ASSESSMENTS OF MACULAR FUNCTION BY FOCAL MACULAR ELECTRORETINOGRAPHY AND STATIC PERIMETRY IN EYES WITH RETINITIS PIGMENTOSA

SATOSHI OKADO, MD, PhD,* YOSHITO KOYANAGI, MD, PhD,*† TAIGA INOOKA, MD,*
TARO KOMINAMI, MD, PhD,* HIROKO TERASAKI, MD, PhD,* KOJI M. NISHIGUCHI, MD, PhD,*
SHINJI UENO, MD, PhD*

Purpose: To assess the macular function by focal macular electroretinography and static perimetry in eyes with retinitis pigmentosa.

Methods: Eighty-eight eyes of 88 retinitis pigmentosa patients were analyzed. The relationships between the focal macular electroretinography components and the mean deviations (MDs) of the Humphrey Field Analyzer 10-2 were determined. Spectral-domain optical coherence tomography was used to determine the integrity of the ellipsoid zone (EZ) and the interdigitation zone.

Results: Forward-backward stepwise regression analyses showed that the amplitudes (r = 0.45, P < 0.01) and implicit times (r = −0.29, P < 0.01) of the b-waves were significantly correlated with the MDs. Some of the eyes had reduced b-wave amplitudes (<1.0 μV) and disrupted interdigitation zone, despite having a better MD (≥−10.0 dB) and intact EZ. Subgroup analyses of eyes with better MD (≥−10.0 dB) showed that the EZ width was correlated with the MDs but not with the b-wave amplitude. The thickness of the EZ-retinal pigment epithelium as an alternative indicator of interdigitation zone was correlated with the b-wave amplitude (r = 0.32, P = 0.04) but not with the MDs (r = −0.10, P = 0.53).

Conclusion: The fact that the focal macular electroretinography amplitudes are reduced before the shortening of the EZ in the early stage of retinitis pigmentosa indicates that the focal macular electroretinography amplitudes are an earlier indicator of macular dysfunction than the Humphrey Field Analyzer 10-2 findings.

RETINA 42:2184–2193, 2022

Retinitis pigmentosa (RP) is a hereditary retinal disease that affects about one in 4,000 individuals, and it is the most common hereditary retinal disease. Assessments of the visual fields by static perimetry are essential for evaluating the status of the retinal degeneration. We and other groups have conducted longitudinal studies and have found that the mean deviations (MDs) of the Humphrey Field Analyzer (HFA; Carl Zeiss Meditec, Dublin, CA) 10-2 program decrease by 0.46 to 0.70 dB/year in eyes with RP. Based on these rates of progression of the visual field defects, HFA has been used to determine the therapeutic effects of some potential therapies. Because of the recent advancements of optical coherence tomography, the relationships between visual sensitivities and the morphology of the microstructures of the photoreceptors obtained by spectral-domain optical coherence tomography (SD-OCT) have been investigated in eyes with RP. Among the microstructures examined in the OCT images, the width of the ellipsoid zone (EZ)
has received extensive attention in RP studies because it was found to be significantly correlated with the diameter of the residual visual fields.7

Several groups have evaluated the central visual field in eyes with RP by electroretinography (ERG) including multifocal ERGs (mERGs) and focal macular ERGs (FMERGs).8–10 Although static perimetry can evaluate the retinal function subjectively, ERGs can determine the retinal function objectively. Focal macular electroretinograms are elicited by photopic stimulation of only the macular area, and it has been used to evaluate the function of the macula. We have reported that the extent of the amplitude reduction and prolongation of the implicit times of the FMERGs were proportional to the extent of the central visual field impairment.11–14 However, the relationship between the HFA 10-2 and FMERGs has not been analyzed in detail.

Thus, the purpose of this study was to determine the relationship between the MDs of the HFA 10-2 and the components of the FMERGs. We also analyzed the SD-OCT images in some of the cases to determine the relationships between the FMERG components, the MDs, and the integrity of the microstructures of the photoreceptors in more detail.

**Methods**

**Subjects**

We reviewed the medical records of RP patients who were examined in the Nagoya University Hospital from March 2013 to January 2020. We excluded patients whose scotopic b-wave amplitude of the full-field ERGs elicited by a 300-cd-s/m² bright flash (PE-3000; TOMEY, Nagoya, Japan) was >100 μV. Patients who had macular edema or an epiretinal membrane in the SD-OCT images or other retinal complications such as glaucoma were excluded. We identified 124 patients who met the inclusion criteria and had all the FMERG, HFA 10-2 program, and SD-OCT findings recorded. When an interval between the date of recording the FMERGs and that of recording HFA and SD-OCT was more than two years, the data were excluded. The HFA 10-2 data with more than two years, the data were excluded. The HFA 10-2 data with 20% or more of false-positive errors or false-negative errors were also excluded. In patients whose two eyes met the inclusion criteria, the findings in the right eye were used for the statistical analyses. Based on these criteria, 88 eyes of 88 patients with RP were analyzed.

**Humphrey Visual Field Analyzer 10-2**

The procedures of HFA 10-2 were performed with the Swedish Interactive Thresholding Algorithm (SITA) standard test strategy. The mean deviation (MD in dB), false-positive errors (%), and false-negative errors (%) were determined. As the decibel values are on a logarithmic scale, we converted the MD values to 1/Lambert (1/L) linear scale for further analysis using the following equation:

\[
\text{MD (1/L) = 10}^{\frac{\text{MD(dB)}}{10}}.
\]

**Focal Macular Electroretinograms**

The procedures used for recording FMERGs (ER-80; Kowa, Nagoya, Japan) have been described in detail in our earlier study.12 The diameter of the stimulus spot was 15°, and the correspondence between the FMERG stimulus area and the HFA 10-2 measurement area is shown in Figure 1A. For the analyses of the a- and b-waves, the waveforms with frequencies ≤70 Hz were extracted from the raw FMERGs by fast Fourier transform (Figure 1B) as reported in detail in our earlier study.14 For the oscillatory potentials (OPs), the amplitude of each OP after a fast Fourier transform of >70 Hz analysis was used (Figure 1B). When the FMERG amplitude of the different components was less than 0.10 μV, these waves were taken to be noise, and the amplitudes were set to 0.00 μV, and the implicit time was not analyzed (17 eyes for a-wave and 15 eyes for b-wave).

**Measurements of Ellipsoid Zone Width and Ellipsoid Zone–Retinal Pigment Epithelium Thickness in Spectral-Domain Optical Coherence Tomography Images**

We recorded cross-sectional OCT images of 30° diameter of all eyes with the Spectralis SD-OCT instrument (Heidelberg Engineering, Heidelberg, Germany). We evaluated only the horizontal and vertical scans centered on the fovea. To compare the FMERGs and SD-OCT findings, the 15° diameter SD-OCT images centered on the fovea were analyzed.

The width of the EZ (EZ width) and thickness between the EZ and retinal pigment epithelium (EZ–RPE thickness) were measured to evaluate the relationship among FMERG, HFA 10-2, and the SD-OCT findings. These two parameters were measured manually in the SD-OCT images that were within 15 degrees of the fovea using the built-in caliper function in the Spectralis OCT. For the EZ width, the borders of the EZ were set where the EZ band met the upper surface of the RPE (Figure 3). If the EZ width was longer than 15°, the lateral border of the EZ was set as the edge of analyzed area of 15°. Then, we defined the EZ width as the lateral distance between the borders. The EZ–RPE thickness was defined as the distance between the lower edge of
the EZ and the upper edge of the RPE in the fovea (Figure 5). The average of the EZ width and the EZ–RPE thickness in the horizontal and vertical scan images was used for the statistical analyses.

Statistical Analyses

Student’s t-tests were used to determine the significance of the difference between normal subjects and RP patients for each parameter. Linear regression analysis was used to determine the correlations between the FMERG and HFA 10-2 findings. Spearman correlation tests were used to determine the significance of the correlations between the components of the FMERGs, MDs of HFA 10-2, EZ width, and EZ–RPE thickness. Forward–backward stepwise regression analyses were used to determine the independent variables including all FMERG parameters that were significantly correlated with the MD values. A $P < 0.05$ was taken to be statistically significant. All statistical analyses were performed with the Statcel software (Statcel, 4th edition; OMS, Inc, Tokyo, Japan), which is an add-in module for Microsoft Excel.

Results

Clinical Data

The data of the patients and control subjects from a former study of our laboratory are shown in Table 1. The average age of the 88 RP patients (42 men and 46 women) was 46.3 ± 16.7 years (range, 13–75 years), and the mean visual acuity was 0.09 ± 0.16 logarithm of the minimum angle of resolution units (Snellen 20/25). The average age of the 43 normal subjects (23 men and 20 women) was 49.5 ± 16.7 years (range, 11–75 years), and the mean visual acuity was 0.01 ± 0.05 logarithm of the minimum angle of resolution units (Snellen 20/20).

The amplitudes of the a- and b-waves were significantly smaller, and the implicit times of the b-wave were
Table 1. Clinical Data of Eyes With RP and Normal Subjects

| Clinical Data          | RP          | Normal Subjects | P       |
|------------------------|-------------|-----------------|---------|
| No. of patients        | 88          | 43              |         |
| Sex                    |             |                 |         |
| Male                   | 42          | 23              |         |
| Female                 | 46          | 20              |         |
| Age (y), mean ± SD     | 46.3 ± 16.7 | 49.5 ± 16.7     | 0.29    |
| Visual acuity (logMAR), mean ± SD | 0.09 ± 0.16 (Snellen 20/25) | 0.01 ± 0.05 (Snellen 20/20) | <0.01 |
| FMERG parameters       |             |                 |         |
| a-wave                 | 0.43 ± 0.37 | 1.46 ± 0.46     | <0.01  |
| b-wave                 | 1.09 ± 0.79 | 3.25 ± 0.96     | <0.01  |
| OPs                    | 1.09 ± 1.02 | —               |         |
| Implicit times (ms), mean ± SD | 23.77 ± 2.33 | 22.11 ± 0.98 | 0.06   |
| a-wave                 |             |                 |         |
| b-wave                 | 46.65 ± 3.19 | 42.95 ± 1.85 | <0.01  |
| HFA 10-2 parameters    |             |                 |         |
| Mean deviation (dB), mean ± SD | -6.35 ± 5.72    | 1.17 ± 1.94   |         |
| Mean false-positive errors (%), mean ± SD | 2.99 ± 4.28 |                 |         |

Student’s t-test was used for statistical analysis.

logMAR, logarithm of the minimum angle of resolution.

significantly longer in the RP eyes than that of the normal eyes recorded under the same conditions. More specifically, the mean a-wave amplitude was 0.43 ± 0.37 μV (range, 0.00–1.69 μV) in the RP patients and 1.46 ± 0.46 μV (range, 0.51–2.71 μV) in the controls (P < 0.01). The mean b-wave amplitude was 1.09 ± 0.79 μV (range, 0.00–3.30 μV) in the RP patients and 3.25 ± 0.96 μV (range, 1.36–5.66 μV) in the controls (P < 0.01). The mean implicit time of the a-wave was 23.77 ± 2.33 milliseconds (range, 19.6–32.9 ms) in the RP patients and 22.11 ± 0.98 milliseconds (range, 19.9–24.3 ms) in the controls (P = 0.06), and the mean implicit time for the b-wave was 46.65 ± 3.19 milliseconds (range, 40.3–56.6 ms) in the RP patients and 42.95 ± 1.85 milliseconds (range, 39.4–46.7 ms) in the controls (P < 0.01). The mean amplitude of OPs in the RP patients was 1.09 ± 1.02 μV (range, 0.00–3.57 μV).

The mean of the MDs for the HFA 10-2 measurements was -6.35 ± 5.72 dB (0.23 ± 0.27 [1/L]) with a range of -32.16 dB (0.00 [1/L]) to +0.20 dB (1.05 [1/L]) in the RP patients.

Determination of Significance of Correlations Between Focal Macular Electroretinography Components and Mean Deviations of Humphrey Field Analyzer 10-2

We examined whether the correlations between the amplitudes and implicit times of the a- and b-waves and OPs of the FMERGs and the MDs (1/L) of the HFA 1-2 were significant (Figure 2). The MD values were significantly correlated with the amplitudes of the a-waves (r = 0.65, P < 0.01), the b-waves (r = 0.70, P < 0.01), the OPs (r = 0.61, P < 0.01), and the implicit times of the b-waves (r = -0.47, P < 0.01) of the FMERGs. However, the MD values were not significantly correlated with the implicit times of the a-waves (r = 0.18, P = 0.09).

Forward–backward stepwise regression analysis was performed to analyze which FMERG components were significantly correlated with the MD values (Table 2). The results indicated that the b-wave amplitudes (r = 0.45, P < 0.01) and the implicit times (r = -0.29, P < 0.01) were significantly correlated with the MD values.

Subgroup Analysis of Patients with Well-Preserved b-Wave Amplitudes

Analyses of the amplitudes of ERGs have been helpful in determining the status of the residual retinal function in RP patients.14,15 Although both the b-wave amplitudes and implicit times were significantly correlated with the MD in the stepwise regression analysis, we focused on the b-wave amplitudes in this subgroup analysis. Our results showed that none of the patients with preserved b-wave amplitudes of >2.0 μV had reduced MD values of < -20 dB (0.01 [1/L]), but there were 8 patients (9.1%) who had preserved MD values of > -10 dB (0.1 [1/L]),...
despite having reduced b-wave amplitudes of <1.0 μV. This indicated that some patients had relatively good retinal function determined subjectively but impaired visual functions determined objectively.

To determine the cause for this discrepancy, we evaluated the structure of the photoreceptors in the SD-OCT images of eyes with relatively well-preserved MDs. The OCT findings of two representative eyes (Figure 3, A and B) with preserved b-waves (>1.5 μV) and two representative eyes (Figure 3, C and D) with reduced b-waves (<0.5 μV) are shown in Figure 3. The MD values of these four cases ranged from −9.20 dB to −5.72 dB (0.12–0.27 [1/L]). Comparisons of these cases showed that the EZ width was present in almost the entire 15° diameter in each case; however, the interdigitation zone (IZ, red arrows in Figure 3, A and B) was detected only in the eyes with a preserved b-wave. These findings suggested that the visual fields were
maintained in eyes with preserved EZ, despite the absence of the IZ, whereas the amplitude of the b-waves was not dependent on the extent of the EZ width but probably on the integrity of the IZ in these eyes. Therefore, we examined whether there were significant correlations between the EZ width and the MDs of HFA10-2 and between the EZ width and the amplitude of the b-waves of the FMERGs. We analyzed the EZ width of 43 eyes with relatively well-preserved MDs of \( > -10 \text{ dB (0.1 [1/L])} \) as the cutoff value because it was approximately the median of the MD values. Our results showed that the MD values were strongly correlated with the EZ width \( (r = 0.69, P < 0.01; \text{Figure 4A}) \), but the amplitudes of the b-waves were not significantly correlated with the EZ width \( (r = 0.22, P = 0.16; \text{Figure 4B}) \). However, the EZ width was significantly correlated with both the MDs and the b-wave amplitudes in all 88 eyes (Figure 4, C and D). For the EZ, the density of the IZ was too low to evaluate its width in these 43 eyes, which made it difficult to evaluate the EZ width accurately. Therefore, we measured the EZ–RPE thickness in the fovea as an alternative indicator and evaluated its correlation between the amplitude of the b-waves and the MD values (Figure 5). The results showed that the EZ–RPE thickness was significantly correlated with the b-wave amplitudes \( (r = 0.32, P = 0.04) \) but not with the MD values \( (r = -0.10, P = 0.53) \).

### Table 2. Results of Forward–Backward Stepwise Regression Analysis for Independence of Factors Significantly Correlated With the HFA 10-2 MD Values

| Variable                  | Standardized Partial Regression Coefficient |
|---------------------------|---------------------------------------------|
| MD values (1/L)           | 0.05                                        |
| a-wave amplitudes         | 0.45*                                       |
| b-wave amplitudes         | 0.07                                        |
| OP amplitudes             | 0.03                                        |
| a-wave implicit times     | -0.29*                                      |
| b-wave implicit times     |                                             |

\* \( p < 0.01 \).

![Fig. 3. Four representative eyes with retinitis pigmentosa (RP) that had HFA 10-2 MD values better than \(-10.0 \text{ dB (0.1 [1/L])}\). The SD-OCT images, gray scale of HFA 10-2, and FMERGs are shown. Magnified images of the yellow dashed rectangles in the upper SD-OCT images are shown below. The amplitudes of the FMERG b-waves are larger than 1.30 \( \mu \text{V} \) in (A) and (B) (1.97 \( \mu \text{V} \) and 1.83 \( \mu \text{V}, \text{respectively} \), and those with reduced b-waves less than 0.50 \( \mu \text{V} \) are shown in (C) and (D) (0.41 \( \mu \text{V} \) and 0.43 \( \mu \text{V}, \text{respectively} \)). The implicit times of FMERG b-wave of these four cases are 43.9 milliseconds, 46.2 milliseconds, 56.6 milliseconds, and 49.9 milliseconds respectively. Although the ellipsoid zone (EZ, white two-direction arrows) was identified in almost the entire 15° diameter in each case (range of EZ width, 3.08–4.20 mm), the interdigitation zone (red arrows) was clearly detected only in the eyes in (A) and (B).]
Discussion

Our results showed that the amplitudes of the different components of the FMERGs were reduced and the b-wave implicit times were prolonged in the RP patients as reported.\textsuperscript{14,16} Because the FMERGs and HFA 10-2 have been successfully used to evaluate the progression of the RP, correlations between most of the FMERG components and the MD values of HFA 10-2 were expected.

In an earlier study using mfERGs to evaluate 8 RP patients, Hood et al\textsuperscript{8} reported that the reduction in the amplitudes of the mfERGs was not significantly correlated with a decrease in visual field sensitivity. However, if the implicit times of the mfERGs were normal, then the visual field sensitivities would also be expected to be normal. However, if the implicit times were prolonged, the visual field sensitivities would also be expected to be reduced. In our stepwise regression analysis, both the b-wave amplitudes and implicit times were significantly correlated with the MD, and it is possible that the increase in the number of patients in our study may explain the differences from the earlier study.

Examinations of the eyes that had an inconsistency between the FMERG amplitudes and the visual sensitivities showed that the preserved amplitudes of the FMERGs were accompanied by a preservation of the visual fields in general, but preserved visual fields were not always accompanied by preserved amplitudes of the FMERGs.

The photoreceptor is composed of an inner segment and an outer segment. The inner segment is mainly responsible for the cell metabolism and protein production, whereas the outer segments are highly specialized cilia made up of stacks of discs containing opsins, the photosensitive transmembrane proteins. The amplitudes of the FMERGs are highly dependent on the integrity of the cone outer segments that give rise to the electrical potentials. The results of two of our earlier studies showed that a reduction in the amplitudes of FMERGs is accompanied by disruptions of the IZ rather than the EZ in diseased retinas, for

---

**Fig. 4.** Relationships between EZ width and visual functions. In eyes with preserved HFA 10-2 MD values ($\geq -10.0 \, \text{dB (0.1 [1/L]); n = 43}$), the EZ width was significantly correlated with the MDs (1/L) of HFA 10-2 (A) but not with the b-wave amplitudes of the FMERG (B) (Spearman correlation test). However, the EZ width is significantly correlated with both the HFA 10-2 MD values (C) and b-wave amplitudes (D) of the FMERGs for all 88 eyes (Spearman correlation test).
example, in RP and after retinal reattachment in eyes with fovea off rhegmatogenous retinal detachment. However, the visual field diameter was found to be significantly correlated with the EZ width in several earlier studies, which indicated that the EZ width was related to the visual sensitivity.

We have reported that the length of the inner segment/outer segment (IS/OS) line in the time-domain OCT images was weakly but significantly correlated with the amplitude of the FMERGs, and a preserved macular morphology did not necessarily indicate normal FMERG amplitudes in eyes with RP. We have also reported that some RP patients had a severe reduction of the FMERG amplitudes, although the EZ was relatively well-preserved. We called such EZs as “dysfunctional EZs” and demonstrated that eyes with “dysfunctional EZs” tended not to have a visible IZ. In the current study, we found several eyes that had preserved visual sensitivities (MD $>-10$ dB) with reduced b-wave amplitudes (<1.0 $\mu$V). Optical coherence tomography analysis showed some of these eyes had a “dysfunctional EZ” as shown in Figure 3, C and D. The existence of eyes with a relatively well-preserved visual sensitivity despite a “dysfunctional EZ” suggests that eyes with “dysfunctional EZ” can still have good visual function determined subjectively. These findings agree with the results that there was a significant correlation between the EZ width and the value of the MDs, but not with the b-wave amplitude of the FMERGs.

The EZ is part of the inner segments of the cones, and the IZ is part of the cone outer segments. An earlier study showed that the photoreceptor outer segments were lost in the earliest stage of RP followed by a loss of the inner segments and finally a loss of the photoreceptor nuclei. In addition, several recent studies showed that the cone density in the images recorded by adaptive optics scanning laser ophthalmoscopy in RP patients ranged from normal to

Fig. 5. The analysis of the thickness between ellipsoid zone and retinal pigment epithelium (EZ–RPE thickness) in eyes with preserved HFA 10-2 MD values ($\leq -10.0$ dB (0.1 [1/L]); $n = 43$). The EZ–RPE thickness was defined as the distance between the lower edge of the EZ and the upper edge of the RPE in the fovea (red two-direction arrow) (A). The EZ–RPE thickness was significantly correlated with the b-waves of FMERG (B). However, the EZ–RPE thickness was not correlated with the MDs (1/L) of HFA 10-2 (C) (Spearman correlation test).
severely reduced, despite the presence of intact EZ in the OCT images.\textsuperscript{22} Thus, a “dysfunctional EZ” probably indicates a loss of the cone outer segments before disturbances of the cone inner segments in the earliest stage of retinal degeneration. Although it was difficult to measure the IZ width in this study, the fact that the EZ–RPE thickness, as an alternative indicator of IZ, was correlated with the b-wave amplitude of FMERG but not with the MD values of HFA 10-2 supports this. Therefore, our results suggest that in the early stage of RP, there are alterations of the visual functions determined objectively before that determined subjectively.

A similar discrepancy of the visual function tests was reported for the relationship between the foveal structural and psychophysical measurements. Recent studies have used adaptive optics scanning laser ophthalmoscopy to measure the cone density near the fovea in eyes with retinal degeneration, and the findings demonstrated that the cone density was reduced by up to 50% to 62% below the normal density at or near the fovea, although the retinal sensitivity remained within the normal limits.\textsuperscript{23,24}

There are several limitations in this study. First, we did not determine the genotype–phenotype correlations because the number of patients who were identified by the causative gene was too few to obtain meaningful evaluations of their correlations. It is known that the great heterogeneity of macular involvement among RP patients can be related to the large number of causative genes, which alters different underlying biochemical pathways.\textsuperscript{2,25,26} In certain RP subtypes, the macular degeneration occurs relatively early in the course of the disease process.\textsuperscript{27} This is especially true in eyes with ciliopathy, which is caused by dysfunction of the proteins involved in the biogenesis, function, or maintenance of the photoreceptor primary cilium.\textsuperscript{28} In this type, the EZ in the macular area might not be detected evenly, which is different from a shortening of the EZ width.\textsuperscript{29} Future studies on the differences of macular function because of a specific causative gene are needed.

A second limitation was the mismatch between the area of the FMERG stimuli and the HFA 10-2 measurement points. The analyzed points of HFA 10-2 were wider than the stimulus size of the FMERGs, which may have affected the results. However, an exact method for determining MD values of HFA has not been published. Therefore, the MD values of the HFA 10-2 were used directly because it was not possible to recalculate the MD values at the FMERG measurement points.

Third, the dates on which FMERG, HFA 10-2, and SD-OCT were recorded were different. Using the date of FMERG recordings as a reference, the difference from the date of HFA measurements was $-31.47 \pm 263.6$ days, and the difference from the date of SD-OCT recording was $-1.63 \pm 299.6$ days, with no significant bias among them. From previous studies, the progression of MD values for HFA 10-2 in RP is 0.46 to 0.70 dB/year and 0.92 to 1.40 dB/2 years.\textsuperscript{2,3}

Given that the mean MD values for the present case was $-6.35 \pm 5.72$ dB, the period setting of HFA 10-2 recording date within 2 years before and after the FMERG recording date is considered acceptable. The EZ width in the present case was 3214 $\mu$m ± 1,163 $\mu$m, and EZ width has been reported to decrease by $-151$ $\mu$m/year in eyes with RP.\textsuperscript{30} Therefore, the period setting of SD-OCT recording date within 2 years before and after the FMERG recording date was also considered acceptable.

In conclusion, we found that the macular function determined by static perimetry was significantly correlated to that found by FMERGs in eyes with RP. However, the visual sensitivities are not altered in the earliest stages of RP, despite a reduction of the amplitudes of the FMERGs. The FMERGs are a helpful method to evaluate the macular function objectively, but its usage is limited. To determine the macular function in RP eyes more accurately, evaluations by static perimetry and evaluations of the EZ in the SD-OCT images would be helpful.

**Key words:** focal macular electroretinography, optical coherence tomography, retinitis pigmentosa, static perimetry.

**References**

1. Hartong DT, Berson EL, Dryja TP. Retinitis pigmentosa. Lancet 2006;368:1795–1809.
2. Sayo A, Ueno S, Kominami T, et al. Longitudinal study of visual field changes determined by Humphrey Field Analyzer 10-2 in patients with Retinitis Pigmentosa. Sci Rep 2017;7:16383.
3. Ogino K, Otani A, Oishi A, et al. Concentric division of 10° visual field tests in retinitis pigmentosa. Jpn J Ophthalmol 2013;57:268–274.
4. Birch DG, Bernstein PS, Iannacone A, et al. Effect of oral valproic acid vs placebo for vision loss in patients with autosomal dominant retinitis pigmentosa: a randomized phase 2 multicenter placebo-controlled clinical trial. JAMA Ophthalmol 2018;136:849–856.
5. Akiyama M, Ikeda Y, Yoshida N, et al. Therapeutic efficacy of topical unoprostone isopropyl in retinitis pigmentosa. Acta Ophthalmol 2014;92:e229–e234.
6. Hara A, Nakazawa M, Saito M, Suzuki Y. The qualitative assessment of optical coherence tomography and the central retinal sensitivity in patients with retinitis pigmentosa. PLoS One 2020;15:e0232700.
7. Hood DC, Ramachandran R, Holopigian K, et al. Method for deriving visual field boundaries from OCT scans of patients.
with retinitis pigmentosa. Biomed Opt Express 2011;2:1106–1114.
8. Hood DC, Holopigian K, Greenstein V, et al. Assessment of local retinal function in patients with retinitis pigmentosa using the multi-focal ERG technique. Vis Res 1998;38:163–179.
9. Sandberg MA, Jacobson SG, Berson EL. Foveal cone electroretinograms in retinitis pigmentosa and juvenile macular degeneration. Am J Ophthalmol 1979;88:702–707.
10. Falsini B, Galli-Resta L, Fadda A, et al. Long-term decline of central cone function in retinitis pigmentosa evaluated by focal electroretinogram. Invest Ophthalmol Vis Sci 2012;53:7701–7709.
11. Hibi N, Ueno S, Ito Y, et al. Relationship between retinal layer thickness and focal macular electroretinogram components after epiretinal membrane surgery. Invest Ophthalmol Vis Sci 2013;54:7207–7214.
12. Kominami A, Ueno S, Kominami T, et al. Restoration of cone interdigitation zone associated with improvement of focal macular ERG after fovea-off rhegmatogenous retinal reattachment. Invest Ophthalmol Vis Sci 2016;57:1604–1611.
13. Terasaki H, Kojima T, Niwa H, et al. Changes in focal macular electroretinograms and foveal thickness after vitrectomy for diabetic macular edema. Invest Ophthalmol Vis Sci 2003;44:4465–4472.
14. Kominami T, Ueno S, Kominami A, et al. Associations between outer retinal structures and focal macular electroretinograms in patients with retinitis pigmentosa. Invest Ophthalmol Vis Sci 2017;58:5122–5128.
15. Oishi A, Nakamura H, Tatsumi I, et al. Optical coherence tomographic pattern and focal electroretinogram in patients with retinitis pigmentosa. Eye (Lond) 2009;23:299–303.
16. Sugita T, Kondo M, Piao C-H, et al. Correlation between macular volume and focal macular electroretinogram in patients with retinitis pigmentosa. Invest Ophthalmol Vis Sci 2008;49:3551–3558.
17. Birch DG, Locke KG, Wen Y, et al. Spectral-domain optical coherence tomography measures of outer segment progression in patients with X-linked retinitis pigmentosa. JAMA Ophthalmol 2013;131:1143–1150.
18. Iftekhar M, Usmani B, Sanyal A, et al. Progression of retinitis pigmentosa on multimodal imaging: the PREP-1 study. Clin Exp Ophthalmol 2019;47:605–613.
19. Staurenghi G, Sadda S, Chakravarthy U, Spaide RF; International Nomenclature for Optical Coherence Tomography IN OCT Panel. Proposed lexicon for anatomic landmarks in normal posterior segment spectral-domain optical coherence tomography: the IN OCT consensus. Ophthalmology 2014;121:1572–1578.
20. Hood DC, Lazow MA, Locke KG, et al. The transition zone between healthy and diseased retina in patients with retinitis pigmentosa. Invest Ophthalmol Vis Sci 2011;52:101–108.
21. Milam AH, Li ZY, Fariss RN. Histopathology of the human retina in retinitis pigmentosa. Prog Retin Eye Res 1998;17:175–205.
22. Kubota D, Matsumoto K, Hayashi M, et al. High-resolution photoreceptor imaging analysis of patients with autosomal dominant retinitis pigmentosa (adRP) caused by HK1 mutation. Ophthalmic Genet 2020;41:629–638.
23. Ratnam K, Carroll J, Porco TC, et al. Relationship between foveal cone structure and clinical measures of visual function in patients with inherited retinal degenerations. Invest Ophthalmol Vis Sci 2013;54:5836–5847.
24. Foote KG, Loumou P, Griffin S, et al. Relationship between foveal cone structure and visual acuity measured with adaptive optics scanning laser ophthalmoscopy in retinal degeneration. Invest Ophthalmol Vis Sci 2018;59:3385–3393.
25. Cai CX, Locke KG, Ramachandran R, et al. A comparison of progressive loss of the ellipsoid zone (EZ) band in autosomal dominant and x-linked retinitis pigmentosa. Invest Ophthalmol Vis Sci 2014;55:7417–7422.
26. Sun X, Park JH, Gumerson J, et al. Loss of RPGR glutamyltransferase underlies the pathogenic mechanism of retinal dystrophy caused by TTLL5 mutations. Proc Natl Acad Sci U S A 2016;113:E2925–E2934.
27. Ueno S, Koyanagi Y, Kominami T, et al. Clinical characteristics and high resolution retinal imaging of retinitis pigmentosa caused by RP1 gene variants. Jpn J Ophthalmol 2020;64:485–496.
28. Besharse JC, Baker SA, Luby-Phelps K, Pazour GJ. Photoreceptor intersegmental transport and retinal degeneration: a conserved pathway common to motile and sensory cilia. Adv Exp Med Biol 2003;533:157–164.
29. Takahashi VKL, Xu CL, Takiuti JT, et al. Comparison of structural progression between ciliopathy and non-ciliopathy associated with autosomal recessive retinitis pigmentosa. Orphanet J Rare Dis 2019;14:187.
30. Iftekhar M, Usmani B, Sanyal A, et al. Progression of retinitis pigmentosa on multimodal imaging: the PREP-1 study. Clin Exp Ophthalmol 2019;47:605–613.