Extended Abstracts of the 2005 International Conference on Solid State Devices and Materials, Kobe, 2005, pp.464-465

H-6-3

Evaluation of Electrical Stimulus Current to Retina Cells for Retinal Prosthesis

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1. Introduction

With the progress of ageing society, the number of blind patients due to retinitis pigmentosa (RP) and age-related macular degeneration (AMD) is dramatically increasing. However, medical cures for these diseases have not yet been established. In the retina of these blind patients, photoreceptor cells that convert optical signal into electrical signal are almost or sometimes completely absent, while other retinal cells survive with high probability. Several implantable retinal prostheses have been reported in recent years [1]. The retinal prostheses can enable such blind patients to restore visual sensation by electrical stimulation of remaining retinal cells via an electrode array.

We have already proposed a novel multiple stacked retinal prosthesis chip based on three-dimensional integration technology [2]. The retinal prosthesis consists of retinal prosthesis chips, a flexible cable with a secondary coil for power supply and a stimulus electrode array as shown in Fig. 1. In this system, photodetectors receive visual scenes and convert them into image data, followed by the conversion of the image data into appropriate patterns of electrical current using image processing circuits. Remaining retinal cells are stimulated with the electrical current *via* the stimulus electrode array to activate the remaining retinal cells.

In order to design and fabricate retinal prosthesis chips, it is essential to determine optimum stimulus current. Therefore, it is very important to perform some fundamental animal experiments such as recording of electrically evoked potential (EEP) which expresses electrical activity in primary visual cortex. In this paper, we describe the experimental results of EEP recording on a rabbit by using a fabricated stimulus electrode array formed on a biocompatible flexible cable.

2. Fabrication of an implantable flexible cable with a stimulus electrode array

The overall structure of our designed flexible cable for stimulating the retina to record EEP is shown in Fig. 2. The cable is 140mm in length, 2mm in width, and 30μm in thickness. Biocompatible polyimides are employed as a flexible substrate. A stimulus electrode array and three rings to fix the flexible cable on the surface of retina are formed at the head of the cable, and pads for connection to stimulator are formed at foot of the cable.

The flexible cable with a stimulus electrode array was fabricated on a 2-inch silicon wafer by using standard photolithography and MEMS techniques. First, polyimide precursor was spin-coated on a silicon wafer and cured at 320˚C. The polyimide layer with a thickness of ~30 μm was formed into the shape of the flexible cable by Reactive Ion Etching (RIE). Then, Al wirings with a thickness of 1μm were formed by wet etching. After that, the Al wirings were covered with photosensitive polyimide, followed by the formation of an Al stimulus electrode array and Al pads. Finally, the silicon wafer was immersed in buffered HF solution for several hours to remove the flexible cable from the wafer. As a result, the biocompatible flexible cable with a stimulus electrode array was obtained.

3. Results and Discussion

Stimulus current parameters can be optimized by comparing a waveform of EEP with that of visual evoked potential (VEP) that would be cased by incident light. We measured EEP detected when the retina of a rabbit was electrically stimulated with the fabricated stimulus electrode array on the flexible cable. The rabbit was anesthetized using ketamine hydrochloride (66mg/kg) and xylazine hydrochloride (33mg/kg) and was maintained by additional injections. The apparatus for EEP recording is schematically shown in Fig. 4. The stimulus electrode array, which was connected to a stimulator through the flexible cable, was fixed on the surface of the retina by a retinal tack as shown in Fig. 5. An active electrode and a reference electrode over the occipital cortex of a rabbit and a GND electrode at the tip of the nose were connected to a recorder for evoked potentials. The EEP response was successfully recorded by stimulating the retina with electrical current, 200 μA in amplitude and 0.5msec in duration, as shown in Fig. 6. Comparison of the waveforms recorded before and after axotomy of optic nerve indicates that the rabbit could perceive light by electrical stimulation of the retina, which gives a great expectation to restore visual sensation with retinal prosthesis. Figure 7 shows the relationship between amplitude of recorded EEP and amplitude of stimulus current. The increase in charge quantity of stimulus current increases amplitude of EEP, indicating that the charge quantity of stimulus current can represent the intensity of perceived light in retinal prosthesis. The study on effect of electrode materials such as Al, Pt and Ir on biocompatibility and charge density is in progress and will be described in our future work.

4. Summary

We successfully recorded EEP on the rabbit by using the fabricated stimulus electrode array on the biocompatible flexible cable. The experimental results indicated that the charge quantity of stimulus current can represent the intensity of perceived light in retinal prosthesis. This gives a great expectation to restore visual sensation with retinal prosthesis.

Acknowledgements

This work was partially supported by the 21st Century COE Program "Future Medical Engineering based on Bio-nanotechnology", from the ministry of Education, Culture, Sports, Technology and Science, Japan and Venture Business Laboratory, Tohoku University, Japan.

References

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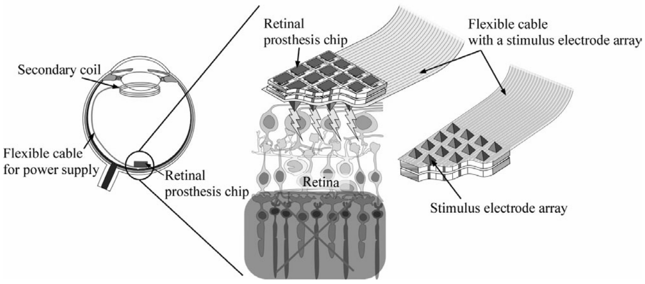

Fig. 1. Configuration of retinal prosthesis with three-dimensional structure.

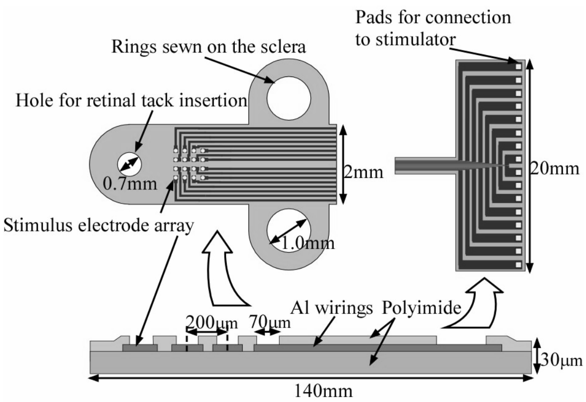

Fig. 2. Design of implantable flexible cable with a stimulus electrode array.

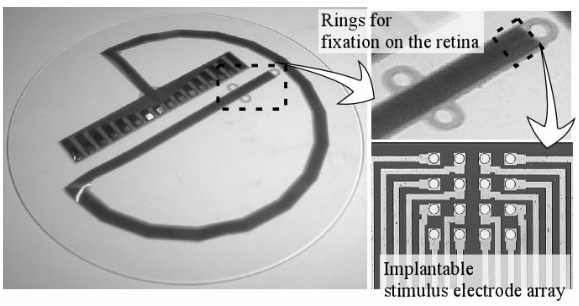

Fig. 3. Photograph of fabricated implantable flexible cable with a stimulus electrode array.

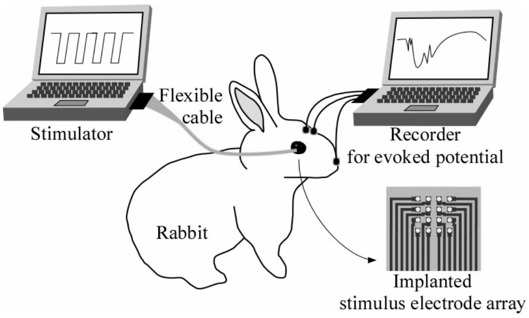

Fig. 4. Schematic diagram of apparatus for EEP recording.

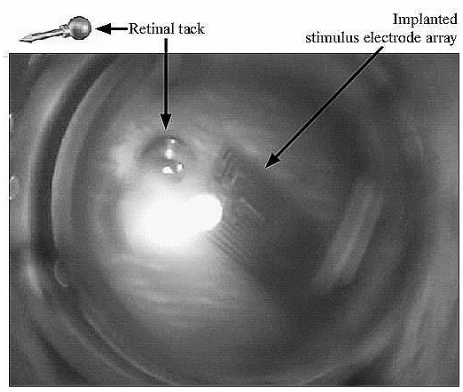

Fig. 5 Fundus photograph of the stimulus electrode array fixed on the surface of the retina.

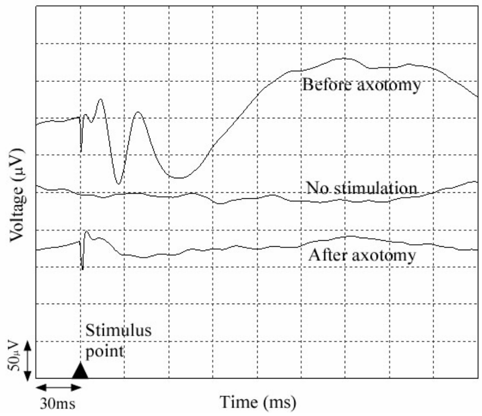

Fig. 6 Waveforms of recorded EEP before and after axotomy of optic nerve.

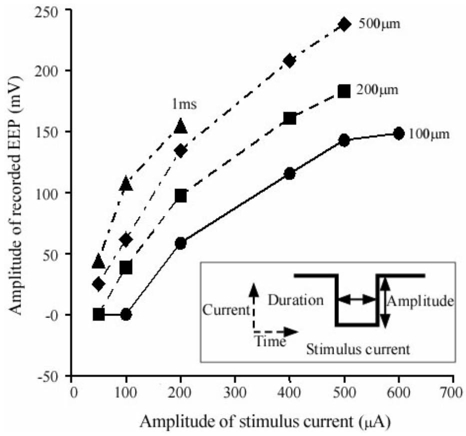

Fig. 7 Relationship between the amplitude of recorded EEP and the strength of stimulus current amplitude.