# Current materials used in artificial vascular tissue engineering

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**Abstract.** A commonly employed approach in the field of vascular tissue regeneration involves the utilization of artificial vascular tissue implants. These implants are designed to replicate the natural architecture of blood vessels through the use of artificial scaffolds, followed by cell growth induced onto these scaffolds, which are subsequently introduced into the body to replace damaged blood tissue. One of the primary obstacles encountered in implementing this technique pertains to the selection of materials that most nearly mimic the characteristics of naturally occurring tissue. Specifically, the aim is to develop an artificial device that closely emulates the biological functionality while eliciting minimal immunological reaction. A wide range of materials for constructing scaffolds has been extensively documented, encompassing natural, synthetic, and composite materials, as well as decellularized extracellular matrix. This study aims to conduct a comprehensive analysis of the existing literature in the field of vascular tissue engineering, utilizing methods of literature review and analysis. The examination will focus on evaluating the strengths, flaws, and availability of the available resources in this area of research.

**Keywords:** Blood Vessel Engineering, Material, Scaffold, Extracellular Matrix.

## 1. Introduction

In recent decades, diseases associated with the obstruction of blood vessels have consistently remained the primary cause of mortality. The coronary artery bypass graft (CABG) surgery is considered a highly effective treatment option for patients diagnosed with coronary artery disease. Its origins can be traced back to the 1950s, when the first successful bypass surgery was performed. This procedure involves the replacement of damaged blood vessel tissues with autografts, which are vascular tissues obtained from other parts of the patient's own body [1]. Subsequently, there has been a significant increase in curiosity on other sources of blood vascular tissue. The year 1954 represents a significant milestone in the field of bypass surgery, as it witnessed the initial triumph of utilizing polyester as an artificial graft. This breakthrough laid the groundwork for further advancements in blood channel engineering, leading to the creation of a diverse collection of materials [2].

In actual clinical scenarios, a significant number of patients face the challenge of insufficient healthy vascular tissue that can be extracted. As a result, researchers have redirected their efforts towards the development of artificial grafts [3]. Before integration into native blood vessels, artificially made blood vessel tissues must satisfy certain criteria. In order to mitigate the risk of thrombogenic mechanisms, it is imperative that the artificial tissue surface exhibits biocompatibility with the blood. Furthermore, the replication of the natural arrangement of cells plays a crucial role in optimizing cell proliferation and viability, as it ensures the potential for future tissue self-regeneration upon successful implantation.

Ultimately, the graft must possess mechanical qualities that are capable of withstanding the hemodynamic forces exerted by blood pressure [4]. The current state of meeting these standards is insufficient, leading to a noticeable deficiency in long-term effectiveness as observed in clinical practice. According to the article, a study involving a cohort of 1041 patients who underwent aortocoronary bypass surgery revealed that 12% of these individuals necessitated a subsequent bypass operation subsequent to the initial procedure. This paper provides a comprehensive overview of the latest materials utilized in the field of blood vessel engineering. It critically evaluates their advantages and disadvantages, offering a holistic perspective on the advancements made in this particular area of research. Significantly, this document delineates the prevalent challenges encountered by various materials, so facilitating subsequent researchers in discerning the optimal study trajectory that expeditiously yields heightened efficacy. The attainment of greater potency is a crucial factor in diminishing the need for subsequent surgical procedures, hence enhancing the overall post-treatment life expectancy. In the interim, this will concomitantly contribute to the expansion of the repository of resources accessible for the development of artificial tissue for various organs.

## 2. scaffold design in artificial vascular tissue engineering

### 2.1. *Scaffold generation*

A proficient scaffold offers a tridimensional structure that facilitates cell-biomaterial interaction, cell adhesion, and biodegradation, by emulating the extracellular matrix (ECM) seen in blood vessels. In order to facilitate the circumferential adherence of smooth muscle cells (SMCs) and endothelial cells, it is essential for the scaffold to exhibit both low-thrombogenicity and properties that are conducive to cell adhesion [5]. The design of scaffolds encompasses the selection of appropriate materials and the architectural configuration by which these materials are fashioned to emulate the natural biological environment, hence regulating cellular behavior. After considering the choice of materials, many methods can be employed to create the scaffold architecture, including electrospinning, decellularization, lyophilization, as well as three-dimension printing and bioprinting [6]. Decellularization and electrospinning procedures are considered to be the most effective at replicating the natural extracellular matrix (ECM), which is crucial for achieving successful integration into the human body. The electrospinning technique facilitates the production of fibers with diameters on the nanoscale scale, which aligns with the dimensions of the extracellular matrix (ECM). The best interaction between cells and materials occurs when the diameters of the fibers are similar to or smaller than those of the cells. This implies that an ideal scaffold should accurately mirror the dimensions of the natural extracellular matrix (ECM) [7].

### 2.2. *ECM*

Before embarking on the replication of natural extracellular matrix (ECM), a comprehensive understanding of its intricate intricacy is required. The extracellular matrix (ECM) plays a crucial role in the integrity and functionality of blood vessels, performing several actions that are vital for the optimal operation of these vascular structures. The complex biological constituents and arrangement facilitate the provision of structural reinforcement, enabling the blood vessel walls to withstand the considerable mechanical pressures generated by the arterial blood flow and vasoconstriction. The regulation of blood flow and blood pressure is primarily facilitated by the existence of an intricate network of elastic fibers. The biological constituents of the extracellular matrix also serve as sources of informational signals for vascular cells, governing their proliferation and differentiation through the regulation of growth factors, which are the key for the capacity to repair, regenerate, and respond to physiological stimuli [8].

### 2.3. *Cell seeding*

After the fabrication of the scaffold, the subsequent essential procedure involves cell seeding, which facilitates the colonization of the scaffold with blood vessel cells capable of differentiation and

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proliferation, ultimately leading to the development of a fully functional blood vessel. Supporting the growth of new tissue is important in this context. The presence of seeded cells on the scaffold can facilitate the integration of the graft and mitigate the risk of thrombosis. Various cell kinds have been examined in clinical studies, which include endothelial cells, smooth muscle cells, fibroblasts, and stem cells. Each of these cell types plays a distinct role in determining the specific characteristics of the tissue under investigation. Endothelial cells play a leading role in the integration of artificial tissue with native blood vessels and in the prevention of thrombosis. Smooth muscle cells and fibroblasts are primarily responsible for maintaining mechanical integrity by contributing to physical strength, elasticity, and extracellular matrix synthesis. In contrast, stem cells possess the capacity to undergo differentiation into many cell lineages and potentially play a role in the regulation of tissue repair and regeneration [9]. The structural design and material characteristics of the scaffold are significant factors in the process of cell seeding. The presence of a porous and permeable network structure facilitates the rapid saturation of the culture medium, resulting in the attainment of high-density and evenly distributed cell populations during the initial seeding phase. In addition, it has been observed that it facilitates the transportation of oxygen and essential nutrients throughout the cultivation stage [10].

## 3. Materials

Blood vessel engineering encompasses a classification of materials that can be categorized into three primary divisions: artificial material, biomaterial, and composite material. Artificial polymers, in general, have enhanced mechanical strength that enables them to retain their structural integrity under the influence of blood pressure, albeit at the expense of biological functionality. On the contrary, natural materials exhibit superior ability to replicate the natural biological environment of the extracellular matrix, albeit with more challenges in terms of their processing into scaffolds. Additionally, they exhibit reduced physical strength and a shorter biodegradation duration. In order to address these issues, researchers have developed bio-composite materials with the aim of producing more versatile and comprehensive materials [5].

### *3.1. Artificial polymer*

Polylactic acid (PLA) is an aliphatic hydrophobic polyester polymer that is derived from the synthesis of L, D lactic acid monomers. The material exhibits biodegradability, as it undergoes hydrolysis in the presence of water, resulting in the generation of non-toxic by-products. The adjustment of molecular weight and stereochemistry permits the attainment of flexibility in the toughness of a material. The rate of degradation of the compound is impeded by the presence of a methyl group, hence posing a drawback for short-term implantation. The presence of hydrophobic properties additionally impeded the ability of cells to adhere and proliferate. The inherent brittleness of the polymer necessitates its blending with other polymers to augment hydrophilicity, flexibility, and elasticity. PLA, which is currently a subject of ongoing research [11], can be combined with several different materials, including natural and synthetic polymers, as well as inorganic materials.

Polyglycolic Acid (PGA) has structural similarities to PLA (Polylactic Acid), albeit with a lesser number of methyl groups. This structural difference results in a shorter breakdown period in the presence of water for PGA, as compared to PLA. It has exceptional structural integrity in withstanding blood pressure. The compound's limited solubility in organic solvents enables it to maintain its structural integrity upon implantation. One limitation of this polymer pertains to its byproduct, which, while non-toxic, has the potential to alter the local pH and thereby elicit an inflammatory response. Furthermore, the rapid rate of degradation negated the benefits conferred by its robust physical capabilities. In a manner akin to the practice observed in the case of PLA, this particular polymer has been subjected to blending with alternative materials in order to address the inherent restrictions associated with its singular polymer composition [11]. Polycaprolactone (PCL) is a highly versatile substance that finds use not only in tissue engineering but also in medication delivery, surgical sutures, and wound dressings [11]. This particular polymer has sufficient mechanical strength, biocompatibility, and exceptional stability throughout the processes of manufacturing and preservation, making it the prevailing choice for constructing artificial blood vessels. According to a study published in the Pub Med database from 2016 to 2021, around 29% of the artificial grafts utilized were derived from polycaprolactone (PCL). The hydrophobic action of the substance, however, results in its reduced ability to interact with cells and may potentially lead to platelet aggregation [5]. In addition to its rather extended degradation period, which typically spans 2-3 years, this material still falls short of being an ideal candidate and necessitates further amalgamation with other substances [11].

### *3.2. Natural polymers*

The process of decellularization is a commonly employed technique in the development of vascular scaffolds. This method entails the removal of cells from the tissue, while ensuring the preservation of the extracellular matrix composition and arrangement. It is widely acknowledged that this approach effectively maintains the biological features of the tissue [5]. The sources of tissue for decellularization encompass a spectrum that includes allografts, autografts, and animal tissues [12]. The utilization of a diverse array of sources provides the opportunity for selecting materials based on their size and mechanical properties. However, it is important to note that the level of flexibility offered by these sources is not as advanced as that achieved through the creation of artificial scaffolds using electrospinning techniques. Scaffolds fabricated with decellularized tissue exhibit a substantial capacity to facilitate cell adhesion and growth. The successful seeding of endothelial cells (ECs) and smooth muscle cells (SMCs) onto the scaffold has been observed. One of the primary challenges associated with this procedure pertains to the technical intricacy involved in effectively decellularizing cells while also preserving the extracellular matrix in its entirety. The determination of the most effective concentration and combination of agents is a subject of ongoing research [5].

Collagen represents the predominant natural polymer employed in the field of vascular tissue engineering. The protein in question is highly prevalent in mammals and consists of a total of 28 distinct variants. Vascular tissue has been observed to have a significant role in the formation of the natural extracellular matrix. The collagen scaffold demonstrates exceptional biocompatibility due to its chemical makeup, leading to enhanced cellular adhesion and proliferation, as well as a higher likelihood of successful integration with adjacent tissues. Notwithstanding its inherent benefits, this technology is constrained by its subpar mechanical characteristics and accelerated deterioration. Consequently, it is employed with more frequency in conjunction with other polymers. As an illustration, gelatin, a derivative of the substance in question, is employed as an additive in the process of electrospinning, with the purpose of augmenting the biocompatibility of synthetic polymers [11].

The exceptional strength and flexibility of silk can be attributed to its structural arrangement, characterized by the stacking of beta-sheet polypeptides and their linkage by disulfide bridges. This unique arrangement contributes to the promising mechanical properties of silk in the field of tissue engineering. The mechanical strength and degradation time of the beta-sheet can be regulated by the manipulation of its creation. The primary factor contributing to the degradation of this polymer is its exposure to protease enzymes. Although the material has high mechanical strength, its biocompatibility is significantly constrained. Thrombogenicity has been demonstrated in several investigations. The occurrence of fibrosis tissue formation is observed during the initial stages of implantation, however it tends to diminish as time progresses [11].

### *3.3. Composite polymer*

In order to address the limitations of individual polymers, it is common practice to blend artificial polymers with either natural polymers or other artificial polymers. Artificial polymers exhibit more adjustability in terms of rigidity, although they demonstrate little capacity to replicate biological attributes that align with physiological conditions, such as thrombogenicity and low cell adhesion. Consequently, a significant body of research has been dedicated to the identification of an optimal blend of polymers and the determination of the optimum proportions of each constituent [11].

An example of a study conducted on composite polymers involves the combination of elastic polyurethane (PU) with silk fibroin. This particular composite has demonstrated improved biocompatibility in comparison to pure PU when implanted in rats. Yang et al. utilized the remarkable biocompatibility of fibrin and the stiffness of polyurethane (PU) to create an electrospun blend with a ratio of 85:15 PU to fibroin. After a period of three months following implantation in rats, the graft exhibited a visual resemblance to the original arteries, displaying comparable functionality and mechanical integrity to the naturally occurring vessels. The in vivo investigation also demonstrated enhanced deposition of extracellular matrix protein in comparison to the unpurified polymer [12]. In a manner akin to the amalgamation of various polymers, the incorporation of medicinal additives with specific functionalities into a polymer matrix can likewise be employed to enhance overall functionality. An illustrative instance involves the incorporation of a specific anticoagulant compound known as heparin, which has been employed to mitigate the propensity for thrombus formation in some scaffolds. The methods employed for achieving inclusion include immobilization, plasma treatment, and coaxial electrospinning. The effective immobilization of heparin has been observed to significantly decrease the likelihood of platelet aggregation within the blood vessel [13].

## 4. Conclusion

The selection of material for the fabrication of artificial blood vessel scaffolds holds significant significance within the domain of vascular tissue engineering. This review has examined different materials and their respective advantages, disadvantages, and accessibility with the objective of developing functional and biocompatible replacements for vascular tissue. The creation of artificial blood arteries has been influenced by the historical setting of vascular surgery, particularly in the case of procedures like coronary artery bypass grafting. The primary obstacle in this particular domain is to the attainment of three key objectives: biocompatibility, replication of natural cell composition and arrangements, and the provision of adequate mechanical strength. Blood vessel engineering encompasses three primary kinds of materials: artificial, natural, and bio-composite materials. The functioning of the ECM is not adequately present in either artificial or natural materials alone. Consequently, the most viable approach would involve combining diverse materials to address the deficiencies in each other's performance. A single polymer has been identified as exhibiting excellent performance in possessing one or two of these features. However, challenges persist in identifying a composite polymer that possesses the complete spectrum of these properties. The absence of any one of these factors establishes the maximum efficacy of a scaffold. The inclusion of these characteristics is imperative in order to establish a vascular graft that is capable of sustaining long-term viability, as indicated by the necessity for subsequent bypass procedures in certain individuals.

Decellularization stands out as the most effective technique among the current methods for scaffold production due to its superior ability to replicate the ECM. The electrospinning technique has the potential to produce fibers that closely resemble the dimensions of the natural ECM. However, the selection of materials capable of replicating the complex composition of the ECM is still in its early stages of development. Hence, it is imperative to comprehend the intricacy of the natural ECM. ECM performs various functions, such as providing structural support, regulating blood flow and pressure, and supplying informational cues to vascular cells to facilitate growth and differentiation. The field of vascular tissue engineering exhibits significant promise in its ability to tackle the complex issues associated with cardiovascular disorders. The field of regenerative medicine is currently witnessing significant advancements in the areas of materials, fabrication processes, and cell-based approaches. These continuing research and innovation efforts have generated much excitement and promise in the development of artificial blood arteries that are both functional and durable.

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