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A Review Study of Soft Electronic Materials for Epicardial Devices

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Abstract

Purpose: 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. To alleviate the physical burden to heart due to ventricular pacing, epicardial electronic system made of soft and elastic materials is needed.

Methodology: In this review, we discuss candidate materials for novel epicardial sensing/stimulation system that matches similar mechanical properties of heart. Materials are categorized as soft conductive materials consist of elastomer and conductive filler and tissue-like low modulus materials. Like hydrogel and its conductive composites.

Main Findings: The soft nanocomposites integrated with nanomaterials as filler and elastomer/hydrogel as matrix show 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.

Implications: 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.

Novelty: This review study is focused and written in simple terms for readers.

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 (Matsuhisa et al, 2019). 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 (Jaishankar et al, 2014)

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, 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, we categorized the advanced soft materials as listed below:

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

Soft elastomeric conductor

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

Elastomer

An elastomer refers to an elastic polymer whose intermolecular force is weak, thus having both elasticity and viscoelasticity. According to IUPAC, it is more intuitively expressed as a polymer that has "rubber-like elasticity". Elastomer mainly consists of long polymer chain with weak physical or chemical bonds, providing dynamic movements to polymer chains when it is stretched. Elasticity is mechanical property to recover its shape under external strain. In macro-scale, the broken weak bonding under strain could reform each other due to elasticity. Elastomers can also have dynamic mechanical or chemical properties depending on the intermolecular force and the interaction between polymer chains. For example, strong intermolecular force and less entanglement of polymer chains of elastomer show the mechanically tough and less elastic. Conversely, if the intermolecular force is weak and the polymer chains are entangled severely, the elastomer is mechanically soft and elastic. Generally, elastomer is an insulator so that it can be used as stretchable encapsulation layer of bio-implantable system.

Elastomer/Carbon-based materials

Carbon-based nanomaterials show both mechanical flexibility and high electrical 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 (Kayat et al, 2011). 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.

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 (Sutter et al, 2009). 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.

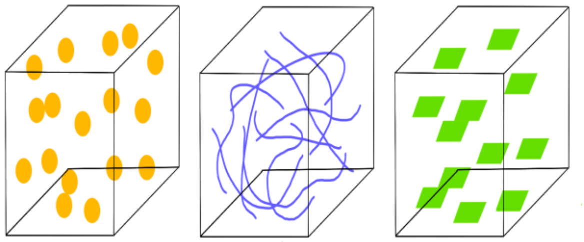

Figure 1: Composite mixed with various dimension of conductive nanomaterials

Elastomer/metallic materials

Similar to carbon materials, metal nanomaterials have various shapes such as 0-dimension, 1-dimension, and 2-demension. Metal nanomaterials have extraordinary electrical conductivities. 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 (Park et al, 2016). 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 (Choi et al, 2018)

Conductive polymer

In pursuit of making high-performance flexible devices, scientists have researched for new desirable materials that are cost-effective and light-weight as well as showing remarkable electrical properties. Conducting polymer (CP) is an organic material that successfully meets these conditions. The intrinsically conducting polymers provide both high electrical performance and mechanical flexibility. These unusual properties have attracted considerable interests in material scientists. CPs are often termed as conjugated polymers because they possess alternate single and double bonds along the polymer chains. The conductivity of CPs is dominantly affected by their delocalized double-bond arrangements (Gochnauer et al, 2018). The well-known CPs are polypyrrole (PPy), polyaniline (PANI), poly(3,4-ethylene dioxy thiophene) (PEDOT) and polynaphthalene (PN). Basically, CPs have insulating behavior in their pristine state; however, post-treatments by using dopant and acid could provide high electrical conductivity. CP could also be functionalized with biocompatible molecules, imparting biocompatibility to sensor and electrical stimulator of bio-implantable electronic system.

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.

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, such as temperature, electric field (Yang et al, 2022) light (Ryplida et al, 2019) 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 (Sun et al, 2012). 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.

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. For example, Lim et al. presented material and device strategies to form a tissue-like interface between wearable bioelectronics and human skin. Hydrogel is used to transport molecules as a mass-permeable media with its intrinsic nature of swelling in the fluidic environment. The low impedance of hydrogel allows ion to flow from the medium to skin (Lim et al, 2021) 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. Ohm et al, improved the conductivity of the hydrogel-Ag flake composite through the dehydration process of the hydrogel network. The condensed volume of hydrogel created high percolation conductive pathways in the hydrogel matrix with only a small amount of filler material (Ohm et al, 2021) This dehydration method is applicable for other dimensions such as 0D and 1D metals (Figure 2). 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.

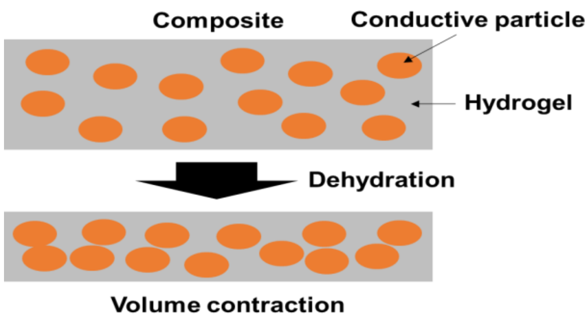

Figure 2: Dehydration of hydrogel metallic composite

CONCLUSION

In this review, we discuss the promising soft materials of next-generation bio-implantable electronic device. First, we introduce elastomer as a basic material for stretchable and flexible electronics. To provide the electrical conductivity, various conductive nanofillers in different dimensions are addressed to realize conductive elastomeric nanocomposite. 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 of biological tissues. Both electrical conductivity of filler and ionic conductivity of bio-fluid in swelling state of hydrogel matrix allow superior electrical performance of hydrogel nanocomposite. The soft nanocomposites integrated with nanomaterials as filler and elastomer/hydrogel as matrix show 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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