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Implantable Triboelectric Nanogenerators in the Biomedical Field

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ABSTRACT

Implantable Triboelectric Nanogenerators (TENGs) have revolutionized the biomedical field by providing innovative power solutions for medical devices and enhancing diagnostic and therapeutic applications. Internally implanted TENG transforms kinetic energy from the body into electrical power, providing a constant energy supply for Implantable Medical Devices (IMD). Their ability to generate high voltage and low current makes them particularly effective for applications in biosensing, patient monitoring, and therapeutic interventions. Therapeutically, TENGs power cardiac pacemakers, promote wound healing, enhance bone regeneration, and support muscle and nerve stimulation. They also enable controlled drug release, particularly in targeted cancer treatments.

This paper reviews the working principle, operation mode and the importance of material selection of implantable TENG for biomedical applications, emphasizing biocompatibility, stability and flexibility. Recent advances in TENG materials and technologies are highlighted, showcasing their potential in biomedical applications and addressing future development challenges.

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Introduction

The rapid development of implantable triboelectric nanogenerators (TENG) has led to new breakthroughs in the biomedical field, providing innovative power solutions for medical devices and enabling advanced monitoring, diagnostic and therapeutic applications [1,2]. Due to its high efficiency, biocompatibility, flexibility and miniaturization, TENG has been widely used in IMplantable medical devices (IMD), effectively reducing the installation, maintenance and longterm implantation infection risk and thus showing broad application prospects in the biomedical field [3]. These nanogenerators collect bio-mechanical energy and convert it into electrical energy through tiny movements of the human heart, lung or muscle providing a sustainable power source for various IMDs and their high voltage and low current output characteristics are unique advantages in biosensing monitoring and biotherapy [4-10]. To minimize the need for surgical removal or replacement of IMDs, various types of implantable TENGs are being utilized in areas like electrical stimulation therapy and the monitoring of physiological signals. This approach not only decreases the discomfort experienced by patients but also enhances the safety and ease of use [11,12].

The sensor-integrated TENG shows great potential for continuous health monitoring and diagnosis [13-15]. Biosensors provide continuous and real-time physiological information through biological biochemical markers or mechanical movements, enabling doctors to more intuitively understand relevant data and make diagnoses, and determine treatment plans in a timely manner, shortening the rehabilitation cycle and reducing patients' economic and physical pain [16,17]. The TENG-based implanted sensor is integrated with the human body to obtain biomechanical energy such as cartilage displacement, heartbeat, lung contraction, muscle stretching and blood vessel dilation while meeting the biocompatibility and providing a measurement of measuring physical parameters such as the degree of cartilage damage, pulse, heart rate, breathing, muscle tension, body temperature, and blood pressure in real-time [18]. Implantable TENG is suitable for the development of efficient and economical new health monitoring technology due to its advantages such as easy availability of materials, low cost and good biocompatibility [19]. The stable electrical output generated by the TENG ensures the high sensitivity and accuracy of the biosensor. These self-powered diagnostic tools enable early monitoring and diagnosis of diseases, thereby improving patient treatment.

In addition to monitoring and diagnosis, TENG also shows great promise in therapeutic applications. TENG has a high voltage characteristic, so one of the applications in the therapeutic field is as a continuous power supply for IMD. Traditional IMD batteries need to be replaced periodically through surgery when they run out of power, putting patients at greater risk. The TENG can significantly extend the service life of these devices by continuously harvesting biomechanical energy, such as the cardiac pacemaker system [20]. TENG can also promote wound healing by providing electrical stimulation, accelerating tissue regeneration and shortening healing time [21]. In the field of orthopedics, TENG promotes the proliferation and differentiation of osteoblasts and enhances bone regeneration and repair [22,23]. In addition, TENG has been used for muscle and nerve stimulation and to provide new treatments for muscle atrophy and neurodegenerative diseases [24,25]. They can provide precise, local stimulation, improve therapeutic effectiveness and reduce side effects. In addition, for implantable therapy, most implantable devices with temporary therapeutic purposes are expected to be wirelessly manipulated and biodegraded to avoid secondary surgical removal and the risk of infection [4,26]. Therefore, bioabsorbable or biodegradable implantable TENG sensors have also been extensively studied. In addition, the TENG can also provide power to drug delivery systems for controlled and sustained drug release, thereby improving therapeutic efficiency for precision treatment purposes, such as stimulating targeted drug delivery systems for cancer treatment [24,4,27,28].

In summary, advances in TENG materials and technologies have the potential to be transformative in terms of monitoring, diagnosis, and treatment. As this emerging field continues to evolve, it will improve medical outcomes and improve patient quality of life. This review summarizes the development, technical characteristics and applications of TENG-based materials in implantable devices. We first briefly introduce the working principle of the TENG. Then, according to the structure of the TENG, the types of materials used to make the friction layer and electrode are introduced respectively. Based on the type of application of implantable TENGs, representative studies of TENG-based implantable devices in the past year as sensors to monitor heart signals, as pacemakers for IMD energy supply, drug delivery, electrical stimulation to promote recovery from neurological diseases, inhibition of muscle atrophy, prevention of surgical wound infection, and simulation of tactile recovery will be presented in turn. Finally, the needs, challenges and prospects of TENG-based IMD are further discussed.

Working Principle

The Triboelectric Nanogenerators (TENGs), first introduced by Professor Wang Zhonglin and his team in 2012, represent an innovative energy technology [29,30]. TENGs operate on the principles of triboelectricity and electrostatic induction. Typically, they are composed of two distinct material layers that serve as the friction layers. These materials should exhibit contrasting tendencies to either gain or lose electrons, which is crucial for TENG functionality [24,31]. Through contact, friction, and separation, these layers enable the accumulation of charge, thereby generating an electric current. The TENG's driving force, known as the Maxwell displacement current, arises from the temporal variation of the electric field in conjunction with dielectric polarization [32]. When utilized in implantable medical devices, TENGs facilitate the conversion of biomechanical energy into electrical energy. This conversion is achieved through the interaction of biomechanical motion induced triboelectrification and electrostatic induction.

Triboelectrification, the process where two distinct materials accumulate opposite charges upon contact and subsequent separation initiates the functioning of a TENG [33]. During contact with the electrode, the triboelectric layer of the TENG undergoes electron transfer due to varying electron affinities, leading to its charging. This charging is quantified by the surface charge density, which is the charge per unit area and is formulated as $Q = \sigma \cdot A$ (where Q is the amount of charge transferred, σ is the surface charge density, and A is the contact area). Following triboelectrification, the charged triboelectric layer's proximity to the electrode induces a charge redistribution within the electrode because of the electric field created by the layer. This results in the formation of an opposite charge on the electrode, establishing a potential difference. The connection of an external circuit allows this potential difference to propel an electric current. This phase harnesses the mechanical energy from the contact-separation motion and transforms it into electrical energy through a process known as electrostatic induction, mathematically represented as $I{=}dQ/dt$ (where I is the current, dQ the change in charge, and t the change in time).

In general, TENG can be divided into vertical Contact-Separation (CS) mode, Lateral Sliding (LS) mode, single-electrode (SE) mode, and Freestanding Triboelectric-layer (FT) mode Four basic types [6,29,33-35]. In the vertical contact-separation configuration of a TENG, the frictional layer interacts by making contact and then separating along a vertical axis. Conversely, in the transverse sliding mode, the frictional layer slides back and forth in a parallel motion. TENGs operating in the single-electrode mode are capable of harnessing energy from objects in motion without the need for any connecting wires. Meanwhile, the independent triboelectric layer mode TENG operates by integrating both the transverse sliding and vertical contact-separation mechanisms, utilizing the electrostatic induction between a pair of symmetrically arranged electrodes to capture kinetic energy.

Bioimplantable TENG devices usually operate in hybrid mode to achieve high current and low current output characteristics, improving the accuracy and accuracy of IMD devices [33].

Material Properties of Implantable TENG

The choice of materials is crucial to the performance of the TENG, which mainly includes friction layer materials and electrode materials. In the field of medical devices and IMD, crafting a superior TENG hinges on the careful selection of materials [18,36,37]. The surface texture, polarity, and micro-architecture of these materials play a pivotal role in determining the efficiency of the resulting devices. It is crucial to balance the pursuit of optimal performance with other essential attributes such as biocompatibility, durability, and pliability, all of which must be taken into account during the material selection process. Currently, materials such as elastomers with similar flexibility to the surrounding tissues are ideal for manufacturing TENG devices [11]. When considering the BDTENG it is also necessary to balance the degradation mechanism and dissolution rate of the friction layer, substrate, electrode, interconnect, encapsulation and bonding layer materials [38].

Friction Layer Material

The two materials of the friction layer should have different electron gain and electron loss capabilities of TENG and the characteristics of different materials affect their ability to form current through contact, friction and separation [24,31]. Friction layer materials can be divided into polymer materials and biological materials.

Polymer Materials

Commonly used triboelectric polymer materials include Polyvinylidene Fluoride (PTFE), Polydimethylsiloxane (PDMS), Fluorinated Ethylene Propylene (FEP), Perfluoroalkoxyane (PFA), Polyvinylidene Fluoride (PVDF), etc [29-39]. Most of them have good electron gain ability and are triboelectronegative [40]. It is relatively easy to transfer charge, non-toxic and biocompatible and can produce implantable TENG with excellent properties.

Due to its extremely high electronegativity and low coefficient of friction, and high wear resistance, PTFE can work in a chemically inert environment, and the surface of PTFE is very smooth and nonviscous, which helps to reduce the friction between the implanted device and the surrounding tissue, reducing the risk of damage during the implantation process [41,42]. It also has good electrical insulation, which helps to improve the energy conversion efficiency of TENG and reduce charge loss, and is an excellent IMD material.

PDMS is a commonly used flexible polymer with good biocompatibility and mechanical properties. Its surface can be chemically modified to increase charge density and improve the output performance of TENG [43]. Its surface roughness can be increased or specific nanostructures introduced [44-46]. This helps to increase the efficiency of charge transfer when it comes into contact with another friction material. PDMS also allows oxygen and water vapor to pass through, which helps maintain the physiological environment at the implant site and reduces the risk of infection.

Although PTFE and PDMS are not biodegradable materials by themselves, their stability and biocompatibility make them ideal for use in TENG designs [47,48], as well as their good durability, ability to withstand long-term mechanical stress and the environment in the organism, making them suitable for long-term use in implanted devices. In 2018, Liu et al. proposed a new TENGimplantable endocardial pressure monitoring technology, which uses tribon-electric layer PTFE films [49]. The output performance of the self-powered endocardial pressure sensor (SEPS) was increased from 1.2V to 6.2V. The aluminum film is chosen as another triboelectric layer. The device is encapsulated using PDMS. The endocardial pressure of pigs was measured with excellent linearity (R2 = 0.997) and sensitivity (1.195 mV mmHg −1).

Zheng et al. reported the first fully biodegradable TENG composed of synthetic polymers (poly (lactate-co-glycolic acid) (PLGA), poly (3-hydroxybutyrate co-2016 hydroxyvalerate) (PHBV) and polycaprolactone (PCL)) [26]. For example, Polylactic Acid-Glycolic Acid Copolymer (PLGA), polylactic acid (PLA) , Polyglycolic Acid (PGA) , Polyvinyl Alcohol (PVA) have been widely studied for TENG due to their biodegradability and biocompatibility [3,27,41,50-55]. The degradation rate of completely degradable materials is related to the environment, and the degradation rate can be controlled by changing the physical environment or the chemical environment to achieve the desired effect.

With the continuous development of modern medical treatment existing polymer materials are not enough to meet people's specific needs for medical equipment, so emerging polymers are also being explored, such as poly (2-hydroxyethyl methacrylate) (HEMA), Polyethylene Glycol Diacrylate (PEGDA) citric acid, 1,6-hexanediol, glutaric acid and 1, 2-Propanediol (CHGP), Poly (hexanediol-co-citric acid) (PHC) prepolymer, Poly (sorbitol sebacate) (PSS), etc. HEMA stands out as a biocompatible and biodegradable polymer that has been cleared for applications in contact and intraocular lenses, as well as in drug storage, and is utilized in soft tissue engineering and drug delivery systems without causing significant adverse effects. To enhance the positive triboelectric characteristics of HEMA, ionic Methacrylic Acid (MAA) is always incorporated. PEGDA hydrogels have gained traction in tissue engineering and regenerative medicine due to their high water retention, biocompatibility, and ease of fabrication [14,45,56]. The copolymers PSS and PHC have demonstrated reduced cytotoxicity and improved cell viability, making them more suitable for the development of Implantable Medical Devices (IMDs).

Biomaterials

Biomaterials used for manufacturing TENG include cellulose , chitin or chitosan , silk , rice paper and egg white etc [54,55,57,58]. These materials come from nature, so most of the materials have strong bioabsorbability in biology and are suitable for making degradable and implantable TENG.

Cellulose is a natural polymer compound with good biocompatibility and biodegradability and it is compatible with human tissues without causing obvious immune reactions and can be degraded into harmless small molecules in the body, which helps to reduce the risk of long-term implantation [57,59]. Cellulose materials have good flexibility in biological friction layer materials. Therefore, it is suitable for use in flexible and stretchable TENG devices.

Chitin is a natural polysaccharide extracted from crustaceans [60]. Chitosan is the deacetylation product of chitin, which is generally obtained by hydrolyzing part of the n-acetyl group of chitins under alkaline conditions. Chitin has natural antibacterial properties that help reduce the risk of infection during implantation. It is also highly processable, chitosan has the properties of film formation and hydrogel formation. It can be made into a variety of shapes and structures to adapt to different types of TENG designs [61].

Silk, one of the earliest animal fibers used by humans, exists in the glands of arthropods such as pupae, scorpions and spiders, and is solidified by the liquid silk secreted during the cocooning process [62]. Silk is made up of two main proteins, sericin (25wt %) and sericin (75wt%), which exhibit excellent toughness and tensile strength since the proteins are connected to adjacent peptides by hydrogen bonds [63]. Modified or carbonized or composite regenerated silk fibroin proteins or cocoons have good electrical conductivity and excellent performance in energy storage and wearable electronics [64].

With the continuous development of materials science and nanotechnology, more and more biological materials have been studied and applied to triboelectric layers that can be implanted in TENG. Among them, polysaccharides are alginate hyaluronic acid and hyaluronic acid agar and collagen [62,65-68]. Proteins such as gelatin, due to their excellent biocompatibility and inherent enzymatic iodegradability in the human body, have also begun to be used in the friction layer of TENG [69]. Most implantable biomaterials are already widely used in other research fields, such as drug delivery, stimulation-response materials, and chemistry, which not only have good biocompatibility, but also have excellent properties of biodegradation, and greatly reduce pain in patients [41].

Other Materials

Covalent Organic Frameworks (COFs) are not polymers in the traditional sense [70,71]. Among the different nano-catalysts used for nanozymes, covalent organic frameworks (COFs) composed of light elements such as C, H, N, B and O have the advantages of low density, high stability and adjustable porosity [4,72,73]. COF has good stability in aqueous solution, and some COFs have degradability in living organisms. COFs are highly ordered two-dimensional or three-dimensional network structures that typically appear as porous crystalline materials. High specific surface area: The high specific surface area of COFs helps to increase the frictional contact area, which may improve the charge transfer efficiency and output power of the TENG. COFs can integrate multiple functions, such as drug slow release, imaging guidance, etc., to provide additional biomedical functions for TENG. The synthesis of COFs is generally more complex than conventional polymers, requires precise control of reaction conditions to obtain the desired structure and properties, and can be costly to synthesize, limiting their popularity in large-scale biomedical applications. Sathiyanathan et al. this year proposed a sensor based on a disposable Triboelectric Nanogenerators (TENG) manufactured with a chitosan covalent organic skeleton (CS-NSCoF), which combined with an Artificial Intelligence (AI) algorithm is a novel method for evaluating urination status.

With the different needs of TENG in the medical field, it is usually difficult for a single material to meet the current individual needs. As the friction layer that can be implanted in TENG, composite materials can effectively improve the energy conversion efficiency, biocompatibility and mechanical stability by combining the characteristics of different materials, providing new possibilities for improving the performance of TENGs. It is expected to promote the development of implantable medical devices in the direction of self-energy, high efficiency and good biocompatibility.

Electrode Materials

Metallic Materials

At present, biodegradable metals are still used as the main electrodes in TENG [74]. These metals can be gradually degraded in vivo through chemical or enzymatic reactions and eventually converted into a form that is harmless to the body [75]. New alloy composition, surface modification technology, and composite methods with other materials can make them have mechanical properties that match the application scenario, such as sufficient strength and toughness and degradation rate [27].

Magnesium (Mg) membrane is the most used electrode material, magnesium as one of the essential elements in the human body, degradation in the biological body, to produce harmless magnesium ions [76,77]. In addition, metallic nanowires such as Silver Nanowires (Ag NW) and gold nanowires (AuNW), which have high electrical conductivity and good flexibility, are not only efficient at collecting charge, but also adaptable to different biological environments through flexible design, and are also a common choice for implantable TENG electrodes[25,50].

Conductive Polymers

Polymer electrode materials for implantable triboelectric nanogenerators (B-TENGs) need to have sufficient conductivity to achieve efficient charge transfer but also need to meet the basic conditions of biocompatibility, processability, stability and so on. Commonly used conductive polymers are poly (3, 4-ethylenedioxythiophene) (PEDOT) and Polypyrrole (PPy) [78,79].

PEDOT is a commonly used conductive polymer, which has a high conductivity, even comparable to some metals, which makes it very suitable as a conductive material for electrodes. It also has good flexibility and biocompatibility, making it suitable for use in implantable TENG and biological tissue adaption TENG [80].

PPy is a P-type semiconductor that can adjust its conductivity by doping, has excellent electrical conductivity, and is sensitive to environmental factors such as humidity, pH value, etc., and can be used in the production of sensors in vivo for detecting biomolecules and cells and manufacturing neural electrodes to record and stimulate nerve signals [81]. Some PPy also have antibacterial properties.

There are also many polymers with excellent electrical conductivity that are used to make electrodes, For example, Polyaniline (PANI), Polyp-Styrene-Ethylene (PS), polyimide (PI), Polylactic Acidglycolic Acid Copolymer (PLGA), polycaprolactone (PCL), polyacrylic acid (PAA), poly (4vinylpyridine) (P4VP), poly (3-hydroxybutyrate - co-3-hydroxyvalerate) (PHBV), and poly Ethylene glycol diacrylate (PEGDA), etc [56]. Most of these materials will combine the advantages of different materials to make composite materials to improve the comprehensive properties of TENG. For example, PEGDA/Lap hydrogel serves as both the electrode and triboelectric layer. To enhance the range and linearity of the device, a PEGDA/Laponite composite material is employed, which leads to enhanced performance [82,14]. In the case of chemically crosslinked hydrogels, adjusting the molecular weight of the crosslinking agents is crucial for dictating the mechanical robustness of the material. This manipulation is essential for ensuring the hydrogel is well-suited for integration into a soft biological context and for reducing potential harm to the surrounding tissues.

TENG Structure

According to the working principle of the TENG, most of the structures used for the biomedical implantable TENG are thin-film based. Most TENGs consist of two thin films with large electron affinity differences, and multilayer structures can be used to further improve the output performance of the TENG [6]. In general, TENG prepared from a soft membrane is flexible enough to fit well to the skin or organs.

The pore structure of microscopic nanomaterials can increase the contact area and generate electrostatic induction, so the thin films of TENG are mostly void structures. The void structure effectively enhances the triboelectric effect because the friction layer not only induces charge at the contact surface when it contacts but also generates additional charge on the porous surface within the film due to pore compression, with an accompanying electrostatic effect. The release process leads to a greater potential difference between the upper and lower electrodes [24,83]. Additionally, porous polymer films undergo greater deformation under identical compressive forces. This enhanced deformation boosts the relative capacitance, consequently amplifying the triboelectric output. This increase is due to the extra frictional charge generated by electrostatic induction on the inner surfaces of the pores, coupled with the substantial change in capacitance under mechanical pressure [84].

The hollow structure of the void is also conducive to the storage and release of drugs when they are used as drug carriers.

Electrospinning, as a simple and versatile technique for fabricating fiber nanomaterials, has been widely used and implantable in the fabrication of TENG due to its ideal properties such as extremely high porosity and large surface area [42,85].

Application

Nanogenerators have been widely used in biomedical fields, especially in the research of implantable TENG. This review summarizes, classifies and describes in detail the applications of implantable triboelectric nanogenerators in biomedical fields.

Monitoring and Diagnostics (Biomedical Sensing)

The implantable TENG can be used as a biosensor to realize real-time monitoring of patient's health status by monitoring physiological parameters such as heartbeat and blood pressure [86,87]. For example, several Research teams have developed TENG-based electrocardiogram (ECG) sensors capable of efficiently collecting and analyzing heart signals. Sensing characteristics such as response hysteresis, response time, strain response sensitivity and response range to pressure are key parameters of flexible sensors [14,15]. Since the signal source of the TENG's self-powered sensor is very close to the organism, and the organism exhibits a high response to slight forces, pressures and mechanical deformation of the order of one thousandth or one millionth, it has a low response time and high sensitivity [50]. The TENG-based heart rate monitor can continuously track heart activity and can be used for real-time remote heart monitoring, providing key data for managing heart disease and preventing adverse events [88,89]. In diabetes management, the TENG-powered glucose sensor can monitor glucose levels in real-time, reducing dependence on external power sources and improving patient compliance and convenience.

A recent study by Ouyang Yue and colleagues developed a smart nanoengineered electronic scaffold based on TENG for integrated cartilage therapy [50]. The multi-convex TENG sensor demonstrates excellent pressure sensing capability over the pressure range of joint motion, achieving a highly sensitive voltage output of 52.5 V MPa^{-1}. The collager-chitosan hydroxyapatite (CA-CS-HA) and poly (ε-caprolactone)/poly (dimethylsiloxane)/ poly (ε-caprolactone) -fluorapatite (PCL/PDMS/PCL-FA) are used as positive and negative friction layers, respectively, and silver nanowire is used as electrode material to generate electrical energy. Ag NWs collect, act as an ES energy source, and transmit electrical signals to a receiver outside the body. In addition, the tissue battery can collect electrical energy converted from mechanical energy, which stimulates the proliferation of chondrocytes and accelerates the process of cartilage repair. It is worth noting that the device can monitor the repair status of cartilage in real-time, providing a new type of medical rehabilitation tool for patients with cartilage injury. Although there may be challenges in terms of long-term stability and signal persistence, this work certainly provides a promising direction for the development of bioelectronic implants that promise to reduce patient suffering and reduce treatment costs.

Treatment

IMD Power

Pacemakers

The first implantable pacemaker, invented by Rune Elmqvist had a limited charge life and toxicity issues, and the first patient has undergone nearly 30 pacemaker replacement surgeries [90]. In order to solve these problems, nuclear batteries, lithium iodine batteries, and lithium batteries were successively invented, but they could not fully achieve a self-electric power supply. In 2019, Ouyang et al. introduced a pioneering symbiotic pacemaker utilizing the TENG to collect and store energy from cardiac movement, using an external wireless magnetic switch to activate the pacemaker, maintaining stable cardiac pacing in an animal model [91]. In 2024, Liu et al. also reported a battery-free, transcatheter, self-powered intracardiac pacemaker based on an implantable TENG for the treatment of arrhythmias in a large animal model [92]. The energy harvesting unit is made of a gold electrode deposited by a film of Polyformaldehyde (POM) particles and Polytetrafluorovinyl (PTFE). The movement of POM particles between electrodes, driven by the rhythm of a heartbeat, produces an alternating current, in accordance with the principles of triboelectric nanogenerators outlined by Maxwell. The self-powered intracardiac pacemaker achieves an open circuit voltage of approximately 6.0V and a short circuit current of 0.2μA. Employing a capsule-like device weighing 1.75 grams and with a volume of 1.52 cubic centimeters, which can be delivered via a catheter and implanted into the pig's right ventricle, this technology effectively harnesses the kinetic energy of the heart to generate electricity. This innovative method showcases the latest strides in IMDs, addressing the energy limitations typically faced by implantable pacemakers and other bioelectronic devices designed for therapeutic and sensing purposes.

Drug Delivery

In the field of biomedicine, TENG is emerging as a new potential energy source for precision drug delivery. The use of the TENG to generate electric fields to control the loading and release of drugs can enable more precise delivery of drugs to the target location, preventing the accumulation of drugs in healthy tissues and reducing potential adverse effects.

Chemotherapy is the most commonly used way to treat cancer, but chemotherapy has serious side effects and can develop resistance after long-term chemotherapy, reducing the effectiveness of treatment. Targeted Drug Delivery Systems (DDS) are designed to minimize the adverse effects of chemotherapy. Gang et al. studied a Biodegradable Triboelectric Nanogenerator (BI-TENG) made of natural and synthetic biodegradable materials for targeted drug delivery in cancer treatment [76]. The device's triboelectric layer was composed of reed film, primarily cellulose, and Polylactic Acid (PLA). Upon implantation in mice, the motion of the mice induced an open circuit voltage of 0.176 V and a short circuit current of 192 nA. This research underscores the potential of BI-TENG in harnessing biological motion for energy generation, facilitating a more sustainable approach to drug delivery systems. BI-TENG, as a power source, is connected to the interdigital electrode to generate an electric field, which stimulates the accelerated release of Doxorubicin (DOX) from red blood cells in the targeted Drug Delivery System (DDS) and increases the speed of DOX release from red blood cells by the DDS system. Once the electric field application ceases, the release rate of DOX reverts to its baseline, allowing for controlled drug delivery timing and targeting. This approach can mitigate the impact on healthy tissues during cancer therapy and ensure the precise elimination of cancer cells. The research highlights the significant potential of BI-TENG in the fields of cancer therapy and targeted medication administration.

Electrical Stimulation Promotes Repair

Electrical stimulation can enhance tissue regeneration and contribute to nerve disease recovery, wound healing soft tissue injury, muscle regeneration and other processes, and play a great role in the accurate treatment of various clinical diseases [93]. However, the limited-service life and buckling size of implanted devices remain significant barriers to long-term clinical use. Advances in implantable TENG have paved the way for self-sustaining closed-loop electrical stimulation in vivo [94].

Implantable TENG for nerve stimulation therapy has shown surprising advantages in the stimulation, inhibition and perception of neural activity. They treat Parkinson's disease, obesity and other diseases by generating a micro-current to stimulate neurons and perform nerve modulation through Deep Brain Stimulation, vagus nerve stimulation, etc [25,95]. In the study of Chen, P. et al. they developed an ultrasound-driven battery-free nerve stimulator based on PVDF/ TMCM-MnCl3 soft piezoelectric-triboelectric hybrid nanogenerator (PTNG) without any flexion auxiliary control circuit [25]. Soft PTNG implanted under the skin can be used as a wireless-powered nerve stimulator. The adjustable stimulation current of 0.9 mA can be achieved by allowing the stimulation parameters to be adjusted by an externally programmable ultrasonic pulse. The device was implanted in the Subthalamic Nucleus (STN) of Parkinson's rats for Deep Brain Stimulation (DBS) and then recorded electrophysiological signals during their daily activities, and the results showed that ultrasound-driven DBS can effectively modulate abnormal beta oscillations and improve motor dysfunction in PD rats.

Direct stimulation of muscles with a small current through the TENG has been shown to be effective in treating muscle injuries. Zhang et al. In a recent study, Shuai Zhang et al developed a novel implantable heterogeneous triboelectric nanogenerators (h-TENG), which uses Polyvinyl Alcohol (PVA) and Polycaprolactone-Zein (PCL &Zein) as friction layer materials [24]. The device effectively prevents muscle atrophy caused by denervation through electrical stimulation. They placed it in the gastrocnemius muscle of mice to prevent muscle atrophy in vivo verification, and found that this device can up-regulate the expression of the FGF6 gene, thereby promoting muscle cell proliferation and effectively preventing muscle atrophy.

Antibacterial

Surgical Site Infection (SSI) is a common and frequently occurring disease in wound healing after surgery, which will significantly increase morbidity and mortality [96]. In order to prevent this problem, it is essential to eliminate microorganisms. Various antibiotics are used to control the proliferation of microorganisms, but with the discovery of antibiotic resistance, this has become one of the most serious global health problems. Studies have shown that electrical stimulation can effectively inhibit bacterial growth, and the inhibitory effect of ES on bacterial growth has been proposed as a mechanism to explain the beneficial effect of ES on wound healing [97,98].

Imani et al. outlined a method for combating soft tissue microorganisms using an ultrasounddriven, implantable, biodegradable vibratory triboelectric nanogenerator (IBV-TENG) [99]. The device produces electrical stimulation in vitro and in vivo to address Surgical Site Infection (SSI). The IBVTENG is capable of producing a voltage of about 4 volts and a current of about 22 microamps at a frequency of 20 kHz and a power density of 2 watts per square centimeter, operating at a depth of 3 millimeters underwater from the ultrasonic probe. This technique has been shown to eradicate up to 100 percent of Staphylococcus aureus and 99 percent of E. coli in vitro. In addition, in laboratory evaluations, it is effective in inhibiting bacterial growth in pig tissues. Once its antibacterial function is complete, IBV-TENG degrades and is absorbed by the body. This not only effectively targets the bacteria at the deep surgical site, but also relieves the physical and financial stress of the surgical patient. This antimicrobial approach is expected to serve as an effective strategy against SSI, potentially extending life and improving the quality of care by preventing the colonization of microorganisms in deep tissues.

Simulated Sensations

The absence of tactile sensation is frequently observed among individuals who have sustained injuries to their peripheral nerves or experienced a loss of soft tissue [100]. The advancement of wearable or implantable neuroprosthesis devices designed to replicate the sense of touch is anticipated to help restore this sensory function. These devices operate by transforming pressure signals from the vicinity of the injury into electrical impulses, which are subsequently interpreted by the brain. Shlomy and colleagues [16] explored the use of implantable triboelectric nanogenerators (TENGs) to restore tactile sensation. They developed an integrated tactile TENG (TENG-IT) device, which is placed beneath the skin. This device transforms tactile pressure into an electric potential. By employing cuff electrodes, it transmits impulses to intact sensory nerves, mimicking the sensation of touch. This approach holds significant promise for aiding patients who have suffered a loss of tactile sensation due to traumatic peripheral nerve damage or soft tissue injuries. They chose polydimethylsiloxane (PDMS) as the negative friction layer, cellulose acetate butyrate (CAB) as the positive friction layer, and gold film as the electrode. The output voltage of this TENG is 0.97± 0.03V. Listening to them demonstrate TENG-IT in rats, immunohistochemical staining results showed that it provided tactile ability to rats who blocked posterior foot sensation by severing the distal tibial nerve. These findings suggest that self-powered TENG-based implants hold great potential as a means of restoring the sense of touch.

Challenges and Developments

TENG technology has experienced rapid development and optimization since it was first proposed in 2012. The initial TENG design was relatively simple and inefficient. With the development of materials science and nanotechnology, researchers have developed a variety of highly efficient TENG materials and structures, improving the efficiency and stability of electrical energy conversion. In addition, advances in integrated circuits and miniaturization technology have also promoted the application of TENG in implantable devices. However, with the growing demand for renewable energy and self-powered technologies in the biomedical field, TENG has also faced some challenges and issues during its development.

In order to more effectively implant or attach to the human body, it is necessary to further miniaturize the structural design of the TENG and further improve the packaging strategy of the nano-TENG devices to ensure the long life of the implanted system, resist body fluid corrosion, and reduce energy loss. With the development and needs of precision medicine, IMD equipment needs higher stability and accuracy, and the development of multi-functional integrated triboelectric nanogenerators to achieve functions such as energy collection, sensor monitoring and treatment at the same time. In the process of promoting the clinical trial and commercialization of implantable TENG, its biosafety and performance need to be continuously tested and verified, so that it can be applied in practical medical treatment as soon as possible to benefit more patients.

In the future, the development of implantable TENGs will likely be in the following aspects: TENG based hybrid technologies, the development of new materials and structures, and multi-functional integration. The use of ultrasound to transmit energy to implantable bioelectronic devices has strong penetration depth and higher security [26], but the research on the material properties of TENG driven by this method is still in its infancy. The development of TENG can also be combined with other nano power generation, such as piezoelectric and other effects, to obtain implantable medical power generation devices with better performance [101]. Implantable triboelectric nanogenerators (iTENG) research focuses on the development of novel biodegradable polymer materials, bioabsorbable materials, and triboelectric nanogenerators using natural materials to improve device biocompatibility, degradability, miniaturization design, and improved packaging strategies. These advances indicate that iTENG has great application potential in biomedical monitoring, treatment and health management in the future, and the integration of TENG with other sensors, and medical devices, and the integration of IoT and smart medical systems will form a multi-functional, integrated intelligent system to achieve a wider range of applications.

Conclusion

This review briefly summarizes the application of implantable TENG in biomedical field in recent years, including the working principle, material properties, structure, application and so on. Through the continuous efforts of researchers, the idea of collecting human machinery to power biomedical systems has been applied to reality. The implantable, biocompatible TENG enables continuous monitoring of physiological signals, as well as timely disease diagnosis, and revolutionizes medical treatment technology. With the development of material science, engineering technology, textile science and biomedical technology, implantable TENG is expected to play a greater role in practical medical applications, providing stable and sustainable electrical energy support for IMD, and has broad application prospects.

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