IMPROVED SURFACE COATINGS FOR DEEP BRAIN STIMULATION MICROELECTRODES

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INTRODUCTION

Neurological Disorders, Psychiatric Illnesses and the Deep Brain Stimulation Device

Neurological disorders are conditions that affects the brain, the nerves across the body and the spinal cord, and these affects can be either biochemical, structural or electrical [1]. Some of the most commonly known neurological disabilities and diseases include epilepsy, Alzheimer's, Parkinson's (PD), stroke and cerebral palsy, and some psychiatric illnesses include attention deficit disorder and obsessive compulsive disorder (OCD) [1]. In 2011, an estimated 100 million people in the US were affected by 1 in more than 1000 neurological disorders [2], and in 2016, some of the neurological diseases were the leading cause of DALYs and the second leading cause of death, globally [3]. In order to reduce symptoms of these conditions in people, innovation in medical devices have emerged within the past two decades in search of providing therapeutic reliefs to suffering patients [4].

One of those devices include deep brain stimulation (DBS), which is a widely used medical device approved by the FDA to treat PD, dystonia, essential tremors and OCD [4]. It is intended to induce neuromodulation in the targeted neural circuitry by providing electromagnetic energy through neurostimulation into the corresponding anatomical sites [4]. This is an invasive approach where the DBS device is implanted inside the patient using these three components: 1.) DBS stimulating microelectrodes; 2.) electrode extensions; and 3.) chest implanted stimulator or internalized pulse generator (IPG) [4]. With the aid of MRI scans and neuroimaging techniques, surgeons establish trajectory pathways and inserts the DBS microelectrode through a carefully drilled out burr hole into the brain structure, and electrode extensions are tunneled via the neck muscles and attached to the IPG which is implanted below the clavicle, as shown in Figure 1 [4].

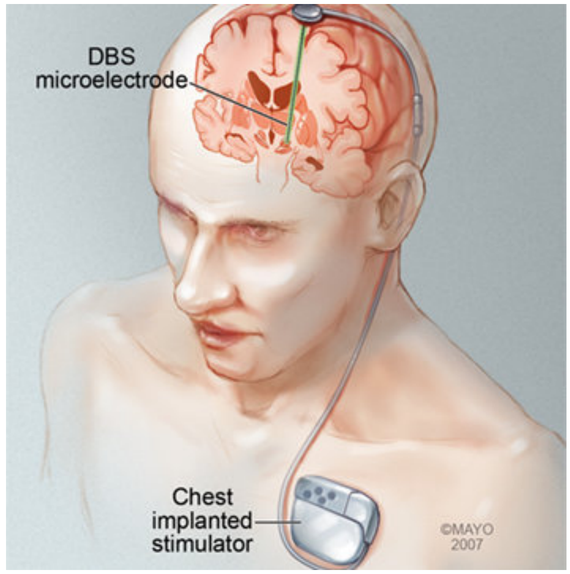

Fig. 1. Deep Brain Stimulation Device. The placement of the DBS microelectrode, which is connected to the electrode extensions. The extensions are tunneled via neck muscles before attaching to the chest implanted stimulator. This picture is taken from google images.

DBS device so far has shown to accomplish the reduction of symptoms in patients suffering from neurological disorders. However, the device itself may not be completely free from not causing adverse effects inside the body of patients due to poor device performance, which raises biocompatibility concerns. Some of the concerning areas of biocompatibility problems spur from the delamination of conducting polymer poly(3,4-ethylenedioxythiophene) (PEDOT), a conductive polymer coating that is generally used on neural recording and stimulating electrodes, from the surface of the DBS microelectrodes and electrochemical instability when PEDOT is coated on metal substrates of DBS microelectrodes [5], which is the topic of this proposal paper.

PEDOT, Delamination of PEDOT Coatings and Electrochemical Instability

PEDOT are widely researched unique, conductive, organic polymers not only known for their high conductivity (research has shown lower impedance than biologically significant frequencies (1-1000Hz)) and large charge storage capacity but also for their reduced foreign body response in the body, compared to inorganic metals used as the only interacting component with tissues [6,9]. This conducting polymer serves as good biocompatible interfacing layer between the metal and the living tissues and have been greatly used as surface coatings in recording and stimulating neural electrodes due to its good electrochemical stability and easy processing [7,8]. To deposit this polymer on a metal substrate, the PEDOT coating is electropolymerized on the DBS microelectrodes by that use of an electrochemical cell containing a solution of monomers, doping ions and a solvent [5]. Despite their benefits, electropolymerized PEDOT coatings faces the issue of delamination due to their poor adherence with inorganic metal substrates when implanted device stays for extended periods of time in the body [5,9]. This loss of PEDOT layer has shown to cause degradation of electrical signal quality [9]. Furthermore, over extended periods of time, PEDOT coatings lose their electrochemical stability, which is an important factor to consider since stimulating electrodes must have good electrochemical stability and stay functional for long periods of time [5]. These issues may lead to eventual failure of DBS device, which may cause frequent replacements of DBS microelectrodes or any potential harm to the patient.

Optimization of Adhesion and Electrochemical Stability

Delamination of an organic material such as PEDOT off an inorganic metal arises due to poor ‘adhesion strength’ [9]. The adhesion strength can be measured using scratch testing, indentation testing, sonication etc. However, it is very hard to measure. Therefore, very little research has been conducted to understand the mechanism of the delamination. On the other hand, electrochemical stability can be measured using PBS solution immersion test, etc. The optimization of adhesion and electrochemical stability largely depends on the solvents used to electropolymerize PEDOT on the metal surface since the solvents also get incorporated into the interfacing layer [5]. The solvents play a huge role in bringing the chemical structural changes in the polymer [5]. Adjusting the experimental parameters such as solvent, techniques, dopant concentration may help improve the adhesion strength of these surface coatings and may make them durable for extended implantation [5].

PROPOSED ALTERNATIVE

Electropolymerization of PEDOT:tetrafluoroborate (PEDOT:BF_4) using propylene carbonate solvent

One possible solution to optimize adhesion of PEDOT coating is to use PEDOT:BF4, where BF_4 is the doping ion, and an organic solvent such as propylene carbonate (PCs) via galvanostatic electropolymerization to deposit the polymer. Galvanostatic electropolymerization has shown to allow precise control of how much polymer deposition without causing overoxidation of the polymer, according to Bodart et al [5], making it ideal for use. The polymer will be deposited on platinum-iridium (PtIr) for DBS microelectrodes. The chosen dopants and solvent are ideal in this case since PEDOT:BF_4 coating deposited using PC solvent has shown to pass adhesion test through ultrasonication [5]. The use of BF_4 as dopant ion and PC as solvent is almost a necessity since microelectrodes processed just in deionized water have shown to create chemical properties of the polymer with the weakest of adhesion strength to metal substrates and very poor electrochemical stability [5,9]. Therefore, these changes in parameters may help optimize the surface coatings on metal microelectrodes.

JUSTIFICATION & RATIONALE

PEDOT vs PEDOT:BF_4

Current PEDOT coating processed without any dopants have suffered from electrochemical instability and delamination. Bodart et al [5] was able to determine the impedance of the modified PEDOT coatings, such as PEDOT:BF_4 through potential electrochemical impedance spectroscopy (EIS) to show conduction stability of the polymer coating. For DBS stimulation, low impedance is a must to help the charge transfer at the electrode-tissue interface and to reduce the energy consumption during stimulation [5]. According to the investigation carried by Bodart et al [5], the PEDOT:BF4 on PtIr microelectrodes showed a significant decrease of impedance within the required frequency range (1-10^5 Hz) even without the aid of any organic solvent. These results are also consistent with the literature when BF_4 is used as dopant ion for PEDOT [10].

Delamination of PEDOT

The use of BF_4 as dopant ion and PC as solvent has been shown to stay physically stable after 5 minutes of sonication and was also able to retain more than 80% of their ability to charge storage capacity (CSC), a charge measure that was used in this research to determine adhesion strength [5]. On the contrary, coatings processed with deionized water as solvent has shown to survive sonification for only 2-3 mins [5]. This gives evidence that using a dopant like BF4 is beneficial and not using one.

Electrochemical Stability of PEDOT

Using the same combination of coating formulations as mentioned above, electrochemical stability was tested through 2-week immersion of PEDOT:BF4 coating PtIr microelectrodes in phosphate buffer solution (PBS) pH 7.4 solution, and the impedance was measured [5]. The impedance of PC processed microelectrode was shown to only get affected by a factor of 2-3, which indicated significantly lower than that of microelectrodes processed without PC [5]. These evidences prove that usage of the aforementioned solvents and doping ions may improve existing microelectrodes and help prolong DBS device stability in biological environment for extended periods of time compared to the DBS devices that exist in the market.

Cost Analysis

The cost of all the materials used will depend on the concentration of dopants, and solvents used along with PEDOT and PtIr microelectrodes. All costs should be feasible enough to incorporate them into mass production. The evidence presented so far suggests great improvements, therefore, the costs can be outweighed by the profit made if the DBS devices achieve their intended functions and frequent replacements is no more needed with the suggested solution.

PROPOSED VERIFICATION TESTING

Since this is a novel approach, animal and clinical testing will be necessary to demonstrate long term benefits in patients before seeking approval from the FDA. The following verification method is adopted from Bodart et al research. Ultrasonication test must be conducted on PEDOT:BF_4 coatings by immersing them in ultrasonic bath to determine adhesion capability with PtIr metal. Then coatings should be soaked in PBS pH 7.4 for prolonged amounts of time to determine electrochemical stability. Finally, after sterilization tests were performed by autoclaving, the microelectrodes should be implanted into the brain of rats to perform in Vivo stimulations. The stimulations should be recorded and compared to the standard charge storage capacity required in actual patients. The outline of the aforementioned methods is shown in Figure 2. These processes should be sufficient to capture the benefits or adverse effects of using PEDOT:BF_4 in PC solvent.

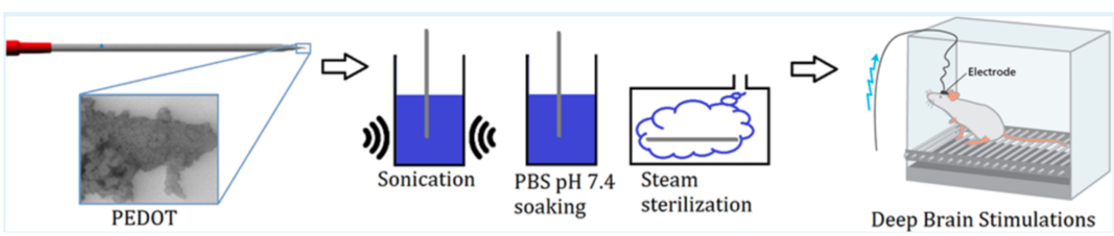

Fig. 2. **Verification testing process outline.** This image is retrieved from reference 5.

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