and between each pair of sequential time points for BT values. Ultimately, no significant correlations were observed ($P>0.05$ for all).

DISCUSSION

This observational study showed that BT did not significantly influence CT from 9:00 to 17:00 according to hourly measurements taken using EDI spectral-domain OCT in the healthy patients. We did not find daily alterations in BT according to hourly measurements during this period either. We did, however, find significant diurnal variation in SF-CT and N-CT according to SD-OCT, despite finding no difference in T-CT.

Recent studies have expanded current understandings of circadian rhythms according to CT in humans. Previous studies were reported that CT was greatest in the evening and least in the morning[15-16]. On the other hand, some studies were determined a circadian rhythm in CT with a maximum thickness early in the morning and a minimum thickness later in the evening[12,17-18]. By contrast, Osmanbasoglu *et al*[19] found no significant diurnal variation in CT in their study population. Usui *et al*[12] and Tan *et al*[17] determined that mean CT decreased during the day, whereas Chakraborty *et al*[15], Toyokawa *et al*[16] and Lee *et al*[18] found increases in their populations.

In the present study, we found diurnal variation in SF-CT and N-CT. All parts of the choroid were found to be thickest at 9:00 and to become progressively thinner over the course of the day. SF-CT became thinner at 13:00, 14:00, 16:00, and 17:00, while N-CT statistically became thinner at 13:00. T-CT had no statistically alteration during the daytime. We determined that CT was greatest in the morning and thinned as the afternoon and evening progressed. As our results show, all parts of the choroid were thickest at 9:00; SF-CT was thinnest at 17:00, T-CT at both 13:00 and 16:00, and N-CT at 13:00.

Other studies have reported that CT correlated significantly with AL[15,17,20] while others still have determined that increased age, eyes with longer AL or myopic refraction, lower diastolic perfusion pressure, and thicker CCT correlated with thinner choroids[4,9,20].

Though many physiological parameters have been shown to affect CT, there is limited evaluation of the potential effect of various physiological factors on diurnal changes in CT. Lee *et al*[18] determined that the pattern and amplitude of CT's diurnal rhythm correlated significantly with AL, while Vural *et al*[10] reported that drinking coffee causes a significant decrease in CT for at least 4h after consumption.

Table 2 Mean BT and choroidal thickness values at different measurement times Mean±SD

Parts of the choroid	Measurement times (hours)								
	9:00	10:00	11:00	12:00	13:00	14:00	15:00	16:00	17:00
BT(℃)	36.7±0.5	36.7±0.5	36.8±0.4	36.7±0.4	36.7±0.4	36.7±0.4	36.6±0.5	36.6±0.5	36.7±0.4
SF-CT(μm)	347±80	337±75	338±81	336±73	320±78	321±78	324±84	324±84	315±84
T-CT(μm)	338±68	335±67	336±69	332±65	320±67	325±65	320±71	319±68	321±69
N-CT(μm)	338±84	330±82	327±82	325±76	306±80	317±71	316±81	317±82	314±78

BT: Body temperature; SF-CT: Subfoveal choroidal thickness; T-CT: Fovea to temporal 500μm; N-CT: Fovea to nasal 500 μm.

Table 3 Changes of BT and choroidal thickness between the sequential measurement Mean±SD

Parts of the choroid	Measurement times (hours)							
	9:00-10:00	10:00-11:00	11:00-12:00	12:00-13:00	13:00-14:00	14:00-15:00	15:00-16:00	16:00-17:00
BT(℃)	0.1±0.3	0.02±0.3	-0.1±0.3	0.02±0.4	-0.01±0.4	-0.08±0.4	0.02±0.5	0.07±0.4
SF-CT(μm)	-9±29	1±35	-2±35	-16±42	1±26	4 ±34	-1±34	-8±37
T-CT(μm)	-4±29	2±45	-5±39	-12±42	5±28	-5±42	-1±41	2±38
N-CT(μm)	-8±34	-3±33	-2±35	-19±43	10±29	0±31	1±27	-3±40

BT: Body temperature; SF-CT: Subfoveal choroidal thickness; T-CT: Fovea to temporal 500μm; N-CT: Fovea to nasal 500 μm.

The primary circadian pacemaker is the suprachiasmatic nucleus located within the hypothalamus, which receives direct input regarding the solar cycle from the retina[21]. The retino-hypothalamic pathway coordinates daily biological rhythms such as hormone secretion, temperature fluctuation, and neural activation[22]. Several studies have reported that BT also exhibits diurnal rhythms[21] and is controlled within a highly limited range[23]. Miyazaki *et al*[24] reported that beagles' BTs were higher after feeding but decreased by 0.2℃ by the following early morning. It has been reported that BT in humans rises during the day and declines during the night, data which were found to be related to locomotor activity[23]. Direct relationships between temperature and blood flow are also well determined in peripheral tissues[25]. Potent linear correlation between increases in blood flow and during local temperature increases have been shown in the skin[26], muscular tissue[27], and in the brain of humans[28]. However, to the best of our knowledge, the present study is the first to investigate the association between diurnal CT changes and BT. SF-CT thinned by the afternoon and early evening, and nasal parts of the choroid statistically thinned by the afternoon. It may thus be expected that CT is affected by BT due to its affecting the blood flow either by active vasodilatation or by releasing the vessels' vasoconstrictor tone[13].

In our study, we did not identify any significant alteration in BT according to measurements taken hourly during 9:00-17:00, and CT was not found to be significantly associated with changes in a range of BTs during the same daily period. The variation amplitude of BT is regulated within a narrow range by a complex feedback system.

Our study poses several limitations. CT was assessed only during daylight and evening hours and not at midnight. Furthermore, all measurements were taken using direct inverted scans. Since the software used for CT did not involve an algorithm, measurements were processed manually, which could have resulted in differences that may have affected results. In some eyes, it was difficult to identify the choroid-sclera borderline clearly. The other limiting factors of our study include its small sample size, and lack of body mass index (BMI), and blood pressure values of cases studied. The study can be expanded by including these factors.

In conclusion, our study indicated that CT shows diurnal variation during the daytime. BT does not affect CT or alter daily according to measurements taken hourly from 9:00-17:00. In addition, our results found by using EDI-OCT show a significant pattern of diurnal variation in SF-CT in healthy patients.

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