Evaluation of Macular Function Using Focal Macular Electroretinography in Eyes with Macular Edema Associated with Branch Retinal Vein Occlusion

Ken Ogino, Akitaka Tsujikawa, Tomoaki Murakami, Yuki Muraoka, Yumiko Akagi-Kurashige, Kenji Ishihara, Kazuaki Miyamoto, Hajime Nakamura, and Nagabisa Yoshimura

Purpose. To study the usefulness of focal macular electroretinography (fmERG) for evaluation of macular function in eyes with macular edema (ME) associated with branch retinal vein occlusion (BRVO).

Methods. The authors prospectively performed fmERG on 34 patients with untreated unilateral BRVO at the initial visit and 12 months later. Amplitudes and latencies of the a-wave, b-wave, and photopic negative response (PhNR) were compared with visual acuity, with retinal sensitivity measured by microperimetry, and with measurements obtained by optical coherence tomography.

Results. In eyes with ME from BRVO, amplitudes of the a-wave, b-wave, and PhNR were reduced significantly and latencies were prolonged significantly compared with those of healthy fellow eyes \((P < 0.05)\). Relative amplitudes and latencies were not correlated with visual acuity but, rather, tended to be correlated with retinal sensitivity within the macular area. Among all parameters studied by fmERG, relative amplitude of the PhNR was most strongly correlated with central foveal thickness \((r = -0.465; P = 0.007)\). In addition, the height of the serous retinal detachment showed a correlation with the relative amplitude of the PhNR \((r = -0.376; P = 0.034)\). At 12 months, the amplitude of the b-wave and the PhNR improved significantly, in parallel with resolution of the ME \((P = 0.015; P = 0.033)\).

Conclusions. In eyes with ME from BRVO, amplitudes and latencies seen by fmERG were correlated with other biological parameters. Based on findings of the present study, fmERG appears to be useful as a functional examination within the macular area affected by BRVO. (Invest Ophthalmol Vis Sci. 2011;52:8047–8055) DOI:10.1167/iovs.11-8143

Macular edema (ME) is one of the most vision-threatening complications associated with branch retinal vein occlusion (BRVO). Since the Branch Vein Occlusion Study Group reported the efficacy of grid laser photocoagulation, it has been recognized as the standard treatment for ME from BRVO,\(^1\) but, recently, an increasing number of reports have shown the efficacy of newer treatments on ME from BRVO, such as intravitreal injection of triamcinolone acetonide, bevacizumab, or ranibizumab.\(^2\)–\(^4\) Generally, both the severity of the ME and the effect of the treatment have been evaluated by quantitative measurement of foveal thickness using optical coherence tomography (OCT).\(^5\)–\(^6\) As a functional parameter, we typically use visual acuity (VA) measurement. Although ME associated with BRVO usually involves the larger macular area, VA measurement reflects only foveal function. In addition, physicians sometimes note a discrepancy between the morphologic severity of ME and VA. 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.\(^7\)–\(^8\)

Full-field electroretinography (ffERG), which allows examination of the entire retinal function, is used widely as a functional examination in various diseases.\(^9\) Using ffERG, Chen et al.\(^10\) reported an abnormal photopic negative response (PhNR), which is thought to reflect the function of the inner retina in eyes with BRVO. In contrast to ffERG, the focal macular ERG (fmERG) allows examination of retinal function within only the macular area.\(^11\)–\(^12\) Using fmERG, Terasaki et al.\(^13\)–\(^14\) demonstrated a correlation between increased foveal thickness from diabetic ME and decreased macular function. Thus far, as a functional measurement of a focal area within the macula, multifocal ERG has been used in various retinal diseases,\(^15\)–\(^17\) especially retinal dystrophies.\(^18\)–\(^20\) Compared with multifocal ERG, fmERG allows more reliable recording of the whole macular area, even from patients with poor fixation or poor VA, by monitoring the fundus through an infrared camera and manually adjusting the stimulus at the fovea.\(^15\)–\(^14\)–\(^21\)–\(^25\) We hypothesize that fmERG might enable us to evaluate more effectively the impaired macular function due to ME secondary to BRVO. Little information, however, is available about macular function examined by fmERG in eyes with BRVO. In the study described herein, fmERG in eyes with ME associated with BRVO was performed during the acute phase and at 12 months, at which time ME was resolved in most eyes, and we studied the correlations of fmERG with other biological parameters. Based on our findings, we evaluated the usefulness of fmERG to better define macular function of these eyes.

Patients and Methods

This prospective study consisted of 34 patients with ME secondary to untreated unilateral BRVO who made their initial visit to Kyoto University Hospital between May 2009 and March 2010. This study was approved by the Institutional Review Board at Kyoto University Graduate School of Medicine and adhered to the tenets of the Declaration of Helsinki. From the Department of Ophthalmology and Visual Sciences, Kyoto University Graduate School of Medicine, Kyoto, Japan.

Submitted for publication June 29, 2011; revised August 24, 2011; accepted September 4, 2011.

Disclosure: K. Ogino, None; A. Tsujikawa, None; T. Murakami, None; Y. Muraoka, None; Y. Akagi-Kurashige, None; K. Ishihara, None; K. Miyamoto, None; H. Nakamura, None; N. Yoshimura, None.

Corresponding author: Akitaka Tsujikawa, Department of Ophthalmology, Kyoto University Graduate School of Medicine, Sakyoku, Kyoto 606-8507, Japan; tsujikawa@kuhp.kyoto-u.ac.jp.
Fluorescein angiography was performed using a confocal laser scanning system (HRA-2; Heidelberg Engineering, Heidelberg, Germany). At each scheduled visit, the entire macular area was examined with multimodality imaging (Spectralis+OCT; Heidelberg Engineering). Using a vertical sectional image centered on the fovea obtained at the initial visit and at 12 months, we performed three measurements in the fovea; these consisted of center point thickness, height of the serous retinal detachment, and sensory retinal thickness. Center point thickness was defined as the distance between the internal limiting membrane and the retinal pigment epithelium (RPE) at the center of the fovea; height of serous retinal detachment was defined as the distance between the RPE and the bottom of the detached neurosensory retina, just beneath the fovea; sensory retinal thickness was calculated by subtracting the height of the serous retinal detachment from the center point thickness.

In 31 eyes with BRVO, retinal sensitivity within the macular area was examined with a fundus-monitored micrometer (Micro Perimeter 1 [MP1]; Nidek, Gamagori, Japan). A 4-2-staircase strategy with Goldmann III size stimuli was used, and 57 stimulus locations within the central 10° were examined by microperimetry. Each stimulus was located according to the measurement points in Humphrey 10-2, with some additional points (Fig. 1A). The white background illumination was set at 1.27 cd/m². The differential luminance, defined as the difference between stimulus luminance and background luminance, was 1.27 cd/m² 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 (2° cross for central fixation, 4° or 6° cross for paracentral fixation) according to the VA of the individual patient. There were 17 and 37 measurement points within the central 4° and 8° areas.

Recording of fmERG has been reported in detail previously. Briefly, after the pupils of both eyes were maximally dilated, a Burian-Allen bipolar contact lens electrode (Hansen Ophthalmic Laboratories, Iowa City, IA) was placed in the conjunctival sac of each eye under topical anesthesia. A chloride silver electrode was attached to the left earlobe as a ground electrode. fmERG was elicited by 15° circular stimuli positioned on the macular area, using a prototype of the ER-80 (Kowa, Tokyo, Japan), which 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/m², respectively. The 15° circular stimulus was carefully and constantly centered on the fovea, as observed through the infrared camera (Fig. 1B). The fmERG was recorded with 2-Hz rectangular stimuli (150 ms with the light on and 350 ms with the light off). Affected eyes were examined before 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. Black arrowhead: beginning of stimulation; red arrow: amplitudes of the waves.

Recording of fmERG has been reported in detail previously. Briefly, after the pupils of both eyes were maximally dilated, a Burian-Allen bipolar contact lens electrode (Hansen Ophthalmic Laboratories, Iowa City, IA) was placed in the conjunctival sac of each eye under topical anesthesia. A chloride silver electrode was attached to the left earlobe as a ground electrode. fmERG was elicited by 15° circular stimuli positioned on the macular area, using a prototype of the ER-80 (Kowa, Tokyo, Japan), which 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/m², respectively. The 15° circular stimulus was carefully and constantly centered on the fovea, as observed through the infrared camera (Fig. 1B). The fmERG was recorded with 2-Hz rectangular stimuli (150 ms with the light on and 350 ms with the light off). Affected eyes were examined before 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 PhNR and with a band-pass filter of 50 to 500 Hz for oscillatory potentials. The amplitudes of the a-wave and b-wave were measured, respectively, from the baseline to the peak of the a-wave and from the trough of the a-wave to the peak of the b-wave (Fig. 1C). The amplitude of PhNR was measured from the peak of the b-wave to the trough of PhNR, based on our previous reports (Fig. 1C). 26–28 Latency was defined as the time from the beginning of stimulation to the peak of each component.

Statistical analysis was performed (PASW Statistics, version 17.0; SPSS, Chicago, IL). All values are presented as mean ± SD. Paired t-test with Bonferroni correction was used to compare amplitudes and latencies of the a-wave, b-wave, and PhNR between affected eyes and unaffected fellow eyes. The initial fmERG parameters, VA, and OCT parameters with values obtained at 12 months were also compared with a paired t-test with Bonferroni correction. To compare the fmERG parameters with other measurement values (VA, retinal sensitivity, OCT parameters), we used 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 because of BRVO, the relative latency of PhNR was not compared with the other values. P < 0.05 was considered statistically significant.

### RESULTS

In the present study, we examined 34 eyes with BRVO and 34 healthy fellow eyes of 34 patients (18 men, 16 women), who ranged in age from 45 to 78 years (66.8 ± 9.0 years). The mean duration of symptoms was 3.8 ± 7.0 months. At the initial visit, VA in logMAR fashion was 0.49 ± 0.38 in affected eyes and −0.07 ± 0.13 in healthy fellow eyes. All affected eyes had ME with cystoid spaces at the fovea, in which mean center point thickness was 553 ± 192 μm. Twenty-five (74%) of the 34 affected eyes had serous retinal detachments beneath the fovea; the mean height of these detachments was 160 ± 110 μm. Mean sensory retinal thickness was 416 ± 140 μm. In the fellow eyes, OCT showed a physiologic shape of the fovea, and the mean center point thickness in these healthy eyes was 235 ± 35 μm.

To evaluate the reproducibility of fmERG, the intraclass correlation coefficient (ICC) was calculated from the initial fmERG and from recordings obtained at 12 months from 24 unaffected fellow eyes. In these unaffected fellow eyes, amplitudes of the a-wave, b-wave, and PhNR were 1.29 ± 0.43, 3.05 ± 0.92, and 3.78 ± 0.22 μV, respectively, at the initial visit and 1.48 ± 0.58, 3.46 ± 0.87, and 3.99 ± 1.04 μV, respectively, at 12 months. Latencies of the a-wave, b-wave, and PhNR were 21.2 ± 1.3, 40.3 ± 2.1, and 75.9 ± 8.2 ms, respectively, at the initial visit and 21.1 ± 1.4, 40.6 ± 2.5, and 75.7 ± 9.1 ms, respectively, at 12 months. ICCs were 0.219, 0.490, and 0.635, respectively, in amplitude and 0.445, 0.422, and 0.533, respectively, in latency of the a-wave, b-wave, and PhNR.

Of the 34 affected eyes, reliable fmERG recordings could be obtained from 32 (94%) of the eyes at the initial visit and from 24 (100%) of 24 affected eyes at 12 months. In two eyes, reliable fmERG could not be obtained because of low reproducibility or a slanted baseline. In eyes with BRVO, a flat ERG was not seen, but oscillatory potentials were diminished in 12 eyes at 12 months. None of our

-------------------

**TABLE 1.** Correlation of Parameters in Focal Macular Electroretinogram with Visual Acuity or Retinal Sensitivity Examined with MP1 at the Initial Visit

<table>
<thead>
<tr>
<th></th>
<th>Visual Acuity (logMAR)</th>
<th>Center Point</th>
<th>Within 4°</th>
<th>Within 8°</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P</td>
<td>r</td>
<td>P</td>
</tr>
<tr>
<td>Relative amplitude</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a-Wave</td>
<td>0.015</td>
<td>0.938</td>
<td>0.036</td>
<td>0.635</td>
</tr>
<tr>
<td>b-Wave</td>
<td>0.066</td>
<td>0.720</td>
<td>-0.127</td>
<td>0.512</td>
</tr>
<tr>
<td>PhNR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relative latency</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a-Wave</td>
<td>0.014</td>
<td>0.938</td>
<td>-0.155</td>
<td>0.422</td>
</tr>
<tr>
<td>b-Wave</td>
<td>0.066</td>
<td>0.720</td>
<td>-0.127</td>
<td>0.512</td>
</tr>
</tbody>
</table>

Pearson correlation coefficient. logMAR, logarithm of the minimum angle of resolution.

---

**FIGURE 3.** Relationship between relative amplitude and retinal sensitivity in the macular area (A) or mean retinal thickness (B) in eyes with ME associated with BRVO. Relative amplitude is calculated as amplitude in the affected eye divided by that in the fellow eye. Mean sensitivity within 8° was obtained with the MP1. Center point thickness was obtained with a vertical section of OCT.
patients reported eye pain or loss of vision after the fmERG recording.

At the initial visit, amplitudes of the a-wave, b-wave, and PhNR in affected eyes were 0.95 ± 0.39, 1.66 ± 0.70, and 2.22 ± 1.06 μV, respectively (Fig. 2A), and were reduced significantly compared with those in the fellow eyes (P < 0.001). Latencies of the a-wave, b-wave, and PhNR in affected eyes were 22.8 ± 2.5, 43.8 ± 3.6, and 84.0 ± 11.7 ms, respectively (Fig. 2B), and were significantly prolonged compared with those in the fellow eyes (P = 0.009; P < 0.001; P = 0.012).

To compare the initial fmERG parameters with other measurements (VA, retinal sensitivity, OCT parameters), relative amplitudes and latencies (affected eye/fellow eye) were calculated. At the initial visit, relative amplitudes and latencies were not correlated with VA, although both relative amplitude and latency of each wave at the initial visit showed some correlation with retinal sensitivity within the macular area (Table 1). Relative amplitudes of the b-wave and of PhNR had the best correlation with the mean sensitivity within the central 8° area (r = 0.546, P = 0.002; r = 0.525, P = 0.003), which is compatible with the area of fmERG stimulation (Fig. 3A).

Furthermore, we compared initial fmERG parameters with OCT measurements, also obtained at the initial visit (Table 2). Center point thickness showed a correlation with relative amplitudes of the b-wave and PhNR. In fact among all parameters measured, relative amplitude of the PhNR was most strongly correlated with center point thickness (r = 0.465; P = 0.007) (Fig. 3B). In addition, the height of the serous retinal detachment showed a correlation with amplitudes of the b-wave and PhNR.

### Table 2. Correlation of Parameters in fmERG with Measurements of OCT at the Initial Visit

<table>
<thead>
<tr>
<th></th>
<th>Center Point Thickness (μm)</th>
<th>Sensory Retinal Thickness (μm)</th>
<th>Height of Serous Retinal Detachment (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P</td>
<td>r</td>
</tr>
<tr>
<td>Relative amplitude</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a-Wave</td>
<td>−0.026</td>
<td>0.886</td>
<td>0.156</td>
</tr>
<tr>
<td>b-Wave</td>
<td>−0.580</td>
<td>0.032</td>
<td>−0.227</td>
</tr>
<tr>
<td>PhNR</td>
<td>−0.465</td>
<td>0.007</td>
<td>−0.345</td>
</tr>
<tr>
<td>Relative latency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a-Wave</td>
<td>0.014</td>
<td>0.938</td>
<td>0.087</td>
</tr>
<tr>
<td>b-Wave</td>
<td>0.066</td>
<td>0.720</td>
<td>−0.059</td>
</tr>
</tbody>
</table>

Pearson correlation coefficient.

**FIGURE 4.** BRVO with extensive serous retinal detachment. (A) A 59-year-old man had a 1-month history of blurred vision due to BRVO in the left eye (0.7 on a Landolt chart, equivalent to 20/29 on a Snellen chart). (B) Retinal thickness map shows severe ME. (C) Microperimetry map shows decreased retinal sensitivity in the larger macula area beyond the area affected with BRVO. (D) Initial OCT shows ME with extensive serous retinal detachment. (E) ME and serous retinal detachment were resolved at 12 months. (F) fmERG obtained from the eye affected with BRVO (red, at initial visit; purple, at 12 months) and from the healthy fellow eye (gray, at initial visit). Black line: beginning of stimulation. The fmERG was severely affected at the initial visit and was only partially improved at 12 months. Relative amplitude of PhNR was 0.45 at initial visit and 0.71 at 12 months.
wave ($r = -0.388; P = 0.028$) and of PhNR ($r = -0.376; P = 0.0034$). However, neither relative amplitudes nor relative latencies had a correlation with sensory retinal thickness. In affected eyes, swelling of the sensory retina did not result in a reduction of amplitude or a prolongation of latency, but amplitudes did become reduced in parallel with the height of the foveal serous detachment. In addition, some eyes with BRVO showed an extensive serous retinal detachment that, in some cases, extended to the unaffected side of the retina. Retinal sensitivity was substantially reduced in the area involved by the serous retinal detachment, and there was a substantial decrease in fmERG amplitude (Figs. 4, 5).

At 12 months after the initial examination, all affected eyes showed substantial reduction in ME, and center point thickness was reduced to 313 $\pm$ 151 $\mu$m ($P < 0.001$; Fig. 6). No eye had a serous retinal detachment, but nine eyes showed residual cystoid spaces. At 12 months, VA was significantly improved to 0.27 $\pm$ 0.41 ($P = 0.005$). Amplitudes of the a-wave, b-wave, and PhNR were 0.99 $\pm$ 0.55, 2.13 $\pm$ 0.90, and 2.66 $\pm$ 1.21 $\mu$V in affected eyes, respectively. In affected eyes, amplitudes of the b-wave and PhNR were significantly improved compared with values at the initial visit ($P = 0.015; P = 0.033$) (Fig. 6). Latencies of the a-wave, b-wave, and PhNR were 22.6 $\pm$ 2.8, 43.6 $\pm$ 3.0, and 81.5 $\pm$ 11.1 ms in affected eyes, respectively; these latencies were not significantly improved. Table 3 shows the VA, center point thickness, and focal macular electroretinogram at the initial visit and at 12 months in each group stratified by the treatment modality. Although the change of fmERG parameters showed a similar tendency in each group, most were not statistically significant, perhaps because of the small number of eyes.

In this study, 15 affected eyes of 34 patients with BRVO showed an area of nonperfusion that measured >5 disc diameters on fluorescein angiography. Table 4 shows each parameter of the fmERG obtained at the initial visit and 12 months later in ischemic and nonischemic BRVO. Between ischemic BRVO and nonischemic BRVO, there were no differences in parameters of the fmERG taken at the initial visit and at 12 months.

**DISCUSSION**

Visual prognosis in eyes with BRVO is thought to be better than that of eyes with CRVO. Nevertheless, some patients with BRVO have severely impaired visual function because of ME. VA is the most common functional examination but reflects only foveal function, and the ME caused by BRVO usually

---

**Figure 5.** BRVO with localized serous retinal detachment. (A) A 45-year-old man had a 2-month history of blurred vision due to BRVO in the left eye (0.9 on a Landolt chart, equivalent to 20/22 on a Snellen chart). (B) Retinal thickness map shows severe ME. (C) Micoperimetry map shows decreased retinal sensitivity in the fovea. (D) Initial OCT shows ME with localized serous retinal detachment. (E) ME and serous retinal detachment are resolved at 12 months. (F) fmERG obtained from the eye affected with BRVO (red, at initial visit; purple, at 12 months) and from the healthy fellow eye (gray, at initial visit). Black line: beginning of stimulation. The fmERG in the affected eye was relatively preserved both at the initial visit and at 12 months. The relative amplitude of PhNR was 0.88 at the initial visit and 1.16 at 12 months.
involves the larger macular area, leading to functional impairment of the entire macular area. With the use of microperimetry, Yamaike et al.\cite{8} reported a close correlation between retinal sensitivity in the macular area and retinal thickness in eyes with ME associated with BRVO. In the present study, we performed fmERG and studied the correlations between fmERG and other biological parameters and evaluated the usefulness of fmERG as a possible examination to better define the macular function of these eyes. fmERG allows us to perform accurate macular stimulation with monitoring of the macula through an infrared fundus camera.\cite{12} In addition, an fmERG system has been commercially available since 2008, and its clinical usefulness for several retinal diseases has been reported.\cite{13,14,21–25}

However, it is generally recognized that amplitude of the ERG does not have high reproducibility, even in subjects with healthy eyes.\cite{31} In the present study, we used the relative amplitudes (affected eyes/fellow eyes) to minimize this variability of measurements. In addition, to confirm the reproducibility of fmERG, we assessed the ICC in parameters of fmERG.

**Figure 6.** Comparison of VA, retinal thickness of the fovea, and fmERG at the initial visit and at 12 months. VA was converted to logarithm of the minimum angle of resolution (logMAR). Center point thickness, height of the serous retinal detachment, and sensory retinal thickness were obtained with a vertical section of OCT. *P < 0.05, †P < 0.01 in paired t-test.
With the use of fellow eyes, which were examined at both the initial visit and at 12 months. The ICCs in amplitude and latency of the a-wave, b-wave, and PhNR were 0.219 and 0.445, 0.490 and 0.422, and 0.635 and 0.533, respectively. Based on this assessment, we confirmed that PhNR was the most stable parameter in fmERG.

In the acute phase of ME associated with BRVO, each parameter of the fmERG showed a substantial decrease in macular function. Although the relative amplitude and latency of each wave were not correlated with VA, the relative amplitude of PhNR did show a correlation with retinal sensitivity within the macular area. PhNR is a negative, large, slow wave that follows the b-wave and that typically has a larger signal/noise ratio than do other waves. Moreover, PhNR is reported to reflect inner retinal function. Machida et al. re-ported the usefulness of PhNR in fmERG for evaluation of the severity of glaucoma in which ganglion cells are primarily damaged. Because BRVO primarily causes damage in the inner retina, we hypothesized that PhNR in fmERG may be a useful parameter with which to evaluate objectively the macular function in eyes with BRVO. However, there is no consensus about how to measure the amplitude of PhNR. In previous experiments using monkeys treated with tetrodotoxin, the PhNR trough did not reach baseline. Severe inner retinal damage possibly resulted in PhNR trough levels above baseline. In preliminary experiments, some ischemic eyes showed such a pattern of PhNR. In the present study, therefore, the amplitude of PhNR was measured from the peak of b-wave to the trough level of PhNR.

Recent advances in OCT technology have revealed the pathomorphology of ME associated with BRVO, including the location of cystoid spaces and the usefulness of the junction between the inner and outer segments of the foveal photoreceptor layer as a hallmark of integrity of the outer retina. Recent advances in OCT technology have revealed the pathomorphology of ME associated with BRVO, including the location of cystoid spaces and the usefulness of the junction between the inner and outer segments of the foveal photoreceptor layer as a hallmark of integrity of the outer retina.

### Table 3. Comparison of Visual Acuity, Retinal Thickness, and fmERG at the Initial Visit and at 12 Months in Each Group Stratified by the Treatments

<table>
<thead>
<tr>
<th>Eyes, n</th>
<th>No Treatment</th>
<th>Grid Photocoagulation</th>
<th>Vitrectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>12</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>7/5</td>
<td>7/1</td>
<td>0/4</td>
</tr>
<tr>
<td>Age, y</td>
<td>60.9 ± 8.7</td>
<td>69.3 ± 9.1</td>
<td>73.0 ± 5.8</td>
</tr>
<tr>
<td>Duration, mo</td>
<td>5.0 ± 2.8</td>
<td>4.9 ± 2.8</td>
<td>2.0 ± 1.0</td>
</tr>
<tr>
<td>Visual acuity, logMAR</td>
<td>Initial visit</td>
<td>0.52 ± 0.47</td>
<td>0.58 ± 0.22</td>
</tr>
<tr>
<td></td>
<td>12 months</td>
<td>0.07 ± 0.33*</td>
<td>0.39 ± 0.27</td>
</tr>
<tr>
<td>Center point thickness, µm</td>
<td>Initial visit</td>
<td>455 ± 137</td>
<td>588 ± 181</td>
</tr>
<tr>
<td></td>
<td>12 months</td>
<td>270 ± 99*</td>
<td>295 ± 143*</td>
</tr>
<tr>
<td>a-Wave amplitude, µV</td>
<td>Initial visit</td>
<td>0.9 ± 0.4</td>
<td>1.0 ± 0.5</td>
</tr>
<tr>
<td></td>
<td>12 months</td>
<td>1.2 ± 0.5</td>
<td>0.8 ± 0.6</td>
</tr>
<tr>
<td>b-Wave amplitude, µV</td>
<td>Initial visit</td>
<td>1.7 ± 0.6</td>
<td>1.5 ± 0.8</td>
</tr>
<tr>
<td></td>
<td>12 months</td>
<td>2.4 ± 0.7*</td>
<td>1.8 ± 1.0</td>
</tr>
<tr>
<td>PhNR amplitude, µV</td>
<td>Initial visit</td>
<td>2.4 ± 1.1</td>
<td>1.8 ± 1.0</td>
</tr>
<tr>
<td></td>
<td>12 months</td>
<td>3.1 ± 1.2</td>
<td>2.2 ± 1.3</td>
</tr>
<tr>
<td>a-Wave latency, ms</td>
<td>Initial visit</td>
<td>21.5 ± 1.5</td>
<td>24.2 ± 3.3</td>
</tr>
<tr>
<td></td>
<td>12 months</td>
<td>25.2 ± 3.5</td>
<td>22.6 ± 2.3</td>
</tr>
<tr>
<td>b-Wave latency, ms</td>
<td>Initial visit</td>
<td>42.8 ± 2.9</td>
<td>46.3 ± 4.2</td>
</tr>
<tr>
<td></td>
<td>12 months</td>
<td>43.5 ± 4.1</td>
<td>43.7 ± 1.7</td>
</tr>
</tbody>
</table>

logMAR, logarithm of the minimum angle of resolution.

* *P* < 0.05, compared with values at initial visit.

with the use of fellow eyes, which were examined at both the initial visit and at 12 months. The ICCs in amplitude and latency of the a-wave, b-wave, and PhNR were 0.219 and 0.445, 0.490 and 0.422, and 0.635 and 0.533, respectively. Based on this assessment, we confirmed that PhNR was the most stable parameter in fmERG.
Therefore, we speculate that this correlation with retinal detachment might have contributed primarily to the correlation of center point thickness with relative amplitude. In addition, Table 2 indicates that macular function is negatively correlated with height of serous retinal detachment. As was shown in Figure 4, the extent of the serous retinal detachment may be associated with impairment of function in the macular area. In eyes with CRVO, it has been reported that the relative latency has a cross-correlation with sensory retinal thickness.34 In eyes with ME associated with BRVO, however, the relative latency was not correlated with any of the OCT parameters. This may be explained partially by the fact that the extent of sensory retinal swelling is milder in BRVO.

At 12 months after the initial visit, center point thickness was reduced significantly, with marked recovery of VA. OCT examination at 12 months revealed that all affected eyes showed substantial reduction in ME and complete absorption of the previously seen serous retinal detachment. In parallel with the morphologic recovery of the macular area, fmERG at 12 months also showed a recovery of some parameters; for example, the amplitudes of the b-wave and of PhNR improved significantly compared with those at the initial visit. The initial amplitude of the PhNR showed a correlation with the final amplitude ($r = 0.448; P = 0.035$). Similar to VA, macular function after resolution of the ME associated with BRVO appears to be determined by the severity of impairment of function during the acute phase. In the present study, persistent ME was treated with grid photocoagulation in 11 eyes and with pars plana vitrectomy in four eyes. Table 3 shows parameters of fmERG at the initial visit and at 12 months in each group stratified by the treatment modality. Although the changes of fmERG parameters showed a similar tendency in each group, most were not statistically significant, perhaps because of the small number of eyes.

In addition, we assessed whether initial parameters of fmERG served as prognostic factors of final VA. Unfortunately, however, we found no parameters of fmERG at the initial visit to be correlated with VA at 12 months (data not shown).

In the present study, initial fluorescein angiography showed an area of nonperfusion of >5 disc diameters in 44% of eyes with BRVO. Between ischemic BRVO and nonischemic BRVO, there were no differences in fmERG parameters obtained at the initial visit and at 12 months. Nonperfusion in the inner retina could well cause functional impairment of the retina and would have a substantial effect on the PhNR. Retinal ischemia caused by BRVO, often seen outside the vascular arcade, did not result in decreased fmERG, which reflected the only function of the macular area.

Major limitations of the present study are its small sample size and the various treatment regimens used. Although age, duration of disease, treatments, and other factors possibly influenced the parameters of fmERG, small sample size did not allow multivariate regression analysis. However, this is the first report of fmERG used to evaluate macular function in eyes with ME associated with BRVO and to compare the parameters of fmERG with other measurements. We have demonstrated, with the use of fmERG, that the amplitudes of each wave were significantly decreased in eyes with acute BRVO and showed improvement after reductions in ME. Furthermore, impaired amplitudes of PhNR were correlated not with VA but, rather, with macular sensitivity, as measured with the MP1; thus, the PhNR in fmERG would effectively reflect the decreased macular function from ME caused by BRVO. Recently, clinical trials using anti-vascular endothelial growth factor agents have been performed for the treatment of ME secondary to retinal vein occlusion.4.38–39 Such treatment, however, requires frequent intravitreal injection but does maintain a very low level of vascular endothelial growth factor in the eye for a long time, which might be a survival factor for the retinal neurons.40 fmERG, which allows for evaluation of macular function, may be useful for monitoring the safety of these treatments.

References


