Retinal Cases & Brief Reports

Identification of increased blue light reflectivity in macular telangiectasia type 2 using a scanning laser ophthalmoscopy versus red free fundus photography

--Manuscript Draft--

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Abstract:	Purpose To compare two modalities used for detection of the characteristic parafoveal hyperreflective area seen in macular telangiectasia type 2 (MacTel). Methods Scanning laser ophthalmoscope blue light reflectance (SLO-BLR) was compared with red free fundus photography (RF) imaging. Images were obtained as part of the international Natural History Study of Macular Telangiectasia (Mac Tel Study). Results The hyperreflective area can more frequently be seen with SLO-BLR than with RF imaging. However, the frequency of detection is similar in good quality RF images. Conclusion Detection of the hyperreflective area might help to identify MacTel in earlier disease stages. SLO-BLR should be preferred as diagnostic tool when the suspicion of MacTel arises. However, RF imaging offer a viable option to SLO BLR when good quality is achieved.
Response to Reviewers:	Reviewer #1: Soorma et al. compared differences of an SLO system and a fundus camera in identifying a specific sign - increased blue light reflectance - in patients with macular telangiectasia type 2. 1) Why do the authors not choose a more specific title - e.g. "Identification of increased blue light reflectivity in macular telangiectasia type 2 using a scanning laser ophthalmoscopy versus red free fundus photography". 1) Thank you for suggesting the change of title, we also feel this new title is more appropriate and this has been changed accordingly. 2) Based on the table, SLO imaging is far superior compared to the fundus camera in

	all aspects - and this should be clearly summarized in the main text. Picking only those fundus camera images with ideal image quality appears inappropriate because it is likely that the same photographers have recorded the images form individual patients. This should result in an overall similar technical quality of the two imaging procedures for each patient. If the fundus camera images are worse for other reasons, e.g. because patients had cataract, the worse detection rate of the investigated phenomenon would simply reflect the inferiority of the method for this purpose. The abstract should also be changed accordingly. 2) Thank you for suggesting the above point, after reviewing this we agree that including only those images with good quality into analysis does not seem appropriate. For this reason, we have removed these results from the table and from the text. We have removed it from the methods and the conclusion section. We agree that SLO-BLR seems superior to RF photography and therefore we have added : “In all other aspects, SLO-BLR images seemed superior to detect the characteristic signs of MacTel (Table 1). In particular, the hyperreflective area was visible more frequently and outlined more clearly in SLO-BLR images’”. However, we feel it is necessary to state that ‘RF imaging, however, offers a viable alternative to SLO BLR if the latter is not available’ and have therefore added this into the conclusion. We look forward to hearing your thoughts regarding this, and welcome any suggestions for amendments. 4) The abbreviation "hra" in the table is not necessary. 4) We also feel this is not necessary and this has been removed accordingly, both in the table and in the table legend. 5) The last sentence of the discussion is not necessary - this is obvious. 5) Thank you for this comment ‘The sentence was deleted.

Identification of increased blue light reflectivity in macular telangiectasia type 2 using a scanning laser ophthalmoscopy versus red free fundus photography

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Key words

Macular telangiectasia type 2;

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Summary statement

Redfree (RF) fundus photography is useful for detection of the hyperreflective pattern seen on blue light reflectance imaging in macular telangiectasia type 2 (MacTel) and might help clinicians to diagnose early cases of MacTel, given that sufficient imaging quality can be achieved.

Abstract

Purpose To compare two modalities used for detection of the characteristic parafoveal hyperreflective area seen in macular telangiectasia type 2 (MacTel).

Methods Scanning laser ophthalmoscope blue light reflectance (SLO-BLR) was compared with red free fundus photography (RF) imaging. Images were obtained as part of the international Natural History Study of Macular Telangiectasia (Mac Tel Study).

Results The hyperreflective area can more frequently be seen with SLO-BLR than with RF imaging.

Conclusion Detection of the hyperreflective area might help to identify MacTel in earlier disease stages. SLO-BLR should be preferred as diagnostic tool when the suspicion of MacTel arises. However, RF imaging offer a viable option to SLO BLR when good quality is achieved.

Macular telangiectasia (MacTel) type 2 is a bilateral neurodegenerative macular disease that typically presents in the fifth or sixth decade of life and may eventually result in legal blindness. Epidemiologic, functional and clinical findings have been described in detail recently.[1] Diagnosis of early MacTel disease remains a challenge even with more advanced techniques such as spectral domain optical coherence tomography (SD-OCT).[1, 2] It has been shown that blue light reflectance (BLR) reveals a pathognomonic hyperreflective area (figure) which correlates to loss of macular pigment as seen in dual-wavelength autofluorescene (DWAF). This pattern is believed to be one of the first detectable signs of MacTel.[2-5] Although DWAF seems superior in detection of this characteristic pattern,[5, 6] it is not widely available limiting its clinical utility, leaving BLR to be the diagnostic tool of choice for early detection of MacTel. Theoretically, only scanning laser ophthalmoscopes (SLO) produce "pure" blue light, usually at 488nm.[5] However, SLO systems such as the HRA Spectralis® are not available to all therefore it is essential to evaluate if there is an alternative to SLO for detection of the characteristic early sign of MacTel. Some fundus cameras offer the option of "red free photography". Red free imaging is created with a blue or green filter (in Topcon fundus cameras this is a *green filter* with a maximum transmission of 540nm, thus it creates *green* light). We compared a red free (RF) camera with SLO BLR in order clarify if RF is also useful for detection of the characteristic sign of MacTel.

Methods

SLO BLR and RF fundus photography were performed in MacTel patients as part of the multicenter MacTel Natural History Observation Study (NHOS).[7] SLO BLR was taken with HRA Spectralis® (Heidelberg Engineering, Germany, setting: HS mode, central field, 30°x 30°). Red free images were taken with Topcon TRX-50 (Topcon Medical Systems, Tokyo, Japan, setting: green filter, central field, 30^0 angle) during the same imaging session. Image quality was graded based on visibility of the nerve fibre bundles around the optic disc and the visibility of the third order vessels around the fovea (figure). Presence and visibility of

different characteristics as presented in table 1 were compared between the two devices. (non-parametric Chi-squared testing, SPSS, IBM version 22.0, p-value <0.05 = statistically significant). A subset of 31 images was re-graded to calculate intra-grader agreement (Linear weights for calculating weighted κ-values, MedCalc Windows 12.5).

Results

A total 327 images of eighty-three patients were selected from three sites. Seven images were not gradable. Third order vessels were seen in 100% of both RF and SLO-BLR images and thus seem not to be suitable as sign for quality of the image. In all other aspects, SLO-BLR images seemed superior to detect the characteristic signs of MacTel (Table 1). In particular, the hyperreflective area was visible more frequently and outlined more clearly in SLO-BLR images. A high intragrader agreement was seen in all analysed parameters.

Conclusion

Our comparison shows that RF fundus photography is useful for detection of the hyperreflective area as early sign of MacTel, but SLO BLR was superior to RF photography in detection of this area. RF imaging , however, offers a viable alternative to SLO BLRif the latter is not available. Both technicians and clinicians should be aware of the opportunity that RF imaging provides and at the same time of the problems it presents when considering a diagnosis of MacTel.

References

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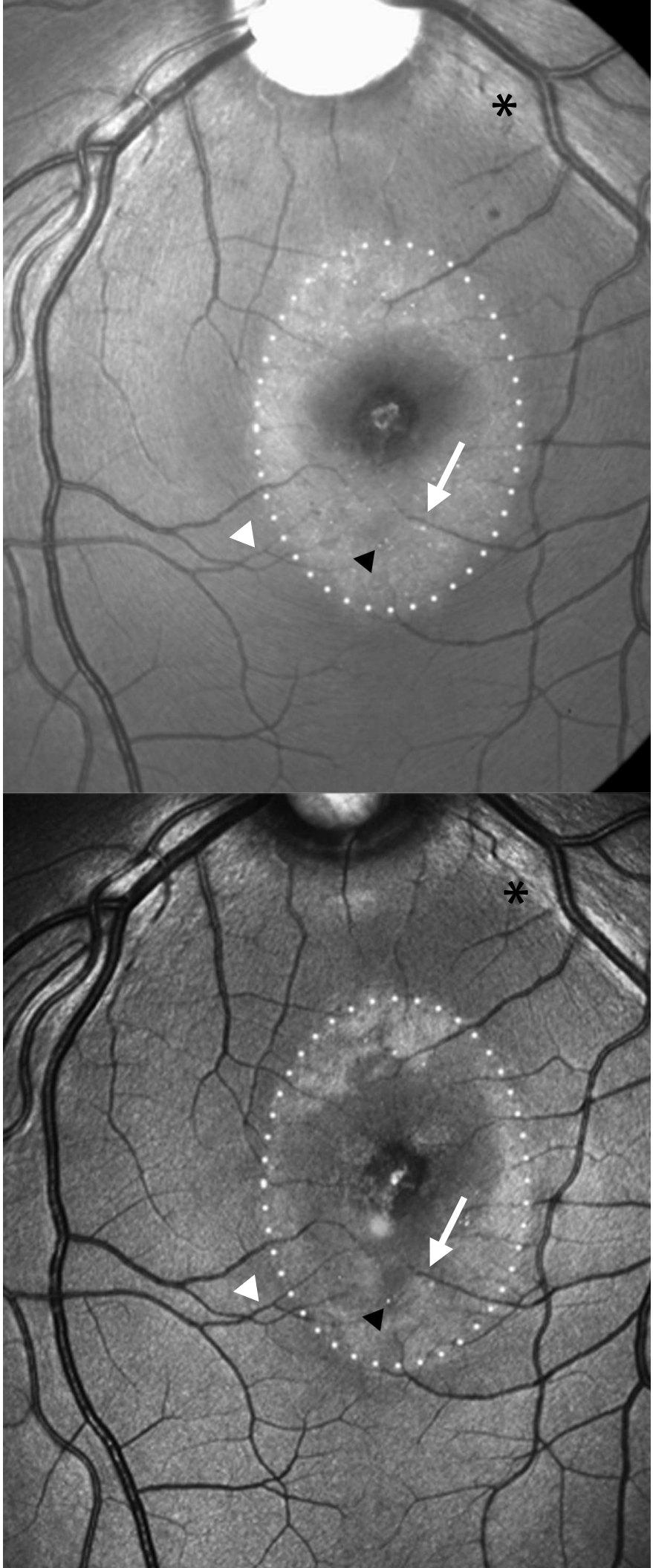
Figure Comparison between 488nm blue light reflectance (BLR) (left) and red free fundus photography with green filter (right) in an eye with macular telangiectasia type 2. The characteristic area of increased reflectance (outlined by dotted line) is clearly visible. Third order vessels (white arrowheads), nerve fibres (asteriscs), blunted right angled venules (arrows) and crystalline deposits (black arrowheads) can be identified.

Figure



Table

Characteristics	SLO	Topcon	Significance	(Kappa-value)	
				SLO	Topcon
Nerve fibers visible	70%	35%	Yes , *p*<0.0001	0.925	0.913
3rd order vessels visible	100%	100%	No , *p* = 1	1.0	0.936
Hyperreflective area	85%	45%	Yes *p*<0.0001	1.0	0.710
• border clearly defined	60%	25%	Yes , *p*<0.0001	1.0	0.717
• border complete	55%	20%	Yes , *p*<0.0001	1.0	0.796
Crystalline deposits	30%	20%	Yes *p*<0.0001	0.920	0.796
Right-angled venules	40%	15%	*Yes p*<0.0001	0.929	0.714

Table 1 n= 327 images of eighty-three patients. Kappa-values from a sample of 31 images (κ < 0, poor agreement; κ values 0–0.20 “slight,” 0.21–0.40 “fair,” 0.41–0.60 “moderate,” 0.61–0.8 “substantial,” and k > 0.81 “almost perfect” agreement (nerve fibres visible, n=106) show the *hyperreflective area*