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Choroidal morphology and the outer choroidoscleral boundary in dry age related maculopathy in Swept Source Optical Coherence Tomography

Ocena morfologii naczyniówki oraz granicy naczyniówkowo-twardówkowej za pomocą optycznej koherentnej tomografii z użyciem lasera strojonego u chorych na suchą postać zwyrodnienia plamki związanego z wiekiem

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Abstract: Background and objective: To report on details of the choroid in dry age-related macular degeneration imaged with Swept Source Optical Coherence Tomography.
Material and methods: Swept Source Optical Coherence Tomography was performed in 28 eyes with dry age-related macular degeneration (Group 1), who were age and refractive error-matched with 28 eyes of 28 healthy controls (Group 2). The visibility and contour of the outer choroidoscleral boundary and suprachoroidal layer was estimated.
Results: Choroidoscleral boundary was visible in all eyes, irregular in 78% in Group 1 and in 18% in Group 2. Suprachoroidal layer was visible in 36% eyes in Group 1 and in 7% eyes in Group 2. Mean choroidal thickness did not differ between groups ($p=.11$).
Conclusions: The outer choroidoscleral boundary is irregular in most cases of age-related macular degeneration. Suprachoroidal layer and suprachoroidal space are more often visible in dry age-related macular degeneration than in healthy controls.
Key words: Swept Source Optical Coherence Tomography (SS-OCT), age-related macular degeneration (AMD), choroidal boundary (CSB), suprachoroidal layer (SCL).
Abstrakt: Cel: ocena naczyniówki u chorych na suchą postać zwyrodnienia plamki związanego z wiekiem za pomocą optycznej koherentnej tomografii z użyciem lasera strojonego.
Materiał i metody: porównano wyniki badania optycznej koherentnej tomografii z użyciem lasera strojonego 28 oczu chorych na suchą postacią zwyrodnienia plamki związanego z wiekiem (grupa 1.) oraz 28 oczu osób zdrowych dopasowanych pod względem wieku oraz wady refrakcji (grupa 2.). Ponadto oceniano granicę naczyniówkowo-twardówkową oraz warstwę nadnaczyniówkową.
Wyniki: granica naczyniówkowo-twardówkowa była widoczna u wszystkich badanych. Oceniono ją jako nieregularną u 78% osób z grupy 1. oraz 18% osób z grupy 2. Warstwę nadnaczyniówkową uwidoczniono w 36% oczu z grupy 1. i w 7% oczu z grupy 2. Średnia grubość naczyniówki nie różniła się istotnie statystycznie między grupami ($p = 0,11$).
Wnioski: granica naczyniówkowo-twardówkowa jest częściej nieregularna u chorych na suchą postać zwyrodnienia plamki związanego z wiekiem. Warstwa nadnaczyniówkowa i przestrzeń nadnaczyniówkowa są częściej obserwowane u chorych na suchą postać zwyrodnienia plamki związanego z wiekiem niż u osób z grupy kontrolnej.
Słowa kluczowe: optyczna koherentna tomografia z użyciem lasera strojonego (SSOCT), zwyrodnienie plamki związane z wiekiem (AMD), granica naczyniówkowo-twardówkowa (CSB), przestrzeń nadnaczyniówkowa (SCL).

Introduction

Recently introduced, Swept Source Optical Coherence Tomography (SS-OCT, DRI-OCT, Topcon, Tokyo, Japan), uses a longer wavelength (1050 nm) as compared to conventional SD-OCT systems (840 nm). This enables visualization of deeper lying structures such as the choroid or even the sclera (1).

The choroid is a highly vascular structure that provides nutrients and oxygen to the photoreceptor layer, is responsible for the thermoregulation of retinal tissue, and eliminates waste products from the retinal pigment epithelium (RPE) (2). The choroid comprises: the innermost Bruch's membrane, choriocapillaris, Sattler's layer (layer of medium diameter blood vessels), Haller's layer (layer of larger diameter blood vessels). The visibility of suprachoroidal layer was recently described by our group (3). It consists of an inner hyporeflective band and an outer hyperreflective one. SS-OCT and SD-OCT enable particular choroidal layers to be distinguished *in vivo* (3, 4). The ability to visualize the sub-RPE space may be useful in the longitudinal monitoring and eventual management of chorioretinal disorders such as age-related macular degeneration (AMD).

AMD is a chronic, progressive disease that leads to loss of vision among individuals aged over 50. Dry AMD is the most common subtype of macular degeneration, characterized by aging changes of photoreceptors, retinal pigment epithelium (RPE), Bruch's membrane and the choroid. This results in early focal hyperpigmentation or formation of yellow, nodular deposits (drusen) localized between the basement membrane of the RPE and the inner collagenous layer of Bruch's membrane.

Earlier studies suggested that inadequate choroidal perfusion and decreased choroidal blood flow might result in the RPE degeneration and photoreceptor damage and further lead to visual dysfunction and exudative form of the disease (5). SD-OCT evidence confirms that choroidal thickness is altered in dry AMD (6, 7). We hypothesized that besides thickness, other morphological details of the choroid may characterize patients with dry AMD. In this paper, we will focus on the details of the outer choroidoscleral boundary and the structure and thickness of particular choroidal layers. Our secondary goal is to compare choroidal thickness measurements obtained with SS-OCT in patients with dry AMD and age and refractive error-matched normal volunteers and determine parameters characteristic for dry AMD.

Material and methods

This was a prospective, cross-sectional study. The macular areas of 28 eyes of 28 patients with dry AMD (Group 1) and 28 normal eyes of 28 age-matched controls (Group 2) were examined with SS-OCT (DRI-OCT, Topcon, Tokyo, Japan).

All enrolled participants underwent thorough ophthalmic examinations, including a spherical equivalent refractive error measured with an autorefractometer (NIDEK Co, Ltd, Japan), slit-lamp examination, fundus photography, fluorescein angiography and SS-OCT (DRI-OCT, Topcon, Japan). Preoperative refraction was used in pseudophakic patients with a history of previous cataract surgery. In phakic patients, the most recent refraction was used.

Dry AMD was diagnosed if any of the following features were noted: soft drusen bigger than 125 microns in diameter, retinal pigment epithelium alternations or drusenoid pigment epithelial detachment. Exclusion criteria were: refractive error higher than 6.0 diopters, the presence of choroidal neovascularization (CNV) in the study eye, any other retinal or vitreoretinal diseases in the study eye (such as diabetic retinopathy, epiretinal membrane, vitreoretinal traction syndrome, macular hole etc.), history of previous ocular surgery despite uncomplicated cataract surgery.

The control group was recruited from healthy volunteers. The study eye was randomly selected in each patient.

To exclude diurnal variations in choroidal thickness all examinations were performed at the same time (3–6 p.m.) Choroidal thickness was estimated automatically and manually using an SS-OCT system with a resolution of 1.0 μm. Additionally, we analyzed the thickness of particular choroidal vascular layers. Manual choroidal thickness was estimated on the single line scan with a resolution of 1.0 μm built from 1024, 12.0 mm long A scans centered in the fovea. Choroidal thickness was measured subfoveally as the distance between the posterior edge of RPE and the outer choroidoscleral boundary (CSB) (Fig. 1). Choroidal thickness was also measured automatically on the 3-dimensional scanning protocol with 3.0 μm axial resolution and speed of 100 000 scan/sec. It consists of 256 horizontal scans covering an area of 12.0 mm. The ETDRS grid was applied to the scanned area and mean choroidal thickness for each area was documented. ETDRS grid divides the macula into 9 regions with three rings measuring 1.0 mm (central ring diameter), 3.0 mm (inner ring) and 6.0 mm (outer ring). The inner and outer regions are further divided into superior, inferior, temporal and nasal quadrants. (Fig. 2).

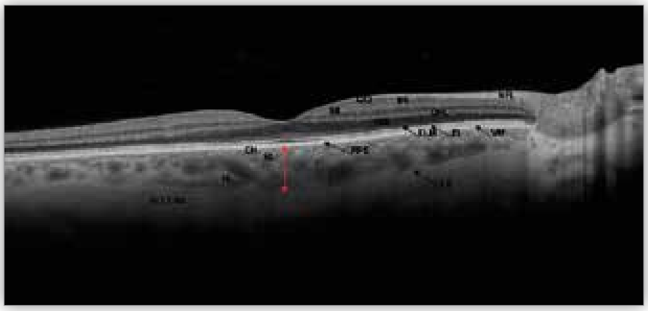

Fig. 1. SS-OCT image of a healthy eye showing the manual measurement of choroidal thickness at the fovea on the single line scan as a distance between posterior edge of RPE and the outer CSB (red arrow) (NFL – nerve fiber layer, GCL – ganglion cell layer, IPL – inner plexiform layer, INL – inner nuclear layer, OPL – outer plexiform layer, ONL – outer nuclear layer, ELM – external limiting membrane, VM – Voerhoff's membrane, RPE – retinal pigment epithelium, CH – choriocapillaries layer, SL – Sattler's layer, HL – Haller's layer, LS – suprachoroid lamina).

Ryc. 1. Obraz badania SS-OCT zdrowego oka pokazujący metodę ręcznego pomiaru grubości naczyniówki (mierzonej poddołkowo) jako odległości między nabłonkiem barwnikowym siatkówki a granicą naczyniówkowo-twardówkową (czerwona strzałka) (NFL – warstwa włókien nerwowych, GCL – warstwa komórek zwojowych, IPL – warstwa splotowata wewnętrzna, INL – warstwa jądrzasta wewnętrzna, OPL – warstwa splotowata zewnętrzna, ONL – warstwa jądrzasta zewnętrzna, ELM – błona graniczna zewnętrzna, VM – błona Voerhoffa, RPE – nabłonek barwnikowy siatkówki, CH – warstwa choriokapilar, SL – warstwa Sattlera, HL – warstwa Hallera, LS – blaszka nadnaczyniówkowa).

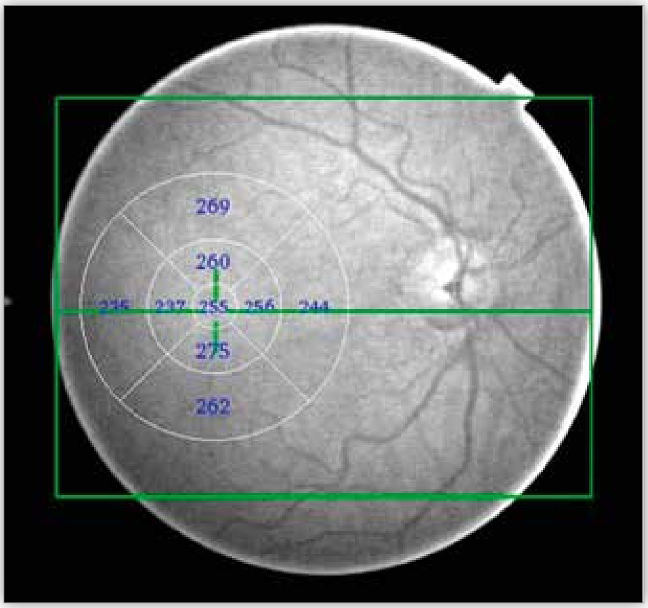

Fig. 2. The mean choroidal thickness located in the center of each representative point of each area of the ETDRS grid.

Ryc. 2. Średnia grubość naczyniówki oceniana w centrum obszaru ETDRS.

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In both healthy eyes and eyes with dry AMD, individual choroidal layers were recognizable on a single, high-resolution B-scan. Haller's Layer (large choroidal vessels) was identified precisely and measured by drawing a perpendicular line to the fovea from the inner border of the Haller's Layer to the outer CSB. The combined thickness of Sattler's Layer (of medium choroidal vessels) and the choriocapillaris complex was calculated by subtracting Haller's Layer from the total choroidal thickness (Fig. 3).

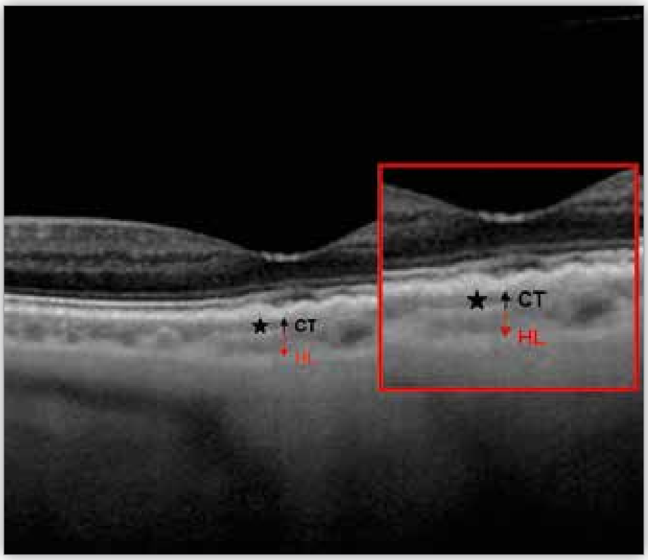

Fig. 3. Method used to analyze the individual vascular layers of the choroid. Haller's Layer (large choroidal vessels, red arrow) was identified precisely and measured by drawing a perpendicular line to the fovea from the inner border of the Haller's Layer to the outer CSB. The combined thickness of Sattler's Layer (of medium choroidal vessels) and the choriocapillaris complex (black star) was calculated by subtracting Haller's Layer from the total choroidal thickness (black arrow).

Ryc. 3. Ilustracja metody użytej do oceny pojedyńczych warstw naczyń naczyniówki. Warstwa Hallera (duże naczynia naczyniówki, czerwona strzałka) została dokładnie zidentyfikowana poprzez narysowanie linii prostopadłej do dołka od wewnętrznej granicy warstwy Hallera do granicy naczyniówkowo-twardówkowej. Łączna grubość i grubość warstwy choriokapilar zostały obliczone poprzez odjęcie grubości warstwy Hallera od całkowitej grubości naczyniówki (czarna strzałka).

Statistical analysis was performed with SigmaStat 3.5 for Windows.

Results

The mean age in Group 1 was 75.5 ± 7.5 years and the mean refractive error was 1.3 ± 2.0 diopters. The mean age in Group 2 was 75.1 ± 7.5 years and the mean refractive error was 1.5 D ± 1.9 diopters. The age and refractive error differences between groups were not statistically significant (p =.83 and p = .70, respectively). In each group, 13 eyes were pseudophakic and 15 eyes were phakic.

Analysis of individual choroidal layers

We evaluated the thickness of individual choroidal vascular layers in patients with AMD and in age-matched controls. The thickness of medium choroidal vessels layer and choriocapillaris complex tended to be lower in patients with AMD, as compared to healthy subjects (31.3 ± 23.4 μm vs. 42.6 ± 23.7 μm, p = .064). The thickness of large choroidal vessels layer was 174.7 ± 69.1 μm in the AMD group and 193.1 ± 101.6 μm in the healthy control group (p = .45).

Choroidal thickness measurements

Mean central choroidal thickness measured manually at the fovea in the AMD group did not differ significantly from age-matched controls (205.9± 76.8 μm vs. 239.8 ± 86.0 μm, p = .12)

The mean choroidal thickness was evaluated subfoveally and in 8 quadrants: inner and outer nasal, inner and outer temporal, inner and outer superior, and inner and outer inferior in both groups. We observed the same choroidal thickness pattern in both groups, with the choroid being the thickest subfoveally and the thinnest in the outer nasal quadrant. Moreover, the inferior choroid was thinner than its superior area. Central choroidal thickness in both groups correlated negatively with age (r = -.42, p = .023 vs. r = -.45, p = .019 in AMD and control groups, respectively). Furthermore, in the dry AMD group no statistically significant correlation was demonstrated between subfoveal choroidal thickness and refractive error (r = .12, p = .56) whereas in the age-matched controls, we observed a weak correlation (r = .37, p = .053).

We performed multiple regression analysis in order to determine the most important factors associated with choroidal thickness. All analyzed data were included in the analysis (age, refractive error, phakic status, geographic atrophy, glaucoma, presence of CNV in fellow eye, visibility of the suprachoroidal space – SCS). In Group 1, multiple regression analysis revealed that choroidal thickness in patients with dry AMD is associated with their phakic status (p = .003; F = 10.95). Choroidal thickness was significantly lower in pseudophakic than in phakic eyes (167 μm vs. 250 μm, respectively), regardless of patient's age. In Group 2, multiple regression analysis revealed, as anticipated, that choroidal thickness depended on patient's age (p = .01; F = 6.28).

As mentioned above, five patients with dry AMD had choroidal neovascularization in their fellow eye. The estimated mean choroidal thickness of 175.8 μm ± 69.8 in this group did not differ significantly (p = .34) from the patients without CNV in fellow eye (212.5 ± 78.1 μm).

Analysis of the choroidoscleral boundary (CSB)

CSB was recognized in all eyes and classified as regular, if it followed the natural shape of the globe (Figure 4a) or irregular, if it followed the alternating shape of choroid (Figure 4b). We observed irregular CSB in 22 eyes (78%) from Group 1 and in 5 eyes (18%) from Group 2. Suprachoroidal layer was recognized as two bands, an inner hyperreflective and an outer hyporeflective band, indicating the boundary between choroid and sclera. The outer hyporeflective band probably correlates with SCS (3) (Fig. 5). SCS was visible in 36% eyes in Group 1 and in 7% in Group 2. We performed multiple regression analysis to identify independent variables correlating with the visibility of the SCS. This revealed that in Group 1 SCS occurs more often in pseudophakic eyes (p = .02; F = 5.98). Multivariate analysis did not reveal any variables associated with the visibility of SCS in healthy eyes.

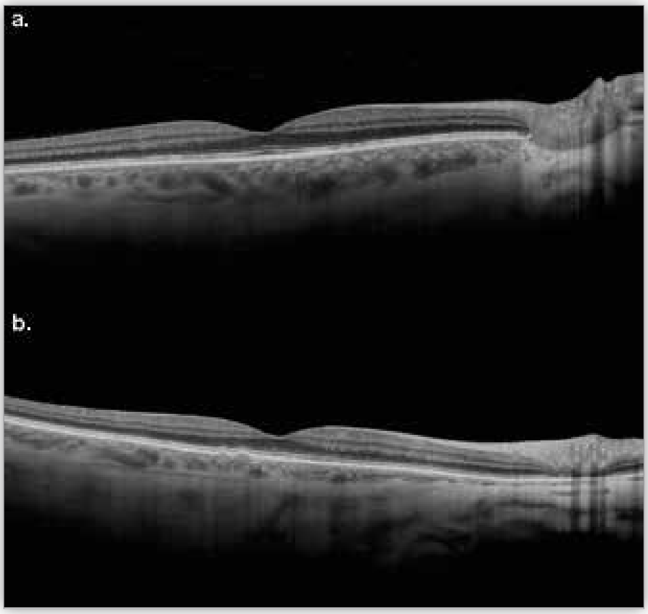

Fig. 4. Illustration of different morphology of CSB: a. regular CSB follows the natural oval contour of the globe, b. irregular CSB varies in thickness from point to point.

Ryc. 4. Przedstawienie różnych morfologii CSB: a. regularne CSB naśladuje naturalny owalny kształt gałki ocznej, b. nieregularne CSB różni się grubością od punktu do punktu.

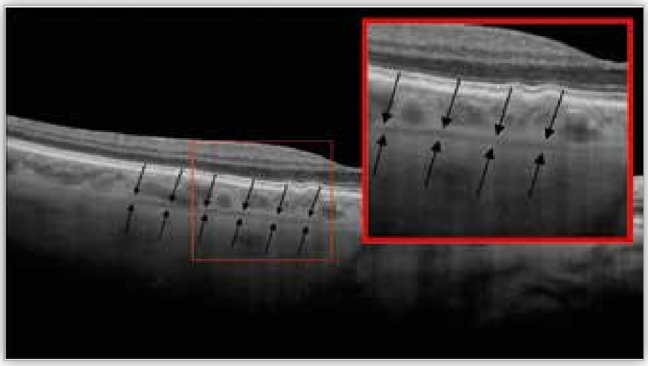

Fig. 5. Illustration showing the additional outer hyporeflective line recognized as SCS (black arrows).

Ryc. 5. Zdjęcie przedstawiające dodatkową zewnętrzną hyporefleksyjną linię uznaną za SCS (czarne strzałki).

Discussion

In this study, we observed that the choroid is thinner in pseudophakic than in phakic eyes with AMD. Despite lack of significant differences in choroidal thickness between eyes with drusen in dry AMD and healthy subjects, choroidal morphology is altered in dry AMD cases. The outer CSB is more often irregular and suprachoroidal layer is more often visible in eyes with dry AMD than in healthy age matched subjects.

Abnormalities in choroidal circulation have been postulated to play an important role in the pathophysiology of AMD (8, 9). Using Doppler techniques Grunwald et al. noticed that eyes with AMD have decreased choroidal blood flow (9). Reduced choroidal thickness has been reported in geographic atrophy and in eyes with choroidal neovascularization (10). In a histological study, Sarks reported that choroidal thinning may occur in late stages of dry AMD (11). In our group, we did not observe statistically significant thinning of the choroid in any quadrant in eyes with dry AMD when compared to age and refractive error matched controls. This may be explained by the fact that most patients in our study group had moderate, dry AMD.

Currently available SD-OCT and SS-OCT devices are unable to automatically delineate thickness of particular choroidal layers, thus we had to perform the segmentation manually. Our study, using SS-OCT, showed a trend towards thinning of the choriocapillaries/ medium choroidal vessels complex. This confirms earlier histological studies suggesting decreased choriocapillaries density below drusen (8).

We observed the outer CSB is more frequently irregular in eyes with drusen than in healthy subjects. This is probably because of the varying blood vessel diameter in Haller's layer. As SD-OCT choroidal thickness measurements are performed manually with the in-built caliper, the values presented by earlier authors might have been affected by the point-to-point variation of choroidal thickness in eyes with AMD. Enabling automated measurement, SS-OCT probably presents more unified data of choroidal thickness in each measured quadrant. Stating that choroidal thickness is altered in AMD, earlier authors investigated more severe AMD cases than ours. This may also explain why we did not find a statistically significant difference between healthy eyes and eyes with dry AMD. We must also consider the possibility of selection bias, which may occur in any cross-sectional study. The ideal model would be to compare study eyes with their unaffected fellow eyes. Unfortunately, however, AMD is a bilateral disease and elderly patients with unilateral AMD are rarely found. Phacoemulsicfication may have an influence on the dilution of anti-VEGF drugs due to intraoperative fluidics. In our group, we estimated that the phakic status is the most important independent factor, having influence on choroidal thickness in eyes with AMD. It requires further studies, but it may be speculated that cataract extraction is associated with choroidal thinning in susceptible eyes with AMD. Earlier reports have suggested choroidal thickening after cataract extraction in eyes without macular diseases (12, 13).

In conclusion, the outer CSB is more often irregular and SCS is more often visible in dry AMD, which may suggest varying diameter of large choroidal vessels. Furthermore, central choroidal thickness is lower in pseudophakic eyes with AMD.

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