

Changes in choroidal thickness following trabeculectomy and its correlation with the decline in intraocular pressure

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Abstract

Purpose Evaluate whether there are significant changes in choroidal thickness following trabeculectomy, and how they relate to the decline in intraocular pressure.

Methods This was a prospective evaluation of 28 eyes who underwent Moorfields modified trabeculectomy. The choroidal thickness was measured via OCT with enhanced depth imaging, before surgery and 1 day, 1 week and 1 month after surgery. Measurements were taken at the fovea, 1000 μm temporal to the fovea and 1000 μm nasal to the fovea. The relationship between choroidal thickness and intraocular pressure was statistically evaluated.

Results The mean intraocular pressure before surgery was 25.07 ± 4.64 mmHg; 8.57 ± 3.62 mmHg after 1 day; 10.36 ± 4.39 mmHg after 1 week and 13.71 ± 5.13 mmHg after 1 month. Mean choroidal thickness increased after trabeculectomy with maximal values at 1 week. The largest increase was found at the fovea, with an average before surgery of 253.54 ± 62.01 μm ; 286.75 ± 64.20 μm at 1 day, 286.36 ± 63.14 μm at 1 week and 271.00 ± 60.31 μm at 1 month. Increase in choroidal

thickness was significant 1 day and 1 week after surgery in the foveal ($p = 0.012$, $p = 0.007$) and temporal ($p = 0.040$, $p = 0.000$) locations and 1 week postoperatively on the nasal location ($p = 0.016$). None of them were significant at 1 month after surgery. Preoperative IOP and choroidal thickness were correlated at all macular locations ($\rho = 0.449$ – 0.525 , $p = 0.004$ – 0.016) yet no correlation was found between increase in choroidal thickness and decline in intraocular pressure in the postoperative period.

Conclusion Choroidal thickness appears to increase temporarily after trabeculectomy and these changes were not correlated with the decline in intraocular pressure. Further research is required to fully understand this phenomenon.

Keywords Choroidal thickness · Glaucoma · Intraocular pressure · Optical coherence tomography · Trabeculectomy

Introduction

In trabeculectomy, a scleral flap guarded filtration procedure, a fistula that allows drainage of the aqueous humor into the subconjunctival/sub-Tenon space by a sclerostomy is obtained, thereby reducing the intraocular pressure. Though superior to unprotected surgeries, drainage control is not perfect, with the

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possibility of hyperfiltration and associated complications [1–3]. Decompression and the resulting changes in the hydrostatic pressure gradient may lead to anatomical and functional alterations that have been described previously, such as reduced axial length, expansion of choroidal tissue and increased ocular perfusion pressure [4, 5]. Recently, with the advent of spectral domain OCT with enhanced depth imaging (EDI) technology and the feasibility of determining choroidal thickness objectively [6, 7], this parameter has become subject to study, as it is speculated that axial length reduction after trabeculectomy is related to the expansion of choroidal tissue [8, 9]. It is also thought that choroidal thickness is a dynamic parameter, which may reflect vascular alterations related to intraocular pressure oscillations in the postoperative period [8]. Previous studies have shown a significant increase in choroidal thickness following trabeculectomy both in open [8–10] and closed-angle glaucoma patients [11]. Analysis of the relation between this increase and decreased IOP has produced contradictory results, however [8–11].

The goal of our study is to characterize the changes in choroidal thickness following trabeculectomy and their relation to IOP.

Methods

We studied 28 eyes of 23 patients that underwent trabeculectomy and were prospectively evaluated in Hospital Professor Doutor Fernando da Fonseca (Amadora-Sintra, Lisbon, Portugal) between March 2015 and December 2016. The study was approved by our institutional ethical committee and it was in accordance with the ethical principles of the declaration of Helsinki. Informed consent was obtained from all participants. Eligibility criteria were diagnosis of primary open-angle glaucoma poorly controlled with medical therapy, refractive error with a spherical equivalent up to 4 diopters, transparent media and absence of previous ocular pathology. Glaucoma diagnosis was established upon joint evaluation of the standard clinical examination, optic nerve retinal nerve fiber layer assessment by OCT, and visual field testing.

Exclusion criteria were combined phacoemulsification and trabeculectomy surgery, history or signs of any retinal or chorioretinal pathology, neovascular

glaucoma and low-quality image due to hypermature cataract or unstable fixation. The registered systemic diagnosis of our participants included hypertension, dyslipidemia, osteoarthritis and primary benign prostatic hyperplasia. All patients underwent Moorfields modified trabeculectomy with 0.4 mg/mL mitomycin, given that they met the criteria for its application. Postoperative complications included two cases of hyphema that resolved with conservative treatment. Complications such as seidel in the postoperative period, choroidal detachment or hypotony maculopathy were not registered.

Before and after surgery, patients were clinically evaluated. Visual acuity testing, refraction, slit lamp biomicroscopy, gonioscopy, fundoscopy under pharmacological mydriasis and applanation tonometry were performed on all patients.

Choroidal thickness was determined by spectral domain OCT (*Spectralis*, wavelength: 870 nm; Heidelberg Engineering Co, Heidelberg, Germany) in EDI mode, which by moving the OCT lens closer to the eye, produces a mirror image of the eye allowing a greater signal depth in a procedure that has been previously described [7]. All measurements were performed by the same experienced examiner. Choroidal thickness was defined as the vertical distance between the external portion of the hyper-reflective line corresponding to the retinal pigment epithelial complex—Bruch membrane and the internal portion of the hyper-reflective line corresponding to the scleral internal surface. For better image quality, the *eye-tracking* and *image-averaging* features of OCT *Spectralis* were enabled. Only images with a signal-to-noise ratio > 20 dB were considered for evaluation.

Choroidal thickness was measured at the fovea, 1000 μm nasal to the fovea and 1000 μm temporal to the fovea at the day of the surgery; and at 1 day, 1 week and 1 month after surgery. Choroidal thickness measurements were compared to the preoperative value obtained at the day of surgery, by analyzing their differences.

Statistical analysis was performed in *IBM SPSS Statistics* version 22 (SPSS, Inc, Chicago, IL, USA). Shapiro–Wilk normality test ($\alpha = 0.05$) was used to attest the normality of the distribution of the IOP and choroidal thickness measurements. The differences were then compared with the ANOVA test for repeated measures.

The choroidal thickness measurements (preoperatively and at the first day, first week, and first month after surgery) and the corresponding mean intraocular pressure were tested for correlation with the Pearson's correlation test.

Significance threshold was set at $p < 0.05$.

Results

The average patient age was 64.36 ± 9.58 (range: 46–84 years) with a balanced male: female distribution. The registered systemic diagnosis of our participants was arterial hypertension (21 patients), dyslipidemia (11 patients), osteoarthritis (17 patients) and primary benign prostatic hyperplasia (5 patients). Demographic characteristics are summarized in Table 1.

Mean preoperative IOP was 25.07 ± 4.64 mmHg; 8.57 ± 3.62 mmHg 1 day after surgery; 10.36 ± 4.39 mmHg 1 week after surgery and 13.71 ± 5.13 mmHg 1 month after surgery. Mean choroidal thickness increased postoperatively at the three macular locations, with higher increases during the first day and first week for all locations (Fig. 1).

A summary of the mean choroidal thickness measurements at the evaluated locations is presented in Table 2. Preoperatively, the mean choroidal thickness was greatest at the fovea (253.54 ± 62.01 μm), followed by the temporal (234.50 ± 47.39 μm) and nasal (215.64 ± 55.01 μm) locations.

Central choroidal thickness after surgery increased and a statistical significant difference was registered 1 day ($p = 0.012$) and 1 week after surgery ($p = 0.007$), but not 1-month postoperatively ($p = 0.493$).

The mean temporal choroidal thickness showed an increase in the postoperative period that was

statistically significant at 1 day ($p = 0.040$) and 1 week after surgery ($p = 0.000$), but not 1 month postoperatively ($p = 0.142$).

Finally, mean choroidal thickness nasal to the fovea also increased after surgery; however, a statistically significant difference was observed only 1 week postoperatively ($p = 0.003$), not in the measurements 1 day ($p = 0.088$) and 1 month after surgery ($p = 0.154$).

Mean choroidal thickness differences and the corresponding p values are summarized in Tables 3, 4 and 5.

We analyzed the correlation between choroidal thickness and IOP at all three macular locations preoperatively, as well as at day one, 1 week and 1 month after surgery (Table 6). We verified that, preoperatively, choroidal thickness correlated moderately with the IOP at the subfoveal location ($\rho = 0.518$, $p = 0.005$) and nasal location ($\rho = 0.525$, $p = 0.004$). Temporal choroidal thickness also correlated with the IOP preoperatively, though weakly ($\rho = 0.449$, $p = 0.016$). In the postoperative period, we verified that IOP and choroidal thickness did not correlate at all three macular locations at day one, 1 week and 1 month after surgery ($\rho < 0.3$ and $p > 0.05$) as described in Table 5. Scatter plots displaying the correlation analysis between choroidal thickness and IOP at all three macular locations can be seen in Figs. 2, 3 and 4.

Discussion

The study of changes in choroidal thickness is a recent development, with a small number of studies suggesting postoperative changes after trabeculectomy [8–11]. In accordance with previous studies [8–11], we observed an increase in choroidal thickness after trabeculectomy. This increase was present at the first day, first week and first month after surgery and was statistically significant at 1 day and 1 week in the subfoveal and temporal locations and on the one/week measurement in the nasal location.

Choroidal thickness is a dynamic parameter [8], influenced by various factors. It has been previously observed that it correlates negatively with advanced age, increased axial length, increased IOP and increased corneal thickness [12–16]. Previous studies hypothesize about the generic physiology of choroidal

Table 1 Demographic data summary

Demographic data ($N = 28$)	
Age	64.36 ± 9.58
Gender	
Male	11 (47.83%)
Female	12 (52.17%)
Race	
Caucasian	19 (82.61%)
African	4 (17.39%)

Fig. 1 Mean choroidal thickness evolution in the postoperative period

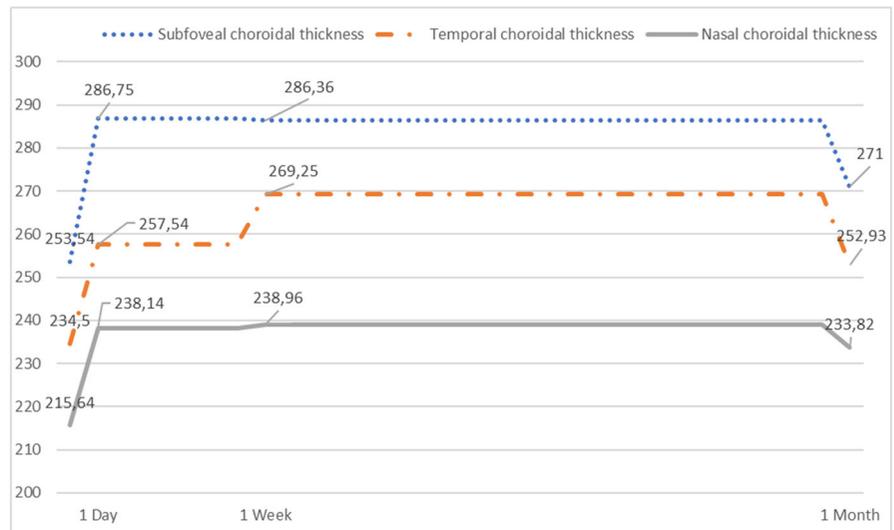


Table 2 Mean choroidal thickness measurements at the evaluated locations

Mean choroidal thickness measurements (μm) at the fovea, temporally and nasally

	Mean central choroidal thickness (μm)	Mean temporal choroidal thickness (μm)	Mean nasal choroidal thickness (μm)
Preoperative	253.54 ± 62.01	234.50 ± 47.39	215.64 ± 55.01
1 day after surgery	286.75 ± 64.20	257.54 ± 54.69	238.14 ± 57.94
1 week after surgery	286.36 ± 63.14	269.25 ± 42.38	238.96 ± 10.76
1 month after surgery	271.00 ± 60.31	252.93 ± 50.35	233.82 ± 56.47

Table 3 Central choroidal thickness differences and significance level

Central choroidal thickness	Mean difference (μm)	<i>p</i> value
1 day—preoperative	33.21 ± 51.23	0.012
1 week—preoperative	32.82 ± 47.92	0.007
1 month—preoperative	17.46 ± 51.18	0.493

Table 4 Temporal choroidal thickness differences and statistical significance level

Temporal choroidal thickness	Mean difference (μm)	<i>p</i> value
1 day—preoperative	23.04 ± 41.53	0.040
1 week—preoperative	34.75 ± 31.41	0.000
1 month—preoperative	18.43 ± 40.66	0.142

thickness increases [17], pointing at possible factors underlying this alteration, such as increased synthesis of scleral proteo-glycans with greater osmotic retention in this tissue; higher number of fenestrations of the choriocapillaris, with an increase in the circulation of osmotically active substances and corresponding

greater water flow towards this tissue; higher transportation of retinal fluid by retinal pigment epithelium; and alterations in the non-vascular smooth muscle tissue tonicity at this level [8, 17].

Regarding the modification of choroidal thickness after trabeculectomy specifically, Kara et al. [8] were

Table 5 Nasal choroidal thickness differences and statistical significance level

Nasal choroidal thickness		
	Mean difference (μm)	<i>p</i> value
1 day—preoperative	22.50 ± 45.65	0.088
1 1 week—preoperative	23.32 ± 37.34	0.016
1 month—preoperative	18.18 ± 40.75	0.154

the first to study the modifications in this layer and its relation to IOP, axial length and ocular perfusion pressure. The authors analyzed 39 eyes of 39 patients with primary open-angle glaucoma before and after surgery and a month after trabeculectomy and

observed an increase in choroidal thickness, correlating positively with the decrease in intraocular pressure and the increase in ocular perfusion pressure. They suggest that the observed modifications are explained by vascular alterations associated with the sharply decreasing IOP after surgery.

Similarly, Saedi et al. [10] (2014) studied a sample of 17 eyes with primary open-angle glaucoma, measuring the choroidal thickness before surgery, and at the first week, third month and 6 months after surgery. Increased choroidal thickness was observed in every patient, correlating with the decrease in IOP, with each 1 mmHg drop in IOP corresponding to an average increase of 3.4 μm in choroidal thickness (*p* < 0.0001 for the univariate regression analysis, confidence interval between 2.5 and 4.3), thus representing a

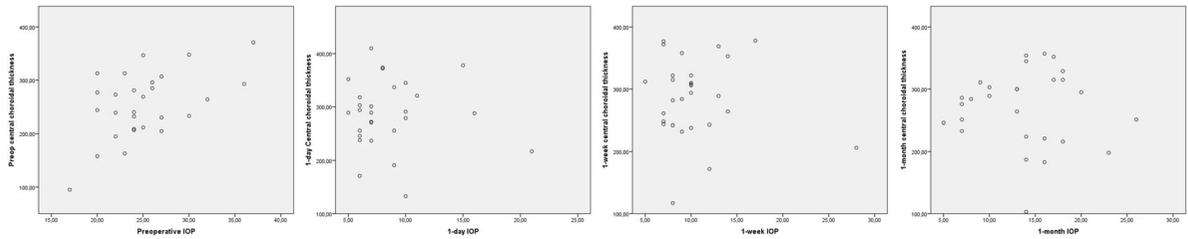


Fig. 2 Scatter plot of the relationship between IOP and central choroidal thickness preoperatively, 1-day, 1-week and 1-month after surgery

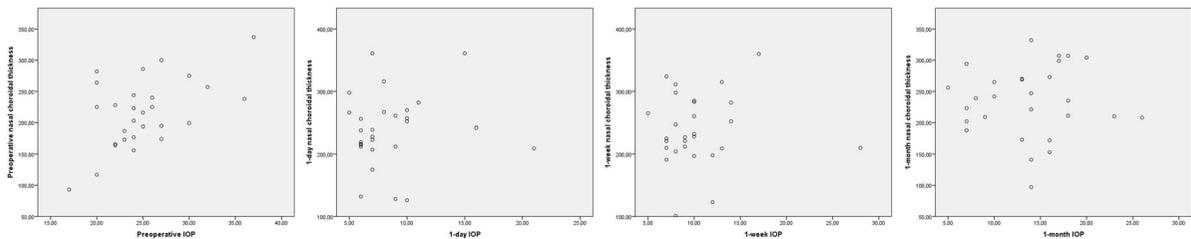


Fig. 3 Scatter plot of the relationship between IOP and nasal choroidal thickness preoperatively, 1-day, 1-week and 1-month after surgery

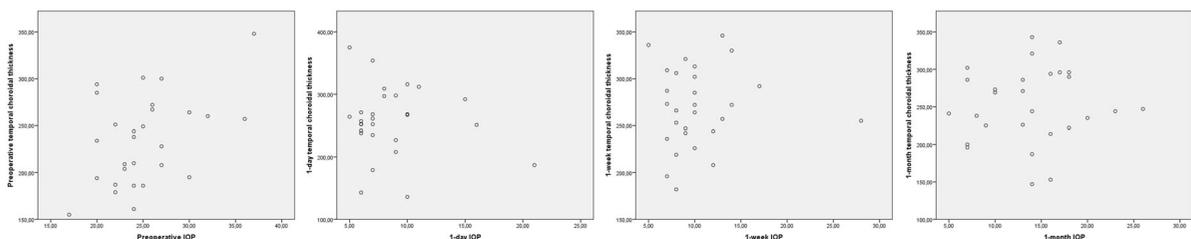


Fig. 4 Scatter plot of the relationship between IOP and temporal choroidal thickness preoperatively, 1-day, 1-week and 1-month after surgery

Table 6 Choroidal thickness and IOP correlation analysis

Choroidal thickness and IOP correlation		
	Pearson correlation ρ	p value
Preoperative		
Subfoveal choroidal thickness	0.518	0.005
Temporal choroidal thickness	0.449	0.016
Nasal choroidal thickness	0.525	0.004
1 day		
Subfoveal choroidal thickness	0.037	0.851
Temporal choroidal thickness	0.020	0.918
Nasal choroidal thickness	0.093	0.638
1 week		
Subfoveal choroidal thickness	– 0.019	0.923
Temporal choroidal thickness	0.095	0.631
Nasal choroidal thickness	0.065	0.741
1 month		
Subfoveal choroidal thickness	– 0.040	0.841
Temporal choroidal thickness	0.069	0.726
Nasal choroidal thickness	0.030	0.880

1.7% increase for each mmHg decrease ($p < 0.0001$; 95% confidence interval between 1.3 and 2.0%).

In spite of the above-mentioned results, in other studies preceding Kara et al. [9, 11], the same increase in choroidal thickness was observed, but with no observed correlation to the decreasing intraocular pressure. Usui et al. [9] (2013) studied 14 eyes of 14 primary open-angle glaucoma patients, before surgery and 6 days after trabeculectomy, with the measurements of choroidal thickness at the fovea and in 4 locations around the optic disc. A statistically significant increase was observed in all locations, with no correlation with the IOP. In 2014, Chen et al. [11] studied a sample of 23 eyes of 23 primary closed-angle glaucoma patients. They measured choroidal thickness before surgery and 1 week after surgery in 9 macular locations. Statistically significant differences were found in the 9 locations, yet with no correlation to IOP.

Authors of these studies suggest some explanations for this phenomenon, such as different study designs, small sample size and timing of choroidal thickness measurements (1 week versus 1 month after surgery) [9]; higher circadian variation of choroidal thickness after surgery due to quick changes in intraocular pressure [9]; and finally, they attribute alterations in choroidal thickness to ocular perfusion following

surgery, with modification of the uveoscleral pathway, resulting in choroidal thickness increase [9, 11].

Our study is in line with the referred studies [9, 11], with no observed correlation between choroidal thickness in the various macular locations and IOP decrease.

As for the choroidal thickness measurements, following the practice of previous studies [9–11], they were taken preferentially in the morning to minimize the effects of circadian variations in the results. Although ocular perfusion measurements were not taken in this study, the absence of correlation to IOP may suggest that choroidal thickness is related to the hemodynamic changes following surgery, as pointed out by previous research. The fact that in our study choroidal thickness was distinctively and consistently correlated with the IOP in the preoperative period in all locations, with this correlation subsiding in the postoperative period favors this hypothesis. Further research is still required to clarify this relationship.

In addition, by characterizing modifications at the first day, first week and first month after surgery, our study shows a pattern of peak choroidal thickness at the first week, and even though it remains higher than before surgery at the end of the first month, the mean difference was not statistically significant in all locations and, therefore, it appears to follow a

declining trend. Thus, one should question whether the modification in choroidal thickness after surgery is actually a temporary alteration or if eventual vascular modifications remain for a long period of time. Further research is needed where this parameter is followed during a broader timescale for us to obtain a better understanding of the phenomenon.

Our work is a preliminary study, limited to a small sample, which limits the statistical strength of some conclusions, namely the correlation with IOP decrease. The small number of participants may also justify the fact that nasal choroidal thickness measurements were not statistically significant at the 1-day evaluation. Additionally, choroidal thickness was measured manually, which might affect the reliability of the study, although there are studies that show good levels of inter-observer correlation, repeatability and inter-individual reliability of manual choroidal thickness measurements [7, 18, 19]. Regarding the influence of systemic diseases in choroidal thickness measurements, our population included patients with arterial hypertension and dyslipidemia which can influence choroidal thickness measurements [20, 21]. However, we believe that since we are comparing the baseline choroidal thickness of each participant with their subsequent evaluations after trabeculectomy, the influence of the systemic disease profile in our results is minimized.

Conclusion

We observed an increase in choroidal thickness that was statistically significant at 1 day and 1 week at the subfoveal and temporal locations, and at 1 week at the nasal location. Choroidal thickness measurements did not correlate with the IOP decrease in the postoperative period. Choroidal thickness appears to peak at the first week of the postoperative period, decreasing subsequently. There are only a small number of studies in this area, with contradictory results, and as a result the significance and pathophysiological basis of these alterations remain undefined. In the absence of correlation to IOP, this phenomenon might be explained by an increase in ocular perfusion and modification of the uveoscleral pathway and consequent increase in choroidal thickness.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

- Pederson JE (1984) Hypotony. In: Duane TD (ed) Clinical ophthalmology, chapter 58, vol 3. Harper & Row, Philadelphia, pp 1–8
- Stamper RL, McMenemy MG, Lieberman MF (1992) Hypotonous maculopathy after trabeculectomy with subconjunctival 5-fluorouracil. *Am J Ophthalmol* 114:544–553
- Suner IJ, Greenfield DS, Miller MP, Nicolela MT, Palmberg PF (1997) Hypotony maculopathy after filtering surgery with mitomycin C. Incidence and treatment. *Ophthalmology* 104:207–214
- Cashwell LF, Martin CA (1999) Axial length decrease accompanying successful glaucoma filtration surgery. *Ophthalmology* 106:2307–2311
- Berisha F, Schmetterer K, Vass C, Dallinger S, Rainer G, Findl O et al (2005) Effect of trabeculectomy on ocular blood flow. *Br J Ophthalmol* 89:185–188
- Margolis R, Spaide RF (2009) A pilot study of enhanced depth imaging optical coherence tomography of the choroid in normal eyes. *Am J Ophthalmol* 147:811–815
- Spaide RF, Koizumi H, Pozzoni MC (2008) Enhanced depth imaging spectral-domain optical coherence tomography. *Am J Ophthalmol* 146:496–500
- Kara N, Baz O, Altan C, Satana B, Kurt T, Demirok A (2013) Changes in choroidal thickness, axial length, and ocular perfusion pressure accompanying successful glaucoma filtration surgery. *Eye* 27(8):940–945
- Usui S, Ikuno Y, Uematsu S, Morimoto Y, Yasuno Y, Otori Y (2013) Changes in axial length and choroidal thickness after intraocular pressure reduction resulting from trabeculectomy. *Clin Ophthalmol* 7:1155–1161
- Saeedi O, Pillar A, Jefferys J, Arora K, Friedman D, Quigley H (2014) Change in choroidal thickness and axial length with change in intraocular pressure after trabeculectomy. *Br J Ophthalmol* 98(7):976–979
- Chen S, Wang W, Gao X, Li Z, Huang W, Li X, Zhou M, Zhang X (2014) Changes in choroidal thickness after trabeculectomy in primary angle closure glaucoma. *Investig Ophthalmol Vis Sci* 55(4):2608–2613
- Esmaelpour M, Povazay B, Hermann B, Hofer B, Kajic V, Kapoor K et al (2010) Three-dimensional 1060-nm OCT: choroidal thickness maps in normal subjects and improved posterior segment visualization in cataract patients. *Investig Ophthalmol Vis Sci* 51:5260–5266

13. Fujiwara T, Imamura Y, Margolis R, Slakter JS, Spaide RF (2009) Enhanced depth imaging optical coherence tomography of the choroid in highly myopic eyes. *Am J Ophthalmol* 148:445–450
14. Ikuno Y, Tano Y (2009) Retinal and choroidal biometry in highly myopic eyes with spectral-domain optical coherence tomography. *Investig Ophthalmol Vis Sci* 50:3876–3880
15. Mwanza JC, Hochberg JT, Banitt MR, Feuer WJ, Budenz DL (2011) Lack of association between glaucoma and macular choroidal thickness measured with enhanced depth-imaging optical coherence tomography. *Investig Ophthalmol Vis Sci* 52:3430–3435
16. Ikuno Y, Kawaguchi K, Nouchi T, Yasuno Y (2010) Choroidal thickness in healthy Japanese subjects. *Investig Ophthalmol Vis Sci* 51:2173–2176
17. Nickla DL, Wallman J (2010) The multifunctional choroid. *Prog Retin Eye Res* 29:144–168
18. Rahman W, Chen FK, Yeoh J, Patel P, Tufail A, Da Cruz L (2011) Repeatability of manual subfoveal choroidal thickness measurements in healthy subjects using the technique of enhanced depth imaging optical coherence tomography. *Investig Ophthalmol Vis Sci* 52(5):2267–2271
19. Karaca EE, Özdek Ş, Yalçın NG, Ekici F (2014) Reproducibility of choroidal thickness measurements in healthy Turkish subjects. *Eur J Ophthalmol* 24(2):202–208
20. Wong IY, Wong RL, Zhao P, Lai WW (2013) Choroidal thickness in relation to hypercholesterolemia on enhanced depth imaging optical coherence tomography. *Retina* 33(2):423–428
21. Akay F, Gundogan FC, Yolcu U, Toyran S, Uzun S (2016) Choroidal thickness in systemic arterial hypertension. *Eur J Ophthalmol* 26(2):152–157