Wearable Technology (2022) Volume 3 Issue 2, *pp. 39–45.*
doi: 10.54517/wt.v3i2.2106

Asia Pacific Academy of Science Pte. Ltd.

REVIEW ARTICLE

Research progress of electrode coating for cochlear implant

Zhiyi Wang, Yong Fu*

Department of Otolaryngology Head and Neck Surgery, Children's Hospital of Zhejiang University School of Medicine, Hangzhou 310000, Zhejiang, China. Email: 1307022@zju.edu.cn

ABSTRACT

As the standard treatment of severe sensorineural hearing loss, the cochlear implants (CI) has been widely accepted. However, many factors affect the effect of CI implantation, including mechanical damage caused by CI electrode implantation, inflammatory reaction in the cochlea, tissue fibrosis and new bone formation, and even the formation of fibrous tissue on the electrode surface. These factors damage residual spiral ganglion cells, auditory hair cells, and stria vascularis cells and increase electrical impedance. In recent years, the use of electrode coating to reduce the effect of these adverse factors on CI implantation has become a research hotspot. For example, different coating embedded genes were used to recombine dry cells, drugs, growth factors and neurotrophic factors to reduce electrode implantation resistance, reduce electrode surface protein adhesion, and reduce electrode electrical impedance. In this paper, the characteristics of electrode coatings on different materials that have been studied in recent years are reviewed.

Keywords: cochlear implants; coatings; material

1. Introduction

Cochlear implants directly stimulate spiral ganglion cells through microelectrodes implanted in the scala tympani to transmit auditory information to the central nervous system. The number of residual spiral ganglion neurons (SGN) is small[1], the distance between nerve fibers and electrodes is large[2], the damage of auditory hair cells and spiral ganglion cells caused by electrode implantation resistance, and the possible inflammatory reaction[3–5], the fibrosis and ossification in the tympanic scale, and the increase of electrical resistance caused by the formation of fiber tissue on the electrode surface[6] all affect the hearing experience after cochlear implantation. Precision minimally invasive cochlear implantation[7], bone marrow mesenchymal stem cell transplantation SGN and hair cell regeneration[8], drug loading through cochlear electrodes[9] and other schemes have provided new ideas and directions to solve the above problems. With the development of material science, people also continue to explore the role of electrode coating in improving the effect of cochlear implantation. This article will review the electrode coating materials that have been studied and their advantages and disadvantages.

2. Alginate coating

Verena et al.[10] embedded mesenchymal stem cells (MSCs) that can produce brain-derived neu-

ARTICLE INFO
Received: May 6, 2022 | Accepted: June 25, 2022 | Available online: July 11, 2022

CITATION
Wang Z, Fu Y. Research progress of electrode coating for cochlear implant. Wearable Technology 2022; 3(2): 39–45.

rotrophic factor (BDNF) in ultra-high viscosity alginate as electrode coating and implanted them into the inner ear of guinea pigs. After 4 weeks, the SGN density was significantly higher than that of the group implanted with uncoated electrodes, without causing fibrosis around the electrodes and electrode resistance changes.

Jana et al.[11] put alginate in the simulated inner ear environment for 28 days, and the diameter of alginate beads and the elasticity of alginate layer did not change significantly, showing good stability. The MSCs overexpressing BDNF were embedded in alginate, and the BDNF produced was sufficient to protect SGN and promote its synaptic formation. MSCs embedded in alginate can survive for more than 3 weeks, but after 21 days, the survival rate of MSCs in alginate is only 40%. When using clinical maximum pulse width (400 μs), the number of MSCs was significantly reduced when the electrodes were stimulated with 2 mA and current intensity (2 mA), and alginate was destroyed. The current intensity of 1 mA, 0.88 mA, 0.66 mA also reduced the number of MSCs, while 0.33 mA had no significant effect on the survival of MSCs. Silke et al.[12] used the human cochlear model to prove that the alginate electrode coating can increase the hydrophilicity of the electrode surface, reduce the electrode implantation resistance, and reduce the incidence of electrode bending and tip folding. The alginate coating shows good stability and can avoid the separation and migration of the embedded MSC.

3. Nanometer coating

3.1. Triethoxysilane terminated polyethylene oxide with 44 ethylene oxide units, PEO44–TES

Alessandra[13] et al. treated the surface of the polydimethylsiloxane (PDMS) electrode with plasma, making the nano coating PEO44–TES covalently combine with the electrode surface. The prepared electrode surface has a good anti fouling ability, which can effectively inhibit the adhesion of bovine serum albumin and fibrinogen. Even after 2 months, it still maintains a strong anti-protein adhesion ability, and effectively inhibits Staphylococcus aureus. The growth of Staphylococcus epidermidis and Pseudomonas aeruginosa on the electrode surface. The coating has good stability under continuous bending stress. In the light wavelength range of 900–2,000 nm, PEO44–TES coating can basically transmit all, which is suitable for light triggered optical cochlear implants.

3.2. Calcium phosphate hollow nanospheres (CPHS)

Hao[14] et al. used the drug carrying CPHS as the electrode coating to store and release BDNF and glia cell line—derived neurotrophic factor (GDNF). Research shows that every 1ng of CPHS can store 0.1 ng of GDNF. The coating has explosive release of GDNF on the surface of the nanosphere for the first 6 hours, releasing about 50% of GDNF, and then 6–17 hours is the linear slow release of GDNF in the nanosphere. Finally, with the further release of GDNF by calcium phosphate degradation, the release will be slower in this stage. After 14 days of culture, GDNF or BDNF released from the coating can make SGN synapses grow towards the coating surface. GDNF–CPHS coating can make contact between the electrode surface originally with 0.7 mm and SGN synapses, while the distance between the general neural pore and the electrode is 0.5mm, and the distance between the cochlear axis and the electrode is 1–1.5 mm.

3.3. Star-shaped polyethylene glycols (sPEG)

Antonina et al.[15] in vitro tests showed that DMS and sPEG coating could reduce the growth of fibroblasts on the electrode surface by more than 90%, while DMS plus sPEG coating could reduce the number of cells by 99%, effectively inhibit cell adhesion and reduce the fibrosis on the electrode surface. The sPEG electrode coating slows down the release rate of DMS in the electrode. Whether there is sPEG coating or not, DMS will be released explosively in the first week. After 90 days of the experiment, DMS will continue to release. According to the

release rule of DMS in PDMS without sPEG coating, it is speculated that the continuous release time can exceed 2 years, and covering sPEG will make the release time longer. Antonina et al.[16] also tested the above-mentioned sPEG-coated DMS combined with PDMS electrodes in vivo and implanted them into the inner ear of guinea pigs and found that DMS, DMS + sPEG, and sPEG all reduced the adhesion of tissue and other indeterminate material on the surface of the implanted electrodes by 85%, 75%, and 30%, respectively. DMS + sPEG electrodes had a worse inhibitory effect on tissue formation than DMS alone, which may be related to the fact that sPEG slows down the release of DMS. This suggests that it does not increase implantation damage.

4. Degradable material coating

Biodegradable material coating can be used for short-term cochlear local administration. The direct injury or inflammation caused by injury of electrode implantation, as well as the inflammation caused by foreign body reaction, may cause the degradation of SGN, auditory hair cells and stria vascularis cells at the early stage of electrode implantation. Therefore, local drug intervention at the early stage of implantation is very valuable for improving the implantation effect. Other short-term local drug delivery methods have shortcomings such as uneven drug concentration, difficult drug dosage control, and increased risk of infection[17]. The biodegradable electrode coating may become an ideal short-term local drug delivery method after cochlear implantation. The above CPHS is also a degradable material and will not be repeated.

4.1. Poly (L-lactide, PLLA) and poly (4-hydroxybutyrate), P (4HB)

Ceschi et al.[18] implanted PLLA, P (4HB) coated electrodes into the inner ear of guinea pigs for 1–6 months. Compared with the control group of uncoated electrodes, they did not change the ABR threshold, and only a small amount of fibrous tissue was formed around the coated electrodes, indicating that the coating and its degradation products did not cause a strong tissue reaction and had good biocompatibility. After 6 months in the guinea pig inner ear, PLLA did not degrade, while P (4HB) was almost completely degraded. In addition, during the electrode implantation process, the PLLA coating showed weak bonding with the silicon surface of the electrode, so it was speculated that P (4HB) was more suitable for local administration as a degradable coating. In vitro tests by Anne et al.[19] also showed that P (4HB) has stronger biodegradability and is more suitable for electrode coating. PLLA increases the surface roughness of the electrode, while P (4HB) makes the surface smooth and uniform. The porous rough surface will increase the bacterial reproduction, which further limits the use of PLLA. P (4HB) also showed good stability; P (4HB) released dexamethasone at a fast rate, and there was an explosive release of drugs in the first 24 hours. PLLA released at a slow rate, and there was no explosive release stage. The explosive release of P (4HB) at the initial stage could reduce the hearing loss caused by CI surgery trauma.

4.2. Poly lactic-co-glycolic acid (PLGA)

Haoran et al.[20] used PLGA and chloroform as the coating of drug loaded electrode, and the drug loaded was dexamethasone sodium phosphate, cytarabine hydrochloride, or nicotinamide adenine dinucleotide. PLGA coating increased the thickness and quality of the electrode, surface smoothness, hydrophilicity, and did not increase the electrode impedance. In vitro drug release test showed that the drug was released rapidly on the first day, with 63.4% release rate. The drug was released stably on the 14th day, and basically released within 15 days. The drug release rate had no significant relationship with the coating thickness, drug type and drug dose. The coating can be quickly customized according to the needs of different patients within 15 minutes during the operation. The 50:50 lactic acid and glycolic acid polymer showed the fastest degradation rate. The 50:50 polymer degraded in 30 days, covering the postoperative inflammatory edema period.

4.3. Gelatin

Yayoi et al.[21] used gelatin as the electrode coating to adsorb insulin-like growth factor and hepatocyte growth factor. In vitro tests showed that the gelatin coating can effectively adsorb insulin-like growth factor. In the collagenase environment, there was explosive release in the first hour, and then continued to release slowly for 48 hours. Increasing the coating thickness can improve the drug absorption and release. The guinea pig inner ear electrode implantation test showed that the gelatin coating can reduce the ABR threshold increase caused by electrode implantation, while the coating containing growth factors can continuously reduce the ABR threshold, which may be the result of growth factors continuing to promote SGN survival and synaptic formation. The coating can increase the survival number of SGN after electrode implantation, and the coating did not cause adverse reactions on cochlear function and histology in the experimental period of 4 weeks.

5. Conductive polymer coating

The CI electrode is implanted into the scala tympani filled with perilymph, and there is a certain distance from the target neuron. The electrical stimulation generated by the electrode needs to be conducted by liquid, bone, and soft tissue. These conductive mediums increase the resistance

Plus, to reduce the precise transmission of signals, it is necessary to increase the stimulation voltage, which will lead to tissue damage and cause non-specific SGN stimulation. Conductive polymers can improve charge transmission, increase the ratio of stimulus signal intensity, reduce non-specific SGN stimulation, and reduce fibrosis[22].

5.1. Poly (3,4-ethylenedioxythiophene), PEDOT

PEDOT is a new type of organic conductive material with good conductivity, electrochemical stability and biocompatibility[23]. Jennifer et al.[24] mixed arginine glycine-aspartic acid, RGD functionalized alginate hydrogel with PEDOT polymer to make hydrogel/PEDOT electrode coating, which is used to deliver BDNF. In vitro experiments showed that the coating could reduce the electrode resistance, and BDNF could be released for more than 2 weeks, with explosive release at the early stage. In the 6-month guinea pig in vivo test, the resistance of the uncoated electrode gradually increased with time, while the resistance of the hydrogel/PEDOT coated implanted electrode remained low at all frequencies. BDNF release protected SGN and other cells in a short period of time. The long-term implantation of the hydrogel/PEDOT coated electrode did not affect SGN survival, and there was no cytotoxicity. Rachel et al.[25] used two hydrogels, poly (vinyl alcohol), PVA and heparin methacrylic acid, and a mixture of PEDOT and para-tolu-enesulfonate pTS to form a hydrogel/conductive polymer electrode coating. In vitro tests on the conductive polymer electrode coating showed that the coating reduced the electrode resistance, improved its charge transfer capacity, and increased the electrode charge storage capacity, and the coating was not significantly damaged during the electrode implantation into the cochlear model, indicating its good stability.

5.2. Platinum iridium alloy

Curtis et al.[26] used a platinum-iridium alloy as an electrode coating that was electrodeposited onto the surface of a platinum electrode, and in vitro experiments showed that the coated electrode reduced the polarization electrical impedance by more than 90% compared to an uncoated platinum electrode under clinically used electrical pulses. Ashley et al.[27] implanted the above coated electrode into the rat cochlea for 5 weeks and gave appropriate electrical stimulation. The results showed that compared with the uncoated platinum electrode, the coated electrode had higher charge storage capacity and charge injection limit before and after implantation, but the voltage transient impedance was only lower within one week after implantation, which may be related to the formation of fibrin on the electrode surface. The coating does not increase the tissue reaction caused by electrode implantation. It does not in-

crease the loss of spiral ganglion cells and the damage of neuronal function.

Ashley et al.[28] conducted an in vitro study on the electrochemical characteristics of PEDOT/pTS-PVA conductive hydrogels and electrodeposited platinum iridium alloy conductive coatings. The results showed that, compared with uncoated platinum electrodes, the two conductive coated electrodes had higher charge storage capacity, charge injection limit, and lower electrical impedance before and after 21 days of strong electrical pulse stimulation, and the coatings had no obvious corrosion.

6. Coating of other materials

6.1. Polydopamine (PD)

PD can improve the hydrophilicity of different substrate materials, promote cell surface adhesion, and has good biocompatibility[29]. Philipp et al.[30] studied the PD coated electrode in vitro, which showed that PD could increase the hydrophilicity and adhesiveness of the silicon electrode surface, maintain the normal morphology, distribution and function of the adherent adipose stem cells, increase the survival number of stem cells, and the coating slightly reduced the implantation resistance of the electrode drum, and there was less cell shedding after the implantation of the electrode.

6.2. Poly ([2–methacryloyloxy) ethyl] trimethylammoniumchloride), PMTA)

Hadler et al.[31], studied in vitro the effects of three polymer films, poly(N, N-dimethylacrylamide), poly(2-ethyl oxazoline), and PMTA, on fibroblast, glial cell, and SGN growth, respectively, and found that only PMTA showed significant attachment of glial cells on the surface, high SGN survival, and significant synaptic growth, while the former two significantly reduced SGN survival and synapse formation were significantly reduced by the former two, while fibroblast growth was observed on the surface of poly (2-ethyl oxazoline).

6.3. 2–methacryloyloxyethyl phosphorylcholine, MPC

MPC is a new type of biomaterial that mimics the structure of cell membrane. The strong polarity of phosphorylcholine in MPC makes it have a high affinity for water, and the acrylic group provides the possibility of forming polymers with other monomers[32]. Makoto et al.[33] implanted the guinea pig cochlea with MPC as the electrode coating. The experiment showed that the coating significantly reduced the electrode implantation resistance, which may be related to the increase of electrode hydrophilicity; the survival rate of SGN around the bottom of the cochlea in the coating group was significantly higher than that in the uncoated group. There was no significant difference in the survival rate of the inner and outer hair cells around the bottom of the cochlea, but the survival rate of the outer hair cells around the top of the cochlea was significantly higher than that in the uncoated group. It may be that the damage caused by electrode implantation and the inflammatory reaction did not spread upward in the coating group. Under the condition of mechanical stress and electric stimulation, the coating shows good stability.

7. Conclusions

Many electrode coating materials have been studied so far, mainly for loading neurotrophic factors or other drugs, loading adult stem cells, reducing implantation resistance, inhibiting fibrin adhesion, increasing electrode conductivity, etc. On the one hand, the coating materials that have been studied need to be further explored, including the physicochemical properties and biological properties of the coating in the cochlear environment, drug release rules, local pharmacokinetics, the properties of the coating under conventional voltage and current stimulation, the effects of electrical stimulation on the embedded cells and drugs, the long-term performance of the coating after implantation, and the effects on normal tissue cells, cochlear internal environment and hearing, etc. More perfect basic research is needed in the future to promote the realization of further clinical research. On the other hand,

it is necessary to continue to find new materials that are more suitable for the coating of cochlear implants. With the rapid development of nanotechnology, nano materials have shown many unique properties, and nano coatings have shown good antifouling ability, drug loading and drug release ability. Degradable materials are also an ideal choice. They can be used for short-term local administration, and can also be used to reduce electrode implantation resistance. There is no need to worry about the uncertain consequences caused by the long-term existence of the coating. However, when studying biodegradable materials to embed living cells or even allogeneic recombinant cells, it is necessary to ensure that living cells are effectively wrapped with degradable materials during their survival, otherwise cell migration or immune attack from autologous cells will result. How to combine the advantages of the two materials is worth further exploring. In a word, electrode coating has a broad development prospect in improving the effect of cochlear implant, but the research is still in its infancy. To explore appropriate coating materials and apply them to clinical practice will be a new hotspot and direction in the field of cochlear implant.

Conflict of interest

The authors declare no conflict of interest.

References

1. Seyyedi M, Viana LM, Nadol Jr JB. Within-subject comparison of word recognition and spiral ganglion cell count in bilateral cochlear implant recipients. Otology & Neurotology 2014; 35(8): 1446–1450.
2. O'Leary SJ, Richardson RR, McDermott HJ. Principles of design and biological approaches for improving the selectivity of cochlear implant electrodes. Journal of Neural Engineering 2009; 6(5): 055002.
3. Dhanasingh A, Jolly C. An overview of cochlear implant electrode array designs. Hearing Research 2017; 356: 93–103.
4. Bas E, Dinh CT, Garnham C, et al. Conservation of hearing and protection of hair cells in cochlear implant patients' with residual hearing. The Anatomical Record 2012; 295(11): 1909–1927.
5. Bas E, Goncalves S, Adams M, et al. Spiral ganglion cells and macrophages initiate neuro-inflammation and scarring following cochlear implantation. Frontiers in Cellular Neuroscience 2015; 12(9): 303.
6. Somdas MA, Li PM, Whiten DM, et al. Quantitative evaluation of new bone and fibrous tissue in the cochlea following cochlear implantation in the human. Audiology and Neurotology 2007; 12(5): 277–284.
7. Liu J, Yang S. Development of cochlear implantation and its related technique. Chinese Journal of Otorhinolaryngology-skull Base Surgery 2018; 5(10): 449–455.
8. Wang M, Wang X, Zhong C. Research advances in convergence of cochlear implantation with human induced pluripotent stem cell transplantation in treatment of sensorineural hearing loss. Chinese Journal of Otology 2020; 18(05): 972–976.
9. Xu M, Zhang H. Research progress in cochlear electrode drug delivery. Chinese Journal of Otology 2018; 16(4): 570–574.
10. Scheper V, Hoffmann A, Gepp MM, et al. Stem cell-based drug delivery for protection of auditory neurons in a guinea pig model of cochlear implantation. Frontiers in Cellular Neuroscience 2019; 13: 177.
11. Schwieger J, Hamm A, Gepp MM, et al. Alginate-encapsulated brain-derived neurotrophic factor-overexpressing mesenchymal stem cells are a promising drug delivery system for protection of auditory neurons. Journal of Tissue Engineering 2020; 11: 1–15.
12. Hügl S, Scheper V, Gepp MM, et al. Coating stability and insertion forces of an alginate-cell-based drug delivery implant system for the inner ear. Journal of the Mechanical Behavior of Biomedical Materials 2019; 97: 90–98.
13. Griffo A, Liu Y, Mahlberg R, et al. Design and testing of a bending-resistant transparent nanocoating for optoacoustic cochlear implants. ChemistryOpen 2019; 8(8): 1100–1108.
14. Li H, Edin F, Hayashi H, et al. Guided growth of auditory neurons: Bioactive particles towards gapless neural-electrode interface. Biomaterials 2017; 122: 1–9.
15. Wrzeszcz A, Dittrich B, Haamann D, et al. Dexamethasone released from cochlear implant coatings combined with a protein repellent hydrogel layer inhibits fibroblast proliferation. Journal of Biomedical Materials Research 2014; 102(2): 442–454.
16. Wrzeszcz A, Steffens M, Balster S, et al. Hydrogel coated and dexamethasone releasing cochlear implants: Quantification of fibrosis in guinea pigs and evaluation of insertion forces in a human cochlea mode. Journal of Biomedical Materials Research Part B: Applied Biomaterials 2015; 103(1): 169–178.
17. Plontke SK, Salt AN. Local drug delivery to the inner ear: Principles, practice, and future challenges. Hearing Research 2018; 368: 1–2.
18. Ceschi P, Bohl A, Sternberg K, et al. Biodegradable polymeric coatings on cochlear implant surfaces and their influence on spiral ganglion cell survival. Jour-

nal of Biomedical Materials Research Part B: Applied Biomaterials 2014; 102(6): 1255–1267.
19. Bohl A, Rohm HW, Ceschi P, et al. Development of a specially tailored local drug delivery system for the prevention of fibrosis after insertion of cochlear implants into the inner ear. Journal of Materials Science: Materials in Medicine 2012; 23(9): 2151–2162.
20. Yu H, Tan H, Huang Y, et al. Development of a rapidly made, easily personalized drug-eluting polymer film on the electrode array of a cochlear implant during surgery. Biochemical and Biophysical Research Communications 2020; 526(2): 328–333.
21. Kikkawa YS, Nakagawa T, Ying L, et al. Growth factor-eluting cochlear implant electrode: impact on residual auditory function, insertional trauma, and fibrosis. Journal of Translational Medicine 2014; 12: 280.
22. Duan Y, Clark GM, Cowan RSC. A study of intracochlear electrodes and tissue interface by electrochemical impedance methods in vivo. Biomaterials 2004; 25(17): 3813–3828.
23. Wallace GG, Kane-Maguire LAP. Manipulating and monitoring biomolecular interactions with conducting electroactive polymers. Advanced Materials 2002; 14: 953–960.
24. Chikar JA, Hendricks JL, Richardson-Burns SM, et al. The use of a dual PEDOT and RGD-functionalized alginate hydrogel coating to provide sustained drug delivery and improved cochlear implant function. Biomaterials 2012; 33(7): 1982–1990.
25. Hassarati RT, Dueck WF, Tasche C, et al. Improving cochlear implant properties through conductive hydrogel coatings. IEEE Transactions on Neural Systems and Rehabilitation Engineering 2014; 22(2): 411–418.
26. Lee CD, Hudak EM, Whalen JJ, et al. Low-impedance, high surface area Pt-Ir electrodeposited on cochlear implant electrodes. Journal of the Electrochemical Society 2018; 165(12): G3015-G3017.
27. Dalrymple AN, Huynh M, Nayagam BA, 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.
28. Dalrymple AN, Huynh M, Robles UA, et al. Electrochemical and mechanical performance of reduced graphene oxide, conductive hydrogel, and electrodeposited Pt-Ir coated electrodes: An active in vitro study. Journal of Neural Engineering 2019; 17(1): 016015.
29. Liu Z, Zhang T. Research progress of polydopamine modified polymers in nerve repair. China Biotechnology 2020; 40(10): 57–64.
30. Schendzielorz P, Rak K, Radeloff K, et al. A polydopamine peptide coating enables adipose-derived stem cell growth on the silicone surface of cochlear implant electrode arrays. Journal of Biomedical Materials Research Part B: Applied Biomaterials 2018; 106(4): 1431–1438.
31. Hadler C, Aliuos P, Brandes G, et al. Polymer coatings of cochlear implant electrode surface—An option for improving electrode-nerve-interface by blocking fibroblast overgrowth. PloS One 2016; 11(7): e0157710.
32. Iwasaki Y, Ishihara K. Cell membrane-inspired phospholipid polymers for developing medical devices with excellent biointerfaces. Science and Technology of Advanced Materials 2012; 13: 064101.
33. Kinoshita M, Kikkawa YS, Sakamoto T, et al. Safety, reliability, and operability of cochlear implant electrode arrays coated with biocompatible polymer. Acta Oto-Laryngologica 2015; 135(4): 320–327.