

# Focal Macular Electroretinogram in Macular Edema Secondary to Central Retinal Vein Occlusion

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**PURPOSE.** To evaluate the usefulness of focal macular electroretinography (fmERG) for evaluation of macular function in eyes with central retinal vein occlusion (CRVO).

**METHODS.** fmERG recordings were made prospectively in 24 patients with unilateral CRVO. The amplitudes and latencies of the a-wave, b-wave, and photopic negative response (PhNR) were compared with other biological parameters, including visual acuity (VA), retinal sensitivity measured with a microperimeter, and optical coherence tomography.

**RESULTS.** In eyes affected by CRVO, amplitudes of the a-wave, b-wave, and PhNR were reduced significantly, and latencies were prolonged significantly compared with those of healthy fellow eyes ( $P < 0.001$ ). Relative amplitudes (affected eye/fellow eye) of each wave showed a cross correlation with VA. Furthermore, both relative amplitudes and latencies of each wave tended to correlate with retinal sensitivity within the macular area. Central foveal thickness showed a correlation with both relative amplitude and relative latency. Among all parameters, relative amplitude of the PhNR correlated most strongly with central foveal thickness ( $r = -0.598$ ,  $P = 0.0042$ ). In addition, sensory retinal thickness showed a correlation with relative latencies, and height of the retinal detachment (when present) showed a correlation with relative amplitudes. In ischemic CRVO, relative amplitudes were reduced more severely than were those in nonischemic CRVO.

**CONCLUSIONS.** In eyes with CRVO, amplitudes and latencies of the fmERG correlated with other biological parameters. Based on the present study, fmERG appears to be useful for the examination of the macular edema that accompanies CRVO. (*Invest Ophthalmol Vis Sci.* 2011;52:3514–3520) DOI:10.1167/jovs.10-7142

Macular edema (ME) is one of the most vision-threatening complications associated with central retinal vein occlusion (CRVO).<sup>1,2</sup> Generally, the severity of the ME has been evaluated by using optical coherence tomography (OCT) for the quantitative measurement of foveal thickness. In addition, recent advances in the technology of OCT have revealed the pathomorphology of ME that is associated with CRVO, including the location of each cystoid space, the frequent presence of a serous retinal detachment, and the usefulness of the junction between the inner and outer segments of the foveal photore-

ceptor layer as a hallmark of the integrity of the outer retina.<sup>3–6</sup> As a functional parameter in eyes with ME associated with CRVO, we typically use visual acuity (VA), which primarily reflects foveal function. However, ME usually involves the larger macular area. To evaluate the severity of ME and its response to treatment, it is essential to establish another functional examination that reflects not only the fovea but also the larger macular area.<sup>7</sup>

Electroretinography (ERG) is used widely to evaluate the function of the retina. In eyes with CRVO, many reports have shown that full-field (ff)ERG is useful in predicting the development of neovascular glaucoma.<sup>8–14</sup> Recently, Chen et al.<sup>15</sup> reported that the amplitude of the photopic negative response (PhNR), which is a negative wave that follows the b-wave, was markedly more reduced than were other components in eyes with retinal vein occlusion. Because PhNR in the photopic ERG is reported to reflect inner retinal function,<sup>16–19</sup> PhNR may be an ideal parameter with which to evaluate retinal function in eyes affected with CRVO, in which the inner retina is the portion of the retina that is most affected.<sup>17–19</sup>

In contrast to the ffERG, the focal macular (fm)ERG allows examination of the retinal function only within the macular area. In eyes with diabetic macular edema, Terasaki et al.<sup>20</sup> demonstrated a correlation between the functional changes detected by fmERG and foveal thickness. So far, however, little is known about macular function examined by fmERG in eyes with CRVO. We hypothesized that fmERG would enable us to evaluate more effectively the macular function in eyes with ME secondary to CRVO. In the study described herein, we examined the correlation of fmERG with other biological parameters in eyes with ME secondary to CRVO, to evaluate the usefulness of fmERG, especially PhNR and better define macular function in these eyes.

## PATIENTS AND METHODS

This prospective study consisted of 24 patients with ME secondary to untreated unilateral CRVO who were examined at Kyoto University Hospital between May 2009 and August 2010. Patients with co-existing ocular disease (i.e., epiretinal membrane, glaucoma, proliferative diabetic retinopathy, or senile cataract) that resulted in poor quality OCT images and fmERG in either eye were excluded from the present study. Eyes with hemi-CRVO were also excluded from the present study. The diagnosis of CRVO was based on the fundus examination and fluorescein angiography findings of two retina specialists (AT, TM). At the initial visit, after the medical history was obtained, each patient had a complete examination, including best corrected VA measurement, slit lamp biomicroscopy, indirect fundus ophthalmoscopy, fluorescein angiography, OCT, microperimetry, and fmERG.

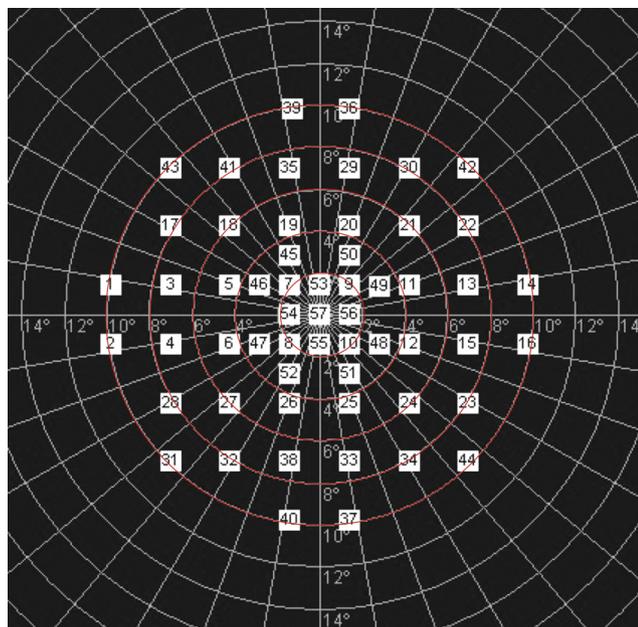
Best corrected VA was measured with a Landolt chart and was converted to logarithm of the minimum angle of resolution (logMAR). Fluorescein angiography was performed on each patient with a confocal laser scanning system (HRA-2; Heidelberg Engineering, Heidelberg, Germany). Eyes with CRVO were judged to be ischemic when

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**FIGURE 1.** A total of 57 locations covering the central 10° were examined with microperimetry. Five measurement points were located within the central 2° of the macula, 17 were located within the central 4°, 29 were located within the central 6°, and 37 points were located within the central 8°.

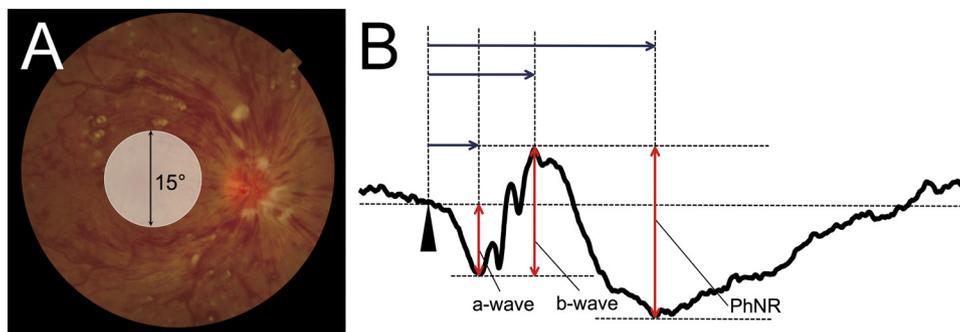
initial fluorescein angiography revealed more than 10 disc areas of nonperfusion. All patients were examined by spectral domain-optical coherence tomography (Spectralis OCT; Heidelberg Engineering). Using these images obtained at the initial visit, we performed three measurements in the fovea, including the center point thickness (CPT), height of the retinal detachment (HRD), and sensory retinal thickness (SRT). CPT was defined as the distance between the internal limiting membrane and the retinal pigment epithelium (RPE) at the center of the fovea; HRD was defined as the distance between the RPE and the bottom of the detached neurosensory retina just beneath the fovea. SRT was calculated by subtracting the HRD from the CPT.

In 17 eyes with CRVO, fundus-monitored microperimetry was performed (MP1; Nidek, Gamagori, Japan). The software for this system contains an automatic tracking system for fundus movements that evaluates every acquired frame for shifts in the *x*- and *y*-directions of the fundus with respect to a reference frame obtained by an infrared camera at the start of the examination. A 4-2-staircase strategy with Goldmann III size stimulus was used, and 57 stimulus locations that covered the central 10° were examined by microperimetry. Each

stimulus is located according to the measurement points used in Humphrey 10-2, with some additional points. The white background illumination was set at 1.27 cd/m<sup>2</sup>. The differential luminance, defined as the difference between stimulus luminance and background luminance, was 127 cd/m<sup>2</sup> at 0 dB stimulation, and the maximum stimulus attenuation was 20 dB. The duration of the stimulus was 200 ms, and the fixation target varied in size (a 2° cross for central fixation and a 4° or 6° cross for paracentral fixation) according to the VA of the patient. The 5, 17, 29, 37, and 57 measurement points were assigned within the central 2°, 4°, 6°, 8°, and 10° areas (Fig. 1).

For fmERG recording, the pupils of both eyes were dilated with 0.5% tropicamide and 0.5% phenylephrine hydrochloride. After the pupils were maximally dilated, a Burian-Allen bipolar contact lens electrode (Hansen Ophthalmic Laboratories, Iowa City, IA) was placed in the conjunctival sac while the eye was under topical anesthesia induced by 0.4% oxybuprocaine. A chloride silver electrode was attached to the left earlobe as a ground electrode. The fmERG was elicited by 15° circular stimuli positioned on the fovea (Fig. 2). The fmERG system used in this study was the prototype of the ER-80 (Kowa, Tokyo, Japan). It was composed of an infrared camera (Kowa) and a stimulation system (Mayo Co., Nagoya, Japan). The luminances of white stimulus light and background illumination were 181.5 and 6.9 cd/m<sup>2</sup>, respectively. A background field of 45° visual angle was projected to the eye from the fundus camera. The fmERG was recorded with 2-Hz rectangular stimuli (150 ms with the light on and 350 ms with the light off). The 15° circular stimulus was carefully and constantly centered on the fovea, as observed through the infrared camera. The affected eyes were examined before the fellow eyes. The recording (100–150 responses) was made twice to confirm reproducibility, and a total of 200 to 300 responses were averaged by the signal processor (Neuropack MEB-2204; Nihon Kohden, Tokyo, Japan). The fmERG response was digitized at 10 kHz with a band-pass filter of 5 to 500 Hz for the a-wave, b-wave, and photopic negative response, and at 50 to 500 Hz for oscillatory potentials (OPs). The amplitudes of the a-wave, b-wave, and PhNR were measured, respectively, from the baseline to the peak of the a-wave, from the trough of the a-wave to the peak of the b-wave, and from the peak of the b-wave to the trough of the PhNR (Fig. 2). Latencies were defined as the time from the beginning of the stimuli to the peak of each component.

The amplitudes and latencies of the a-wave, b-wave, and PhNR were compared between the affected eye and the fellow eye with a paired *t*-test. To compare the fmERG parameters with other measurement values, we converted to the relative amplitude and latency (affected eye/fellow eye) and calculated the Pearson correlation coefficient. Because PhNR is a slow wave and does not have a sharp peak in eyes with decreased function due to CRVO, the relative latency of PhNR was not compared with the values obtained by others. The difference between ischemic and nonischemic cases was shown by an



**FIGURE 2.** (A) Area of macular stimulation. The fmERG was elicited by 15° circular stimuli positioned on the fovea. (B) fmERG obtained from a normal fellow eye. A total of 200 to 300 responses were averaged by a signal processor. *Black arrowhead*: the beginning of the stimuli; *red arrows*: amplitudes of each wave; *blue arrows*: latencies of each wave.

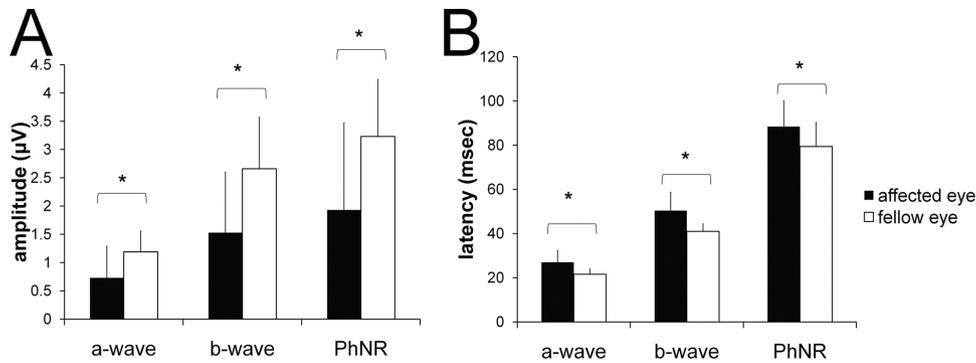


FIGURE 3. Amplitudes (A) and latencies (B) of focal macular electroretinograms obtained from eyes with macular edema associated with CRVO and from fellow eyes. Error bar, SD; \* $P < 0.01$ , by paired  $t$ -test.

unpaired  $t$ -test.  $P < 0.05$  was considered to be statistically significant (PASW Statistics, version 17.0; SPSS, Chicago, IL).

## RESULTS

In the present study, we examined 24 eyes with CRVO and 24 healthy fellow eyes of 24 patients (15 men and 9 women) who ranged in age from 35 to 80 years (mean,  $67.2 \pm 13.0$ ). The median duration of symptoms was 1 month (range, 0.5–12). At the initial visit, VA in logMAR fashion was  $0.62 \pm 0.47$  in the affected eyes and  $-0.07 \pm 0.12$  in the healthy fellow eyes. All affected eyes had ME with cystoid spaces at the fovea, in which mean CPT was  $771 \pm 281 \mu\text{m}$ . Eighteen (75%) of the 24 eyes had a serous retinal detachment, the mean HRD of these being  $218 \pm 215 \mu\text{m}$ . The SRT was  $610 \pm 180 \mu\text{m}$ . In the fellow eyes, OCT showed a physiologic shape of the fovea and a mean CPT of  $223 \pm 25 \mu\text{m}$ .

Of the 24 affected eyes, reliable fmERG recordings could be obtained from 22 (92%). In two eyes, a reliable fmERG could not be obtained because of low reproducibility or a slanted baseline. Of the remaining 22 eyes, a flat ERG was recorded in 2 (9%) and OPs were diminished in 14 (64%). None of our patients noted any eye pain or loss of vision after the fmERG recording. Amplitudes in the 20 eyes with reliable ERGs (except for the 2 eyes with flat ERGs) were used for the statistical analysis.

Amplitudes of the a-wave, b-wave, and PhNR were  $0.73 \pm 0.56$ ,  $1.53 \pm 1.07$ , and  $1.93 \pm 1.54 \mu\text{V}$  in the affected eyes and  $1.19 \pm 0.37$ ,  $2.66 \pm 0.91$ , and  $3.23 \pm 1.01 \mu\text{V}$  in the fellow eyes, respectively (Fig. 3). In the affected eyes, the amplitudes of the a-wave, b-wave, and PhNR were reduced significantly compared with those of the healthy fellow eyes ( $P = 0.0010$ ,  $P < 0.001$ , and  $P = 0.00053$ , respectively). Latencies of the a-wave, b-wave, and PhNR were  $27.0 \pm 5.3$ ,  $50.4 \pm 8.3$ , and  $88.4 \pm 11.7 \text{ ms}$  in the affected eyes and  $21.6 \pm 2.4$ ,  $41.0 \pm 3.4$ , and  $79.4 \pm 10.9 \text{ ms}$  in the fellow eyes, respectively (Fig. 3), showing that latencies were prolonged significantly in the affected eyes compared with those in the fellow eyes ( $P < 0.001$ ,  $P < 0.001$ , and  $P = 0.0066$ ).

To compare the fmERG parameters with other measurements (OCT, microperimetry, and VA), we calculated the relative amplitudes and latencies (affected eye/fellow eye). The relative amplitudes of the a-wave ( $r = -0.470$ ,  $P = 0.027$ ), b-wave ( $r = -0.525$ ,  $P = 0.012$ ), and PhNR ( $r = -0.598$ ,  $P = 0.0033$ ) showed a cross-correlation with VA in logMAR. In the affected eyes, the amplitudes of fmERG became lower, in parallel with the level of decreased VA. Relative amplitude of PhNR correlated the most strongly with VA (Fig. 4). However, the relative latencies of the a- and b-waves showed no correlation with VA (Table 1). In addition, retinal sensitivity in the

macular area was measured with the microperimeter in 17 affected eyes. Relative amplitudes and latencies of each wave showed a tendency to correlate with retinal sensitivity within the macular area, and some correlations were nearly statistically significant (Table 1). The relative amplitudes of PhNR correlated in a statistically significant way with mean sensitivity within the central  $8^\circ$  area ( $r = 0.482$ ,  $P = 0.050$ ) and within the central  $10^\circ$  area ( $r = 0.521$ ,  $P = 0.032$ ).

We then compared fmERG parameters with OCT measurements. CPT showed a correlation with both the relative amplitude and the relative latency of each wave (Table 2). Among all parameters, however, the relative amplitude of PhNR was correlated the most strongly CPT ( $r = -0.598$ ,  $P = 0.0042$ ). In addition, SRT showed a correlation with the latencies of the a-wave ( $r = 0.440$ ,  $P = 0.052$ ) and the b-wave ( $r = 0.608$ ,  $P = 0.0045$ ). However, the relative amplitudes of neither were correlated with SRT. Swelling of the sensory retina resulted in the prolongation of both a- and b-wave latencies. In contrast, HRD had no correlation with the relative latency of either wave. However, relative amplitudes of the a-wave ( $r = -0.442$ ,  $P = 0.045$ ), b-wave ( $r = -0.588$ ,  $P = 0.0051$ ), and PhNR ( $r = -0.675$ ,  $P = 0.00078$ ) correlated significantly with HRD. In the affected eyes, the amplitudes of fmERG became lower in parallel with the extent of foveal retinal detachment.

Fluorescein angiography revealed the CRVO to be ischemic in five eyes. In these eyes, ME was more severe ( $P < 0.001$ , CPT) and VA was more deteriorated ( $P = 0.019$ ) than in eyes with nonischemic CRVO (Table 3). Furthermore, all eyes with

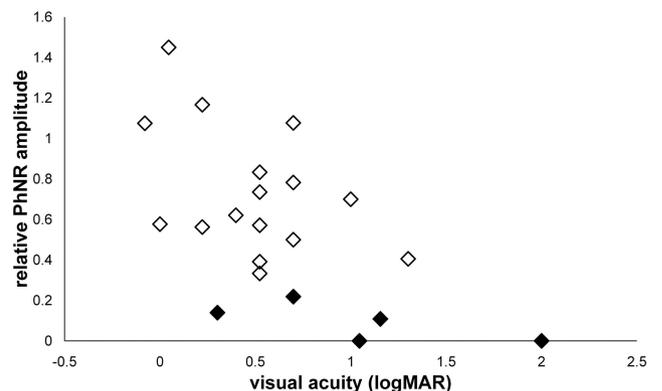


FIGURE 4. Relationship between relative amplitudes of PhNR and VA. Relative amplitude was calculated by dividing the amplitude in the affected eye by that in the fellow eye. VA was converted to logMAR. VA expressed as logMAR fashion showed cross-correlation with relative amplitudes of PhNR ( $r = -0.598$ ,  $P = 0.0033$ ). (◆) Ischemic cases; (◇) nonischemic cases.

TABLE 1. Comparison of Parameters in the fmERG with VA and Retinal Sensitivity Obtained by Microperimetry

	Visual Acuity (logMAR)		Mean Retinal Sensitivity									
			Within 2° Area		Within 4° Area		Within 6° Area		Within 8° Area		Within 10° Area	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Relative a-wave amplitude	-0.470	0.027	0.395	0.117	0.412	0.100	0.412	0.100	0.417	0.096	0.444	0.074
Relative b-wave amplitude	-0.525	0.012	0.459	0.064	0.367	0.147	0.374	0.139	0.394	0.118	0.422	0.092
Relative PhNR amplitude	-0.598	0.0033	0.474	0.055	0.427	0.087	0.454	0.067	0.482	0.050	0.521	0.032
Relative a-wave latency	0.203	0.391	-0.500	0.058	-0.416	0.123	-0.420	0.119	-0.423	0.116	-0.398	0.142
Relative b-wave latency	0.260	0.268	-0.496	0.060	-0.455	0.088	-0.461	0.084	-0.460	0.084	-0.448	0.094

ischemic CRVO showed a serous retinal detachment beneath the fovea. HRD was greater with ischemic CRVO (486 ± 274 μm) than with nonischemic CRVO (96 ± 115 μm; *P* < 0.001). In ischemic eyes, the relative amplitudes of the a-wave (*P* = 0.041), b-wave (*P* = 0.0040), and PhNR (*P* < 0.001) were reduced more severely than in the nonischemic eyes, although PhNR was the most severely affected (Fig. 3). Of the 24 affected eyes, a flat ERG was recorded in two. Both of these eyes showed severe ischemic CRVO with a VA of less than 0.1 on a Landolt chart (20/200 on a Snellen chart).

**Representative Cases**

**Case 1.** A 39-year-old man had a 1-month history of blurred vision in the left eye (1.2 on the Landolt chart, which is equivalent to 20/16 on a Snellen chart), and a retinal hemorrhage characteristic of CRVO was seen. Fluorescein angiography showed small areas of nonperfusion, and OCT revealed a small cystoid space at the fovea; SRT was 322 μm. FmERG was well preserved in the affected eye. The relative amplitude of PhNR was 1.08 and the relative latency of the b-wave was 1.05 (Fig. 5).

**Case 2.** A 76-year-old woman had a 1-month history of decreased vision in the right eye (0.3 on the Landolt chart, equivalent to 20/66 on a Snellen chart), and an extensive retinal hemorrhage associated with CRVO was seen. Fluorescein angiography showed only a minimal area of nonperfusion, and OCT revealed large cystoid spaces with no retinal detachment. SRT was 451 μm. In the affected eye, amplitude of the fmERG was decreased and latency was prolonged. The relative amplitude of PhNR was decreased to 0.83, and relative latency of the b-wave was 1.27 (Fig. 5).

**Case 3.** A 73-year-old man had a 2-week history of severely decreased VA in the left eye (0.05 on a Landolt chart; equivalent to 20/400 on a Snellen chart). At the initial visit, an extensive retinal hemorrhage and many cotton wool spots associated with CRVO were seen. OCT showed thickening of the outer retina with a retinal detachment beneath the fovea. In the affected eye, SRT was 360 μm and HRD was 441 μm, and the amplitude of the fmERG was markedly

decreased. The relative amplitude of PhNR was also markedly decreased (to 0.41), and the relative latency of the b-wave was 1.13 (Fig. 5).

**Case 4.** A 65-year-old man had a 2-week history of severe visual impairment in the right eye (0.09 on a Landolt chart, which is equal to 20/222 on a Snellen chart), and a retinal hemorrhage with numerous cotton wool spots associated with CRVO was seen. Fluorescein angiography showed extensive areas of nonperfusion, and OCT revealed marked cystoid edema with severe retinal detachment. SRT was 645 μm and HRD was 889 μm; fmERG in this eye was nonrecordable (Fig. 5).

**DISCUSSION**

Despite various treatments, ME secondary to CRVO often results in severely impaired visual function. A number of investigators have recently reported the efficacy of antivascular endothelial growth factor therapy for this condition,<sup>21-23</sup> but to evaluate the effectiveness of this treatment, most studies have used a change in both VA and retinal thickness as measured by OCT.<sup>24</sup> However, VA reflects only foveal function, whereas the ME secondary to CRVO usually involves the larger macular area. To evaluate the efficacy of treatment for ME, it is essential that another functional examination that reflects the larger macular area be established.<sup>7</sup> Recently, Yamaike et al.<sup>7</sup> reported the retinal sensitivity as examined with a microperimeter (MP1; Nidek) in the macular area of eyes with branch retinal vein occlusion. The MP1 software contains an automatic tracking system for fundus movements that evaluates every acquired frame for shifts in the *x*- and *y*-directions of the fundus. In their report, retinal sensitivity in the macular area correlated closely with retinal thickness. The fmERG provides accurate stimulation of the macula while monitoring the macula through the infrared fundus camera.<sup>25</sup> We hypothesized that fmERG may be useful for examination of macular function in eyes with CRVO.

The fmERG system, which was developed by Miyake et al,<sup>26-28</sup> has been commercially available since 2008. With the

TABLE 2. Comparison of fmERG with Foveal Measurements Obtained with OCT

	CPT		SRT		HRD	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Relative a-wave amplitude	-0.447	0.042	-0.196	0.395	-0.442	0.045
Relative b-wave amplitude	-0.497	0.022	-0.101	0.665	-0.588	0.0051
Relative PhNR amplitude	-0.598	0.0042	-0.160	0.487	-0.675	0.00078
Relative a-wave latency	0.473	0.035	0.440	0.052	0.225	0.341
Relative b-wave latency	0.678	0.0010	0.608	0.0045	0.353	0.127

Data are the Pearson correlation coefficient.

TABLE 3. Comparisons of OCT and fmERG Measurements between Ischemic and Nonischemic CRVO

	Ischemic CRVO	Nonischemic CRVO	P
Number of eyes	5	17	
Age, y	68.0 ± 12.7	67.0 ± 13.5	0.88
Gender, men/women	3/2	11/6	0.99
Visual acuity, logMAR	1.04 ± 0.63	0.49 ± 0.35	0.019
CPT, $\mu\text{m}$	1185 ± 234	673 ± 207	<0.001
Eyes with retinal detachment, <i>n</i>	5 (100%)	11 (65%)	0.27
SRT, $\mu\text{m}$	699 ± 76	577 ± 199	0.23
HRD, $\mu\text{m}$	486 ± 274	96 ± 115	<0.001
Relative a-wave amplitude	0.26 ± 0.33	0.74 ± 0.45	0.041
Relative b-wave amplitude	0.22 ± 0.28	0.69 ± 0.29	0.0040
Relative PhNR amplitude	0.09 ± 0.09	0.73 ± 0.31	<0.001
Relative a-wave latency	1.49 ± 0.21	1.24 ± 0.27	0.148
Relative b-wave latency	1.50 ± 0.10	1.21 ± 0.23	0.048

use of fmERG, Machida et al.<sup>29</sup> reported the usefulness of focal macular PhNR in the evaluation of glaucoma, in which the ganglion cells are primarily the cells that are damaged. PhNR, which is a negative wave that follows the b-wave, is reported to reflect inner retinal function. Because CRVO causes damage primarily within the inner retina, PhNR may well be a useful parameter in evaluating the function of the inner retina.<sup>17-19</sup> Using various stimulus durations on monkeys, Kondo et al.<sup>30</sup> reported the characteristics of PhNR obtained by both brief and long flashes. In agreement with their report, our preliminary experience with CRVO showed that PhNR obtained by a long flash (150 ms) was larger and slower than that obtained by a brief flash (3 ms). Based on this previous report and on our preliminary data, we evaluated macular function in CRVO by measuring fmERG, with emphasis on PhNR obtained by a long (150-ms) flash.

In our patients with ME secondary to CRVO, both the amplitudes and the latencies of all components of the fmERG reflected the decreased macular function. However, it has been noted that the amplitudes and latencies have some variance even among normal subjects. To compare the fmERG measurements with other parameters, we used the relative amplitudes and latencies (affected eye/fellow eye). In macular pseudohole, Suzuki et al.<sup>31</sup> reported a correlation between VA and relative b-wave amplitudes in fmERG, and a correlation between retinal thickness and these relative b-wave amplitudes. In the present study, we found similar correlations in eyes with CRVO. However, some changes in the fmERG may be characteristic of the disease, so it may be necessary to accumulate data on each disease.

In the present study, foveal thickness (CPT) showed a correlation with both the relative amplitude and the relative latency of each wave. In addition, relative amplitude correlated with HRD, but not with SRT. Therefore, the correlation of HRD would contribute primarily to the correlation of CPT with relative amplitude. Similarly, because relative latency correlated with SRT, but not with HRD, the correlation of CPT with relative latency could be explained by the correlation of HRD. We do not know exactly how ME affects visual function. Murakami et al.<sup>32</sup> indicated that obtaining good VA requires an intact foveal photoreceptor layer in acute branch retinal vein occlusion. ME with acute CRVO frequently accompanies serous detachment.<sup>33</sup> Our finding suggest that subretinal fluid accumulation within the macula may impair macular function, depending on the height of the detachment. In addition, prolonged latency may be explained by the delay in conduction from the first to the next neuron, depending on the increased retinal thickness due to CRVO.

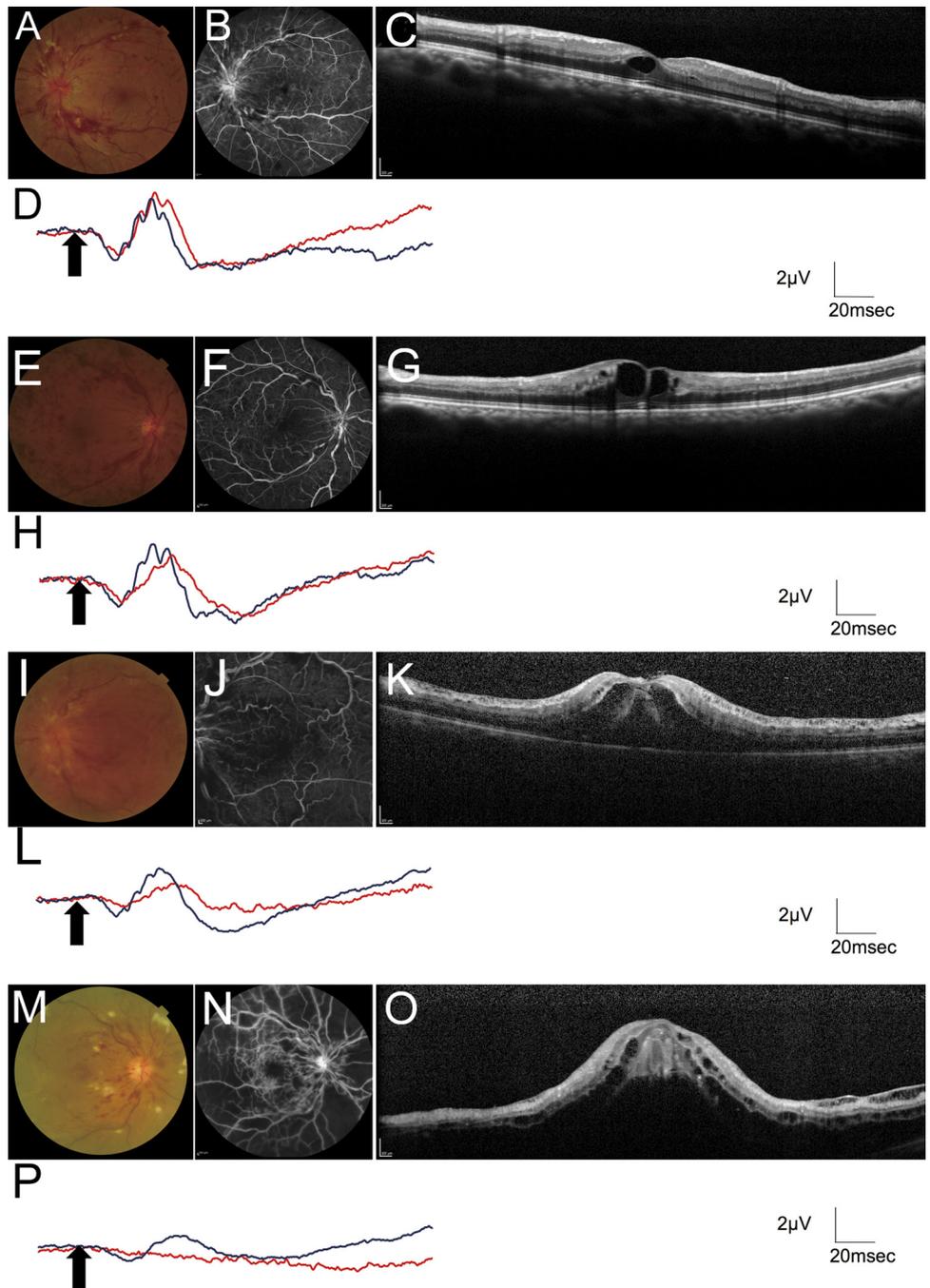
From the fmERG recordings, we can obtain the a-wave, b-wave, and PhNR, although it is not yet known which wave most effectively reflects macular function. Among these three

waves, the amplitudes of PhNR correlated more closely with VA and HRD, but only the PhNR amplitude showed a significant correlation with retinal sensitivity by the use of microperimetry (MP1; Nidek). Because the amplitude of the a-wave was smaller than that of the b-wave or of PhNR, the signal-to-noise ratio in the a-wave may have been greater. Because CRVO causes damage primarily within the inner retina, PhNR, which originates from ganglion cells, may be a useful parameter with which to evaluate macular function in CRVO. However, the fmERG showed the most marked change in the amplitude of PhNR in CRVO. PhNR is a slow wave and does not have a sharp peak, especially in eyes with decreased function due to CRVO, so, when using the latency of fmERG to evaluate macular function in CRVO, the latency of the b-wave might be more appropriate.

Neovascularization is such a severe complication of CRVO that many previous investigators have reported its predictive factors. The latency of the 30-Hz flicker in ffERG is reported to be useful in predicting the occurrence of new vessels in CRVO.<sup>13,14,34,35</sup> In our patients, we encountered five eyes with ischemic CRVO that showed no new vessels on fluorescein angiography. These eyes had lower amplitudes, particularly in PhNR, which represents inner retinal dysfunction. PhNR may thus be a predictor of neovascularization in eyes with CRVO. However, the present study was cross-sectional, and it is necessary to confirm in future studies the association of PhNR with the development of new vessels.

Major limitations of the present study are its small sample size and lack of control individuals. In the present study, we used a Landolt chart, which is based on an uneven spatial gradient scale, for the measurement of VA. A logMAR chart, such as an ETDRS chart, may allow us to obtain a more powerful correlation of fmERG measurements with VA. In addition, because this was a cross-sectional study, it is necessary to perform a longitudinal study to better define the role of fmERG recordings in the prediction of visual prognosis and in the development of new vessels. However, this is the first report of macular function in ME secondary to CRVO using the fmERG system and is also the first to compare the parameters of fmERG with other measurements, even though the statistical tests were not corrected for the number of comparisons. To establish fmERG as a more common examination, the conditions of recording must be improved. The fmERG system at present requires the use of a contact lens, and the patient being tested tends to feel some stress. In the current setting, we demonstrated that both the amplitudes and the latencies of fmERG were decreased markedly in CRVO and that they correlated with VA and with some OCT measurements. Based on the present study, fmERG appears to be a useful functional examination

**FIGURE 5.** Fundus photographs (A, E, I, M), fluorescein angiography (B, F, J, N), and OCT (C, G, K, O) in eyes with macular edema associated with CRVO. (D, H, L, P) fmERG obtained from an eye with CRVO (red) and from the healthy fellow eye (blue). Arrow: beginning of stimulation. (A–D) Case 1. An eye with mild nonischemic CRVO (1.2 on Landolt chart; equivalent to 20/16 on Snellen chart). OCT showed a small cystoid space at the fovea; CPT was 322  $\mu\text{m}$ . fmERG was well preserved in the affected eye. Relative amplitude of PhNR was 1.08, and relative latency of the b-wave was 1.05. (E–H) Case 2. An eye with moderate nonischemic CRVO (0.3 on Landolt chart, equal to 20/66 on Snellen chart). OCT showed large cystoid spaces without retinal detachment. SRT was 451  $\mu\text{m}$ . In the affected eye, amplitude of the fmERG was decreased, and latency was prolonged. The relative amplitude of PhNR was decreased to 0.83, and the relative latency of the b-wave was 1.27. (I–L) Case 3. An eye with severe nonischemic CRVO (0.05 on Landolt chart, which is the equivalent of 20/400 on Snellen chart). OCT showed marked thickening of the outer retina with a retinal detachment located beneath the fovea. SRT was 360  $\mu\text{m}$ , and the HRD was 441  $\mu\text{m}$ . In the affected eye, the amplitude of the fmERG was markedly decreased. The relative amplitude of the PhNR was markedly decreased to 0.41, and relative latency of the b-wave was 1.13. (M–P) Case 4. An eye with severe ischemic CRVO (0.09 on Landolt chart; equivalent to 20/222 on Snellen chart). OCT revealed marked cystoid edema with severe retinal detachment. SRT was 645  $\mu\text{m}$  and HRD was 889  $\mu\text{m}$ . The fmERG in the affected eye was nonrecordable.



with which to evaluate the severity of ME in CRVO and the effect of treatment, such as anti-VEGF therapy.

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