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Comparison of multicolor scanning laser imaging and color fundus photography in evaluating vessel whitening in branch retinal vein occlusion

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Abstract

Introduction: Few studies have explored Multicolor™ imaging (MCI) in evaluating retinal vascular diseases, particularly branch retinal vein occlusion (BRVO). This study aimed to compare the identification of retinal vessel whitening in BRVO using MCI by scanning confocal laser versus conventional white flash color fundus photography (CFP).

Methods: Paired images of consecutive patients diagnosed with BRVO who underwent same-day MCI and CFP were reviewed. Visualization of vessel whitening on MCI and CFP was graded and scored using a scale by two masked graders. A longitudinal analysis of the vessel grading score was performed to evaluate the vessel whitening detection by MCI. A correlation analysis was conducted between vessel whitening on MCI and the measured area of retinal ischemia on fluorescein angiography to evaluate the MCI performance.

Results: Forty-four eyes of 41 patients (mean age 69±14 years; 61% female) were analyzed. MCI demonstrated superior vessel whitening visibility score than CFP ($p<0.001$). Longitudinal analysis showed no significant changes in vessel whitening visibility scores over a mean follow-up time of 430 ± 648 days ($p=0.655$). There was a significantly positive correlation between the

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AUTHOR CONTRIBUTIONS

Nobuyoshi Unno: data curation, formal analysis, investigation, methodology, visualization, writing original draft.
Leonardo Lando: data curation, formal analysis, software, visualization, writing original draft, editing.
Varsha Alex: data curation, formal analysis, investigation, editing.
Peng Yong Sim: formal analysis, writing original draft, editing.
Mahima Jhingan: data curation, formal analysis, investigation, editing.
William R. Freeman: data curation, formal analysis, funding acquisition, investigation, editing.
Shyamanga Borooah: conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, supervision, editing.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

grading score of vessels whitening by MCI and the area of ischemia by fluorescein angiography (r^2=0.15; p=0.036).

Conclusion: MCI appears to provide a superior detection of whitening BRVO compared to CFP, serving as a rapid and non-invasive correlate of retinal ischemia.

Keywords

Multicolor scanning laser imaging; color fundus photography; branch retinal vein occlusion; vessel whitening; retinal ischemia

INTRODUCTION

Retinal vascular occlusions encompass the second most common cause of sight-threatening retinal vascular disorder after diabetic retinopathy, [1] and result from a block in the retinal venous circulation. [2] Globally, the prevalence of retinal occlusions is approximately 3.7 per 1000 people, with an estimated 13.9 million adults affected worldwide by branch retinal vein occlusion (BRVO), one of its frequent types of manifestation. [2]

BRVO results in the classical clinical findings of venous dilation and tortuosity, capillary non-perfusion, flame-shaped retinal hemorrhages, and macular edema. [3] In this process, the occluded vasculature may be sufficiently severe to cause retinal ischemia, which has important implications for ocular therapy, complications, and visual prognosis. [4] A common sequela of retinal ischemia is vessel sclerosis, which manifests clinically as vessel whitening and is recognized by changes in the vessel wall color or sheathing on fundoscopy. These changes are most attributable to perivascular remodeling of the vascular tunica, as determined by animal models. [5] Close monitoring of this clinical correlate may facilitate early detection of complications and timely treatment to prevent vision loss.

Visualization of chronic vascular features can be challenging due to media opacity, poor color contrast with the background retina, small vessel caliber, or simultaneous artifacts leading to a blockage such as retinal hemorrhage or exudation. [6] Conventional color fundus photography (CFP), which utilizes broad-spectrum white light to capture in true color the retinal surface, optic nerve, and vascular arcades, has been the gold standard tool to image retinal diseases. [7, 8] However, the identification of clinical features using CFP is limited by light scattering, the lack of penetration of different retinal layers, [9] and the absence of automated eye tracking, which renders it susceptible to motion blur. [10]

The recent development of Multicolor™ imaging (MCI) (Spectralis HRA-OCT; Heidelberg Engineering, Heidelberg, Germany) allows the acquisition of pseudo-color images by combining confocal scanning laser ophthalmoscopy utilizing three different wavelengths – blue (486 nm), green (518 nm) and infrared (815 nm). [11] These three monochromatic wavelengths facilitate light penetration through the various retinal layers, enhancing contrast and enabling the appreciation of distinct details from specific retinal and choroidal layers. Blue laser captures details of the inner retina and vitreoretinal interface, being used to identify features including epiretinal membrane and retinal nerve fiber layer thinning [12, 13]. In contrast, green laser is highly absorbed by hemoglobin, assisting in visualizing

retinal blood vessels and intraretinal exudation. [14] Finally, the infrared laser penetrates more profoundly through the retina due to its longer wavelength, allowing for retinal pigment epithelium and choroidal imaging. [15–17] Few studies have explored MCI in evaluating retinal vascular diseases, particularly BRVO. [11] In this study, we assess the utility of MCI in detecting vessel whitening associated with BRVO and investigate the correlation between vessel whitening visibility by MCI and the area of ischemia by fundus fluorescein angiography (FFA).

METHODS

In this retrospective case study, consecutive patients diagnosed with BRVO by a senior ophthalmologist (W.R.F.) between April 2013 to September 2019 were identified from the imaging database at the Jacobs Retina Center, Shiley Eye Institute, University of California San Diego. Institutional Review Board (IRB) approval was acquired from the University of California San Diego to review and analyze patient data. Patient consent was obtained per usual institutional policy and was waived for the analysis of retrospective data as per IRB. All data and images were anonymized for patient safety. The study complied with the Health Insurance Portability and Accountability Act of 1996. The standard clinic protocol, where possible, was for CFP, MCI, spectral-domain optical coherence tomography (SD-OCT), and oral FFA to be performed on the same day of the patient's first visit. In follow-up visits, patients would conventionally undergo only MCI and SD-OCT imaging. For CFP vs. MCI analyses, cases were only included if imaged by both techniques on the same day and displaying good quality images, denoted by the second-order retinal vessels being clearly visible. CFP was performed by Topcon TRC-50DX digital fundus camera (Topcon, Tokyo, Japan), whereas MCI and FFA were acquired using the Spectralis SD-OCT (Heidelberg Engineering, Heidelberg, Germany) with a 30° of field of view. MCI was set for an ART of 15 in all wavelengths. All imaging was obtained after pupil dilation using 1 drop of tropicamide (1%) plus 1 drop of phenylephrine (2.5%), spaced by 5–10 minutes.

MCI and CFP images were respectively saved as TIFF and JPG files without any modifications (N.U.). The anonymized images were randomized using a Visual Basic for Applications macro on PowerPoint 2016 (Microsoft Office) and subsequently graded for vessel whitening visibility and image quality by two independent masked retinal specialists (V.A., M.J.), with a third senior retinal specialist (S.B.) casting a consensus in cases of disagreement. Image grading was conducted using the same computer screen by both graders (1,440 × 900 pixels, 15-inch, 2019, Apple MacBook with Retina display) according to reference images, which are shown in Fig. 1.

In the grading process, vessel whitening was defined as whitening which extended completely across the vessel. This differentiation was chosen to try to reduce chances of vessel whitening by masqueraders, such as early hypertensive changes or sheathing from vasculitis, which may sometimes affect vessels in a segment. [18, 19] The visualization of vessel whitening was quantified according to the most affected branch or segment and scored from 0 to 2, as following: 'grade 0' = vessel whitening was not visible; 'grade 1' = vessel whitening was slightly visible; and 'grade 2' = vessel whitening being clearly visible. Presence of vessel whitening was considered in cases where the vessel was graded 1 or 2. In

cases of whitening detected on CFP, graders were asked to select the preferred MCI channel (blue, green or infrared) which best identified vessel whitening.

To understand changes in vessel whitening on MCI over time, follow-up images from patients with identified vessel whitening at their initial visit were randomized and graded following the same process described above. In a final further analysis, the area of ischemia identified using FFA, was evaluated in cases where vessel whitening was identified at initial visit. The FFA images were taken at the initial visit as previously described. [20] The images were analyzed by a trained ophthalmologist (V.A.) using the Heidelberg software (6.15.7.0). The ischemic areas were identified first by visual inspection of the FFA and then marked using the region marker in the overlay mode on the Heidelberg software. The area estimates were calculated by the Heidelberg software and used for the correlation analysis.

The agreement between the two graders for the visualization of vessel whitening and image quality was calculated using Cohen's kappa coefficient (k). For non-normally distributed data, the Wilcoxon signed-rank test was used to compare the grading scores between MCI and CFP and longitudinal changes. A 2×2 table was used to evaluate the sensitivity, specificity, and predictive values. The correlation between vessel whitening visibility score on MCI and area of ischemia on FFA was evaluated using the Pearson correlation coefficient. Analyses were indicated by central values (mean or median) with confidence intervals or distribution (standard deviation, SD). Calculations were performed on SPSS software version 25 (SPSS Inc, Chicago, IL) with significance assigned at $p<0.05$.

RESULTS

A total of 44 eyes from 41 BRVO patients were included in the different sets of analyses of this study, as indicated in the following sub-sessions. The patients mean age was 69±14 (28–89) years, being 61% females. No case was excluded after review.

Vessel whitening visualization on MCI versus CFP

Twenty-six eyes of 23 BRVO patients (mean age 69±12; 61% females) who underwent same-day MCI and CFP images were considered for this analysis.

Twelve cases had vessel grading as whitening not visible, 13 as slightly visible, and 1 as clearly visible on CFP. As for MCI, 10 were graded as not visible, 10 as slightly visible, and 6 as clearly visible. The results of the visibility of vessel whitening using the two imaging modalities are detailed in Supplementary Table 1 and exemplified in Fig. 2. The agreement among the retinal specialists in grading the visualization of vessel whitening was high for both MCI (k=0.64; 95% CI 0.39–0.90; $p<0.001$) and CFP (k=0.63; 95% CI 0.39–0.93; $p<0.001$).

Vessel whitening grading was consistent between the two imaging modalities in 14 eyes (54%), being identified in 16 eyes (62%) on MCI versus 14 eyes (54%) on CFP (Table 1). The sensitivity and specificity of MCI for vessel whitening identification was 100% and 83.3% respectively using CFP as the gold standard imaging modality. The positive and negative predictive values for MCI as screening technique for vessel whitening visualization

was 87.5% and 100%, respectively. Amongst the 14 eyes (64% females; mean age 68±14 years) with vessel whitening visualized by both imaging techniques, the average grading score for vessel whitening was found to be significantly higher using MCI (1.4; 95% CI 1.1–1.7) than CFP (1.0; 95% CI 0.9–1.2) ($p<0.001$).

Vessel whitening visualization on MCI in BRVO patients versus healthy controls

Although MCI imaging appeared to be highly sensitive at detecting vessel whitening, MCI was noted to generate some false positives in the MCI versus CFP comparison analysis above. To confirm whether MCI generated false positives we first looked back at the corresponding CFP images which were graded as not identifying whitening. We did not identify any whitening on review of these CFP images.

Next, we performed MCI on 14 control patients (14 eyes; 64% females; mean age 66±16 years) who had been examined by an ophthalmologist, imaged with CFP and not noted to have any known ocular pathology. All 14 control eyes were graded as whitening not visible using MCI supporting the high sensitivity of MCI for identifying vessel whitening in BRVO patients.

MCI channel preference for vessel whitening visualization

MCI imaging generates a pseudo-color image from three channels (blue, green and infrared). Next, we tried to see if a particular channel was preferred to identify vessel whitening. The fourteen eyes of 14 patients, with confirmed vessel whitening using both imaging modalities, were included in this analysis. The preferred channel for graders to visualize whitening was found to be the green reflectance (71%) channel, followed by blue (29%) (Fig. 3). No preference for infrared reflectance (0%) was made. Substantial intergrader agreement was observed for channel preference on MCI (k=0.65; CI 0.2–1.1; p=0.015).

Longitudinal changes in vessel whitening visualization using MCI

Having confirmed that MCI is sensitive and specific at detecting vessel whitening in BRVO, we performed a longitudinal analysis to understand how vessel whitening using MCI changed with time. MCI from 23 eyes of 23 BRVO patients with more than one visit had longitudinal images graded from first presentation to latest clinic visit.

The mean follow-up period was 430±648 days. The median baseline and follow-up grading score for vessel whitening visualization were both 1.0 (p=0.655). The mean grading at baseline and follow-up was, 0.61 (95% CI 0.36–0.86) and 0.57 (95% CI 0.31–0.82) respectively, with no significant difference in the grading score over time (p=0.856).

Correlation of vessel whitening on MCI with area of ischemia on FFA

Twenty-nine eyes of 29 patients (62% females; mean age 68±15 years) who underwent same-day MCI and FFA were included in this analysis. The mean area of ischemia on FFA was 10.27 mm^2 (95% CI 4.7–15.8). The grading score for vessel whitening on MCI was significantly correlated to the area of ischemia on FFA, with a higher grading score associated with a larger area of ischemia (r^2=0.15; p=0.036).

DISCUSSION

Although CFP remains a common imaging technique for documenting retinal findings, it may be labor-intensive and time-consuming when the patient requires several imaging modalities such as SD-OCT, autofluorescence, and increasingly digital widefield imaging. CFP may also be limited when the view is restricted by coexisting media opacities such as cataracts or vitreous hemorrhage. [21] Some of these limitations are circumvented by MCI, which can be performed nearly simultaneously with SD-OCT, is less affected by media opacities due to suppression of light scatter and can enable better resolution by eye tracking. [22]

To investigate the validity of MCI in identifying vessel whitening secondary to BRVO, we opted to evaluate its detection rate only in BRVO eyes manifesting vessel whitening in the entire extent of a vascular segment, given other conditions such as hypertensive retinopathy and vasculitis may sometimes present with segmental or focal vessel whitening. [18, 19] This differentiation of vessel whitening clinically may be challenging and variable in the context of retinal vascular diseases. Nonetheless, using these criteria, no false positives were found in the control group compared to the BRVO cohort. Results also suggested that MCI has a high specificity for vessel whitening when appropriately identified with careful differentiation from artifacts and physiological variants.

In this study, we demonstrated that MCI had a superior detection rate of vessel whitening compared to CFP, with a significantly higher vessel whitening visibility score. To our knowledge, only one previous study has compared MCI to CFP in BRVO. Tan and colleagues [11] compared CFP and MCI in multiple macular and retinal disorders, describing a single case of ischemic BRVO in which CFP demonstrated better visualization of collateral and sclerosed vessels than MCI. It is, however, unclear from their paper's methods whether the images of this single case were taken on the same day, as the hemorrhages do appear markedly different.

Interestingly, despite a lower pixel density than CFP (3,000 × 2,672 pixels for all colors combined on Topcon Color camera vs. 768 × 768 pixels x 3 colors on the Spectralis), MCI was able to better detect vessel whitening resulting from BRVO in our present study. This may be due to the in-built automated eye-tracking technology and noise-reduction techniques, which enhance image clarity and reduce the effect of light scatter. [10] This knowledge, in conjunction with our findings, attests to the emerging role of MCI in evaluating chorioretinal vascular diseases, as supported by previous authors. [23–26] As for MCI channel preference, we found a predilection for the green and blue channels. One explanation is likely due to the optimized visualization of inner retinal surface changes and blood vessels with shorter wavelengths, such as green and blue reflectance. This explanation is corroborated by similar studies focusing on color fundus image analysis that have established the green channel as the best contrast provider for blood vessels. [27, 28]

Based on the longitudinal analysis of grading scores in BRVO patients, we demonstrated that MCI offers consistent grading over an extended follow-up period. This conclusion may support the use of MCI in the long-term monitoring of vessel whitening in BRVO, possibly

extending its utility to aid in the work-up of previously undiagnosed cases with delayed presentation. Furthermore, we found a slight reduction in vessel whitening visibility at the end of follow-up, which was not statistically significant but could reflect a phenotypic change in response to the long-term retinal vascular remodeling seen in retinal ischemia. [29] This study also found a significant correlation between vessel whitening visibility on MCI and ischemic area size on FFA, highlighting the potential role of the former as a non-invasive surrogate marker for retinal ischemia, which may have important therapeutic and prognostic implications.

There are limitations to the findings in our study; the most important is the inherent discrepancy in image appearance between CFP and MCI. In addition, despite an attempt to increase objectivity by utilizing a grading scale, it was impossible to mask the observers regarding the modality being graded. It is also likely that MCI and CFP failed to detect all cases of vessel whitening secondary to BRVO in our study, which might be explained by the limited field of view with both imaging modalities precluding evaluation of vessel whitening in the peripheral retina. Further studies using alternative imaging, such as ultra-widefield retinal imaging, may overcome this limitation.

In summary, the present study finds that MCI is highly sensitive and specific in detecting vessel whitening in BRVO and provides better visualization of vessel whitening in eyes with BRVO than CFP. We also show that MCI can achieve a high interobserver agreement in the visibility of vessel whitening and provide a reliable, long-term evaluation of this parameter, serving as a non-invasive correlate of retinal ischemia. Finally, the present study suggests that MCI can be a valuable adjunct to current imaging modalities to assist in identifying vessel whitening in BRVO, which is potentially useful in cases where the diagnosis is suspected but still inconclusive after fundoscopy or CFP evaluations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this article and its supplementary material files. Further enquiries can be directed to the corresponding author.

ABBREVIATIONS

BRVO	branch retinal vein occlusion

CFP	color fundus photography
FFA	fundus fluorescein angiography
IRB	institutional review board
MCI	Multicolor™ imaging
SD-OCT	spectral-domain optical coherence tomography

REFERENCES

1. Rogers SL, McIntosh RL, Lim L, Mitchell P, Cheung N, Kowalski JW, et al. Natural history of branch retinal vein occlusion: an evidence-based systematic review. Ophthalmology. 2010;117(6):1094–101.e5. [PubMed: 20430447]
2. Rogers S, McIntosh RL, Cheung N, Lim L, Wang JJ, Mitchell P, et al. The prevalence of retinal vein occlusion: pooled data from population studies from the United States, Europe, Asia, and Australia. Ophthalmology. 2010;117(2):313–9.e1. [PubMed: 20022117]
3. Rehak J, Rehak M. Branch retinal vein occlusion: pathogenesis, visual prognosis, and treatment modalities. Curr Eye Res. 2008;33(2):111–31. [PubMed: 18293182]
4. Argon laser scatter photocoagulation for prevention of neovascularization and vitreous hemorrhage in branch vein occlusion. A randomized clinical trial. Branch Vein Occlusion Study Group. Arch Ophthalmol. 1986;104(1):34–41. [PubMed: 2417579]
5. Genevois O, Paques M, Simonutti M, Sercombe R, Seylaz J, Gaudric A, et al. Microvascular remodeling after occlusion-recanalization of a branch retinal vein in rats. Invest Ophthalmol Vis Sci. 2004;45(2):594–600. [PubMed: 14744903]
6. L Srinidhi C, Aparna P, Rajan J. Recent Advancements in Retinal Vessel Segmentation. J Med Syst. 2017;41(4):70. [PubMed: 28285460]
7. Group ETDRSR. Grading Diabetic Retinopathy from Stereoscopic Color Fundus Photographs - An Extension of the Modified Airlie House Classification: ETDRS Report Number 10. Ophthalmology. 2020;127(4S):S99–S119. [PubMed: 32200833]
8. Group A-REDSR. The Age-Related Eye Disease Study system for classifying age-related macular degeneration from stereoscopic color fundus photographs: the Age-Related Eye Disease Study Report Number 6. Am J Ophthalmol. 2001;132(5):668–81. [PubMed: 11704028]
9. Abràmoff MD, Garvin MK, Sonka M. Retinal imaging and image analysis. IEEE Rev Biomed Eng. 2010;3:169–208. [PubMed: 22275207]
10. Sergott RC. Retinal segmentation using multicolor laser imaging. J Neuroophthalmol. 2014;34 Suppl:S24–8. [PubMed: 24275984]
11. Tan AC, Fleckenstein M, Schmitz-Valckenberg S, Holz FG. Clinical Application of Multicolor Imaging Technology. Ophthalmologica. 2016;236(1):8–18. [PubMed: 27404384]
12. Song JH, Moon KY, Jang S, Moon Y. Comparison of MultiColor fundus imaging and colour fundus photography in the evaluation of epiretinal membrane. Acta Ophthalmol. 2019;97(4):e533–e9. [PubMed: 30565886]
13. Basu T, Shah D, Das D, Saurabh K, Roy R. Multicolor imaging for retinal nerve fiber layer defect in glaucoma. Indian J Ophthalmol. 2018;66(9):1345–9. [PubMed: 30127168]
14. Kousha O, Delle Fave MM, Cozzi M, Carini E, Pagliarini S. Diabetic maculopathy: multicolour and SD-OCT versus fundus photography. BMJ Open Ophthalmol. 2021;6(1):e000514.
15. Pang CE, Freund KB. Ghost maculopathy: an artifact on near-infrared reflectance and multicolor imaging masquerading as chorioretinal pathology. Am J Ophthalmol. 2014;158(1):171–8.e2. [PubMed: 24631479]
16. Graham KW, Chakravarthy U, Hogg RE, Muldrew KA, Young IS, Kee F. IDENTIFYING FEATURES OF EARLY AND LATE AGE-RELATED MACULAR DEGENERATION: A Comparison of Multicolor Versus Traditional Color Fundus Photography. Retina. 2018;38(9):1751–8. [PubMed: 28834946]

17. He L, Chen C, Yi Z, Wang X, Liu J, Zheng H. CLINICAL APPLICATION OF MULTICOLOR IMAGING IN CENTRAL SEROUS CHORIORETINOPATHY. Retina. 2020;40(4):743–9. [PubMed: 30608348]
18. Henderson AD, Bruce BB, Newman NJ, Biousse V. Hypertension-related eye abnormalities and the risk of stroke. Rev Neurol Dis. 2011;8(1–2):1–9. [PubMed: 21769065]
19. Stanford MR, Mathew R. Patterns of Retinal Vascular Involvement in the Diagnosis of Retinal Vasculitis. Uveitis and Immunological Disorders. Berlin, Heidelberg: Springer Berlin Heidelberg; 2009. p. 87–96.
20. Amador-Patarroyo MJ, Lin T, Meshi A, Dans KC, Chen K, Borooah S, et al. Identifying the factors for improving quality of oral fluorescein angiography. Br J Ophthalmol. 2020;104(4):504–8. [PubMed: 31272951]
21. Toffoli D, Bruce BB, Lamirel C, Henderson AD, Newman NJ, Biousse V. Feasibility and quality of nonmydriatic fundus photography in children. J AAPOS. 2011;15(6):567–72. [PubMed: 22153402]
22. Saurabh K, Roy R, Chowdhury M. Efficacy of Multicolor Imaging in Patients With Asteroid Hyalosis: Seeing the Unseen. JAMA Ophthalmol. 2018;136(4):446–7. [PubMed: 29522059]
23. Kilic Muftuoglu I, Bartsch DU, Barteselli G, Gaber R, Nezgoda J, Freeman WR. VISUALIZATION OF MACULAR PUCKER BY MULTICOLOR SCANNING LASER IMAGING. Retina. 2018;38(2):352–8. [PubMed: 28151841]
24. Muftuoglu IK, Gaber R, Bartsch DU, Meshi A, Goldbaum M, Freeman WR. Comparison of conventional color fundus photography and multicolor imaging in choroidal or retinal lesions. Graefes Arch Clin Exp Ophthalmol. 2018;256(4):643–9. [PubMed: 29492687]
25. Ben Moussa N, Georges A, Capuano V, Merle B, Souied EH, Querques G. MultiColor imaging in the evaluation of geographic atrophy due to age-related macular degeneration. Br J Ophthalmol. 2015;99(6):842–7. [PubMed: 25586715]
26. Govindahari V, Singh SR, Rajesh B, Gallego-Pinazo R, Marco RD, Nair DV, et al. Multicolor imaging in central serous chorioretinopathy - a quantitative and qualitative comparison with fundus autofluorescence. Sci Rep. 2019;9(1):11728. [PubMed: 31409843]
27. Alam M, Son T, Toslak D, Lim JI, Yao X. Combining ODR and Blood Vessel Tracking for Artery-Vein Classification and Analysis in Color Fundus Images. Transl Vis Sci Technol. 2018;7(2):23.
28. Walter T, Massin P, Erginay A, Ordonez R, Jeulin C, Klein JC. Automatic detection of microaneurysms in color fundus images. Med Image Anal. 2007;11(6):555–66. [PubMed: 17950655]
29. Ishida S, Yamashiro K, Usui T, Kaji Y, Ogura Y, Hida T, et al. Leukocytes mediate retinal vascular remodeling during development and vaso-obliteration in disease. Nat Med. 2003;9(6):781–8. [PubMed: 12730690]

STATEMENT OF ETHICS

Study approval statement:

Institutional Review Board (IRB) from the University of California San Diego has reviewed and granted exemption from ethics approval for the review and analysis of retrospective anonymized patients' data. This retrospective cross-sectional study was conducted according to the principles of the Declaration of Helsinki. The study complied with the Health Insurance Portability and Accountability Act of 1996.

Consent to participate statement:

Exemption from requiring written informed consent was obtained following review of the study by IRB of the University of California San Diego.

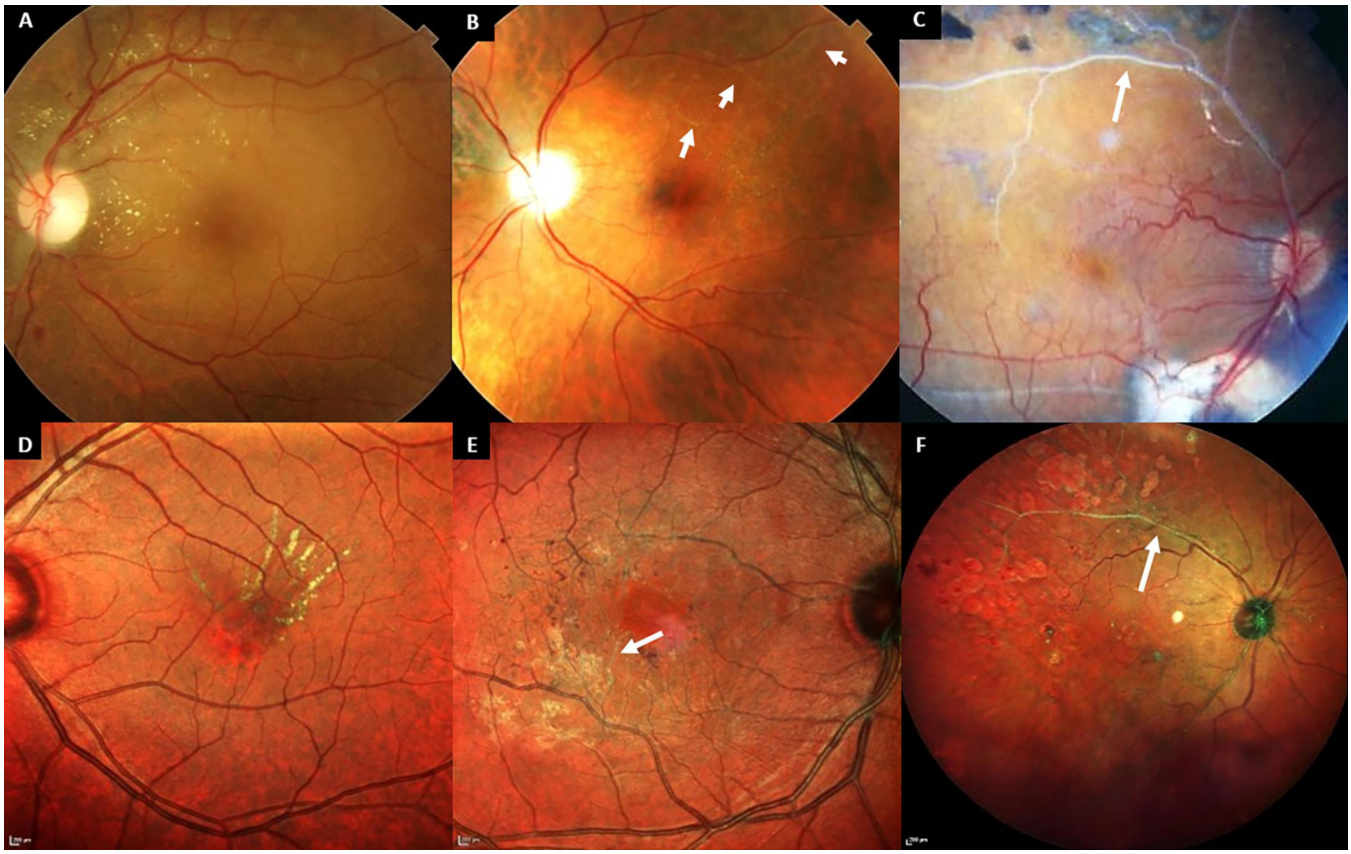

Figure 1.

Standard images by color fundus photography (A-C) and Multicolor technique (D-F) employed by the two independent graders as a reference in the in the process of vessel whitening identification. The arrowheads point to the occluded vessels analyzed. Grade 0 corresponds to no visible vessel whitening (A, D). Grade 1 consists of slightly visible vessel whitening (B, E). Grade 2 indicates clearly visible vessel whitening (C, F).

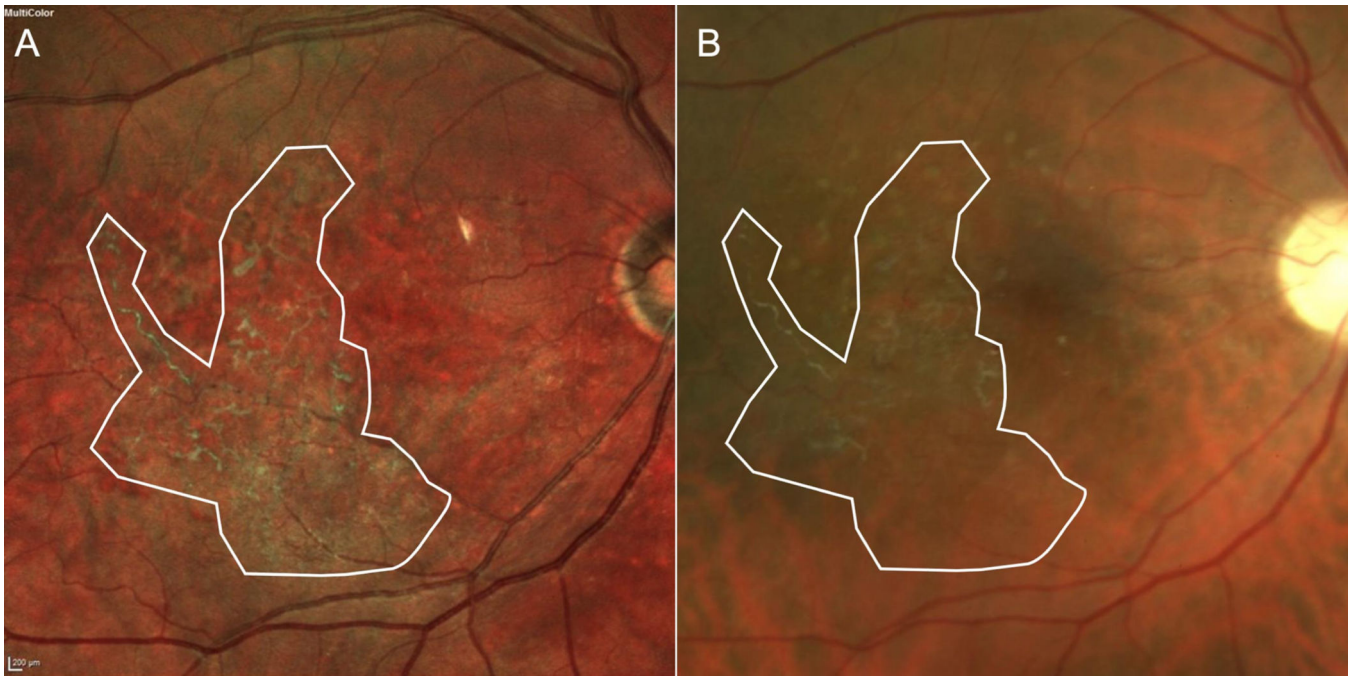

Figure 2.

Same-patient paired images showing incongruent appearance of vessel whitening following branch retina vein occlusion captured by Multicolor imaging (A) and color fundus photo (B). The sclerotic changes indicated by the area encircled with a white line shows that the ischemic area is clearly visible on the Multicolor and only slightly noticeable on the conventional fundus photo. Differences in color rendition are also evident between the two imaging techniques.

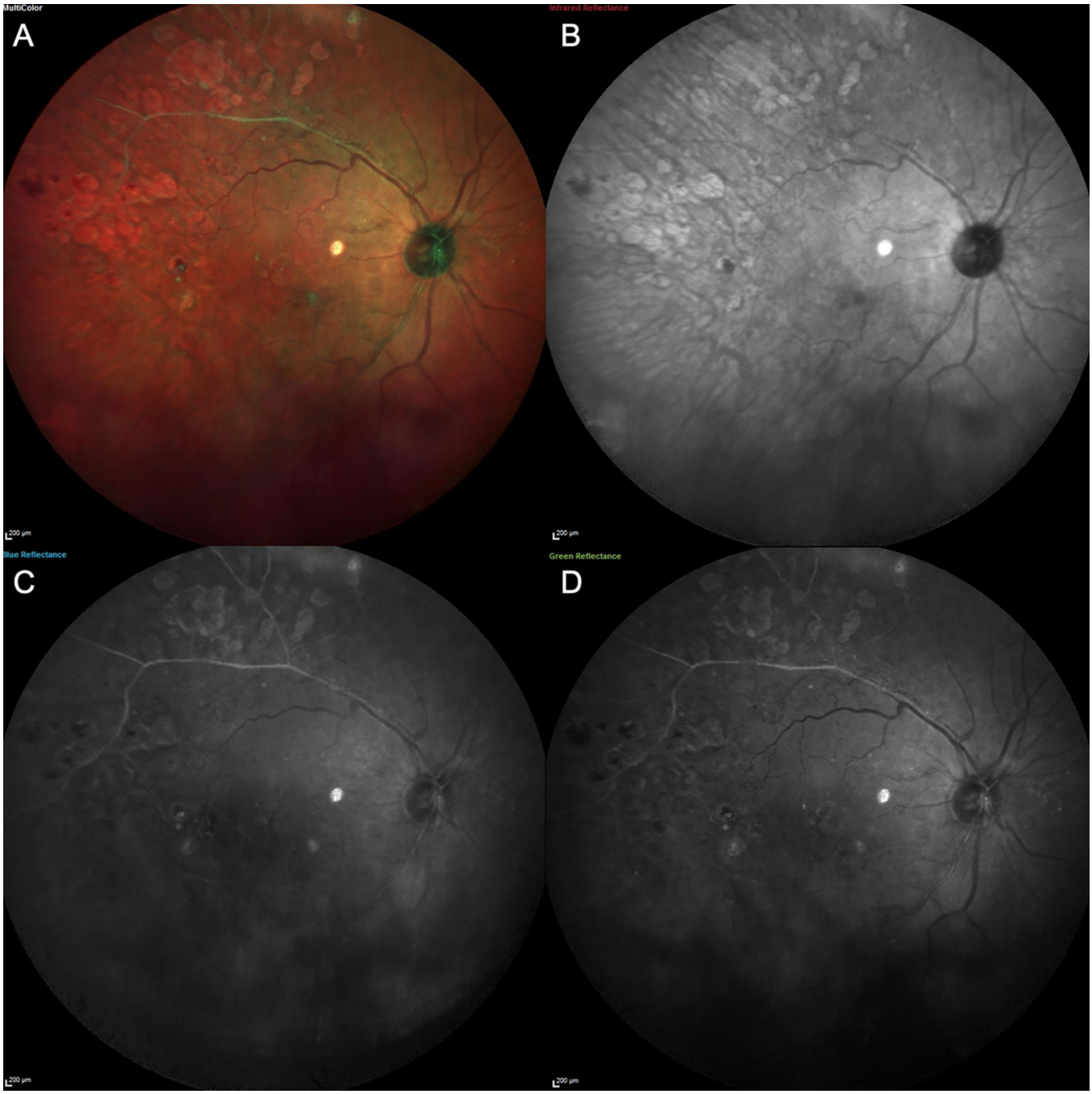

Figure 3.
Photo-composite showing the standard Multicolor photo (A) and the three-color channels (B-D) in a case of branch retinal vein occlusion affecting the superotemporal arcade. As displayed, while vessel whitening is most clearly visible on the blue (C) and green (D) channels, it appears less noticeable on the infrared reflectance (B).

Table 1.

Visualization of vessel whitening using multicolor imaging and color fundus photography (n=26)

		Vessel whitening on color fundus photography		Total
		Presence	Absence	
Vessel whitening on multicolor imaging	Presence	14	2	16
	Absence	0	10	10
Total		14	12	26