Encapsulation of Flexible Biomedical Microimplants with Parylene C

T. Stieglitz[1], S. Kammer[1], K. P. Koch[1], S. Wien[2], A. Robitzki[2]

Neural Prosthetics Group[1], Biohybrid Systems Department[2]
Fraunhofer-Institute for Biomedical Engineering
Ensheimer Strasse 48, D-66386 Sankt Ingbert, Germany
thomas.stieglitz@ibmt.fhg.de

Abstract

Parylene has been used as encapsulation material since several decades, e.g. for wires, needles and pacemaker coatings. Within this paper, its use as insulation and protection layer for flexible biomedical microimplants is described. Investigations on the deposition, structuring with reactive ion etching and the cytotoxic behavior of the etched layers led to promising results. Parylene seems to be an appropriate material to protect hybrid assemblies of microimplants from water and ions.

Keywords: parylene, polyimide, cytotoxicity, microimplant, neural prostheses

1. Introduction

Parylene is a polymer that is available for more than 25 years, but its biomedical use has been limited to the United States of America (USA) for no obvious reasons [1]. Only recently has it found increased applications in Europe beyond its traditional use in pacemakers.

Applications of parylene coatings range from the encapsulation of electronic circuits under harsh environments to the insulation of implantable wires and electrodes. It has to be found as a chronically stable, reproducible microelectrode insulator [2] with a good *in vivo* biocompatibilty [3] in the subdural space. Even though widely used in cardiac pacemakers, a certain contact sensitivity of parylene to skin reactions was reported [4]. A good biostability of the coatings could be observed in the absence of mechanical stresses. Electrical leakage tests on thin and flexible wires under cyclic stressing (up to 11 % strain while bending at an angle of 170°) led to increased currents that indicated a deterioration of the insulation [5]. Recording electrodes with parylene coating were often exposed by laser ablation [6] that might not be suitable for thin-film metallization.

Within the last years, we developed polyimide-based substrates with integrated thin-film electrodes for the use in neural prostheses [7]. Building up functional systems with a hybrid integration of microelectronic circuits and components, we need a reliable encapsulation that insulates the electronics and blocks water and ions. Parylene was chosen to be an appropriate candidate that should be investigated in combination with our polyimide-based electrodes.

In this paper, we present the first results on parylene deposition and patterning with reactive ion etching, some investigations on adhesion on different substrate materials and a preliminary *in vitro* cytotoxicity testing of the material after plasma etching.

2. Materials and Methods

2.1. Parylene Deposition and Patterning

Parylene has become the generic name of the poly-para-xylylenes. Three different types of dimer types are available: Parylene N, C, and D. For biomedical implants, parylene C (Fig. 1) with one chlorine atom on the benzene ring has favorable properties due to lowest permeability to moisture and corrosive gases. The films are (theoretically) pinhole-free even at a thickness of less than 1 µm.

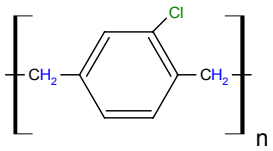

Fig. 1: Chemical structure of Parylene-C monomer.

The deposition of parylene C took place in a "Lab Top 3000" parylene coater (Paratec, Inc.) that uses the standardized Gorham-process [8]. We used no adhesion promoter, the A-174 Silane adhesion promoter and/or plasma activation (49 sccm O_2, 70 W, 10 s) before parylene deposition, respectively. Parylene films were deposited on different test substrates like glass, FR4 printed circuit boards, aluminum oxide ceramics, polyimide, silicon, and different silicones. Reactive ion etching (RIE) was used to pattern the parylene films. Investigations were done mainly with different ratios of oxygen and CF_4 gases in a STS 320 PC (Surface Technology Systems) reactor.

2.2. Adhesion of Parylene

The adhesion between the parylene layer and the underlying substrates was measured on test structures with a bond pull tester (Dage PC 2400). Therefore, the substrate with the parylene layer was glued with epoxy resin upside

down on a carrier (Fig. 2). The shear tests were performed with a velocity of 500 µm/s.

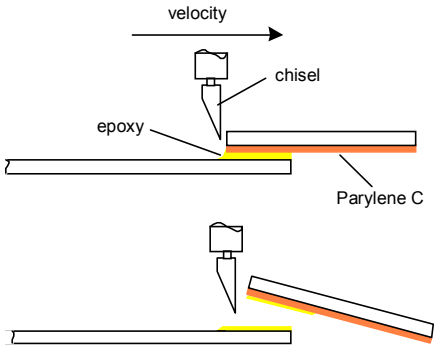

Fig. 2: Shear test to investigate adhesion of Parylene C on different substrates.

2.3. Cytotoxicity Testing

To asses the *in vitro* cytotoxicity of the material directly after deposition and after reactive ion etching, we have established qualitative and quantitative means according to the international standard ISO 10993. The effects were compared with negative (non-toxic) and positive (toxic) control material, e.g. PU tube and HEMA.

3. Results

3.1. Parylene Deposition and Patterning

We have deposited parylene C layers on planar test substrates and on hybrid assemblies of flexible polyimide substrates with electronic components (Fig. 3)

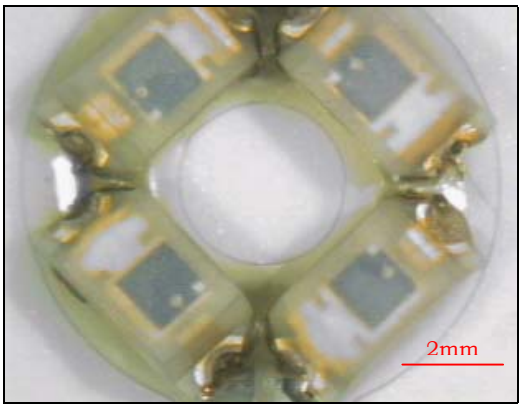

Fig. 3: Encapsulation of four photodiodes that have been soldered onto gold contact pads on a polyimide-based substrate.

The parylene C coating was deposited conformal over the devices with a high aspect ratio. Measurements with an spectroscopic ellipsometer showed transmission of the layers of approximately 80 % in the near infrared (NIR) and the visible light (VIS) region.

Contact angle measurements with drops of water proved the hydrophobic surface properties. We obtained a contact angle of 89°. After RIE the contact angles changed. Etching with pure oxygen led to a nearly unchanged contact angle of 86° while a CF_4/O_2 mixture led to a hydrophilic surface with a contact angle of 4°.

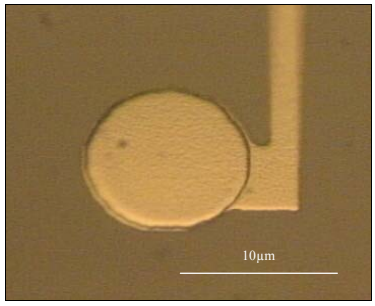

Fig. 4: Gold thin-film electrode between two layers of Parylene C. The electrode site has been opened by RIE (O_2, 150 W, 85 mTorr, 49 sccm).

The different etching rates with pure O_2, CF_4 or mixtures of both were measured. Electrodes with a diameter of 10 µm were patterned with pure O_2 plasma (Fig. 4) with steep edges and smooth wall surfaces.

3.2. Adhesion of Parylene

The adhesion of the parylene C on glass, silicon, aluminum oxide ceramic, and FR4 was between 450 N for glass up to 600 N for FR4 with Silane A-174 adhesion promoter. The limiting parameter was the strength of the epoxy glue. Using polyimide PI 2611 (HD microsystems), SU-8 and different silicones (Nusil MED 100, MED 6015, Dow Corning MDX 4210) nearly no adhesion was obtained without and with adhesion promoter. Only a plasma activation of the surfaces led to a good adhesion of parylene C on polyimide (460-640 N) and on the silicones (up to 280 N). The combination of plasma and adhesion promoter led to the best adhesion on SU-8 (530 –630 N).

3.3. Cytotoxicity Testing

The *in vitro* cytotoxicity testing revealed no toxic effect of the deposited and plasma etched parylene C layers. The qualitative direct contact tests showed good viability of the L 929 cells on all layers. The adhesion of the cells was diminished on the untreated surfaces (Fig. 5). The hydrophobic surface led to an altered cell morphology with round cells that cluster. The more hydrophilic surfaces after plasma treatment resulted in a normal cell morphology with good cell adhesion (Fig. 6). The quantitative measurements have been done with extracts tests. Cell vitality (WST-1 test) and DNA synthesis rate (BrdU-test) were in the range of the negative (i.e. non-toxic) control material. Parylene C that has been etched with a O_2/CF_4 gas mixture was slightly more inhibiting (11%) the cell metabolism and DNA synthesis rate than the oxygen plasma.

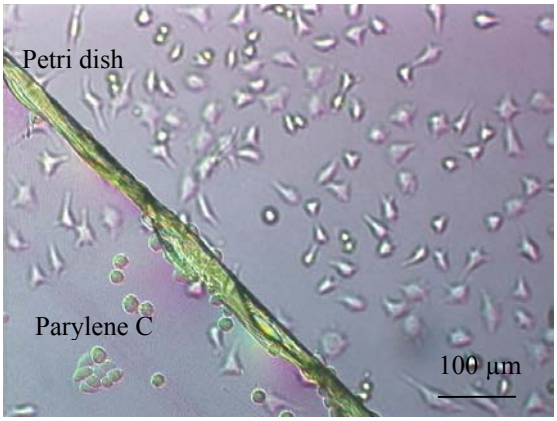

Fig. 5: Direct contact test with L 929-cells on Parylene C. Vital cells but hardly cell processes and accumulation of cells.

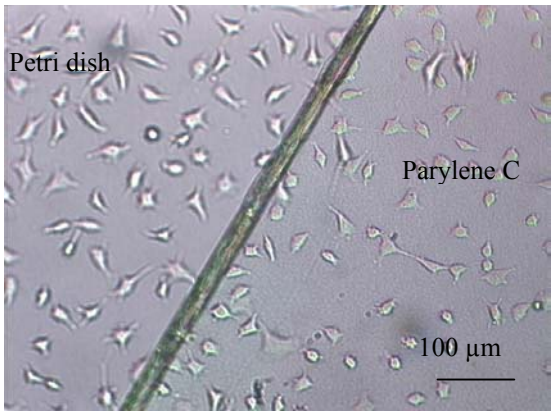

Fig. 6: Direct contact test with L 929-cells on Parylene C after O_2 dry etch. Vital cells.

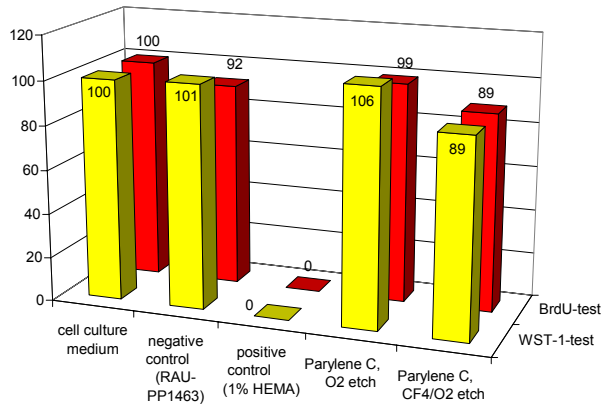

Fig. 7: Extract testing of Parylene C after dry etching. DNA-synthesis (BrdU-test) and vitality (WST-1 test) with L 929-cells.

4. Summary and Conclusions

Parylene C seems to be a suitable encapsulation material for biomedical microdevices. However, the use of adhesion promoter and surface plasma activation of the substrates is recommended to ensure an appropriate adhesion and a reliable hermetic encapsulation in combination with other materials. Hybrid assemblies of microelectronic components on flexible polyimde-based substrates of 15 µm thickness were conformal coated. Reactive ion etching allows parallel patterning of many structures on a wafer with high accuracy. The parylene C before and after reactive ion etching showed excellent *in vitro* cytotoxicity.

Within the next steps, we will characterize the adhesion of parylene C to polyimide and to silicone elastomers in detail. The mechanical and electrical biostability will be investigated with regard to applications of long-term stable microimplants, e.g. in a retina implant for the blind or in smart electrodes [9] for limb control in quadriplegic persons.

References

[1] J. Noordegraaf, "Conformal Coating Using Parylene Polymers," Med. Device Technol., 8(1), pp. 14-20, 1997.

[2] G.E. Loeb, M.J. Bak, M. Salcman, E.M. Schmidt, "Parylene as a chronically stable, reproducible microelectrode insulator," IEEE Trans. Biomed. Eng., 24 (2), pp. 121-128, 1977.

[3] T.G. Yuen, W.F. Agnew, L.A. Bullara, "Tissue Response to Potential Neuroprosthetic Material Implanted Subdurally," Biomaterials, 8 (2), pp. 138-141, 1987.

[4] N. Iguchi, H. Kasanuki, N. Matsuda, M. Shoda, S. Onishi, S. Hosoda, "Contact Sensitivity to Polychloroparayxlene Coated Cardiac Pacemakers," Pacing Clinic. Electrophysiol., 20 (2 Pt 1), pp. 372-373, 1997.

[5] M.F. Nichols, "Flexible and Insulative Plasmalene Wire Coatings for Biomedical Applications," Biomed. Sci. Instrum., 29, pp. 77-86, 1993.

[6] E.M. Schmidt, M.J. Bak, P. Christensen, "Laser Exposure of Parylene-C Insulated Microelectrodes," J. Neurosci. Meth., 62 (1-2), pp. 89-92, 1995.

[7] T. Stieglitz, H. Beutel, M. Schuettler, J.-U. Meyer, "Micromachined, Polyimide-based Devices for Flexible Neural Interfaces," Biomedical Microdevices, 2 (4), pp. 283-294, 2000.

[8] W.F. Gorham, J. Polym. Sci., A4, pp. 3027, 1966.

[9] M. Schuettler, K. P. Koch, T. Stieglitz, O. Scholz, W. Haberer, R. Keller, J.-U. Meyer, "Multichannel Neural Cuff Electrodes with Integrated Multiplexer Circuit," Proc. 1st Ann. Int. IEEE-EMBS Special Topic Conference on Microtechnology in Medicine & Biology, October 12-14, Lyon, France, pp. 624-629 (2000).