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ORIGINAL RESEARCH

Hyperreflectivity of Inner Retinal Layers as a Quantitative Parameter of Ischemic Damage in Acute Retinal Vein Occlusion (RVO): An Optical Coherence Tomography Study

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Purpose: To investigate the reflectivity changes of inner retinal layers in acute retinal vein occlusion (RVO) on spectral-domain optical coherence tomography (SD-OCT) and to correlate these values with other known parameters of acute ischemic damage.

Patients and Methods: In this retrospective and observational case series, 230 eyes from 115 patients with acute RVO (central or branch) were categorized as ischemic or non-ischemic depending on fluorescein angiography (FA) images at baseline. Thickness and reflectivity of selected retinal layers were measured from SD-OCT images at baseline. Reflectivity values were correlated with other parameters of acute ischemic damage (best-corrected visual acuity (BCVA), retinal thickness, extent of macular edema, ischemic area on fluorescein angiography). The data were compared with contralateral eyes (controls). Prominent middle limiting membrane sign (p-MLM) was also registered.

Results: RVO reflectivity values differed significantly in all retinal layers compared to controls ($P<0.001$). Ischemic RVO eyes had higher optical intensity values for the innermost retinal layer (IMRL; $P=0.008$) and inner retinal layer ($P=0.019$) compared to non-ischemic cases. For all RVO eyes as well as central RVO, severity parameters like BCVA, central and total retinal thickness showed a strong correlation with the IMRL reflectivity. In branch RVO, BCVA remained significantly correlated with the IMRL reflectivity, while the thickness values showed significant correlation only for central foveal thickness in non-ischemic branch RVO type. The p-MLM was seen on OCT in 94% of the ischemic and in 66% of the non-ischemic RVO cases.

Conclusion: Acute RVO leads to increased reflectivity of inner retinal layers with significantly higher values in the ischemic vs non-ischemic type. Increased inner retinal layers' reflectivity correlated significantly with BCVA, retinal thickness of separate retinal layers, as well as ischemic area on FA. Quantitative non-invasive measurement of inner retinal layers' reflectivity might be used to determine the extent of acute ischemic retinal damage in RVO.

Keywords: retinal vein occlusion, optical coherence tomography, retinal layers' reflectivity, acute retinal ischemia

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Introduction

Retinal vein occlusion (RVO) is very common, but despite a lot of knowledge being accumulated about this vascular disease, its management still remains challenging.[1,2] The course of the disease is very different depending on the absence or presence of retinal ischemia. While the non-ischemic RVO type usually has a good disease course

with visual recovery up to 100%, the ischemic RVO type often shows a very poor visual outcome with sometimes severe complications up to painful neovascular glaucoma with consecutive enucleation.[3]

Better understanding of the disease process will help to predict the long-term outcomes and the needed disease management. Many studies have been searching for reliable markers of retinal ischemia in the past years. The most important clinical trial providing guidelines for management of RVO is the Central Vein Occlusion Study (CVOS). In CVOS, the fluorescein angiography (FA) was used to assess the perfusion status of the retina and to distinguish the ischemic from non-ischemic RVO type.[4,5] Nowadays, FA still remains the gold standard for providing detailed information about non-perfused areas of the retina. However, the rule of at least "10 disc areas of capillary non-perfusion" for defining clinically relevant ischemic central retinal vein occlusion (CRVO) does not always correlate with the visual outcome and might therefore be misleading.[1,6] Furthermore, FA is an invasive diagnostic tool with possible adverse reactions and a subjective assessment of non-perfused areas. Welch and Augsburger[7] found that the proportion of agreement between eight retinal specialists in assessing the extent of retinal capillary non-perfusion on fluorescein angiography was less than 60% for all the specialists.

Several other parameters help to assess the severity of acute retinal damage in RVO, such as visual acuity, relative afferent pupillary defect (RAPD), extent of macular edema, perimetry, and full-field electroretinography (ERG). However, most of them remain subjective and represent only indirect hints of possible extent of retinal ischemia in acute RVO.

A recent study of Seknazi et al[8] showed that OCT-angiography (OCT-A) might be a useful tool for identifying high-risk RVO patients who may benefit from further FA evaluation. The most important limitation of OCT-A nowadays remains the smaller image field compared to that of FA, which does not always allow one to reliably classify the perfusion status of peripheral retinal areas.

Some studies reported inner retinal thinning on OCT in the non-perfused areas of RVO, suggesting this criterion for recognition of existing retinal ischemia.[9–11] However, this is a late sign, which develops in the course of the disease and cannot be taken into consideration in acute RVO, when the patient's observation plan including possible acute treatment should be considered.

Some studies observed increased inner retinal layers' reflectivity in acute retinal vascular disorders including RVO.[12–16] In our previous study, we could also show that retinal ischemia in acute retinal artery occlusion results in hyperreflectivity of inner retinal layers, which is significantly different depending on the disease grade and might therefore be used to assess the grade of acute ischemic damage to the retina.[17,18]

Regarding the need for a stable, objective, and easily measurable parameter with strong probability value for severe RVO course, we analyzed the hyperreflectivity of selected retinal layers in acute RVO as a value of acute ischemic retinal damage and measured its correlation with other known RVO severity parameters.

Methods

The present study adhered to the tenets of the Declaration of Helsinki and has been approved by the Institutional Review Board of Technische Universität Dresden (Dresden, Germany). Informed patients' consent was waived because of the retrospective design and because no study-related investigations were necessary. The accessed patient data complied with relevant data protection and privacy regulations. The investigation was 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 CRVO and branch retinal vein occlusion (BRVO) according to the International Classification of Diseases, 10th Revision, between September 2011 and December 2017. Included patients met the following criteria: a) diagnosed with acute CRVO or BRVO (symptom onset within 7 days of the initial visit); and b) SD-OCT and FA at initial visit with SD-OCT image quality score >30. Patients with a) a history of ocular trauma or presence of b) macular disease, c) other retinal vascular diseases, d) glaucoma, e) myopic retinopathy, or f) other diseases interfering with OCT images in any one of the eyes (eg, vitreomacular traction, epiretinal membrane,) as well as g) one-eyed patients, were excluded from the analysis. The contralateral eyes served as controls to provide the best match regarding concomitant cardiovascular diseases, which might influence the retinal perfusion status.

Ophthalmic Examination

All patients underwent a comprehensive ophthalmic examination at baseline (before any treatment) including best-corrected visual acuity (BCVA) in decimal numbers, applanation tonometry, slit-lamp biomicroscopy, indirect binocular ophthalmoscopy, SD-OCT imaging, and FA (Spectralis®, Heidelberg Engineering Inc., Heidelberg, Germany).

Fluorescein Angiography and Assessment of Retinal Ischemic Area

FA was performed on Spectralis HRA (Heidelberg Engineering Inc., Heidelberg, Germany) using a 55° objective. The area of retinal non-perfusion was assessed by the same author (O.F.) and was measured in mm^2 using the built-in software tool of the device (Figure 1). Regarding the absence or presence of retinal nonperfusion on FA, RVO eyes were classified into ischemic and non-ischemic. The retinal nonperfusion areas were defined as parts of the retina with loss of retinal arterioles or capillaries and resulting hypofluorescence.

Optical Coherence Tomography

SD-OCT examination was performed using Spectralis OCT. 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° × 20° centered on the fovea with standard nine frames. The eye tracking system (ART Module, Heidelberg Engineering Inc.) was used to minimize motion artifacts.

Thickness and Reflectivity Measurements

The detailed method for measuring thickness and reflectivity of separate retinal layers is described elsewhere.[11,12] All thickness and reflectivity measurements were done by the same author (E.M.). For nomenclature of analyzed

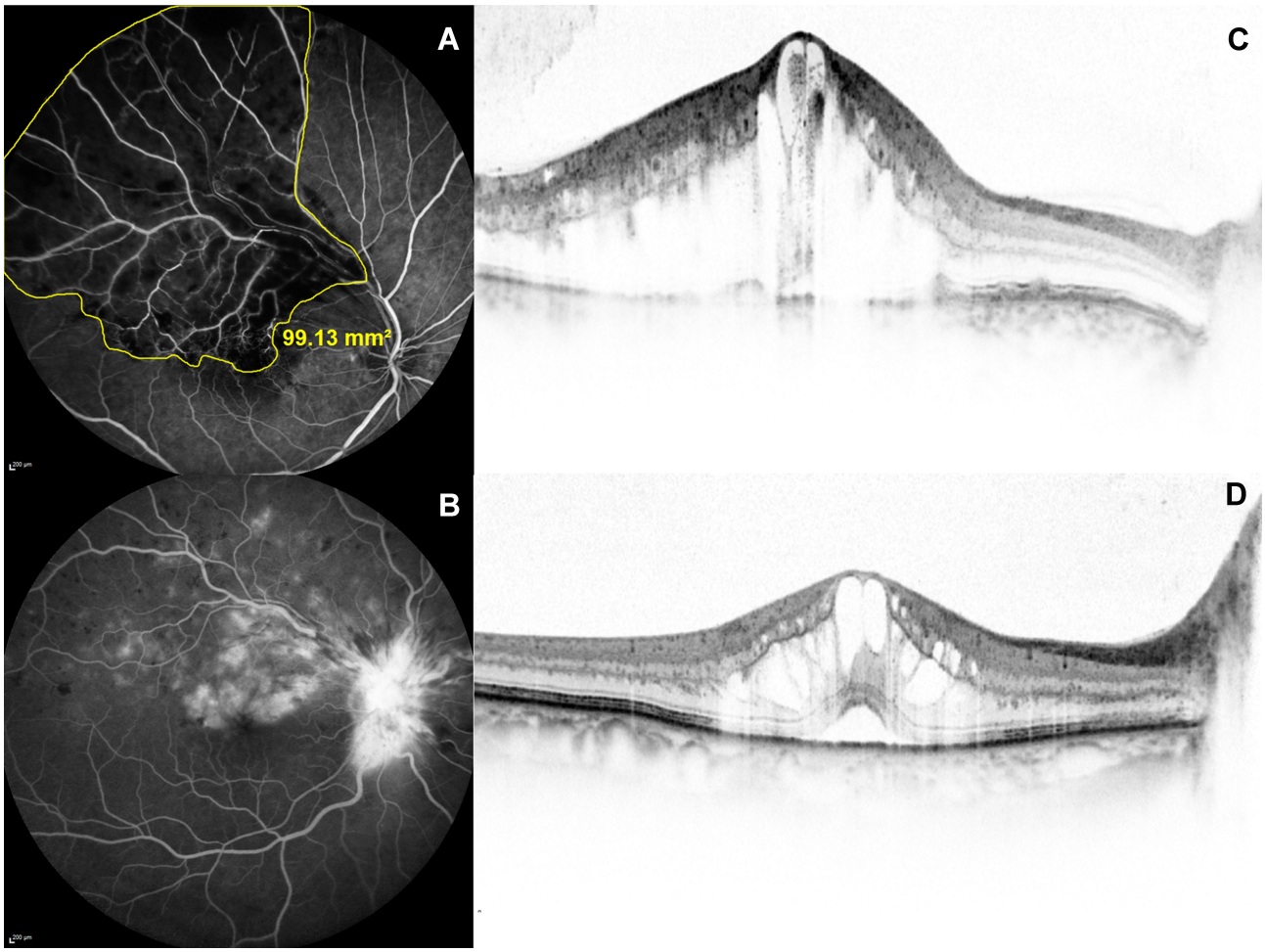

Figure 1 Fluorescein angiography images and SD-OCT scans of ischemic and non-ischemic branch retinal vein occlusion (BRVO). Shown is the FA image (**A** – With visible ischemic area marked and measured manually using built-in software; **B** – Non-ischemic occlusion) and the macular scan (**C** – Ischemic BRVO, **D** – Non-ischemic BRVO).

retinal layers please see Table 1. 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.

The presence or absence of the "prominent middle-limiting membrane sign" (p-MLM sign) on the OCT images was also noted.

Statistical Analysis

Data for continuous variables are expressed as mean±standard deviation (SD). Visual acuity measurements were converted from decimal numbers to logMAR for analyses. Mann–Whitney *U*-test was performed to compare different values between all RVO eyes and healthy contralateral eyes. Pearson correlation coefficient was used to determine the correlation between the retinal ischemic area, BCVA, retinal thickness measurements, and reflectivity values. 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

In total, 230 eyes from 115 patients were included in this study. Table 2 shows demographic and clinical characteristics of study participants.

Tables 3 and 4 outline the retinal thickness and reflectivity measurements of the different retinal layers in RVO eyes as well as healthy controls. RVO eyes show a statistically significant increase in thickness of all measured retinal layers compared to control eyes. Moreover, in ischemic RVO type there was a significantly increased total retinal thickness due to increased thickness of CFT and ORL compared to non-ischemic occlusion type.

Table 1 Nomenclature of Analyzed Retinal Layers in Both Retinal Vein Occlusion (RVO) and Contralateral Healthy Eyes

Ganglion cell layer (GC)	**Innermost retinal layer (IMRL)**	**Inner retinal layer (IRL)**
Inner plexiform layer (IPL)		
Inner nuclear layer (INL)	**Middle retinal layer (MRL)**	
Outer plexiform layer (OPL)		
Outer nuclear layer (ONL)	**Outer retinal layer (ORL)**	
External limiting membrane (ELM)		
Ellipsoid layer		
Retinal pigment epithelium (RPE)		

Regarding optical intensity measurements, there was also a statistically significant increase (lower values mean darker images with more reflectivity) in all layers in RVO eyes compared to contralateral eyes. Comparing the ischemic with the non-ischemic RVO type, we observed statistically significant differences in the IMRL and IRL with higher reflectivity values in the ischemic group (Figure 3, Table 4).

The optical intensity of the vitreous body was significantly higher in the RVO group compared to contralateral eyes with no difference between the non-ischemic and the ischemic RVO types. To eliminate the influence of image quality on the reflectivity of separate retinal layers, we calculated the optical intensity ratios (OIR) for inner and outer retinal layers reflectivity values (Table 5). Note the high statistically significant differences in the ratio values across all compared groups.

The mean retinal ischemic area in the ischemic RVO type was 151.2±128.1 mm^2 with a range from 1.7 mm^2 to 503.6 mm^2.

As IMRL reflectivity showed the strongest differences between the ischemic and the non-ischemic RVO type, we further analyzed the Pearson's correlation coefficient of IMRL reflectivity to other severity parameters in RVO (Table 6). For the whole RVO cohort, ischemic and non-ischemic RVO, as well as ischemic CRVO, all other assessed severity parameters such as BCVA, central, and total retinal thickness showed strong statistically significant correlation with the IMRL reflectivity. In non-ischemic CRVO and BRVO, BCVA remained significantly correlated with the IMRL reflectivity, while the thickness values showed significant correlation only for central foveal thickness in non-ischemic BRVO type. The peripheral ischemic area measured on FA did not show any significant correlation with IMRL reflectivity.

The p-MLM was seen on OCT in 94% of the ischemic and in 66% of the non-ischemic RVO cases.

Discussion

Assessment of retinal ischemia in RVO still remains the biggest challenge. Eyes at high risk of possible neovascular complications should be monitored more closely and treated more aggressively. Clinical assessment of retinal ischemia includes BCVA, RAPD, visual field, and full-field ERG.[19,20] However, these signs do not help to reliably determine the extent of ischemic retinal damage. FA

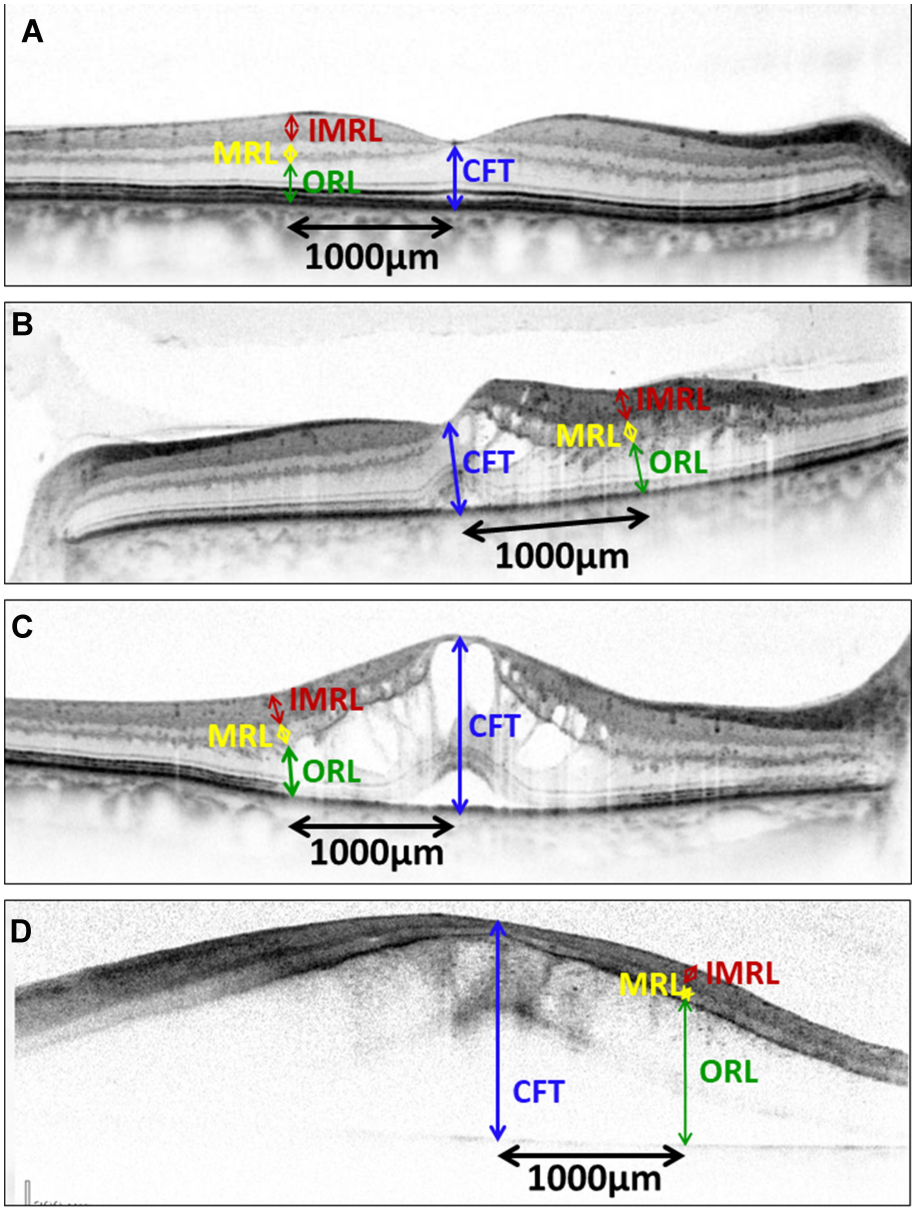

Figure 2 Definition of region of interest for measurement of the retinal layers' thickness and reflectivity on SD-OCT images of a healthy contralateral eye (**A**), an eye with branch retinal vein occlusion (BRVO; **B**), an eye with non-ischemic central retinal vein occlusion (CRVO; **C**), and an eye with ischemic CRVO with pronounced macular edema (**D**). All measurements were done manually using built in software of SD-OCT. Central foveal thickness was measured as shown (CFT). In case of CRVO, measurements of separate retinal layers' thickness and reflectivity were done 1000 µm temporal to the fovea. In the case of BRVO, the values were obtained 1000 µm superior or inferior of the fovea in cases of no fovea involvement, depending on which area had been hit by the occlusion. The innermost retinal layer (IMRL) included a retinal nerve fiber layer, ganglion cell layer, and inner plexiform layer. The inner nuclear layer and the outer plexiform layer were combined to build the so-called middle retinal layer (MRL). The outer retinal layer (ORL) included the structures from the inner border of the outer nuclear layer till the outer border of retinal pigment epithelium. All thickness measurements are given in micrometers.

as the gold standard for assessing the peripheral retinal perfusion status has some severe disadvantages.[21,22] Furthermore, defining RVO into two types according to FA – ischemic and non-ischemic – does not give us detailed information about the extent of ischemic retinal damage, as recent studies showed continuous gradation of ischemia reflected in the VEGF concentration in the extracellular retinal fluid and the vitreous.

The need for reliable markers of acute ischemic retinal damage with predictive value regarding neovascular complications still remains unmet. Recent studies have been looking for other criteria to better characterize ischemic changes in RVO.[9,10,23]

Lim et al[9] found significantly reduced thickness of the macula and inner retinal layers in ischemic BRVO compared to non-ischemic BRVO. However, these findings

Table 2 General Characteristics of Included Patients with Both Types of RVO

Characteristics	All Patients (N=115)	Ischemic RVO (N=60)	Non-Ischemic RVO (N=55)	*P*-value
Mean age±SD, years (range) CI (95%)	65.12±14.08 (28–86)	64.48±13.20 (28–86) 61.23–68.09	66.80±13.90 (31–86) 63.11–70.60	0.374
Gender, n (%): Male Female	 43 (37) 72 (63)	 27 (45) 33 (55)	 25 (45) 30 (55)	0.244
RVO type, n (%): BRVO CRVO	 60 (52) 55 (48)	 29 (48) 31 (52)	 31 (56) 24 (44)	0.471
BCVA, affected eye, logMAR, mean±SD CI (95%)	0.74±0.56	0.95±0.64 0.75–1.06	0.56±0.39 0.45–0.66	<0.001***
BCVA, healthy eye, logMAR, mean±SD CI (95%)	0.09±0.26	0.09±0.37 0.00–0.19	0.09±0.16 0.04–0.14	0.893

Notes: Differences between ischemic and non-ischemic RVO types were calculated using Mann–Whitney *U*-test. Statistically significant (*P*<0.001***).
Abbreviations: BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; BCVA, best-corrected visual acuity; logMAR, logarithm of minimal angle of resolution; CI, confidence interval.

Table 3 Retinal Thickness Measurements on SD-OCT in Both RVO Types and Contralateral Eyes

RVO Type/Retinal Layer	Contralateral Eyes (N=115)	All RVO (N=115)	*P*-value[a]	Ischemic RVO (N=60)	Non-Ischemic RVO (N=55)	*P*-value[b]
CFT, µm (mean±SD) CI (95%)	220±26 215–225	612±268 566–669	<0.001***	670±283 596–747	559±241 490–628	0.029*
IMRL, µm (mean±SD) CI (95%)	94±14 92–97	135±34 128–141	<0.001***	139±38 128–149	130±22 124–136	0.168
MRL, µm (mean±SD) CI (95%)	63±8 62–65	113±41 105–120	<0.001***	116±45 103–127	110±35 101–119	0.485
IRL, µm (mean±SD) CI (95%)	158±17 155–161	248±59 236–258	<0.001***	256±71 235–272	240±45 228–252	0.214
ORL, µm (mean±SD) CI (95%)	164±15 161–167	309±140 284–338	<0.001***	336±163 296–379	283±114 251–314	0.037*
Total retinal thickness, µm (mean±SD) CI (95%)	322±26 317–327	556±174 526–590	<0.001***	592±201 450–643	523±129 487–559	0.031*

Notes: Differences between groups were calculated using Mann–Whitney *U*-test. Statistically significant (*P*<0.05*, *P*<0.001***). [a]Comparison of all RVO eyes and healthy contralateral eyes. [b]Comparison of ischemic and non-ischemic RVO type.
Abbreviations: SD-OCT, spectral-domain optical coherence tomography; CFT, central foveal thickness; IMRL, innermost retinal layer; MRL, middle retinal layer; IRL, inner retinal layer; ORL, outer retinal layer; SD, standard deviation; CI, confidence interval.

were observed in BRVO eyes after 2 years of follow-up and cannot be used in the acute phase.

A recent study of Hasegawa et al[24] described a significant correlation of low reflective spaces in the RNFL with the presence of non-perfused areas on FA in RVO. It has been postulated that these spaces could be apoptotic changes in the RNFL due to retinal nonperfusion. In this study, the low reflective spaces have been seen in RVO eyes 1 month after symptom onset.

Ko et al[23] introduced the concept of p-MLM sign as a diagnostic tool to distinguish the ischemic from the non-ischemic RVO type. Fifty-seven per cent of the eyes having the p-MLM sign were classified into ischemic RVO type. However, this sign is not always identifiable in cases of

Table 4 Reflectivity Measurements in Both Types of RVO and Contralateral Eyes

RVO Type/Retinal Layer's Reflectivity	Contralateral Eyes (N=115)	All RVO (N=115)	*P*-value[a]	Ischemic RVO (N=60)	Non-Ischemic RVO(N=55)	*P*-value[b]
IMRL, mean±SD CI (95%)	155±21 151–159	117±35 108–120	<0.001***	108±31 96–113	125±31 117–134	0.001**
MRL, mean±SD CI (95%)	184±16 181–187	161±30 154–165	<0.001***	157±31 146–162	164±30 157–174	0.066
IRL, mean±SD CI (95%)	166±18 163–170	137±30 131–141	<0.001***	130±27 121–136	144±24 137–151	0.004**
ORL, mean±SD CI (95%)	221±9 220–224	234±17 230–236	<0.001***	234±19 229–238	232±14 229–237	0.790
Vitreous body, mean±SD CI (95%)	249±5 248–250	245±9 243–247	<0.001***	244±8 242–246	245±8 243–248	0.479

Notes: Differences between groups were calculated using Mann–Whitney *U*-test. Statistically significant (*P*<0.01**, *P*<0.001***). [a]Comparison of all RVO eyes and healthy contralateral eyes. [b]Comparison of ischemic and non-ischemic RVO type.

Abbreviations: RVO, retinal vein occlusion; IMRL, innermost retinal layer; MRL, middle retinal layer; IRL, inner retinal layer; ORL, outer retinal layer; SD, standard deviation; CI, confidence interval.

massive retinal hemorrhages or severe macular edema. Furthermore, this diagnostic tool does not give us information about the extent of the ischemic damage, as it can be just registered as present/non-present. In our dataset, the p-MLM was seen in 94% of the ischemic eyes, but in 66% of the non-ischemic RVO, suggesting some extent of acute retinal ischemia in eyes without visible capillary dropout in FA as well.

Seknazi et al[8] demonstrated for the first time a significant correlation between vascular density parameters on OCT-A and peripheral nonperfusion on FA. The limitation of this study was the patient sample including eyes with long-standing RVO. OCT-A still leads to artifacts and mistakes in segmentation in cases of macular edema, which is common in acute RVO. Furthermore, OCT-A provides information on

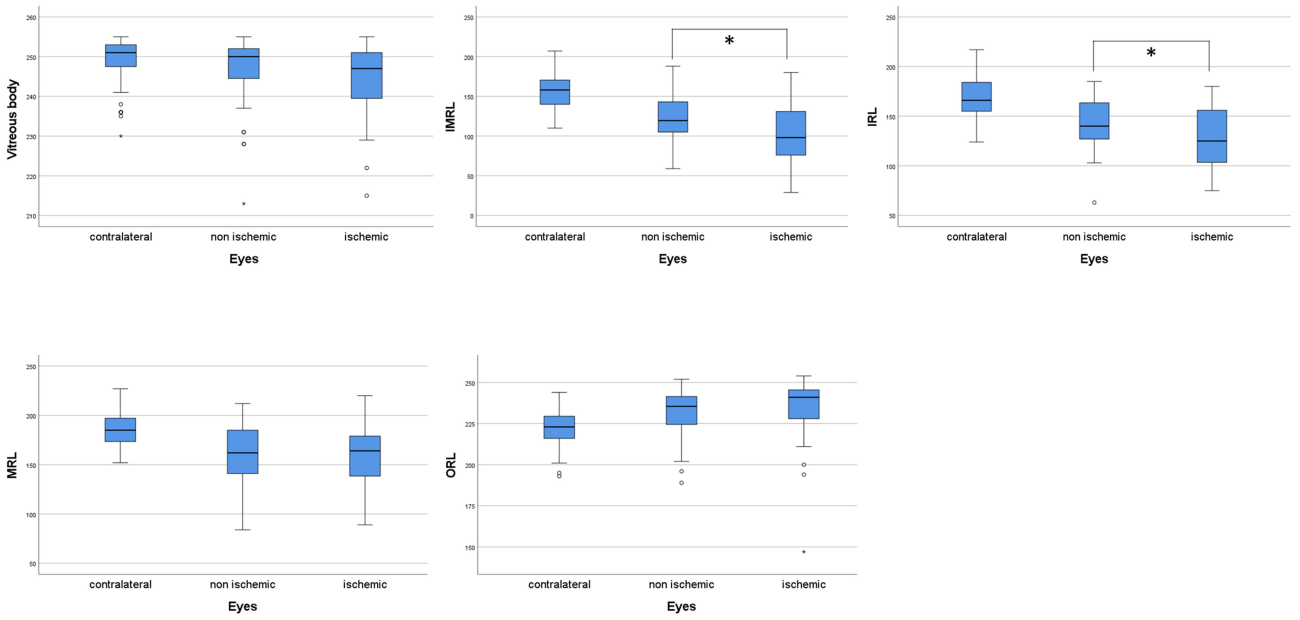

Figure 3 Bar graphs showing the optical intensity of vitreous body and selected retinal layers in different types of retinal vein occlusion and contralateral eyes. X-axis shows different groups for comparison. Y-axis shows the optical intensity levels, ranging from 0 (absolute black) to 255 (absolute white) for different retinal layers. Brackets with asterisks mark statistically significant values with *P*<0.005. Differences between the ischemic and non-ischemic groups were calculated using Mann–Whitney *U*-test. Outliers are marked as small circles, small asterisks without brackets are used for extreme outliers.

Table 5 Optical Intensity Ratios (OIR) in Both RVO Types and Contralateral Eyes

RVO Type/ Reflectivity Ratio	Contralateral Eyes (N=115)	All RVO (N=115)	*P*-value[a]	Ischemic RVO (N=60)	Non-Ischemic RVO (N=55)	*P*-value[b]
ORL/IMRL,			<0.001***			<0.001***
Mean±SD	1.46±0.19	2.19±0.79		2.42±0.94	1.98±0.51	
CI (95%)	1.42–1.49	2.09–2.39		2.25–2.74	1.83–2.11	
Interquartile range	0.24	0.84		1.25	0.73	
ORL/IRL,			<0.001***			0.002**
Mean±SD	1.35±0.13	1.78±0.41		1.89±0.46	1.67±0.33	
CI (95%)	1.32–1.37	1.72–1.87		1.79–2.03	1.58–1.76	
Interquartile range	0.17	0.49		0.60	0.39	

Notes: Differences between groups were calculated using Mann–Whitney *U*-test. Statistically significant (*P*<0.01**, *P*<0.001***). [a]Comparison of all RVO eyes and healthy contralateral eyes. [b]Comparison of ischemic and non-ischemic RVO type.
Abbreviations: RVO, retinal vein occlusion; SD, standard deviation; IMRL, innermost retinal layer; IRL, inner retinal layer; ORL, outer retinal layer; CI, confidence interval.

flow signal showing non-perfused areas, but it does not give information about the tissue status in the non-perfused areas.

Several recent studies described increased retinal layers' reflectivity in cases of acute retinal ischemia caused by retinal perfusion disorders.[12–16] The exact mechanism of reflectivity change in acute ischemia remains poorly understood. One possible explanation is intracellular edema and cell disorganization in acute ischemia, resulting in loss of transparency on OCT images.

Chen et al[25] previously described significantly higher optical intensity values of inner retinal layers in ischemic BRVO in the affected region compared to the unaffected control region. In the non-ischemic BRVO, there were no differences between the affected and unaffected region. This study suggests that optical intensity changes on OCT correlate with retinal ischemia in ischemic BRVO.

We previously reported a novel method of assessment for acute retinal ischemia in retinal artery occlusion disease[17] – we could find strong differences in retinal layers' reflectivity depending on the extent of acute retinal ischemia. In the present study, we applied the same method to measure the possible acute ischemic damage in cases of retinal vein occlusion disease.

The reflectivity of all selected retinal layers differed significantly between RVO and contralateral control eyes, irrespective of the presence or absence of retinal ischemia on FA, suggesting some extent of ischemic damage in all RVO cases. Looking at the ischemic and non-ischemic RVO type separately, the reflectivity of inner retinal layers remained statistically significantly different with the highest optical intensity values of the inner retina in the ischemic RVO type.

The reflectivity of inner retinal layers showed significant correlation with BCVA and retinal thickness measurements in acute RVO. Even in the subgroups of ischemic RVO, non-ischemic RVO as well as ischemic CRVO this strong correlation remained statistically significant. Regarding the subgroup of BRVO, the correlation of inner retinal layers' reflectivity remained significant for BCVA, but not for the retinal thickness values. The discrepancy of these correlation data with strong significant correlation coefficients in RVO and CRVO and weak correlation in most BRVO cases might be explained with better analysis of the study method. While in CRVO, the area of reflectivity/thickness measurements is affected in more or less in the same manner because of ischemia in whole retina, in cases of BRVO the area of measurements might not be representative for the amount of the general ischemic damage to the retina.

Regarding the result of the present study, we suggest that measuring the reflectivity of inner retinal layers in acute RVO gives detailed information about the ischemic tissue damage. This parameter might be useful to determine the stage of ischemic damage in RVO eyes in the acute phase.

A key question not addressed in this study is whether or not reflectivity values – showing acute ischemic damage extent – do have prognostic value for the disease course and whether it might help us to achieve better outcomes in the course of especially ischemic RVO by using a modified approach with more aggressive treatment strategies. Browning et al[26] were searching for possible predictors of subsequent anterior segment neovascularization in CRVO patients. They could not show any prognostic value of SD-OCT signs of ischemia in acute CRVO. However, the level of ischemia on SD-OCT images of CRVO was graded subjectively and the reflectivity of retinal layers was not quantitatively measured.

Table 6 Correlation Between IMRL Reflectivity and Other Parameters of Acute Ischemic Damage in RVO Eyes

Parameters	All RVO (N=115)		Ischemic RVO (N=60)		Non-Ischemic RVO (N=55)		Ischemic CRVO (N=31)		Non-Ischemic CRVO (N=24)		Ischemic BRVO (N=29)		Non-Ischemic BRVO (N=31)	
	r	P	r	P	r	P	r	P	r	P	r	P	r	P
BCVA	−0.517[a]	<0.001***[a]	−0.425[a]	0.001**[a]	−0.559[a]	<0.001***[a]	−0.533[a]	0.002**[a]	−0.623[a]	0.016*[a]	−0.410[a]	0.027*[a]	−0.470[a]	0.008**[a]
CFT	−0.478[a]	<0.001***[a]	−0.438[a]	<0.001***[a]	−0.451[a]	0.002**[a]	−0.554[a]	0.001**[a]	−0.423	0.087	−0.345	0.067	−0.458[a]	0.010*[a]
ORL thickness	−0.440[a]	<0.001***[a]	−0.446[a]	<0.001***[a]	−0.348[a]	0.015*[a]	−0.580[a]	0.001**[a]	−0.432	0.070	−0.320	0.091	−0.301	0.100
TRT	−0.418[a]	<0.001***[a]	−0.404[a]	0.001**[a]	−0.351[a]	0.016*[a]	−0.563[a]	0.001**[a]	−0.464	0.062	−0.229	0.232	−0.293	0.109
Ischemic area	N/A		−0.221	0.09	N/A		−0.238	0.198	N/A		−0.367	0.050	N/A	

Notes: Statistically significant ($P<0.05$*, $P<0.01$**, $P<0.001$***). [a]Statistically significant correlation.

Abbreviations: IMRL, innermost retinal layer; RVO, retinal vein occlusion; BCVA, best-corrected visual acuity; CFT, central foveal thickness; ORL, outer retinal layer; TRT, total retinal thickness; CRVO, central retinal vein occlusion; BRVO, branch retinal vein occlusion; *P*, statistical value of Pearson's correlation test; r, Pearson's correlation coefficient between IMRL reflectivity and other parameters of acute ischemic damage in RVO eyes.

Whether quantitative assessment of inner retinal layers' hyperreflectivity in acute RVO will help to better predict the disease course and optimize the disease management, still remains unknown. In order to try to answer this complex issue, our study group is now investigating the further course of the included RVO eyes over time and its correlation to the optical intensity measurements at baseline.

Our study has several limitations. The first one is the retrospective nature of the study. Second, due to several reasons it was not always possible to examine the complete retina from ora serrata to ora serrata on FA, which means that the area of ischemia might be underestimated, as it was measured on the available pictures only. Furthermore, we did not analyze the central retinal ischemia on OCT angiography (OCT-A).

In summary, we could observe increased inner retinal layers' reflectivity in RVO, with significantly higher values in the ischemic vs non-ischemic type. Increased inner retinal layers' reflectivity correlated significantly with BCVA, retinal thickness of separate retinal layers, as well as ischemic area on FA. We suggest that quantitative measurement of inner retinal layers' reflectivity helps to determine the extent of acute ischemic retinal damage in RVO.

Data Sharing Statement

The authors report that no further data besides what is included in the manuscript will be shared.

Disclosure

The authors report no conflicts of interest in this work.

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