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REVIEW ARTICLE

Vascular System Tissue Engineering: A Comprehensive Review

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ABSTRACT: Underlying complications constitute a significant factor contributing to the damage of blood vessel tissue. Tissue engineering is, therefore, essential for comprehending the various solutions to regenerate impaired tissue. Clinical applications have shown promising results in animal and human trials, but challenges remain in scaling production to achieve long-term success. Methods to gradually regenerate blood vessel tissue consist of synthetic polymer scaffolds, cell sheet assembly, natural protein scaffolds, and decellularized and recellularized matrices. Despite current progress, several limitations and challenges must be addressed, such as biocompatibility, immunogenicity, vascularization, cell source, and cell differentiation: continued research and innovative approaches toward tissue engineering hold great potential for transforming and improving patient outcomes. Overall, this review aims to establish a concrete understanding of the various approaches in vascular tissue engineering.

KEYWORDS: Biomedical Engineering; Cell and Tissue Engineering; Vascular System; Scaffolds; Biomaterials.

Introduction

Cardiovascular disease (CVD) is the foremost cause of morbidity and mortality in the United States.[1] CVD includes a wide range of conditions that could affect blood vessels, such as peripheral artery diseases, coronary artery diseases, hypertension (high blood pressure), congestive heart failure, and hemorrhagic stroke. More than one million coronary arterial-related bypass procedures (CABGs) are performed annually in the United States, where synthetic grafts or autologous veins replace arteries in the peripheral circulation and coronary artery.[1] However, transplantations are complex and expensive. Patients often may not respond to transplantation as expected. It is also challenging to find a donor. These are some reasons researchers have been focusing on different avenues for tissue regeneration, such as grafts, tissue mimics, and bioprinting. Vascular tissue engineering using autologous cells holds a significant promise for producing biological grafts that can be used in bypass surgery. Scientists have developed different methods for increasing the efficiency of these different approaches. In the past, researchers have successfully tested engineering blood vessels using collagen and vascular cells.[2] This review paper focuses on different approaches for tissue engineering of blood vessels in terms of different cell types that can assist vascular tissue regeneration, the role of synthetic grafts, biological and mechanical requirements for regenerating the vascular tissue, and the limitations and future directions in the field.

A. Anatomy of Vascular Tissue:

Blood vessels supply blood throughout the living tissues inside the human body. Blood vessels are composed of three distinct layers, each providing unique benefits. These three layers are the Tunica Adventitia, the Tunica Intima, and the Tunica Media. The thickness of these layers depends on the type of blood vessels (arteries, veins, and capillaries). Each layer has its own set of cells and responsibilities. The endothelial cells (ECs) consist of monolayer epithelial cells that are located on the insides of the tunica intima, which helps to develop the growth of the tissue of the vessel and to transport the blood inside the vessel using receptors, such as VEGFR-1, VEGFR-2, and factor VIII.[3] The endothelial layer is a selectively permeable layer that excels in absorbing special nutrients and conveying blood throughout the body.[4] The smooth muscle cells (SMCs) visible in the tunica media (middle layer) provide structural stability and vary in layer depending on the arteries or veins. The markers of SMCs include smooth muscle α-actin, myosin 1, and calponin. Finally, the fibroblasts in the tunica adventitia (outermost layer) distribute and maintain collagen fibers for nutrition and stability of the vessel. This layer produces an extracellular matrix (ECM) and regulates blood vessel cell proliferation (Figure 1).[5]

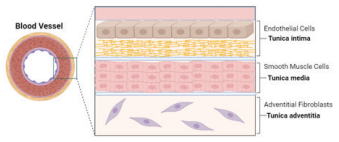

Figure 1: Blood vessel wall composition: The structure has three distinct layers. (1) tunica intima, which contains endothelial cells in the subendothelial area; (2) the tunica media, primarily made up of vascular smooth muscle cells and extracellular matrix proteins; and (3) the tunica adventitia, housing fibroblasts and connective tissues. This figure was created using Biorender by Ishan Ghosh.

B. Cell Sources:

Stem cells are an important component of vascular tissue engineering. There are two main types of stem cells: Adult Somatic Stem Cells (ASCs) and Embryonic Stem Cells (ESCs). ASCs have essential properties that allow them to self-renew and transform into mature cells, which is ideal for tissue regeneration.[4] These types of cells are readily available as a source of seeding cells. ESCs have the potential to differentiate into

DOI: 10.36838/v6i8.6

various cell types, including those that produce ECM components like collagen fiber and elastin.[6]

- ***1. Embryonic Stem Cells:***

ESCs are not naturally found in the ECM-rich environment like adult tissues.[7] Human embryonic stem cells (hESCs) can transform into endothelial cells (ECs) when exposed to appropriate signaling cues. ECs are a critical component of blood vessels and play an important role in forming tube-like structures on Matrigel, known as capillary-like structures *in vitro* and microvessels *in vivo*. There are some limitations and ethical concerns to using human embryonic stem cells. Also, ESCs have immunogenic and tumorigenic problems that need to be addressed.[4]

- ***2. Adult Stem Cells:***

Adult stem cells can be directly collected from adult patients. They are mostly found in the bone marrow and various body tissues and can transform into specialized cells in the tissue in which they are located.[8] The availability of these cells in adult tissue solves the ethical concerns and immune-rejection problems associated with embryonic stem cells. Adult stem cells do not contain a tumorigenic nature.

Adult stem cells, Endothelial Progenitor Cells (EPCs), can differentiate into mature endothelial cells.[4] EPCs can be found in the peripheral blood and the bone marrow, eliminating the need for harvesting native vessels directly from patients.[9] Conducted studies have demonstrated that EPCs collected from the peripheral blood of sheep can be used to construct vascular grafts *in vitro*. Adult stem cells also have limitations. They have limited abundance in adult blood and bone marrow. The proliferative capacity of endothelial progenitor cells (EPCs) tends to decline with age.[8]

- ***3. Autologous ECs and SMCs:***

Harvesting autologous Endothelial Cells (ECs) and Smooth Muscle Cells (SMCs) from a patient's tissue are common and preferred choices for engineering blood vessels. Autologous ECs and SMCs in vascular tissue engineering offer several benefits: immuno-compatibility, improved integration, and ethical considerations. Building biodegradable scaffolds by seeding cultured bovine aortic ECs, SMCs, and adventitial fibroblasts is a common approach in vascular tissue engineering.[7] However, the limited proliferation capacity of ECs limits the growth of many cells in the culture. Moreover, ECs can change and lose some functional and phenotypic qualities during cell expansion in culture.[4] Furthermore, an invasive procedure is required to conduct blood vessel biopsies to collect these cells, which may result in complications at the donor site. These challenges have swayed researchers to find alternative solutions, such as stem cells.[9] Figure 2 illustrates proposed interactions in the vasculature with stem and progenitor cells.

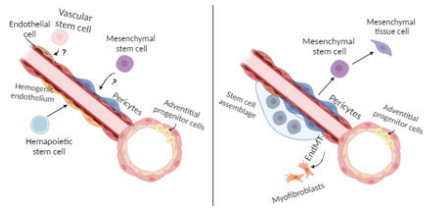

Figure 2: This illustration represents the proposed interactions in the vasculature with stem and progenitor cells. (a) Several types of stem and progenitor cells reside in the developing vessel within the embryonic blood vessel. There is a potential for both stem and progenitor cells to contribute to vascular endothelial cells, Pericytes, and hemogenic endothelium. In turn, hemogenic endothelium may produce HSCs. (b) Adult blood vessels interact with stem and progenitor cells in myriad ways. Vessels create a specialized environment for organ-specific stem cells, store pericytes and endothelial cells that might play a role in mesenchymal lineages, and hold adventitious progenitor cells. Interactions that need to be more established and indicated with a question mark.[10] This figure was created using Biorender by Ishan Ghosh.

- ***4. Other Cell types:***

Induced pluripotent stem cells (iPSCs) have made significant vascular and cardiac tissue regeneration breakthroughs. The nuclear DNA of adult somatic cells can be reprogrammed to induce pluripotency, resulting in the generation of induced pluripotent stem cells (iPSCs).[8] The most significant advantages of using iPSCs are their availability and the potential for self-renewal. iPSCs can be generated from readily accessible tissues like skin or peripheral blood and have self-renewal capability.

Researchers can precisely modify the genetic makeup of iPSCs to correct disease-causing mutations or to introduce specific beneficial changes using CRISPR-Cas9. While iPSCs have the potential, it has tumorigenesis risk, which can be further aggravated by the risk of reprogramming causing chromosomal rearrangement. Moreover, the cost of preparing such iPSCs is high, and iPSC formation yield is low. Therefore, these drawbacks currently make them unsuitable for vascular tissue engineering clinical applications. Such concerns must be addressed to utilize iPSCs effectively.[11]

Other cell types, such as human fibroblasts harvested from skin biopsies, were also tested to construct tissue-engineered blood vessels. These vessels were antithrombogenic and demonstrated stability for eight months *in vivo*. Histological analysis proved the presence of smooth muscle-specific α-actin positive cells. However, these studies have been done only in animal models, not human beings.[4]

■ Discussion

A. Functional requirements in blood vessel tissue engineering:

- ***1. Mechanical Properties:***

Design parameters should focus on the functional requirements of mechanical and biological performance to successfully implement tissue-engineered blood vessels (TEBV). Mechanical requirements include burst pressure, mechanical strength, elasticity, tensile strength, kinking radius, cell-ECM interaction, suture retention, fatigue resistance, and compliance.[12] Blood vessels are generally categorized into three parts: arteries, capillaries, and veins. Arteries consist of three-layer architecture: tunica intima, tunica media, and

tunica adventitia. Collagen fibers are present in the tunica adventitia to support the tensile strength of blood vessels, especially arteries.[13] Tissue-engineered vascular grafts (TEVGs) should undergo a process including cell seeding on scaffolds, bioreactor cultivation, tissue maturation, biocompatibility, and mechanical testing to achieve the mechanical requirements.[9] Similarly, chemical pretreatments like dehydration by cross-linking with glutaraldehyde (GA) and ethanol (ET) have increased the mechanical stability of vascular grafts.[14] Using biodegradable polymers has also been effective in achieving mechanical requirements. Porous ε-caprolactone and L-lactide copolymer reinforced with a polyglycolic acid (PGA) fabric and seeded with autologous cells resulted in the first clinically effective TEBV, which adhered to the mechanical properties.[12]

- ***2. Biological Properties Requirement:***

Like mechanical properties, the biological properties of TEBVs are also critical to producing successful grafts. Vessel structures and functions are defined at the biomolecular level. An essential biological requirement is constructing a biocompatible surface with the necessary anti-thrombogenic mechanisms when the surface connects with the blood. The focus should also be on the manufacturing technique of these biocompatible surfaces with maximum cell survival. The arrangement of cells within tissue-engineered blood vessels is both challenging and complex. Smooth muscle cells (SMCs) and endothelial cells (ECs) reside inside the tunica intima, the inner vascular layer, and the tunica media, the middle vascular layer. These cells' arrangement requirements must be satisfied to create TEBVs.[13] Biological failure occurs when non-specific protein adsorption, thrombosis, or blood clotting occurs on the luminal surface. Combining hydrophilicity and resistance to protein adsorption through surface modifications has shown efficacy in preventing thrombus formation. ECs are also an essential factor in the biocompatibility of the surface. How these cells are seeded will predict the likelihood of long-term graft survival. Moreover, SMCs are responsible for the vessel's medical compliance. Research has shown that SMC-seeded grafts have shown better host integration and medical cellularization.[12]

B. Scaffold Types:

The basic principle of using a scaffold in tissue engineering and regenerative medicine is to implant a natural or biodegradable material into a damaged or injured body area to support tissue repair and regeneration. The crucial design requirements for blood vessel scaffolds include biocompatibility, mechanical strength, appropriate porosity for cell infiltration and nutrient diffusion, and the ability to promote the formation of a confluent EC's cell layer to prevent thrombosis.[15] The biomaterial must be biodegradable to allow the pre-existing tissue to flourish and be biocompatible, as harmful mutations could arise without the proper precautions. Scaffold porosity and the release of ECM collagen fibers are also vital design considerations in tissue engineering. The developing tissue can regenerate over time as the scaffold gradually degrades. Membranes play diverse roles in supporting cell growth, transport, and regeneration in various biological and biomedical applications. In vascular tissue engineering, a few types of scaffolds are used: cell sheet assembly, natural protein scaffolds, synthetic polymers, and decellularized natural scaffolds.

- ***1. Tissue engineering by self-assembly /cell sheet:***

Cell sheet assembly: Studies have shown that cell sheet engineering provides sufficient burst pressure, suture strength, cell-matrix, and cell-cell interactions that are critical for the mechanical requirements of tissue-engineered blood vessels.[17] In cell sheet engineering, a monolayer of endothelial cells is stacked and cultured on a temperature-responsive material, and a cell sheet is formed and successfully harvested.[16]

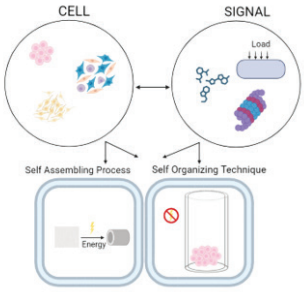

Figure 3: Illustrated in this context are sample methods within this framework, utilizing similar or varied cell groups alongside mechanical forces (such as compressive loading) and biochemical cues (like transforming growth factor β1 [TGF-β1] or sucrose) to amplify new tissue characteristics. There are two clear types of scaffold-free tissue engineering: the self-assembling process (SAP) and the self-organization technique (SOT). While self-organization needs external energy input, self-assembly occurs in a self-contained system.[17] This model was created using Biorender by Ishan Ghosh.

Self-assembling or self-organizing techniques are scaffold-free approaches in vascular tissue engineering that allow the organization and formation of three-dimensional structures without using an external scaffold.[17] Scaffold-free approaches in vascular tissue engineering offer several benefits, such as mimicking natural tissue architecture, scalability, personalization, and reduced foreign body response.[17] The challenge of the self-assembly process is that the lack of a physical scaffold can make it harder to engineer large and complex tissue constructs precisely. As a result, scaffold-free techniques are often used for smaller-scale applications. A summary of the self-assembly method has been provided in Figure 3.

- ***2. Natural Protein Scaffolds:***

In tissue engineering applications, ECM proteins, such as collagen fibers, fibronectin, elastin, and laminin, play an important role in creating functional tissue structures or scaffolds. Natural proteins help re-form stable connections between cells to regenerate tissues.[18]

Collagen-based scaffolds can provide a supportive structure for endothelial cell growth and tissue regeneration. Collagen fibers can be engineered into various configurations to mimic the native architecture of the tunica intima and provide mechanical stability.[19] Collagen is a fibrous, triple-helical protein composed of amino acids, primarily glycine, proline, and hydroxyproline.[6] The specific arrangement of these amino acids gives collagen its characteristic triple-helical structure, which is vital for maintaining structural integrity.[20] Fibronectin is an essential glycoprotein that plays a crucial role in providing adhesive, migration ECM assembly, and signal transduction

DOI: 10.36838/v6i8.6

(abilities and supporting the structure of the vascular system).[21] Elastin is a structural protein found in the aorta. It provides unique properties contributing to these tissues' mechanical integrity and elasticity. When elastin works with collagen, it gives tensile strength to the aorta. Elastin and collagen create a stable extracellular matrix (ECM), providing structural support and elasticity to blood vessels.[22]

- ***3. Synthetic Polymer Scaffolds:***

Synthetic polymer scaffolds (SPSs) are extensively used in vascular tissue engineering to treat damaged tissues. SPSs offer several advantages that make them popular choices for scaffold materials. These advantages include tailored properties (mechanical properties, degradation rates, and porosity), biodegradability, flexibility, durability, and scalability.[23] SPSs often have a hydrophobic surface rather than hydrophilic surfaces, which may limit their intrinsic bioactivity, such as adhesion and protein binding.[24]

There are five commonly used synthetic polymers for vascular tissue engineering: PLGA (Poly lactic-co-glycolic acid) is a biodegradable lactic acid and glycolic acid copolymer. It has excellent biocompatibility, tunable degradation rate, and mechanical properties.[25] PLA (Polylactic acid): PLA is a biodegradable and biocompatible polymer that degrades into non-toxic lactic acid. PLA scaffolds provide mechanical support during tissue regeneration and gradually degrade as new tissue is formed.[26] PCL (Polycaprolactone): PCL is a slow-degrading synthetic polymer with good mechanical support and can be designed to maintain its integrity while the new tissue forms around it.[27] PEG (Polyethylene glycol): PEG is a hydrophilic polymer often used in combination with other materials or as a surface modification to improve the hydrophilicity of scaffold surfaces.[26]

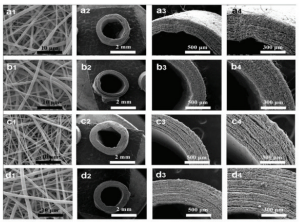

Figure 4: Four SEM images of the PCL/PLGA blended scaffolds. a 95/5, b 90/10, c 80/20, d 60/40. a1–d1: electrospun mats; a2–d2, a3–d3, a4–d4: cross sections of tubular grafts.[28]

SPSs can be engineered to regulate the healing process and address issues, such as excessive or uncontrolled fibroblast deposition.[29] SPSs could be manufactured using advanced techniques, such as Laser Stereolithography (SLA) and 3D Printing (Fused Deposition Modeling – FDM). Manufacturing using 3D printing has advantages over SLA, such as material flexibility, no liquid resin, no need for support structures, reduced post-processing, and agility.[30]

- ***4. Decellularized & Re-cellularized Matrices:***

Decellularizing natural matrices is one of the most promising methods for revitalizing vascular scaffolds. Decellularization means the elimination of antigenic cellular materials from the tissues while maintaining and preserving the structural, functional, mechanical, and biological characteristics of the ECM.[31] In the decellularization process, a wide range of chemical compounds (detergents, diluents, acids, bases, and hypertonic solutions), biological agents (chelating agents and enzymes), and physical methods (pressure, agitation, and abrasion) are used.[32] ECM contains collagen, elastin, laminin, fibronectin, and matricellular proteins, and once decellularized and successfully recellularized, these natural scaffolds can be implanted back into the patients to restore and even replace damaged organs.[33] Figure 5 shows the decellularization and recellularization process.

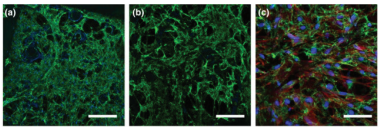

Figure 5: Assembly of a robust ECM before (a) and after (b) decellularization on Day 7. Scaffolds were recellularized with MSC for 24 hr (c). Scaffolds were fixed and stained for fibronectin (green), nuclei (blue), and actin (red, c only). Scale bars are 200 μm (a,c) and 100 μm (b).[5]

- ***5. Comparison of Materials and Scaffolds Type:***

Several advantages and disadvantages are associated with using different materials and scaffolds for vascular tissue engineering. The following tables illustrate such types (Table 1):[34-36]

Table 1: Advantages and disadvantages of regenerative blood vessels using different scaffolds and materials:

Scaffolds type	Materials	Advantages	Disadvantages
Synthetic polymers	ePTFE, PET, PU, PCL, PLCL, PLA, PGS.	Superior mechanical properties. Availability. Suitable for mass production. Easy surgical suturing. They prevent vascular bursts—off-the-shelf use.	Causes thrombosis, intimal hyperplasia, calcification, and chronic inflammation. No growth potential. Poor hemocompatibility. Compliance mismatch.
Natural biomaterials	Silk fibroin, collagen, elastin, chitosan, bacterial cellulose	Optimal biocompatibility. We have enhanced biological signaling. Tunable mechanical properties.	Weak mechanical strength. Causes vascular graft dilation and aneurysms. Quick degradation. Overly complex designs. Translation difficulties.
Decellularized Vessels	Animal artery, umbilical artery, umbilical vein	Low immunogenicity. Preserved extracellular matrix, meso- and microvasculature.	Increased thrombogenicity. Host immune response. Precision difficulty recellularization. Calcification.

Note: ePTFE: expanded polytetrafluoroethylene; PCL: polycaprolactone; PET: poly(ethylene terephthalate); PGS: poly(glycerol sebacate); PLA: polylactic acid; PLCL: poly(L-lactide-co-caprolactone); PU: polyurethane.[34-36]

- ***C. Clinical Applications:***

The application of biodegradable scaffolding materials has tremendous potential in vascular tissue engineering. It has widespread applications due to the expeditious advancement of several tissue-engineered scaffolds, such as natural and synthetic polymer-based scaffolds.[33] One of the earliest reported successful clinical applications of modern synthetic scaffold implantation in patients occurred when the medical professional implanted a biodegradable construct to help support the arteries in the patient's body. The construct was composed of a special synthetic polymer mixture. One of the earliest reported successful clinical applications of modern synthetic scaffold implantation in patients occurred when the medical professional implanted a biodegradable construct to help support the arteries in the patient's body. The construct was composed of a special synthetic polymer mixture. In several months, numerous implants have been conducted, in which there have been no mortalities.[2,7] DCM grafts have been implanted in femoral arteries for approximately a year.[37] Three months after the im-

plantation, the development of the endothelial layers resulted in a progression of elastin fiber and collagen production over time as the blood vessel gradually regenerates.[38] In addition, patients provided with commercially available ECM implants showed no signs of failure or concern for several months; however, later, they showed blood vessel complications, such as hemodialysis.[32] The following tables illustrate various available products in the market (Table 2):[34]

Table 2: Commercially available tissue-engineered blood vessels in clinical use

Company	Product name	Materials	Details and modification	Indications for use
Atrium Medical Corporation	Flixene IFG Vascular graft	ePTFE	Very robust and durable with three layers	Arterial vascular reconstruction/segmental bypass/arteriovenous vascular access
Bard Peripheral Vascular, Inc.	Venaflo™ II Vascular graft	ePTFE	Cuffed to promote good hemodynamic performance	Subcutaneous arteriovenous conduits for blood access only
Edwards Life Sciences	Edwards Lifespan reinforced expanded PTFE vascular graft	ePTFE	Higher crush and kink resistance	Bypass or reconstruction of diseased or occluded blood vessels/ arteriovenous shunts
Maquet Cardiovascular, LLC	FUSION Vascular Graft	ePTFE	Two layers fused with a proprietary polycarbonate urethane adhesive	Peripheral artery repair or replacement/vascular access
	FUSION™ and FUSION™ Bioline Vascular Grafts	ePTFE and PET	Two layers with heparin/albumin coating on the interior surface	Peripheral artery repair or replacement
	EXXCEL™ Soft ePTFE Vascular Grafts	ePTFE	featuring a GUIDELINE® stripe to facilitate proper graft alignment.	Peripheral arteries (iliac, femoral, popliteal, infra geniculate vessels, axillary, renal) repair or replacement/vascular access
InterVascular SAS	InterGard Heparin	PET	Heparin-bonded collagen coating	Peripheral artery replacement
PECA Labs, Inc.	ExGraft and ExGraft Carbon EPTFE Vascular Graft	ePTFE	A radiopaque ink and the exGraft Carbon ePTFE vascular graft coating with carbon were applied to the surface.	Peripheral artery repair or replacement/dialysis access
Vascular Flow Technologies Ltd.	Spiral Flow™ Peripheral Vascular Graft	ePTFE	Propagating spiral flows through the graft and into the distal circulation reinforced.	Bypass or reconstruction of occluded or diseased peripheral arterial blood vessels above or below the knee
Vascutek Ltd.	Vascutek Gelsoft Plus ERS Vascular Graft	PET	External polypropylene support, gelatine-sealed, knitted polyester grafts	Indicated for extra anatomical vascular repair, primarily for ax-illo-femoral/bi-femoral bypass and femoropopliteal reconstruction
	Vascutek Gelseal Vascular Grafts	PET	Knitted, gelatine integrated	Indicated for replacement or bypass of abdominal arteries afflicted with aneurysmal or occlusive disease
	Vascutek Gelsoft Vascular Grafts	PET	Knitted, gelatine impregnated, zero porosity	Indicated for abdominal and peripheral vascular repair
	Vascutek Gelsoft Plus Vascular Grafts	PET	Knitted, gelatine impregnated, dilation resistant	Indicated exclusively for abdominal and peripheral vascular repair
W.L. Gore & Associates, Inc.	Gore-Tex	ePTFE	Unmodified	Vascular access
	Gore-Tex Stretch	ePTFE	Stretch	
	Gore Propaten	ePTFE	Reduced thrombogenicity through covalently binding to bioactive heparin	

Note: All the products above are registered with the US Food and Drug Administration's 510(k). ePTFE: expanded polytetrafluoroethylene; PET: poly(ethylene terephthalate).[34]

D. Limitation and Future Perspective:

Research on regenerative cells has made significant progress since its starting days. One of the promising methods for future cell regeneration is the usage of grafting / biodegradable scaffolds. Cell manipulation technologies, such as cell seeding, genetic engineering, and cell programming, can be used to control the integration of such grafts in the host body.[2] However, grafting isn't available to meet the demands of many patients. For example, Cytograft's Lifeline® graft has properties similar to native blood vessels, but the production time is around 6 to 9 months.[13] Vascular tissue engineering often faces challenges that include biocompatibility, immunogenicity, mechanical properties, vascularization, cell source, and cell differentiation. One of the critical factors in the successful implementation of vascular grafting is the role of the host immune system response. Study shows that the potential of immunotolerant stem cells can be effectively utilized to control the immune acceptance of cell-based implants.[7]

To build a successful vascular construct, it is essential to reconstruct the complexity of native vascular tissue, which includes incorporating the fibroblasts, endothelial cells, smooth muscle cells, and biomaterials to mimic the extracellular matrix (ECM). However, available constructs are now limited to only one layer of endothelial cells. Creating multi-layered vascular tissue that accurately imitates the structure and function of native blood vessels is a complex task that faces challenges, including cell source, cell alignment, tissue architecture, nutrient diffusion, vascularization, and host integration.

3D bioprinting has emerged as a potential solution to this problem. The capabilities of 3D bioprinting will allow researchers to produce desired anatomical models.[13] 3D bioprinting has a huge potential since it will eliminate the need for organ donors. This is important because there is a high risk of disease or infection associated with donated organs.[39,40] However, some factors need to be addressed for bioprinting. The challenge will be to print tissues that maintain their integrity and not use growth factors that increase the risk of tumorigenesis and cancer development.[21] Further research will be needed to explore the capabilities of bioprinting fully.

In animal studies, seeding vascular cells on biodegradable scaffolds has proven effective for creating functional vascular tissue. That is why future tissue engineering research needs to focus on having these scaffolds with endothelial cells and smooth muscle cells, eliminating the need for manual seeding.[39] Scientists should research designing vascular constructs with pre-seeded endothelial and smooth muscle cells, paving the way for improved vascular grafts and tissue-engineered blood vessels to improve the patient's quality of life and reduce the complexity of vascular tissue engineering procedures. However, it's important to remember that while this vision is promising, continued research and rigorous testing will be required before these techniques become widely available for clinical use.

■ Conclusion

Illnesses such as CVD may lead to vascular tissue damage, which in turn impairs the blood vessels. The implementation of tissue engineering via scaffold implantation is fundamental in healing the affected area. Scaffolds can be constructed through various methods, but certain mechanical and biological factors must be addressed before scaffold production. Mechanical factors include burst pressure, elasticity, tensile strength, cell-ECM interaction, and fatigue resistance, while

DOI: 10.36838/v6i8.6

biological factors include biocompatibility, structural support, and effective cell arrangement. Multiple challenges hinder us from producing the optimal scaffold, including structural durability and efficient vascularization. Future outlooks yield fruitful results, as vascular cell infusion on biodegradable scaffolds proves to be effective in generating functional vascular tissue.

In conclusion, tissue engineering offers a transformative path toward revolutionizing vascular disease treatment. Through continual research, refinement of methodologies, and collaboration between disciplines, the vision of personalized, efficient, and accessible interventions for CVD can become a reality. As the complexities are navigated and the challenges surmounted, the potential for improved patient outcomes and enhanced quality of life becomes a powerful incentive to drive this field forward.

Acknowledgments

I want to thank my mentor, Dr. Birol Ay (Harvard Medical School) and Dr. Cigdem Sahin (Joslin Diabetes Center), for their guidance and valuable feedback when writing this paper.

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DOI: 10.36838/v6i8.6