A trial of objective visual field measurement by pupillary reaction

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ABSTRACT We created pupil perimetry that could objectively analyze the visual fields utilizing the light reflex with the Visual Evoked Response Imaging System (VERIS).

Nineteen hexagonal stimulating elements were used to stimulate up to 15 degrees of eccentricity at 2 Hz. The evoked light reflex was recorded by the infrared camera, and the changes in the maximum transverse diameter of the pupil were measured using a pupillometer. Then, the amplitude of the light reflex evoked by local retinal stimulation was calculated using VERIS Science 4.1.

The variation coefficient of the light reflex was the smallest in healthy individuals and its amplitude was greatest when white-black stimuli were delivered with an indoor luminance of 5 asb. Therefore, this was established as the optimal testing condition for the present perimetric system. In patients with visual field defects, the amplitude of the light reflex at areas of visual field loss was significantly smaller than that at normal areas, but minute defects could not be detected.

Pupil perimetry utilizing VERIS could objectively analyze the visual fields, but the size of the stimulated field must be expanded and the resolution must be improved before it can be used clinically.

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Key words : **Objectively , Visual field , Pupil perimetry , Visual evoked response imaging system**

INTRODUCTION

Since all current perimetric techniques rely on subjective responses, their reliability is low when the test subjects are small children, uncooperative, or cannot follow directions. In some of these cases it may be difficult to analyze test results. To solve this problem, various experiments have been performed to objectively analyze the visual fields. To date, development of the following objective perimetric techniques has been reported, but none of them has been accepted widely: pupil perimetry consisting of an automatic perimeter and an infrared pupillometer[1－5], multifocal electroretinography (ERG)[7－10] utilizing the Visual Evoked Response Imaging System (VERIS) introduced by Sutter *et al.*[6], multifocal visual evoked potential (VEP)[11－14], and pupillary response[15]. Herein, we describe a pupil perimetric method that we developed which could objectively analyze the visual fields by recording the pupillary light reflex using VERIS.

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No major modifications to the existing hardware were necessary and the commercially available software, Veris Science, could be used. Pretreatment was unnecessary and the testing procedure was less invasive than other methods. We used this perimetric system to examine and compare the visual fields of healthy individuals and patients with visual field defects.

SUBJECTS AND METHODS

Subjects

The pupil field of the right eye of 22 healthy individuals, 12 men and 10 women with an average age of 38.0 years (range: 22-67 years), was analyzed. These subjects had neither ophthalmological diseases, except for errors of refraction, nor systemic diseases that could affect their eyes. Errors of refraction ranging between -5 diopters and +5 diopters were correctable using the lens in the infrared camera, and subjects with errors of refraction exceeding this range were excluded from the present study.

Next, to confirm the differences in the test results of the healthy individuals and patients with visual field defects and to clarify the relationship between the present perimetric method and conventional subjective perimetry, the pupil field of 11 patients with visual field defects, 9 men and 2 women with an average age of 55.5 years (range: 14-79 years), was analyzed. The breakdown of causes of visual field defects was as follows: five patients had cerebral tumors, one had cerebral hemorrhage, one had cerebral infarction, one suffered a head trauma, one had anterior ischemic optic neuropathy, one had subretinal hemorrhage, and one had branch retinal vein occlusion. These patients had relatively large visual field defects, such as hemianopsia, quadrantanopsia and central scotoma.

Patients who were taking drugs that could affect their pupils and those with a past history of ophthalmological surgery were excluded from the present study.

Pupil perimetry

As shown in Fig. 1, we attached an infrared camera (E.D.I. refractor /camera: Electro-

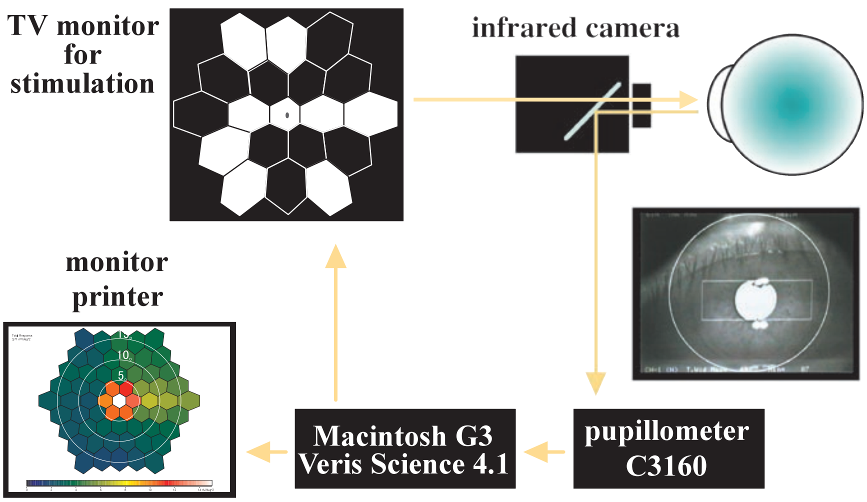

Fig. 1. Summary of pupil perimetry
Through the use of a television monitor, 19 hexagonal elements were shown on the screen. Each test subject was then asked to look at the screen through an infrared camera. The amplitude of the pupillary light reflex evoked by the local retinal stimulation was measured by an pupillometer, and then expressed as two- and three-dimensional topographic images using Veris Science 4.1.

Diagnostic Imaging, Inc., San Mateo, CA, USA) and an electropupillometer (C3160: Hamamatsu Photonics Inc., Hamamatsu, Japan) to VERIS III (MAYO Corp., Inazawa, Japan). Veris Science 4.1 software (E.D.I. Inc. San Mateo, CA, USA) was used to control a series of perimetric procedures (i.e., stimulation, recording and analysis). Using a CRT monitor (QB 1781: Chuo Musen Inc., Tokyo, Japan), hexagonal stimulating elements were projected onto the screen by choosing the option of "hexagon 19", which is preregistered in Veris Science 4.1. This particular stimulation condition was chosen because it could be done more quickly. Although resolution is better when more elements are used, the test takes longer to complete and the noise becomes greater. Also, to obtain a sufficient pupillary light reflex in the periphery, the area of elements was small in the center and large in the periphery (the area ratio of stimulating elements along the horizontal diameter = 26.476 : 37.88 : 53.312). Each element was designed to reverse light-to-dark by the binary M sequence, and a small gray fixation point was placed in the center of the stimulated field. Since the latency of the light reflex was about 250-300 msec, the stimulation frequency was made slightly longer at about 2 Hz (427 msec) to stimulate the visual field up to 15 degrees of eccentricity. To suppress blinking, anesthetic eye drops were placed in both eyes, and an eye patch was placed over the left eye. Then, the head of each subject was fixed so that the distance between the monitor and the eye was 38 cm (each subject looked at the monitor through the infrared camera equipped with a plus lens. Since its magnification was 1.28, the head was placed 49 cm away from the monitor). Errors of refraction ranging between -5 diopters and +5 diopters were corrected using the other plus lens in the infrared camera without affecting the image magnification on the retina. Based on the pupillary light reflex evoked by retinal stimulation, the maximum transverse diameter of the pupil was calculated using the pupillometer. The amplitudes of the light reflex were calculated using VERIS Science 4.1, and shown as topographic images. When assessing the visual fields, to make it easier to visually identify mild reductions in amplitudes, "refined mode" topography was used (topographic images were created using the mean values between two elements to increase the number of elements). A total of eight measurements were made, and since each measurement took 30 seconds, the entire test required about four minutes. The test subjects took a short break between each two successive measurements. A measurement was repeated if any noise, such as eye movement or blinking, was observed more than two times within a 30-second period.

Informed consent was obtained from each subject prior to the start of the study.

Determining the optimal testing condition for the present perimetry

Initially, perimetry was performed on the healthy individuals to determine the optimal indoor luminance. By fixing the stimulating element at white (100 cd/m^2) - gray (20 cd/m^2), the indoor luminance varied: light, 5 apostilb (asb: It is the brightness of a perfectly diffusing surface reflecting or emitting one lumen per square meter), or dark. Subsequently, to determine the optimal brightness of the stimulating elements, the indoor luminance was set at 5 asb, and brightness varied: high contrast = white (100 cd/m^2) - black (0.09 cd/m^2), and low contrast = white (100 cd/m^2) - gray (20 cd/m^2). As shown in Fig. 2, the amplitudes and variation coefficients of the light reflex at the central, intermediate and peripheral regions were calculated to ascertain the optimal testing condition.

Analysis of the pupil field of patients with visual field defects

Under the optimal testing condition established

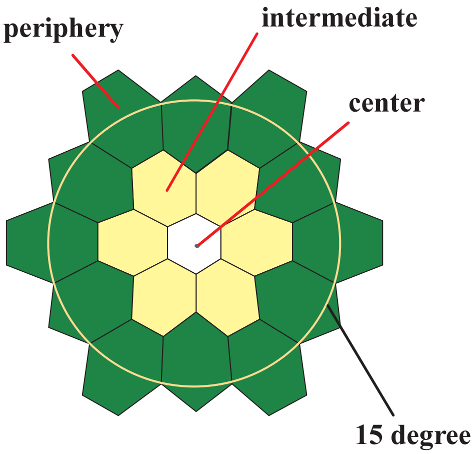

Fig. 2. The visual field up to 15 degrees of eccentricity was divided into three regions (central, intermediate and peripheral regions) to determine the amplitude and variation coefficient of the light reflex in each region.

based on the results of the previous preliminary experiments, the pupil field of the patients was analyzed.

RESULTS

Optimal testing condition

The amplitudes and variation coefficients of the light reflex in the central, intermediate and peripheral regions were calculated under three indoor luminance settings. The amplitude of the light reflex was the largest in all regions with indoor luminance of 5 asb (Fig. 3a). The variation coefficient of the light reflex was also the smallest in all regions with indoor luminance of 5 asb (Fig. 3b).

Next, the relationships between the brightness of stimuli and the amplitudes and variation coefficients of the light reflex were examined. The amplitude was greater in all regions when the contrast was high (white-black) than when it was low (white-gray) (Fig. 3c). Also, even though there were no

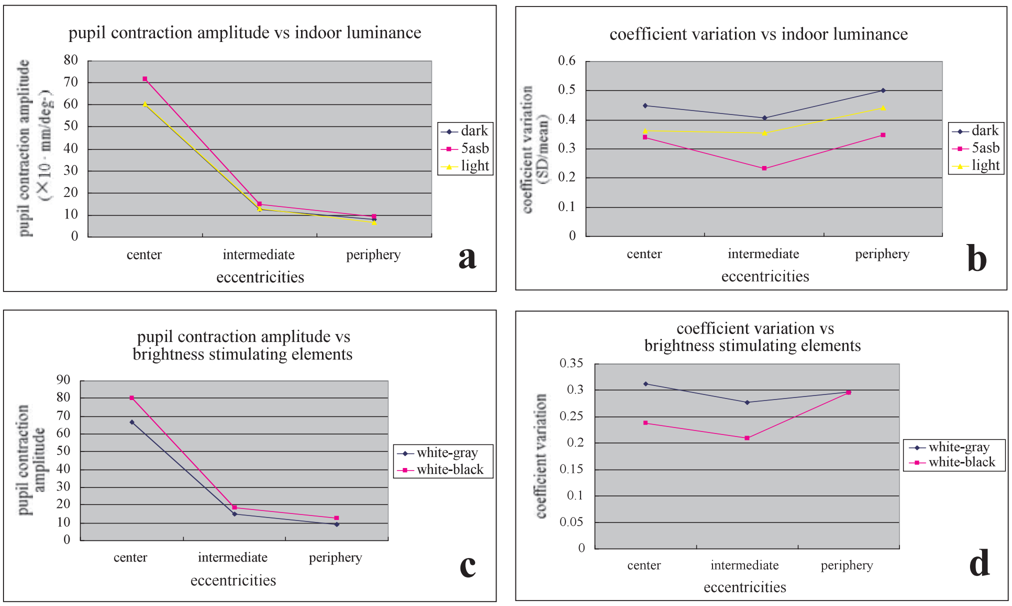

Fig. 3. Differences in the amplitude and variation coefficient of the light reflex in terms of eccentricity.
Comparison of the amplitude (a) and variation coefficient (b) of the light reflex under different indoor luminance settings.
There were no marked differences among the three luminance settings, but the amplitude of the light reflex was the greatest with the luminance of 5 asb, and the variation coefficient was the smallest with the luminance of 5 asb, even though it was fairly high at 20-40%.
Comparison of the amplitudes and variation coefficients under two brightness settings.
As was the case with indoor luminance, there were no marked differences between the two settings, but the amplitude was high and the variation coefficient was low when white-black stimuli were used.

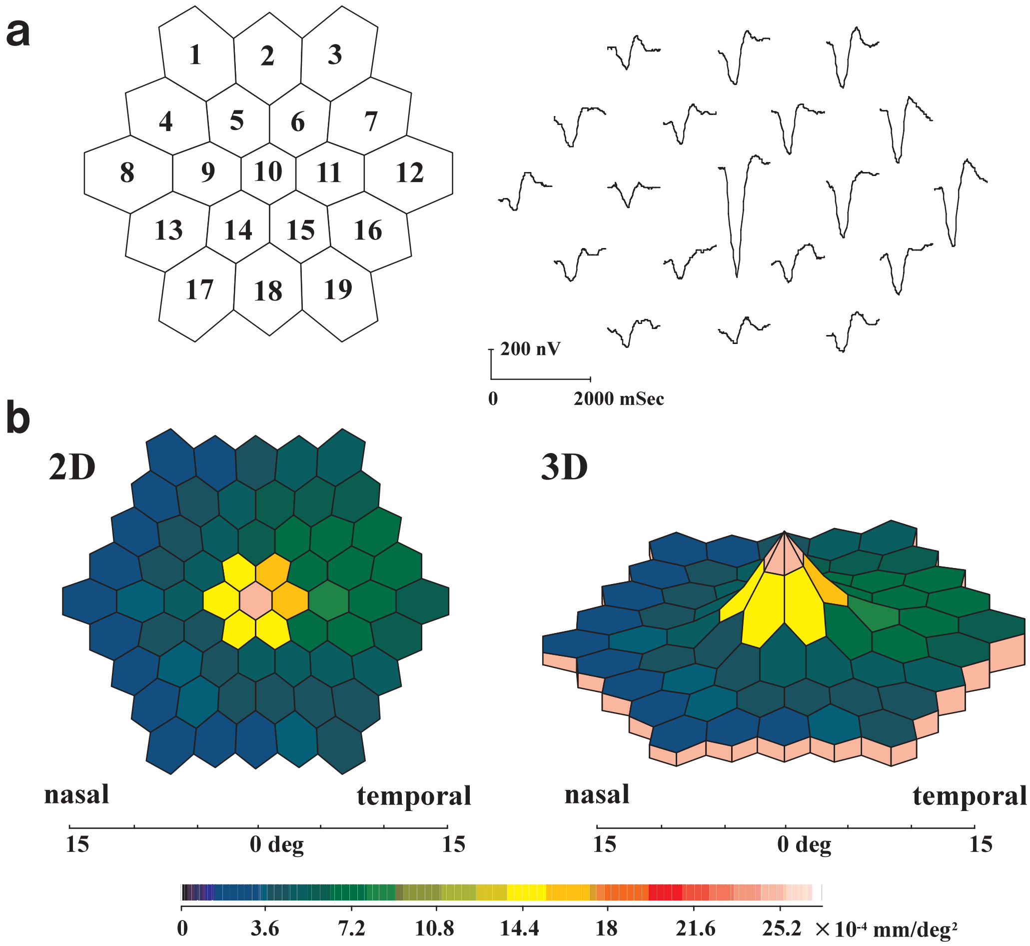

Fig. 4. The pupil field of the right eye of healthy individuals
a: A Trace Array display of the pupillary light reflex of healthy individuals.
This shows the average waveforms of 19 light reflexes that were generated when the retina was stimulated locally by hexagonal elements by the binary m sequence.
b: Two and three-dimensional topographic images of healthy individuals.
Black indicates a small amplitude and white a high amplitude. In the healthy individuals, the amplitude was the greatest at the central region, and became smaller as it moved toward the periphery. Since up to about 15 degrees of eccentricity was stimulated, Mariott blind spots were undetectable. Among the four quadrants, the amplitude was the greatest in the upper temporal quadrant and the smallest in the lower nasal quadrant.

significant differences in the variation coefficient in the peripheral region, it was smaller in the central and intermediate regions when the contrast was high (white-black) (Fig. 3d).

However, there were no statistics significant difference in these results, because the light reflex was large and the variation coefficient small, the indoor luminance of 5 asb and the brightness of white (100 cd/m^2) - black (0.09 cd/m^2) were established as the optimal testing condition. The subsequent tests were performed under this condition.

Pupil fields of the healthy individuals (Fig. 4)

The pupil fields of the right eye of the 22 healthy individuals were analyzed, and the average amplitude of 19 light reflexes were recorded (Fig. 4a). Based on their waveforms, two- and three-dimensional topographic images were then prepared (Fig. 4b). The amplitude was the greatest at the center, and became lower is the amplitude moving toward the periphery. Also, among the four quadrants, the amplitude was the greatest in the upper temporal quadrant, and the smallest in the lower nasal quadrant.

Pupil fields of patients with visual field defects

Then, the pupil fields obtained by our perimetry and those obtained by the conventional subjective perimetry were compared among the patients with various visual field defects.

Case 1: A 56-year-old man had bitemporal hemianopsia caused by a pituitary adenoma. The static visual field of the right eye, obtained by the Humphrey field analyzer program 30-2 (Fig. 5a), showed reduced sensitivities in the temporal half, and temporal hemianopsia, accompanied by macular splitting, was confirmed. His pupil field (Fig. 5b) showed that the light reflex in the upper temporal quadrant was smaller than that in the nasal quadrant, thus agreeing with the results of the static visual field. However, the light reflex in the hemianoptic area did not completely disappear, and we could not ascertain the presence of macular splitting. Nonetheless, when the topographic image of this patient was compared with that of healthy individuals (Fig. 5c), reductions in the amplitude of the light reflex in the temporal half were very clear, and those at the central region were also noticeable when compared with the topographic images of the

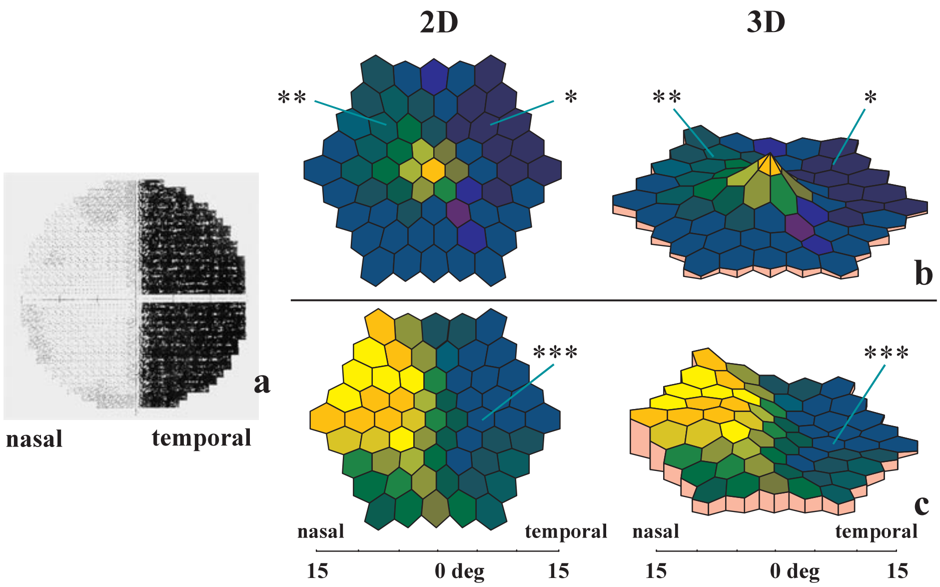

Fig. 5. Case 1. A 56-year-old man had right hemianopsia caused by a pituitary adenoma.
a: A static visual field obtained by the Humphrey Field Analyzer showing reduced sensitivities in the temporal half, accompanied by macular splitting.
b: A pupil field showing that the amplitude in the upper temporal quadrant (*) was lower than that in the upper nasal quadrant (**).
c: A topographic image comparing the amplitude of the light reflex of this patient with that of the healthy individuals. Yellow indicates ± 0 (since the degree of individual and age-related differences are great for the pupillary light reflex, colors other than yellow do not necessarily represent abnormalities). Reductions in the amplitude were seen in the temporal half (***), and when compared with the regular three-dimensional topographic images, the area and severity of visual field defects were more clearly identified.

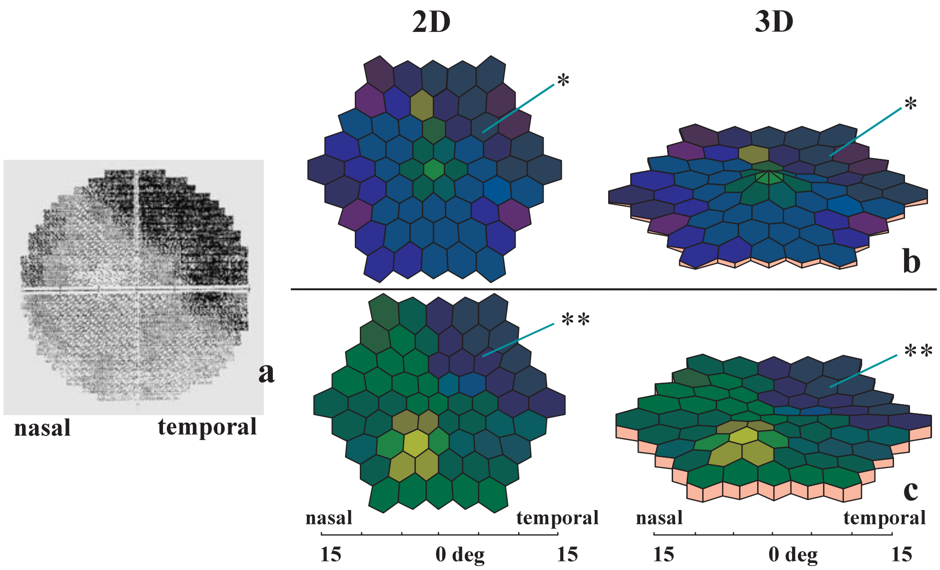

Fig. 6. Case 2. A 56-year-old woman had right upper quadrantanopsia caused by ablation of a brain tumor in the left parietal region.
a: Reductions in the amplitude, accompanied by macular sparing, are seen in the upper temporal quadrant.
b: Since the amplitude of the light reflex was generally small, visual field defects were unclear, but reduced amplitudes in the upper temporal quadrant (*) were observed.
c: When compared to healthy individuals, reduced amplitudes in the upper temporal quadrant (**) were clear. However, it was difficult to ascertain whether or not the visual field defects affected the macula.

healthy individuals.

Case 2: A 56-year-old woman underwent ablative surgery to remove a brain tumor in the left parietal region. The static visual field of the right eye taken by a Humphrey field analyzer (Fig. 6a) confirmed upper right quadrantanopsia, and her pupil field (Fig. 6b, 6c) showed reduced amplitudes in the matching area. However, a complete loss of the light reflex was not seen.

DISCUSSION

Many investigators have attempted to objectively analyze the visual fields: by pupil perimetry, equipped with an automatic perimeter and an infrared pupillometer, that objectively measures the visual fields utilizing the light reflex [1-5], by multifocal ERG using VERIS[7-10], and by multifocal VEP[11-14]. In perimetry utilizing multifocal ERG, the multifocal retinal function is expressed as a topographic image. Therefore, retinopathy-induced visual field defects can be detected, but those caused by visual pathway disorders past the retina cannot be detected. In the strictest sense of the word, the "visual field" does not apply to this perimetric technique. Unlike ERG, it is difficult to obtain even responses with multifocal VEP, and the degree of individual differences at the periphery is great[14]. Multifocal stimulation is more complicated than pattern-reverse stimulation, and with this technique, multiple polarity dipoles may be generated in the brain. There is a question as to whether or not they can simply be analyzed as electrode polarity components on the scalp. A method employing the light reflex was first reported by Harms[16] in 1949, and there have been many reports since then [17-21]. However, the degrees of individual and age differences are large, and test results are easily influenced by psychological factors. Therefore, a method a practical and appropriate method must be determined in the future. In the present study, we decided to measure the pupillary light reflex to objectively analyze the visual fields. Pretreatment was unnecessary, the perimetric procedure was non-invasive, VERIS was used to analyze the pupil fields with no major modifications in hardware being necessary, and the commercially available software could be used to perform a series of perimetric procedures, including stimulation, recording, and analysis.

First, preliminary experiments were carried out to ascertain the type of waveforms obtained by VERIS since the stimulation methods and equipment used were different from the conventional automatic perimetry. When white-black stimuli were delivered under 5 asb of indoor light, the pupillary response was the greatest at the central region and got smaller toward the periphery. Also, among the four quadrants, the amplitude was the greatest in the upper temporal quadrant, and the smallest in the lower nasal quadrant, thus agreeing with the results of a previous study[1]. These findings show that the pupil fields obtained by the present perimetric system were comparable to those obtained by the conventional technique. As far as the variation coefficients of these two different systems are concerned, Kardon *et al.*[1] reported that when -10 dB of stimuli were used, the variation coefficient was less than 20% at all degrees of eccentricity. This level is much lower than that (20-30%) with our system. This discrepancy is due to the fact that the brightness of the white-black reverse stimuli was about one third that of light stimuli used with the conventional method, thus making the resultant pupillary response smaller and increasing the standard deviation. This issue of large variance in the light reflex is always pointed out in studies on pupil perimetry[1,21]. Therefore, it will be necessary to adjust the brightness and area of stimulating elements to evoke large responses while considering the scattering of light stimuli in the eye.

The pupil fields of patients with visual field defects were analyzed. The amplitude of the light reflex in visual field defect areas was significantly lower than that in healthy areas. Thus we could obtain results that were very similar to those obtained by subjective perimetry. Although the present perimetric system was effective in detecting relatively large visual field defects such as hemianopsia or quadrantanopsia, the pupillary light reflex did not completely disappear in the anopic areas, thus suggesting that it would not be possible to detect abnormalities such as absolute or relative scotomas on the pupil fields. Therefore, the present pupil perimetry would not now be suitable for assessing minute reductions in retinal sensitivity, such as early-stage glaucoma. At this point in time, subjective perimetry with high spatial resolution is needed for this type of application. However, if the reliability of subjective perimetry is compromised (e.g., ambiguous responses or child subjects), the present pupil perimetry, as a supplemental test, could very useful.

Before the present perimetric system can be used in clinical settings, the stimulated field must be expanded and the resolution must be improved. Due to the structural limitations of the infrared camera, the stimulated field is limited to 15 degrees of eccentricity. Consequently, peripheral visual field defects cannot be detected, and it will be necessary to expand the stimulated area by optical means, such as the use of a half-mirror or the expansion of the monitor. Furthermore, the results of the present study showed that visualization of visual field defects on the pupil fields is more difficult when compared to subjective fields, and that the present pupil perimetry cannot identify minute defects such as macular splitting. As documented in previous reports, this was caused by scattering of the light stimuli and low resolution. Nevertheless, we could assess the pupil fields more accurately not only by analyzing three- dimensional topographic images, but also by comparing the topographic images of the patients with those of healthy individuals. In any case, while suppressing the scattering of light by adjusting the brightness of stimuli, the resolution must be improved by increasing the number of elements or reducing the area of elements. In addition, at this point in time, it takes about four minutes to complete the entire test. Since the pupils are easily influenced by psychological factors and are easily fatigued, perimetry should not take any longer than this to complete. Therefore, the longer test time required for higher resolution is another important issue for clinical application of the present pupil perimetry.

In conclusion, many problems still remain with objective perimetry using the light reflex, and we believe that it will take some time before it can be put into practical use, but the present perimetric system can be used when subjective perimetry fails to achieve desirable results.

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