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A Comparison of Retinal Prosthesis Electrode Array Substrate Materials

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Abstract

Simulations of artificial vision suggest that 1000 electrodes may be required to restore vision to individuals with diseases of the outer retina. In order to achieve such an implant, new technology is needed, since the state-of-the-art implantable neural stimulator has at most 22 contacts with neural tissue. A critical component of this system is the multi-channel, stimulating electrode array. This array must meet very challenging, competing requirements for manufacturing, integration, surgical handling, and biocompatibility. Our lab has evaluated 3 polymers as retinal prosthesis substrates: polyimide, parylene, and silicone.

Introduction

Several incurable eye diseases result in blindness for 100,000's of individuals each year.[1] One proposed treatment for these conditions is a retinal prosthesis that will stimulate the retina at many distinct locations to create a pattern of neural activation and thus a visual perception.[2,3] In order to function properly, a retinal prosthesis will require the presence of cells in the retina. Therefore, diseases primarily limited to the outer retina are potentially treatable with a retinal prosthesis. The two most common outer retinal degenerative diseases are age-related macular degeneration (AMD) and retinitis pigmentosa (RP). AMD is more prevalent but RP is more severe. Electrical stimulation in human test subjects with these conditions, has demonstrated the feasibility of an electronic retinal prosthesis as a means of providing some degree of vision. [4]

Retinal prostheses consist of external and implanted components. The external component has video capture, processing, and transfer capability. The video data is transmitted via a wireless link to the implant. Power is also wirelessly transmitted. Inductively coupled coils are typically used for this wireless link, although some systems use an optical link. The implanted system has the necessary circuitry to receive both power and data from the wireless link. The electronic circuits are hermetically packaged with enough vias through the package to connect electrodes to the current drivers. Typically, a ribbon cable is used with conducting lines for an interconnect from package to electrodes. The flexible cable and electrode array are typically formed in a single process, yielding a subcomponent we will call the flex electrode (which includes a ribbon cable).

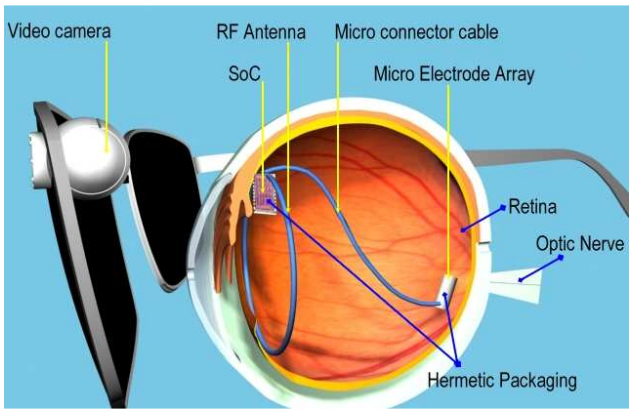

Fig. 1 Conceptual diagram of retinal prosthesis system. A video camera on a pair of glasses captures information. A wearable computer (not shown) processes video information and transmits it to the implant. Power is also sent wirelessly via inductive coils. The implanted electronics decode the information and produces DC chip power from the induced AC voltage on the power coil. The implanted chip produces a pattern of stimulation based on the received data. The stimulus pulse pattern is applied to the retina via a microelectrode array.

Methods

It is important to consider the system requirements with respect to the number of pixels needed for the patient to have useful vision. A number of studies have been performed that assess the visual task performance of normally sighted individuals while immersed in a simulated environment. These studies have been recently reviewed.[5] The combined results suggest that a retinal prosthesis must have 600-1000 individual pixels to restore function such as face recognition, reading, and unaided mobility. A handmade electrode array, like that used in a clinical trial [4], is not feasible with so many individual electrode sites required. Micromachining approaches are needed.

The flex electrode has several competing requirements with respect to mechanical properties. The flex electrodes must be robust enough to be assembled with a rigid electronics

case and handled with forceps during implantation. However, if the flex electrode is too stiff, it can damage the fragile retina. We have evaluated 3 materials for flex electrode substrates: polyimide, parylene, and silicone. In this paper we review the results of these studies.

Polyimide flex electrodes were developed and manufactured by Premitec Inc. (Raleigh, NC) in a microfabrication laboratory under clean room conditions. A drawing of the wide-field array is shown in figure 2. The microelectrode arrays consisted of gold traces connecting electrode sites with respective bondpads on opposing ends, sandwiched between two patterned layers of polyimide films (each about 10 μm thick). Standard microfabrication techniques were utilized to deposit and pattern the various layers involved, i.e. base polyimide film, gold traces and top polyimide film. A photodefinable polyimide material was spin-coated onto a sacrificial substrate material, such as a glass plate or silicon wafer, in order to maintain enough mechanical stability during subsequent processing steps. A thin film of chromium served as an adhesion promoting film between the polyimide surface and gold layer with thicknesses of 10nm and 200nm, respectively. The second polyimide film contains openings to define the size of individual electrode sites as well as openings for corresponding bondpads. As a final processing step, each device was removed from the sacrificial substrate by immersion into a metal etch bath, which removed the metal release film the sacrificial substrate was coated with.

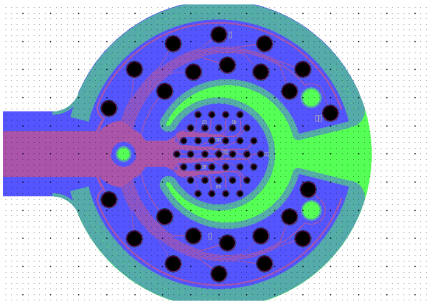

Fig. 2 - CAD drawing of polyimide wide-field array.

Parylene has been fabricated with multiple metal layers, which can address routing issues for conducting lines to a 1000 electrode array. Figure 3 shows the basic process steps. A sacrificial photoresist layer is spun on a silicon wafer. A 10 μm parylene layer is deposited on the entire wafer. 20nm of titanium followed by 200nm of platinum are patterned with a lift-off process. A 1 μm parylene layer is deposited between metal layers and 6 μm x 6 μm vias are patterned where interconnection between metal layers is needed. A second metal layer is patterned as before. A final layer of parylene forms the top insulating layer and electrode openings are created with a photoresist mask and reactive-ion etching in an oxygen plasma. If a sacrificial layer is used, then acetone is used to dissolve this layer for release. With no sacrificial layer, the devices can be peeled from the wafer. A post-processing annealing step (200 deg. C for 2 days in a vacuum oven) has been shown to greatly improve adhesion between the parylene layers.

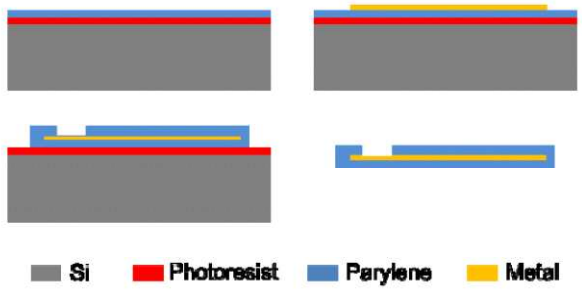

Fig. 3 – Simple diagram of photolithography steps for parylene flex electrode fabrication. Multiple metals layers require repetition of some steps.

Unlike the polyimide and parylene electrodes, which use photolithography, the silicone implants we have tested are fabricated using a novel technique based on laser treatment of silicone followed by electroless plating of metal that is restricted to the area of lasing. Medical grade silicone from Nusil is cured on a wafer to form a 50 μm film. Laser irradiation results in selective surface decomposition of silicone that preserves the (inorganic, Si-O) backbone structure of the polymer and eliminates its organic part (C-radicals). Use of a UV laser source at 248nm (corresponding to 5.0eV photon energy) limits photon absorption to Si-C bonds. The end product of that decomposition is a polymeric chain (i.e. poly-silica) that is formed of Si-O monomers. The irradiated silicone surface, which is now recessed a few μm below the original silicone surface, is readily metalized with electroless plating. Use of automated X-Y microcontroller facilitates patterning of metal lines (fig. 4).

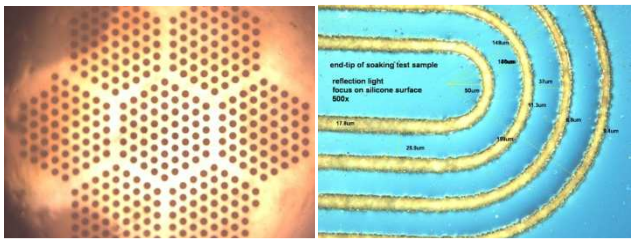

Fig. 4- Laser patterning allows metallization for (left) electrodes and (right) conducting lines on silicone

Flex electrodes can be evaluated in a number of ways, what we discuss here are basic biocompatibility tests that involve implantation in of the prototype devices in animal eyes to assess surgical handling. Long-term implants assess chronic pressure effects and stability. Only the flex electrode portion of the implant was tested (i.e. no electronics package or coil was included). Direct comparison of materials would require fabrication of components with similar dimensions. This was not done due to limited resources and differing project goals,

however we did model the different electrodes composed of each material in a recently developed Solidworks finite element model used to predict and compare mechanical interaction between arrays and the retina.

Results

The polyimide implants tested were wide-field arrays, measuring 11 mm in diameter, twice as wide as human retinal prosthesis arrays. A thermal forming process is used to pre-curve the arrays to match eye curvature. The arrays had a central portion and two wings, which allows folding to insert through a sclerotomy (eye wall incision) less than 4 mm. Arrays have been successfully inserted and unfolded in a canine eye (Figure 5). A retinal tack is used to attach the array to the retina. The wide-field allows stimulation in peripheral retina, which may be important for mobility. Difficulty was noted in matching the curvature of the device to the retina. Too much curvature resulted in unacceptable separation between the array and the retina (which leads to high thresholds). Too little curvature increased the chances of retinal damage due to force exerted by the array when conforming to the retina.

Parylene flex electrodes were implanted in 2 canines. The arrays were precurved using a thermal forming process. Array size was 5 mm x 6 mm. 1000 electrode sites were arranged in a pattern that matches the density of the retinal ganglion cell layer. The array was well-formed to the retina and the angiogram (Figure 6) showed good blood vessel integrity underneath the array.

To date, only short term (acute) implants have been done with silicone flex cables. A silicon flex cable measuring 4 mm x 5 mm was implanted. Figure 7 shows imaging data. Fluorescent imaging of the retinal vasculature shows good preservation of blood flow. OCT imaging shows close apposition between the array and the retina.

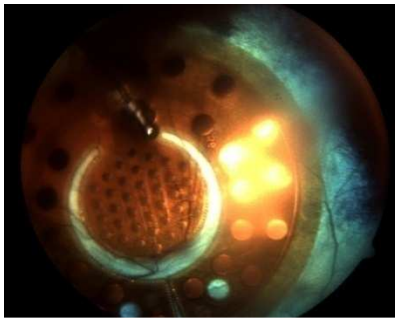

Fig. 5 – Polyimide, wide field array, photographed through the dilated pupil in a canine eye. Photo was taken 3 months post-operative.

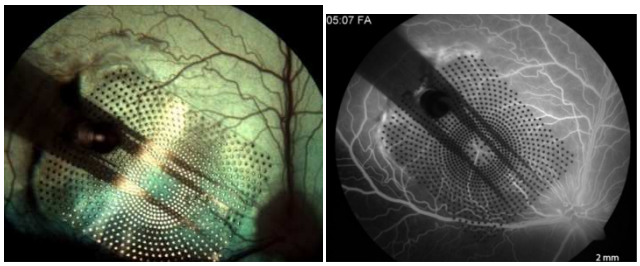

Fig. 6 – (Left) Fundus photo through a dilated pupil shows a 1000 electrode, parylene substrate array implanted on the retinal surface. Electrodes covers 5x6 mm area. Photo was taken 5 months post-operative (Right) Fluorescein angiogram of parylene array on the retina. Fluorescent dye appears white and shows the vasculature.

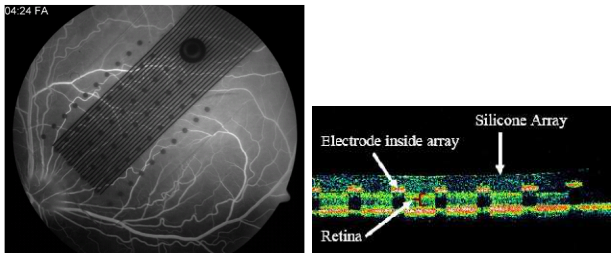

Fig. 7 – (Left) Fluorescein angiogram of silicone array on the retina. Fluorescent dye appears white and show the vasculature. (Right) Optical coherence tomography shows a cross section of array and retina. Photo was taken immediately after implantation.

A Solidworks model of the posterior eyeball was constructed with 4 layers: retina, choroid, sclera, and orbital fat. Literature values were used for Young's modulus. The force exerted by the retinal tack was directly measured using a load cell (Bose Electroforce 3100). Figure 8 shows Von Mises Stress in the retina for the three different materials when tacking a 5 mm x 6 mm array. The model predicts that parylene and polyimide arrays will distribute stress about the electrode array, while the silicone array concentrates stress around the tack site.

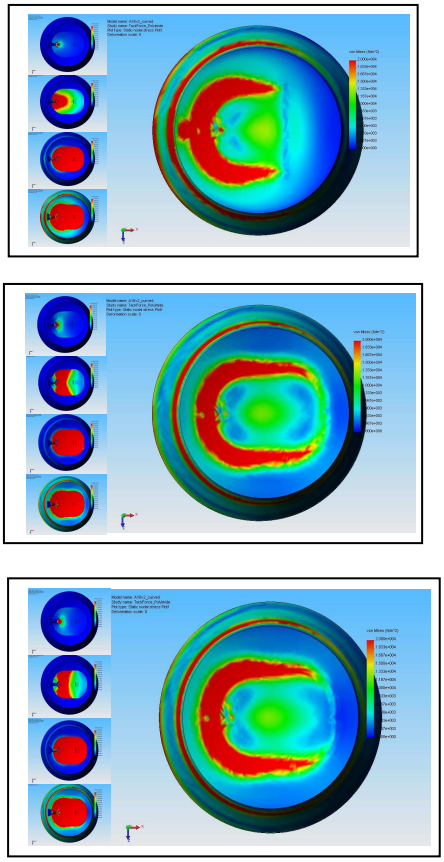

Fig. 8 – Mechanical model of (top) silicone, (middle) parylene, and (bottom) polyimide arrays tacked to the retina. Von Mises stress is shown, with red more intense stress in red.

Conclusions

Three polymers are used as substrates for retinal prosthesis flex electrodes. Comparing the manufacturing of the different substrates, polyimide is the easiest to fabricate, possibly due to its long history in flex circuits and the large number of labs working in this area. Parylene requires an annealing step for several days to fuse the parylene layers. Photolithography, used for parlyene and polyimide, is a well-established technique for patterning metal on polymer, but silicone has not been amenable to traditional metallization processes like sputtering or e-beam deposition. The novel laser treatment process solves this problem, but it is not clear if this can be incorporated into a mass production process. Also, the silicone metallization process is not mature and it remains to be proven. Comparing surgical handling, the silicone array is the most compliant and produces the least damage to the retina when incidental contact is made between the array and retina. Parylene also showed excellent long-term biocompatibility. Polyimide is the stiffest material, and extreme care was required when inserting these devices in the eye. Too much compliance may not be an advantage, however. The finite element modeling suggests that the pure silicone array may unacceptably distort during fixation to the retina with a tack. If only a single polymer can be used, parylene may have the best combination of properties, although it is not optimal. In separate studies in our group and by others, all three materials have shown acceptable insulation properties under conditions of long-term soak test. An alternative approach would be to combine polymers to take advantage of the favorable properties of each. A multi-polymer approach has been done in other implantable systems. [6]

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