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Flexible Thin Film Electrode Arrays for Minimally-Invasive Neurological Monitoring

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***Abstract*—We present approaches for using thin film polymeric electrode arrays for use in applications of minimally invasive neurological monitoring. The flexibility and unique surface properties of the thin-film polyimide substrate in combination with a compact device platform make them amenable to a variety of surgical implantation procedures. Using a rapid-prototyping and fabrication technique, arrays of various geometries can be fabricated within a week. In this paper we test two different approaches for deploying electrode arrays through small cranial openings.**

I. Introduction

About 1% of the United States population is afflicted with epilepsy, and at least one-third of these patients are likely candidates for epilepsy surgery [1]. Despite advances in antiepileptic drug development, only 50 to 70% of epileptic patients are controlled with medications [2]. For medication refractory patients, epileptogenic brain areas can be addressed surgically through non-invasive or invasive neurological functional mapping. Electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) are safe and noninvasive, but sometimes lack the spatial resolution to localize the regions of epileptogenesis. In such circumstances, subdural grids and strips are used to locate neocortical epileptogenic areas. While subdural girds have gained increasing popularity, they require a relatively large craniotomy, increasing the risk of intra-cerebral hemorrhage, infection and increased intracranial pressure [3, 4].

Various devices and platforms to record signals from the brain have been developed for brain-computer interface applications [5-8]. Flexible thin film electrodes have shown promising results in cortical recording tests: they are less invasive than penetrating microelectrode arrays, and show better signal quality than EEG [9-11]. In this paper, we present a flexible micro-electrode array for minimally-invasive neurological monitoring. Using a rapid-prototyping fabrication technique, arrays of various geometries can be fabricated within a week. These novel devices are expected to induce a smaller tissue response and be less invasive than current devices, and the high electrode density will provide spatial cortical information on a scale unavailable in current clinical electrode arrays. Finally, the flexibility and unique surface properties of the thin-film polyimide substrate in combination with a compact device platform make them amenable to a variety of surgical implantation procedures. In this paper we test two different deployment techniques that are suitable for minimally invasive surgical approaches.

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II. Materials and Methods

A. Flexible Thin Film Electrode Microfabrication Process

Polyimide PI-2729 (HD Microsystems) was chosen over other polyimides to fabricate flexible thin film electrode arrays because of its excellent insulation characteristics and because it can be microstructured by photolithography. The multilayer process for integrating metal tracks, micro-vias and interconnection pads is illustrated in Fig. 1.

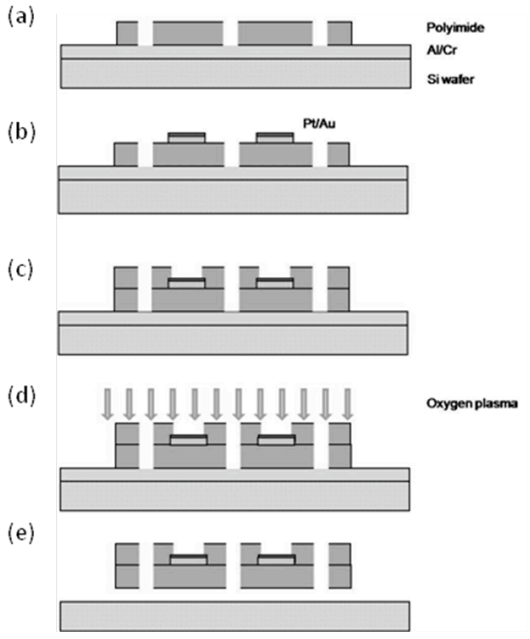

Fig. 1. Microfabrication process of flexible thin film electrode arrays; (a) Photo-patterning of polyimide on Al/Cr coated Si wafer (b) A lift-off process after Cr/Au/Pt metallization (c) Photo-patterning of polyimide as top layer (d) Oxygen plasma treatment (e) Substrate release by metal dissolution technique

For release of the microstructures, chrome (10nm) and sacrificial aluminum (300nm) were evaporated on 100 mm silicon substrates. On the aluminum surface, a 20 μm thick layer of PI-2729 polyimide was applied for the base layer,

photo-structured and then cured in a nitrogen atmosphere oven. The interconnection pads, connecting lines, and electrode sites were patterned by a lift-off technique after metallization (10 nm Cr/250 nm Au/50 nm Pt) by e-beam evaporation. After metallization, a second upper polyimide layer was spun onto the wafer and photo-defined to insulate the metal interconnects. Oxygen plasma treatment was applied to remove remaining polyimide or solvent. The flexible thin film electrode arrays were released by an anodic metal dissolution technique. The wafer containing the devices to be released was immersed in a concentrated sodium chloride solution together with a Pt counter electrode. A positive 0.8 V was applied to the aluminum layer using a constant-voltage supply. During the anodic metal dissolution process of the aluminum layer, the chrome remained on the substrate due to the difference in electrochemical potential compared to aluminum. After their release, the arrays were rinsed in DI water and subsequently dried.

B. Benchtop Electrode Deployment Testing

PDMS (Sylgard 184) was mixed in a 10:1 ratio of base and curing agent in a disposable plastic boat for use as a flexible brain surface phantom. To degas the bubbles in the PDMS mixture, a desiccator connected to a rotary pump was used to apply a vacuum to the PDMS mixture until no bubbles remained. Degassed PDMS was poured into a Petri dish until the gap with the top cover reached 5 mm, to replicate the gap between the brain and the cranium, and then cured at room temperature. A hole with a 10 mm diameter was made in the top cover to simulate a craniotomy for insertion of the flexible electrode arrays. The dish was filled with saline solution (HyQ Phosphate buffered saline, Hyclone) to simulate cerebrospinal fluid.

C. Cadaver Monkey Testing of Electrode Deployment

Two electrode deployment techniques were tested in fresh Rhesus macaque (Macaca mulatta) cadavers. All procedures were approved by the University of Wisconsin Animal Care and Use Committee. The animal's head was held in a stereotaxic frame while a craniotomy 1-2 cm in diameter was made with a burr drill. For the first technique, a looped electrode was delivered into the craniotomy with a brass tube oriented perpendicular to the cranium, 1 cm in diameter. Advancing the electrode into the tube delivered the looped electrode radially from the craniotomy, above the dura. For the second deployment technique, a stiff guide introducer was guided by hand through the craniotomy. Both epidural and subdural approaches were used. Video was captured with an endoscopic camera inserted into another distal craniotomy, approximately 5 cm from the electrode deployment site.

D. Mechanical Bending Testing

The surface of the thin film electrode array was lowered, following contact with saline solution, until the electrode is submerged. Subsequently, the thin film electrode array was slowly raised, but maintains an electrical connection due to surface interaction with the saline. Electrical impedance measurements were made with a two-electrode cell configuration using an Autolab potentiostat (PGSTAT12, Eco Chemie, Netherlands) in saline solution. The impedance was measured at a range of frequencies from 100 Hz to 100 kHz at every 1mm movement.

III. RESULTS AND DISCUSSION

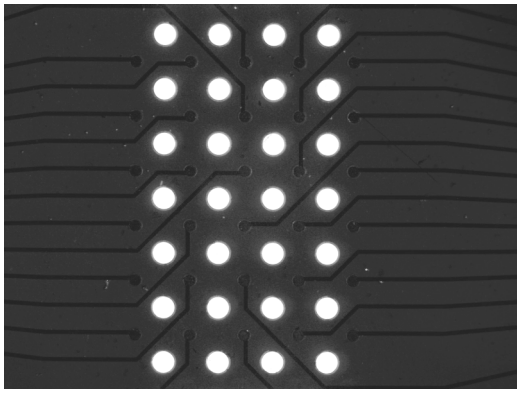

Fig. 2. Example of flexible thin film electrode arrays.

A. Flexible Thin Film Electrode Microfabrication Process

Implanted microelectrode arrays must be mechanically and electrically stable in the physiological environment, and also flexible enough to conform to the soft, convoluted structures of the brain. Among other polymers, photo-definable polyimide PI 2729 was particularly chosen because of high resolution and wide range of thickness (over 20μm). It exhibits excellent insulation characteristics and good chemical/thermal resistance as well as high flexibility. As seen in Fig. 2, flexible electrode arrays consist of electrode sites and holes, which are intended to facilitate consistent brain surface perfusion, as well as allowing other micro-electrode recording or imaging techniques through the array. Rapid prototyping, combined with microfabrication techniques, allows for more variation in electrode size and spacing in electrode structure that can be customized for a given application or animal. Mask prototyping is a flexible technique that expedites the implementation of new designs and decreases overall design cycle time, allowing new device designs to be tested and either accepted or rejected within a very short time frame.

The microfabrication process for flexible electrode arrays did not include any wet or dry etching steps. Traditionally a wet etching method using a HF solution is utilized to release completed structures from oxidized silicon wafers [12]. This technique may lead to over-etching and critical damage to the device. Since releasing the device is usually the final step, small defects can jeopardize the integrity of the final device. Dry etching by chlorine gas is also a common technique to make structures in polyimide, but requires an additional mask set and could be harmful to biological

tissues. Therefore, the metal dissolution technique chosen for releasing completed devices is a gentle and safe process. Release was carried out at room temperature, and devices are smoothly released and float in the solution when it was finished.

B. Benchtop Electrode Deployment Testing

Two key points to consider in minimally-invasive neurological monitoring applications are the tradeoffs between producing a small insertion site in the skull and providing extensive coverage of the brain surface. The flexibility of the thin-film polyimide electrode arrays allowed expansive radial coverage of targeted brain regions from a small insertion site. Before testing the device in a primate model, the deployment of flexible electrode arrays were tested in a closed Petri dish filled with cured PDMS; a 5 mm gap was left between the PDMS surface and the dish lid. The electrode was then inserted through a 10 mm opening in the dish lid, and deployed onto the PDMS surface (see Fig 3). Since fully cured PDMS is elastic and transparent, it is possible to observe the contact between the flexible electrodes and the surface of PDMS, prior to use in a real brain. When flexible electrode arrays were inserted through the small opening, we observed the two arms of the electrode bending and the electrode surface making full planar contact with the PDMS surface. As the array was pressed down, the total contact area expanded laterally from the 10 mm opening to cover approximately 20-30 mm (See Fig. 3 for a depiction of the array).

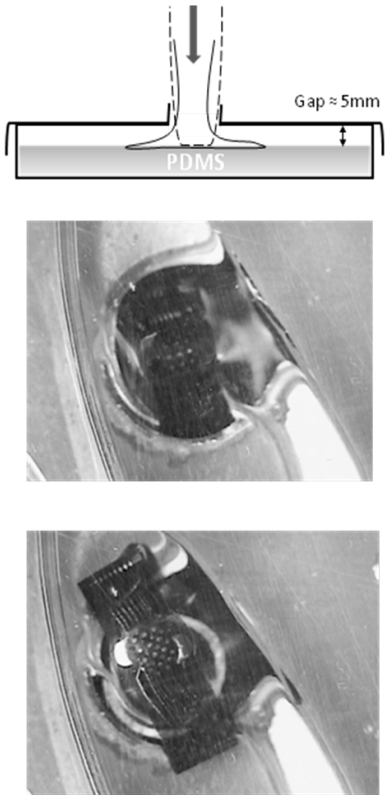

Fig. 3. (above) Schematic of the Petri dish test setup. (middle and below) Insertion of flexible thin film electrode arrays into the petri dish.

C. Cadaver Monkey Testing of Electrode Deployment

Two deployment techniques were tested in which electrode arrays were deployed through a small craniotomy. The surface of the looped electrode arrays made good contact with the dura (see Fig. 4), and the two arms containing electrical leads bent naturally. This bending will likely provide mechanical stability for future chronic implantation in humans and animals.

The second deployment technique worked both epidurally and subdurally (see Fig. 5), but it required a thicker introducer to prevent buckling during advancement. We found that small placement corrections could be made laterally, following insertion (Figs. 5 b-c), so the electrode array would not have to be removed and replaced to correct small placement errors.

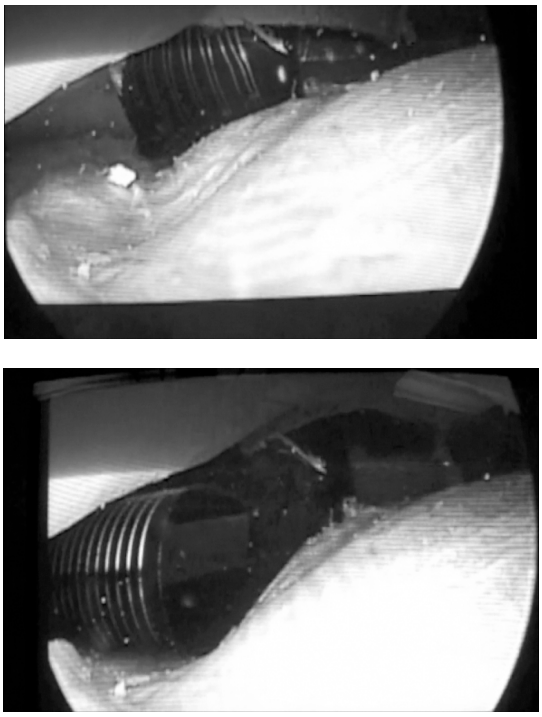

Fig. 4. The looped electrode bends naturally as it deploys under the cranium. The bottom surface of the electrode can be seen making good contact with the dura.

D. Mechanical Bending Testing

The consistency of the electrode electrical impedance properties was tested under wide range of vertical movement while maintaining contact with saline solution. Figure 6 shows the change in impedance, normalized to its initial value, versus its vertical displacement position. The electrode contact with the saline surface is sustained up to a vertical displacement of 8 mm, with just less than 4% change in impedance. When the cable arms of thin film electrode arrays are deflected, the inside portions of arm are forced into compression by the bending, while the outside

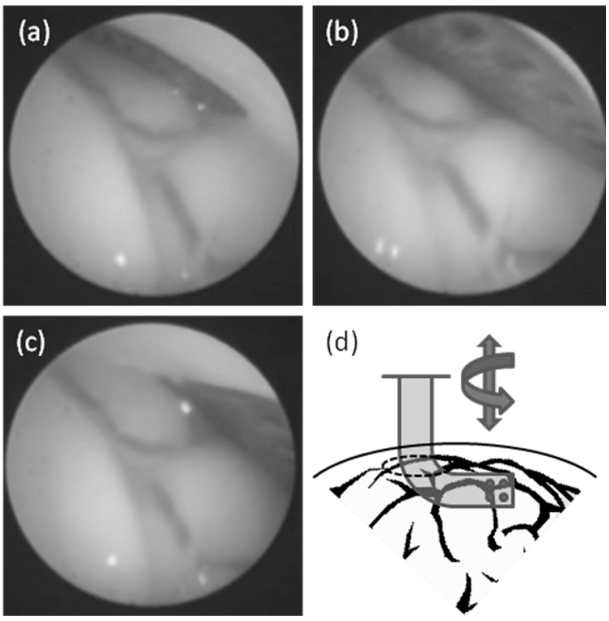

Fig. 5. (a-b) The electrode array advances subdurally. (b-c) The electrode can be shifted laterally. (d) A schematic showing the deployment of the electrode array.

portions of the arms are extended in tension. Since the metal lines are located closer to the top side of electrode structure (Fig. 1), the electrical lines received tensile stress in either stretching or bending. Under the tensile stress condition, the cross-sectional area becomes smaller, and thus makes the impedance values larger [13]. As a result, impedance values increased in both lowering and raising the electrode arrays while maintaining tight contact with the saline solution. Due to the negligible mass of the array, surface tension dominates this contact mechanism. This is an advantage for possible long-term implants, because the brain will not be compressed by the thin electrode arrays due to the pulsatile micromotion of the brain surface.

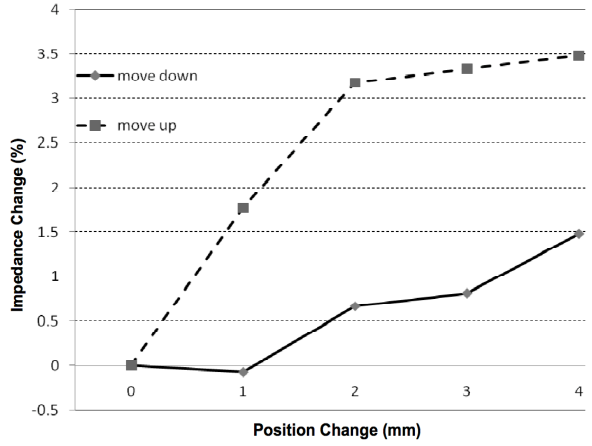

Fig. 6. Change in the normalized impedance at 1KHz of thin film electrode arrays vs. the movement of micromanipulator. The zero position indicates the natural bending without additional stress or strain.

The buckling arms and the adhesive surface have potential advantages during long-term implantation, because the brain is not motionless; it undergoes minute changes in position based on pressure fluctuation due to just heartbeat and respiration. This steady contact of thin film electrode arrays may help maintain long-term contact with the cortex with minimal mechanical effects felt by the brain.

IV. CONCLUSION

The mechanical properties of polyimide thin-film electrode arrays make them suitable for use in less invasive intracranial deployment strategies. The choice of fabrication materials and techniques should provide a biocompatible and MRI compatible device. Future work will include testing these devices in live animal models.

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