

# Effects of Stimulus Blocking, Light Scattering, and Distortion on Multifocal Electroretinogram

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**Purpose:** To investigate how the multifocal electroretinogram (ERG) is altered in conditions of blocking, light scattering, or distortion of the stimulus that are seen in ocular pathologies.

**Methods:** A central 40°-diameter stimulus pattern consisting of 61 hexagons was presented on a cathode ray tube monitor at a rate of 75 Hz according to the pseudo-random binary M sequence by the Veris computer program. Localized responses corresponding to each hexagon and ERG topographies were displayed on the computer screen. Central scotoma was simulated by blocking the central area of the stimulus, visual field constriction by blocking the outer area of the stimulus, mild cataract by using acrylic filters that caused light scatter, and epiretinal membrane by using a wavy plastic plate that produced metamorphopsia.

**Results:** The responses from the blocked area were nonrecordable whether blockage was central or peripheral; responses from the adjacent unblocked area had a larger amplitude when large areas of the stimulus were blocked. The light scatter that decreased vision from 20/20 to 20/70 did not significantly decrease response amplitudes. Responses from areas in which the stimulus pattern was distorted were minimally affected.

**Conclusions:** The results show that the system records local ERGs from the macula and outside the macula. It can detect the area where the stimulus is blocked. Moderate light scattering and distortion do not cause loss of local ERG characteristics. **Jpn J Ophthalmol 1999;43:481-489** © 1999 Japanese Ophthalmological Society

**Key Words:** Central scotoma, light scatter effect, multifocal electroretinogram, stimulus distortion, visual field constriction.

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## Introduction

Sutter and Tran<sup>1</sup> have recently introduced a multifocal electroretinogram (ERG) system that records local responses from multiple retinal areas and provides ERG topography in fine resolution. This technique, which is based on binary M sequences that record responses from a large number of small retinal areas simultaneously, can detect impaired retinal function in relatively small retinal areas within a short recording time. Kondo et al<sup>2</sup> reported that this technique showed retinal impairment in retinitis pig-

mentosa and branch retinal artery occlusion. Bearse and Sutter<sup>3</sup> reported that the focal ERG was absent in the areas of unmodulated stimuli and depressed in areas of desensitization that were bleached before the recording. These authors also found depression or loss of the ERG in the area corresponding to the fundus anomaly caused by age-related macular degeneration and other fundus diseases.

To interpret the results obtained from patients, it is essential to know how the stimulus parameters that are altered by various ocular diseases affect multifocal ERG responses. For instance, How exactly does the visual field defect affect the ERG topography? How does the light scatter by cataract affect the results? and so forth.

We recorded multifocal ERGs in normal subjects in response to various abnormal stimulus conditions

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such as blocking, light scattering, and distortion of the stimulus.

### Materials and Methods

A 35-year-old man (MA, left eye) and a 27-year-old woman (JF, right eye) served as subjects of this study. Neither subject had any ocular abnormality except for mild myopia.

The stimulus pattern consisted of 61 hexagons generated by the Veris system in a computer system (Power Macintosh 7100/80; Apple, Cupertino, CA, USA) and displayed on a 17-inch cathode ray tube monitor (Multiscan 17se; Sony, Tokyo). The sizes of the hexagons were smallest in the center of the pattern and largest toward the periphery, so that the usually small peripheral responses could be well recognized. The stimulus covered an area  $40^\circ$  in diameter. The luminance ranged from a high of  $92 \text{ cd/m}^2$  to a low of  $2 \text{ cd/m}^2$ , with a contrast of 95.7%. A red dot 3 mm in diameter in the center of the pattern served as the fixation target. The hexagons were presented at a rate of 75 Hz according to the pseudo-random binary M sequence.<sup>1</sup> This stimulus technique makes it possible to record the ERG from the area of the retina that corresponds to each hexagonal element.<sup>1</sup>

In testing, the subject's pupil was fully dilated with 2.5% phenylephrine hydrochloride. A Burian-Allen bipolar contact lens electrode was used with a ground electrode on the left earlobe. The subject was asked to fixate on the red dot. Refractive errors were fully corrected by a lens with a frame placed in front of the eye fitted with the contact lens electrode. The fellow eye was occluded. The total recording time was 4 minutes with an artifact rejection technique. During the recording, the subjects tended to lose concentration and even became sleepy. As a result, the tested eye deviated from the fixation dot. To overcome this problem, the subject was permitted to have a break between the recording sessions. The responses were amplified 100,000 times with bandpass filters of 6 and 100 Hz (Grass, Quincy, MA, USA). The ERGs were recorded five times for each subject to confirm reproducibility.

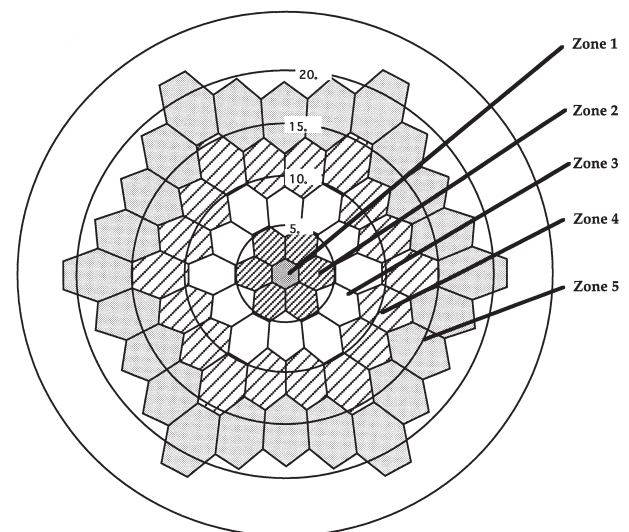
Local responses to each hexagon were extracted from the raw data by cross-correlational computation between the M sequence and the response cycle.<sup>1</sup> The amplitude of each local response was estimated as the dot product of the normalized response template and each local response (scalar product method).<sup>1</sup> The responses were converted to response densities (amplitude per unit of retinal area) and plotted on the computer screen. The ERG color or

gray scale topography in response density was displayed in three dimensions.

### Alteration of Stimulus

**Central scotoma.** The stimulus field was blocked by the masking program in the Veris system to simulate a central scotoma in macular diseases. This simulation of a central scotoma with stimulus blocking has been used previously in recording pattern ERG and visual evoked response (VER) or sweep VER.<sup>4</sup> Blocking a particular area of stimulus or leaving the area unmodulated does not influence data acquisition; namely, the system continues to accumulate the responses from each area of the retina whether certain stimulus areas are blocked or not.<sup>3</sup> The luminance of the blocked area was the same as the mean luminance of the stimulus. We divided the 61 responses into five groups, ie, the central hexagon and four concentric rings, to analyze responses from each area (Figure 1). Starting from zone 1 (the central hexagon approximately  $1.5^\circ$  in radius) and extending to the next larger ring of stimulus (zones 1 and 2 with a  $5^\circ$  radius), the stimulus was covered up to zone 4 ( $15^\circ$  radius), which, therefore, simulated four different sizes of central scotoma.

**Visual field constriction.** Using the same masking program as in the central scotoma experiment, the stimulus field was narrowed by blocking the outer



**Figure 1.** Responses from 61 stimulus hexagons are divided into five groups of concentric rings for analysis. Number on each ring indicates radius of circle, zone 1 having a  $1.5^\circ$  radius.

zones, which simulated a constricted visual field usually seen in eyes with retinitis pigmentosa. A multifocal ERG was recorded using three different stimulus fields, approximately 5° (zones 1 and 2), 10° (zones 1 to 3), and 15° (zones 1 to 4) in radius. Again, the system continued to record from the blocked area even when not stimulating the retina in that area.

**Scattered light effect.** Transparent acrylic sheets, which can induce the scattering light effect when placed in front of the eye, were used to simulate the scattering effect resulting from cataract.<sup>5</sup> Three degrees of light scatter were produced by increasing the number of sheets to 5, 10, or 15. The mean luminance level decreased approximately 37% (0.2 log unit) with 10 sheets.<sup>5</sup> The multifocal ERG was recorded by placing these sheets in front of the tested eye.

**Distortion.** A clear Plexiglas™ plate cut on one surface into a uniform wave-like pattern<sup>6</sup> was placed on the center of the stimulus screen to induce distortion of the stimulus pattern, simulating metamorphopsia in the eye with an epiretinal membrane. The waves of the plate were oriented at 45°, producing alternating enlarged and minimized stimulus hexagons along the waves without defocusing them. This plate covered an area of 20 × 20° in the center of the stimulus pattern.

The work in this study was carried out in conformity with the tenets of the Declaration of Helsinki. The procedures were explained fully to both subjects and informed consent was obtained before the multifocal ERG recordings.

## Results

The ERG responses from the 61 hexagons in the right eye of subject JF contained an initial corneal negative wave followed immediately by a positive wave, referred to as N1 and P1, respectively, as reported by Nagatomo et al<sup>7</sup> (Figure 2, top row, middle). In the ERG topography, a slight depression of the responses was seen in the area of the optic nerve head (Figure 2, top right). The responses from the area of the optic nerve head were recordable because the geometric images of the hexagon stimulus did not fit exactly into the optic nerve head, and more than one hexagon stimulated part of the optic nerve head and part of the adjacent retina.

Table 1 shows the mean amplitudes measured from the trough of N1 to the peak of P1 and the standard deviations in each zone. The standard devia-

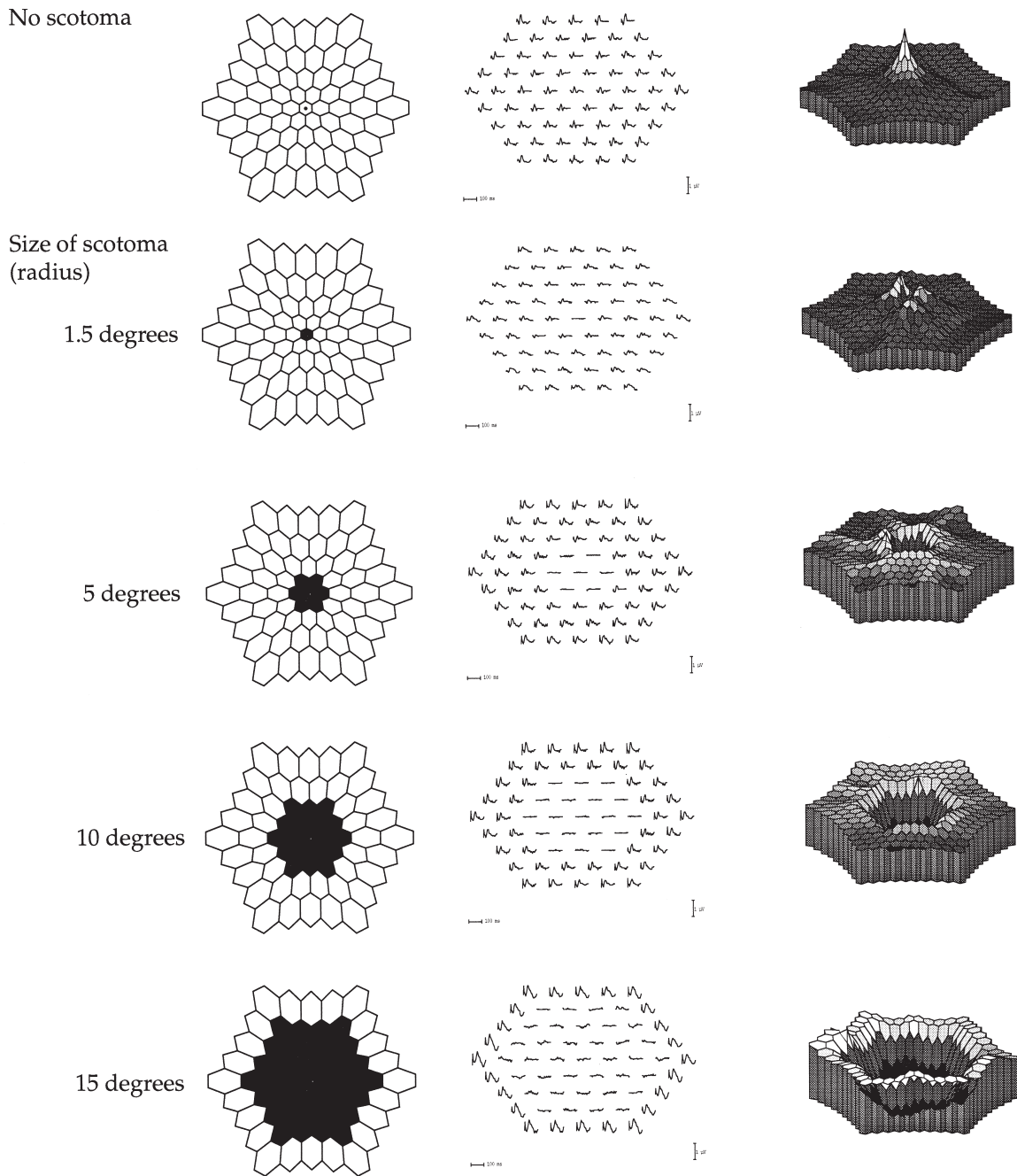
tions were similar to those reported previously.<sup>2,7</sup> The results indicate relatively good reproducibility in the same subject, although the values differed between subjects.

### *Alteration of Stimulus*

**Central scotoma.** Central scotoma in the stimulus field, the trace arrays, and ERG topographies are shown in Figure 2 (rows 2–5). Responses from the simulated scotoma were nonrecordable in the presence of scotoma of any size. The ERG topography showed a chopped central peak when only the central hexagon was blocked. As the scotoma enlarged, the depression in the center of the ERG topography also enlarged. In subject JF, the mean amplitude of the ERG from zone 5 with the remainder of the zones blocked was 29.0 nV/deg<sup>2</sup>, which was much larger than that of the responses from the same zone without the central area blocked. No significantly enlarged responses from the outside area were found when the small central area of the stimulus was blocked. The responses did not enlarge when the central portion of the stimulus was blocked in subject MA.

The recordings were performed in one subject (MA) by actually covering the portions of the stimulus field with black paper instead of electronically blocking the fields. The results are indicated in Figure 3. Upper recording indicates that zones 1 and 2 were blocked and the lower recording indicates that zones 1, 2, 3, and 4 were blocked. The responses from the area covered by black paper were nonrecordable and those from the unblocked area showed no significant changes compared with the results in the same subject when the stimulus fields were blocked by the system used in this study.

**Visual field constriction.** Figure 4 shows the changes of the stimulus field, the array of responses, and ERG topography. Responses were recorded only from the uncovered areas with every size of stimulus. The shapes of waveforms in this experiment were somewhat different from those of the central scotoma experiments especially in the upper two arrays of responses (Figure 4), showing broader positive waves with some having double peaks, instead of a spiky single peak. When zones 1 and 2 or zones 1, 2, and 3 were stimulated there was no central peak in the ERG topography because all the recordable responses from the edge of the field became very large in both subjects. The mean amplitudes from zones 1 and 2 were 47.2 nV/deg<sup>2</sup> (subject MA) and 89.1 nV/deg<sup>2</sup> (subject JF) compared with 30.3 and



**Figure 2.** Left column: Stimulus patterns of normal (no scotoma) multifocal electroretinogram (ERG) stimulus field (recording) (top) and simulations of central scotoma of various degrees. Middle column: Array of responses from 61 hexagons in response to normal stimulus field without scotoma and with different scotomata from subject JF. Only blocked areas produced nonrecordable ERGs. Right column: Three-dimensional ERG topographies. Central hole-like depressions correspond to the blocked areas.

50.2 nV/deg<sup>2</sup>, respectively, from the same central area without blocking the peripheral field. The mean amplitudes from zones 1, 2, and 3 were 28.9 (subject MA) and 54.5 nV/deg<sup>2</sup> (subject JF), compared with

22.4 and 36.4 nV/deg<sup>2</sup>, respectively, in the normal stimulus field without peripheral blockage. The ERG topography showed a tower-like shape in these narrowed stimulus fields in both subjects. When only

**Table 1.** Mean Amplitudes Per Square Degree (nV/deg<sup>2</sup>) From Five Electroretinograms From Five Stimulus Zones in Both Study Subjects

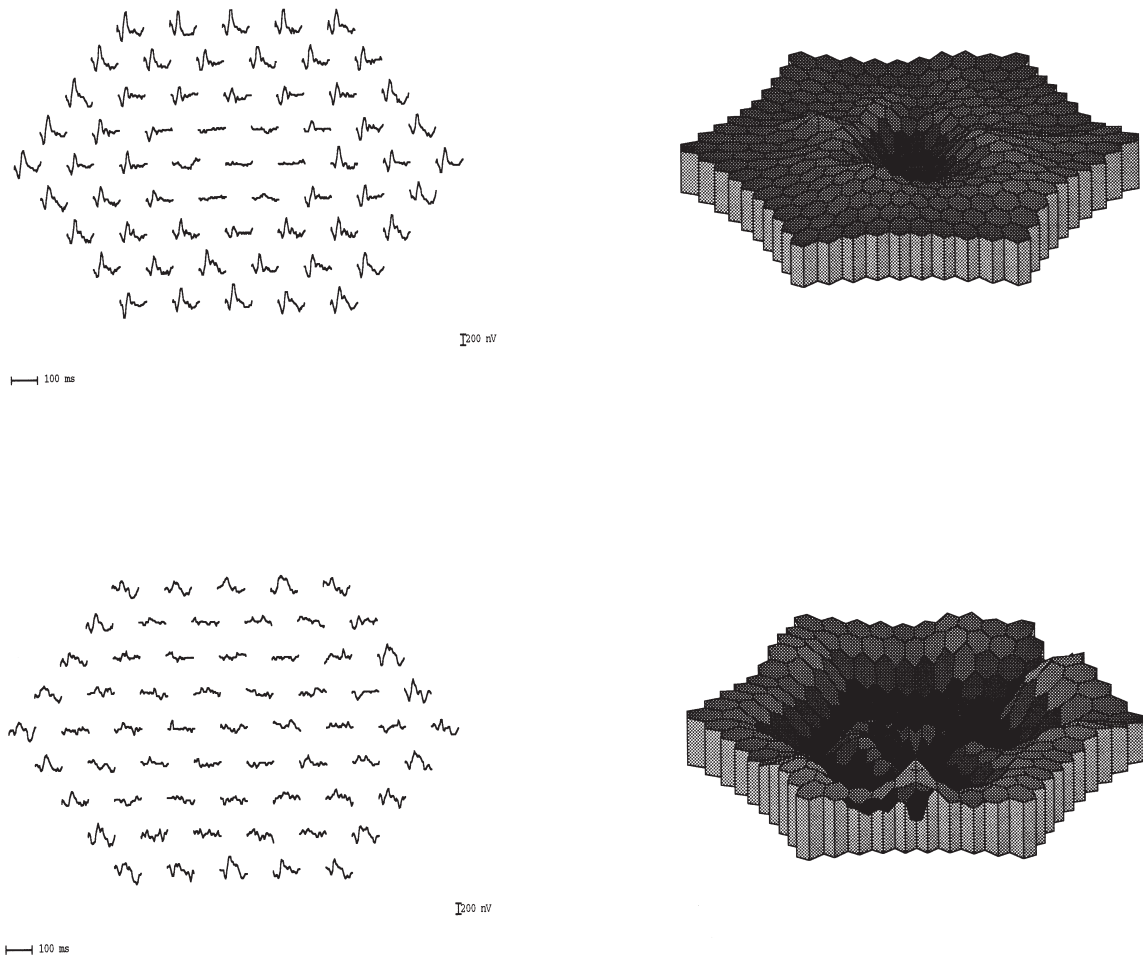
Subject	Zone				
	1	2	3	4	5
MA	47.4 (10.5)	26.6 (3.4)	18.4 (3.3)	14.3 (1.5)	13.3 (1.5)
JF	84.0 (21.3)	45.3 (7.9)	28.9 (6.4)	21.5 (4.5)	19.2 (3.5)

Values in parentheses are standard deviations.

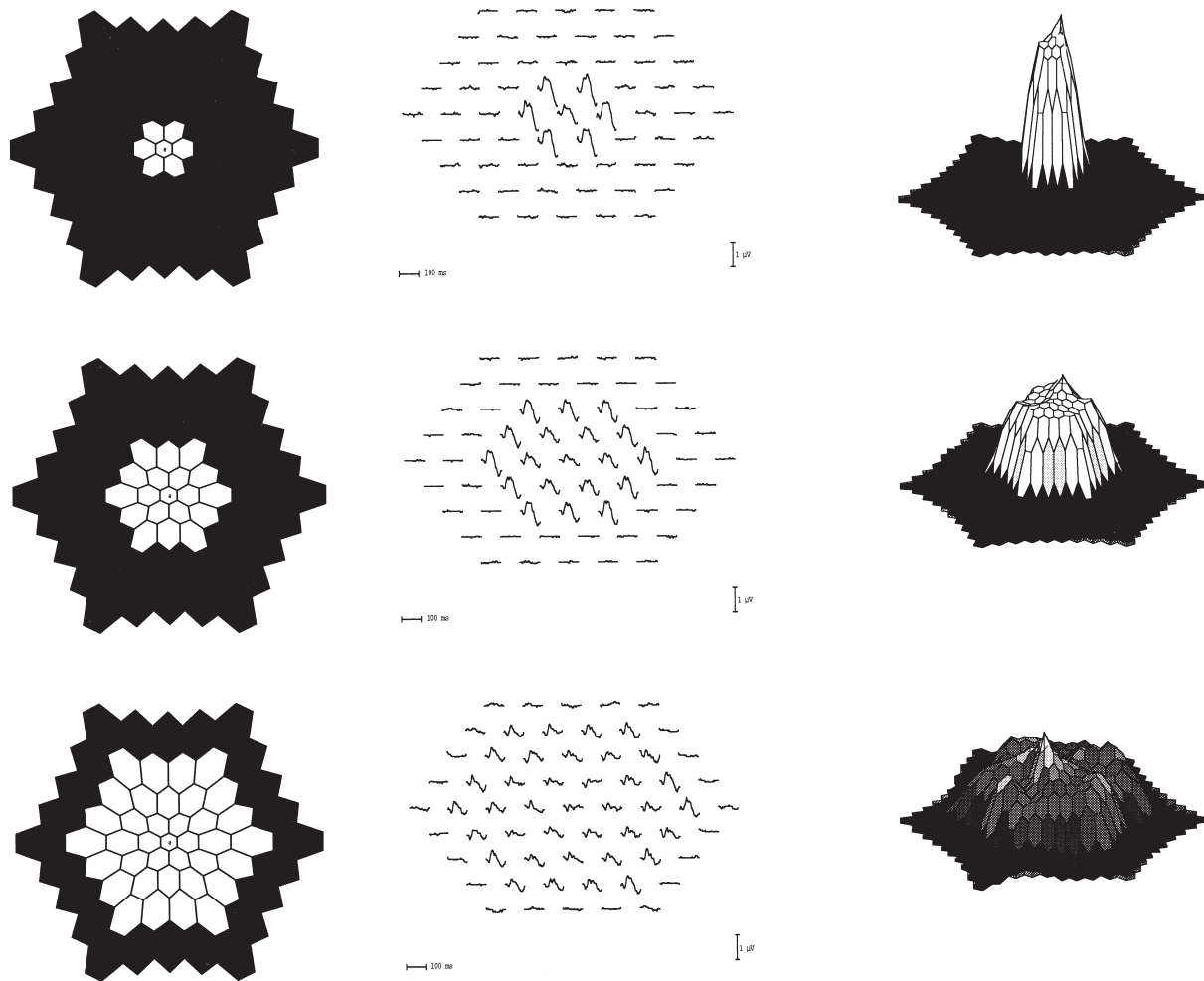
the outer ring was blocked, there was no significant difference in the amplitudes between the blocked and unblocked conditions in both subjects.

**Scattered light effect.** The visual acuity declined to 20/30 in both subjects with 5 acrylic sheets placed in front of the eye, to 20/70 with 10 sheets, and to 20/

125 with 15 sheets. The mean luminance of the stimulation decreased to 30 cd/m<sup>2</sup> with 5 sheets, 20 cd/m<sup>2</sup> with 10 sheets, and 17 cd/m<sup>2</sup> with 15 sheets, and the contrast was 83%, 70%, and 58%, respectively. Table 2 shows the amplitudes from each condition in both subjects. A slight decrease in amplitude was observed from the central areas when 5 acrylic sheets were used. Figure 5 shows the array of responses and ERG topographies with 5, 10, and 15 translucent acrylic sheets, respectively. There was a central peak that was slightly reduced in height in each condition, and the responses from the perimacular and peripheral areas were slightly reduced. There were variations between the two subjects in the results with an increase of acrylic sheets. In subject MA, the amplitude decreased in the central zone when the number of sheets was increased from 10 to 15, but in subject



**Figure 3.** Left: Arrays of responses. Right: Three-dimensional electroretinogram topographies. Recording performed by actually covering portions of stimulus field with black paper in one subject (MA). Top: Zones 1 and 2 were covered. Bottom: Zones 1, 2, 3, and 4 were covered. Responses are recordable in uncovered areas and showed no significant change compared with blocking the stimulus electrically by the Veris system.



**Figure 4.** Left column: Stimulus pattern blocked in periphery. Middle column: Array of responses corresponding to blocked stimulus fields shown on left. Those from blocked areas are nonrecordable. Responses from unblocked areas tend to enlarge. Right column: Three-dimensional electroretinogram topographies show tower (top) or butte (middle) configuration.

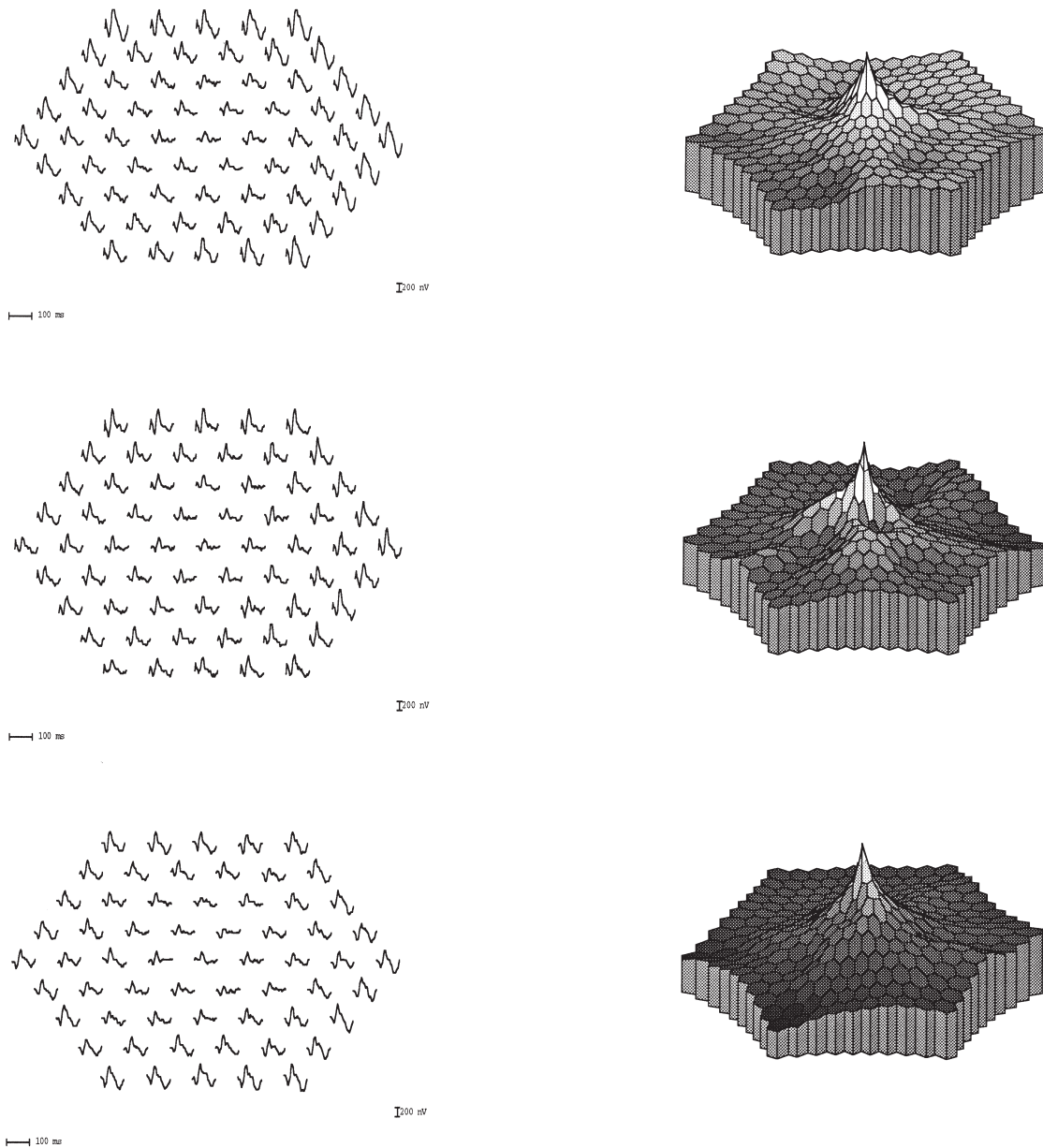
**Table 2.** Amplitudes (nV/deg<sup>2</sup>) From Each Zone Under Four Recording Conditions With Light Scatter in Each Subject

Subject	No. of Sheets	Zone				
		1	2	3	4	5
MA	0	47.4	26.6	18.4	14.3	13.3
	5	40.6	22.5	16.1	12.5	11.0
	10	41.1	21.1	16.2	12.8	12.5
	15	29.7	17.3	17.1	14.5	13.4
JF	0	84.0	45.3	28.9	21.5	19.2
	5	61.2	39.5	29.1	24.0	23.5
	10	56.2	33.7	24.8	19.9	18.7
	15	60.1	38.4	31.1	24.4	20.2

JF amplitude did not decrease. However, the general configurations of the three-dimensional topography was maintained with the central peaks always present (Figure 5). Responses from the periphery (zones 3, 4, and 5) were not much reduced by these acrylic sheets.

**Distortion.** Responses were recordable even from the area distorted by Plexiglas™, although the responses from the area fluctuated (Figure 6). Relatively large responses and small responses were found along the wave of the Plexiglas™ in the trace array. The responses from the magnified area tended to be larger, and those from the minimized area smaller. Even with these response fluctuations, the



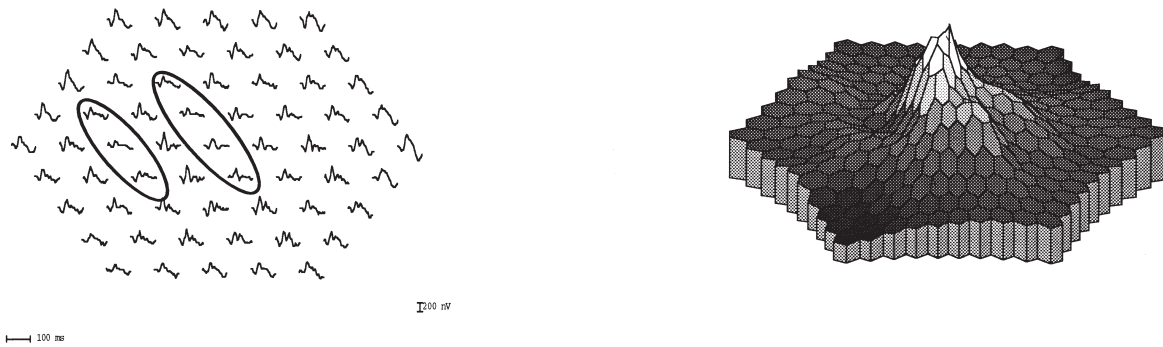


**Figure 5.** Left: Arrays of responses. Right: Three-dimensional electroretinogram (ERG) topographies, from top, with 5, 10, or 15 transparent acrylic sheets, respectively, placed in front of tested eye. Responses are all recordable and central peaks in ERG topography are shown in three recording conditions.

ERG topography showed a central peak. However, this peak was not as sharp as that under normal recording conditions without distortion, and was surrounded by some upheavals and depressions resulting from these fluctuations in the responses. Responses from all zones were observed, and those from the central hexagon decreased in both subjects (Table 3).

## Discussion

Some successful attempts had been made in the past to record the ERG from the local peripheral retina by stimulating each small retinal area individually.<sup>8</sup> However, as the peripheral responses were small and time required to accumulate the responses was long, ERG topography had never become a clinical reality. Sutter and Tran<sup>1</sup> ingeniously overcame



**Figure 6.** Left: Array of responses. Right: Three-dimensional electroretinogram (ERG) topography with distorted stimulus patterns. Responses in circles in array are from stimulus elements minimized by Plexiglas™ and are smaller than adjacent responses. Although responses along wave of Plexiglas™ fluctuated, they were all recordable and produced central peak in ERG topography.

this shortcoming by stimulating the multiple areas of the retina randomly at the same time and successfully accumulated the responses generated in each part of the retina in a relatively short period of recording time. They also proved that the recordings were coming from the local area by demonstrating that the responses became smaller when the retinal area was desensitized by pre-exposure to light. The multifocal ERG responses also became smaller in the area of scotoma in patients with field defect resulting from retinal abnormality.<sup>3</sup> The method appears to have some potential clinical value. However, to interpret the results obtained from patients, it is helpful and important to know the effects of various parameters, such as those used in our study on this multifocal ERG system.

Our results indicate that the blocked stimulus areas correspond to the unstimulated retinal areas, which produced no responses, being well isolated from the stimulated area that produced the responses. Blocking a certain area of stimulus does not influence the data acquisition process; namely, the system continues to accumulate the responses from the nonstimulated area as well as stimulated area.<sup>3</sup>

**Table 3.** Response Amplitudes (nV/deg<sup>2</sup>) From Central and Paracentral Areas Where Stimulus Image Was Distorted

Subject	Zone				
	1	2	3	4	5
MA	39.0	24.1	16.6	12.9	11.3
JF	52.5	37.5	24.3	16.5	12.2

Since the same results were obtained by covering a part of the stimulus field with black paper, nonrecordable ERG from the blocked area really indicates that this system did not pick up any responses from the blocked area. The timing of stimulus hexagon is different between the blocked area and unblocked area because the response from each location is recognized by a temporal encoding of the light that stimulates each hexagon. Even though this blocking experiment may not simulate a real scotoma resulting from macular degeneration, the multifocal ERG would detect the location and extent of dense scotoma or visual field defect caused by retinal abnormalities such as epimacular hemorrhages.

In the present study, the blocked areas did not affect the responses from the unblocked area when the blocked area was small. However, blocking a larger part of the stimulus field resulted in larger response amplitudes from the unblocked retinal areas. We do not know if this phenomenon is due to the biological nature of the retina—the responses from the normal retina are enhanced by the neighboring nonfunctional retina—or if this is purely a result of the stray light effect, that is, the scattered light from the unblocked areas of stimulus stimulated the blocked area of the retina by scattering. This would make the responses from the unblocked area larger in spite of maintaining the luminance at the blocked area the same as the mean luminance of the entire screen. The scattered light cannot be completely eliminated even though the luminance outside the stimulus pattern on the screen is also maintained at the same luminance as the mean luminance of stimulus. The responses may be too small to affect the response from each element because the response per unit is very



small in the peripheral retina. On the other hand, the responses to the scattered light may be large enough to affect the result when the blocked area is within the stimulus field where sufficient responses are regularly recordable. Then what happens in actual disorders such as age-related macular degeneration or retinitis pigmentosa? For instance, no increase in responses was reported from the residual functioning retinal area in retinitis pigmentosa<sup>2</sup> or macular degeneration.<sup>9</sup> However, the responses were compared with those for other normal individuals. It is quite possible that the area that does not have field defect may not be entirely normal, so no enhancement of ERG responses would occur.

Regarding cataract simulation, Tetsuka et al<sup>5</sup> reported that the pattern reversal visual evoked responses (PVER) became abnormal when three acrylic sheets used to create the light scatter were placed in front of the eye although the visual acuity remained normal. Those authors cautioned about interpreting PVERs recorded in patients with a mild cataract and relatively good vision. In contrast, our results using the same acrylic sheets showed only a slight decrease in the amplitudes of responses from the central areas even with 10 acrylic sheets, which decreased the visual acuity to as low as 20/70. These findings appear to suggest that the multifocal ERG is not as sensitive to the light-scattering effect as the PVER, and the presence of a mild nuclear sclerosis of the lens may not be a concern when an elderly patient undergoes ERG testing for evaluation of retinal topography.

Simulating the visual phenomena resulting from the epiretinal membrane is complex. The membrane may have light-filtering, scattering, and defocusing effects, besides image distortion or metamorphopsia. The distortion of the stimulus did not affect the responses drastically. Only the amplitudes of the responses from the area where the stimulus pattern was distorted fluctuated, but they were recordable. These findings suggest that the multifocal ERG test result might indicate whether the retina beneath the epiretinal membrane is functioning or not, and may

be helpful in predicting potential recovery of vision after the membrane is surgically removed.

Our results appear to further support the theory that this system records the local ERG not only from the macula but also from outside the macula. The results also showed that mild scattered light or distortion did not cause the ERG to lose its local electrophysiologic features and this technique might be helpful to evaluate retinal function behind an epiretinal membrane.

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