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Multifocal Electroretinograms in Early Primary Open-angle Glaucoma

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Purpose: To determine the utility of multifocal electroretinograms (mfERGs) in patients with early primary open-angle glaucoma (POAG) with unilateral visual field abnormalities.

Methods: mfERGs were recorded from 24 eyes of 12 cases of early POAG (stage I for 1 eye and stage II for the other eye on the Kosaki scale). The implicit times and amplitudes of the second-order kernel summed for the whole visual field, for the superior and inferior hemifields, and for quadrantic fields of the stage I and stage II eyes were compared.

Results: Neither the first- nor the second-order kernels of the mfERGs showed any changes reflecting glaucomatous visual field abnormalities. The implicit times and amplitudes of the second-order kernel summed for the whole visual field, the superior and inferior hemi-visual fields, and quadrantic visual fields of the stage I and stage II eyes were also not significantly different.

Conclusions: We conclude that because the second-order kernel of the mfERG does not correlate with the visual field abnormality in early POAG, the second-order kernel of the mfERG that can be recorded at present is highly unlikely to reflect the function of the ganglion cells in the inner retinal layers. **Jpn J Ophthalmol 2002;46:443–450** © 2002 Japanese Ophthalmological Society

Key Words: Multifocal electroretinograms, primary open-angle glaucoma, second-order kernel, unilateral visual field defect.

Introduction

Pattern electroretinograms (PERGs) are used to test the function of the inner retinal layers because PERGs are considered to reflect mainly the electrical activity of the retinal ganglion cells.[1–3] However, PERGs are not widely used clinically, probably because PERGs are very small (2 μV) even when they are summated many times.

It was recently reported that the second-order kernel of the multifocal electroretinogram (mfERG) reflects the activity of inner retinal layers,[4,5] and the question arose whether the examination of the second-order kernel of the mfERG can replace the PERG for detecting primary open-angle glaucoma (POAG). However, earlier basic studies on the first-order kernel of the mfERG[6–8] are not sufficient to answer this question, and only a few investigations have been conducted correlating the second-order kernel of the mfERG to the PERGs.[9]

To determine whether an examination of the second-order kernel of the mfERG can replace the PERG for detecting patients at an early stage of POAG, the second-order kernel of the mfERGs recorded from 24 eyes in 12 cases of early stage POAG with unilateral visual field abnormalities were studied.

Materials and Methods

Twelve patients (4 men and 8 women), ages 35 to 60 years (average = 54.2 years), were studied (Table 1) All these patients were diagnosed with early-stage

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Table 1. Studied Cases*

Case	Age (y)	Sex	Right Visual Field†		Left Visual Field†	
			MD	Lens	MD	Lens
1	60	M	II		I	
			−4.92,	−0.25	−1.35,	−1.00
2	52	F	I		II	
			+0.94,	+2.75	−3.13,	+3.00
3	57	F	II		I	
			−16.50,	+0.75	−2.18,	+0.50
4	52	M	I		II	
			−2.81,	+0.50	−7.53,	+0.00
5	60	F	II		I	
			−3.74,	+4.25	+0.16,	+4.50
6	56	F	I		II	
			−1.00,	+3.00	−3.58,	+2.50
7	54	F	I		II	
			−1.74,	+2.25	−2.88,	+2.50
8	60	F	I		II	
			−0.56,	+1.00	−6.59,	+0.75
9	60	M	I		II	
			+0.80,	−1.25	−3.88,	−1.50
10	57	F	I		II	
			−2.17,	+3.50	−4.48,	+4.00
11	35	M	I		II	
			−1.74,	−0.75	−9.71,	−0.75
12	47	F	I		II	
			+0.40,	+0.00	−2.23,	+1.00

*Visual field stages were rated on Kosaki scale.
†MD: mean deviation calculated from the result of Humphrey perimetry. Lens: ones used for corrected visual acuity.

POAG with corrected vision of 1.0 or better. No abnormalities were observed in the anterior segment or the optic media. One eye had a normal-appearing fundus and the other eye had glaucomatous changes, such as an enlarged optic nerve cup and nerve fiber bundle defects.

Kinetic perimetry (Goldmann perimetry) and static perimetry (program 30-2; Humphrey 740 perimetry) were performed on all subjects, and the visual fields showed that 1 eye of each subject was at stage I and the other eye was at stage II on the Kosaki scale.[10] All subjects were using only topical beta-blockers twice daily in both eyes, and eye drops affecting the pupil diameter were not being used.

mfERGs were recorded using the VERIS III™ system (Mayo, Inazawa, Aichi). For stimulation, a pattern of 103 hexagonal elements was chosen, and the mfERGs were displayed on a CRT monitor. The stimulated field had an overall visual angle of 42° × 45°. Each hexagonal element was designed to turn on and off pseudorandomly at a frequency of 75 Hz. The mean luminance of the pattern was 91 cd/m^2 (L_{max} = 178 cd/m^2 and L_{min} = 4 cd/m^2), and the contrast was 95%. The pupil was maximally dilated by topical tropicamide and phenylephrin (Midrin-P®).

A bipolar contact lens electrode (Kyoto Contact, Kyoto) was used after corneal surface anesthesia with oxybuprocaine hydrochloride (Benoxil®) for recording the mfERGs. The ground electrode was placed on the right earlobe. During the mfERG recordings, the subject sat with chin and forehead tightly fixed. The subject was instructed to fixate on a point at the center of the CRT monitor with the eye being stimulated. The other eye was patched. The eye movement during multifocal stimulation was strictly monitored using a routine Veris monitoring system. The distance from the testing eye to the CRT monitor was 32 cm.

The signals were amplified with the 12-4 Neurodata Acquisition System™ (Astro-Med; Grass Instrument Division, West Warwick, RI, USA) with the band-pass filter set at 10–300 Hz. For the comfort of the patient, the 4 minutes required for recording one mfERG were divided into eight sets of 30-second recordings. The responses were displayed as a topographic array using the Power Macintosh 7100/80 computer system. The topographic displays were compared with the results of Humphrey perimetry.

The mfERGs were analyzed by summating different groups of responses: an all-traces response (all visual field groups), a superior and an inferior hemi-field group, and four quadrantic visual field groups. The waves of the second-order kernel were linearly added spatially for each group, utilizing a computer to obtain the waveform for each individual group.

Results

The cases studied are listed in Table 1 showing that 1 eye was at stage I and the other eye was at stage II on the Kosaki scale. The stage was determined from the results of kinetic and static perimetry.

Examples of individual first- and second-order kernels are shown in Figure 1. The second-order kernels (Figure 1 right) of the mfERG were noisy and considerably smaller in amplitude than the first-or-der kernels (Figure 1, left). For a subject who had 1 eye that was normal by kinetic and static perimetry and the other eye abnormal due to early stage glaucoma, the decrease in the response density of either the first-order kernel or the second-order kernel did not correlate with the visual field abnormalities. A right-to-left eye difference in the same subject could

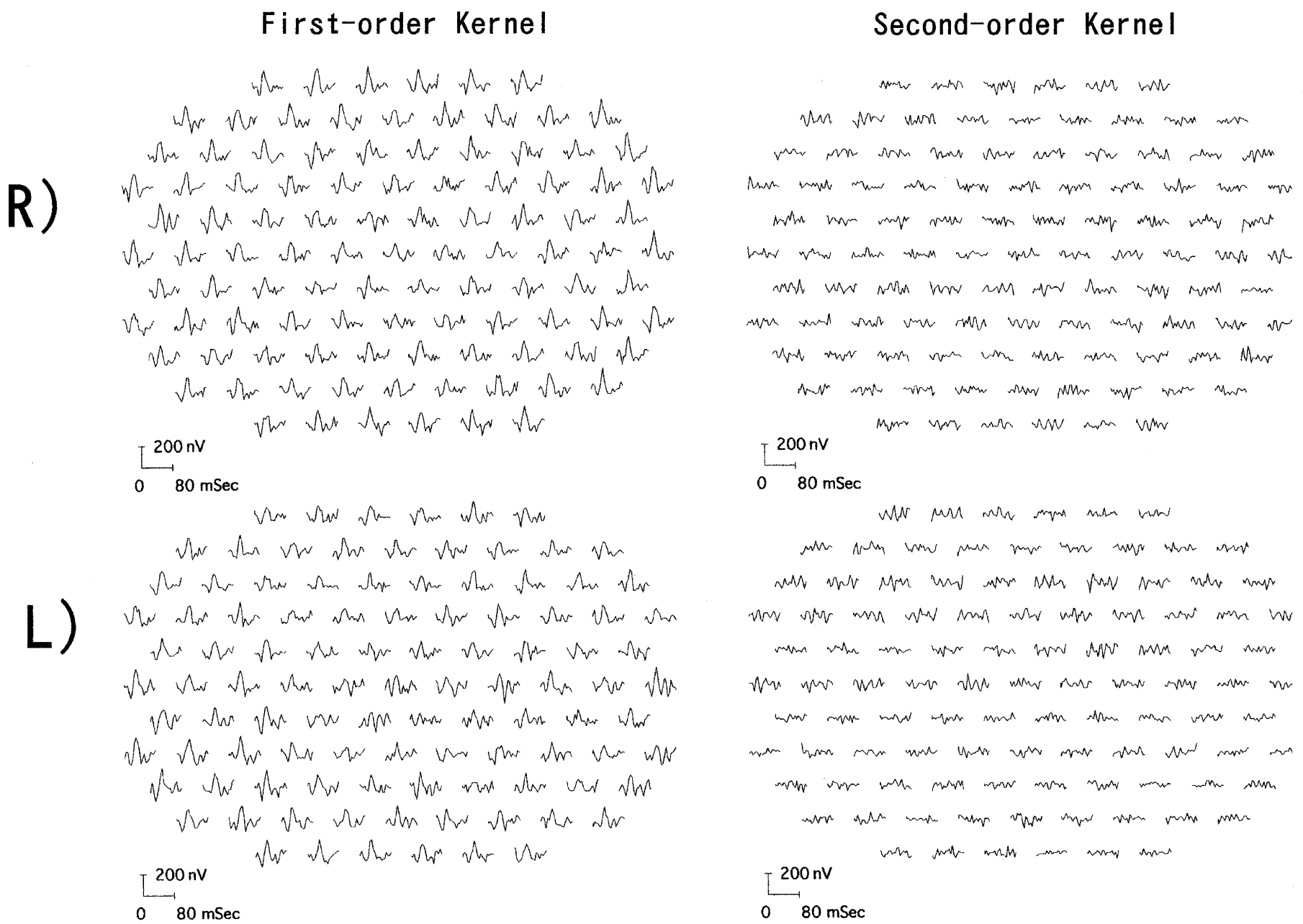

Figure 1. Individual first- and second-order kernel components of the multifocal electroretinogram in case 1.

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Table 2. Mean and SD of the Amplitude and Latency of the Waveform Obtained by Addition of Multifocal Electroretinogram Second-order Kernel Components for All Cases in the Individual Divided Visual Field Group

	Latency (ms)			Amplitude (μV)	
	P1	N1	P2	P1–N1	N1–P2
Whole visual field					
Stage I (n = 12)					
Mean	21.7	28.1	39.1	4.56	4.42
SD	0.8	1.0	3.0	1.12	1.24
Stage II (n = 12)					
Mean	21.7	28.1	39.3	4.78	4.83
SD	0.8	0.7	3.9	1.08	1.48
Superior hemi-visual field					
Stage I (n = 12)					
Mean	22.1	28.2	38.0	2.09	2.09
SD	1.2	1.2	2.0	0.41	0.56
Stage II (n = 12)					
Mean	22.0	28.1	38.1	2.24	2.44
SD	0.8	0.6	2.9	0.51	0.57
Inferior hemi-visual field					
Stage I (n = 12)					
Mean	21.8	28.0	41.1	2.27	2.17
SD	0.9	1.1	2.9	0.64	0.55
Stage II (n = 12)					
Mean	21.5	28.2	40.8	2.33	2.42
SD	0.7	0.7	4.1	0.52	0.61
Superior auricular visual field					
Stage I (n = 12)					
Mean	22.3	28.3	39.1	1.07	1.08
SD	1.6	1.3	3.8	0.22	0.26
Stage II (n = 12)					
Mean	21.9	26.8	36.9	1.14	1.23
SD	2.1	6.0	2.6	0.26	0.31
Inferior auricular visual field					
Stage I (n = 12)					
Mean	21.4	28.7	41.6	1.15	1.18
SD	0.8	1.4	2.9	0.22	0.26
Stage II (n = 12)					
Mean	21.1	28.3	44.3	1.14	1.21
SD	1.4	1.1	4.8	0.31	0.35
Superior nasal visual field					
Stage I (n = 12)					
Mean	22.0	27.7	40.1	1.13	1.22
SD	1.2	1.4	4.2	0.39	0.43
Stage II (n = 12)					
Mean	22.1	28.3	40.7	1.11	1.23
SD	2.1	0.8	3.4	0.31	0.35
Inferior nasal visual field					
Stage I (n = 12)					
Mean	21.9	28.0	39.3	1.18	1.08
SD	0.9	1.0	3.0	0.46	0.32
Stage II (n = 12)					
Mean	22.1	28.0	39.2	1.13	1.18
SD	0.7	0.6	4.5	0.25	0.28

not be detected even when the second-order kernel component was used.

The amplitudes and implicit times of the second-order kernel (Table 2) of the all traces group, the upper and lower hemi-visual field groups, and the four quadrantic field groups (Figures 2 and 3) were not significantly different between the stage I and stage II eyes for all groups.

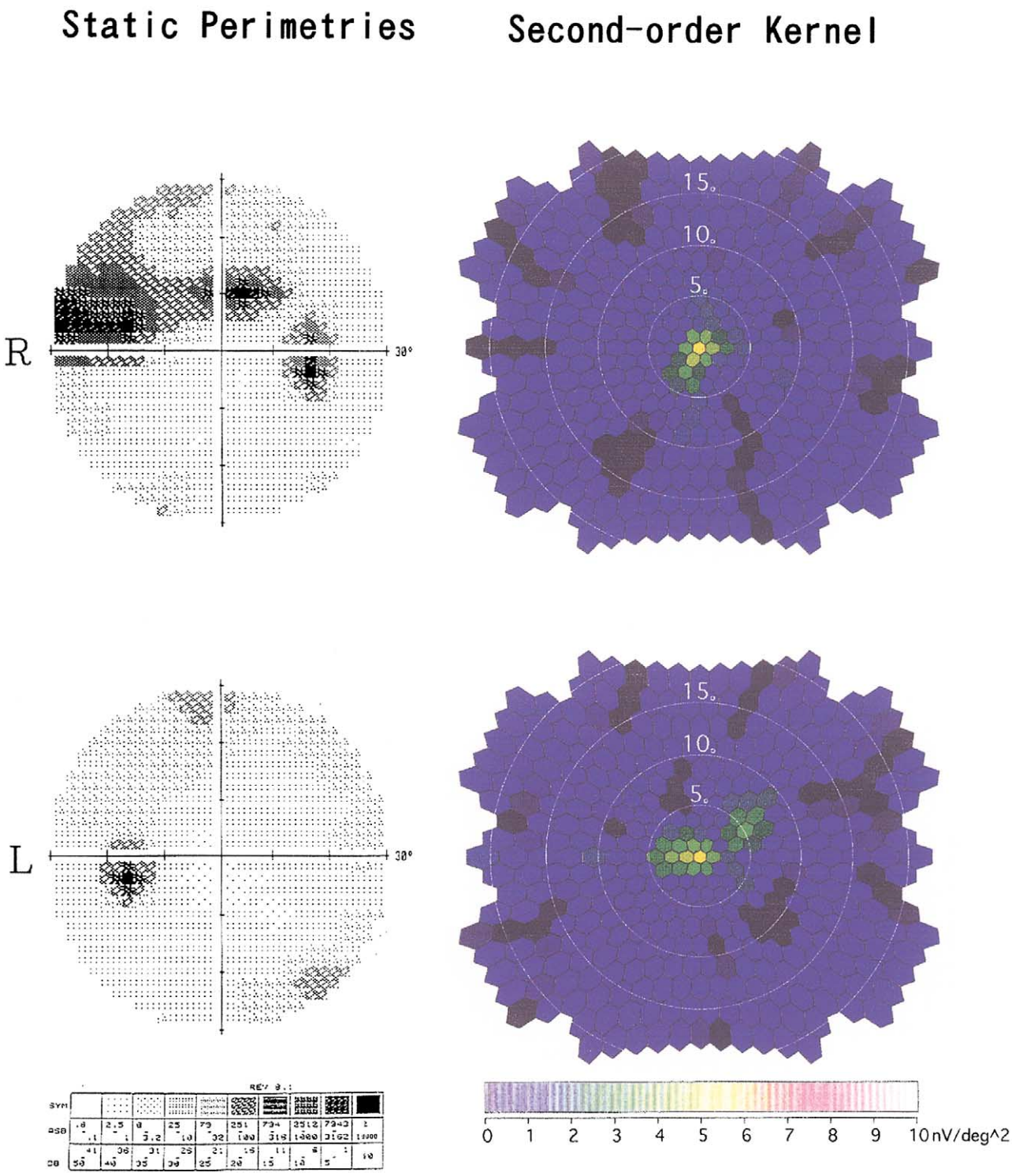


Figure 2. The static perimetric findings and the second-order kernel of the multifocal electroretinogram in case 1.

Discussion

The use of patients with POAG for testing the significance of the differences between stage I and stage II eyes is advantageous because the stage I eyes had virtually no abnormality of the optic media and no visual field abnormality, and thus could be regarded as age-matched control eyes.

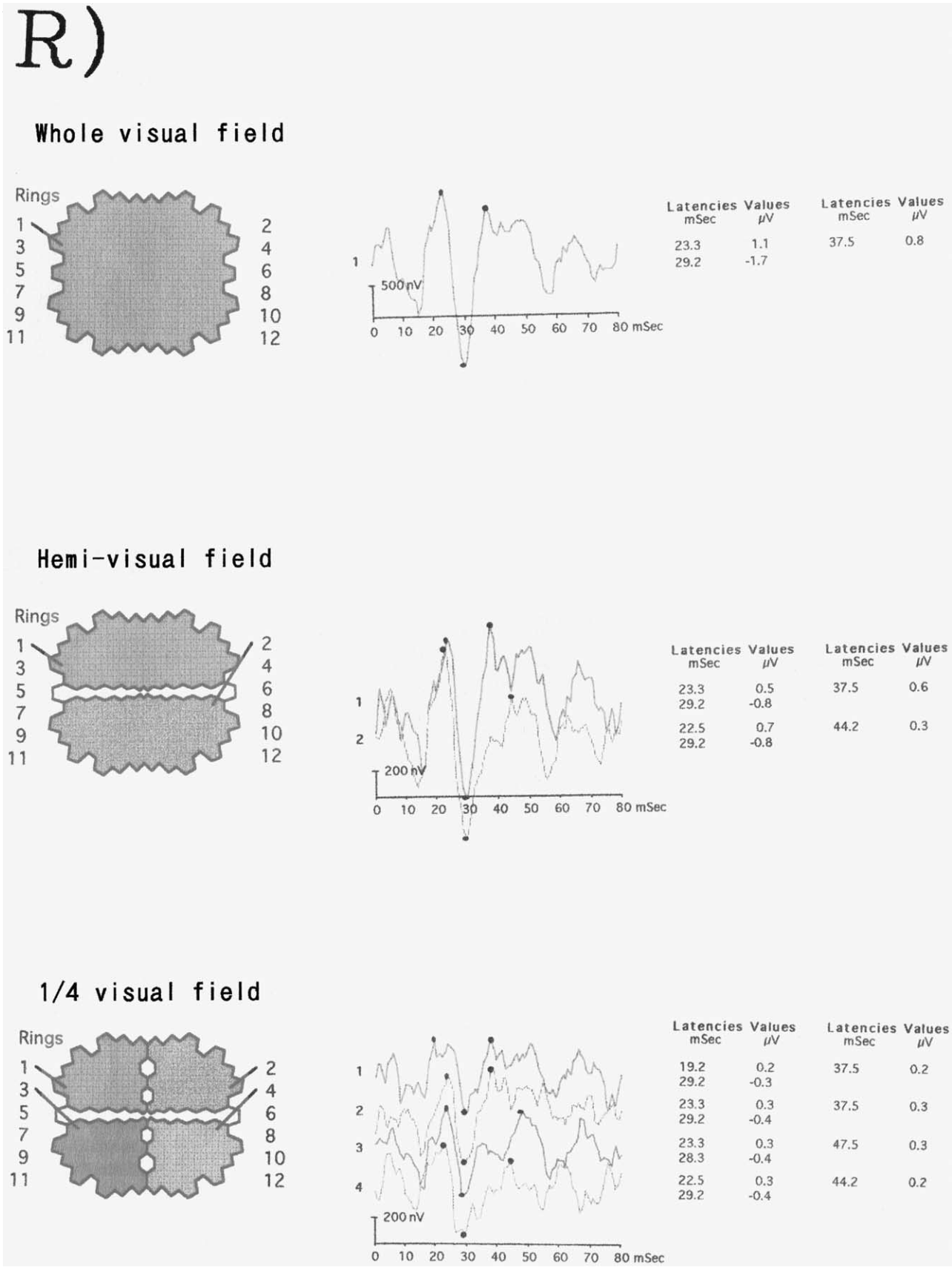
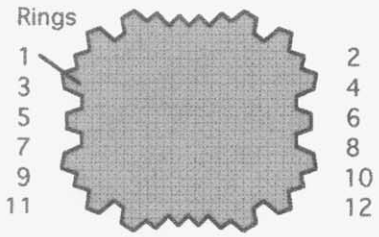
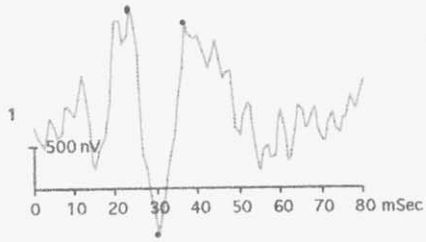


Figure 3. The waveform obtained by adding data on the second-order kernel components in the individual divided visual field groups for case 1, right and left eyes.

L)

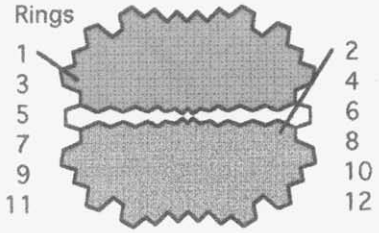
Whole visual field

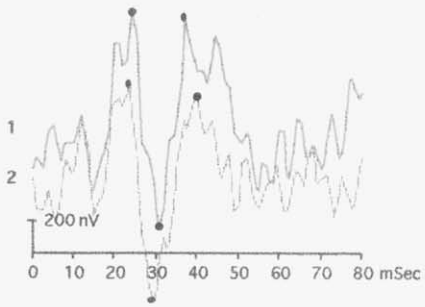




Latencies mSec	Values μV	Latencies mSec	Values μV
23.3	1.2	36.7	1.0
30.0	-1.4		

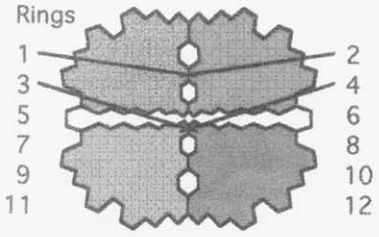
Hemi-visual field

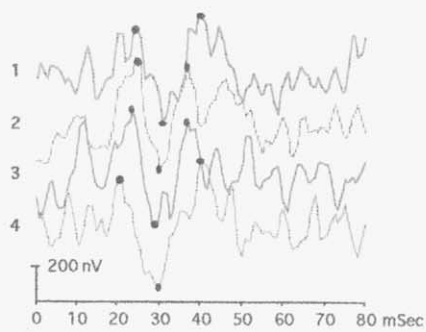




Latencies mSec	Values μV	Latencies mSec	Values μV
24.2	0.7	36.7	0.6
30.8	-0.6		
23.3	0.6	40.0	0.5
29.2	-0.7		

1/4 visual field





Latencies mSec	Values μV	Latencies mSec	Values μV
24.2	0.2	40.0	0.3
30.8	-0.3		
25.0	0.4	36.7	0.3
30.0	-0.3		
23.3	0.4	36.7	0.3
29.2	-0.3		
20.8	0.3	40.0	0.4
30.0	-0.4		

Figure 3. Continued

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The second-order kernel of the mfERGs is a relatively small response, and the individual traces of the second-order kernel are considerably noisy even when the second-order kernel is obtained from a first-order kernel with very low noise and a high response density.[11] In fact, the second-order kernel of stages I and II eyes were almost at the baseline noise level except for the responses from the central retina. A decrease in the response density of the mfERGs could not be detected in the field topographic response which is equivalent to the Humphrey visual field, as reported in our previous paper.[9] Because the individual waves of the second-order kernel were very noisy, the waveforms obtained by spatial linear addition of all-traces, or the several waveforms obtained by adding the individual responses within rings from the center towards the periphery, were used for analysis.[5] A comparison of the summated waves for the different fields showed no significant difference between stage I and stage II eyes. We believe, however, that it is not possible to detect a focal abnormality corresponding to an actual visual field abnormality by this method because the entire retinal region to be added must be spatially linear. Therefore, it is necessary to prove that the waveform obtained by stimulating the entire retinal region simultaneously is identical to the waveform obtained from the all-traces response.

According to previous studies on the generation of PERGs in different clinical cases, PERGs can be considered to reflect well the function of the inner retinal layers when the retinal outer layer is functioning nearly normally. It has also been reported that the P50 amplitude of the PERG recorded from normal subjects by pattern stimulation of nasal/temporal hemi-visual fields showed a significant difference in correlation with the cell density of the retinal ganglion cells,[12] suggesting a correlation between PERG and the function of the inner retinal layers. Holder has recorded PERGs from 72 cases of different types of ophthalmological diseases and reported that the amplitude of the P50 component of the PERG is a good index of retinal dysfunction.[13] In our earlier study of patients with early POAG, no correlation was observed between the PERGs and either the first- or the second-order kernels of the mfERGs. Thus, the second-order kernel of the mfERG was found to have a low possibility of reflecting the function of the ganglion cells. However, the possibility that the stimulating and recording conditions suitable for the analysis of the second-order kernel component may differ from the conditions employed in the present study cannot be ruled out. It is necessary to record mfERGs from healthy subjects under varied stimulating and recording conditions and to investigate whether there are better conditions for obtaining larger amplitude and less noisy second-order kernels.

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