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Feasibility of 2nd Generation STS Retinal Prosthesis in dogs

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Abstract— **We developed a 2nd generation suprachoroidal transretinal stimulation (STS) system with a 49 channel electrode array and implanted in 2 dogs. One month after surgery, all electrodes were functioning and the ocular fundus was normal in both dogs. The results indicate the 2nd generation STS retinal prosthesis is feasible and can be considered for clinical use.**

I. Introduction

Retinitis pigmentosa (RP) is one of the leading causes of blindness in developed countries and is characterized by a progressive degeneration of the photoreceptors.[1,2] To restore some vision to these patients, stimulating the residual functional retinal neurons by electrical currents delivered through a retinal prosthesis is being extensively studied.[3-5]We have developed our original method of retinal prosthesis named suprachoroidal transretinal stimulation (STS) and demonstrated that STS system with 9 channel platinum electrode array allowed 2 patients with advanced RP resolve to white bar targets.[6] In STS retinal prosthesis, electrode array is placed in a scleral pocket, which allows the stability of electrode[7] , so STS may be a safer approach compared with epi- or subretinal approaches. In order to attain the reading vision, we have developed a 2nd generation STS system with 49 channel electrodes, in which the surface of electrodes is processed by a femtosecond laser to increase the capability of charge injection. A multiplexer was attached to the electrode array and distributes electric pulses to each electrode, which allowed the internal system to reduce the number of lead wires. The purpose of this study was to determine the feasibility of the new STS retinal prosthesis using dogs.

II. Methods

A. Implant

The internal device consisted of a secondary coil which receives signals from the external coil and a decoder which generates biphasic pulses. (Fig.1) The electrode array (size, 5.8 × 5.8 mm; Nidek, Gamabori, Japan**)** consisted of 49 electrodes made of 0.5 mm diameter platinum bulk with a surface processed by femtosecond laser. The center-to-center separation of a pair of electrode was 0.7 mm. Each electrode protruded from the silicon base by 0.3 mm. A multiplexer was attached to the electrode array and distributes electric pulses to individual electrode. The return electrode was a 0.5 mm diameter, 6 mm long platinum wire that was insulated except for 3 mm of the tip.

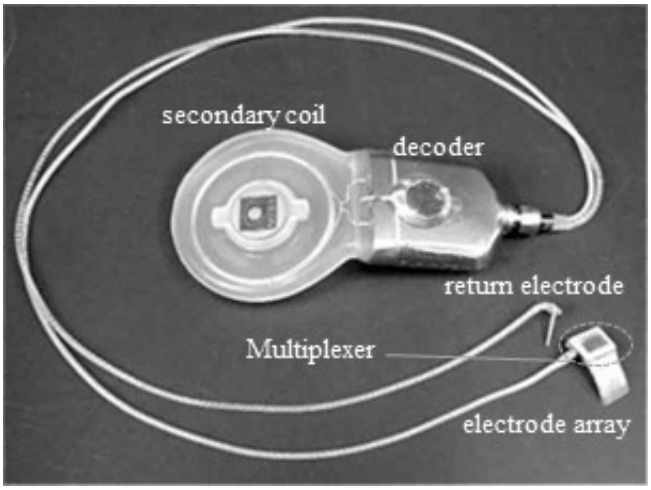

Figure 1. Photograph of the internal device

B. Surgical procedure

Two healthy adult male beagle dogs in weight from 10 to 12 kg were used. All procedures conformed to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research, and the procedures were approved by the Animal Care and Use Committee of Osaka University. Implantation was made to the left eye of each dog. The surgical procedures included insertion of the microelectrode array into a deep lamellar scleral pocket created 11.5mm from the corneal limbus, and placing the return needle electrode into the vitreous body. The microelectrode array and the return electrode were combined into one bundle and the cables were passed under the skin of the forehead and through the brow. The Internal coil and the decoder were set on the surface of the left temporal muscle and cables from electrode array and return electrode were connected to the decoder. (Fig. 1)

C. Examination of Ocular fundus

Color fundus photographs were taken under general anesthesia before surgery and monthly after surgery. Fluorescein angiography (FA) was performed at 1 month after surgery. For both procedures, the eyes were dilated with topical 2.5% phenylephrine hydrochloride and 0.5% tropicamide (Midrine P; Santen Co., Ltd., Osaka, Japan), and fundus photographs were taken with a fundus camera

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(TRC-50IX; Topcon Corporation, Tokyo, Japan). For FA, photographs were taken after the injection of 0.075 mL/kg of 10% sodium fluorescein solution (Fluorescite; Alcon Japan Ltd., Tokyo, Japan) into a vein.

D. Electroretinography

Bright-light flash electroretinograms (ERG) were recorded 1 month after the implantation of the STS electrode array. Under general anesthesia with pupil dilation, corneal contact lens electrode/LED mini-Ganzfeld stimulator (WLS-20; Mayo Corporation, Nagoya, Japan) was used for ERG recording. The animal was dark-adapted for 30 minutes before the ERG recordings. Responses elicited by bright flash stimuli were amplified, band pass filtered from 0.5 to 1000 Hz, and digitized at 3.3 kHz. Five responses were averaged.

E. Functional Testing of STS System

The voltage in the microelectronic circuit of the decoder was monitored by an external circuit. The maximum voltage of this circuit was 10.0 V, and we set 9.5 V as a saturation voltage. Just after and at 1month after implantation, we checked to be sure that the voltage did not exceed the saturation voltage of 9.5 V. Each of the 49 electrodes was activated with balanced, cathodic-first biphasic pulses of up to 1000 uA, with a duration of 0.5 ms/phase and pulse duration of 0.5 ms. The frequency of the pulses was 20 Hz for 0.5 seconds that was controlled by the extraocular stimulator driven by the external transmitter. If the voltage in the electric circuit in the microstimulator was less than the saturation voltage, the device set the current as pass, but if the voltage exceeded the saturation voltage, the device set the current as failure. Next the artifacts evoked by electrical stimulation were recorded with a contact lens corneal electrode/LED mini-Ganzfeld stimulator (WLS-20; Mayo Corporation).

III. RESULTS

A. Implantation Surgery

All prostheses were safely implanted and no intraoperative complications occurred. The electrode array was inserted in the scleral pocket without bleeding (Fig. 2) and the multiplexer attached with electrode array was kept stably under the conjunctiva. The cable was flexible and encircled the globe. No sign of infections or wound dehiscence was observed.

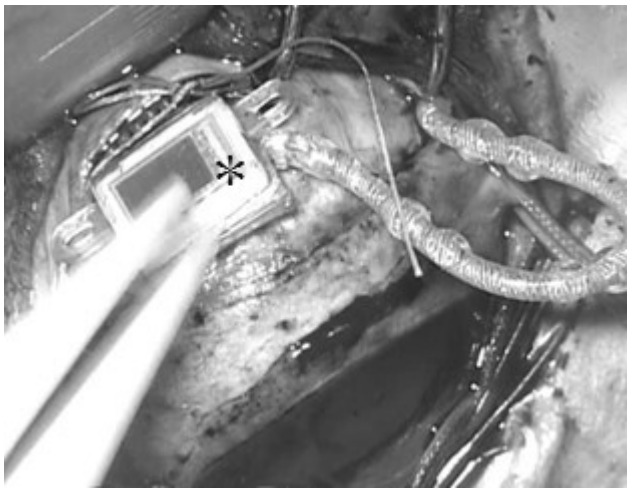

Figure2. Photograph taken during implantation surgery. An electrode array was inserted into the scleral pocket, and the multiplexer was sutured (＊) to the sclera. Asterisk mark indicates the multiplexer.

B. Postoperative ocular fundus

Fundus photographs of the two dogs showed that the implanted electrode array was not detectable, and there was no obvious indication of surgical damage or side effects. FA showed intact vasculature without signs of inflammation, leakage, obstruction, or formation of new vessels in the area overlying and surrounding the implant in all dogs.

C. Electroretinography

The electroretinograms had normal a-wave and b-waves, and the shapes did not differ from those of electroretinograms recorded from the unoperated fellow eye 1 month after implantation in all two animals. (Fig. 3)

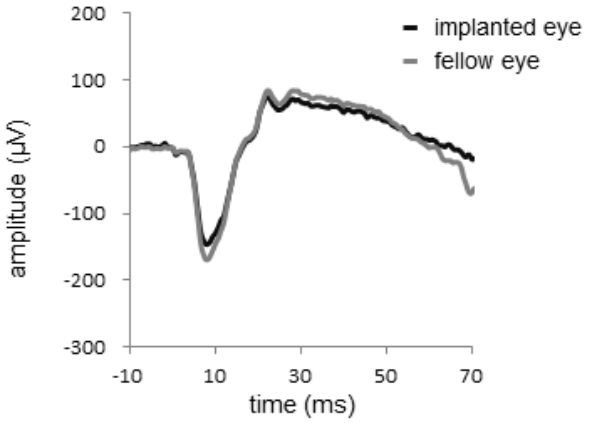

Figure 3. Representative electroretinograms recorded of the implanted eye and fellow eye of dog 1 after one month implantation.

D. Functional Testing of STS System

The voltage in the microelectronic circuit of the decoder was less than the saturation voltage in all electrodes and in all cases throughout the observation period. Representative stimulus artifact waveforms recorded with a contact lens electrode are shown in Figure 4. All the electrodes could deliver the electric currents.

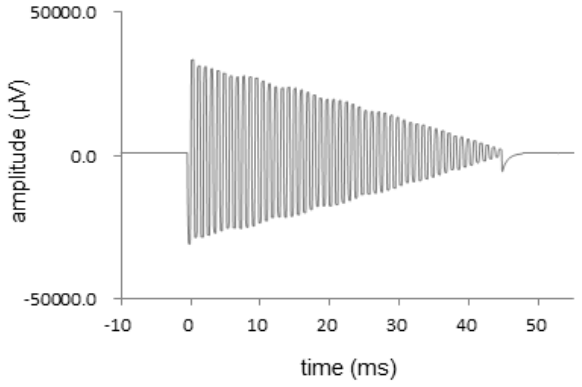

Figure 4. Representative waveforms of the stimulus artifacts of dog 1. Drawing of the waveforms of artifacts derived from each of 49 electrodes sequentially. Amplitudes of artifacts increase with increasing current intensity.

IV. Discussion

Our results showed that it is possible to implant our 2nd generation STS device into the scleral pocket of beagle dogs without intraoperative or postoperative complications.

The device were consisted of 49 channel electrode array with multiplexer and a decoder with internal coil. The device was different from that of 1st generation in that multiplexer was added to deliver electrical pulses to each 49 channel electrodes without increasing the number of lead wires.

The multiplexer have 5.7 × 4.4 mm in area and set close (10.5 mm) to the corneal limbs, so a possibility exists that the device is exposed from the conjunctiva if the friction between the lid and conjunctiva is increased. However the multiplexer was covered by the conjunctiva stably for 1 month, suggesting that the new device is able to be implanted stably in human trial.

The new device equipped a junction between the decoder and the lead wires, so a possibility exists to disconnection between the device and wires. However, the device was functional 1 month after the implantation, suggesting that the new device is kept functional at least 1 month.

Further observation is necessary to confirm the long-time safety and efficacy of our 2nd generation STS retinal prosthesis.

V. Conclusion

The 2nd generation STS system with a 49 channel electrode array is implanted successfully in 2 dogs. One month after surgery, all electrodes were functioning and the ocular fundus was normal in both dogs, suggesting that the 2nd generation STS retinal prosthesis is feasible and can be considered for clinical use.

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