Implanted Electrodes and Microneedle Array Electrodes for the Neuromodulation

Huanqun Zhu *

Department of Electronic and Electrical Engineering, Lancaster University, Lancaster, United Kingdom

* Corresponding author: zhuh11@lancaster.ac.uk

Abstract. In the human body, nerve conduction plays an important role. A range of physiological reactions and movements in the human body require nerves for transmission. Nerves realize the function of conduction by transmitting bio-electrical signals. If the nerves are damaged, the biological signals will not be transmitted, so the human body's reactions cannot be carried out, causing serious consequences. Neuromodulation is an effective treatment modality for patients with nerve damage. Neuromodulation has been proven to have effective therapeutic effects in various brain and neurological diseases. Among them, the electrodes in the neuromodulator regulate the abnormalities of the brain or neurons by releasing electromagnetic pulses, which are an important part of the whole device. However, various electrodes can be used for neuromodulation, and different electrodes have different characteristics from one another. In this study, several electrodes that can be used as wearable/implantable neuromodulators and their properties will be investigated and whether there is a relationship between them.

Keywords: Inorganic electrode, Flexible electrodes, Micro-needle array electrode.

1. Introduction

In the human body, the brain and spine are the main organs of the nervous system and the most complex organs. It contains many neurons and biological response receptors that manage the body's functions. These neurons and cells complete the It transmits information through electrical and chemical signals through neurotransmitters and is responsible for complex reactions such as speaking language, analyzing various information and the secretion of various hormones and even changes in mood. Up to now, there are still many unknowns about the neurological function of the brain and spine, and there are still many studies on these organs and related to them [1].

The body's reaction consists of several steps: bioelectrical or chemical signals from the brain or spine; These signals go into neurons; The terminals of the neurons are connected to receivers on the organ that performs the response, and these signals are transmitted to the organ for the response [1]. In this process, nerve injury can lead to signal failure or transmission of wrong signals. Disease or injury of the brain or spine can also lead to wrong signals, affecting people's daily activities and physiological reactions. The inability to control body parts and their reactions can lead to serious consequences. Brain disorders can sometimes cause a person to lose basic skills, such as movement, memory, and language, and are even life-threatening.

However, as medical science advances, people have also been exploring how to treat brain and neurological diseases [2]. There are already possible solutions for many neurological and brain disorders, in which the implantation of electrodes into the nervous system or a region of the brain has been shown to treat various conditions, such as Parkinson's disease, essential tremor, dystonia, epilepsy, and obsessive-compulsive disorder. Meanwhile, implanted electrodes can be used to treat movement disorders and psychiatric disorders [1]. Therefore, implanted electrodes are being investigated for treating Tourette's syndrome, Huntington's disease, and chronic headaches. Scientists are also studying whether implanted electrodes can help treat a variety of difficult brain and neurological conditions today, so that people with these conditions can be as healthy as possible.

An important part is implantable/wearable electrode therapy, which modulates brain or neuronal abnormalities by releasing electromagnetic pulses [2]. And this is done by electrodes in the device.

Different electrodes have different conductivity and electrical conductivity. Similarly, there will be different requirements for electrode materials in different use scenarios. Wearable/implantable medical devices have been greatly improved in recent years [2]. With the progress of science and technology and the continuous research of scientists in the field of bioelectronics, the conductivity of wearable/implantable medical devices has been improved [1]. At the same time, this also makes using these devices more efficient, improving the treatment effect. In some cases, it can even control other medical devices that patients may access, such as robotic arms and other devices that help the body's only neuroreceiver to respond and move. At the same time, the special research on materials has also promoted the advent of more biocompatible materials, so the equipment has been improved, such as conductive polymers, silicon, carbon nanowires, graphene and organic-inorganic composite nanomaterials [1]. The combination of various conductive and biological materials has also resulted in different types of electrodes, which can treat more diseases or better affect a particular disease [2]. This paper will conduct research about various categories of electrodes in wearable/implantable medical devices, especially in the following fields: inorganic electrodes, flexible electrodes, material for inorganic electrodes and microneedle array electrodes.

2. The electrodes in the neuromodulation

2.1. Inorganic Electrodes

Inorganic electrodes are a type of electrode that is often used in wearable/implantable electrode devices. Normally, electrodes in the device convert the energy of the ionic current into a biological current. The converted current can be scaled up or down as needed [2]. The devices work by contacting the patient with an external power supply. Inorganic electrodes can be composed of a variety of materials. Especially ceramics and various precious metals made of inorganic electrodes are the most common. In general, lead, superconducting metals and electrode conductive paste are common materials used as inorganic electrodes. Among them, precious metals such as titanium have good electrical conductivity and body adaptability. Inorganic electrodes made of titanium usually do not produce repulsion in the human body. Platinum material (a new type of inorganic material) can be well used to manufacture cochlear implants [3]. The malleability and conductivity of these materials enable medical devices to maintain efficiency by reducing electrical conduction losses. Inorganic electrodes can be used in various medical devices, such as discs [4], disposables, hair bands, etc.

Silicon is a common element often used in chips and batteries and the main material for semiconductors. It has the characteristics of both inorganic and organic materials - non-toxic, tasteless, and oxidative stability - which make it suitable for biomedical devices [5]. With the research of nervous system and the progress of biological biomaterials and silicon micro processing technology, today's neuromodulators based on electroless electrodes have been able to stimulate and/or record neurons for a long time. The Utah Electrode Array (UEA) is a good example.

For adequate conductivity, the fabrication process of inorganic electrodes and the arrangement between electrodes are usually specially treated. In the case of UEA, electrical isolation between electrodes is achieved by a moat surrounding the bottom of the electrode [5]. In addition, to facilitate ion conduction, UEA uses aluminium foil as a mask to selectively coat the tip of each electrode with conductive material. At the same time, for biocompatibility, UEA will use Parylene-C to reduce the rejection of the human body. But to ensure efficiency, the device's tip will be exposed, and the Parylene-C on it will be removed using oxygen ions. The length of the inorganic electrode is either constant or variable, and the UEA that can change its length is called Utah slant electrode array, or in convoluted configurations.

2.2. Flexible Electrodes

Flexible electrodes are another type used for wearable/implantable electrode devices. In treatment, neural microelectrodes bridge the human body and medical devices. All control of medical devices requires the recording and transmission of neural signals through ladder electrodes [6]. Electrodes can also provide electrical stimulation of nerve tissue to treat patients with long-term brain diseases safely and reliably. However, in some cases, the traditional rigid electrode probe cannot match Young's modulus of human tissue, which leads to immune rejection of the tissue. At the same time, because sometimes the body area where the device is implanted or worn is not flat, the rigid electrode probe cannot be fully attached to the implanted/worn area, resulting in poor contact. These can affect the treatment effect and reduce efficiency [7]. Therefore, to avoid the above things, in recent years, with the research and progress of flexible materials and special electrode structure design, flexible electrodes have become a commonly used device in the medical field. Flexible electrodes are usually metal films on flexible substrates (polymers), such as Ag-AgCl; a conductive adhesive on one side of the substrate holds the electrode to the skin, and an insulating layer on the side connecting the impression. Flexible electrodes are usually thin and can remain on the patient for a long time.

Although silicon-based electrode arrays have high mechanical hardness and biocompatibility, such as Michigan electrodes and UEA. Silicon-based electrodes [6] play an important role in restoring patients' normal and accurate recording and treatment. However, due to the rigid characteristics of silicon (the young's modulus of single crystal silicon is ~170 GPa, while the young's modulus of brain tissue is ~3 kPa), it cannot be matched with biological tissue. At the same time, because the surface of biological tissue is usually curved, it is difficult for silicon-based electrodes to tightly connect with cortical neural tissue, thus triggering an immune response. In this case, flexible electrodes can eliminate these problems as much as possible to improve the treatment efficiency.

Flexible electrodes are mainly used in long-term treatment [6][7], usually composed of three parts: substrate, electrode and package. Flexible electrodes are often made of low Young's modulus materials, such as Perylene-C, polyamide and SU-8 photoresist. They typically have a young's modulus of 1 to 10 GPa and are commonly used as underlining. In addition, flexible electrode structures are usually designed as waves, snakes, origami and kirigami, which can also help reduce Young's modulus of the original rigid array.

2.3. Material for Inorganic Electrodes

Generally, inorganic electrodes have a material composition with strong conductivity and strong biological adaptability. Inorganic electrodes will use silicon, titanium and so on as the basic materials for manufacturing [5]. They are helping patients to see and hear. In the current study, scientists focused on finding materials with good electrical conductivity and biological adaptability. Among them, electrodeposited Pt-Ir (platinum-iridium) [4] plays an important role in the application of cochlear implants. It is often used for chronic stimulation of cochlear implants in humans.

Pt-Ir is a platinum-based binary alloy containing iridium, which can improve the corrosion resistance of the alloy due to its non-volatilized and non-oxidized characteristics. It has high hardness, high melting point and high corrosion resistance. At the same time, the low contact resistance makes it a good conductive material. And its corrosion resistance is also capable of being suitable for wearable/implantable medical devices. The role of cochlear implants is to provide important auditory cues for patients with severe hearing loss. To understand speech and accept environmental sounds. These devices selectively stimulate primary auditory neurons through longitudinal arrays of platinum electrodes in the scala tympani. However, platinum has relatively strong biocompatibility and electrochemical stability under active conditions, which makes electrodeposition Pt-Ir competent. The electrochemical properties of the electrodeposited Pt-Ir electrode were significantly improved compared with the uncoated alloy on the experimental bench and in vivo [4].

However, electrodeposited Pt-Ir also has certain defects. The too rigid material leads to a large difference in Young's modulus from brain tissue [4], leading to the immune system's rejection. This will directly affect the efficiency of the equipment. At the same time, it has been shown that the use of electrodeposited Pt-Ir leads to accumulation in vivo. But it doesn't affect neurons.

Pt-Ir and other materials have been considered for use in inorganic electrodes in the present scientific research. Ruthenium oxide [8] is one such example. It is an important material for making resistors and capacitors and has good electrical conductivity. At the same time, its insoluble property in acid also means that it has good stability. "According to ISO 10993-5: Biological evaluation of medical devices, this substance has no significant effect on neuronal cell activity or cortical network function and therefore poses a low risk of rejection by the immune system." The better conductivity of ruthenium oxide makes it suitable for use as an inorganic electrode compared to other materials. Iridium oxide and ruthenium oxide were used to modify indium tin oxide sites to establish an in vitro microelectrode series. After testing, the impedance of ruthenium oxide coating detected by electrochemical impedance spectroscopy was lower than that of iridium oxide and indium tin oxide, thus demonstrating that ruthenium oxide has a more stable extracellular recording ability in the outer cortical network and has a better therapeutic quality.

2.4. Microneedle Array Electrodes

Although the scale of clinical medical devices related to nerve stimulation is relatively large, the clinical application of devices based on microneedle array electrode systems is being investigated. In general, microneedle array has the advantage of small stimulation [9] volume in treatment due to its size, which can improve the selectivity of stimulation position and increase the treatment efficiency. At present, microneedle arrays are often associated with chronic tissue [9] [10] responses in humans, but this can also limit the recording and therapeutic effect of these medical devices in the nervous system. The solution is to reduce the physical size of the device. In the current level of medical technology, electrode miniaturization is an important goal for researchers. The smaller size of the device makes it more convenient for precise treatment, and the smaller size of the electrode can also reduce the contact area as much as possible, which avoid the immune rejection. It has been shown that layers with high electric core capacity, made of emerging polymers and non-silicon carbide, may have an important role in ultramicroelectrodes.

Microneedle arrays are of great help in the field of artificial retina [10]. Microneedle array electrodes can help stimulate a subset of visual neurons in patients with photosensor degeneration using an artificial retina. Therefore, the fabrication of microneedle arrays will also use materials with strong conductivity and high biocompatibility. In the artificial cornea, to minimize the damage of ophthalmic surgery and form better contact with the retina. Various studies have shown that the flexible polyimide multi-electrode array has good stability and safety on the biological retina. Multi-electrode array is a microneedle array electrode material commonly used in microelectronics technology [10] [11], which is often used in microelectronics technology materials. It has good electrical conductivity. At the same time, the non-toxic and harmless characteristics of the material make it a good medical device. The material is malleable, which can reduce Young's modulus of the material and reduce immune rejection.

In the future, renewable and expandable fibers will be used for microneedle arrays [9]. Amorphous silicon carbide has been investigated as a microneedle electrode for brain implants. Amorphous silicon carbide has strong stability, high electronic resistivity and corrosion resistance. At the same time, in the medical field, it has been used as a coating for coronary artery stents, which has been proved to have good biocompatibility. Devices made from it have the potential to achieve highly spatially selective neural stimulation under chronic conditions. And because the device's physical size is small, its contact with the body is also small, which can minimize immune rejection.

3. Discussion

Inorganic electrodes are the most common type of electrode used in wearable/implantable medical devices. It is also the earliest type of electrode used. They have good electrical conductivity, have as good stability as possible, and are biocompatible enough to avoid rejection. Conventionally, high-performance conductive metal combined with the biological coating is the basic structure [5] of inorganic electrodes. With the development of electronic technology, silicon is also used as a material for inorganic electrodes because of its conductivity and stability. Moreover, it has become a trend in the development of medical devices for new materials to be tested to whether they can be used as inorganic materials [8].

Flexible electrodes are mostly used to fit the patient's body. Their initial purpose is to make medical devices more suitable for the damaged/need-to-be treated parts of the patient to treat diseases more accurately. Because the human body is not completely flat, hard electrodes can sometimes lead to poor contact and reduce the effectiveness of treatment or even trigger rejection by the immune system. In addition, flexible electrodes are often used in emerging materials [7], which are often soft and have Young's modulus similar to human tissue [6], so that rejection can be avoided as much as possible.

In the current research, the material is universal. That is, the material used by the inorganic electrode can also be used in other electrodes [4]. These materials are often new materials, which have higher electrical conductivity than ordinary metals, and at the same time, have more biocompatibility than previous materials. The application of these materials may lead to changes in the structure of inorganic electrodes. Although these materials may not be similar to Young's modulus of human tissue [8], the rejection can still exist. Now, these materials are also being continuously improved and studied.

Electrode miniaturization [9] is the primary goal of scientists in electrode research, and microneedle array electrode is the product of research to achieve this goal. Microneedle array electrodes have the advantage of small stimulation volume, which can reduce the contact area with the patient, avoid rejection, and perform a more accurate treatment. These properties make it possible to treat small but critical human body parts, such as the artificial cornea [10]. This electrode can avoid the recording/stimulation efficiency caused by human chronic tissue as much as possible, so the treatment effect can be improved [11].

The use of three electrodes is often chosen based on the patient's needs. Inorganic electrodes have good electrical conductivity due to their structure and materials, so they can bring more effective treatment effects. However, for patients with long-term treatment, materials that do not match Young's modulus of human tissue will lead to rejection in long-term use, even if they have strong biological inclusion. Therefore, the materials used in general inorganic electrodes are not fully suitable for long-term treatment. Although the newly developed materials used in inorganic electrodes have also been applied to microneedle array electrodes, if the contact area with the patient is not small enough, it still cannot guarantee that the Young's modulus is similar to that of human tissue. Microneedle array electrodes and flexible electrodes are now commonly used for long-term treatment because they are usually similar to Young's modulus of human tissue. However, there are still differences between them. Microneedle array electrodes are often not flexible, so it is difficult to fully match the Young's modulus of flexible electrodes. They can only be used by reducing the area and sometimes cannot fully contact with the patient to meet the treatment needs. In the treatment process that requires a large area of contact with the patient, only flexible electrodes are often more able to fit the site of the patient to achieve the best effect.

4. Conclusion

In summary, the wearable/implantable medical device composed of the three electrodes can carry out effective treatment, which is of great help to the rehabilitation of patients. The choice of which electrode constitutes a wearable/implantable medical device for patients should be related to their own needs. No electrode is more advanced or less advanced than any other. Different electrodes have different therapeutic effects on different diseases. Sometimes one electrode is more effective for a particular disease but not so effective for others. It's not just a variety of diseases; different patients and patients respond differently to different electrodes and electrode materials. Doctors should choose the most effective device for treatment based on the patient's condition while avoiding rejection caused by the patient's immune system. Sometimes patients need to use more than one device at a time. In the future, materials that simultaneously meet the conductivity, biocompatibility and Young's modulus of human tissues are the research goals of scientists. Suppose such materials can be used in electrodes. In that case, they will be able to improve the functionality and efficiency of each electrode, and even change the structure of these electrodes and enable them to treat more difficult diseases that cannot be solved at present. At the same time, this will make the electrode function more comprehensive, improve the efficiency of the treatment and reduce the cost.

References

[1] Shi Yue, Liu Ruping, He Liang, et al. Recent development of implantable and flexible nerve electrodes. In Smart Materials in Medicine, Smart Materials in Medicine, 2020, 1: 131 - 147.

[2] Wu Nan, Wan Shu, Shi Su, et al. Electrode materials for brain-machine interface: A review. InfoMat, 2021, 3 (11): 1174 - 1194.

[3] Rylie A. Green, Nigel H. Lovell, Gordon G. Wallace, et al. Conducting polymers for neural interfaces: Challenges in developing an effective long-term implant. Biomaterials, 2008, 29 (24): 3393 - 3399.

[4] Ashley N. Dalrymple, Mario Huynh, Bryony A. et al. Electrochemical and biological characterization of thin-film platinum-iridium alloy electrode coatings: A chronic in vivo study. Journal of Neural Engineering, 2020, 17 (3): 036012.

[5] Negi S., Bhandari R., Rieth L., Solzbacher F. In vitro comparison of sputtered iridium oxide and platinum-coated neural implantable microelectrode arrays. Biomedical Materials (Bristol, England), 2010, 5(1): 15007.

[6] Zhao Huiqiang, Liu Ruping, Zhang Huiling, et al. Research progress on the flexibility of an implantable neural microelectrode. Micromachines, 2022, 13 (3): 386.

[7] Klas Tybrandt, Dion Khodagholy, Bernd Dielacher, et al. High-density stretchable electrode grids for chronic neural recording. 2018, Advanced Materials, 30 (15): 1706520.

[8] Rahul Atmaramani, Bitan Chakraborty, Rashed T. Rihani, et al. Ruthenium oxide-based microelectrode arrays for in vitro and in vivo neural recording and stimulation. Acta Biomaterialia, 2020, 101: 565 - 574.

[9] Joseph J. Pancrazio, Deku, Felix, Atefeh Ghazavi, et al. Thinking small: progress on microscale neurostimulation technology. Neuromodulation: Technology at the Neural Interface, 2017, 20 (8): 745 - 752.

[10] Jong-Mo Seo, Sung June Kim, Hum Chung, et al. Biocompatibility of polyimide microelectrode array for retinal stimulation. Materials Science and Engineering C, 2004, 24 (1): 185 - 189.

[11] Gao Fei, Luo Jinping, Song Yilin, et al. Microelectrode arrays for monitoring neural activity in neural stem cells with modulation by glutamate in vitro. Nanotechnology and Precision Engineering, 2020, 3 (2): 69 - 74.