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Development of Moving Multifocal Electroretinogram with a Precise Perimetry Apparatus

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***Abstract*—**A decline in visual sensitivity at arbitrary points on the retina can be measured using a precise perimetry apparatus along with a fundus camera. However, the retinal layer associated with this decline cannot be identified accurately with current medical technology. To investigate cryptogenic diseases, such as macular dystrophy, acute zonal occult outer retinopathy (AZOOR), and multiple evanescent white dot syndrome (MEWDS), we evaluated an electroretinogram (ERG) function that allows moving the center of the multifocal hexagonal stimulus array to a chosen position. Macular dystrophy is a generalized term used for a variety of functional disorders of the macula lutea, and the ERG shows a diminution of the b-wave in these disorders. AZOOR causes an acute functional disorder to an outer layer of the retina, and the ERG shows a-wave and b-wave amplitude reduction as well as delayed 30 Hz flicker responses. MEWDS causes acute visual loss and the ERG shows a decrease in a-wave amplitude. We combined an electroretinographic optical system and a perimetric optical system into an experimental apparatus that has the same optical system as that of a fundus camera. We also deployed an EO-50231 Edmund infrared camera, a 45-degree cold mirror, a lens with a 25-mm focal length, a halogen lamp, and an 8-inch monitor. Then, we also employed a differential amplifier with gain 10, a 50 Hz notch filter, a high-pass filter with a 21.2 Hz cut-off frequency, and two non-inverting amplifiers with gains 1001 and 11. In addition, we used a USB-6216 National Instruments I/O device, a NE-113A Nihon Kohden plate electrode, a SCB-68A shielded connector block, and LabVIEW 2017 software for data retrieval. The software was used to generate the multifocal hexagonal stimulus array on the computer monitor with C++Builder 10.2 and to move the center of the array toward the left and right and up and down. Cone and bright flash ERG results were observed using the moving ERG function. The a-wave, b-wave, c-wave, and the photopic negative response were identified with cone ERG. The moving ERG function allowed the identification of the retinal layer causing visual alterations.

***Keywords*—**Moving ERG, multifocal ERG, precise perimetry, retinal layers, visual sensitivity.

I. Introduction

PRECISE perimetry can be used to measure visual sensitivity in a target area. With Perimetry, the examination target is projected in visual field areas, whereas an ophthalmologist observes a patient's fundus directly during an examination. Precise perimetry is used to measure visual sensitivity in a target area [1]. However, the retina consists of 10 layers, as shown in Fig. 1. To date, there would be few examination methods that can precisely identify the retinal layer that is associated with the decline in visual sensitivity [1]-[5]. It is important to find an examination method that can perfectly identify the retinal layer causing a decline in visual sensitivity. The ERG uses a multifocal hexagonal stimulus array with intermittent flashes of light and is able to measure the electric potential of the reactions through a contact lens or plate electrodes.

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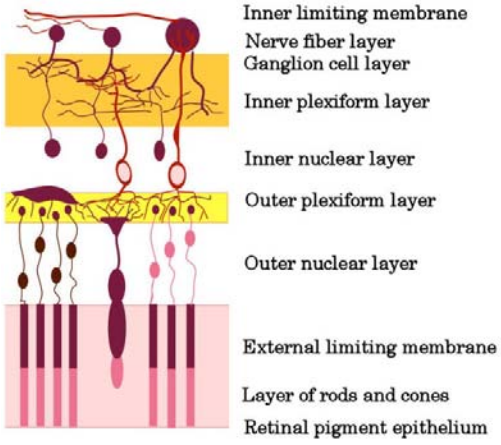


Fig. 1 Ten-layer retinal structure

Four different waveforms of ERG reflect the decline in visual sensitivity of separate layers of the retina, as shown in Fig. 2.

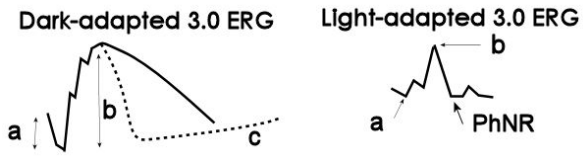


Fig. 2 Example of an ERG waveform

The a-wave represents signals from the layer of rods and cones, the b-wave represents signals from the inner nuclear layer, the c-wave represents signals from the retinal pigment epithelium, and the photopic negative response represents signals from the ganglion cell layer [2]-[4]. However, conventional ERG cannot be used to move the position of the multifocal hexagonal stimulus array; therefore, it is limited and can just measure ERG waveforms at predetermined positions, as shown in Fig. 3 (a). The source of the decline in visual sensitivity can be detected if the center of the multifocal hexagonal stimulus array of ERG is adjusted to the same position as the examination target, as shown in Fig. 3 (b).

The pathogenic mechanisms of cryptogenic diseases, such as macular dystrophy, AZOOR, and MEWDS are reviewed here. Macular dystrophy [6] affects both eyes and is a generalized

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term used for functional disorders of the macula lutea, including Stargardt's disease [7], [8], occult macular dystrophy [9], vitelliform macular dystrophy [10], and cone-rod dystrophy. When patients with macular dystrophy receive a full-field ERG, the functions of the cone and rod areas are normal, but the function of the macula lutea is abnormal. Familial internal limiting membrane dystrophy is type of macular dystrophy. ERG shows a selective diminution of the b-wave [6]. AZOOR is a disease that causes an acute functional disorder to an outer layer of the retina [11], [12]. It usually affects in young women and tends to be accompanied by photopsia. The disease is accompanied by a rapid visual loss and visual field defect. The fundus of the eye is almost normal, and ERG shows an unusual result; this unusual result is effective for diagnosis. ERG shows a characteristic reduction in the a-wave and b-wave amplitude followed by a delayed 30 Hz flicker responses [12]. MEWDS affects young women, causing acute visual loss and a reduced visual field [13], [14]. In addition, the Mariotte blind spot is enlarged. When the symptoms of the disease appear, white dots are scattered from a deep layer of the retina to the retinal pigment epithelium. The white dots disappear within a few days or weeks. Focal ERG results show an amplitude decline in the areas of the abnormal visual field [15]. ERG shows a decrease in a-wave amplitude, which returns to a normal pattern within a few weeks [14].

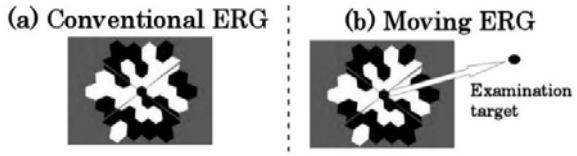


Fig. 3 Conventional ERG and Moving ERG

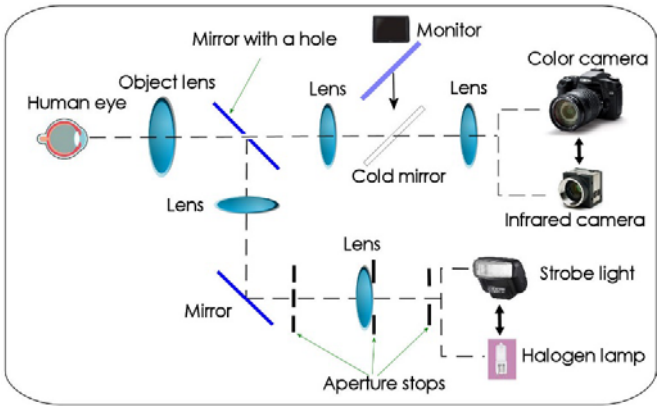


Fig. 4 Ophthalmological examination apparatus

As shown in Fig. 4, an ophthalmological examination apparatus that displays multifocal hexagonal stimulus arrays and examination targets on a monitor is currently being developed. This apparatus can perform three kinds of functions: a moving ERG, precise perimetry, and a fundus photography. Moving ERG aligns the central position of the multifocal hexagonal stimulus array with the position of the examination target in precise perimetry. To take a color image, the apparatus uses a color camera and a strobe light. However, to take an infrared image, it uses an infrared camera and a halogen lamp. Suzuki et al. performed basic research that integrated moving ERG functions with their experimental ophthalmology apparatus. With this apparatus, it was possible for them to measure ERGs in the same positions of precise perimetry [5].

II. Methods

A. Experimental Apparatus and Artificial Eye

We constructed an experimental apparatus [Fig. 5 (a)] comprising three ophthalmologic devices: a fundus camera, an ERG device and a precise perimeter. This experimental apparatus had illumination and photographic optical systems, separated by a mirror with a 4-mm diameter hole. Moreover, the apparatus had a precise perimetry optical system and an ERG optical system separated by a cold mirror. The apparatus consisted of an EO-50231 Edmund infrared camera, a lens with a 25-mm focal length, a halogen lamp, an object lens with a 50-mm focal length, four double-convex lenses with a 100-mm focal length, two aperture stops, a mirror, a 45-degree cold mirror, an 8-inch monitor, and an artificial eye. The artificial eye was based on the Gullstrand's artificial eye model, as shown in Fig. 5 (b). Fig. 5 (c) shows the chin mount.

B. Electrical Measuring Equipment

We developed an equipment to measure the electrical activity of the retina, as shown in Fig. 5 (d). In addition, we used a USB-6216 National Instruments multifunction I/O device, SCB-68A shielded connector block, an electronic amplifier, the NE-113A Nihon Kohden plate electrode, and LabVIEW 2017 software for data retrieval. The electronic amplifier comprised a differential amplifier with a gain of 10, a high-pass filter with a 21.2 Hz cut-off frequency, a 50 Hz notch filter, and two non-inverting amplifiers with gains of 1001 and 11.

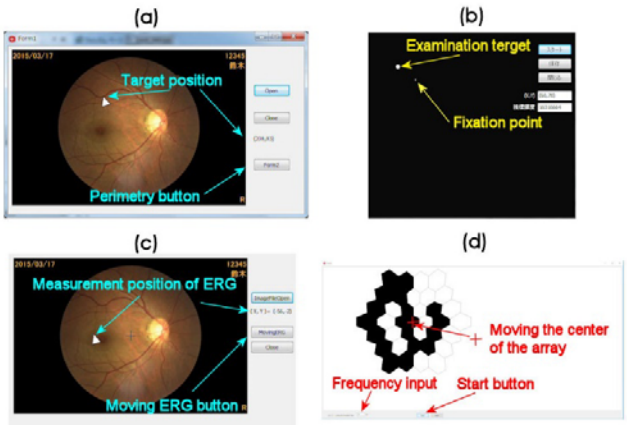


Fig. 6 Precise perimetry and moving ERG

C. Software Development

We developed a software using C++Builder 10.2 to assess the data obtained from moving ERG and precise perimetry examinations. This software can be used to adjust the arbitrary

position for both examinations on a fundus image. The position of the examination target in precise perimetry is shown in Fig. 6 (a), and Fig. 6 (b) shows this target displayed on a desktop computer. The center of the multifocal hexagonal stimulus array of moving ERG is shown in Fig. 6 (c), whereas its movement is depicted in Fig. 6 (d).

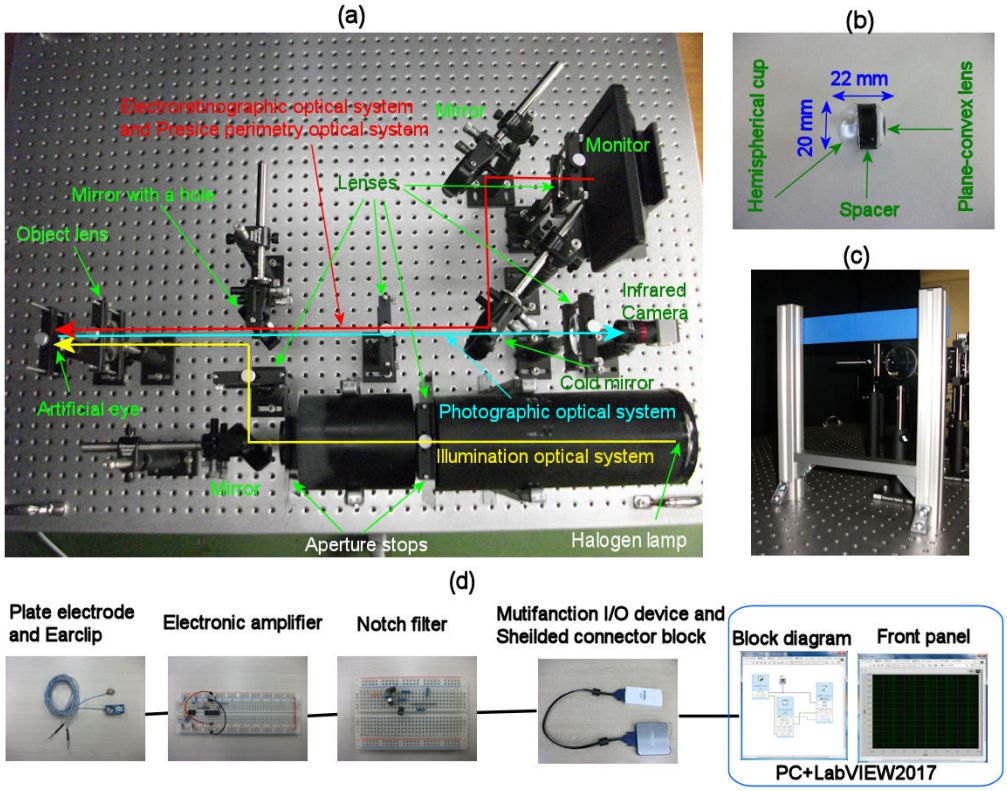


Fig. 5 Experimental apparatus with an artificial eye and a chin mount, and electrical measuring equipment

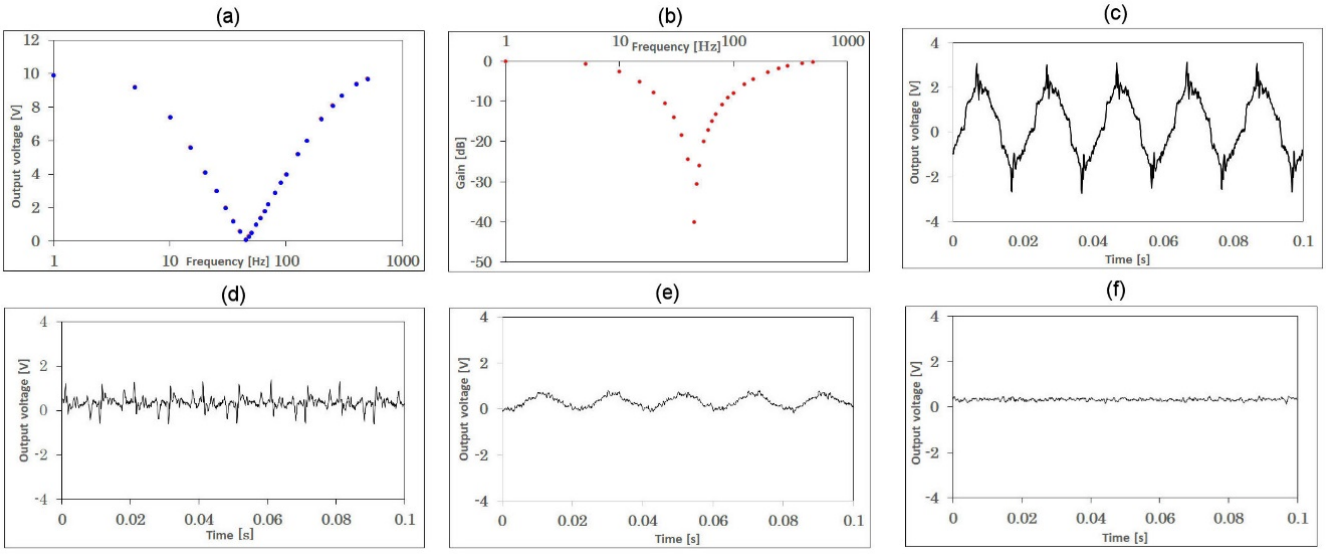


Fig. 7 Verification to filter out the mains hum and white noise

III. Results

A. Verification of Electrical Measuring Equipment

We conducted experiments to verify the efficiency of the notch filter. Fig. 7 (a) shows the relationship between frequency and output voltage, and Fig. 7 (b) shows the results of the frequency analysis. The notch filter was very effective. Furthermore, we conducted a verification experiment to filter out the 50-Hz mains hum. Fig. 7 (c) shows the results from connecting the plate electrode and ear clip with the electronic amplifier without an effective countermeasure against noise.

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Fig. 7 (d) shows the output voltage when the notch filter was connected to the electronic amplifier. This arrangement filtered out the hum noise considerably compared with the former instance. Finally, we conducted a verification experiment to filter out white noise. Fig. 7 (e) shows the output voltage during the use of Y047 shield sheet (made by Nihon Kohden). The white noise was reduced compared with that shown in Fig. 7 (c). Furthermore, Fig. 7 (f) shows the output voltage during the use of the shield sheet and the notch filter. The hum noise and white noise were completely filtered out. This electrical measuring equipment was very effective for ERG measurements.

B. Measurements Using Moving ERG

Fig. 8 (a) shows the moving ERG that was displayed on a 23-inch ThinkVisionT2324d display (Lenovo Corp.). The distance between the eye and the display was 30 cm. Three healthy men aged 21–22 years and a man in his 40s were tested. Plate electrodes and ear clips were attached to the participants and were subjected to dark adaptation for approximately 5 minutes in a darkroom [Fig. 8 (b)]. The voltage was ±9 V [Fig. 8 (c)].

An example of the measurement results is shown in Fig. 9. Cone and bright flash ERG results were observed using the moving ERG function. The a-wave, b-wave, and c-wave, as well as the photopic negative response, were identified with cone ERG.

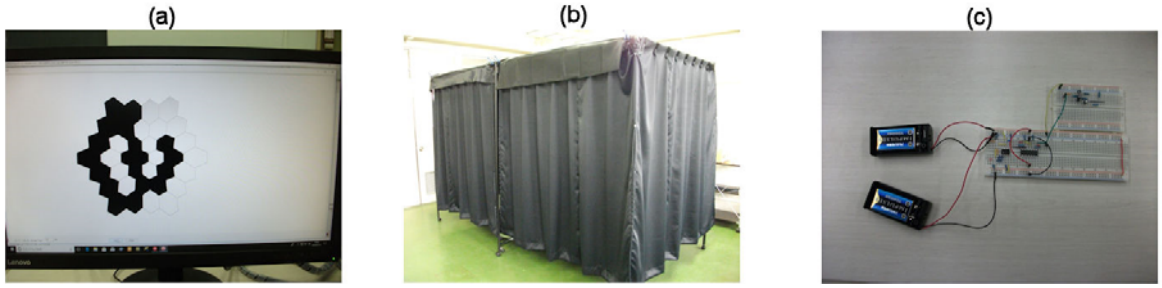


Fig. 8 Some devices of moving ERG

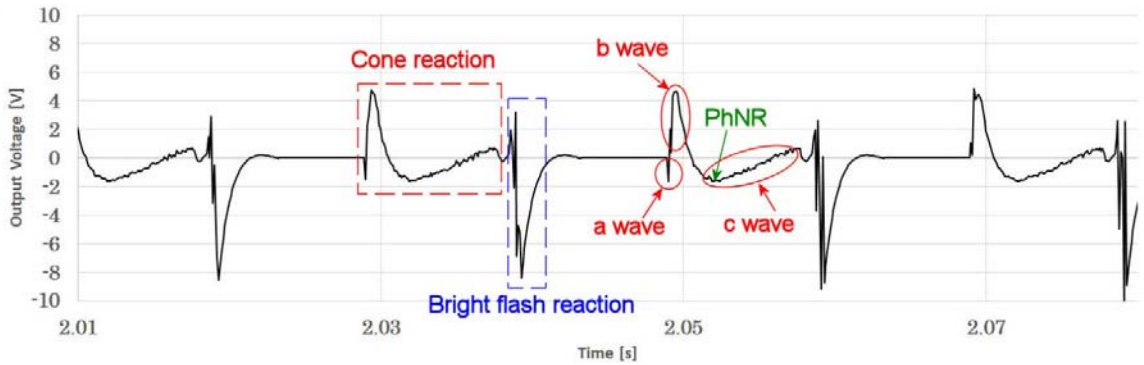


Fig. 9 Measurement result using moving ERG

IV. Conclusion

We developed an apparatus that allows moving ERG and precise perimetry. We also developed a software for data retrieval using this apparatus. The electrical measuring equipment was determined to be very effective because it successfully filtered out the hum noise and white noise. Cone and bright flash ERG results were observed using moving ERG. Moving ERG allows for successful identification of the retinal layer responsible for a decline in visual sensitivity.

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