Reading Performance Is Reduced by Parafoveal Scotomas in Patients with Macular Telangiectasia Type 2

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Purpose. Macular telangiectasia (MacTel) type 2 typically exhibits sharply demarcated parafoveal scotomas. In an investigation of their significance for reading performance, reading acuity and speed were measured and correlated with parafoveal sensitivity and fixation stability.

Methods. In this prospective controlled cross-sectional observational study, 49 eyes of 26 patients with MacTel type 2 were investigated. Twenty-four eyes of 14 age-matched normal subjects served as the control. Reading acuity and reading speed (in words per minute [wpm]) were assessed by Radner charts. Retinal sensitivity was measured using fundus controlled microperimetry (MP1; Nidek Technologies). Fixation stability was quantified by the bivariate contour ellipse area (BCEA). Multiple logistic regression analysis was used to delineate outcome predictors of reading acuity and speed.

Results. Mean reading speed was considerably reduced in patients (to 141 wpm; control speed, 190 wpm; $P < 0.001$) as was reading acuity (patients, 20/63; control subjects, 20/32; $P < 0.001$). Mean best corrected visual acuity (BCVA) was reduced in most eyes (patients, 20/50; control subjects, 20/20; $P < 0.001$). Mean BCEA was not reduced compared with that in the control subjects. BCVA reduction predicted reading acuity loss ($P = 0.02$) and a decrease in maximum reading speed ($P < 0.001$). Parafoveal sensitivity loss resulted in decreased reading acuity ($P = 0.03$) and reading speed reduction ($P < 0.001$).

Conclusions. These findings indicate that parafoveal sensitivity loss in MacTel type 2 is associated with loss of reading performance despite stable central fixation. Reading performance appears to be a sensitive variable of functional impairment in MacTel type 2 and should therefore be considered an outcome measure in future interventional trials. (*Invest Ophthalmol Vis Sci.* 2009;50:1366–1370) DOI:10.1167/iovs.08-2032

Type 2 idiopathic macular telangiectasia (IMT) is a rare condition that usually presents with a slow decrease in visual acuity in the fifth to seventh decade.[1–3] The bilateral disease is defined by parafoveal telangiectatic capillaries with minimal exudation, a hallmark that often is visible only on fluorescein angiography. Typical findings in clinical examination include a loss of retinal transparency, superficial retinal crystalline deposits, right-angled venules, and in later disease stages intraretinal pigment migration and ultimately neovascular membranes. The disease is predominant in the temporal parafoveal area and has been associated with an increased parafoveal confocal blue reflectance,[4,5] possibly due to a decrease in macular pigment density.[4,6] Optical coherence tomography (OCT) may reveal hyporeflective spaces and often a decreased central retinal thickness.[7–10]

Affected patients often complain of reading impairment despite good distance visual acuity and central fixation. Recently, it was shown that patients with MacTel type 2 usually develop paracentral scotomas.[10–12] We hypothesized that such parafoveal sensitivity loss may impair reading ability. Moreover, a scotoma in proximity to the fovea may also destabilize fixation.

As such, MacTel type 2 may serve a model disease for the study of parafoveal scotomas and their impact on function. Central scotomas and adaptive changes in fixation have been studied in artificially created models that have certain limitations when translating findings into clinical relevant practice.[13] Reading and parafoveal scotomas can be studied in vivo in patients with MacTel type 2. The parafoveally reduced retinal sensitivity in MacTel type 2 may be used to study reading ability in the context of a reduced central visual field and thus a reduced perceptual span due to parafoveal scotomas.

We therefore examined reading ability in patients with MacTel type 2 and correlated it with fixation stability, foveal and parafoveal retinal light increment sensitivity, and distance visual acuity.

Methods

In a prospective cross-sectional study, 52 eyes of 26 patients with MacTel type 2 (13 male and 13 female) were included. One randomly selected eye of each of 15 healthy control subjects served as the control. All subjects underwent a complete ophthalmic examination, including BCVA and indirect ophthalmoscopy. Patients underwent fluorescein angiography either by digital photography (model FF450; Carl Zeiss Meditec, Jena, Germany) or by confocal scanning laser ophthalmoscopy (cSLO; HRA2; Heidelberg Engineering, Heidelberg, Germany), fundus photography (FF450l; Carl Zeiss Meditec), OCT (Stratus OCT; Carl Zeiss Meditec), and microperimetry. Diagnosis of MacTel type 2 was ascertained clinically and on fluorescein angiography based on criteria laid out in the definition of the disease entity by Gass et al.[1,14]

The study was approved by the local institutional review boards (ethics committee, University of Bonn). All patients gave informed consent before any study-related activities, in accordance with the Declaration of Helsinki. The study was performed in the context of the worldwide multicenter MacTel Study (The Macular Telangiectasia Project; www.mactelresearch.org).

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Visual Acuity Testing

BCVA was measured with a standard Early Treatment Diabetic Retinopathy Study (ETDRS) protocol at 4 m, with the fellow eye occluded.

BCVA and reading speed in words per minute (wpm) were tested monocularly with standard Radner reading charts at a reading distance of 25 cm, as previously described by Radner et al.[15] The critical print size (CPS) was set at the smallest print size that could be read with maximum reading speed (MRS). The sentences were covered with a piece of paper, and the patients were asked to uncover sentence after sentence, reading each one aloud as quickly and accurately as possible. The patients were instructed to read each sentence to the end without correcting any reading errors. Reading time was measured with a stopwatch. Reading speed in wpm was calculated based on the number of words in a sentence and the time needed to read the sentence. The MRS was the best reading speed achieved in the test. Reading acuity was set at the smallest print size the patient was able to read completely and was expressed in terms of logRAD (logarithm of the reading acuity which is the reading equivalent of logMAR).

Microperimetry and Fixation Testing

Fundus controlled static threshold microperimetry with dilated pupils was performed (MP1, software version 1.5.1; Nidek Technologies, Padova, Italy), using Goldmann III stimuli presented for 100 ms against a white background with a luminance of 1.27 cd/m^2. The range of target luminance was 0 to 20 dB attenuation from a maximum of 127 cd/m^2. The fixation target was a suprathreshold 2° red cross. Perimetric targets were displayed using a 16° macular grid centered on the fovea to assess the central and paracentral visual field and foveal sensitivity. The room was dark during examination. The minimal light increment sensitivity (LIS) temporal to the fovea was defined according to Charbel Issa et al.[11] Microperimetric data on a subset of the patient cohort have been published.[11]

Fixation stability was assessed over a period of 30 seconds and calculated as bivariate contour ellipse area (BCEA), within which the center of the target was imaged 68% of the time.[16,17] The fixation target was the same as for the microperimetry examination (i.e., a suprathreshold 2° red cross with a thickness of 1 unit, as predefined by the MP1) against a white background with a luminance of 1.27 cd/m^2. Fixation was tested before microperimetry or other retinal imaging or visual testing with fully dilated pupils using the MP1. LIS at the point of fixation is referred to as central foveal LIS. The fixation data were further evaluated to determine whether there were multiple fixation loci (preferred retinal loci, PRLs) using the kernel density estimator technique described by Crossland et al.[18] Data were recorded only while the eye tracking was active. Thus, no data were recorded during blinking or loss of tracking.

Statistical Analysis

As the BCEA data were right skewed, a log transformation was used to obtain near normal distribution. Visual acuity calculations were performed with the logMAR (logarithm of the minimum angle of resolution) scale for BCVA and the logRAD (reading equivalent of logMAR) scale for best corrected reading acuity. Temporal LIS was transformed into a binary variable (minimal temporal LIS = 0, absolute scotoma; and minimal temporal LIS > 0, relative scotoma) to be included in the regression models.

Because of the possible dependency between right and left eye of a person the data were analyzed under a generalized linear model approach using generalized estimation equations to account for the correlation structure. Pooled data were used to increase the power of the subsequent performed statistical analyses, taking into account the interocular dependence of intraindividual measurements. Based on this, regression analyses were performed to develop models for the linear prediction of reading speed and reading acuity. The regression analysis included a set of possible variables for the prediction of reading speed and acuity (BCVA, BCEA, and central and temporal LIS). Because of the low number of observations, we fitted only one- and two-factor regression models and used the QIC-criterion[19] to select the best-fitting model. Analyses were performed with commercial software (SAS 9.1; SAS Institute Inc., Cary, NC). Within the patient sample, right and left eyes were analyzed separately to account for possible differences in reading performance caused by scotomas either to the right or to the left of the visual axis. Data were too limited to model complex analyses such as multiple interactions for right or left eyes separately. Cases with missing data were excluded from the respective analysis.

Results

Within the patient group, three eyes were excluded from further analysis: BCEA could not be calculated in one eye due to three PRLs, and the datasets were very noisy in two other eyes (Fig. 1).

Characteristics of the patient and control samples are presented in Table 1. Mean age did not differ significantly between the two groups (patients, 62 years; control subjects, 64 years). However, all functional measures except BCEA were significantly better in the control group. BCVA of the control subjects was 20/20, whereas BCVA was reduced in most MacTel type 2 eyes to a mean of 20/50 ($P < 0.001$). Similarly, reading acuity was 20/32 in the control group and 20/63 in the MacTel type 2 group (logRAD mean control subjects, 0.24; patients, 0.45; $P < 0.001$). The mean maximum reading speed was considerably reduced by almost 50 wpm from an average of 190 wpm in the control group to 141 wpm in the patient group ($P < 0.001$). Median BCEA was 857 minarc^2 (range, 97–2141 minarc^2) for the control group and 529 minarc^2 (range, 132–3142 minarc^2) for the MacTel type 2 group, which exhibited greater intragroup variability although the intergroup difference did not reach statistical significance ($P = 0.057$). Median central foveal sensitivity was found to be 14 dB and median minimal LIS temporal to the foveal center was 7 dB in the patient group.

Analyzing outcome parameters of reading acuity and maximum reading speed in the MacTel type 2 group, best fit regression analysis showed BCVA and minimal temporal LIS to be significant predictors of both variables (Table 2). A reduction of BCVA predicted a reduction of reading acuity ($P = 0.02$) and a decrease in maximum reading speed ($P < 0.001$). Reduced temporal LIS resulted in significant decreases in both reading acuity ($P = 0.03$) and reading speed ($P < 0.001$). Two examples with well preserved central fixation but poor reading acuity in the presence of a parafoveal scotoma are provided in Figure 2. BCEA and central foveal LIS were not found to be good predictors of the investigated outcome parameters.

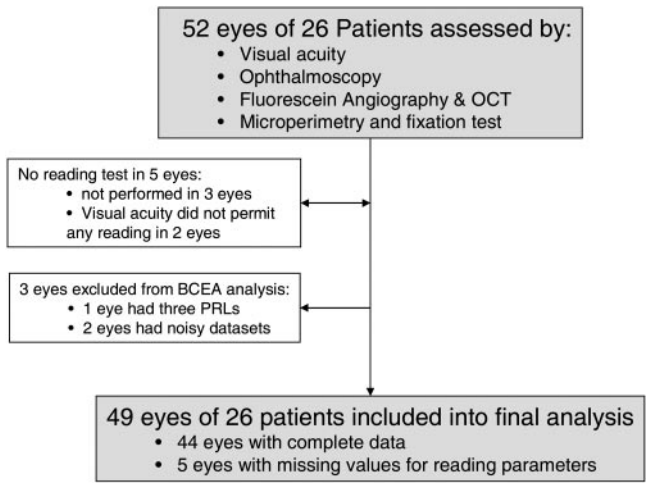

Figure 1. Patient flowchart.

TABLE 1. Characteristics of Patients with MacTel Type 2 and Control Subjects

	MacTel Type 2	Controls	*P**
Age (y)	62 (6.6)	64 (9.0)	0.282
BCVA	20/50 logMAR 0.40 (0.27)	20/20 logMAR 0 (0.1)	<0.001
Reading acuity	20/63 logRAD 0.45 (0.28)	20/32 logRAD 0.24 (0.14)	<0.001
Maximum reading speed (words/min)	140 (48)	190 (21)	<0.001
BCEA (minarc^2)†	529 (range, 132–3142)	857 (range, 97–2141)	0.057

Data are expressed as the mean (SD).
* Two-tailed *t*-test
† Median and range; log transformation used for *t*-test.

In an analysis of the outcome parameters of reading acuity and maximum reading speed separately for right and left eyes in the MacTel type 2 group, best fit regression analysis showed temporal LIS to be a good predictor of both reading acuity ($P = 0.0069$) and speed ($P = 0.0209$) in right eyes, whereas BCVA did not interact with either parameter ($P > 0.15$; Table 2). In left eyes, BCVA did predict both reading acuity ($P < 0.0001$) and maximum reading speed ($P < 0.0001$), whereas temporal LIS was found to be only a good predictor of reading speed ($P = 0.0005$). BCEA and central foveal LIS were not found to interact with either outcome parameter.

DISCUSSION

We have shown previously that temporal parafoveal scotomas typically develop in later disease stages of MacTel type 2.[10,11] Efficient reading requires not only sufficient visual acuity to resolve the letters, but also a sufficient extent of central visual field of usually at least 4° to sufficiently process words and perform adequate eye movements.[20] Therefore, parafoveal scotomas in the proximity of an intact central foveal fixation locus may decrease reading acuity and impair reading performance and may account for the highly significant correlation between parafoveal sensitivity loss and reduced reading speed.

BCVA and parafoveal sensitivity appear to be two independent predictors of reading performance. Recently, we reported that in early stages of MacTel type 2, these variables show a moderate correlation, which is not seen with later stages of the disease.[11] BCVA did not significantly impact reading performance (in right eyes), whereas the parafoveal sensitivity strongly predicted reading performance. This result provides further evidence that BCVA and temporal parafoveal sensitivity were independent in the investigated sample.

Separate analysis of the right and left eyes of the patients showed that temporal LIS interacted significantly with reading performance (acuity and speed) in right eyes and only with reading speed in left eyes, which can be explained by the location of the scotoma in the visual field. Deep paracentral scotomas to the left of the visual axis lead to reading out of the scotoma, which severely impairs reading performance (right eyes), as the start of a line has to be searched for when reading from left to right and line progression is severely impaired. Scotomas located to the right of the visual axis allow for a near normal start at the left-hand end of a line and lead to reduced reading speed only by slowing line progression (reduced reading speed in left eyes).[21] Larger samples are needed to confirm this interpretation.

Sunness et al.[22] investigated the relation of parafoveal scotomas and reading performance in geographic atrophy (GA) due to age-related macular degeneration (AMD). They found that the extent of the limitation of the central field as well as foveal function contributed to the maximum reading rate and remaining central VA in patients with GA. Initial scotoma size was found to be a negative prognostic factor for reading performance at 2 years.[22] The group also found that maximum reading rate correlated highly with size of the atrophic area, but not with age or visual acuity within the limited visual acuity

TABLE 2. Two-Factor Regression Models for Reading Acuity and Maximum Reading Speed for Patients with MacTel Type 2

Models	Parameter	Estimate	SE	95% CI Upper	95% CI Lower	*Z*	$P_r > \|Z\|$
Both eyes							
Reading acuity (logRAD)	BCVA (logMAR)	0.51	0.22	0.07	0.94	2.29	0.0218
	Temporal LIS	−0.16	0.08	−0.31	−0.02	−2.18	0.0296
Maximum reading speed	BCVA (logMAR)	−89.81	24.50	−137.84	−41.79	−3.67	0.0002
	Temporal LIS	41.66	10.11	21.85	61.48	4.12	<0.0001
Right eye							
Reading acuity (logRAD)	BCVA (logMAR)	0.35	0.25	−0.13	0.83	1.42	0.1542
	Temporal LIS	0.28	0.10	0.08	0.49	2.70	0.0069
Maximum reading speed	BCVA (logMAR)	−24.38	20.38	−64.32	15.57	−1.20	0.2316
	Temporal LIS	−39.39	17.05	−72.80	−5.97	−2.31	0.0209
Left eye							
Reading acuity (logRAD)	BCVA (logMAR)	0.87	0.21	0.46	1.28	4.18	<0.0001
	Temporal LIS	0.01	0.09	−0.16	0.18	0.10	0.9181
Maximum reading speed	BCVA (logMAR)	−177.11	37.78	−251.16	−103.05	−4.69	<0.0001
	Temporal LIS	−43.86	12.55	−68.45	−19.27	−3.50	0.0005

Regression models analyzed the predictive value of BCVA and temporal LIS for reading performance (reading acuity and speed). Shown are pooled data from both eyes and single eye analyses.

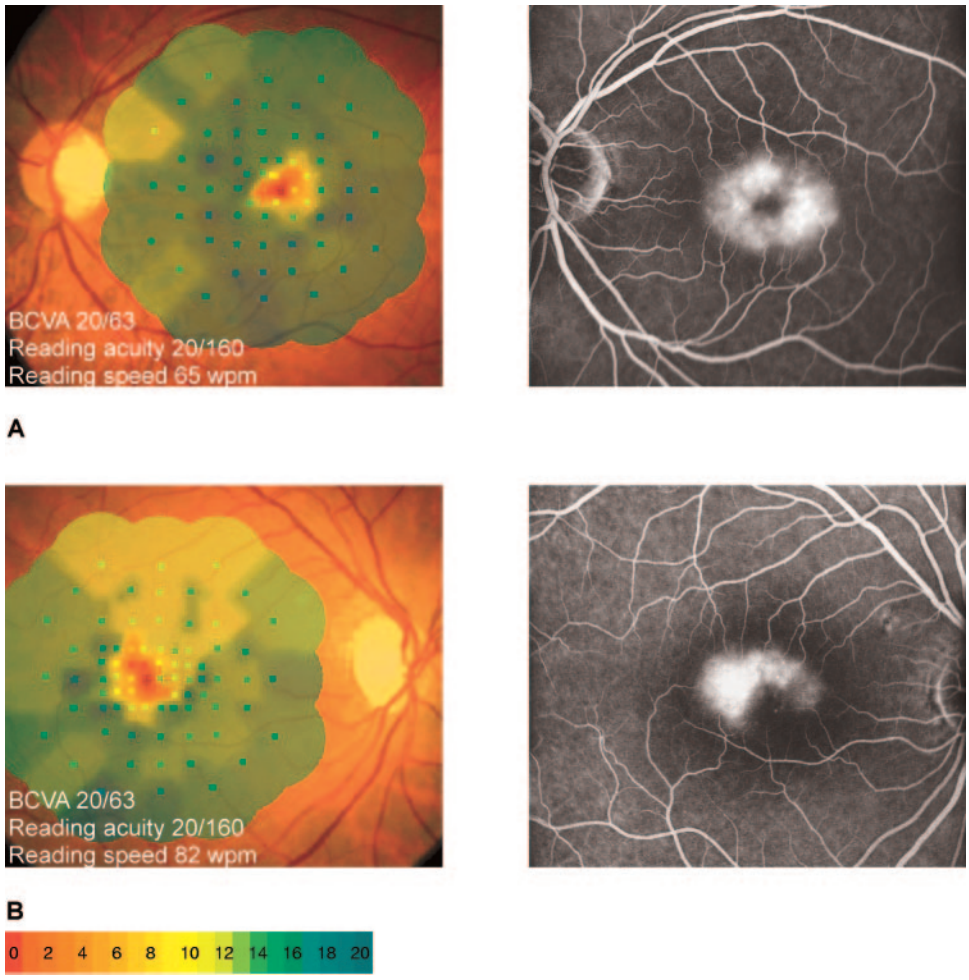

FIGURE 2. Two example cases with relatively good central fixation but poor reading acuity in the presence of a parafoveal scotoma: (**A**) 52-year-old female patient, BCEA 428 minarc^2; (**B**) 58-year-old female patient, BCEA 396 minarc^2. Microperimetric results (*left*) for the central 16° are shown as a false color map, with differential light threshold values superimposed (*colored dots*). The sensitivity range, as shown in the scale, is from 0 to 20 dB. Fluorescein angiography images (*right*) of the same eye at 10 minutes.

range tested,[23] which is in accordance with our findings in MacTel type 2. Sunness et al.[24] further found that eyes fixating with the scotoma to the left tended to have lower reading rates than eyes fixating with right or superior patterns.[24] This finding is mirrored by our observations of lower reading performance (acuity and speed) in right eyes with paracentral scotomas to the left (fixation to the right of the scotoma in relation to the visual axis) compared to left eyes (fixation to the left of the scotoma).

The analysis of the reading process provides important information about perceptual preconditions and cortical adaptive strategies, which are also of significance for rehabilitation.[25] Rehabilitating patients with central scotomas has been shown to be possible by creating a new PRL[26] and was especially successful when the use of eccentric fixation above or below a central scotoma had been trained.[27] As patients with MacTel type 2 typically develop paracentral scotomas that may eventually involve the central macula, rehabilitation, and reading training is difficult.[28] As disease may progress at different speeds in right and left eyes, the better eye could be chosen for rehabilitation once reading becomes difficult bilaterally. Ideally, this would be a left eye, as the PRL could then be moved to a location further nasally from the foveola.

Reading performance is influenced by various factors, including socioeconomic and educational status.[29] In this study, no socioeconomic or educational data were collected, but there was no indication of a specific recruitment bias for these variables in the investigated group of patients and control subjects.

Recent interventional studies examining the effect of intravitreously applied VEGF-inhibitors have shown regression of the parafoveal leakage in fluorescein angiography.[30,31] However, BCVA improved only in a subset of patients. It was furthermore suggested that this treatment approach might also decrease the size of parafoveal scotoma in MacTel type 2.[30–32] Our study further underscores the importance of functional data that do not necessarily reflect morphologic findings. Therefore, functional outcome measures different from BCVA, such as retinal light sensitivity, fixation stability, or reading performance should be included as outcome measures in future therapeutic trials.

Reading performance has been shown to be strongly associated with vision-related quality of life in patients with acquired macular disease,[33] a finding that has been reproduced in other studies mainly focusing on age-related macular degeneration.[34] Many MacTel type 2 patients complain about an impaired reading ability that affects their quality of life. Ultimately, therapeutic interventions in MacTel type 2 should be aimed at maintaining quality of life including the preservation of reading ability.

In summary, our findings indicate that MacTel type 2 is associated with functional impairment of reading in late stage disease despite stable central fixation, suggesting that parafoveal scotomas affect this visual function. Reading acuity and speed are good predictors of reading performance, and thus vision-related quality of life, which appears to be threatened in MacTel type 2.

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