# Bio-textiles for Blood Vessel Tissue Engineering: A Review

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## *ABSTRACT*

*The cardiovascular diseases are increasing and leading to death which increases the social and economical burden of these diseases. The emergence of tissue engineering has opened new possibilities in vascular grafting and tissue engineering provide alternative solution in the condition of natural blood vessel failure by providing synthetic, semi synthetic or natural blood vessels which are fully functional and can mimic natural tissue. The scaffold should act as a substrate to promote cell growth, differentiation, maintain cell function, allow cells to migrate and direct the formation of new extracellular matrix and hence tissue. A fibrous scaffold can provide the highly porous structure required for a scaffold to accommodate a large number of cells.*

*Biotextiles which are defines as the structure made up of fibres and designed to be used under biological conditions can meet all the criteria compulsory for the design of ideal scaffold structures. Textile based scaffolds may be woven, nonwoven, electospun, knitted, braided or composite construction depending on the application. A review of the research going on in the field of the vascular grafts developments will help in understanding relationships between the structure and property in vascular grafts. The purpose of this review is to take a closer look at textile based structures being used as tissue engineering scaffold for blood vessels. Based on ongoing research and existing products, some new approaches in this interesting area are thoroughly discussed.*

***Keywords:*** *Blood Vessels, Tissue Engineering, Scaffolds, Biotextiles.*

## 1. INTRODUCTION

The cardiovascular diseases are increasing and leading to death which leads to increase in the social and economical burden of these diseases. As per American Heart Association report, 16.7 million people die of cardiovascular diseases each year around the world, which represents one third of all deaths all over the world [1-2]. Atherosclerosis is the common cardiovascular disease that is formed by lesion of a raised focal plaque in the intima, which is the innermost layer of blood vessel [3]. Autologous grafts can be used to replace the blocked blood vessel but they are not always available as the patient may also suffer from peripheral vascular disease [4]. Autologous grafts are available in limited number and a autologous graft may have been used previously in case of a bypass surgery[5]. Tissue engineering technique can be used to construct biological substitutes of ailing blood vessels to overcome these limitations. Tissue engineered grafts should be composed of viable tissues and be able to behave like a natural blood vessel under physiological conditions i.e. they should secret normal blood vessel products[6].

The emergence of tissue engineering has opened new possibilities in vascular grafting and tissue engineering provide alternative solution in the condition of natural blood vessel failure by providing natural, synthetic or semisynthetic blood vessels which are fully functional and can mimic natural tissue[7]. Tissue engineering is an interdisciplinary field that applies the principles of engineering and the life sciences toward the development of biological substitutes that restore, maintain, or improve tissue function [8]. In tissue engineering an appropriate cell source is used and the cells are seeded on a biocompatible and biodegradable scaffold developing a blood vessel that can mimic the structure and function of a natural blood vessel. Figure 1 shows the essentials of tissue engineering approach to replace the diseased blood vessel.

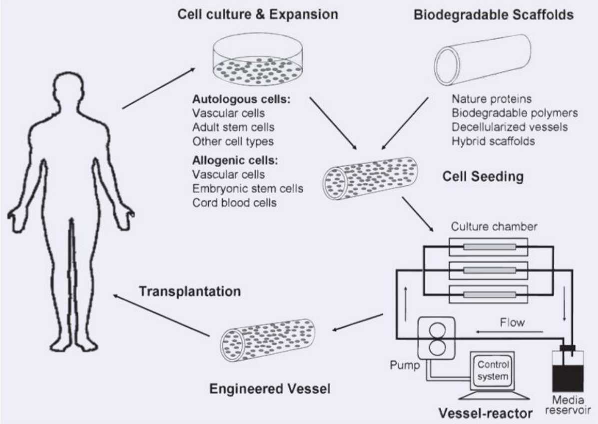

**Figure 1. Tissue-Engineering Approach for Tissue Regeneration**

The requirement of a scaffolds are complex and depends on the tissue intended to be replaced[9]. The scaffold should act as a substrate to promote cell growth, differentiation, maintain cell function, allow cells to migrate and direct the formation of new functional tissue[10,11]. Tissue engineered vascular grafts should be non-thrombogenic, non-immunogenic, bioreceptive, biocompatible and viscoelastic as native blood vessels[12-14]. Furthermore the tissue engineered grafts should be living tissue that will be exactly similar to natural blood vessels for that to the graft should contain cells like endothelial cells and smooth muscle cells.

All layers of blood vessel are required to be regenerated in order to construct a fully functional tissue engineered graft. Scaffold should be able to hold the cells and tissue together in the initial stages which echo the importance of mechanical strength. Research in tissue engineering focuses on scaffolds design to improve biocompatibility by matching compliance and elasticity as well as mechanical properties [15]. A fibrous scaffold can provide the highly porous structure required for a scaffold to accommodate a large number of cells[16]. Textile based vascular graft have many qualities to act as a scaffold for tissue engineering of blood vessels and many implants used as vascular grafts are textile structures. Most of the textile vascular grafts are constructed either of PET (polyethylene terephthalate or Dacron), or PTFE (Polytetrafluoroethylene or Teflon).

## 2. BLOOD VESSEL STRUCTURE

It is important to understand the anatomy and physiology of a natural artery to design a scaffold for tissue engineering of blood vessel. Since the structure of natural blood vessel is complex and depends on the diameter of the artery, the structure of a medium size artery is elaborated. The wall of a medium sized artery consists of three distinct layers called the intima, the media and the adventitia. The intima is the innermost layers which consist of monolayer of endothelial cell lining. The endothelial cells lining is responsible for the non-thrombogenic nature of natural blood vessel and

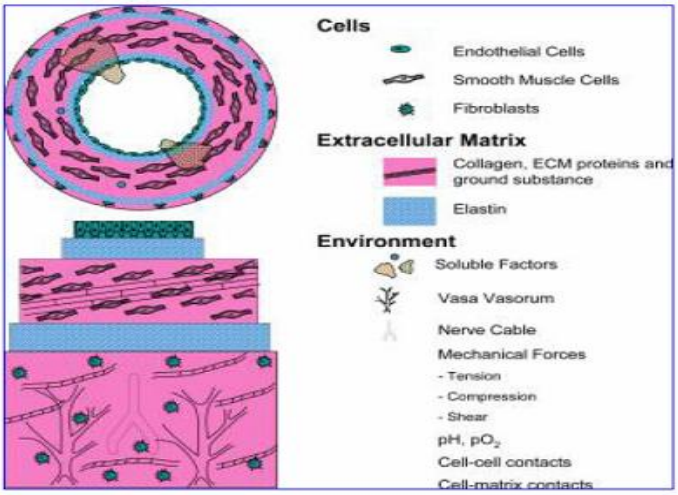

**Figure 2.Schematic of a Medium Sized Artery**

restrict the clotting of flowing blood. The media which is present in between the intima and adventitia contains circumferentially aligned elatin fibers and is populated by smooth muscle cells. The elastin fibres provide the optimal mechanical properties. The adventitia is composed of fibroblasts and connective tissue.The three layers of blood vessels are separated by a layer of elastin in between them[17-19]. Figure 2 shows the structure of a medium sized artery.

## 3. TISSUE ENGINEERING AND SCAFFOLD FOR BLOOD VESSEL

Scaffolds made of polymeric materials mainly provide physical support for the cell adhesion, migration, proliferation, differentiation, and ultimately tissue regeneration [20]. The scaffold is expected to mimic the structure of blood vessel and behave like natural blood vessel to guide the process of tissue formation. The scaffold for tissue engineering of vascular graft should have some specific qualities to effectively serve the purpose of scaffold[21]. Following are the qualities required to possess by a scaffold:

- Scaffolds should be microporous with optimum porosity and proper pore size because the size of the pores affects the speed and extent of peripheral tissue ingrowth [22] and influences the development of endothelial layer in intima.
- It must be non- toxic, that means that the polymer and the fabrication techniques must be non-toxic and free of contaminants.
- Scaffold should be biodegradable with an optimum degradation rate.
- Should possess a proper surface to facilitate cell adhesion and proliferation.
- It should be biocompatible.
- It should be leak proof.
- Scaffold should maintain compliance after tissue ingrowth into the graft[23-24].
- Should be able to constrict or relax in response to stimuli.
- Have optimum fibre diameter,
- have appropriate mechanical properties and flexibility (bursting strength, compliance, good suturability and suture retention [25].

- Should be able to be manufactured cheaply and in sufficient numbers in different size and specifications [26-28].

Biotextiles which are defines as the structure made up of fibres and designed to be used under biological conditions [29], can meet all the criteria compulsory for the design of ideal scaffold structures. Biotextiles are classified according to their fabric structure and surface characterstics. Textile scaffolds can be developed as woven, nonwoven, knitted, braided or of composite construction depending on the apparent application[30]. These are the some of the simple textile structures and in spite of their simplicity they have different structures in terms of porosity, bursting strength, thickness etc [31]. A review of the structures used in the vascular grafts will help in understanding relationships between the structure and property in vascular grafts.

### 3.1 Woven Scaffold

Today, about 45% of the grafts being implanted each year are woven vascular grafts [32]. A woven structure if formed when two set of yarns which are perpendicular to each other are weaved together. Plain weave is the simplest of all weaves. In plain woven fabrics, the vertical yarns lie alternately over and under the horizontal yarn as shown in Figure 3.

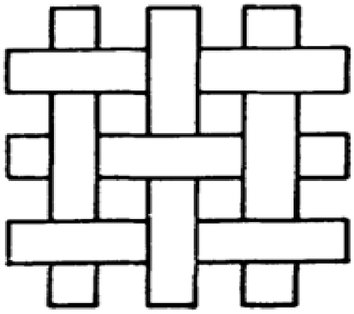

**Figure 3. Plain Woven Fabric Structure**

Plain woven fabric forms the most stable structure since they have highest number of interlacing in spite of their simple structure. Woven grafts have high bursting strength and can be made less permeable. On the other hand they are non compliant and difficult to handle and suture since they have many ends. A major cause for poor performance of woven graft has been shown to be the lack of compliance. Tubular grafts of polyurethane with diameter in the range 4-6 mm were made by a weaving process by Kasyanov et al [33] and the luminal surface was covered with gelatin to minimize permeability.

### 3.2 Knitted Scaffold

The Knitted textile structure composed of an ordered structure made of interlocked loops. A variety of knitted fabrics can be made by varying the modes of interlocking. Each different structure has a different name which is created by lowering and raising of kneedles. The simplest knitted structure is the single weft knit, which consist of sequential left and right interlocks. The interior of the fabric has a rougher surface as compared to the exterior surface. The same fabric is known as reverse single jersey if the inside turned out (Figure 4). Consequently the interior surface becomes smoother and hence woudn’t create turbulence in blood flow. Wefts knitted fabrics are innately more porous than wovens scaffolds. Which accounts for greater yarn mobility and hence knitted grafts are more compliant, and easier to handle and suture [34]. But knitted structure lack dimensional stability, and has a tendency to run (as in hosiery). Moreover these grafts are difficult to suture [35]. Structure made up of warp knitted chitosan is coated with porous chitosan created by freeze drying to form a porous, two-ply tubular chitosan scaffold for guided regeneration of tissue were fabricated by Wang Aijun et al[36]. Ling Zhang et al. [37] developed a chitosan-based tubular scaffold by dipping a knitted chitosan tube into chitosan/gelatin solution then freeze-dehydrated and examined its feasibility of being applied in this field. vSMCs grew and proliferated rapidly on the scaffold.

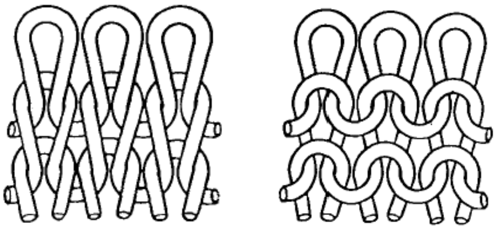

**Figure 4. Loop Diagram of a Single Jersey Structure: (A) Face and (B) Back**

### 3.3 Non-Woven Scaffold

The majority of textile based scaffolds are non-woven structures [38]. Nonwoven fabrics may be defined as flat or porous sheets made up of separate fibers directly or from molten plastic or plastic film. The fibers are not knitted or woven therefore yarn formation is not required in non-woven scaffold formation. Various non woven fabrics can be made by controlling porosity, fibre orientation [39]. The properties of non-woven fabrics are determined by the properties of the polymer and fiber or by the bonding process. Still the non-woven scaffold being used have large porosity and pore size and there is a call for reliable method that can make scaffold with controlled porosity and pore structure. Kim et al. [40] fabricated tubular, macroporous, fibrous scaffold of very elastic biodegradable co-polymer, poly($_L$-lactide-co-caprolactone) (PLCL, 5:5) by using a gel-spinning process. In the another work by Buttafoco et al [41], P(DLLA-*co*-TMC) was spinned into fibres by melt spinning and processed into porous tubular structures by fiber winding.

### 3.4 Electrospun Scaffold

Electrospinning is the well known technique used to produce nanofibrous non-woven fabric[42–45]. Electrospinning can be used to make matrices for blood vessel tissue engineering because the electrospinning produces fibres that mimic the dimension of natural ECM. This is required to allow the exchange of metabolic waste and nutrients between the scaffold and its environment, and to provides a high surface area for delivery of biochemical signals to the seeded cells [46–47]. On the other hand the small pore size of electrospun scaffold leads to difficulty in cell growth and migration. Sang et al. [48] fabricated various scaffolds using blends of collagen, elastin, and several other biodegradable polymers using the electrospinning technique. In results of another study by Bryan et al. [49] it is indicate that electrospun scaffolds support vascular cells to adhere and growth under physiologic conditions and that endothelialized grafts do not allow platelets to adhere when exposed to blood. Nanofibrous scaffold of copolymer P[(LLA-CL)] (75:25) with a unique aligned structure was made by electrospinning by Xu et al [50] by collecting the electrospun fibres on a mandrel rotating at a high speed [51] and using a parallel grid target, which is given a negative charge, behind a rotating mandrel [52]. Teo et al. [53] fabricated tubular scaffolds using a knife-edged counter-electrode. The electrospun nanofibres scaffolds developed were showm to be circumferentially well aligned as well as aligned at an angle to the longitudinal axis of the tube.

### 3.5 Braided Scaffold

Braiding forms simple narrow textile structures. Braiding can bear axial load, reinforce or can be used as protective covers. Braiding form rope like structure and the simplest braiding consist of three or more yarns which are interweaved in a diagonally interlacing pattern when the yarns follow circular paths in opposite directions with crossovers in an overlapping pattern. Design of braiding makes them shear resistant and comfortable [54]. Bini et al. developed the microbraiding by braiding PLGA or chitosan fibers over a microbraiding machine. The developed structure has a high flexibility [55]. X. MO et al. coated a porous layer of PCL (poly (epsilon-caprolactone)) outside the layer of a PGLA (poly (glycolic-co-lactic acid)( with GA:LA =90:10)) fiber braided tube to give a PCL-PGLA composite scaffold and successfully seeded fibroblast cells on them[56].

## 4. SURFACE MODIFICATION OF SCAFFOLD

In tissue engineering, the most important aspect is the interaction between biomaterials and physiological environment. A variety of receptors are present on the surface of cells that bind specific proteins of surrounding cells. As the interaction between cells and extra cellular matrix(ECM) plays a very important role in cell attachment and proliferation and signal transduction. The interactions between the cells and extracellular components are required to be understood to develop bioreceptive and biocompatible scaffolds. In tissue engineering of blood vessel, cell adhesion to vascular graft surface is decisive because cell adhesion occurs prior to other biological events like cell spreading, cell migration and differentiation and cell function. It is commonly accepted that the adhesion of cells to scaffold is affected by several surface properties of scaffold, such as wettability, water contact angle, surface charge, roughness and topography. Surface modification is an efficient method to change biological interactions of a particular material to develop appropriate scaffolds and make them bioreceptive and biocompatible. Surface modifications alters only the surface properties of scaffold whereas the bulk properties remains same. In addition, surface modification can provide chemical functional groups for the immobilization of biologically active species like drugs, enzymes, antibodies etc for a variety of biomedical applications [57-58]. Tseng et. al. [59] examined the effect of surface modification without modifying the graft structure, by amide and amine plasma treatment of expanded polytetrafluoroethylene (ePTFE) vascular grafts on graft patency. Presence of nitrogen-containing functional groups on the surface of plasma modified graft surfaces, along with an increased surface hydrophilicity was prooved in surface analyses by FTIR-ATR ( Fourier transform infrared spectroscopy-attenuated total reflectance), X-ray photoelectron spectroscopy and dynamic contact angle measurements. To rise above the inertness of the PET surface, gelatin was covalently grafted onto the PET NFM (non-woven nanofiber mat )surface by Zuwei et al [60]. On the other hand Zhu et al [61] immobilized covalently *O*-Carboxymethylchitosan (OCMCS) onto expanded poly(tetra-fluoroethylene) (ePTFE) vascular graft using 4-azidobenzoic acid, which is a photosensitive cross linking reagent.

## 5. CONCLUSIONS

Research in tissue-engineering of blood vessels has focused on improving design of scaffold to impart mechanical properties like compliance and elasticity. Textile scaffolds may be knitted, woven, nonwoven, braided or of composite construction depending on the application. These are the some of the simple textile structures and in spite of their simplicity they have different structures in terms of porosity, bursting strength, thickness etc Woven grafts have high bursting strength and can be made less permeable. On the other hand they are non compliant and difficult to handle and suture since they have many ends. A major cause for poor performance of woven graft has been shown to be the lack of compliance. Wefts knitted fabrics are innately more porous than wovens scaffolds. Which accounts for greater yarn mobility and hence knitted grafts are more compliant, and easier to handle and suture. But knitted structure lack dimensional stability, and has a tendency to run (as in hosiery). Moreover these grafts are difficult to suture. Still the non-woven scaffold being fabricated have large porosity and pore size and there is a call for reliable method that can make scaffold with controlled porosity and pore structure. Electrospinning produces fibres that mimic the dimension of natural ECM. On the other hand the small pore size of electrospun scaffold leads to difficulty in cell growth and migration. Surface modification is an efficient method to change biological interactions of a material to develop suitable scaffolds and make them bioreceptive and biocompatible. Surface modifications alters only the surface properties of scaffold whereas the bulk properties remains same. These biotextile structures, like woven, knitted or nonwoven are uniquely suitable to perform the function of tissue engineering scaffolds and to compare favorably with other fabrication techniques. Textile technology has provided a feasible option for vascular surgery and a large number of textile vascular grafts have been implanted in patients.

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