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RETINAL DISORDERS

The outer choroidoscleral boundary in full-thickness macular holes before and after surgery—a swept-source OCT study

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Abstract
Purpose To report on choroidal thickness and the morphology of the outer choroidoscleral boundary in swept-source OCT in patients with full-thickness macular holes (FTMH) before and after surgery.
Methods Single center matched case–control study of 32 patients with FTMH (group 1), fellow eyes (group 2), and 32 eyes of 32 healthy controls (group 3). All eyes from group 1 had vitrectomy with a minimum follow-up of 3 months. Main outcome measures were the visibility and regularity of the outer choroidoscleral boundary (CSB), and additionally the eventual visibility of the suprachoroidal layer (SCL).
Results Choroidal thickness was indifferent between groups. Choroidal thickness did not change after surgery (p=0.1). CSB was visible in all cases. CSB was irregular in 59 % of eyes in group 1, in 40 % of eyes in group 2, and in any eye in group 3. SCL was visible in 34 % of eyes in group 1, and remained visible after surgery. In group 2, SCL was observed in 44 % of eyes, and in group 3 in one eye.
Conclusions Choroidal thickness does not differ between eyes with FTMH and their fellow eyes and healthy controls. CSB is more often irregular and SCL is more often visible in eyes with FTMH and their fellow eyes than in healthy controls. In fellow eyes of FTMH, the visibility of SCL was observed more often in eyes with partial vitreous detachment (p=0.0). Three months after surgery, choroidal thickness does not change, the irregularities of CSB and SCL remain visible. More frequent changes of the outer choroidoscleral boundary in FTMH, and especially in their fellow eyes, may suggest a role of the choroid in the pathogenesis of FTMH.

Keywords Swept source OCT · SS-OCT · Macular hole · Choroidal thickness

Introduction

Full-thickness macular hole (FTMH) is usually regarded as a vitreoretinal interface disease that occurs in the course of posterior vitreous detachment, leading to a full-thickness defect of the central retina [1–3]. In the past, some authors reported that FTMH formation may be additionally due to retinal involutional thinning combined with vascular alternations [4, 5]. This might have explained the rare cases of FTMH in vitrectomized eyes or reopenings of FTMH.

Choroidal thickness was first measured with the inverted image of spectral-domain OCT, i.e., enhanced-depth OCT (EDI-OCT) by R. Spaide [6]. Swept-source OCT is a new device, using a longer wavelength of light (1,024 nm, vs 840 nm in SD-OCT). Longer wavelengths overcome much of the scattering of light on choroidal vasculature, thus enabling a more exact visualization of the choroid and the outer choroidoscleral boundary. This may enhance exact measurement of the choroid.

The role of choroid in FTMH is elusive. Recently, some authors suggested that patients with FTMH have thinner

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choroids than in their fellow eyes and in healthy controls [7, 8]. Other authors stated that there is no correlation between choroidal thickness and the presence of FTMH [9, 10]. We recently observed that choroidal thickness decreases after vitrectomy for idiopathic epiretinal membranes. We speculated that choroidal thickness is increased in eyes with epiretinal membranes, and decreases to normal values after vitrectomy [11]. However, it might also be hypothetized that vitrectomy itself influences choroidal thickness in different conditions.

The purpose of this paper is to estimate whether choroidal thickness changes after vitrectomy with temporal inverted ILM flap technique, and additionally to determine whether the morphology of the outer choroidoscleral boundary and choroidal thickness differs between eyes with FTMH and their fellow eyes, and eyes of healthy controls.

Methods

This is a matched case–control study. The study is coherent with the tenets of the Declaration of Helsinki. Informed consent was obtained, and the Institutional Review Board approved the study. We matched consecutive eyes with idiopathic FTMH (group 1), their unaffected fellow eyes (group 2), and healthy volunteers of the same age, sex, and axial length (group 3). Axial length was measured with optical low-coherence reflectometry (Lenstar LS 900, Haag–Streit, Switzerland).

All patients from group 1 had pars plana vitrectomy performed and at least 3 months follow-up. In patients with bilateral FTMH, the first operated eye was identified as the study eye. We analyzed changes in choroidal thickness and details of the outer choroidoscleral boundary before and 3 months after surgery.

In order to measure choroidal thickness, we used the first commercially available SS-OCT device (DRI- OCT, Topcon, Japan) with a wavelength of 1,024 μm. In all cases, we utilized two scanning protocols. First, we manually estimated choroidal thickness with a single line scan with a resolution of 3 μm, built from 1,024 A-scans with a length of 12 mm. Then, we performed a 3-dimensional scanning protocol with 3 μm axial resolution and a speed of 100,000 A-scans per second. In this protocol, 256 B-scans were taken on an area of 12×9 μm.

We took manual choroidal thickness measurements between the line representing retinal pigment epithelium: the outer most hyperreflective retinal layer, and the outer hyperreflective line of the choroid defined as the outer choroidoscleral boundary. Choroidal thickness and volume was also automatically calculated using the inbuilt software. We calculated numeric averages of the measurements for each of the nine map sectors defined by the Early Treatment Diabetic Retinopathy Study (ETDRS). The inner and outer rings with diameters of 3 mm and 6 mm respectively were segmented into 4 quadrants. Mean choroidal thickness at the fovea was defined as the average thickness in the central 1, 000-μm diameter of the Early Treatment Diabetic Retinopathy Study layout [12]. We also measured the minimum and base diameter of FTMH.

Additionally, we analyzed the regularity of the outer CSB (choroidoscleral boundary), and reported this as either regular (Fig. 1) or irregular (Fig. 2).

We recorded the percentage of eyes with two bands visible at the outer CSB representing suprachoroidal layer (SCL), an upper hyperreflective and a lower hyporeflective (Fig. 3) [13]. All measurements were performed by two experienced examiners (KDC, ZM). In case of any discrepancies, the senior author decided which measurement was correct. Additionally, we measured the intraobserver variability.

Surgical technique—temporal inverted ILM flap technique

This is a modification of the 'inverted ILM flap technique' described by our group [14, 15]. The procedure involves vitrectomy and trypan blue staining (0.06 % solution of trypan blue for 1 min) and peeling of any epiretinal membrane if present. The internal limiting membrane is grasped with ILM forceps and peeled off in a circular fashion on the temporal side of the FTMH. However, the ILM is not removed completely from the retina, but is left attached to the edges of the FTMH on the temporal side. ILM is not removed from the nasal side of the FTMH. The ILM is then massaged gently over the FTMH from all sides until the ILM becomes inverted, i.e., upside-down such that the surface that normally faces the vitreous body now faces the retinal pigment epithelium. In this way, the FTMH is covered with the inverted ILM flap. At the end of surgery, the vitreous cavity is filled with air, and we advise patients to spend 3–4 days in a position in which they can see the air bubble in the center of the visual field at all times.

Statistical analysis was conducted with SPSS 16.0 for Windows.

Results

Thirty-two patients (six male, 26 female, mean age 64.5 years) with FTMH were included in this study.

The mean minimum diameter of the FTMH was 510 μm (245–797 μm). The mean base diameter of the FTMH was 943 μm (403–1,518 μm). The mean refractive error was −0.42Dptr (median +0.5Dsph; range −7.5Dptr to +5Dptr).

Visual acuity improved significantly from a mean of 0.1 Snellen lines to a mean of 0.24 Snellen lines 3 months after surgery (p=0.003). Closure of the FTMH was achieved in 31/

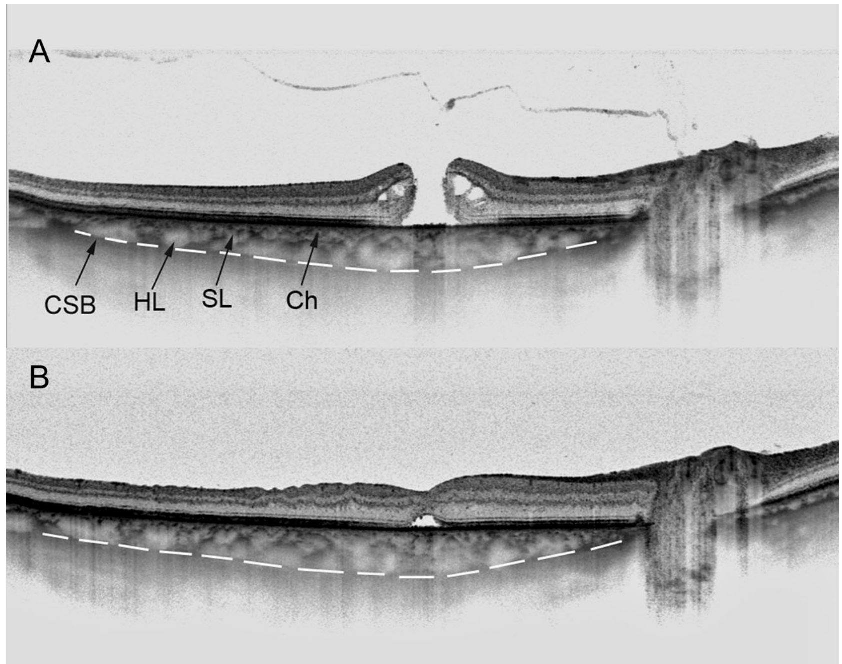

Fig. 1 Swept-source OCT of a macular hole before surgery (**a**) and after surgery (**b**). The *white lines* represent the regularity of the choroidoscleral boundary. *HL* Haller layer, *SL* Sattler layer, *Ch* choriocapillaries *CSB* Choroidoscleral boundary

32 patients after one surgery. One eye had repeated surgery, which enabled a successful closure of the FTMH.

None of the images was excluded because of image quality.

Fellow eyes (Group 2)

In seven eyes, FTMH was diagnosed in the fellow eye (two already successfully treated). Those eyes were excluded from further analysis. In the 25 remaining fellow eyes, vitreomacular adhesion was observed in nine cases, posterior vitreous detachment in nine eyes, lamellar macular hole in two eyes, and drusen in two eyes.

Estimation of outer choroidoscleral boundary and suprachoroidal layer

In all patients in all groups, exact estimation of the outer choroidoscleral boundary was possible.

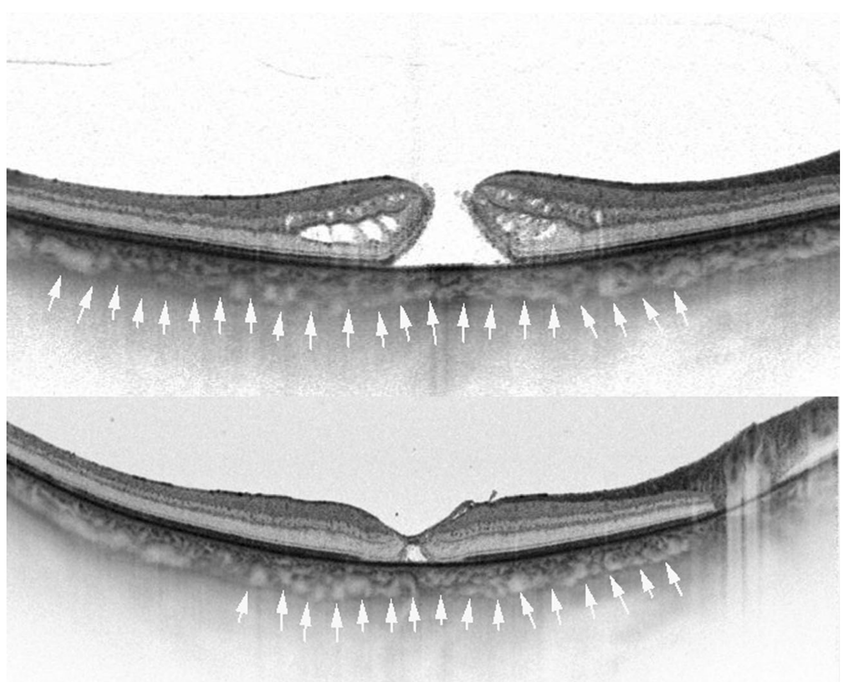

Fig. 2 Swept-source OCT of a macular hole before surgery (*upper image*) and after surgery (*lower image*). The *white arrows* indicate an irregular outer choroidoscleral boundary

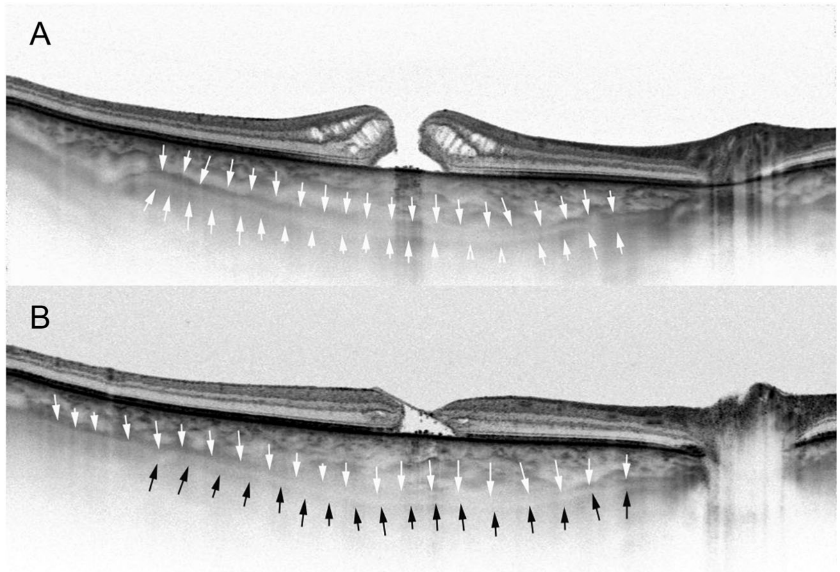

Fig. 3 The *arrows* indicate the suprachoroidal space in an eye with full-thickness macular hole before (**a**) and after (**b**) surgery

We found irregular CSB in 19/32 eyes in group 1 (59 %) (Fig. 2) and in 10/25 eyes in group 2 (40 %). In group 3 we found regular CSB in all 32 cases (100 %).

After surgery, CSB normalized in three cases and CSB remained irregular only in 16/32 eyes (50 %) 3 months post-operatively. In all eyes in which CSB was regular before surgery, it remained regular after surgery (Fig. 2).

SCL was visible in 11/32 eyes in group 1, (34 %) (Fig. 3), in 11/25 cases (44 %) in group 2 (Fig. 4), and in only one case in group 3 (3 %). It remained visible after surgery in all cases (Fig. 3b). (Table 1)

Choroidal measurements before surgery

Manual measurements of choroidal thickness were higher than automatic measurements in group 1 (267 μm vs 220 μm, p=0.03, Mann–Whitney rank sum test), group 2 (262 μm vs 210 μm, p=0.07) and group 3 (249 μm vs 199 μm, p=0.003). There were no statistical significant differences between manual measurement performed by two examiners (p=0.95). Choroidal thickness was estimated correctly by the device included in the software in 46 % of cases before surgery.

One-way analysis of variance was performed to compare choroidal thickness and volume. Mean manually (p=0.687) and automatically (p=0.359) measured choroidal thickness in the fovea was statistically identical between groups 1, 2, and 3. This was also true for choroidal volume (group 1: 0.17 μm^3, group 2: 0.16 μm^3, group 3: 0.16 μm^3; p=0.5).

In group 1, mean choroidal thickness in eyes with FTMH was thickest in the inner ring and thinnest on the nasal side of the outer ring (p=0.004, pairwise multiple comparison Tukey

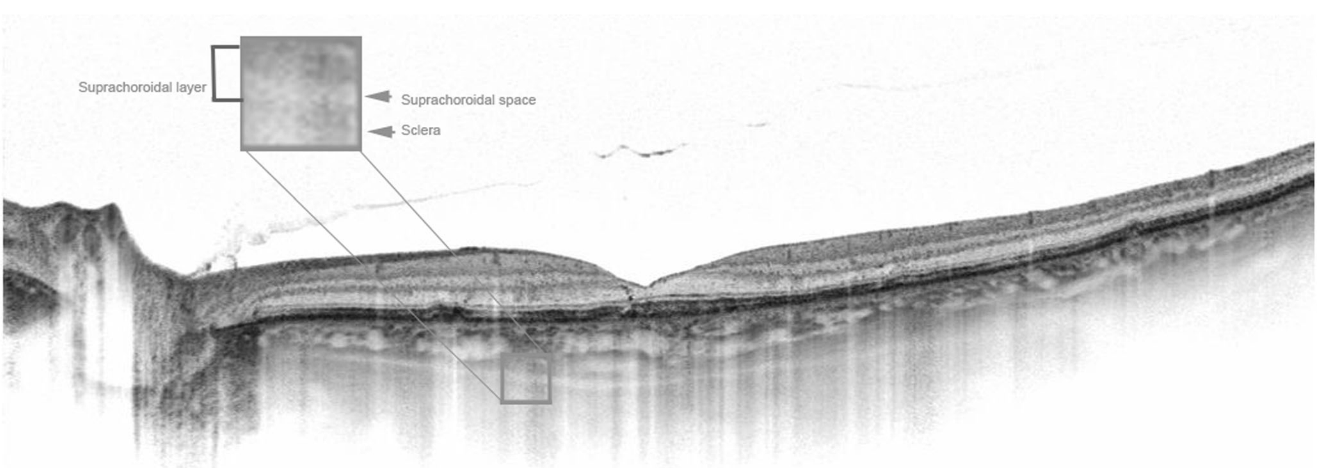

Fig. 4 Fellow eye of an eye with full-thickness macular hole. Posterior vitreous (PH) is partially detached, but adheres to the optic nerve. Irregular fovea contour and drusen are visible. The *enlarged area* presents suprachoroidal layer and suprachroidal space

Table 1 Details of the outer choroidoscleral boundary

	Group 1	Group 1 after surgery	Group 2	Group 3
Irregular CSB	19/32 (59 %)	16/32 (50 %)	10/25 (40 %)	0 %
SCL	11/32 (34 %)	11/32 (34 %)	11/25 (44 %)	1/32 (3 %)

CSB choroidoscleral boundary, *SCL* suprachoroidal layer

test). In the inner ring, choroidal thickness is indifferent between all quadrants. In the outer ring, choroidal thickness was higher superiorly than on the nasal side. Exemptions from this rule could be found in eyes with an irregular choroidoscleral boundary (Fig. 2). Choroid was thickest in the foveola and thinnest in the outer nasal ring in groups 2 (p=0.02) and 3 (p<0.001).

Choroidal volume in different ETDRS subfields is measured from different geometrical figures, and thus cannot be compared. Choroidal volume in the fovea is the volume of a cylinder with an upper and lower diameter of 1,000 μm, and the height of the cylinder is the foveal choroidal thickness ($V=\prod r^2 h$; V = cylinder volume, r = radius, h = height). Choroidal volume in the inner and outer quadrants are volumes of irregular geometrical figures with base diameters bigger than the foveal, which explains why the choroidal volume values in all subfields are bigger than in the center, and that they should not be compared directly [16] (Table 2).

Table 2 Choroidal thickness measurements

	Group 1 (μm)	Group 2 (μm)	Group 3 (μm)
Central choroidal thickness (automatic)	267	262	249
Central choroidal thickness (manual)	220	210	199
S1	221	206	201
N1	200	194	182
T1	216	203	200
I1	199	199.7	188
S2	224	213	206
N2	183	174	162
T2	210	198	195
I2	187	183	186
V central	0.17	0.17	0.15
VS1	0.34	0.32	0.31
VN1	0.33	0.32	0.28
VT1	0.34	0.31	0.31
VI1	0.32	0.359	0.29
VS2	1.25	0.16	1.03
VN2	0.98	0.93	0.82
VT2	1.14	1.0	1.02
VI2	1.08	1.0	0.95

S superior, *N* nasal, *T* temporal, *I* inferior, 1-inner ring, 2- outer ring, *V* volume

Correlations

We found a correlation between choroidal thickness, age (p=0.003), and axial length in all groups (multiple variance analysis) (group 1: p=0.009, group 2: p=0.008, group 3: p=0.001).

Final choroidal thickness did not correlate with the minimum (p=0.7) or base (p=0.8) diameter of the FTMH.

There was no correlation between initial (p=0.7) or final (p=0.6) choroidal thickness and visual acuity.

The regularity of the choroidoscleral boundary did not correlate with neither initial nor final visual acuity. No correlation with the diameter of FTMH was found.

No correlations between the visibility of the suprachoroidal layer and initial or final visual acuity or the diameter of FTMH was observed.

In fellow eyes of FTMH, we observed a strong statistically significant correlation between the status of the vitreous and the visibility of SCL (p=0.0) (Fig. 4). In eyes in which the posterior vitreous was partially attached either to retinal surface or to the optic disc, we always observed SCL. This was also true in healthy subjects, but statistical significance is difficult to estimate as only one healthy eye had SCL visible in our group. This correlation was not true for eyes with FTMH, as all those eyes had partial vitreous attachment.

Choroidal thickness after surgery

Mean central choroidal thickness did not change statistically significantly 1 week after surgery (p=0.2), nor 1 month (p=0.7) nor 3 months after surgery (p=0.3, Wilcoxon signed-rank test). Automated choroidal thickness measurement was estimated as correct in 60 % of eyes.

Distribution of choroidal thickness also remained similar to the preoperative status. Choroidal thickness stayed thickest at the foveal center and thinnest on the nasal side, reaching statistical significance in the outer ring (1.5 mm from the center of the foveola, p=0.01). No statistically significant change in choroidal thickness was observed in any quadrant.

Choroidal volume did not change in a statistically significant way after surgery, neither in the central fovea (p=0.06) nor in any other quadrant.

Discussion

In this study, we confirmed that choroidal thickness measured with SS-OCT is similar in eyes with FTMH when compared to fellow eyes and healthy controls. A new finding is that CSB is more often irregular in eyes with FTMH (59 %) and in their fellow eyes (40 %), whereas it was regular in all cases of healthy controls (Figs. 2). Additionally, SCL is more often visible in FTMH (34 %) and their fellow eyes (44 %) than in healthy controls (3 %) (Figs. 3 and 4). In fellow eyes of FTMH, the visibility of SCL was observed more often in eyes with partial vitreous detachment (p=0.0).

FTMH often occur bilaterally. Other vitreoretinal interface diseases are present with higher frequency in fellow eyes of FTMH than in the general population. Thus, changes of the outer choroidoscleral boundary in fellow eyes of FTMH may cause us to suspect an additional role of the choroid in the etiopathogenesis of vitreomacular interface diseases.

Earlier data reporting on differences of choroidal thickness between eyes with full-thickness macular holes and healthy controls are controversial [7–10]. There are some anecdotal reports from the pre- OCT era of macular hole formation in eyes lacking cortical vitreous [5, 17–22], but no OCT-confirmed studies on that topic have been published (Pubmed Medline). Reibaldi et al. presented a study of 22 eyes with unilateral macular hole with their fellow eyes and age- and sex-matched healthy controls. Zeng et al. [8] compared choroidal thickness of 50 eyes of patients with unilateral macular hole with their fellow eyes and with eyes of healthy controls using EDI-SOCT. They suggested that subfoveal choroidal thickness was lower in affected eyes than in fellow eyes, and both were lower than in healthy controls. However, the studies have several elements of bias. Other authors have questioned the statistics used [23, 24]. The most important bias would be that the authors matched their subgroups in regard to age and sex, without including axial length in their analysis. Previous studies presented a statistically significant correlation between choroidal thickness and age, refractive error and axial length, from which age and axial length were described as the more significant [25–30]. On the other hand, Schaal and coworkers, also using SD-OCT, did not find a difference between eyes with full-thickness macular holes, fellow eyes, and healthy controls in 12 subjects [9]. In our current study, we did not find any differences in any quadrant in mean choroidal thickness between eyes with FTMH, their fellow eyes, and healthy controls. We found that CSB is more likely to be irregular in FTMH. Thus, we believe, that earlier controversies between studies might have been due to the fact that in SD-OCT machines and the SS-OCT prototype, choroidal thickness measurement is possible only manually at certain spots, whereas we were additionally able to measure the mean subfoveal choroidal thickness in all nine map sectors as defined by ETDRS. Additionally, in SD-OCT the identification of the outer choroidoscleral boundary might not be possible in all cases. Due to focal measurements performed in earlier SD-OCT studies, irregularities of the CSB might have been measured and not real thickness, what might have been the reason for differences between studies.

Despite successful treatment, mean choroidal thickness does not change until month 3 after vitrectomy with ILM peeling; CSB has a moderate tendency to become more regular in single cases, whereas it remains irregular in most eyes (Fig. 3). Fujiwara and coworkers, who evaluated 40 eyes with EDI-OCT and followed them also for 3 months presented similar data [10]. Studies with a longer follow- up are needed to confirm the meaning of this finding.

Suprachoroidal layer is a novel finding (Fig. 3 and 4). We previously described it as being localized at the choroidoscleral boundary and consisting of two lines, the upper hyperreflective and lower hyporeflective. This layer was earlier reported to be visible in swept-source OCT in 5 % of healthy eyes [13], with higher frequency in macular diseases. Another author stated that they visualized this layer in 45 % of healthy eyes with the use of EDI-OCT [31]. These differences are difficult to explain with the type or resolution of both devices; SS-OCT has been reported to be advantageous over EDI-OCT [32]. Yiu et al. correlated, in their EDI-OCT supported study, the visibility of SCL with hyperopia and increased choroidal thickness [31]. In the current study, we observed SCL in only one healthy subject; thus, we could not confirm their findings. As SCL was more often visible in fellow eyes of FTMH, we performed an analysis of those cases and found SCL to be more often visible in eyes with partial vitreous attachment to the retinal surface or to the optic nerve (p=0.0). Partial vitreous attachment and SCL are also visible in Fig. 1 of the paper of Yiu et al., which might confirm this finding [31]. We hypothesize that traction may be transmitted through the retina to the choroid and expand the theoretical suprachoroidal space, making SCL visible. This finding requires further studies.

In conclusion, SS-OCT did not confirm any difference between choroidal thickness and volume between eyes with full-thickness macular holes, fellow eyes, and healthy controls. The fact that changes in the outer choroidoscleral boundary are more frequently observed in fellow eyes of FTMH than in healthy controls may indicate a role of the choroid in FTMH etiopathogenesis. Choroidal thickness did not change until month 3 postoperatively; CSB remained irregular in most cases, and SCL remained visible in all eyes. The changes of the choroidoscleral boundary after vitrectomy may require studies with a longer follow-up.

Conflict of interest: The authors have no financial interest to disclose.

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