IMPLANTATION OF THE POLYIMIDE ELECTRODE ARRAY FOR THE ELECTRICAL STIMULATION OF THE RETINA: EPIRETINAL AND SUBRETINAL APPROACHES

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Abstract: Photoreceptor loss due to retinal degenerative diseases is a leading cause of blindness in adults. The feasibility of the electrical stimulation of the remaining retinal neurons is supported by clinical studies. To minimize the damage during ophthalmic surgery and to get better contact to retina, flexible polyimide is selected as the substrate material of microelectrode arrays in our group. Various shapes of microelectrode arrays are designed to reduce the tissue damage and take more intimate contact to the retina. Both subretinal and epiretinal stimulation are under investigation, and the polyimide electrode array showed good surgical properties and *in vivo* biocompatibility.

Introduction

Photoreceptor loss due to retinal degenerative diseases such as age-related macular degeneration (AMD) and retinitis pigmentosa (RP) is a leading cause of blindness in adult. Retinal prosthesis under investigation to rehabilitate this kind of visually impaired patients. The feasibility of the electrical stimulation of the remaining retinal neurons is supported by clinical studies. Controlled electrical signals applied to a small area of the retina of a blind volunteer via the microelectrode resulted in the perception of a small spot of light.

To investigate the usability of the polyimide electrode array for the retinal prosthesis system, epiretinal or subretinal implantation techniques are developed and the b,iocompatibility was tested.

Materials and Methods

A. Polyimide electrode array

Polyimide (PI2525, HD Micro Systems) was prepared as the manufacturer's specification and microelectrode array was fabricated based on semiconductor manufacturing technique. To prevent tearing of edge, polyimide microelectrode array is designed to have rounded corners and circular holes for retinal tack. The polyimde microelectrode array is 18.5 ㎛ in thickness and 3 x 3 mm in size. Each gold electrode is 200 x 200 ㎛ in size and is spaced by 250 ㎛ (Figure 1 & 2).

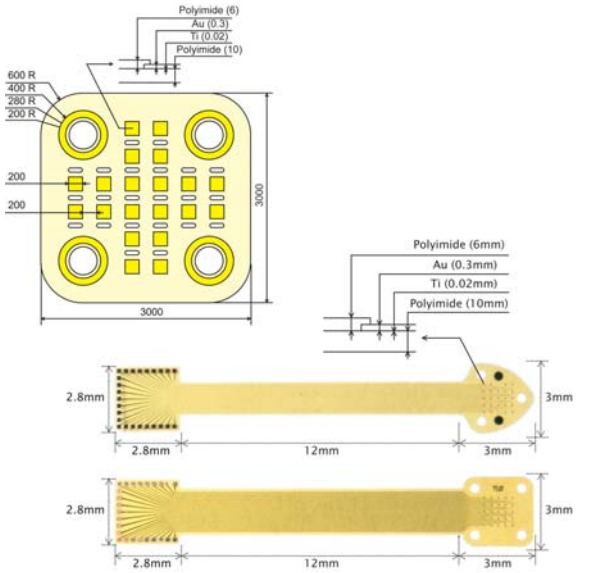

Figure 1: Dimensions and shapes of polyimide electrode arrays. Epiretinal (upper) and subretinal (lower) type electrode array.

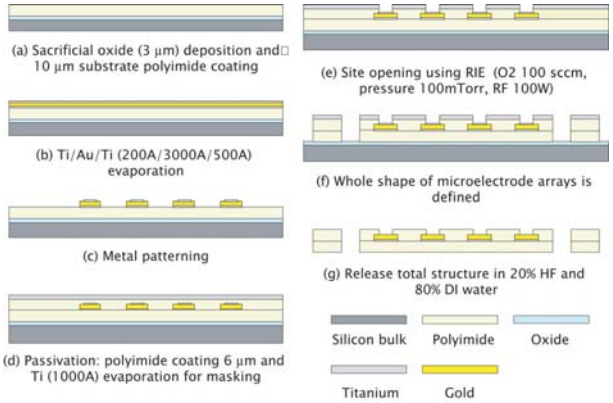

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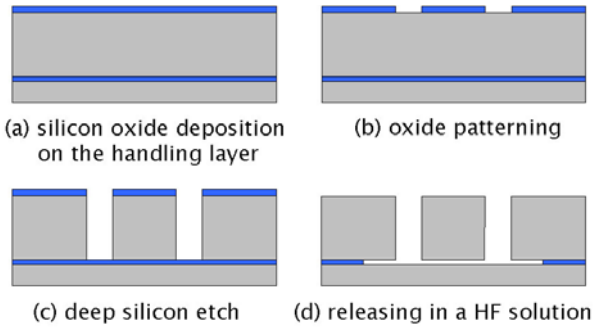
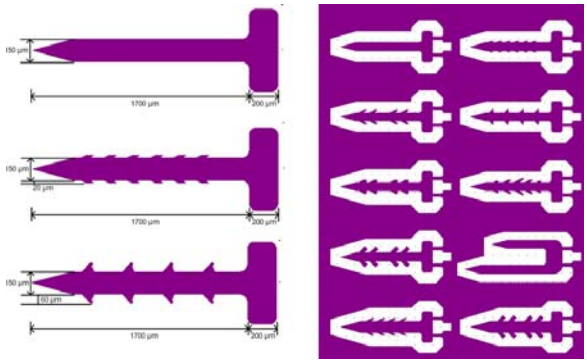
Figure 2: Fabrication process of polyimide electrode arrays

B. Silicon retinal tack

Silicon-micromachined retinal tacks are also developed by micro-electro-mechanical system (MEMS) technology to fix polyimide electrode array, which is a part of the artificial retina. Silicon wafer with the device layer of 100 μm, buried oxide layer of 2 μm, and handle layer of 300 μm was used. 2 μm of silicon dioxide was deposited on the backside by using plasma-enhanced chemical vapor deposition (PECVD), and then the structure was defined by photolithography. After silicon dioxide patterning, deep silicon etch was performed to the bottom of the handle layer, and the buried oxide layer of the SOI wafer was etched via



concentrated (49 %) HF solution in order to release structures. 3 μm-thick parylene film was deposited on



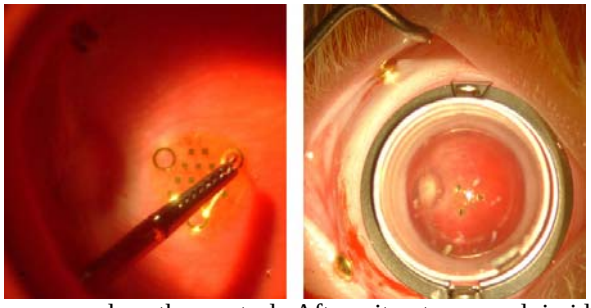
all the fabricated silicon retinal tack surfaces, enhancing the durability and chronic biocompatibility. (Figure 3 & 4).

Figure 3: Fabrication process of silicon retinal tacks

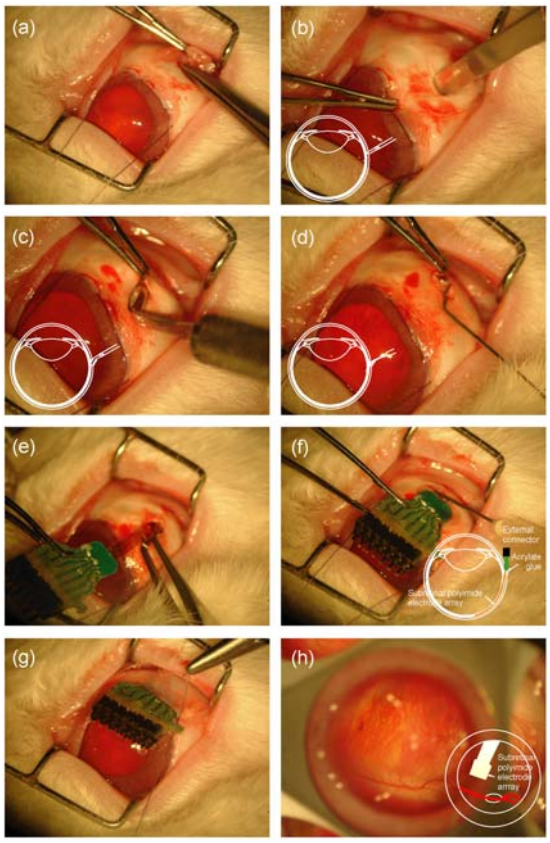
Figure 4: Dimensions and shapes of silicon retinal tacks

C. Epiretinal ans subretinal implantation of the polyimide electrode array

All procedures conformed to the Association for Research in Vision and Ophthalmology (ARVO) Statement on Use of Animals in Ophthalmic and Vision Research. *In vivo* experiment was performed in anesthetized rabbit eyes. Lens-sparing 3 port pars plana vitrectomy was performed in 5 white rabbits under repetitive intramuscular anesthetic injection of 25 mg ketamine and 6 mg xylazine per kg of body weight. The right eye of each rabbit was used for the test and the left



eye served as the control. After vitrectomy, polyimide MEA was inserted into the eyeball through the sclerotomy site and fixed onto the retina by silicon tack.



Sclerotomy site and conjunctiva were repaired with 8-0 vicryl suture (Figure 4).

Figure 4. Epiretinal implantation of the poylimide electrode array with silicon retinal tack

Figure 5. Subretinal insertion of the electrode array. (a) Traction suture and conjunctival incision. (b) Vertical incision of sclera in half thickness. (c) Scleral tunnel formation. (d) Injection of the viscoelastics into the scleral tunnel and the subretinal space. (e) Insertion of the polyimide electrode array with McPherson forceps. (f) Primary fixation of the external part of the

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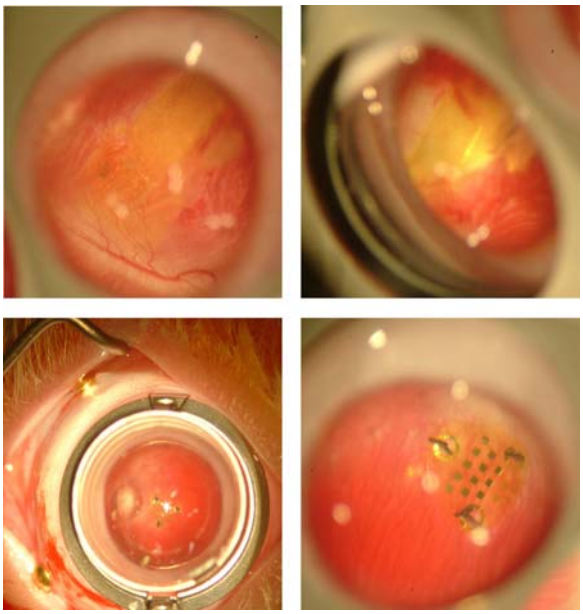
electrode array with acrylate glue. (g) Coverage of the external part of the electrode array with Tenon's capsule and conjunctiva. (h) Goldmann 3 mirror view of the subretinal electrode array.

For the subretinal implantation, electrode array was introduced under the subretinal space via transscleral approach without vitrectomy. At first, traction suture and conjunctival incision were done to expose the targeted scleral site. Sclera was vertically incised in half thickness and the scleral tunnel was formed to guide the electrode array under the retina. A small amount of viscoelastics was injected into the scleral tunnel and the subretinal space, and the polyimide electrode array was inserted into the subretinal space with McPherson forceps. Due to the elasticity and the recoiling characteristics of the polyimide, electrode array can be easily introduced into the subretinal space with gentle snap. The external part of the electrode array was temporally fixed with acrylate glue and after then, permanent fixation was done with 5-0 Dacron and 8-0 Nylon suture. The external part of the electrode array was covered with Tenon's capsule and conjunctiva (Figure 5).

During the follow-up period, regular indirect ophthalmoscopic examination was done to evaluate the inflammatory changes or other complications in vitreous and retina. The histological change of retina was also evaluated.

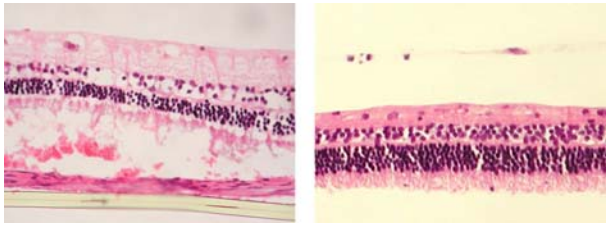
Results



Indirect ophthalmoscopic examination revealed that polyimide microelectrode array had not induced haziness or inflammatory change of vitreous for 2 years after the operations (Figure 6).

Figure 6: Postoperative 2 years of the subretinal electrode insertion (top) and 1 year of the epiretinal implantation of the polyimide electrode array (bottom).

Dissection of eyes also certified that there was no retinal detachment, vitreous haziness, cataract changes in both implantation techniques. There was no



displacement of epiretinally fixed polyimide microelectrode array or subretinally implanted array during follow-up period. Microscopic exam showed well-preserved retinal neurons in both cases. However, the photoreceptors of the eyes with subretinal implant showed degeneration, and it might be due to surgical damage during insertion (Figure 7).

Figure 7. Histological examination after 1 year of the subretinal (left) and epiretinal (right) implantation of the polyimide electrode array.

Discussion

In developing vision prosthesis, suitable nanobioelectronic techniques and fine, less invasive surgical procedures are very important. Choosing biocompatible and durable implant materials is also very essential. The reactions to implanted biomaterials are various according to the characteristic of biomaterial and the site of implantation, thus it is important to certify the biocompatibility of selected biomaterials with the tissues of the eye. It includes the affinity of retinal cells to stimulating electrode, inflammatory or other adverse reaction such as developing cataract, carcinogenic properties and so on.

Polyimide is cheap, easy to produce in large quantity and has well-known biocompatibility and flexibility. Polyimide has been tested as the candidate of substrate for microelectrode in artificial cochlear implant, in neural has not been tested extensively in retinal and associated tissues.

All the polyimide electrode array and silicon retinal tack showed acceptable biocompatibility and durability in *in vivo* test.

Conclusion

Both epiretinal and subretinal implantation of the polyimide electrode array can be done safely in rabbit eyes. Polyimide electrode array showed good biocompatibility in the rabbit eyes for 2 years.

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