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FACULTEIT GENEESKUNDE EN LEVENSWETENSCHAPPEN
master in de biomedische wetenschappen

Masterproef
Microelectrode array system for neuron-muscular application

Promotor :
Prof. dr. Milos NESLADEK

Ali Parsapour
Scriptie ingediend tot het behalen van de graad van master in de biomedische wetenschappen

De transnationale Universiteit Limburg is een uniek samenwerkingsverband van twee universiteiten in twee landen: de Universiteit Hasselt en Maastricht University.



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List of abbreviations

- MEAs : Micro-Electrode Arrays
- CVD: Chemical Vapour Deposition
- PVD: Physical Vapour Deposition
- MWPECVD: Microwave Plasma Enhanced Chemical Vapour Deposition
- NCD: Nano-Crystalline Diamond
- BNCD: Boron-doped Nano-Crystalline Diamond
- PI: Polyimide
- EMG: Electromyography
- SEM: Scanning Electron Microscopy
- EDAX: Energy Dispersive Analysis of X-ray
- AFM: Atomic Force Microscopy
- FTIR: Fourier Transform Infrared Spectroscopy
- PAA: Polyamic Acid
- PDMS: Polydimethylsiloxane
- CNS: Central Nervous System
- PNS: Peripheral Nervous System
- RIE: Reactive Ion Etching
- RMS: Root Mean-Square
- WA: Work of Adhesion
- ECoG: Electrococtogram
- SCCM: Standard Cubic Centimetres per Minute

Abstract

Throughout this thesis, different methods and techniques were employed in order to fabricate flexible polyimide Micro Electrode Arrays (MEAs) with embedded active diamond sites. Diamond is a notable alternative to metal and metal oxide neural interfacing electrodes due to its biocompatibility, resistance to surface bio-fouling and water hydrolysis which leads to tissue damage.

The microelectrodes contain active and connector areas. Active area is made of conductive boron-doped nano-crystalline diamond which is fabricated by means Microwave Plasma Enhanced Chemical Vapour Deposition (MWPECVD) and insulated by polyimide.

Metals such as gold are deposited by using Physical Vapour Deposition (PVD) on polyimide surface for creating connection between active BNCD electrode areas and electrical lead connector . However, Polyimide surface does not have active sites with coupling agent to initiate metal adhesion. Therefore, in this study, two different methods for PI surface treatment are investigated in order to improve adhesion of Cr/Au and Au layer on PI films. The two methods are Oxygen plasma and chemical treatments which are used for improving the adhesion of metal to polyimide by increasing hydrophobicity of polyimide surface.

The surface properties of the electrodes are investigated and characterized using Scanning Electron Microscopy (SEM), Atomic Force Microscopy (AFM), Optical microscope, Fourier Transform Infrared Spectroscopy (FTIR) and Contact angle measurement. Recording sites were characterized by using impedance spectroscopy.

Highly flexible polyimide electrodes with diamond have been successfully fabricated as EMG electrodes for *in-vivo* measurements. Diamond–metal–polyimide sandwich structure provides insulation and mechanical flexibility for bio-interfaces application. This new generation of flexible EMG electrodes is a step forward to improving bio-material techniques for engineering of man – machine interfaces.

1-Introduction:

1-1-General introduction and aim of the thesis

Nervous system disorders affect the quality of life of afflicted people and are the most difficult to treat. Ageing, diseases or health problems can cause some neurological disorders such as Alzheimer and Parkinson or other forms of neural damage that are also largely observed (spinal cord lesions, strokes, etc.) [1].

One of the most important medical challenges is the increase of life expectancy. To handle this issue, innovative therapeutic solutions are still required [2]. Electrical stimulation and recording of nerve cells have been used in neuroscience studies for over a century [3]. On the other hand, neural implants are mainly used to stimulate affected parts and structures of the nervous system with the help of implanted electrical circuitry or record the electrical activity of nerve cells [4].

Neuromodulation and macroscopic neural implant are known concepts used already in neural devices and clinical therapies, developed in last decades. However, only recently, sophisticated modern micro-fabrication technology and advances in material sciences [1-3] facilitated development of microscopic neural devices that lead to significantly lower damage of neural tissue.

The aim of this research is to fabricate flexible nano-materials, specifically nanocrystalline diamond electrode integrated with polyimide for electrical stimulation and recording by using Electromyography (EMG) technique and to use the favourable electrochemical and mechanical properties of BNCD electrode simultaneously. Boron-doped nano crystalline diamond electrodes are designed and successfully fabricated to provide tissue compatible neural implants.

We report on the successful integration of B-doped diamond with polyimide EMG and produce functional devices. These devices are intended to be used for human prosthetic devices with the advantage of diamond biocompatibility and beneficial electrical characteristics for EMG reading.

1-2-Micro-Electrode Array system (MEA)

Microelectrode array techniques have become increasingly important nowadays as they are very promising for applications on the biomedical domain, namely disease diagnostic and molecular biology. In the past decade, many types of neural implantable electrodes which are fabricated by MEAs have been reported [4].

There are different types of implantable MEAs which are based on metal, silicon and polymer. Up to now; MEAs have been fabricated by three different techniques named microwire, micromachined, and flexible arrays [4].

Microwires which are mostly made from tungsten or stainless steel were the first implantable electrodes to record chronically from the brain [5]. Micromachined electrode arrays are mainly silicon or metal based. A flexible multi-electrode array is another type of electrode. In this type, the metal-based electrodes are coated by two layers of polyimide without a silicon structure [6]. Flexible arrays provide an advantage over rigid electrode arrays because of the less/negligible mechanical match with muscle tissue [6-7].

Table 1 shows briefly comparison among different techniques which used for fabricating MEA.

Table 1. Advantages and drawbacks of MEA fabrication methods [7].

| Method | Advantages | Disadvantages |
|-----------------------|--|--|
| Microwire arrays | Access to deep brain structures Multi-neuronal recordings for simultaneous recording at the level of neural populations | Electrode tips location cannot be controlled (to bend during implantation) |
| Micro-machined arrays | Ease of implantation Stimulate more localized regions of tissue | Rigid and may fracture May damage neural tissues during insertion |
| Flexible arrays | Flexibility reduces the chronic tissue inflammation response | Flexibility nature implies difficulty in insertion |

Micro-fabrication technology is the term used to describe the group of technologies or processes for fabrication at the micrometer scale of electronic devices or Microelectrode Array system (MEAs). The fabrication of micro-devices includes many processes which is done in sequence and even repeatedly, as for example photolithography, etching, film deposition, wafer cleaning, etc. [7].

An implantable MEA allows a communication between man and machine, which in all cases are the electronics interfaced to the nerve cells in the body. The microelectrodes can be used to transmit electrical signals to the neurons and modulate their behaviour *in-vivo*, or sense neural signals [8].

Electrodes which are fabricated by MEAs have dimensions of tens of micrometers or less, down to submicrometer range. They are different from macroelectrodes. These differences are caused by changing conditions of the mass transport from solution toward the electrode and have several important practical implications, such as minimizing ohmic IR-drop, fast establishment of a steady-state signal, a current increase due to enhanced mass transport at the electrode boundary, and increased signal-to-noise ratio. These effects make sufficiently small electrodes (Microelectrode) advantageous in the areas of man-machine interfaces [9]. In fact, to be able to use the MEAs efficiently, the electrode must be able to deliver enough charge to exceed the stimulation threshold of nerve cells. Furthermore, many applications require high-resolution stimulation, which means the electrodes need to be small enough, densely packed, and able to produce localized excitation. Therefore, MEA techniques have been developed to have a long-term and stable interface with the nerve cells [8-9].

In this project, polyimide on Boron-doped Nano Crystalline Diamond (BNCD) electrodes have successfully been fabricated which results in production of flexible electrodes for Electromyography (EMG) devices that significantly reduces damaging of tissue and nerve cells at neural interfaces rather than silicon (rigid) - based electrodes.

1-3-Material selection

The essential parameters which should be considered for microelectrodes as neural implant before and after using in the body are as follow:

1-3-1-Biocompatibility

Biocompatibility is the ability of a material to perform with an appropriate host response in a specific application in body implants [10]. In fact, it means that the tissue of the patient that comes into contact with the materials does not suffer from any toxic, irritating, inflammatory, allergic, mutagenic or carcinogenic action.

However, any surgical operation can cause an inflammatory response as a normal physiological response to the operation. In the presence of an implant, this response might be enhanced and extended depending on the chemical composition of the implant's surface [11]. For instance, the materials which are used in this project such as diamond, gold and polyimide are biocompatible.

1-3-2-Biostability

The chemical, electrical and mechanical properties of the material should be stable in long term *in vivo* studies, such as body implants.

The technical term “biostability” summarizes different chemical aspects with respect to material stability and system integrity. Metals should not corrode, and substrate and insulation layers should not delaminate or degrade. In polymers, hydrolytic, oxidative and enzymatic degradation should not occur as it can be accelerated by pH changes and voltages on integrated interconnect lines [12].

1-3-3-Mechanical properties

A neural implant should have enough mechanical flexibility to avoid causing damage to the tissue from relatively small movements in the body as well as avoid damaging from the tissue movements. Structural biocompatibility refers to mechanical interaction between the implant and the surrounding tissue and includes weight, shape and flexibility (Young's modulus). Mechanical mismatch has been reported as leading to cell and tissue damage, followed by a release of mediators as a result of the implantation event initiating the inflammatory response [13].

1-4-Materials for microelectrode arrays

1-4-1-Silicon

Silicon makes up to 25.7% of the earth's crust, by weight, and is the second most abundant element, being exceeded only by oxygen. Silicon is not found free in nature, but occurs chiefly as the oxide and as silicates. Sand, quartz, rock crystal, and opal are some of the forms in which the oxide appears.

A Silicon wafer is a thin slice of silicon crystal which is commonly the basic semiconductor material, used in the fabrication of integrated circuit and other micro devices. The wafer serves as the substrate for microelectronic devices that are built-in and over-the-wafer. This process undergoes many micro fabrication steps such as doping or ion implantation, etching, deposition of various materials, and photolithographic patterning and, etc. [14].

1-4-2-Diamond

Diamond is one of the hardest natural materials, having one of the highest thermal conductivities at room temperature. It is transparent over a very wide wavelength range, one of the stiffest materials, one of the least compressible, and inert to most chemical reagents at room temperature. With these remarkable properties, diamond has been referred to be one of the best natural materials for biological interfacing.

The unique electrochemical properties of diamond such as wide electrochemical potential window in aqueous solution, low voltammetric background current and prolonged stability, make it attractive for applications in electrochemical analysis and biomedical application [15].

It is therefore needless to say that the possibility of growing diamond from the gas phase by using chemical vapour deposition (CVD) has been the starting point of a large number of developments in diamond crystal growth [16].

Nano crystalline Diamond (NCD) films cover a wide variety of materials ranging from films with properties approaching to single crystal diamond, which are useful for specialized applications such as microelectrode array system. However, when the size of the electrode is decreased, the surface/volume ratio increases considerably and the surface phenomena predominate over the chemistry and physics in the bulk. Thus, there are some specific properties for the NCD films that differentiate them from microcrystalline [16-17].

1-4-3- Polyimides

Polyimides are a type of commercially available polymers most widely used in various aspects of biomedical applications. Among the polymers suitable for MEAs applications, polyimide has received a great attention due to its thermal and chemical stability, low dielectric constant, high electrical resistivity, and relative ease of processing into coating and films. For all these reasons,

polyimides have been widely used in microelectronics as dielectric spacing layers, protective coatings and substrates for metal thin films. Moreover, Polyimide is available as photo-definable and non-definable version whereas photo-definable polyimides tend to have a higher moisture uptake that limits their use in vitro [18].

Polyimides are synthesized from two monomers, a dianhydride and a diamine. Commercial products are supplied as soluble polyamic acid (PAA) intermediates, which undergo a thermal imidization with the evolution of water to form the insoluble polyimide. Moreover, they contain in molecules functional group CO-NR₂ called imide. The presence of n- π conjugation between non-pair electron of nitrogen atom and π electrons of the carbonyl group makes them resistant to chemical agents and moisture. Mainly the type of hydrocarbon residues (arenes, aliphatic) and the presence of other functional groups (Cl, F, NO₂, OCH₃, etc.) determine their physical properties and their application in practice [19].

Although polyimide, especially the BPDA/PPD type which is shown in figure 1, is most often used as biomaterial and commercially available under the trademark of DuPont's such as PI2611 and PI2574, various groups have proven its biocompatibility, low cytotoxicity and low hemolytic capacity, both for bulk materials and long-term implanted electrodes.

Existing applications of polyimide are manifold and include peripheral nervous system (PNS) and central nervous system (CNS) implementations, such as cuff and intrafascicular electrodes or shaft and ECoG electrodes, respectively [20].

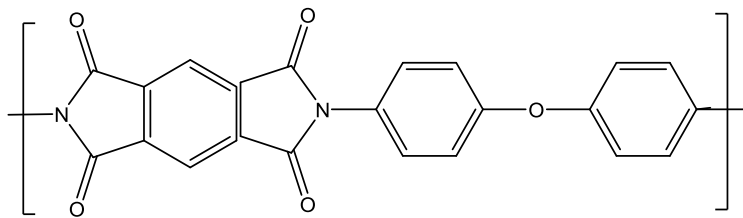


Figure 1: Chemical structure of a typical polyimide

To develop an interface between the electronics and living nerve cells, many aspects are needed to be considered.

In the recent years, silicon-based microelectrodes have not been used, because their rigid structures can lead to problems on *in-vivo* applications due to silicon's brittleness [21]. Since the

material does not deform in the organs, if the recording position shifts slightly, the cells will damage when the body moves. This is why this kind of rigid electrode is not suitable for long-term neural recording [22].

Microelectrodes have a significant impact on biomedical applications as neural devices for recording and stimulation of electrical activity of the muscles. Therefore, these electrodes could incorporate with an appropriate flexibility to prevent one of the major problems in the implantable MEAs.

As micromotion which occurs between electrode and the soft neural tissue during normal activity, might cause tissue damage, and induce the foreign body response. Polymer-based microelectrodes should be applied to comply better with tissue motion by reducing the mechanical mismatch issues which is result of reducing the stiffness of the device substrate ($E_{\text{polymer}} = \sim 1\text{--}4 \text{ GPa}$) besides having appropriate biocompatibility [21-22].

Polymers have been widely used as an alternative to silicon material for implantable MEAs as they have been able to employ flexible materials. Polyimide, Parylene and PDMS on diamond are some examples [23].

Here, Diamond was chosen as a biocompatible and durable platform for fabrication of MEAs. Due to a low baseline current, good chemical stability, biocompatibility and reduced biological fouling and many other interesting properties. Moreover, diamond can be engineered conductive by Boron-doping in the layer [24]. Diamond electrodes allows neural stimulation capabilities at higher applied voltage while avoiding water hydrolysis that leads to tissue damage, and provide long-term stability [25].

In addition to stability in the biological environment, nanodiamond coatings have been shown to promote the formation of neural networks which may be advantageous for maintaining their close contact between the implanted electrode and the surrounding neurons [23-25].

2-Materials and Methods

2-1-Cleaning silicon wafer

Silicon wafers were used as support for the polyimide structures. These wafers were used for materials deposition only. The wafers used had a size of 4 inches which corresponds to approximately 101.6 mm with a thickness 1 mm.

Before depositing silicon dioxide as sacrificial layer, silicon wafer is cleaned by two steps according to standard wafer cleaning procedure:

In the first step, the silicon wafer is immersed in acidic solution which contains miliQ water, hydrochloride acid (20%) and hydrogen peroxide (20%) with ratio of 6:1:1 respectively at 75° C for 10 minute. In the second step, after rinsing well and drying the silicon wafer, it is immersed in basic solution which contains miliQ water, ammoniac (20 %) and hydrogen peroxides (20 %) with ratio of 5:1:1 respectively with the same temperature and time as first step.

Figure 2 shows a cleaned silicon wafer which is washed according to above mentioned procedure



Figure 2: The surface of cleaned silicon wafer

The surface of the wafer is checked under the microscope to assess the cleanness microscopically.

2-2 -Depositing of silicon dioxide

A 500- μm thick SiO_2 was deposited on 4 inch silicon wafer with physical vapour deposition technique for 5 h using a silicon target, depositing the silicon particles using Argon and Oxygen ions of according to the parameters in Table 2.

Table 2. Silicon dioxide growth parameter

| | |
|--------------------------|---------------------------|
| Power | 100 W |
| Pressure | 1.5×10^{-3} mbar |
| Ar flow rate | 75 sccm |
| O ₂ flow rate | 25 sccm |
| Depositing rate | 100 nm/ h |
| Working Temperature | Room temperature |

2-3-Annealing the deposited silicon dioxide

There is a thermal stress in the deposited silicon dioxide due to difference in thermal expansion coefficients of the coating and the substrate [26-27]. To remove the residual stress, the sample is annealed by heating from room temperature to 1000 ° C using heating rate of 5° C/min for 2 hour in the annealing furnace. Cooling was carried out by shutting off the power of the furnace and estimated cooling rate of 2° C/min.

2-4- Coating diamond on the sample

In the next step, we need Boron doped Nano-Crystalline Diamond (BNCD) film as the conductive layer of our electrodes. For that, the sample has to be seeded with nano diamond particles. To do that, the sample is immersed in a solution of nano particles of diamond in milliQ water and then spun dried. After the seeding, the sample is loaded in the ASTEX diamond reactor to grow BNCD with thickness of approximately ~200nm by Chemical Vapour Deposition (CVD) method. Figure 3 shows a picture of the MPECVD reactor (ASTeX AX6500 system) used in this thesis. It consists of a microwave source, a vacuum system, a gas injection control box, a manual control cabinet, and a computer control system. The upper output power limit of the microwave source is 1.2 kW.



Figure 3: ASTeX reactor for BNCD growth

2-5- Patterning conductive diamond

To pattern the conductive diamond as the electrodes, a photolithography step is employed. First of all, the surface of sample should be de-hydrated by placing on hotplate at 180 °C for 5 min. The coating of the photoresist includes a bi-layer stack; the primer -used for adhesion promotion- and the photoresist itself. The prime (MCC primer -MicroChem Corp, Germany) is spun coated on sample in 2 steps; 500 rpm for 5 seconds and then 4000 rpm for 30s and then is baked on hotplate at 110 °C for 120s.

After that the negative lift-off photoresist (ma -N 1420, MicroChem Corp, Germany) is spun coated on the sample again in two steps; 500 rpm for 5 seconds and then 3000 rpm, 30sec, then baked on the hotplate at 100 °C for 120s. Finally, the sample is exposed to the UV light (365nm) for 40 seconds, using the photo mask of the electrodes which is shown in figure 4. In this mask we define 22 BNCD electrodes. Each electrode contains 16 ellipses as active area and each ellipse has the dimension of 50 x150 μ m with spacing of 850 μ m. After development in developer solution (ma-D 533/S, micro resist technology GmbH) for 150 s, the photoresist is not be presented in the conducting area of the electrodes. Then about 300nm Chromium (Cr) is deposited on the sample by PVD method, using the parameters in the table 3.

Table 3. Chromium deposition parameters

| | |
|----------------------|-------------------------|
| Power | 150 W |
| Pressure | 4×10^{-3} mbar |
| Ar flow rate | 50 sccm |
| Deposition time | 20 min |
| Thickness of coating | 340 nm |

Once deposited, the photoresist is lifted-off in acetone; consequently, Cr is used as a mask to protect the conducting area of the electrodes on BNCD film. To pattern the BNCD film, the unmasked BNCD is etched away in Reactive Ion Etching (RIE) in O_2 plasma, according to the parameter in Table 4.

It should be noted that this etching takes place with a faster rate at the edge of the sample than in the centre. Also, the BNCD layer is slightly thicker in the middle of the wafer than in the edge and this is due to the difference in power of the plasma. Thus, one must carefully check for the complete etching of the BNCD on the whole surface.

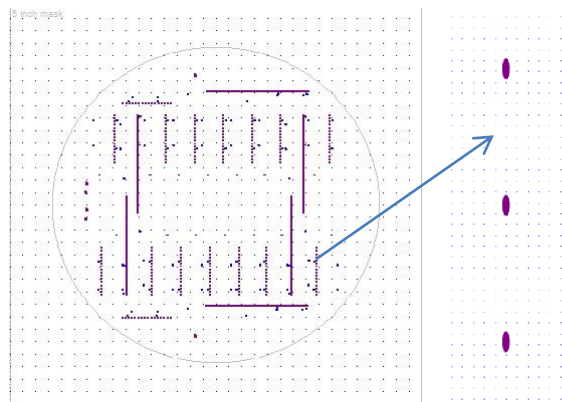


Figure 4: Diamond mask of electrodes

Table 4. Reactive Ion Etching (RIE) O₂ plasma parameters

| | |
|--------------------------|-------------------------|
| Power | 300 W |
| Pressure | 5×10^{-3} mbar |
| O ₂ flow rate | 50 sccm |
| Time of etching | 1:30 h |

2-6-Coating the first insulating layer

To insulate the BNCD electrode, polyimide-2574 (PI-2574-HD microsystems GmbH) is used. PI-2574 is self-priming and does not require an adhesion promoter. Prior to coating, the sample should be cleaned in acetone by ultra-sonification and then de-hydrated on hotplate at 180° C for 5 min. It is spun coated on the patterned sample with diamond electrode by steps followed in Table . The main purpose of doing soft bake of polyimide is partly driving out the solvents in the layer, which makes it adhere partially to silicon dioxide. Since this Polyimide is not photosensitive, there is a need for an imaging resist. For patterning insulating part, a positive photoresist (S1818, MICROPOSIT– MicroChem, and Germany) is then spun –coated on polyimide and is baked on hotplate at 90° C for 1min.

Table 5.PI processing parameters

| | |
|------------------------------------|---------------------|
| Spin-speed | 500 rpm for 5 sec |
| | 3000 rpm for 30 sec |
| Soft bake temperature, followed by | 120° C, 150° C |
| Soft bake time (hot plate) | 30s |
| | 30s |
| Thickness of cured polyimide | 11 μm |

After that the coated sample is exposed to the UV light (365nm) for 16 seconds, using the insulating mask of the electrodes which is shown in figure 5. In this mask we define insulation layer for the 22 BNCD electrodes. Each electrode contains 16 ellipses of $45 \times 135 \mu\text{m}$ which has designed slightly smaller to make sure it covers the BNCD electrodes. Moreover, contact area of each electrode has 16 squares of $700 \times 700 \mu\text{m}$ with spacing of $570 \mu\text{m}$ (vertically) and $1100 \mu\text{m}$ (horizontally). The length of each electrode is 6cm in total- a needle part is defined for insertion of the electrode to the tissue and the thickness of the needle is $150 \mu\text{m}$ with the length of $4650 \mu\text{m}$. Finally, the exposed sample is developed in developer solution (ma-D 533/S, micro resist technology GmbH) for 50S. After the developing, the remaining photoresist will be removed by Acetone.

After developing step, the sample should be hard baked or cured by heating from room temperature to 200°C with heating rate of $4^\circ \text{C}/\text{min}$ and then holding on at 200°C for 30 min. Following, the heating continues from 200°C to 300°C with heating rate of $2.5^\circ \text{C}/\text{min}$ and holding for 1 h, finally, cooling down gradually. The cure process was carried out in N_2 atmosphere.

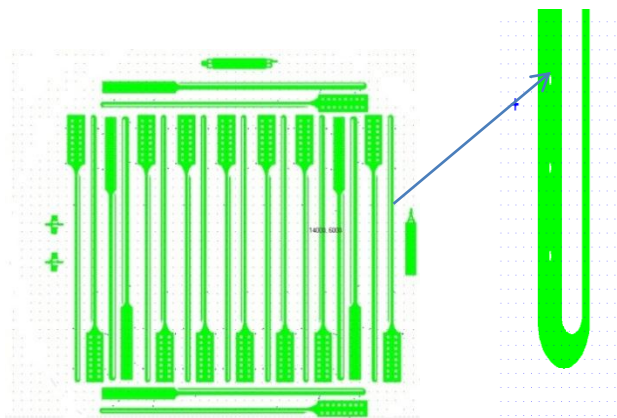


Figure 5: The insulating mask (PI-1) of electrodes

2-7-Surface modification of Polyimide

After patterning polyimide (PI-2574) on the surface of electrodes and curing it, the surface was treated with 10 wt. % KOH aqueous solution at room temperature in the range of 0 to 60 min in order to slightly etch the surface and increase the roughness of surface and polar functional group. The excess amount of KOH was removed by washing with miliQ water (2 - 3 min). Then,

the polyimide was treated with 10 wt. % HCl aqueous solutions at room temperature for 5 min, and the treated samples were (rinsed and) dried and kept under vacuum for 12 h [32].

Physical surface treatments have also used for final polyimide insulating layer which include O₂ plasma treatment of 100 and 50W in 35 sccm of oxygen.

2-8- Metal Patterning as the connecting lines

To connect the BNCD electrodes to the contact measurement areas, metallic lines are patterned. For that, a photolithography step is employed. First of all, MCC-primer and negative photoresist (ma -N 1420) should be spun- coated on treated PI, and baked on hotplate at 110 and 100° C for 120s, respectively.

After that, the sample is exposed to the UV light (365nm) for 50 seconds, using the metal mask of the electrodes to pattern metal part which is shown in figure 6. In this mask we also define 16 ellipses of 50x150µm as electrodes and 16 squares of 700x700µm as connector site. Each electrode is connected to a square with a line of 10µm. After development in developer solution (ma-D 533/S, micro resist technology GmbH) for 150 seconds, the photoresist will not be present in the metal areas of the electrodes.

Finally, the metals (Au in this case) are deposited with thickness of approximately 100 nm to the treated polyimide by PVD method according to parameters in the table 6, then metal is patterned on the polyimide by lift off in acetone to dissolve the photoresist and to remove all excess metal. In this method, the metal is used to connect active area (which is area that will be exposed to neuron or cells-BNCD ellipses) to connector area (which is the part that will be attached to the measurement device outside of the biological environment).

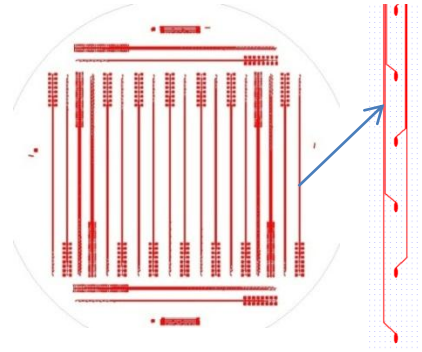


Figure 6: Gold mask of electrodes

Table 6. Gold growth parameters

| | |
|----------------------|-------------------------|
| Working Pressure | 5×10^{-2} mbar |
| Deposition time | 10 min |
| Thickness of coating | 100 nm |

2-9- Polyimide coating for insulating the electrodes

In the final step, Polyimide is coated on the electrode to insulate them. It is exactly patterned like the previous PI procedure, to make a sandwich of polyimide – metal – polyimide, with BNCD as active sites of the electrodes. At this step the polyimide will cover the whole electrodes. A picture of final polyimide mask is shown in figure 7. It covers the whole area of the electrodes with the thickness of the body $500 \mu\text{m}$ and needle $150 \mu\text{m}$.

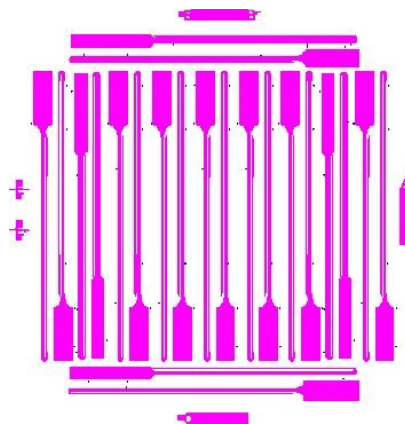


Figure 7: Mask of final polyimide (PI-2) layer

2-10-Surface Characterizations of the electrodes

2-10-1- Optical microscopy

An inverted optical microscope was used to observe the patterns fabricated on the silicon wafer after each step of fabrication. Optical microscopy confirmed the macro-properties of the structures optically.

2-10-2- Atomic Force Microscopy (AFM)

AFM measurement was performed for untreated and treated PI with a Park Systems NX10. In each case, an area of $10 \times 10 \mu\text{m}$ was scanned using the tapping mode in air at room temperature. The surface topography of the treated and untreated polyimide was evaluated in terms of the Root Mean-Square (RMS) of the roughness from the roughness profile by AFM. Moreover, the morphology of the nucleation sites of the diamond -BNCD was characterized by AFM.

2-10-3-Contact angle measurement

Contact angle was measured for untreated and treated samples using the dynamic sessile drop method with the “Contact angle system OCA” from Data Physics instruments GmbH, Germany for an average of 6 measurements per sample with a standard deviation below 1.4° .

2-10-4- Scanning Electron Microscopy (SEM)

Surface morphologies of BNCD, cross section of diamond/PI/SiO₂ and morphology of patterned polyimide on silicon wafer were investigated by SEM using a Fei Quanta 200 F setup.

2-10-5-Fourier Transform Infrared Spectroscopy (FT-IR)

FT-IR spectrum gives information about the chemical structure of the bulk. FT-IR spectra of cured polyimide without any surface treatment were obtained using Vertex 70 series FT-IR spectrometers, from Bruker’s instruments GmbH, Germany. The scans were ranging from 400 to 4000 cm^{-1} .

3-Results and Discussions

3-1-Micro-fabrication

EMG electrodes were fabricated according to step-by-step procedure in a clean room. For the fabrication, several techniques such as Diamond growth, photolithography, metal deposition, Reactive Ion Etching (RIE) and wet etching and lift off have been used. To successfully fabricate the EMG electrodes, a fabrication plan was necessary to be defined. A schematic of micro fabrication steps is shown in figure 8.

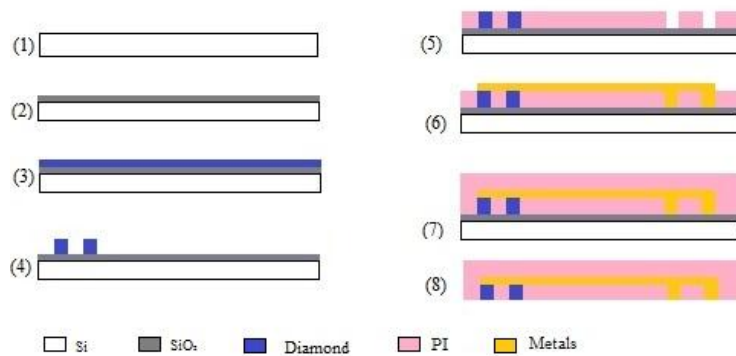


Figure 8: Cross-sectional schematics describing the fabrication of diamond-on polyimide microelectrode arrays

3-2- Flexible diamond electrodes

Flexible diamond electrodes are fabricated using BNCD diamond ellipses, connected with metallic lines and fully insulated with Polyimide. The final electrodes were released from the Si wafer substrates by etching the sacrificial layer (SiO₂) in 4% HF which is shown in figure 9. One attractive aspect of the release process in HF is that it is compatible with the polyimide layer as the insulating layer of the electrodes.

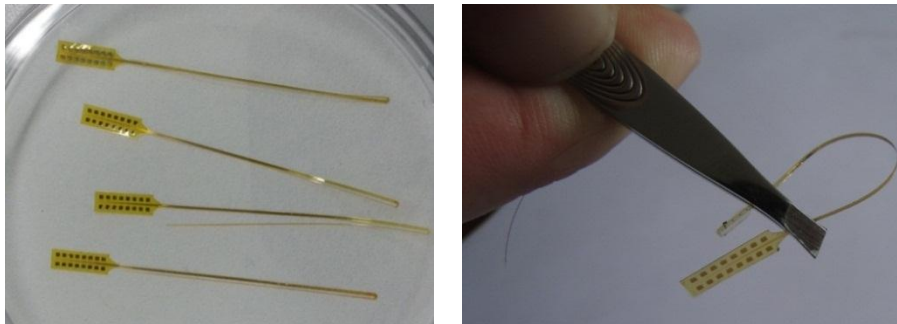


Figure 9: Image of the flexibility and fabricated electrodes

3-3-Characterization of silicon dioxide layer

Silicon dioxide coating has an amorphous structure after sputtering using PVD system. Annealing silicon oxide layer was necessary to release the residual stress and increase the crystallinity of SiO₂ layer on silicon wafer [28]. The thickness of deposited SiO₂ layer was confirmed using SEM which is shown in figure 10. This layer is needed as sacrificial layer to release the devices from wafer by being dissolved it in diluted HF solution.

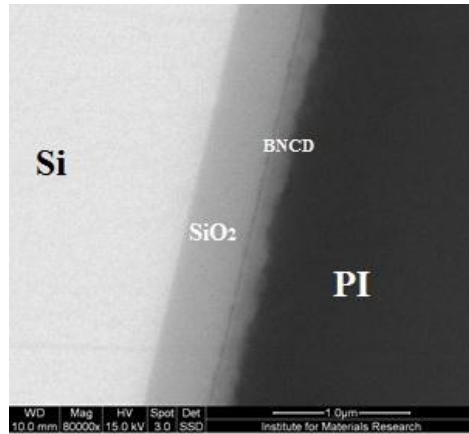


Figure 10: Cross-section of deposited silicon dioxide on silicon wafer

3-4- Surface characterization of patterned BNCD diamond

Several techniques have been used to study the morphology and topography of diamond film in our electrodes (Optical microscopy, SEM, Raman Spectroscopy). These methods help us confirm the decent patterning of the structures.

3-4-1-Reflection optical microscopy

BNCD patterned microscopic image was taken using optical microscopy which is shown in figure 11. In addition, it shows the ellipses which are patterned BNCD electrodes as active electrode sites.

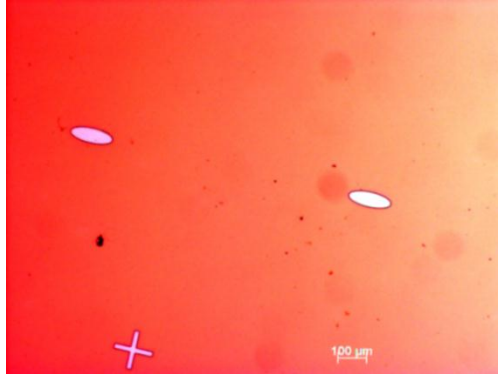


Figure 11: Microscopic image of patterned BNCD

This image represents two ellipses of BNCD which are covered with Cr mask, on a Si/SiO₂ substrate (red back ground colour is due to specific filters used in the microscope). The ‘plus’ sign shown in the image is the alignment mark that is used to align the following photomask on the previously patterned elements. Moreover, this image confirms that BNCD structures have been successfully patterned and the side walls are defined well, using photolithography and negative lift off resist in the developing time of 150s.

3-4-2-SEM

The morphology of BNCD diamond surface has already been widely investigated in the literature [29]. Figure 12 shows the crystalline morphology of diamond surface grown by MPECVD. Moreover, this structure is appropriate for coating the polyimide on the grown site with the thickness of 150 μm for BNCD layer.

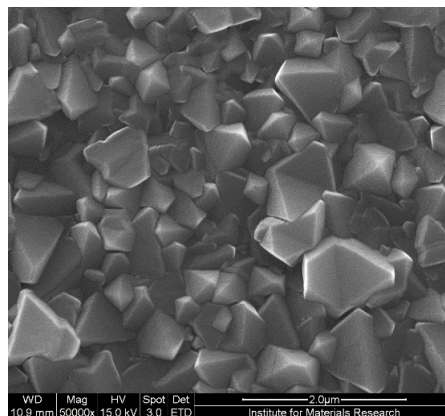


Figure 12: SEM morphology of BNCD surface

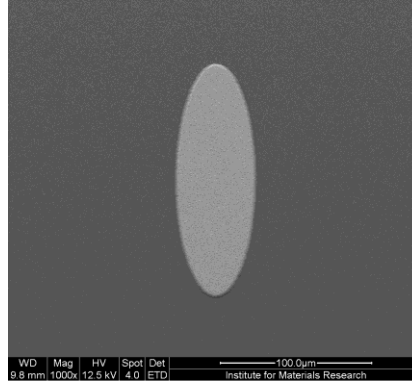


Figure 13: SEM image of the BNCD-active electrode area

Figure 13 is the SEM measurement of the BNCD ellipses, masked with Cr layer. This SEM image demonstrates the patterning of BNCD electrode of 50 μm by 150 μm on silicon dioxide substrate. Fabrication of the BNCD ellipses is performed by means of photolithography, metal deposition and Reactive Ion Etching of diamond.

3-4-3-Raman Spectroscopy

Raman spectroscopy was used to confirm the presence of diamond on the electrode sites which is shown in figure 14. As diamond presents a Raman peak at 1332 cm^{-1} and presents a Raman Peak at 1575 cm^{-1} which is due to presence of carbon in graphite foam (i.e. sp^2 bonded carbon) in diamond film,.

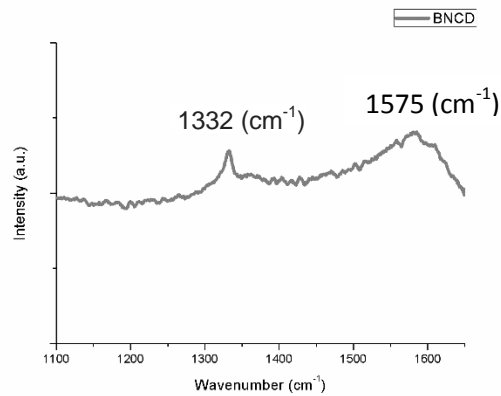


Figure 14: Raman spectroscopy of diamond on polyimide

3-5- Surface characterization of patterned Polyimide

Several methods are used to characterize the polyimide layer (FTIR, Optical microscopy, SEM and AFM) were used

3-5-1-FTIR- Chemical structure

Polyimide was cured after patterning as insulator part to convert polyamic) precursor into polyimide via imidization process and driving out remaining solvent from polyimide film [18-19]

Figure 15 shows the FT-IR spectra of cured polyimide. The key features of the FT-IR spectra of polyimide film are listed in table 6. Moreover, the FT-IR spectra of polyimide film confirm that curing has been completely done the imidization of polyimide.

Table 6. The key features of the FT-IR spectra spectrum of polyimide film are listed in table

| Peak position (cm ⁻¹) | Peak assignment |
|-----------------------------------|-----------------------------|
| 1780 | C=O (asymmetric stretching) |
| 1720 | C=O (Symmetric stretching) |
| 1550 | N-H bending |
| 1513 | C=C in benzene ring |
| 1380 | (C-N) in imide |
| 1244 | (C-O) Stretching |
| 1116 | (C-N) stretching |
| 725 | C=O imide ring deformation |

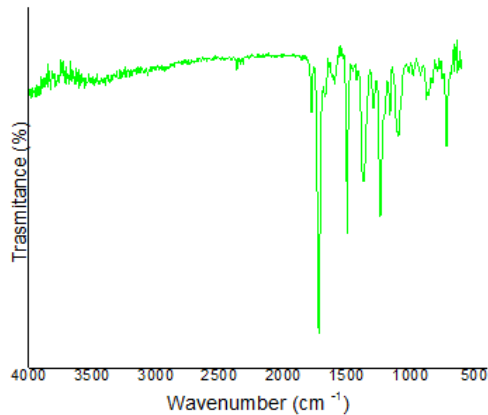


Figure 15: FT-IR spectra of cured polyimide

In figure 15 the characteristic absorption bands of the cured polyimide appear near 1780 cm^{-1} (C=O in phase), 1720 cm^{-1} (C=O out of phase), 1513 cm^{-1} (C=C in C_6H_6), 1380 cm^{-1} (C-N in imide) and 725 cm^{-1} (imide ring deformation).

3-5-2-Reflection optical microscopy

Microscope images were taken from patterned polyimide on BNCD electrodes using optical microscopy. Figure 16 shows patterned polyimide as insulating layer on silicon dioxide substrate. It contains patterned elliptical openings precisely on BNCD electrodes. Since the layer is very smooth and there is no crack in the patterned layer, from the image one can confirm that the surface of polyimide is patterned well, using developer solution with an optimized time for developing (50s).

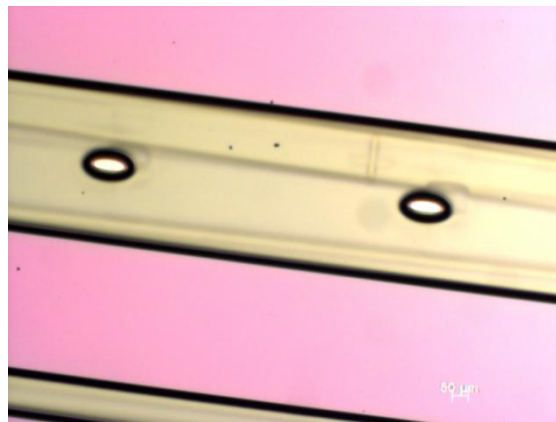


Figure 16: Image of polyimide in the electrodes

3-5-3-SEM morphology

One of the most important steps of the fabrication of the electrodes is the patterning of PI on BNCD ellipses. During the development of the PI many parameters have effect on the quality of the polyimide patterning such as cleanliness level of the substrate surface, baking time and developing time of the polyimide. As a matter of fact, patterning a successful structure of the polyimide is challenging and one has to control and optimize the polyimide patterning conditions to avoid from creating any crack and extra etching of the polyimide during fabrication. SEM measurement was performed on polyimide patterned on BNCD electrodes. It showed successful fabrication by the optimization of UV exposure time and dip development time of polyimide. It can be clearly seen that there is no defect on the surface even after curing.

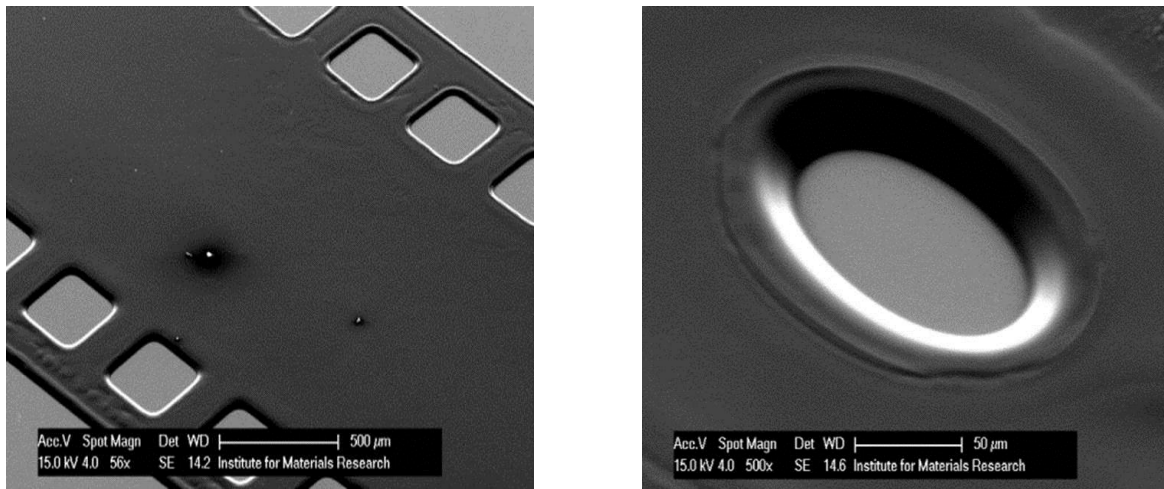


Figure 17: SEM images of the polyimide micro -structure in the electrodes

In Figure 17, elliptical opening of the patterned polyimide with the resolution of 50 μm by 150 μm, and square openings of 250 μm by 250 μm at the left image are demonstrated.

However, the adhesion of metal directly to the polyimide is usually weak due to the inertness of polyimide surfaces and some metals for instance Gold which is used in this research. The metal which is deposited on polyimide surface has normally poor adhesion and is easily cracked, blistered, or otherwise removed. Various surface treatments and modification methods have been used to increase the metal to polyimide adhesion. These include the uses of ion beams, plasmas, and chemical treatments [30]. Therefore, in this research, two different methods for PI surface

treatment are investigated in order to improve adhesion of Cr/Au and Au layer on PI films. The two methods include Oxygen plasma treatment and chemical treatment (KOH treatment). After each treatment, thin layers of Au and Cr/Au were deposited on treated and untreated polyimide surfaces and the adhesion was observed to be excellent on treated films, using a scotch tape adhesion test and ultra-sonication bath.

Wet-process surface modifications are interesting due to its simplicity and low cost. Polyimide films are resistant to most solvents and chemicals, but they react with oxidizing or reducing agents. However, if the concentrations of the chemical reagents, reaction temperatures, and reaction time are well controlled, the reactions can be confined to the surface [31]. We aimed at controlled chemical treatment for surface functionalization of polyimide film in our electrodes. Surface modification of polyimide films can be defined to surface without altering the bulk properties [32].

3-5-4- AFM

The surface morphology is of importance for the surface wettability of the treated polymer films. In this work, AFM was used to examine the topological changes induced on the KOH-treated and O₂ plasma treated polyimide.

Figure 18 shows the three- dimensional AFM image for untreated polyimide surface which was generally smooth with a 0.127 nm RMS roughness. After KOH treatment, the RMS roughness was slightly increased by increasing the time of 40 to 60 min which was 0.191 nm and 0.204 nm respectively. Figure 19 shows RMS of polyimide film generated with AFM, as a function of KOH treatment time and O₂ plasma power. As a matter of fact, the cleavage of imide ring by KOH or O₂ causes increasing the surface roughness of polyimide surface [31].

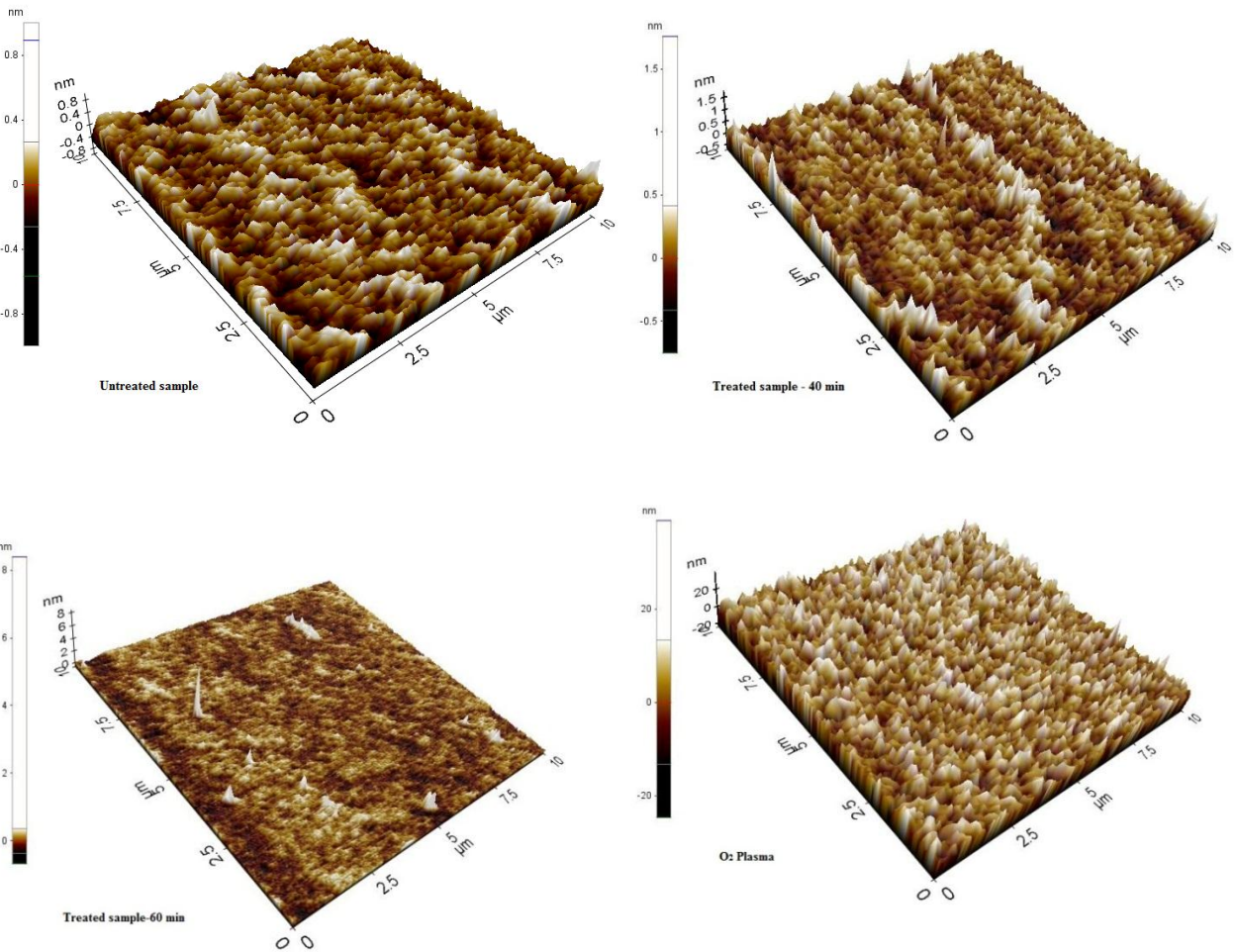


Figure 18: Three-dimensional AFM image of treated and untreated of polyimide surface by KOH and O₂ plasma

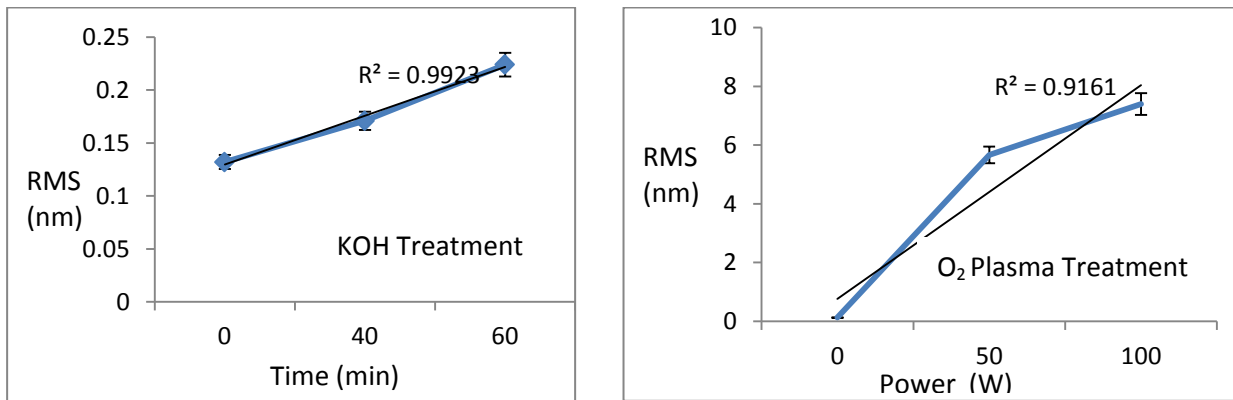


Figure 19: RMS of polyimide as a function of treatment time and power

As a result the RMS of the polyimide was increased with increasing treatment time (for chemical treatment) and treatment power (for Oxygen treatment) which can be attributed to cleave imide ring and increase carbon-oxygen functional groups on polyimide surface by the treatment.

3-5-5- Wettability of treated and untreated polyimide

Contact angle is known to correlate with the surface energy of the material, so that surface free energy may be calculated by using the surface energies at the solid–vapour and solid–liquid interface.

The concept of surface free energy, γ , for physical interactions which can be resolved into a London dispersive component (L) and specific (SP) component is [30-32]

$$\gamma = \gamma^L + \gamma^{SP} \quad (1)$$

In fact, Surface energy of the films also can be calculated by measuring contact angle [30-32].

The change in free energy of the interface is called the work of adhesion (WA) and can be expressed as

$$WA = \gamma^{SV} + \gamma^{SL} - \gamma^{LV} \quad (2)$$

Combining equations (1) and (2) yields the following equation:

$$WA = \gamma^{LV} (1 + \cos\theta)$$

The polyimide films modified by KOH treatment followed by acidification became wet (hydrophilic). As the treatment time increased from 0 to 60 min in 10 wt.% KOH treatment, the Contact Angles (CA) decreased from 64.45 to 48.4 which shown in Figure 20.

The surfaces which were treated by O₂ plasma have become more hydrophilic. To explain the relation between surface roughness and hydrophobicity, the Wenzel model can be used. When contact angle for a flat surface is more than 90 °, increasing surface roughness will result in an increased CA, while for contact angle less than 90°, increasing the surface roughness will decrease the contact angle and consequently the surface will become more hydrophilic [33]

This fact described by the equation 3 as follow:

$$\cos\theta_w = r. \cos\theta_e \quad (3)$$

Where r is the roughness factor, defined as the ratio of the actual area of the total solid surface to the projected area on the horizontal plane, θ_e is the equilibrium contact angle on the flat surface, and θ_w is the Wenzel apparent contact angle on the rough surface.

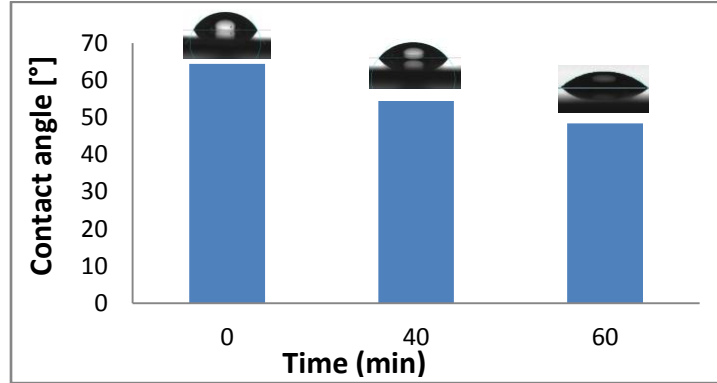


Figure 20: Contact angle as function of time treatment for KOH treatment

3-5-6- SEM and EDX analysis of treated and untreated polyimide

Table 7 shows atomic composition of treated and untreated polyimide which was obtained by Energy Dispersive X-ray spectroscopy (EDAX) in the same conditions. EDX results of polyimide show the existence of carbon, nitrogen, and oxygen. Moreover, it represents the O/C ratio of the polyimide before and after treatment. As a result, the O/C ratio of polyimide increased with treatment which can be attributed to the increase of carbon- oxygen functional group of polyimide surfaces by the treatment.

Table 7. Atomic composition of the polyimide surface obtained by EDX for treated and untreated polyimide

| Wt.% | Control Sample | KOH treatment at 40 min | KOH treatment at 60 min | O ₂ Plasma |
|------|----------------|-------------------------|-------------------------|-----------------------|
| C | 72.37 | 69.82 | 69.82 | 70.72 |
| O | 16.18 | 19.94 | 20.35 | 19.07 |
| N | 11.45 | 10.24 | 9.83 | 10.21 |
| O/C | 0.224 | 0.285 | 0.291 | 0.270 |

3-6-Surface characterization of metal Parts

Several techniques were used to characterize the surface of patterned metal parts such as Optical microscopy and SEM.

3-6-1-Reflection optical microscopy

Microscope images were taken from patterned metal connecting lines using optical microscopy. Figure 21 shows that the surface of metal is developed and patterned well.

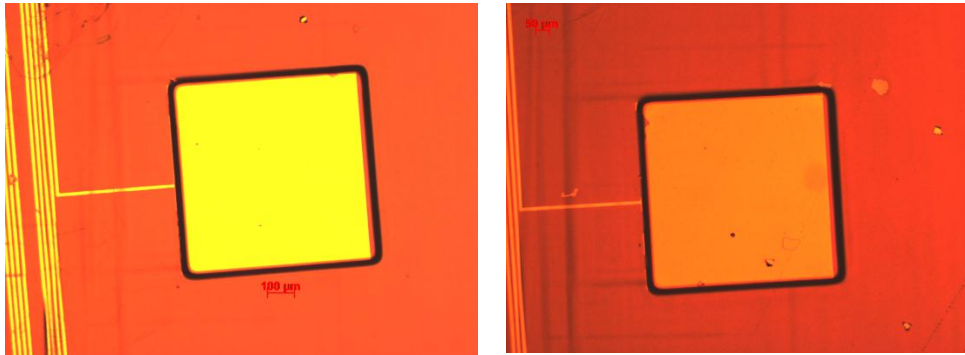


Figure 21: Image of metal parts in the patterned electrodes

Moreover, Fig. 21 shows patterned metal on polyimide as a electric lead connector (square area) and patterned connecting lines which connect the connector area to active area of BNCD electrodes.

3-6-2- SEM morphology

Figure 22 shows that patterning of metal (Gold) connecting structure has been successfully achieved. The metallic lines have been electrically insulated by covering the PI entirely underneath. These lines are responsible to connect the BNCD ellipses to the connector square areas on the electrodes. It is obvious that there is no detaching of metal from polyimide surface after lift-off in acetone due to the application of surface modification.

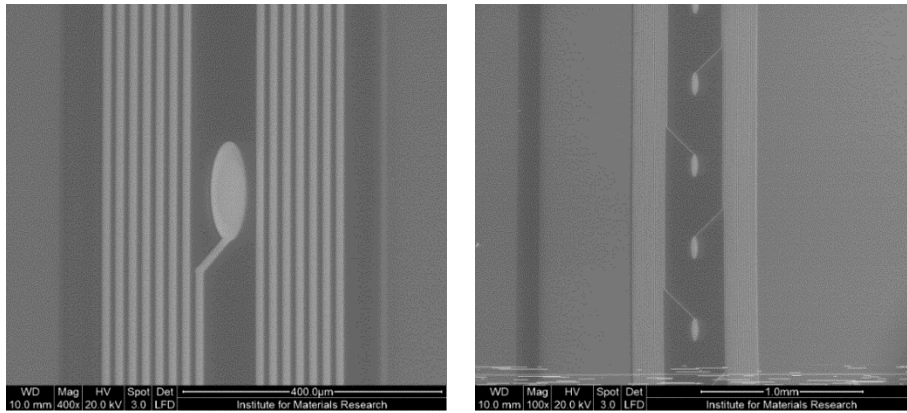


Figure 22: SEM images of the metal micro -structure in the electrodes. Each BNCD ellipse is connected to the square contact by a metallic connecting line with the thickness of 10 μ m.

3-7-Flexibility of the Polyimide/diamond EMG electrodes

Figure 23 shows the flexibility of released electrodes which were bended without resulting in any defects (delamination or crack) in electrode. The achieved flexible electrodes are desired for *in vivo* application.

The newly-designed diamond and polyimide EMG electrodes will be used as implants for recording muscles aimed at deconvoluting motor neuron signals for driving voluntary control artificial prosthetic hand. The device can also be used for a therapeutic stimulation.

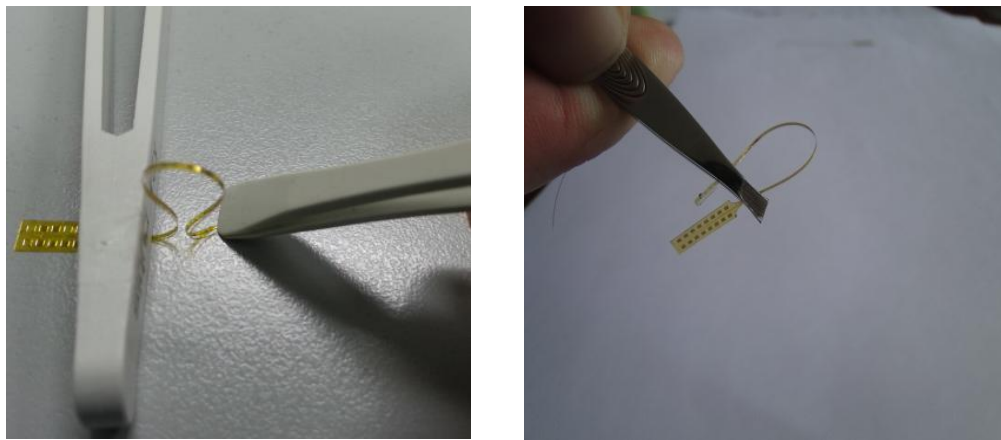


Figure 23: Image of flexible electrodes

4. Conclusion

In summary, in the presented work, the investigation has been carried out in order to fabricate flexible diamond electrodes insulated with Polyimide for Electromyography (EMG) purposes. BNCD layer exposed to muscle tissue or nerve cells can provide active interface for the signal readout. Diamond is anticipated to provide improvement compared to currently used electrode materials.

The thesis report on successful fabrication of Diamond-Polyimide microelectrode arrays for *in vivo* EMG applications. To date, the MEAs technology for therapeutic treatments and restoring lost neural function is still in progress. Improving mechanical flexibility of the implantable electrodes can minimize the tissue damages during implantation and during the device operation. Introducing biocompatible materials would also enhance the functionality of the electrodes and use as chronic implants.

Design, preparation and fabrication of flexible diamond /metal/PI EMG electrodes is presented. Surface treatment of polyimide was performed in order to improve the adhesion of metallic layer to the polyimide electrode.

KOH treatments followed by acidification, as well as O₂ plasma methods were successful to modify polyimide film surface from water-repellent to hydrophilic. This behaviour can be explained by the fact that the KOH treatment and O₂ plasma treatment of the polyimide surfaces produce various oxygen complexes, resulting in decreasing the contact angle and consequently wettability.

The O/C ratio in the elemental analysis of the KOH-treated polyimide was increased as functional of treatment time, resulting in enhancing the surface free energy. The O/C increase was modelled according to Young-Laplace equation and verified by contact angle measurement which confirms the surface of treated polyimide has become more hydrophilic than untreated polyimide. Also, the adhesion at interfaces between the metal and the treated polyimide film was excellent as confirmed using a tape adhesion test.

In the future work, the quality of diamond electrodes integrated with flexible PI can be by impedometry and current pulse testing in order to assess the electrical stimulation properties. Mechanical testing can be further performed in order to investigate mechanical durability of

electrodes. Cyclic voltammetry can be performed for measuring electrochemical properties and chemical stability and biocompatibility of fabricated electrodes *in vitro* and *in vivo* can be evaluated.

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Richting: **master in de biomedische wetenschappen-bio-elektronica en nanotechnologie**

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Voor akkoord,

Parsapour, Ali

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