Retinal Changes in Different Grades of Retinal Artery Occlusion: An Optical Coherence Tomography Study

Olga Furashova¹ and Egbert Matthé²

¹Ophthalmology Department, Hospital Chemnitz, Chemnitz, Germany
²Ophthalmology Department, University Hospital Dresden, Dresden, Germany

Correspondence: Olga Furashova, Ophthalmology Department, Hospital Chemnitz, Flemmingstraße 2, 09116 Chemnitz, Germany; o.furashova@skc.de.
Submitted: June 12, 2017
Accepted: September 11, 2017
Citation: Furashova O, Matthé E. Retinal changes in different grades of retinal artery occlusion: an optical coherence tomography study. Invest Ophthalmol Vis Sci. 2017;58:5209–5216. DOI:10.1167/iovs.17-22411

PURPOSE. To investigate layer-by-layer changes in retinal thickness and reflectivity regarding the severity grade of acute retinal artery occlusion (RAO) using spectral-domain optical coherence tomography (SD-OCT).

METHODS. This study is a retrospective, observational case-control series that took place in an institutional setting and included 148 eyes from 74 patients diagnosed with acute RAO (central or branch). SD-OCT examinations were taken at baseline. Based on OCT findings, RAO was categorized into three grades (incomplete, subtotal, total). The thickness and reflectivity of selected retinal layers were measured from SD-OCT images. The data were compared across the three grades and against the contralateral eyes (controls). The main outcome measures were thickness and reflectivity of selected retinal layers.

RESULTS. The thickness of the inner and middle retinal layers differed significantly across the three RAO groups \( (P < 0.001) \), whereas the outer retinal layer thickness remained not significantly different. Reflectivity values showed statistically significant differences in the inner, middle, and outer retinal layers, but not in the vitreous body \( (P < 0.001) \).

CONCLUSIONS. The reflectivity changes of selected retinal layers differ significantly regarding different grades of RAO. SD-OCT reflectivity measurement may be used as a noninvasive method to estimate the grade of retinal ischemia in RAO.

Keywords: retinal artery occlusion, optical coherence tomography, retinal ischemia, oxidative damage, retinal thickness

Retinal artery occlusion (RAO) leads to severe ischemia of the retina, causing sudden painless loss of vision. At initial presentation, the visual acuity ranges from no light perception to 20/25, with 90% of patients having a visual acuity of 20/400 or less in the case of central RAO. Visual outcome has been shown to be very poor with very low visual improvement. Several studies showed stage-dependent visual outcome of retinal artery occlusion after intraarterial fibrinolysis treatment as well as correlation of baseline and final visual acuity depending on the stage of ischemia. Therefore, a handy and easy grading system of acute ischemia in retinal artery occlusion would be clinically important.

Schmidt and associates classified the central retinal artery occlusion (CRAO) as incomplete, subtotal, and total based on the clinical criteria such as vision loss and extent of retinal edema as well as a delay in arterial blood flow on fluorescein angiography. This grading system has been shown to be related to the prognosis after treatment in eyes with CRAO. However, it is subjective and does not provide quantitative information. Moreover, it cannot be adapted to cases of branch retinal artery occlusion (BRAO). Visual acuity as important criteria is mainly affected in an “on/off” manner, depending on the perfusion stage of the macula. Furthermore, fluorescein angiography is an invasive method subject to rare but sometimes severe complications such as nausea, vomiting, dyspnea, and syncope as well as a possibility of severe anaphylaxis.

Optical coherence tomography (OCT) is a noninvasive technology providing in vivo high-resolution cross-sectional images of the retina. Based on OCT images, microscopic damage to the retina in different layers can be identified and observed over time.

Spectral-domain OCT (SD-OCT) compares a light beam reflected in the investigated medium with a reference beam by interferometry. The higher the differences between investigation beam and reference beam, the higher the optical density (i.e., optical intensity or reflectivity) of the investigated tissue. This optical density, in this article also termed “optical intensity” or “reflectivity,” can be displayed as a more or less arbitrary gray scale image ranging from 0 to 255 for each pixel.

Ahn et al. identified distinctive features of retinal ischemia in CRAO at each grade based on OCT morphologic features, such as layered structure of the inner retina, inner retinal hyperreflectivity, and macular edema. Incomplete CRAO is characterized by minimal loss of the organized layered structure of the inner retina and inner retinal hyperreflectivity without distinct macular edema. Subtotal CRAO showed distinct loss of the organized layered structure of the inner retina and macular edema, whereas total CRAO differed from the other two types by marked macular edema and subfoveal choroidal thinning. However, the degree of inner retinal hyperreflectivity still remains a subjective parameter without established quantitative measurements.

To the best of our knowledge, there is no study that quantitatively evaluated the hyperreflectivity of the inner retinal layers at different grades of acute retinal ischemia. The
purpose of the current study, therefore, is to quantitatively assess the hyperreflectivity of the inner retinal layers regarding different grades of retinal artery occlusion.

**METHODS**

The present study adhered to the tenets of the Declaration of Helsinki and has been approved by the Institutional Review Board of Dresden Technical University (Dresden, Germany). Informed patients’ consent was waived because of the retrospective design and because no study-related investigations were necessary.

The investigation is registered in ClinicalTrials.Gov (ClinicalTrials.gov Identifier NCT03061526).

**Patient Selection**

The patient database in the Dresden University Eye Hospital was reviewed for billing codes of CRAO and BRAO according to the International Classification of Diseases, 10th Revision between September 2010 and December 2016. Patients included in this study had to meet several criteria. First, the patients had to be diagnosed with acute CRAO or BRAO. BRAO was defined as an occlusion of one of the branches of central retinal artery. It should have affected at least in part paramacular regions central of the retinal vessel arcades, but no more than half of the retina. Second, there had to be vision loss or a deficit in the visual field occurring within 7 days of the initial visit. Third, the patient must have had SD-OCT at the initial visit. Fourth, the OCT image quality score had to be >30. Patients with a history of ocular trauma or presence of macular disease, severe nonproliferative or proliferative diabetic retinopathy, other retinal vascular diseases, glaucoma, myopic retinopathy, or other diseases interfering with OCT images in any one of the eyes (e.g., vitreomacular traction, epiretinal membrane) as well as one-eyed patients were excluded from the analysis. The contralateral eye of the patients was chosen as the control eye to provide the best match regarding age, sex, and concomitant diseases (such as coronary artery diseases or arterial hypertension), which might affect the retinal vessel situation.

**Ophthalmic Examination**

All patients underwent a complete ophthalmic examination of both eyes including best-corrected visual acuity (BCVA) in decimal numbers, applanation tonometry, slit-lamp biomicroscopy, indirect binocular ophthalmoscopy, and SD-OCT imaging. Some patients were additionally examined by fluorescein angiography.

SD-OCT examination was performed using Spectralis OCT (Heidelberg Engineering Inc., Heidelberg, Germany). The macula was scanned with an acquisition speed of 40,000 A-scans per second using “fast macular volume” protocol, consisting of a 25-line horizontal raster scan covering 20′ x 20′ centered on the fovea with standard nine frames. The eye tracking system (ART Module, Heidelberg Engineering Inc.) was used to minimize motion artifacts.

**Classification of Disease Grades**

To characterize the disease grade, the eyes with RAO were divided into incomplete, subtotal, and total according to the OCT findings suggested by Ahn et al.11 Table 1 summarizes the criteria for the disease grades. Representative photographic images of the fundus, OCT, and fluorescein angiography are shown in Figure 1.

Although to the best of our knowledge there is no grading system for BRAO, we decided to adopt the system suggested by Ahn et al.11 We believe that the underlying mechanism of CRAO and BRAO are identical, with the only exemption being the degree of visual loss depending on affection of the macular region by the RAO.

**Thickness and Reflectivity Measurement**

For measuring retinal thickness and reflectivity, a spot in 1000 µm distance to the fovea was chosen using the built-in distance measuring tool of the OCT software (Fig. 2). In the case of CRAO, this spot was 1000 µm temporal of the fovea. In the case of BRAO, the region of occlusion was chosen, most often directly superior or inferior of the fovea. The distance of 1000 µm was used in the same manner.

Because in subtotal and total RAO a beginning or severe loss of organized retinal structure is seen, a distinct measurement of each retinal layer—as it is seen in healthy eyes—is impossible. For calculating retinal thickness and layer reflectivity, several retinal layers were combined to represent the inner, middle, and outer retinal structures (Table 2; Fig. 2). The innermost retinal layer, consisting of retinal nerve fiber layer/ganglion cell layer (GC) and inner plexiform layer (IPL), was measured between the internal limiting membrane and the outer border of the inner plexiform layer (IMRL: GC + IPL). The thickness between the inner border of the inner nuclear layer (INL) and the outer border of the outer plexiform layer (OPL) was labeled the middle retinal layer (MRL: INL + OPL). Both of these layers built the inner retinal layer (IRL: GC + IPL + INL + OPL). The outer retinal layer (ORL), consisting of the combined outer nuclear layer, ellipsoid, external limiting membrane, and retinal pigment epithelium, was measured between the inner border of the outer nuclear layer and the outer border of the retinal pigment epithelium. The retinal thickness measurements were done manually using the built-in calipers of the OCT system software. The central foveal thickness was also registered.

In case of total RAO with—by definition—loss of structure, layer thickness and segmentation had to be estimated as well as possible. All thickness measurements were done by one examiner (O.F.).

Representative OCT images defining the segmentation and measurement of the thickness of the retinal layers in the regions of interest are shown in Figure 2.

**Optical Intensity Measurements**

The B-scan image of the region of interest (see above) was exported as lossless grayscale JPEG image in “black-on-white” style. The optical intensity measurements were obtained using Adobe Photoshop Software (CS6 version 13.0 x 64; Adobe Systems Incorporated, San Jose, CA, USA). The optical intensity of the previously defined layers (IMRL, MRL, IRL,
ORL) as well as of the vitreous body was measured by selecting an area at least 5×5 μm in each of the layers and calculating average grayscale, where the scale ranged from 0 (pure black) to 255 (pure white). Same data were obtained from the contralateral eyes. All picture analyses were done by one examiner (E.M.).

**Statistical Analysis**

Data for continuous variables are expressed as mean ± standard deviation. Visual acuity measurements were converted from decimal numbers to the logarithm of the minimal angle of resolution (logMAR) for all analyses. Visual acuity was defined in severe vision loss as the following: counting fingers = 2.3 logMAR, hand motion = 2.5 logMAR, light perception = 2.8 logMAR, and no light perception = 3.0 logMAR. One-way multivariate factorial ANOVA with post hoc Sidak’s test was performed to compare differences across the three RAO groups and with contralateral eyes. For representing statistical significance, $P < 0.05$ was chosen. IBM SPSS Statistics, version 23.0.0.0 for Windows (IBM, Armonk, NY, USA) was used to perform the analysis.

**Results**

**Overall**

In total, 148 eyes from 74 patients were included in this study. Table 3 summarizes the demographic and clinical characteristics of the study participants.

There were no statistical differences between the three groups regarding the mean age at presentation or BCVA of the unaffected eye. In the incomplete and subtotal occlusion

![Representative photographic images of the fundus (left column), fluorescein angiography (FA; middle column), and SD-OCT images (right column) in each group of incomplete, subtotal, and total central RAO. In incomplete CRAO, the photographic image of the fundus (a) shows mild retinal whitening without distinctive cherry-red spot. The FA (b), taken at 20 seconds after dye injection, shows a mild delay in retinal perfusion. On the SD-OCT image (c), hyperreflectivity of inner retinal layers without retinal thickening as well as intact layer-by-layer structure can be observed. In case of subtotal CRAO, note more distinct retinal whitening in the macula with cherry-red spot on color fundus photography (d). Furthermore, subtotal CRAO shows marked delay in retinal perfusion in FA (e) taken at 40 seconds after dye injection as well as central hypofluorescence due to shadowing effect of area with retinal whitening. Observe marked inner retinal layers' thickening on SD-OCT image of subtotal CRAO (f). In total CRAO, fundus photograph (g) shows extreme retinal whitening with a very small area of a cherry-red spot. FA in total CRAO (h), taken at 67 seconds, shows long delay in retinal perfusion. Note here a small area with normal retinal perfusion in papillomacular bundle due to cilioretinal artery (g, h). The SD-OCT image (i) demonstrates complete loss of layer-by-layer structure and extreme retinal thickening in total CRAO.
groups, there were no differences regarding sex and relation of BRAO/CRAO, respectively. In the group with total occlusion, there were statistically significantly more female patients with CRAO. BCVA of the affected eyes differed significantly across the three groups, with lower acuity in higher occlusion grade.

We measured thickness and reflectivity—both parameters change in case of edema—in the given retinal layers. Table 4 outlines the retinal thickness measurements of the different retinal layers in each group of RAO patients.

**Thickness**

As retinal thickness is part of the grading system, we expected changes between healthy eyes and RAO eyes. Preliminary data (manuscript in preparation) show that only ORL thickness did not differ significantly across the three RAO grades, suggesting that increased total retinal thickness in case of acute retinal ischemia is mainly due to increased thickness of the inner and middle retinal layers. After further analysis (post-hoc Sidak’s test), IMRL and IRL thickness remained statistically significantly different across the three RAO groups ($P < 0.05$ and $P < 0.001$ respectively), while total retinal thickness and MRL thickness differed significantly only in total occlusion group compared to incomplete and subtotal (Table 4).

**Optical Intensity**

Table 5 and Figure 3 summarize the optical intensity measurements of the retinal layers at different grades of RAO and the contralateral eyes. Higher values indicate less reflectivity or opacity (whiter in black-on-white-pictures), whereas lower values show more reflectivity or opacity (darker in black-on-white-pictures).

The reflectivity of IMRL, IRL, and ORL showed statistically significant differences between the three RAO grades, whereas MRL and vitreous body reflectivity showed no significant differences in the comparison across the three RAO groups and in comparison with healthy eyes. After analysis of multiple comparisons using the Sidak’s test, the differences in IMRL reflectivity remained statistically significantly different across the three RAO groups ($P < 0.001$). IRL and ORL reflectivity stayed significantly different between the incomplete and subtotal groups ($P < 0.05$) as well as the incomplete and total occlusion groups ($P < 0.001$), but not between the subtotal and total RAO groups ($P = 0.075$ and $P = 0.078$, respectively). The reflectivity of vitreous body showed no differences across the three RAO groups even after the Sidak’s test analysis was performed.

Because vitreous or other opacities (cataracts) might corrupt the absolute optical intensity of the different retinal layers, we calculated ratios of optical intensity of the most affected retinal layers in each eye (Table 6). The ratios were further analyzed performing the Sidak’s test and were statistically significantly different across all the groups of artery occlusion as well as when compared with the contralateral eyes.
Differences between the three RAO grades were calculated using 1-way multivariate factorial ANOVA test. CFT, central foveal thickness.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients, N = 74</th>
<th>Incomplete, n = 27</th>
<th>Subtotal, n = 28</th>
<th>Total, n = 19</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at presentation ± SD, y (range)</td>
<td>71.8 ± 10.6 (43 to 90)</td>
<td>69.7 ± 10.4 (51 to 88)</td>
<td>72.9 ± 10.1 (49 to 86)</td>
<td>73.4 ± 11.6 (43 to 90)</td>
<td>0.849</td>
</tr>
<tr>
<td>Sex, no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>46 (62)</td>
<td>20 (74)</td>
<td>19 (68)</td>
<td>7 (37)</td>
<td>0.038*</td>
</tr>
<tr>
<td>Female</td>
<td>28 (38)</td>
<td>7 (26)</td>
<td>9 (32)</td>
<td>12 (63)</td>
<td></td>
</tr>
<tr>
<td>Artery occlusion type, no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRAO</td>
<td>28 (47)</td>
<td>12 (44)</td>
<td>16 (57)</td>
<td>2 (11)</td>
<td>0.004</td>
</tr>
<tr>
<td>CRAO</td>
<td>32 (53)</td>
<td>15 (56)</td>
<td>12 (43)</td>
<td>17 (89)</td>
<td></td>
</tr>
<tr>
<td>BCVA, affected eye logMAR, mean ± SD (range)</td>
<td>1.28 ± 1.03 (0.00 to 2.80)</td>
<td>0.77 ± 0.70 (0.00 to 2.50)</td>
<td>1.29 ± 1.07 (0.00 to 2.50)</td>
<td>2.03 ± 0.93 (0.00 to 2.80)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>BCVA, healthy eye logMAR, mean ± SD (range)</td>
<td>0.13 ± 0.19 (0.00 to 0.52)</td>
<td>0.13 ± 0.17 (0.00 to 0.52)</td>
<td>0.11 ± 0.21 (0.00 to 1.00)</td>
<td>0.15 ± 0.19 (0.00 to 1.00)</td>
<td>0.741</td>
</tr>
</tbody>
</table>

BRAO, branch retinal artery occlusion; CRAO, central retinal artery occlusion; BCVA, best corrected visual acuity; logMAR, logarithm of the minimal angle of resolution. Differences between the three RAO grades were calculated using 1-way multivariate factorial ANOVA. logMAR, logarithm of the minimal angle of resolution.

* Statistically significant.

DISCUSSION

RAO leads to clinically detectable changes of the retina. Oxygen depletion causes the inner retinal cell homeostasis to collapse, leading to breakdown of Na-K-ATPase, swelling by water intake, and lowering the light transmission. Clinically, edema of the retina is seen as a yellowish tinge in the ischemic areas, especially surrounding the fovea, with the fovea itself seen as “cherry-red spot.” Because OCT is based on reflectivity and transmission measurements, those clinically detectable changes should be found in OCT as well.

In the present study, we analyzed the OCT findings at different grades of acute RAO. We adapted the grading system suggested by Ahn et al. and classified acute RAO in incomplete, subtotal, and total RAO.

The grade of RAO is clinically important because it correlates significantly with the degree of acute retinal ischemia as well as baseline and final visual acuity. Furthermore, there have been studies reporting stage-dependent outcomes of intraarterial thrombolysis in RAO. Intra-arterial thrombolysis may offer functional benefits in eyes with incomplete CRAO, but not in eyes with subtotal or total CRAO.

Schmidt and associates described CRAO as incomplete, subtotal, and total according to the degree of vision loss, extent of retinal edema, and delay in retinal artery filling. Ahn and associates were the first to report pathologic staging of CRAO on the basis of the OCT characteristics at baseline. Incomplete CRAO showed a minimal loss of organized layered structure of the inner retina and inner retinal hyperreflectivity without distinctive macular edema. Subtotal CRAO presented with distinct macular edema and loss of organized layered structure. Total CRAO was distinguished from the other two stages by the presence of marked macular edema and subfoveal choroidal thinning.

The use of visual acuity to grade RAO might lead to problems because in the cases of BRAO, the foveal region might or might not be affected. This could lead to severe differences in grading, although the underlying pathology should be identical. OCT-based measurements would rule out this potential problem because data are taken at the very place of the pathology and are not dependent on foveal function.

Previous studies investigating OCT findings in eyes with CRAO demonstrated an increased reflectivity and thickness of the inner retina in the acute phase. These are consistent with the findings of the present study. We could find statistically significant changes in the thickness and reflectivity of different retinal layers correlating to the grade of acute retinal ischemia.

There was a highly statistically significant increase in the thickness of the inner and middle retinal layers, whereas the thickness of the outer retinal layer did not show any difference across the three RAO groups. Therefore, acute retinal ischemic situations can be detected by an increase in thickness in the inner and middle retinal layers. However, in severe ischemic situations such as subtotal and total RAO, the layer-by-layer structure of the retina might be damaged strongly, preventing clear segmentation of different retinal layers. Thus, the thickness measurement of retinal layers might not always be helpful to access retinal ischemic damage.

### Table 4. Retinal Thickness Measurements (μm) by OCT at Different Grades of RAO

<table>
<thead>
<tr>
<th>Retinal Layer/Disease Grade</th>
<th>Incomplete, n = 27</th>
<th>Subtotal, n = 28</th>
<th>Total, n = 19</th>
<th>P Value</th>
<th>Contralateral Eye, n = 74</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFT, μm</td>
<td>217</td>
<td>234</td>
<td>425</td>
<td>&lt;0.001*</td>
<td>235</td>
</tr>
<tr>
<td>IMRL, μm</td>
<td>101</td>
<td>132</td>
<td>169</td>
<td>&lt;0.001*</td>
<td>95</td>
</tr>
<tr>
<td>MRL, μm</td>
<td>77</td>
<td>105</td>
<td>108</td>
<td>&lt;0.001*</td>
<td>67</td>
</tr>
<tr>
<td>IRL, μm</td>
<td>178</td>
<td>237</td>
<td>279</td>
<td>&lt;0.001*</td>
<td>162</td>
</tr>
<tr>
<td>ORL, μm</td>
<td>172</td>
<td>173</td>
<td>235</td>
<td>0.012</td>
<td>161</td>
</tr>
<tr>
<td>Total retinal thickness (IRL + ORL), μm</td>
<td>349</td>
<td>410</td>
<td>514</td>
<td>&lt;0.001*</td>
<td>524</td>
</tr>
</tbody>
</table>

CFT, central foveal thickness; IMRL, innermost retinal layer; MRL, middle retinal layer; IRL, inner retinal layer; ORL, outer retinal layer. Differences between the three RAO grades were calculated using 1-way multivariate factorial ANOVA. CFT, central foveal thickness.

* Statistically significant across the three grades of RAO.
Furthermore, changes in retinal thickness are seen in many diseases, whereas increased optical reflectivity of the inner retinal layers is specifically seen in retinal ischemia, such as RAO, diabetic retinopathy, retinal vein occlusion, and other vascular retinal diseases. In the present study, we found the strongest changes in the reflectivity of inner retinal layers considering the grade of retinal ischemia. We could show strong statistically significant differences in retinal reflectivity for IMRL across all disease grades with higher levels in the higher RAO occlusion grade. Regarding the OCT technology, the light beam enters the retina by first penetrating the surface of the retina (inner limiting membrane), then crossing all of the retinal layers from the inner limiting membrane to the retinal pigment epithelium. Higher reflectivity of the inner retinal layers in cases of acute ischemia results in less reflectable light for the underlying outer retinal layers. Thus, higher IMRL reflectivity results in lower ORL reflectivity levels. This is consistent with the findings of the present study. ORL reflectivity measurements followed the same pattern as IMRL, but with lower levels in higher RAO occlusion grade and no significant difference between subtotal and total RAO grade (post hoc Sidak’s test).

IRL reflectivity also strongly differed between each RAO group, whereas MRL values showed no significant difference. Therefore, our results suggest that the measurement of IMRL reflectivity might be more useful to define the grade of acute retinal ischemia in cases of RAO. These findings are not consistent with Chen et al. They found the strongest association of optical intensity of the INL with the acute CRAO disease status. The different sample size and different patient population as well as the method of reflectivity measurement may possibly explain the different results among the studies.

The exact mechanism of changes in the optical intensity of retinal layers in acute RAO remains unknown. Ashton et al. demonstrated swelling of cells and axons in the nerve fiber, ganglion cell, inner plexiform, inner nuclear, and outer plexiform layers following 1 hour of embolization of a pig retina.

McLeod suggested the term ‘oncosis’ to describe the swelling that occurs in the cell before death in the majority of acute retinal pathology. In the present study, we could show a

**TABLE 5.** Optical Intensity Measurements in Different Grades of RAO

<table>
<thead>
<tr>
<th>Retinal Layer/Disease Grade</th>
<th>Incomplete, n = 27</th>
<th>Subtotal, n = 28</th>
<th>Total, n = 19</th>
<th>P Value</th>
<th>Contralateral Eye, n = 74</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMRL</td>
<td>124</td>
<td>90</td>
<td>60</td>
<td>&lt;0.001*</td>
<td>157</td>
</tr>
<tr>
<td>MRL</td>
<td>108</td>
<td>116</td>
<td>128</td>
<td>0.065</td>
<td>187</td>
</tr>
<tr>
<td>IRL</td>
<td>113</td>
<td>100</td>
<td>87</td>
<td>&lt;0.001*</td>
<td>168</td>
</tr>
<tr>
<td>ORL</td>
<td>217</td>
<td>228</td>
<td>238</td>
<td>&lt;0.001*</td>
<td>223</td>
</tr>
<tr>
<td>vitreous body</td>
<td>247</td>
<td>247</td>
<td>242</td>
<td>0.057</td>
<td>248</td>
</tr>
</tbody>
</table>

IMRL, innermost retinal layer; MRL, middle retinal layer; IRL, inner retinal layer; ORL, outer retinal layer. Differences between the three RAO grades were calculated using 1-way multivariate factorial ANOVA test.

* Statistically significant across the three grades of RAO.

**FIGURE 3.** Bar graphs showing optical intensity of vitreous body and selected retinal layers at different grades of retinal artery occlusion and contralateral eyes. The x-axis shows different groups for comparison. The y-axis shows the optical intensity levels, ranging from 0 (absolute black) to 255 (absolute white) for different retinal layers. Asterisks mark statistically significant values with P < 0.005. The differences between the three retinal artery occlusion grades were calculated using 1-way multivariate factorial ANOVA test. Outliers are marked as small circles.
statistically significant increase in the reflectivity of the inner retinal layers in each grade of acute RAO. Therefore, we suggest that optical reflectivity measurements correlate strongly with intracellular swelling processes in the retina. Our results support the idea that the optical intensity measurement of the inner retinal layers can be used to estimate the severity of acute retinal ischemia.

The optical intensity on OCT represents the reflective signal strength from tissue. The measurements of optical intensity might therefore be affected not only by the changes of the tissue itself but also by the strength of the underlying laser light signal. The latter depends strongly on media opacities: stronger media opacities result in higher reflectivity levels. To exclude the possible influence of media opacities on the reflectivity measurements in our study, we compared the vitreous body reflectivity, which is not the site of damage in RAO, across all RAO grades and in controls. Similar vitreous body reflectivity levels suggest similar quality of images with negligible differences in media opacity levels between the examined eyes. Therefore, we attribute the changes in retinal layers reflectivity exclusively to ischemic processes in the retina.

Whether the absolute values of retinal reflectivity or the previously mentioned ratios provide the more reliable information regarding retinal ischemia needs to be studied in future work.

The study has several limitations. First, selection bias because of retrospective nature should be considered. Second, the severity scale applied for BRAO was derived from severity scale dealing with CRAO as to the best of our knowledge there is no analogous severity scale for BRAO exclusively. Although the underlying mechanism should be the same, the inclusion of visual acuity in at least some grading systems is not useable for BRAO because the small but important fovea might or might not be affected by BRAO. Furthermore, we used only one SD-OCT device (Spectralis) with the lack of comparison with other SD-OCT as well as time domain OCT devices; the heavy mathematical processing of the laser light information needs to be studied in future work.

The time from symptom onset to the first presentation in the clinic varied from 4 hours to 4 days. The duration of the symptoms before first OCT measurement was made might have influenced the retinal layers’ thickness and reflectivity as retinal edema changes over time.

To the best of our knowledge there are no clinical studies as to at what time after artery occlusions retinal changes begin to show. Ashton et al.15 showed that 3 to 60 minutes after embolization of the pig retinae retinal whitening begin to appear. After 14 days, retinal samples show atrophy of the pig retina. Hayreh and Jonas32 demonstrated irreversible retinal damage from ischemia in the rhesus monkey after about 105 minutes. The earliest signs of atrophy after RAO were given in the histologic study of Ashton (2 weeks), whereas Ahn et al.11 demonstrated this effect in the OCT after 1 month. In the latter study, no earlier measurements were taken. We therefore assume that retinal changes in all of our patients have had enough time to fully develop (minimal time 4 hours), but not enough time to result in atrophy (maximal time 4 days).

In addition, OCT angiography was not used in the present study. Although we believe that short after RAO the vessel density might not be affected and therefore it might not show severe differences, it might provide useful information on perfusion as well as ischemia status of the macula. In case of the complete stop of perfusion in any retinal artery, this stop should be seen in OCT angiography as a vessel occlusion or missing vessels. In the case of reperfused arteries, we do not expect changes shortly after RAO. Finally, follow-up data for retinal thickness is missing, which might be also interesting to compare across the three RAO grades. Last, we cannot rule out changes of severity grades over time because we did not examine the patients’ eyes more than once within the first week after RAO occurred. It might be that there is some sort of change in thickness and/or reflectivity, making the so-called grade stages, which might last for different times.

In conclusion, the present study identified a strong increase in the reflectivity of inner retinal layers in cases of acute RAO. These differences were statistically significant across clinically defined different acute RAO grades. Therefore, we suggest that measurements of optical intensity of retinal layers may be useful to document the severity of acute retinal ischemic damage and to objectively stage eyes with acute RAO. As this method can be used for BRAO and CRAO as well, we suggest that this tool be used in further clinical trials investigating acute ischemic processes in the retina. This would require a built-in software solution to calculate the reflectivity of the retinal layers and the ability to overlay an “ischemic index map” over the retinal image itself.

Acknowledgments

Disclosure: O. Furashova, None; E. Matthé, None

References


