Dark-Adapted Two-Color Fundus-Controlled Perimetry in Macular Telangiectasia Type 2

Tjebo F. C. Heeren, Simone Tzaridis, Roberto Bonelli, Maximilian Pfau, Marcus Fruttiger, Mali Okada, Catherine Egan, Peter Charbel Issa, and Frank G. Holz

1Department of Ophthalmology, University of Bonn, Bonn, Germany
2Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom
3UCL Institute of Ophthalmology, University College London, London, United Kingdom
4The Walter and Eliza Hall Institute of Medical Research, Parkville, Victoria, Australia
5Department of Medical Biology, University of Melbourne, Parkville, Victoria, Australia
6Royal Victorian Eye and Ear Hospital, Melbourne, Victoria, Australia
7Oxford Eye Hospital, Oxford University Hospital NHS Foundation Trust and the Nuffield Laboratory of Ophthalmology, Department of Clinical Neurosciences, University of Oxford, Oxford, United Kingdom

Correspondence: Tjebo F. C. Heeren, Moorfields Eye Hospital NHS Foundation Trust, 162 City Road, London EC1V 2PD, UK; Tjebo.Heeren@moorfields.nhs.uk.

PURPOSE. Macular telangiectasia type 2 (MacTel) is a bilateral neurodegenerative disorder of the central macula. Previous findings indicated more functional impairment in low light conditions. We sought to further characterize retinal dysfunction using dark-adapted two-color fundus-controlled perimetry ("scotopic microperimetry").

METHODS. Participants of the MacTel Natural History Observation Registry study and age-matched healthy controls underwent retinal imaging including dual wavelength autofluorescence macular pigment optical density (MPOD) measurement. Retinal sensitivity was assessed with scotopic microperimetry using cyan (505 nm) and red (627 nm). Disease was graded into classes of MPOD loss (0 to 3). For perimetry analysis, the differences of the mean sensitivities (MacTel minus controls) were compared at each test location and the results were aggregated to global indices.

RESULTS. Thirty-four eyes (19 patients, mean age 62.2 years) were compared with 25 eyes (25 controls, mean age 61.5 years). Both cyan and red sensitivity were lower in MacTel. This was more pronounced at one- and three-degree eccentricity. Eyes with MPOD class 0 did not behave similarly and had impaired cyan and red sensitivity with a relatively higher cyan impairment.

CONCLUSIONS. Rods might be compromised to a greater extent than cones. Linking to previous studies, our results might also hint toward (postreceptoral) dysfunction of the cone system in very early disease stages. Macular pigment loss and global perimetry indices seemed to reflect functional impairment and might be useful as adjunct measures for disease progression.

Keywords: scotopic microperimetry, macular telangiectasia type 2, MacTel, macular pigment optical density, global perimetry index

Macular telangiectasia type 2 (MacTel) is a neurodegenerative disease with secondary typical vascular alterations. Phenotypic characteristics and variations have recently been reviewed and summarized in detail. Functional impairment includes reduced reading performance, metamorphopsia, and a focal paracentral scotoma that enlarges over time. So far, the exact underlying disease mechanism remains unclear.

One aim of the international MacTel Natural History Observation Registry (NHOR) study is to identify earliest structural and functional alterations of the disease, which may shed light on its pathophysiology. In eyes with very early structural disease manifestation, no functional loss was found on visual acuity and mesopic microperimetry testing. In eyes with more advanced disease, areas adjacent to the deep and sharply demarcated scotomata on mesopic microperimetry testing show mild rod dysfunction.

Low light conditions have an overly negative effect on contrast sensitivity and visual acuity in MacTel patients compared with controls. Recently, a two-color dark-adapted fundus-controlled perimetry device was introduced that combines the advantage of fundus-controlled perimetry (so-called microperimetry) with the possibility of retinal sensitivity testing under light- and dark-adapted conditions (so-called scotopic microperimetry). In microperimetry, as opposed to conventional perimetry, stimuli are directly projected onto the retina, which allows creating precise retinal sensitivity maps. There is evidence that the use of two different wavelengths may allow separating cone from rod function. We hypothesized that "scotopic microperimetry" might be able to uncover functional impairment in early disease stages and that dark-adapted cyan sensitivity would be more impaired as sign of more severe rod dysfunction.
Methods

Patients of the MacTel NHOR study were examined in the Department of Ophthalmology, University of Bonn, Germany. The study was conducted in accordance with the Declaration of Helsinki and informed consent was obtained from all participants.

Imaging and Microperimetry

The participants of the study underwent a previously described detailed imaging protocol. The diagnosis of MacTel was based on characteristic patterns on fluorescein angiography, optical coherence tomography, fundus autofluorescence, blue light reflectance, and dual wavelength autofluorescence macular pigment optical density (DWAf MPOD) imaging. Healthy controls were age- and sex-matched. After pupil dilation with phenylephrine 2.5% eye drops and tropicamide 1% eye drops, participants of the study underwent dark-adapted two-color microperimetry. The detailed technical specifications have been described recently. In brief, participants underwent testing under mesopic conditions with white stimuli on white background (the results of which are not presented in this study). Thereafter, they were dark-adapted for 30 minutes before being tested with red (627 nm) and cyan stimuli (505 nm) on a dark background. A perimetry grid with 49 concentrically arranged stimuli was used (Fig. 1).

Microperimetry Results Interpretation

The S-MAIA device is calibrated based on the CIE 1951 scotopic luminosity function or $V(\lambda)$ that shows (in terms of radiance) roughly a 20 dB lower rod threshold for cyan than for red stimuli for healthy observers. This means that the actual radiance of a stimulus at a measured sensitivity value of “0 dB” is approximately 20 dB brighter for red than for cyan stimuli. A healthy retinal area with normal rod and cone function would therefore yield a cyan-red difference of 0 dB for eccentricities $>2^\circ$. The central fovea, including the rod-free zone with a diameter of approximately 1.0 to 1.25 degree, does not contain many rods or S-cones, so the sensitivity for cyan stimuli is very low and can reach absolute scotoma levels even in the healthy retina. Cone and rod sensitivities for long wavelengths (red) are at similar luminance levels in darkness. Thus, an isolated loss of rod function will lead to a relatively stronger loss of cyan sensitivity, yielding negative cyan-red difference scores. If both photoreceptor systems are similarly impaired, the cyan-red difference would become 0 dB again. Table 1 gives an overview of those patterns of sensitivity loss and how we suggest their interpretation.

MPOD Classes

We graded the disease into four different classes of MPOD loss, using a mildly modified version of a previously suggested classification. MPOD class 1 was defined as temporal loss of macular pigment with remaining foveal macular pigment. Additional foveal loss of MPOD defined class 2. Class 3 was defined as MPOD loss in the entire “MacTel area.” Eyes without MPOD loss were defined as stage 0. Those eyes did not show any evidence of MacTel on any of the imaging modalities used in this study and were therefore considered “seemingly unaffected.” It has been shown in an earlier study that those seemingly nonaffected eyes may show functional deficits in

![Figure 1](https://example.com/figure1.png)
low light conditions and show a reduced Stiles-Crawford effect.6,8

Statistical Analysis

All statistical analyses were performed using the R statistical software (R development Core Team, Vienna, Austria). Only eyes with a complete test set with mesopic and dark-adapted microperimetry were used for final analysis. Mixed linear models were used for statistical analysis. Participant category (control versus MacTel) and retinal eccentricity (degree) were used as fixed effects. We included both subject and eye as random intercepts for the model fitting of the sensitivity values. When testing the global indices, only a random intercept for the subject was included. Random term inclusion was tested using likelihood ratio tests. Significance of fixed effect terms were tested using Wald test. A \( P < 0.05 \) was considered as significant.

RESULTS

Thirty-four eyes of 19 patients (mean age 62.2, range 35-76) were compared with 25 eyes of 25 controls (mean age 61.5, range 38-80). Thirty-one eyes presented MPOD and optical coherence tomography pattern typical of MacTel (class 1: 7 eyes, class 2: 9 eyes, class 3: 15 eyes). Three eyes did not show any typical characteristics of MacTel on multimodal imaging (MPOD class 0), but had clinical and imaging features consistent with MacTel in the fellow eye.6

In two-color dark-adapted microperimetry, mean retinal sensitivity for both cyan and red was lower in eyes with MacTel when compared with controls. The effect size was larger for cyan than for red (−4.75 dB versus −2.26 dB) resulting in a negative cyan-red difference (Table 2).

MacTel was associated with a higher reduction of cyan than red sensitivity when compared with controls at each eccentricity, resulting in a negative cyan-red difference at each eccentricity. In MacTel, the largest reduction of both cyan and red sensitivity was found at 1- and 3-degree eccentricity (Table 3). The largest reduction of the cyan-red difference was found at 3 degree, possibly indicating stronger rod than cone impairment in this area. We observed that sensitivity loss seemed more pronounced in the temporal when compared with the nasal retinal sector (Figs. 1, 2).

MPOD class was a relevant predictor of retinal sensitivity (Table 4; Fig. 3). MPOD class 0 was not associated with a change of cyan and red sensitivity. MPOD class 1 was associated with reduced cyan sensitivity, but not with a change in red sensitivity. MPOD classes 2/3 were associated with both reduced cyan and red sensitivity. The effect of MPOD classes 2/3 for cyan was more pronounced than for red sensitivity (higher loss), but MPOD classes 2/3 had a similar effect for each color (Table 4). MacTel patients presented a lower mean deviation (MD) and higher pattern standard deviation (PSD) for both cyan and red. For MD, the effect was more pronounced (more loss) for cyan, but for PSD, the effect was similarly large for both colors (Table 5). In Figure 4, this can be seen as a shift toward lower MD values for cyan: a shift toward the left side of the line of

### Table 2. Effects of MacTel on Retinal Sensitivity for Two Colors in Dark-Adapted Microperimetry

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Cyan Estimates</th>
<th>CI</th>
<th>P</th>
<th>Red Estimates</th>
<th>CI</th>
<th>P</th>
<th>Diff Estimates</th>
<th>CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Intercept)</td>
<td>10.27</td>
<td>9.48 to 11.06</td>
<td>&lt;0.001</td>
<td>11.94</td>
<td>11.01 to 12.87</td>
<td>&lt;0.001</td>
<td>-1.66</td>
<td>-2.56 to -0.77</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MacTel</td>
<td>-4.75</td>
<td>-5.90 to -3.60</td>
<td>&lt;0.001</td>
<td>-2.26</td>
<td>-3.61 to -0.92</td>
<td>0.001</td>
<td>-2.52</td>
<td>-3.78 to -1.26</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The intercept represents the mean sensitivity of the control eyes. The estimates reflect the expected change compared with this intercept when looking at the predictor variables. MacTel was associated with lower cyan and red sensitivity. CI, 95% confidence intervals. \( P \) values below the significance threshold are printed in bold.

### Table 3. Comparing the Sensitivity at Each Retinal Eccentricity, MacTel Versus Control

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Cyan Estimates</th>
<th>CI</th>
<th>P</th>
<th>Red Estimates</th>
<th>CI</th>
<th>P</th>
<th>Cyan-Red Difference Estimates</th>
<th>CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 degree Control (Intercept)</td>
<td>2.08</td>
<td>0.60 to 3.56</td>
<td>0.006</td>
<td>11.96</td>
<td>10.68 to 13.24</td>
<td>&lt;0.001</td>
<td>-9.88</td>
<td>-11.64 to -8.12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MacTel</td>
<td>-2.82</td>
<td>-5.06 to -0.58</td>
<td>0.014</td>
<td>-2.98</td>
<td>-4.70 to -1.26</td>
<td>0.001</td>
<td>0.17</td>
<td>-2.14 to 2.49</td>
<td>0.883</td>
</tr>
<tr>
<td>1 degree Control (Intercept)</td>
<td>5.71</td>
<td>4.96 to 6.45</td>
<td>&lt;0.001</td>
<td>13.66</td>
<td>12.35 to 14.98</td>
<td>&lt;0.001</td>
<td>-7.96</td>
<td>-9.37 to -6.55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MacTel</td>
<td>-5.84</td>
<td>-6.82 to -4.86</td>
<td>&lt;0.001</td>
<td>-4.01</td>
<td>-5.88 to -2.14</td>
<td>&lt;0.001</td>
<td>1.80</td>
<td>-3.79 to 0.18</td>
<td>0.075</td>
</tr>
<tr>
<td>3 degree Control (Intercept)</td>
<td>11.76</td>
<td>10.65 to 12.89</td>
<td>&lt;0.001</td>
<td>12.50</td>
<td>11.53 to 13.47</td>
<td>&lt;0.001</td>
<td>-0.74</td>
<td>-1.86 to 0.38</td>
<td>0.194</td>
</tr>
<tr>
<td>MacTel</td>
<td>-6.45</td>
<td>-8.18 to -4.72</td>
<td>&lt;0.001</td>
<td>-2.78</td>
<td>-4.21 to -1.35</td>
<td>&lt;0.001</td>
<td>-3.67</td>
<td>-5.53 to -2.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5 degree Control (Intercept)</td>
<td>12.25</td>
<td>11.37 to 13.13</td>
<td>&lt;0.001</td>
<td>11.20</td>
<td>10.40 to 12.00</td>
<td>&lt;0.001</td>
<td>1.05</td>
<td>0.34 to 1.76</td>
<td>0.004</td>
</tr>
<tr>
<td>MacTel</td>
<td>-3.61</td>
<td>-4.98 to -2.24</td>
<td>&lt;0.001</td>
<td>-1.54</td>
<td>-2.56 to -0.13</td>
<td>0.031</td>
<td>-2.32</td>
<td>-3.54 to -1.00</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>7 degree Control (Intercept)</td>
<td>12.05</td>
<td>11.23 to 12.87</td>
<td>&lt;0.001</td>
<td>10.38</td>
<td>9.59 to 11.16</td>
<td>&lt;0.001</td>
<td>1.68</td>
<td>1.04 to 2.31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MacTel</td>
<td>-2.30</td>
<td>-3.49 to -1.11</td>
<td>&lt;0.001</td>
<td>-0.87</td>
<td>-2.02 to 0.29</td>
<td>0.141</td>
<td>-1.48</td>
<td>-2.36 to -0.59</td>
<td>0.001</td>
</tr>
</tbody>
</table>

MacTel was associated with lower cyan sensitivity at every location. Red sensitivity was decreased at each location except at 7 degrees. The cyan-red difference was lower at each location; however, this difference did not reach significance at all eccentricities. \( P \) values below the significance threshold are printed in bold.
equality. For PSD, there is a mild bias toward higher values for cyan for both control and MacTel, possibly due to the naturally lower cyan sensitivity in the fovea, as higher PSD values reflect more focal sensitivity losses.

MPOD class seemed relevant for the pattern of MD/PSD change (Table 6). MPOD class 0 was not associated with a change of MD or PSD. MPOD class 1 was associated with a lower MD for cyan color, but not for red color. It was not associated with a change of PSD. MPOD classes 2/3 were associated with lower MD and higher PSD for both colors (Table 6).

Figure 5 shows the cumulative defect curves for all eyes with MacTel (top) and for each MPOD class (bottom). The total of yes showed a global sensitivity reduction in the cumulative defect curve for cyan color, and a more focal loss for red sensitivity. Eyes with MPOD class 0 had normative cumulative defect curves for both cyan and red. Eyes with MPOD class 1 showed a globally reduced cyan sensitivity, but a quasi-normative red sensitivity. Eyes with classes 2 and 3 showed similar curves to one another, with a global deficit for cyan, and a more focal deficit for red color.

**DISCUSSION**

Our results suggest characteristic sensitivity changes for the two tested colors in a dark-adapted state. Sensitivity loss was more pronounced for cyan, and this was strongest at 1- and 3-degree eccentricity from the fovea. This pattern of sensitivity loss is suggestive of more pronounced rod impairment, which could be explained by photoreceptor absence or dysfunction on a cellular level. The lower rod density in the central macula might be one explanation for the latter, maybe due to an increased susceptibility of those rods, or a lack of redundancy. Cones might also partially contribute to cyan responses and using only two wavelengths might not be enough to reliably separate cone from rod function. Moreover, the device used in the study shows both floor and ceiling effect for cyan and red stimuli, challenging the distinction between cone and rod function, especially when reaching brighter cyan levels (i.e., more severe rod dysfunction, or natural absence of rods in the fovea). However, previous studies provided evidence that selective loss of cyan function indeed reflects more pronounced loss of rod-mediated vision. A revised version of the device with an improved dynamic range might be able to quantify severe...
degrees of rod dysfunction more reliably. The results presented here therefore constitute rather conservative estimates for the degree of photoreceptor dysfunction.

Although there remains a degree of uncertainty of which photoreceptor class is actually responding and the device does not fully replace more elaborate psychophysical methods, we uncovered relevant and marked differences between different classes of macular pigment loss, regardless of the responding photoreceptor type. Eyes with preserved macular pigment (MPOD class 0) did not show functional deficits in this study. This finding is interesting and important, because we were previously able to show a marked loss of the Stiles-Crawford effect and an impairment of low luminance contrast sensitivity in those eyes of the same observers. The impaired contrast sensitivity as opposed to the unimpaired microperimetry in those eyes of the same observers. The impaired contrast sensitivity might also be useful from a functional perspective to reduce them to a single category.

The localized retinal dysfunction in MacTel with its temporal predominance represents a peculiar phenomenon. Electrophysiological studies showed normal morphology and retinal function in the retinal periphery of MacTel. Although we are not aware of any MacTel case that extends beyond the so-called “MacTel area,” this remains an observation that warrants systematic analysis. On the other hand, a recent study suggested a disturbance of the RPE-photoreceptor interface extending into the retinal periphery, but the relevance of this finding remains unclear. The MacTel area seems to be anatomically congruent with the area containing Henle’s fibers (unpublished observation from histology studies by one of the coauthors [MF]), which corresponds to the rod-free area before the centripetal photoreceptor migration during embryogenesis. It is conceivable that the photoreceptors in this area might behave differently from “peripheral” photoreceptors, possibly due to differences in metabolism and subsequently higher susceptibility to metabolic dysfunction. Lens opacities might also have influenced the sensitivity for cyan stimuli due to absorption of shorter wavelengths, but one would expect a more global loss of sensitivity and not a focal loss as our results strongly suggested. We therefore decided not to account for cataract as another independent variable lest the linear mixed models contain too many covariates. A limitation of our study was the small numbers of patients with early and earliest disease stages. The results were therefore more of MPOD, and also fit our observation that eyes with MPOD class 0 did not show impaired cyan sensitivity. Figures 3 and 5 show how eyes with MPOD classes 2 and 3 had markedly worse function than eyes with MPOD classes 0 and 1. This correlation suggests that MPOD loss might also be useful as an adjunct parameter for the assessment of disease progression; however, classes 2 and 3 were showing similar results in our study and it might be useful from a functional perspective to reduce them to a single category.

The localized retinal dysfunction in MacTel with its temporal predominance represents a peculiar phenomenon. Electrophysiological studies showed normal morphology and retinal function in the retinal periphery of MacTel. Although we are not aware of any MacTel case that extends beyond the so-called “MacTel area,” this remains an observation that warrants systematic analysis. On the other hand, a recent study suggested a disturbance of the RPE-photoreceptor interface extending into the retinal periphery, but the relevance of this finding remains unclear. The MacTel area seems to be anatomically congruent with the area containing Henle’s fibers (unpublished observation from histology studies by one of the coauthors [MF]), which corresponds to the rod-free area before the centripetal photoreceptor migration during embryogenesis. It is conceivable that the photoreceptors in this area might behave differently from “peripheral” photoreceptors, possibly due to differences in metabolism and subsequently higher susceptibility to metabolic dysfunction. Lens opacities might also have influenced the sensitivity for cyan stimuli due to absorption of shorter wavelengths, but one would expect a more global loss of sensitivity and not a focal loss as our results strongly suggested. We therefore decided not to account for cataract as another independent variable lest the linear mixed models contain too many covariates. A limitation of our study was the small numbers of patients with early and earliest disease stages. The results were therefore more of
### Table 5. Effects of MacTel on MD and PSD in Dark-Adapted Two-Color Microperimetry

<table>
<thead>
<tr>
<th>Predictors</th>
<th>MD Cyan Estimates</th>
<th>CI</th>
<th>P</th>
<th>MD Red Estimates</th>
<th>CI</th>
<th>P</th>
<th>PSD Cyan Estimates</th>
<th>CI</th>
<th>P</th>
<th>PSD Red Estimates</th>
<th>CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Intercept)</td>
<td>0.00</td>
<td>-0.78 to 0.78</td>
<td>1.000</td>
<td>-0.00</td>
<td>-0.85 to 0.85</td>
<td>1.000</td>
<td>2.25</td>
<td>1.90 to 2.60</td>
<td>&lt;0.001</td>
<td>1.68</td>
<td>1.30 to 2.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MacTel</td>
<td>-3.85</td>
<td>-4.99 to -2.70</td>
<td>&lt;0.001</td>
<td>-1.86</td>
<td>-3.08 to -0.63</td>
<td>0.003</td>
<td>1.36</td>
<td>0.86 to 1.86</td>
<td>&lt;0.001</td>
<td>1.38</td>
<td>0.81 to 1.94</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Observations</td>
<td>60</td>
<td>59</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The intercept represents the expected value of the control eyes. The estimates reflect the expected change compared with this intercept when looking at the predictor variables. MacTel is associated with lower MD and higher PSD. MD is more reduced for cyan stimuli. *P* values below the significance threshold are printed in bold.

### Table 6. Effects of MPOD on MD and PSD in Dark-Adapted Two-Color Microperimetry

<table>
<thead>
<tr>
<th>Predictors</th>
<th>MD Cyan Estimates</th>
<th>CI</th>
<th>P</th>
<th>MD Red Estimates</th>
<th>CI</th>
<th>P</th>
<th>PSD Cyan Estimates</th>
<th>CI</th>
<th>P</th>
<th>PSD Red Estimates</th>
<th>CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPOD class 0</td>
<td>-0.94</td>
<td>-2.76 to 0.87</td>
<td>0.309</td>
<td>0.20</td>
<td>-1.88 to 2.28</td>
<td>0.850</td>
<td>-0.13</td>
<td>-1.03 to 0.78</td>
<td>0.786</td>
<td>0.18</td>
<td>-0.74 to 1.11</td>
<td>0.696</td>
</tr>
<tr>
<td>MPOD class 1</td>
<td>-4.74</td>
<td>-6.31 to -3.18</td>
<td>&lt;0.001</td>
<td>-0.51</td>
<td>-2.15 to 1.14</td>
<td>0.545</td>
<td>0.62</td>
<td>-0.05 to 1.28</td>
<td>0.069</td>
<td>0.11</td>
<td>-0.59 to 0.80</td>
<td>0.758</td>
</tr>
<tr>
<td>MPOD class 2</td>
<td>-4.10</td>
<td>-5.45 to -2.75</td>
<td>&lt;0.001</td>
<td>-3.42</td>
<td>-4.84 to -2.00</td>
<td>&lt;0.001</td>
<td>1.56</td>
<td>0.98 to 2.15</td>
<td>&lt;0.001</td>
<td>1.78</td>
<td>1.17 to 2.38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MPOD class 3</td>
<td>-3.98</td>
<td>-5.30 to -2.66</td>
<td>&lt;0.001</td>
<td>-1.89</td>
<td>-3.20 to -0.58</td>
<td>0.005</td>
<td>1.90</td>
<td>1.39 to 2.42</td>
<td>&lt;0.001</td>
<td>1.98</td>
<td>1.44 to 2.52</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Observations</td>
<td>60</td>
<td>59</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The estimates reflect the expected change compared with this intercept when looking at the predictor variables. *P* values below the significance threshold are printed in bold.
observational character and the reliability of statistical inference would therefore remain limited. Future studies including more eyes with early disease are required. Those are likely to be identified because of our increasing knowledge about early stages and potential precursors of the condition.

In summary, we present the first dark-adapted two-color microperimetry study in eyes with MacTel. Our results corroborated evidence that rod function might be compromised earlier and to a greater extent than cone function. The results also point toward an early affection of inner retinal function mainly of the cone system. Categories of macular pigment loss and global perimetry indices might be useful as adjunct measures of functional impairment and thus disease progression. The results are encouraging for further research into retinal function in low light conditions in MacTel, and might help understand the pathophysiology of the disease.

**Acknowledgments**

Supported by the Lowy Medical Research Institute; Melbourne International Research Scholarship and the Victorian State Government Operational Infrastructure Support and Australian Government National Health and Medical Research Council independent research Institute Infrastructure Support Scheme (RB); National Institute of Health Research (NIHR) Biomedical Research Centre (BRC), Oxford, United Kingdom (PCI). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. The funding organizations had no role in the design or conduct of this research. CenterVue SpA, Padova, Italy, has provided the S-MAIA research device used in the conduct of this study. CenterVue had no role in the design, the conduct, nor in the analysis of the experiments.

Disclosures: T.F.C. Heeren, Heidelberg Engineering (F); S. Tzaridis, None; R. Bonelli, None; M. Pfau, None; M. Fruttiger, None; M. Okada, Bayer(R), Allergan(R); C. Egan, None; P. Charbel Issa, None; F.G. Holz, Heidelberg Engineering (C, F, R), Optos (C, F), Zeiss (C, F, R), CenterVue (F).

**References**


