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Soft Conductive Materials for Bio-Implantable Epicardial Devices

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Abstract: Heart failure is a widespread health concern. A person with a heart failure has 5 years shorter life expectancy compared to a person who has a cancer. Specifically, myocardial disease is usually involved with a treatment accompanied by an electrical conduction system. Cardiovascular problems must be found, monitored, prevented, and treated using implantable epicardial devices. When in contact with the epicardium, a typical epicardial bioelectronic device analyzes the electrical and physical properties of the heart, including electrocardiograms (ECGs), mechanical contraction and expansion behaviors, and pathological data. The gadgets can also offer therapeutic remedies. The ideal bioelectronic device should have different sensing capabilities as well as mechanical softness and deformability akin to cardiac tissue. In other words, to alleviate the physical burden to heart due to ventricular pacing, epicardial electronic system made of soft and elastic materials is needed. Newly developed materials are promising candidates to develop an epicardial system that could detect electrical signals of heart rapidly without hindering the physical movement and functions of heart even after few weeks. Multifunctional epicardial system that monitors electrical conduction of epicardium surface and stimulate epicardium simultaneously could be a powerful tool to diagnose and treat myocardial disease. In this review, we discuss candidate materials, which have softness for minimizing the stress to heart inside of our body. To overcome current technologies regarding sensor/therapeutic technology for heart disease, novel epicardial sensing/stimulation system that matches similar mechanical properties of heart was addressed in this article.

Keywords: Heart, Bio-Implantable, Conductor, Myocardial Disease, Epicardial, Soft

1. Introduction

In conventional electronics for bio-implantable system, rigid and brittle materials such as metal and oxide have been used for stable electrical performance, guaranteeing the long-term usability. However, conventional rigid system causes physical burden to epicardium when heart is rapidly expanded or contracted during daily lives. This mechanical mismatch decreases the bioelectronic performance. The conventional technologies are not suitable to be utilized as wearable and implantable bioelectronics because their mechanical stiffness can induce side effects. For example, the rigidity of a wearable device mounted on the skin evokes discomfort and skin irritation [1]. Because stiff and flat electronics cannot intimately follow the contour of soft and curvilinear skin, the pressure is concentrated in a localized area, and friction between the device and the skin may result in allergic reactions. Moreover, rigid and brittle bioelectronic systems cannot make conformal contact with soft and curvilinear skin, lowering the bioelectronic performance owing to high impedance and low signal-to-noise ratio. Besides wearable bioelectronics, the rigidity of implantable bioelectronics can cause inflammatory reactions, particularly in their long-term implantation [2]. For this reason, commercial biventricular pace-maker could not be implanted directly on heart due to rigidity. Instead, it is generally implanted under the skin. In addition, unlike conventional wearable and implantable bioelectronics that consist of metal and/or inorganic materials, biological tissues are hydrophilic, ion rich, and fluidic. This difference in chemical compositions limits the long-term biocompatibility and performance of bioelectronics. To overcome this issue, there have been many progresses in material research to realize the mechanically compatible epicardial bioelectronics system. One of promising materials is an elastomeric material which is suitable for constructing a conformal interface with soft and curvilinear biological tissue due to its intrinsically deformable property. Intrinsically soft electronic systems whose mechanical properties are similar to those of human tissue can be developed using functionalized elastomers. Elastomers can be functionalized by adding appropriate fillers (Figure 1), either nanoscale materials or polymers. Conducting or semiconducting elastomers synthesized and processed with these filler materials can be applied to the fabrication of soft integrated electronic devices. Recently, device components such as sensors, stimulators, power supply devices, displays, and transistors have been developed in a deformable form.

In this review, the advanced soft materials are categorized as listed below.

1) Soft elastomeric conductor: soft conductive materials consist of elastomer and conductive filler.
2) Tissue-like low modulus materials: Hydrogel and its conductive composite.

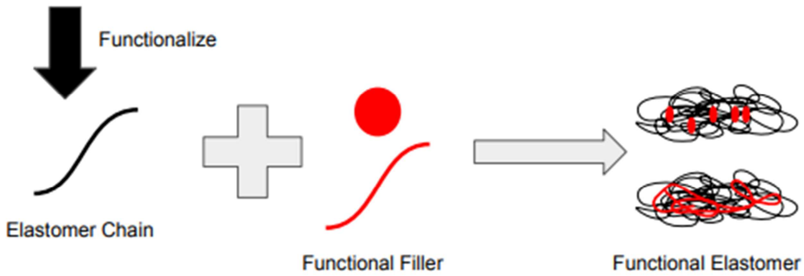

Figure 1. *Functionalizing elastomers with functional fillers for intrinsically soft materials.*

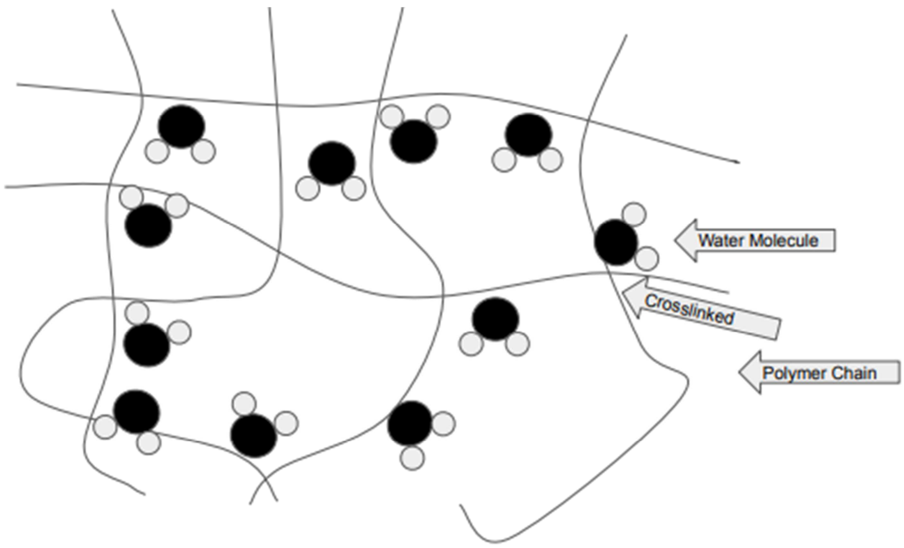

Figure 2. *Schematic showing structure of hydrogel.*

2. Soft Elastomeric Conductor

Sensors and stimulators, which are very important components of biventricular pace-maker, require intimate contact with tissue surface to form high quality interface between biotic-abiotic interactions. The softness of bio-implantable system is a critical factor to operate such systems on curvelinear surfaces of human tissues. Many researchers have been studied soft and elastic materials to develop soft bio-implantable system for a long time. Recently, elastomer and hydrogel have been highlighted as promising materials due to their superior mechanical properties and tunability. Although further researches to optimize those materials are needed, mechanical and electrical performance of current bio-implantable system using elastomer and hydrogel will be tremendously enhanced in the future.

3. Carbon-Based Materials Composite

Carbon-based nanomaterials show both mechanical flexibility and highelectrical conductivity. They can be dispersed in an elastomeric matrix, thereby serving as filler materials in nanocomposite. There are several types of carbon-based nanomaterials, which can be classified into different shape of dimension such as 0-dimension, 1-dimension, 2-dimension (Figure 1). The 0-dimensional carbon materials however are difficult to be utilized as filler materials because they cannot form a percolation network due to their shape and cytotoxicity. As a result, only 1-demensional or 2-dimensional carbon materials are considered for soft nanocomposite. A typical example of 1-dimensionalcarbon material is carbon nanotube (CNT), which has a shape of fiber. It is well-known as a cytotoxic material when inhaled, but no severe cytotoxicity is shown when it is embedded within an elastomer matrix. A previous work studied the cytotoxicity of the nanocomposite containing CNT on a lung tissue in vitro [3]. According to this report, CNT nanocomposite showed high cell viability because CNTs are fixed in the elastomer matrix of thermoplastic polyurethane (TPU). Because the CNTs do not contact with outside of the nanocomposite, no cytotoxic effect of CNTS is applied onto cultured cells on surface of the nanocomposite. The researchers also demonstrated the CNT nanocomposite used as injectable and conductive cardiac patches [4]. They showed the electrical performance of CNT nanocomposite related to electrocardiogram (ECG) measurement and biocompatibility.

Another typical carbon-based nanomaterial shaped in 2-dimensional structure is graphene. Graphene is a sp^2 hybridized carbon atoms arranged in a single-layered honeycomb structure. Graphene is transparent because it is synthesized in a film with single-atom thickness [5]. Due to larger surface area, the 2-dimensional structure provides improved physical contacts within elastomer compared to 0-dimensional materials so that it could enhance the electrical property of nanocomposite. Moreover, the 2-dimensional structure provides freedom of movements in the elastomer so that it can be used as sensitive mechanical sensors for bio-physiological signal detection [6].

4. Metallic Composite

Similar to carbon materials, metal nanomaterials have various shapes such as 0-dimension, 1-dimension, and 2-demension. Metal nanomaterials have extraordinary electrical conductivities [7]. Although general form of metal is stiff and heavy, which are not compatible to soft bioelectronics, metal nanomaterials are flexible and light. Therefore, they can form soft and conductive nanocomposites when they are mixed with elastomer. As illustrated in the above, 1-dimensional or 2-dimensionalmetal nanomaterials have been widely used for conductive nanocomposites. Among those materials, silver nanowire (AgNW) is most widely used as 1-dimensional conductive filler. Choi et al. showed the AgNW-SBS nanocomposite (SBS: Poly (styrene-butadiene-styrene) to fabricate the mechanically integrated epicardial patch to detect an abnormal phenomenon of ventricles and to stimulate the ventricles [8]. As a 2-dimensional filler, Ag flake is also widely used as a filler material for nanocomposite due to its high stretchability and high conductivity for bio-implantable system. Due to cytotoxicity of silver, another research groups have covered the Ag surface with inert metal to improve biocompatibility [9].

5. Tissue-Like, Low Modulus Materials

Modulus is a critical factor to measure the degree of physical burden to our body from wearable or bio-implantable electronic systems. Compared to rigid materials such as metal or flexible polymers, elastomer has lower modulus and higher stretchability. The modulus of elastomer is in the range of hundreds of kilo- to sub mega-pascal. However, the modulus of organ tissue is much lower, which is in a range of sub kilopascal. Therefore, hydrogel has been actively researched as a material that can form very similar mechanical compatibility between abiotic-biotic interfaces due to its low modulus property [10].

6. Hydrogel

Hydrogels are gel-like materials that consist of hydrophilic polymer network embedding the large amounts of water contents in the matrix. It includes covalent cross-linking, ionic interactions, and physical entanglement. Due to their unique structure, mechanical characteristics such as modulus and deformability are similar to those of biological soft tissues. Also, hydrogels have drawn attention as good candidate materials for biomedical applications due to its biocompatibility.

Three-dimensional cross-linked hydrophilic polymer networks are expanded and contracted reversibly in water and retain large volume of liquid in swollen state. They may perform dramatic volume transition in response to a variety of physical and chemical stimuli [11], such as temperature, electric field [12], light [13] and organic solvents. Drastic chance of volume in response to the changes in the external environment of the hydrogel could provide different electrical and mechanical properties. A hydrogel can be stretched to several times longer than its initial length and recovered elastically. Its elastic moduli could be tuned from 1 kPa to 100 kPa, or even beyond this range for different applications. To provide toughness in hydrogel, dual or triple network formation have been studied by combining different types of polymer networks [14]. Although hydrogels have ionic conductivity via solutes in water, challenging challenge is still remained to achieve high conductivity for operating electronic device. To enhance the electrical performance, composite technology could be used as introduced in next section.

7. Conductive Hydrogel Composite

Similar to elastomer, 3-dimensional hydrogel network imparts the softness to nanocomposite. Meanwhile, the electrical properties of nanocomposite are dominantly determined by conductive fillers. There are several strategies to enhance electrical performance and softness of hydrogel based nanocomposite. Lim et al. presented material and device strategies to forma tissue-like, quasi-solid interface between wearable bioelectronics and human skin. They used the hydrogel as mass permeable media to transport molecules using its intrinsic nature of swelling in the fluidic environment [15]. When the hydrogel composite swelled in the bodily fluids, the hydrogel composite show both electrical conductivity of conductive fillers and ionic conductivity of small molecules in water contents. In other words, the electrical performance of hydrogel composite could be enhanced in biological environments containing many ionic molecules in biofluids. Another strategy to enhance the conductivity of hydrogel composite is controlling the expansion of polymeric network [16]. In a previous work, the conductivity of hydrogel-Ag flake composite was improved through the dehydration process of hydrogel network, creating high percolation conductive pathways in the hydrogel matrix. In this manner, hydrogel is another promising candidate as a matrix of nanocomposite that shows high electrical conductivity and mechanical property compatible to soft bio-implantable electric system.

8. Conclusion

In this review, the promising soft materials of next-generation bio-implantable electronic device were discussed. First, elastomer as a basic material for stretchable and flexible electronics are introduced. To provide the electrical conductivity, various conductive nanofillers in different dimensions are addressed to realizeconductive elastomericnanocomposite. Also, conducting polymers that have intrinsic flexibility and conductivity are introduced as low-impedance, biocompatible materials for soft bioelectronics devices. Another promising material is conductive hydrogel composite, which has very low modulus similar to those ofbiological tissues. Both electrical conductivity of filler and ionic conductivity of bio-fluid in swellingstate of hydrogel matrix allow superior electrical performance of hydrogel nanocomposite. The soft nanocomposites integrated with nanomaterials as filler and elastomer/hydrogel as matrixshow potential to open a new pathway in high-performance epicardial electronic system that improve accuracy, stability, and long-term usability in diagnosis and treatment of heart diseases.

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