SEEING ON THE SURFACE OF EYEBALLS: NON-INVASIVE VISUAL SUBSTITUTION WITH THE ELECTRO-TACTILE DEVICE ON CORNEA

Yushi Zhang[1, 2], Yao Chen[3], Boxuan Zhao[1], Yuntao Hu[4], and Zhihong Li[1*]*
[1]National Key Laboratory of Science and Technology on Micro/Nano Fabrication,
Institute of Microelectronics, Peking University, Beijing, CHINA
[2]Institute of Electronics, Chinese Academy of Sciences, Beijing, CHINA
[3]Ophtnalmology Department, Beijing Tian Tan Hospital, Capital Medical University, Beijing, CHINA
[4]Department of Ophthalmology, Beijing Tsinghua Changgung Hospital, Beijing, CHINA

ABSTRACT

In this work, using tactile sensation of the cornea of the blind, a novel visual substitution method and system were proposed for visual reconstruction. Unlike previous tactile-visual substitution, the electro-tactile device attaches on the cornea of the blind, a "useless" organ for a blind, and will not impede intrinsic function of human body. The non-invasive flexible microelectrode array devices for electro-tactility were fabricated and tested. The *in vivo* experiments show that the sensible threshold voltage of the cornea is less than 1.7V, which is much lower than the tactile-visual substitution system previously reported, because of the high sensitivity of the cornea. The experiments also validate the biological safety of the cornea under low voltage.

INTRODUCTION

Visual reconstruction devices and systems are of interest and importance to help the blind restore their vision[1-4]. The visual prosthesis, which can create a sense of vision by electrically activating neural cells in the visual system, was clinically proved effective[1, 2]. However, this invasive and expensive method can only work for the blind on retinal diseases.

Sensory substitution device (SSD) is a device that realizes the transformation of human perception to convey information. The central nerves corresponding to receptors can be used interactively, which is the cross-modal plasticity of the brain. Therefore, the various sensations of the human body, such as vision, touch, hearing, sense of smell, etc., can be replaced by each other. The SSD takes advantage of the plasticity principle of cross-perception in the human brain to realize the perception of mutual replacement and impairment of functional reconstruction[5].

The more widely used is to convert other perceptions to replace vision. According to cross-modal plasticity of the brain, stimulating skin of body can make visual cortex of the trained blind active, which is like to "see".

The tactile-visual sensory substitution system was developed and used in clinical[3, 4]. For example, BrainPort Vision Devices has obtained the license of CE[6]. Using a camera to obtain image information, which is converted to electrical stimulation signals, the device can work on the tongue for recognition image information. Using the technology of Positron Emission Computed Tomography (PET), it was found that the visual area in the blind brain was active during the process of electrical stimulation, that is, the tactile transmission information is processed through the visual area to form the cross-perception.

However, in the existing system, the electrodes should be put on the surface of tongue or fingers, which would impede the use of hand and tongue in the daily life. Also, because of high resistance of stratum corneum, the simulation voltage is as high as tens volts.

In this work, using tactile sensation of the cornea of the blind, a novel visual substitution method and system were proposed for visual reconstruction. Unlike previous tactile-visual substitution, the electro-tactile device attaches on the cornea of the blind, a "useless" organ for a blind, and will not impede intrinsic function of human body.

MATERIALS AND METHODS

The principle of the system

The schematic view of our system is shown in Fig. 1. The principle is the same as the previous tactile-visual substitution and most of the parts of the system is like the existing system. The image information can be caught by the camera and encoded. The cornea is simulated by the encoded electrical pulse. The electrical simulation device for electro-tactility is different from the existing tactile-visual substitution system, which should be designed and fabricated specially.

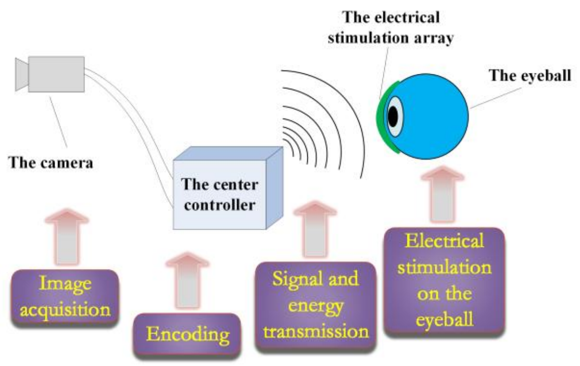

Figure 1: The schematic view of the system.

Device Fabrication

Parylene is a kind of flexible material with biocompatibility, which is suitable as the substrate and package of the device. The platinum (Pt) electrode is widely used for bio-electrical simulation because of the high Charge transfer capability and biocompatibility.

The non-invasive flexible microelectrode array devices were designed and fabricated, as the process shown in Fig. 2. A 4-inch polished wafer was prepared. Using physical vapor deposition (PVD), 1 μm thick aluminum (Al) layer was deposited onto the silicon wafer as the sacrificial layer to facilitate the final Parylene release. After silanization of the surface, a layer of parylene C was deposited in a PDS2010 system (Specialty Coating System, Indianapolis, IN, U.S.) by chemical vapor deposition (CVD) on the aluminum film to a thickness of 10 μm (using 16 g of raw material) as shown in Fig. 2(a).

About 20-nm titanium (Ti) and 400-nm aluminum (Al) were adopted as the first layer to realize undercut under the photoresist layer, an 8-μm-thick AZP4620, where the Ti layer was employed to enhance the adhesion between Al and Parylene. The Al layer was over etched for 5 minutes by the aluminum enchant (H_3PO_4: HAC: HNO_3 = 16: 2: 1, 39 ° C), as shown in Fig.2(b).

After 20-nm-thick titanium, 150-nm-thick gold, and 50-nm-thick platinum were evaporated onto the substrate, the whole structure was bathed in the PRS 3000 stripper at 60 ◦C for about 2 h to obtain the desired pattern. Pt was designed as the electrode and Au was to reduce the stress. (Fig. 2(c)).

After that, the surface of the substrate was treated with oxygen plasma for 35 s. And then the second layer of Parylene C with a thickness of 5 μm was deposite onto the substrate, as shown in Fig. 2 (d), and selectively patterned with lithography, before etching by the oxygen plasma. To avoid the effect of the heat generated during the etching process, each etching process was set as 5 minutes, with 11 times etching in total. During this process, the outline of the device and the sockets for connection were etched out. The electrode point and the pad were exposed and self-stopped during the etching process, as shown in Fig. 2(e).

Finally, the sacrificial layer Al was etched away by 5% TMAH and the flexible electrode device was carefully peeled off from the substrate, as shown in Fig. 2(f).

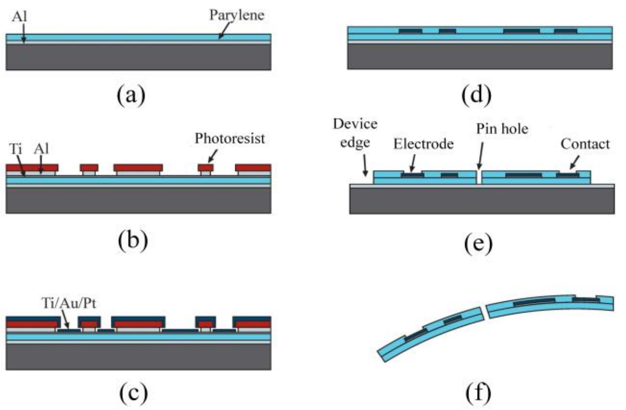

Figure 2: the fabrication process of the device. a) PVD Al (sacrificial layer) and CVD parylene; b) sputtering Ti/Al, coating photoresist, patterning and etching photoresist, and then over etching Al; c) sputtering Ti/Au/Pt; d) lifting off the photoresist, etching Al and Ti, and then CVD parylene; e) etching parylene; f) etching Al (sacrificial layer) and releasing the device.

The device can be designed in different shapes for different experiment cases, as shown in Fig.3(a), and Fig.3(b)~(d) are the partial enlarged photos of the devices. The device with the circularly arranged electrode array is the designed device for this system, which can be much like the device used in the clinical in the future; while the device with the oblong-shaped electrode array can test the sensitivity of different part on the surface the eyeball.

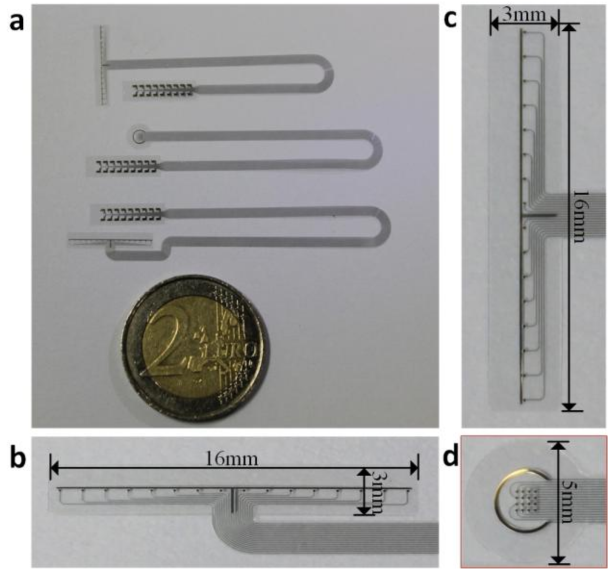

Figure 3. The photos: different types of the devices in (a); parts of the devices in (b)~(d).

Device Properties Testing

To analyze the electrochemical properties of the Pt electrode, the cyclic voltammetry and AC impedance method were used. Electrochemical measurements were performed by a CHI 660 electrochemistry work station (CH Instruments Co., USA) and a three-electrode system in PBS solution (0.01 M, pH 7.4), where the Pt electrode was used as the working electrode, a platinum wire as a counter electrode and an Ag/AgCl electrode as the reference electrode.

***In vivo* Experiments**

In *in-vivo* experiments, New Zealand white rabbits weighing 2.1 kg were anesthetized and the electrodes were attached to the eyes of rabbits for electrical stimulation. The positive and negative pulse signal of 1 kHz (waveform shown in Figure 4) was generated and added on the device.

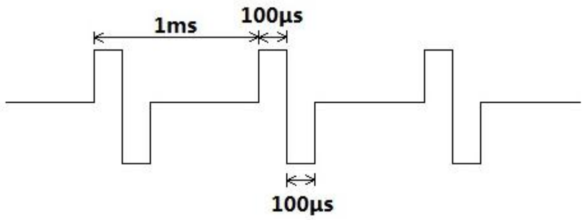

Figure 4: pulse length and period of electrical stimulation.

The device with the circularly arranged electrode array was attached on the surface of the cornea and the sclera to test the sensitivity respectively as shown in Fig. 5(a) and (b)). The oblong-shaped electrode array was attached on the surface of the eyeball, with some part stuck to the cornea and the other part stuck to the sclera (shown in Fig. 5(c) and (d)).

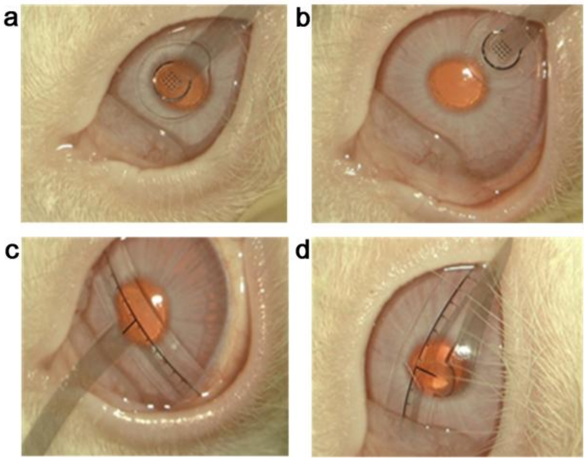

Figure 5: The devices tested on the surface of the eyeball.

In the oblong-shaped electrode array device, the electrode number is shown in Fig.6. Electrode 6~13 were on the cornea. Electrode 2~5 and 14~17 were on the sclera. Electrode 1 and 18 were connected to the ground.

A bipolar pulse stimulation, with 100μs pulse wide and 1 ms period, as shown in Fig.4(b), was added on the electrode. Each electrode was tested as the amplitude of the pulse increased from 0.5V with a step of 0.5V. When the eye blink response of the anesthetic rabbit was observed, the test of that electrode would finish and the voltage which could make the rabbit sensible was recorded. This voltage was as the threshold voltage for the electrical stimulation to react

RESULTS AND DISCUSSION

Device electro-chemical Properties

The electro-chemical properties were shown in Fig.6. The cyclic voltammetry (in Fig.6(a)) shows that Pt electrode has the charge capacity with 2.1 mC/cm^2.

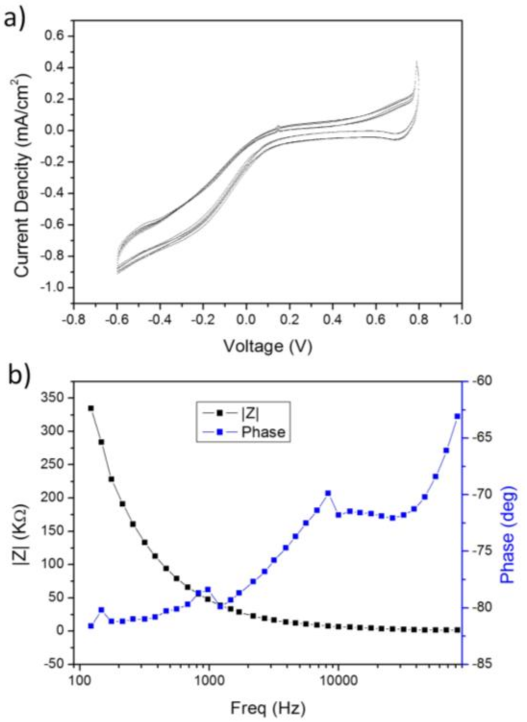

Figure 6: a) the cyclic voltammetry testing result, and b) the impedance of the device.

The electrochemical properties of the electrode demonstrate that the device can also work well for electrical simulation under double-pulse current (usually with the frequent of 1 KHz).The curves in Fig. 6(b) illustrate the Pt electrode has the impedance of 50kΩ under the frequent of 1 KHz.

In vivo Results

The in vivo experiments, as the results in Fig.7, show that the tested sensible threshold voltage on the surface of the eyeball, tested by the oblong-shaped electrode array. The average sensible threshold voltage on the cornea is 1.7V and on the sclera is 2.1V.

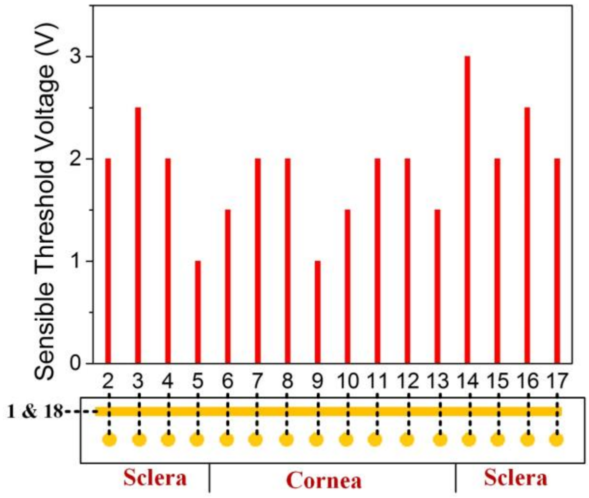

Figure 7: the tested sensible threshold voltages of each electrode on cornea and sclera.

It also indicates that the cornea is more sensible than the sclera for electrical simulation, so the cornea will be selected as the electrical stimulation part of the body in this method. In the experiments, to test and observe the results, a strong electrotactile simulation was used to make the anesthetic rabbit blink. However, in the clinical cases, the method can only make a slight feeling, so the actual sensible voltage is less than the tested voltage 1.7V, which is much lower than the tactile-visual substitution system used before, which is more than 10V used for the fingers and 5~20V used for the tongue[7, 8].

The device with the circled electrode array was also tested. It can be work under less than 1.5V for the cornea and 2V for the sclera.

The threshold voltage of the electrode can be affected by the gap between the device and the eyeball because of the contact resistance. During the experiments, both the cornea and the sclera should be tested with the gap as small as possible. Also, if the “simulation lens” is more suitable for the eyeball, the sensible threshold voltage can be lower.

Electrical Injury Testing

To verify the safety of the electrodes, the corneas of rabbits after simulation with different voltages were examined, using fluorescence staining or biopsy, to find out the safety voltage.

After electrical stimulation with a voltage of 5 V or less, the cornea was fluorescent-stained and no damage spots were observed. However, the cornea dyed point can be observed after 10 V simulation in some cases, which indicating that the corneal epithelium may be damaged. When stimulated with a voltage of 20V, the rabbit was struck by the electric shock at the instant the switch was turned on. The obvious injury of the cornea epidermis can be observed by slicing (Figure 8).

The electrical injury tests show that there was no electrical injury on the surface of the cornea when the voltage is not higher than 5V. As the effective voltage in the method is less than 1.7V, the electrical injury will not occur.

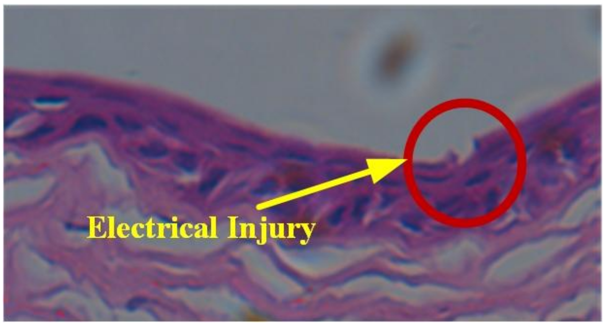

Figure 8: the electrical injury of the cornea epidermis under 10V.

CONCLUSION

The novel visual substitution method can work well with sensible threshold voltage of the cornea is less than 1.7V, which is much lower than the tactile-visual substitution system previously reported, because of the high sensitivity of the cornea. The experiments also validate the biological safety of the cornea under low voltage.

Unlike previous tactile-visual substitution, the electro-tactile device attaches on the cornea of the blind, a "useless" organ for a blind, and will not impede intrinsic function of human body. The non-invasive method for visual reconstruction has a promising prospective.

ACKNOWLEDGEMENTS

This work was supported by the National Natural Science Foundation of China (No. 91323304) and the National Key Research and Development Program of China (No. 2016YFA0200802).

REFERENCES

[1] R. J. Greenberg, M. S. Humayun, L. da Cruz, *et al.*, Five-year data from the Argus II Retinal Prosthesis System Clinical Tria, *Investigative Ophthalmology & Visual Science*, 56 (2015).

[2] J. D. Weiland and M. S. Humayun, Visual prosthesis, *IEEE Transactions on Biomedical Engineering*, 61(2014), pp. 1412-1424

[3] F. Clemente, S. Dosen, L. Lonini, *et al.*, Humans can integrate augmented reality feedback in their sensorimotor control of a robotic hand, *IEEE Transactions on Human-Machine Systems*, 47(2017), pp. 583-589.

[4] B. Nanay, Sensory Substitution and Multimodal Mental Imagery, *Perception*, 46 (2017), pp. 1014-1026.

[5] L. B. Merabet and A. Pascual-Leone, Neural reorganization following sensory loss: the opportunity of change, *Nature Reviews Neuroscience*, 11 (2010), pp. 44-52, 2010.

[6] A. Nau, M. Bach, and C. Fisher, Clinical Tests of Ultra-Low Vision Used to Evaluate Rudimentary Visual Perceptions Enabled by the BrainPort Vision Device, *Translational Vision Science & Technology*, 2 (2013) pp.1-1

[7] K.A.Kaczmarek, The tongue display unit (TDU) for electrotactile spatiotemporal pattern presentation, *Scientia Iranica*, 18(2011), pp. 1476-1485.

[8] Z. Zalevsky, G. Elani, E. Azoulay, *et al.,* Electromechanical tactile stimulation system for sensory vision substitution, *Optical engineering*, 52 (2013), 023202.

CONTACT

*Zhihong Li, Peking University, Beijing, 100871, China, Phone: +86-10-62766581; Fax: 86-10-62751789; E-mail: zhhli@ime.pku.edu.cn

*Yushi Zhang, Institute of Electronics, Chinese Academy of Sciences, Beijing, 100190, China, Phone: +86-10-58887062; Fax: 86-10-58887539; E-mail: zhangyushi@mail.ie.ac.cn.