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A Review: Textile Technologies for Single and Multi-Layer Tubular Soft Tissue Engineering

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In cell-free scaffold tissue engineering (TE), an essential prerequisite is the scaffold design to promote cellular activities and tissue formation. The success is greatly dependent upon the nature of the scaffold including the composition, topography, and mechanical performance. Recent TE approaches use textile technologies to create biomimetic and functional scaffolds similar to the extracellular matrix (ECM). The hierarchical architecture of fiber to yarn to fabric allows precise size-to-scale design. Moreover, textile technologies offer a high degree of manufacturing precision, reproducibility, and potential industrial scalability. Although research in industry and academia has increased significantly over the past years, current fibrous scaffold designs don't fully exploit the potential and diversity of yarn and fabric structures. This review emphasizes hollow tubular textile-based scaffolds that aim to replace vasculature and respiratory tissues. The different techniques, that is, electrospinning, weaving, knitting, and braiding are discussed and the effect of the fiber, yarn, and fabric assembly is highlighted. The design of multi-layer hybrid structures, combining conventional textile techniques and electrospinning can address current challenges. Prospects of structural design in TE scaffold fabrication can anticipate profiled fibers, and complex pattern designs to fully exploit the potential of textile technologies for tissue-engineered scaffolds.

1. Introduction

Tissue engineering (TE), as part of regenerative medicine, aims to create biological tissues through directed cell cultivation to replace or regenerate diseased or damaged tissues.[1] The success of TE is greatly dependent on the interdisciplinary complexity of multiple disciplines, including material science, biology, and engineering. In addition, it requires a fundamental understanding of the structure and function of the target tissue type.

Tubular tissues, such as vascular, respiratory, or intestinal systems supply the body with important nutrients and transport blood, air, food, or fluids. A defect in these tissues can considerably affect the patient's quality of life, for example, the required surgical reconstruction of connecting pathways between two anatomical structures can significantly reduce the patient's mobility. Current treatment strategies for diseased tubular tissues include transplantations of donor organs, autologous tissues, or implantable medical devices to restore tissue function.[2] However, transplants of donor organs or autologous tissue are limited due to availability, donor site morbidity, and risk of disease transmission.[3] Compared to natural body parts, implants have not yet reached the functionality, quality, or longevity (often need replacement after years).[3] Moreover, they must remain in the body for years, and material-specific compatibility problems can cause chronic inflammatory responses, thus limiting their clinical use. Being able to develop tissues outside the body provides a long-term alternative to organ transplantation that could offset the increasing discrepancy between the required number of donor organs needed and availability due to a growing and aging population and the higher life expectancy.[1] Additionally, eliminating the need for time-intensive therapy, for example, immune suppressants, and improving the patient quality of life.[1]

Tubular tissues have many unifying structural and biomechanical characteristics despite their different functions. They consist of a multi-layered muscular wall structure of multiple different cell types. The different cell types are embedded in a surrounding environment, the extracellular matrix (ECM).[1] The ECM serves for the spatial organization of the cells and consists of fibrous structures, for example, collagen or elastin, which are proteins that form fiber bundles.[2] Fibrous structures can be found throughout the human body, whether in the architecture and ECM of specific tissue structures, such as arteries, lymphatic vessels, cartilage, or in the fibrous nature of nerves, muscles, ligaments, tendons.[4] A major aim of TE is to mimic the ECM and develop a 3D scaffold that will be seeded with native cells for tissue formation. Current scaffold designs of tubular tissues include foams, gel mattresses, sponges, meshes, and nanofibrous structures.[5] The scaffold serves as a template

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for temporary structural support and ideally guides cell adhesion, proliferation, and infiltration. mimicking the structural components of ECM. Most of these structures are constructed by techniques that are not characterized by precisely defined and reproducible geometry of the porosity. A successful scaffold design requires a defined geometry and porosity to ensure cell differentiation and functionality of the ex vivo grown tissue.[6]

Given that a vital characteristic of the architecture of biological tissue is its fibrous ECM, it stands to reason to use textile techniques for the development of scaffold-engineered tissues. Textile structures are already widely used as medical implants to support or replace soft and hard tissue.[7] Their application as implants in the biomedical field has only emerged over the past decades.[8] Fibrous structures, due to their structural versatility as well as superior mechanical and biological characteristics, can mimic biological tissues to a large extent.[4] Thus, offer new possibilities in TE, and create alternatives to autologous tissues and prostheses. Textile structures for biomedical applications range from fiber, yarn, filaments, nonwoven, weaves, knits, braids, and embroidered materials.[7] Each offers potential for specific applications. Woven, nonwoven, or knitted tubular prostheses are used for applications in blood vessels, trachea, or esophagus.[4] Complex woven structures are used in heart valve TE.[9] Tubular braided structures are used as implantable stents made from filaments.[7] The choice of textile structure and technology is highly dependent on the specific application and its mechanical properties.

Textiles are hierarchical structures made of fibers, spun into yarn, or mono-/ multifilament, which are engineered into fabrics. The variety of textile construction processes (knitting, weaving, braiding) and appropriate choice of fiber-forming material, allow for a great structural and mechanical variety for their application. Hence, textiles offer, compared to other engineering techniques, great potential in the area of TE, specifically in soft tissue repair, for example, cardiovascular implants, which are used to replace or repair diseased arteries.[4] The design and construction of suitable, biocompatible scaffolds that replicate the native tissues' ECM for spatial cell attachment is a challenging question that has been addressed by many researchers from multiple disciplines.

Textile technologies, such as knitting, weaving, braiding, and electrospinning as a fiber manufacturing technique, hold great promise to create physiological functioning and biocompatible fibrous scaffolds. The interrelation between fiber, yarn, 2D, and 3D spatial fabric structures allows precise size-to-scale design.

A schematic diagram of the role of the textile's scaffold multi-scale parameters for cellular response and behavior is shown in **Figure 1**. The material and fiber should possess biomimetic properties that allow cellular attachment and guidance. The 2D or 3D fabric design should be highly porous, thereby facilitating cellular infiltration and stimulation of tissue formation. Additionally, resemble the mechanical properties of the native tissue. The yarn features should be adequate for

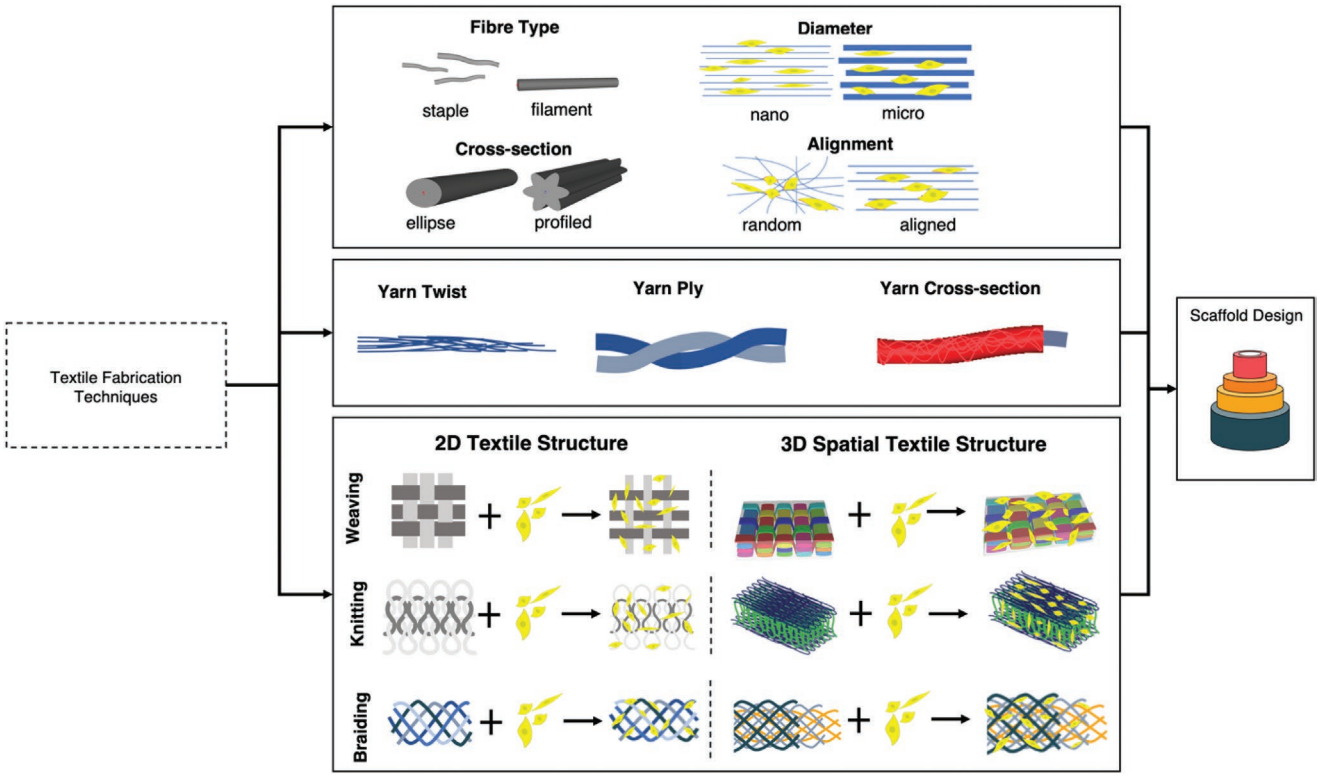

Figure 1. Interrelation of fiber, yarn, and fabric structures. The textile manufacturing process and the design and fabrication parameters on the different levels, that is, fiber, yarn, 2D textile, and 3D spatial textile structures could regulate cell-material interaction and cell behaviors in addition to the design and mechanical properties of the textile-based scaffold.

cellular response and provide sufficient mechanical strength for textile processing, that is, knitting, weaving, and braiding. Considering the precise structural design and pattern diversity of textile-based scaffolds based on fiber, yarn, and fabric technology are important construction techniques where each level can be specifically addressed and tailored to contribute to successful TE.

Engineering fibrous architectures entail fiber fabrication and manufacturing textile structures that will mimic the native ECM and provide a favorable environment for cell growth and differentiation.[10] Recent studies used textile technologies, such as electrospinning,[11–15] braiding,[16,17] knitting,[18,19] weaving,[20,21] or a combination[22–26] to fabricate scaffolds of tubular geometries, with an emphasis on the use of electrospinning. However, scaffold engineering was almost consistently neglected with great focus given on cell attachment and material mechanical properties.

Scaffold design is essential as it creates the environment for cellular activities, including adhesion, growth, infiltration, and differentiation, and supports tissue formation. The scaffold design concept, which was developed by scientists at MIT and Harvard in the early 1990s, when TE pioneered, comprises the following four steps: material selection respective to the demanded requirements, characterization of the material-cell interaction, construction of the 3D design based on the demands of the native tissue, performance evaluation of the design.[27] However, Hollister outlines that the individual aspects have to be considered mutually as they inevitably affect each other.[27] The success is greatly dependent upon the nature of the scaffold including material composition and degradation, macro-and microarchitecture, physical and mechanical properties, morphology, and material characteristics in terms of biocompatibility, degradability, pureness, and non-toxicity.[4,28–30] Moreover, these considerations change over time as the scaffold intentionally degrades and cells proliferate.[28]

Although research in industry and academia has increased significantly over the past years, there are no available designs that sufficiently address the needs of a clinical scale-up. Currently, fabricated tissues still have substantial drawbacks, such as mechanical instability, causing inflammation and resulting in high failure rates. There is a need for more relevant solutions.

There are several existing and newly published reviews on the advantages of textile-based TE and the application of textile technology in different TE applications.[31–36] Akbari et al., categorized materials into synthetic, natural, hydrogel-based fibers, and composite and hybrid reinforced fibers.[31] Whereas Liberski et al., research the process parameters, Jiao et al., review textile patterns, designs, and structure-property relations of textile-based scaffolds for various TE applications.[9] Jiang et al., focus their review on the process technique and parameters and their effect on the scaffold's properties.[33] In addition, various reviews exist for fabricating nanofibrous scaffolds from a wide range of biomaterial.[37,38] This review focuses on the application and adoption of textile patterns and the construction of single and multi-layer hollow tubular textile structures, provides an overview of current textile-based tubular scaffold engineering strategies, and highlights future potential research directions.

2. Textile Technologies for Engineering Hollow Tubular Scaffolds

Fundamental processing techniques in textile engineering include fiber and filament-forming techniques (e.g., electrospinning, melt-spinning, extrusion, etc.), yarn spinning techniques (ring spinning, rotor spinning, etc.), fabric manufacturing techniques (knitting, weaving, braiding), and further processing techniques (e.g., embroidery). **Table 1** shows the textile structures and their processing techniques from fibers, the base unit of textiles, over yarn spinning to fabric forming. Each structure offers unique characteristics and potential for applications in scaffold engineering for tubular soft tissues.

Textile-based scaffolds offer a unique form as cell-carrier substrates compared to other scaffold engineering methods. Fibrous scaffolds provide a high volume to ratio structure. Fibers or filaments can be spun into yarn, multi-ply-yarn, and further processed by weaving, knitting, or braiding. Thus, create a highly adaptable hierarchical structure and closely mimic the ECM of human tissues. The fibers and filaments closely resemble the collagen and elastin fibers of the ECM of tubular tissues.[4] Additionally, electrospun nanofibers ranging from 1µm to several 10nm facilitate cell response.[39] Tamayol et al. reviewed a variety of fiber-forming techniques, including electrospinning, melt spinning, wet spinning, bio spinning, microfluidic spinning, to form cell-free and cell-laden fibers from naturally derived and synthetic polymers.[34] Electrospinning has emerged as the predominantly adopted technique for nanofiber fabrication in TE due to its ease of use, cost-effectiveness, and versatility as well as its great controllability over fiber diameter and morphology.[40]

In general, textiles are anisotropic 2D structures with high in-plane stiffness and low bending stiffness.[39] The variety of textile engineering techniques and wide range of materials in fiber engineering enables the manipulation of surface morphology, structural porosity, and mechanical anisotropy as well as size, shape, and topography. For example, woven fabrics possess excellent dimensional stability, high stiffness, and tear-resistance and are characterized by pores of regular size and shape.[39] Knitted fabrics, on the other hand, are very flexible due to the loop construction and adjust well to changing deformations. Depending on the warp or weft knits and stitch density, they have higher strength and elasticity in the longitudinal or circumferential direction. Compared with woven or knitted fabrics, braided textile composites can better resist twisting, shearing, and impact. However, they exhibit low compression strength in the axial direction.[39] Electrospun nonwoven mats allow the greatest variation, but also the least control over the pore characteristics. Essentially, the scaffold needs to provide sufficient strength and elasticity as well as load-bearing capacity, to ensure adequate structural integrity during in vitro and/or in vivo regeneration.[28] Moreover, textile architecture encompasses besides structural design other aspects, such as morphology and topography, determining the fiber-cell interaction.

2.1. Electrospinning

Electrospinning is a widely employed technique to develop TE scaffolds, due to the ease of processing nanofibers, which have

Table 1. Textile structures and their processing techniques from fiber to fabric.[41]

Structure	Technology	Potential application for TE
Micro-/nanofibers	Natural or man-made fiber fabrication (wet spinning, melt spinning, dry spinning, electrospinning)	Nanofibers are beneficial for cell attachment, fiber diameter, and alignment allowing to control of cell behavior, drug loading capabilities
Web, sliver, roving	Preliminary spinning processes (carding, drawing, roving)	Hybrid nano-micro yarns, modified yarns can be used to produce fabrics for TE
Spun yarn	Spinning (ring spinning, rotor spinning,)	Yarn design is critical to the basic mechanical properties of tubular tissue replacements, organized in a higher-ordered structure and additionally control the morphology
Filament yarn	Formation of filament (extrusion, cutting, etc.)	Smooth tissue-like haptics
Plied, braided, cabled yarn	Assembling, twisting, braiding,	Engineered mechanical properties that correspond to those of the native tissue
Fancy yarn	Spinning, twisting	potentially as a spacer within the scaffold where void volume is needed to cell promote ingrowth
Woven fabric (2D and 3D woven structures)	Weaving	Tubular weaves, bifurcated and honeycomb structures mimic tubular tissues Multi-layered fabrics potentially promote cell migration
Nonwoven membrane	Bonding by friction/ cohesion/ adhesion	Single/ multi-layer nanofiber membranes mimic ECM of tubular tissues
Knitted fabric (tubular structures, spacer textiles)	Knitting (warp or weft)	Tubular knitting to fabricate seamless scaffolds
Braids	Braiding	Hollow braids provide space for cell growth and new tissue regeneration
Embroidered material	Embroidering	Stiffening and pore control
Modified structures (surface treatments)	Modification using various treatment techniques (printing, impregnations, plasma treatment, bonding, etc.)	To impart multifunctional characteristics (for example absorption, hydrophilicity)

been proven to have an increasingly important role in TE.[39] The predominant use of electrospinning in TE is accredited to its simplicity, cost-effectiveness, versatility as well as structural benefits due to high porosity and controllability over fiber diameter and morphology. Moreover, electrospinning easily fabricates seamless tubular conduits. Electrospun scaffolds have been applied in various TE applications, such as skin, bone, cartilage, tendon, ligament, nerve, blood vessel, cardiac tissue, and aortic valve.[42]

The process of electrospinning is based on the electrohydrodynamic of polymer droplets in a high electromagnetic field. The counter-electrode is located at a certain distance, usually a few centimeters, from the needle through which the polymer solution is dispensed at constant pressure and forms a droplet. The discharged droplet elongates to a jet, which, due to bending instability, is drawn further. As the fine solution jet travels toward the counter electrode, the solvent evaporates and produces fibers with a diameter in nanoscale. The fibers accumulate on a rotating drum or collector plate located on top of the counter electrode, producing a dense, randomly aligned structure. The physical, chemical, and mechanical fiber-fiber bonding generates a cohesive nonwoven structure. Electrospun nanofibers can be obtained from a variety of polymers, such as synthetic, natural, and polymer blends, closely mimicking the biochemical environment of the native ECM. Furthermore, the components of the polymer solution can be tailored and loaded with drugs or other biologically active molecules, allowing the manipulation of the properties and performance of the structure.[43] The fiber parameters are primarily controlled by adjusting the electrospinning conditions, such as applied voltage, feed rate, topography and types of collector, diameters of the needle (spinneret), and distance between the needle tip and the collector, as well as solution conditions, such as velocity, polymer concentration, temperature, and humidity.[39] By varying those parameters, several unique morphologies can be achieved, resulting in a variety of morphologies such as porous nanofibers, flattened, ribbon-like fibers, helical fibers, hollow fibers, beads-on string.[39,44] Nanofibers with beads were initially thought of as by-products and were considered unfavorable for TE. However, they have recently gained attention as promising applications in TE due to their drug-loading capabilities.[45]

The surface morphology and cross-sectional shape of the fiber are critical aspects of cell attachment and proliferation. The superior surface-to-volume ratio of nanofibers compared to micro-and macrofibers, surface modification, and tailored chemical constitution provide favorable conditions for cells. Prospective cell cultivation relies considerably on focal adhesion, that is, the contact sites between the cell membrane and ECM, which are characterized by the fiber shape and cell size.[39] Despite the benefits, electrospun nonwoven structures lack precise porosity control, including pore size and pore distribution.[46] However, load-bearing scaffolds require a well-defined porosity, depending on the specific application and the corresponding cell size.

However, it is projected that conventional textile manufacturing techniques, such as twisting, braiding, and weaving, should enable the assembly of electrospun filaments into robust

multifilament yarns with suitable structural and mechanical properties. In the context of soft tissue repair, multifilament scaffolds present an exciting opportunity to design devices that resemble the hierarchical structure as well as physical and mechanical behavior of the natural tissue.[47] Abhari et al. reviewed the manufacture and assembly of electrospun mono- and multifilament and their properties.[47]

2.1.1. Hollow Tubular Shaped 3D Nonwovens

Nonwovens are commonly fabricated as sheets. However, for hollow tubular nonwoven structures, a modified electrospinning set-up using rotating collectors the nanofibers deposit on the circumference or longitude of the rotating collector, forming a tube in its dimensions. Electrospinning with rotating devices such as mandrels, wire drums, wheels, cones, or frames is the most common and simplest method to fabricate hollow tubular nonwovens, in particular in TE small-diameter vascular scaffolds.[48] This technique generally is used to fabricate oriented fibers and multilayered nonwoven structures with fiber alignments of different degrees. Thereby, the fiber alignment is controlled by the specific set-up and collector speed. However, each does not only affect the degree of fiber alignment but also the mechanical properties of the engineered scaffold.[48]

There are various set-ups that allow multi-layered nonwoven tubular. **Figure 2** shows a schematic diagram of the fabrication method of a small-diameter four-layered tubular scaffold for

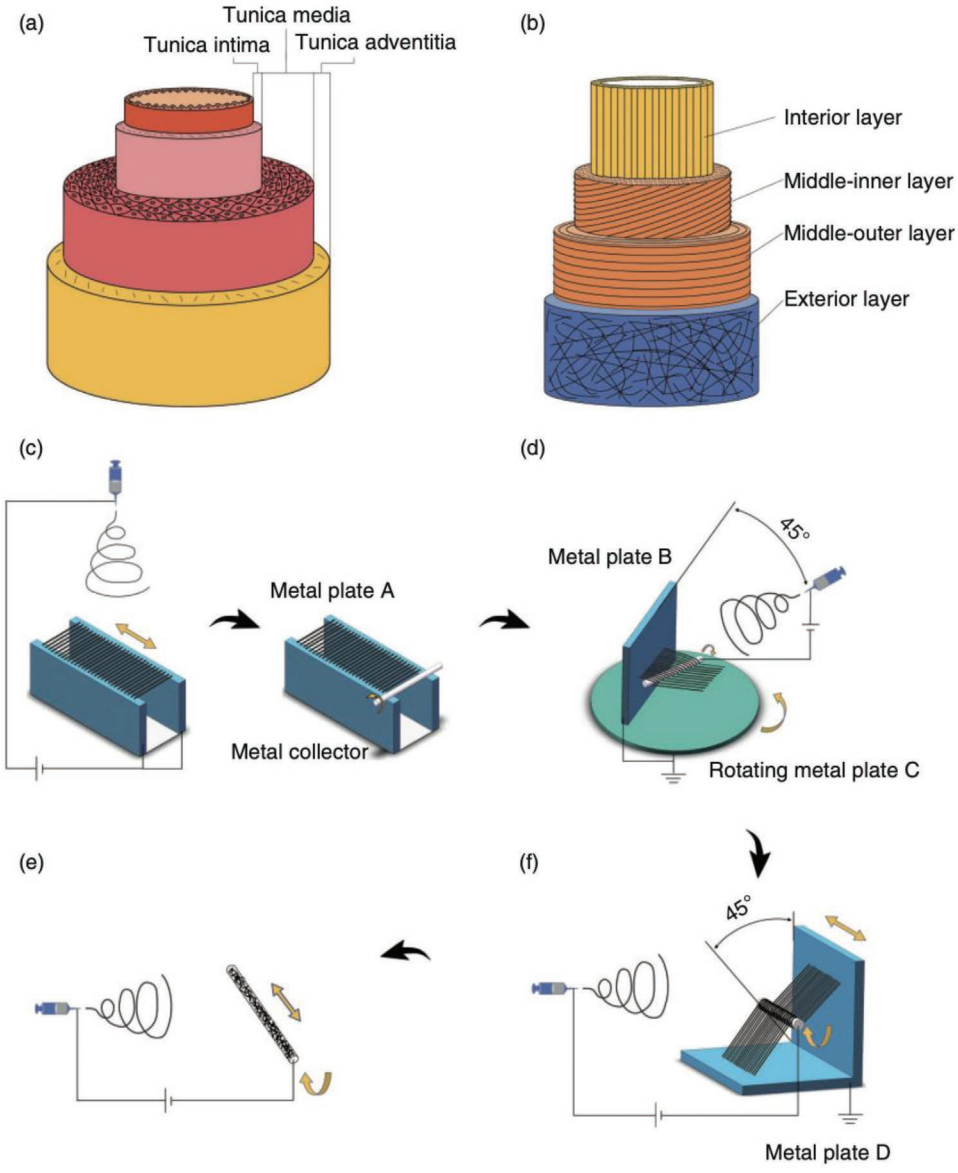

Figure 2. A schematic diagram of a) native blood vessel and b) small-diameter FLTSs that consist of an interior layer with highly longitudinal aligned nanofibers, two middle layers composed of electrospun sloped and circumferentially aligned fibers, and an exterior layer comprising random fibers. The fabrication method of the FLTSs: c) interior layer, d) middle-inner layer, e) middle-outer layer, and f) exterior layer. Reproduced with permission.[12] Copyright 2022, SAGE Journals.

blood vessel TE with aligned nanofibers to guide the growth of endothelial cells.

From a structural design perspective also, electrospinning provides a range of possibilities for mimicking the multilayered construction of arterial walls.[12] The main challenge is to precisely control the fiber distribution and the scaffold properties.

2.2. Knitting

Knitted structures are being used in a variety of medical applications, including for soft tissue applications such as vascular grafts, tracheal stents, hernia nets, ligament repair, artificial skin, cardiac devices, and are the most frequently used type of structures for scaffold-based tissues.[28] Due to their structural diversity and adaptability to specific requirements, for example, elasticity, high flexibility, burst pressure, dimensional stability, and fatigue resistance,[49,50] they are of particular interest as load-bearing support structures and withstand stresses and strains, that is, expand and contract in response to in vivo media flow without losing dimensional stability. Whereas fibrous nonwoven structures lack structural stability and braided or woven scaffolds lack internal space for cell growth, knitted structures offer enhanced porosity, flexibility, and bursting strength.[50] Advanced knitted structures can also exhibit different mechanical properties between axial and transverse directions, emphasizing their anisotropic properties, which might make this technique the manufacturing technology of choice for applications that emulate the intrinsic anisotropy of the tissues, such as for engineering cardiac constructs or for creating artificial muscles with enhanced strain.[51]

Compared to electrospinning, conventional textile engineering, such as knitting, weaving, and braiding, are yarn-based techniques. Knitting is performed by interlooping of one yarn, rather than crossing a set of multiple yarns. Knitted textiles are categorized into warp and weft knits, these differ in structure by the yarn course. In weft knitting, a horizontal row of connected loops is formed by one yarn in a horizontal direction (**Figure 3**A). The needles move individually, and the stitches (interloping of the yarn) are formed one after the other. In warp knitting, the stitches run vertically, each row is formed from an individual yarn system (Figure 3E). The stitches are formed collectively by all needles in a horizontal direction. Because of their single yarn construction, weft knits can unravel, whereas warp knitted fabrics may be defective but won't unravel.

The key binding elements that design the structure and influence its characteristics are stitch, tuck, float, or held stitches (Figure 3B,C). Binding elements other than stitches are used for local changes that increase or decrease the amount of yarn. The knitting parameters include course density, wale density, yarn characteristics, and stitch design which influence the fabric structure and its properties. Basic weft-knit patterns are plain, rib, and purl structures, which are manufactured on a circular and flat-bed knitting machine.[50] Warp knitted structures are made on Tricot or Raschel knitting machines and are classified into three major types of warp knits: tricot, raschel, and nets/laces.

Compared to weft knitted structures, warp-knits generally exhibit better dimensional stability. The loop formation in weft knits holds slightly more yarn, making them easier to displace, thus more flexible and elastic.[50] The 3D loop shape of weft knitted fabrics provides a slightly greater amount of yarn, making them easier to distort and stretch, while warp-knitted

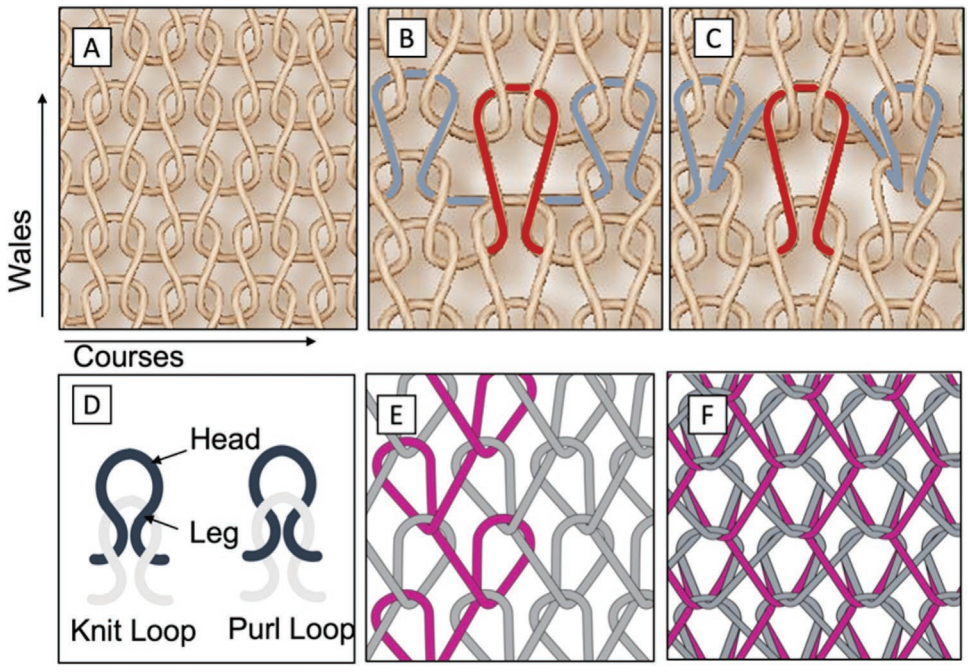

Figure 3. Illustration of different Knit structures and binding elements. A) Plain Knit, B) Knit miss stitch, C) Knit tuck stitch, D) basic loop pattern, E) single jersey warp structure, F) double jersey warp structure—The float is yarn lying over at least one stitch.

loops are bound by the neighboring stitches and are limited in their distortion, thus are more stable and less deformable. Knitted structures have the greatest mechanical diversity among yarn-based structures, ranging from 0% (multiaxial warp-knitted fabrics) to more than several 100% (rib weft-knitted fabrics) tensile elongation, attributed to the 3D shape of the stitch and the structure itself.[52]

In knitted structures, the loop configuration defines the porosity, pore size, and pore distribution as well as the mechanical properties. Yekrang et al. engineered a plain weft-knitted tubular structure for esophageal TE, investigating the parameters of the stitch density on the mechanical properties.[26] It was found that an increase in stitch density causes an increase in strength and a decrease in axial deformation. Therefore, for tubular structures with circumferential expansion and longitudinal strength, it is essential to set the stitch density at an optimum value to have good mechanical properties in both directions.[26] Besides, the manufacturing parameters, such as gauge size, take-up setting, yarn tension, also have a considerable influence. At the same time, the fineness, linear density, twist and morphology of the yarn, and their cross-sectional shape define the micro-level properties. Generally, weft-knitted structures are categorized into three basic structures: plain, rib, and purl structures, which are manufactured on a circular and flat-bed knitting machine. Warp knitted structures are produced on Tricot or Raschel knitting machines and classified into three major types of warp knits: tricot, raschel, and nets or laces.

The versatility allows knitted fabrics to meet most TE requirements. Knitted structures have been characterized by Wang et al. as excellent tissue scaffolds that promote tissue repair and have versatile mechanical properties. On account of the symmetrical loop structure, knits exhibit a high homogeneous porosity. The structure of the pores and the high degree of porosity does have an influence on the mechanical properties.[32] In general, knitted structures have low in-plane strength, which is one of the main concerns relating to the performance of knitted scaffolds. The high porosity and large pores lead to greater permeability, which is inadequate in the case of wall barrier structures.

2.2.1. 3D Knitted Tubular Structures

Both weft and warp 3D knitting technologies enable the production of single, bifurcated, or multibranched seamless tubular structures.[49] Circular weft knitting machines only create single-layer tubes of small to large diameter. Tubular structures of more complex designs are fabricated using flat-bed weft-knitting machines.[52] A variety of designs can be created by using a combination of constituent materials and stitches. For example, plain plating is a typical knitting structure used to obtain a particular effect on tubular structures and used to create an artificial tracheal stent.[53] A plated structure is composed of two or more yarns with different features to influence the morphology and physical properties. In comparison to weft-knitting, warp-knitted structures develop tubular scaffolds with superior radial stability, high compliance, and increased suture retention strength.[39] Compliance is defined in the standard ANSI/AAMI/ISO 7198:2016 (E) as the ability of a prosthesis to elastically expand and contract in the circumferential direction in response to a pulsatile pressure.[13] Lin et al. studied the relation of the fabric structure of warp and weft knits to their circumferential properties.[18] The loop arrangement of weft knits is circumferential, while that of warp knits is axial. Hence, results indicate that weft-knitted structures exhibit more significant variation in diameter, which creates a higher circumferential deformation.[18]

2.2.2. 3D Spacer Fabrics

Multi-layer structures, such as spacer fabrics, offer advanced structural design possibilities and properties, for example, tensile, elastic, compression, and permeability properties.[49] Spacer fabrics are made of two outer layers connected by a third inner spacer layer, providing a certain thickness. Examples of warp-knitted spacer fabric structures with different yarn configurations are shown in **Figure 4**. The structural designs and their mechanical features can be tailored by adjusting knitting parameters.

The thickness is variable and can be modified to match the requirements of the application,[53] but commonly ranges between 100 µm to 60 mm.[8,42] The highly cross-linked, porous structure and the large surface-to-volume ratio are particularly interesting for TE. The spacer yarn/walls that lie in the thickness direction provide the mechanical support and the high total porosity needed for a TE scaffold. In addition, the large surface area enhances cell attachment and proliferation. The knitting constructions of spacer fabrics and the differences in properties and structure have been outlined by Anand.[8] Spacer fabrics can be knitted on both weft and warp knitting machines.[49] However, its more commonly fabricated on warp knitted double-needle Raschel machines, due to their low cost, high output, and wide structural variety.[49] Warp-knitted spacer fabrics have high bursting strength, high porosity, high elongation, and low Young's modulus with a high volume to weight ratio, moisture permeability, compression resistance, and excellent recovery properties. Thus, warp-knitted spacer fabrics are a promising technique with a high potential in complex TE applications such as multi-layer tubular structures.

2.3. Weaving

Weaving is an ancient textile technique that is increasingly used for medical applications, for example, vascular prothesis, heart valves, and textile straps for tissue support.[9] The basic principle of 2D weaving entails the interlacing of two sets of parallel aligned yarns, that is, warp and weft, at a 90° angle to each other (**Figure 5**A).

The number of yarn crossings determines the weave pattern. There are three basic weaves: plain, satin, and twill as illustrated in Figure 5. The variety of weft and warp crossing gives an infinite variety of weaves.[54] In plain weave, the warp and weft yarns pass alternately above and below each other and vice versa (1:1 warp and weft ratio), producing a dense structure with the maximum number of binding points, that is, the crossings of weft and warp, and the shortest floats which results in a high yarn displacement stability. Plain woven structures have been

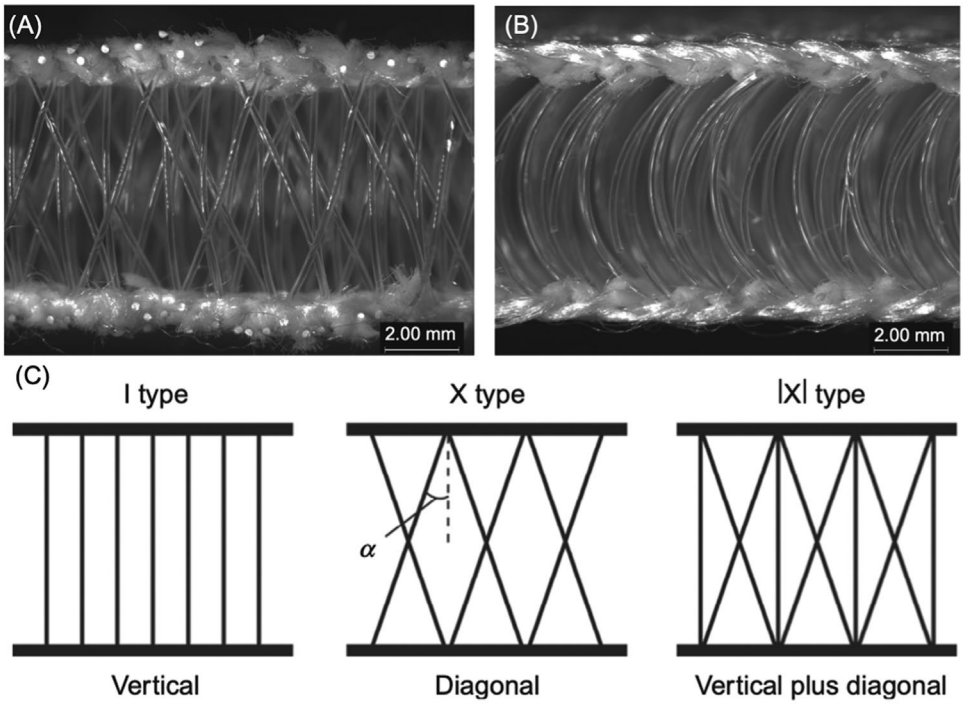

Figure 4. Photographs of warp-knitted spacer fabric and schematics of spacer yarn configurations. A,B) Spacer fabric knitted with six guide bars on a double-needle Raschel machine. Two outer layers with a middle spacer layer. C) Three configurations of spacer yarns: vertical, diagonal, and vertical plus diagonal. Depending on their inclination angle (α) as illustrated. Geometric configurations and their mechanical properties can be tailored by adjusting knitting parameters (i.e., underlapping movements, threading, and knockover comb bar distance). Reproduced with permission.[49] Copyright 2015, Elsevier.

used for vascular prostheses since the beginning of the 1950s.[55] Twill weave is characterized by a recognizable diagonal line on the face of the fabric (3:2 warp and weft ratio). Satin weave has fewer binding points and longer floats. (5:5 minimum warp and weft repeat). Due to the relatively small number of interlacing points, satin has a considerably low resistance to yarn displacement.

Properties, such as thickness, strength, porosity, extensibility, and durability, depend on the weave pattern design and thread spacing (number of threads per cm).[56] The weave pattern influences the stability, strength, flexibility, drape-ability, and permeability of the fabric.[42] Weave parameters that influence the structure and properties include warp and weft density (yarns per centimeter), weave design, yarn fineness, yarn

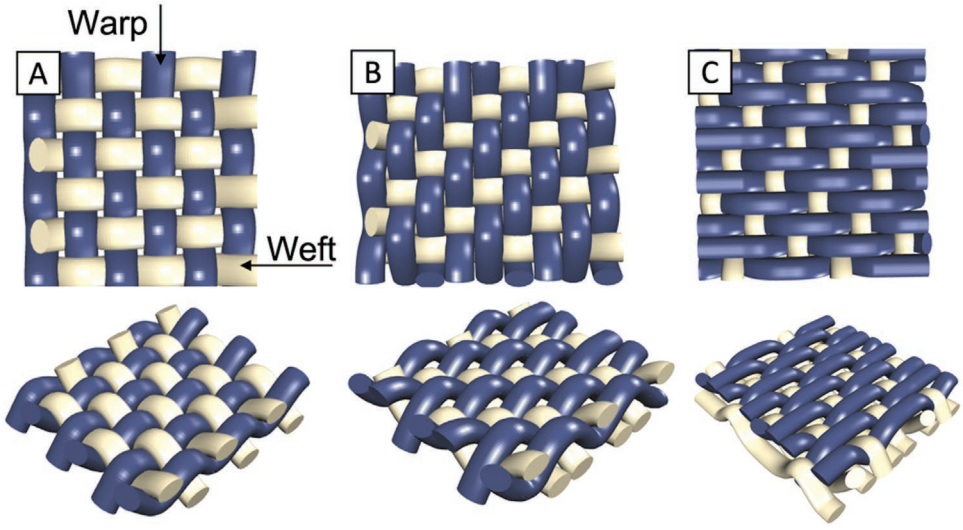

Figure 5. Top-view and 3D illustrations of different weave patterns: A) plain weave, B) twill weave, and C) satin weave. The blue represents the warp yarn and the white the weft yarn.

crimp, yarn twist, and material. Additionally, by using different yarns in warp and weft, location-specific elasticity and anisotropy may be achieved.[9] In that regard, weaving allows utilizing the benefits of a given material to its full extent. The structures in woven fabrics can also be modified to achieve largely different properties in the weft and warp directions.[9]

In general, weaves exhibit high mechanical strength and excellent dimensional stability, but relatively low elasticity.[54] Benefits of weaving include manufacturing precision of yarn alignment, geometrical reliability, reproducibility, and versatility. The area density and surface evenness of the structure is high, compared to knitted or braided structures. In comparison to nonwoven or knitted structures, they exhibit low porosity and poor compliance.

The porosity is defined by the inter-yarn spaces which for weave structures is due to yarn crossing, yarn crimps as well as weft and warp cover factor, that is, the extent to which the one yarn is covered by the other markedly impacted.[34] However, sufficient porosity is vital for cell adhesion and proliferation. Nevertheless, due to the low permeability to blood and less kinking, woven structures are suitable for high-flow and large-diameter arteries.[55] In addition, multi-layer woven fabrics have a load-bearing capacity and could provide enough space for cell or tissue growth. Cells seeded on 3D structures enhance the biological activity, cell migration rate, and proliferation rate, and reduce the requirements of cell adhesion for the integrin.[32]

Woven textile structures have been used reasonably little for the construction of tubular tissue scaffolds, designed to provide an ECM for cells. One primary concern when adopting weave structures for tubular scaffolds construction is adequate compliance to sufficiently perform circumferential deformation. For in vivo implantation, a structure with a stiffness that is too high may pose the risk of failure to the surrounding tissues. Moreover, the open selvedge or fray of yarn ends impacts the suture retention and may cause inflammation. However, weaving technology is capable of producing complex branched tubular structures, such as seamless bifurcated or trifurcated scaffolds.[42]

2.3.1. 3D Woven Tubular Structures

Woven structures are manufactured on looms that form 2D fabrics. Advances in 3D weaving enable the fabrication of complex seamless geometries, including hollow single, bifurcated or multi-branched tubular, nodal, that is, intersection of tubes, and spacer structures[57,58] for applications in tubular soft TE (**Figure 6**).[52] This demand developed from the fact that biomaterial yarns frequently may not be efficiently post-process due to thermal sensitivity, so it is better to weave them in their final shape.[34] Complex tubular structures can be fabricated on modified conventional, shuttle looms, circular looms, or jacquard, as

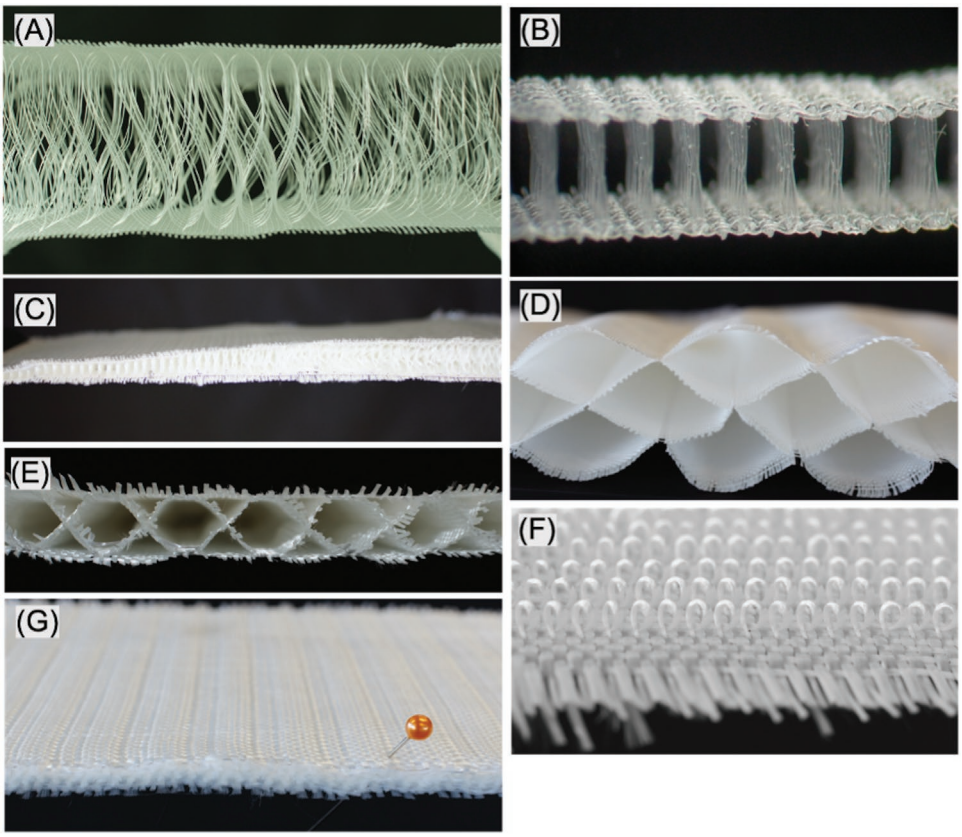

Figure 6. Examples of 3D woven fabrics. A–C) Distance woven fabrics. (A) With constant height with connection yarns at an angle, (B) constant height with vertical connection yarn, and (C) variable height. D,E) Tubular woven fabrics. (D) Honeycomb structure with profiled faces and horizontal connections. (E) Flat-woven faces with a woven connection under an angle. F) Loop pile fabric consists of a woven layer with perpendicular loops of pile yarns. G) Multilayer woven fabric with interlocking yarns in Z-direction. Reproduced with permission.[60] Copyright 2022, 3D Weaving.

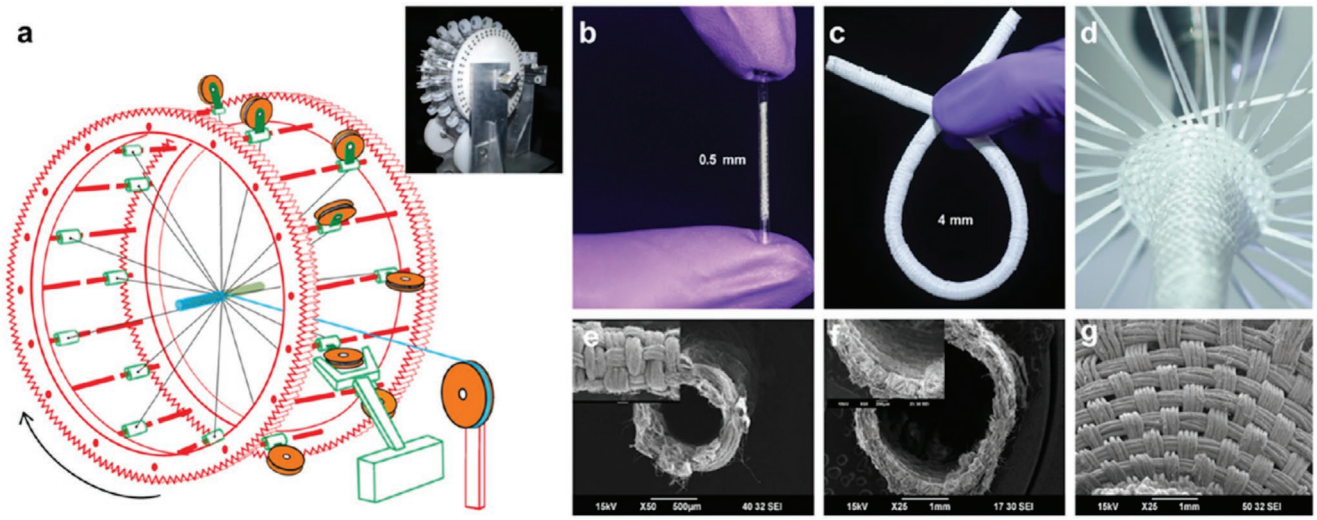

Figure 7. Fabrication of nanotextiles. a) Schematic of the automated weaving system (nanoweaver) that produces continuous woven fabric (blue: circumferential yarn; black: longitudinal yarn). The fabric is formed on the rod placed at the center of the two large rotating disks. Inset: photograph of the robotic system. Optical and SEM images of b,e) the smallest woven fabric (0.5 mm) (inside a capillary tube; the inset shows its lateral view), c,f) a 4 mm flexible woven conduit (the inset shows the cross-sectional view of the inner surface), and d,g) architectures formed due to inadequate tension on yarns during weaving. Reproduced with permission.[21] Copyright 2018, ACS.

well as on advanced 3D looms.[57] An automated circular loom (robotic system) for engineering a small-diameter conduit is shown in **Figure 7**a. The tubular scaffold is formed by interlacing multiple longitudinal warp yarns with one circumferential weft yarn (Figure 7a,c).

The greatest potential of weaving technology for scaffolding includes triaxial fabrics. Yokota et al. developed a small-diameter (4mm) tubular plain-weave patterned scaffold composed of core-sheath PGA and PLLA fibers for enhanced stability and strength to avoid rupture and aneurysm formation, that is, dilation of the artery.[59] Joseph et al. also used a plain weave pattern to fabricate a tubular scaffold with different diameters (from 0.5 to 4 mm) utilizing an automated weave process.[21] The structure consisted of low-strength yarn with multiple longitudinal yarns held in position by one circumferential yarn. The fabric was formed on a rod with corresponding changes in the diameter and changes in the number of longitudinal yarns to circumferential yarns. Testing of the mechanical properties and in vivo application showed superior performance characteristics in terms of flexibility and circumferential strength, radial stiffness, kink resistance, suture-ability, and both cellular attachment and proliferation compared to nonwoven small-diameter scaffolds.[21] Meng et al. proposed a method to weave tapered circular woven structures within a continuous weaving process by changing the weft density for enhanced homogeneous porosity and without any loss in tensile strength.[20] Typically, the transition from one diameter to another occurs at a single point in the weave, creating a sudden change in the weaving pattern in bifurcated and multi-branched structures.

2.4. Braiding

Similar to weaving, braiding is a technique in which a set of yarns is interwoven, but in an angular direction to each other forming a strand or hollow tube. The process entails the interwinding of three or more yarns at a diagonal angle ranging from 0° to 90°.[61] Due to the angle bias of the fiber alignment and yarn or filament arrangement, braided structures provide high flexibility, in comparison to woven structures.[62] Braided tubular structures have the highest axial strength and degree of radial expansion among textiles techniques. Owing to their dense weave-like surface structure, they have lower porosity than knitted structures, but better axial expansion and longitudinal elongation than woven structures.[16] The mechanical and structural properties, including surface density, diameter, and thickness, are controlled by manufacturing parameters, for example, braiding angle. An advantage of braids is their capability to bear loadings and stress in all three dimensions, in addition to high fatigue resistance and stability.[32]

2.4.1. 3D Braided Tubular Structures

Tubular braids are manufactured by an even number of yarns arranged in a circular setup. The bobbins move along sinusoidal tracks in opposing directions, thereby crossing alternately in a regular repeating pattern.

Common braided fabric structures are diamond braid, regular braid, and Hercules braid. **Figure 8** illustrates the basic geometric nature of these structures. Similar to woven fabrics, the yarn is only partially visible on the outside of the tube.[49] The structural versatility is achieved by incorporating floats, increasing the float length, or introducing yarns in a longitudinal direction to form triaxial.[61] Braiding can form 2D and 3D hollow structures. Later are multiple layers which are interlaced in thickness, whereas 2D tubes can be layered but the layers are not interlaced with each other. The 3D braided structure has superior axial support performance, high elasticity, and stability, which improves the functional diversity.[32,63]

Figure 8. Three common tubular 2D braids. Diamond braid has the maximum interlacing density with a 1/1 intersection repeat (the yarn is continuously passing over one and then under one yarn). Regular braid with a 2/2 and Hercules braid with a 3/3 yarn passing. The particular braid pattern is determined by the machine set-up.

Braiding has recently gained increasing attention in the development of biomedical applications for ligament, tendon, or cartilage tissues because of its high tensile strength.[34] Common medical applications of braided textiles are non-compliant metal stents, prostheses, sutures, and bandages.[51] However, stiff metallic stents, in contrast to scaffold engineered tissues, do not match the mechanical properties of the native tissue but brace the tissue open.[64]

Sun et al. developed a composite biodegradable braided stent composed of poly (p-dioxanone) (PPDO) monofilament and PPDO/PCL multifilament to increase mechanical strength and inherent resistance to deformation (vessel recoil) by strengthening the interlacement points.[17] The stent was fabricated by 28 monofilaments and 4 multifilaments at a braiding angle approximately of 55° to improve the friction of the yarns, impede sliding of the interlacing points and produce the desired porosity for cell adhesion. Thus, enhancing the mechanical properties compromises the shortage of suboptimal mechanical properties of the polymers.[17] The braiding pattern was not specified. The stent had an internal diameter of 8 mm suitable for applications in pulmonary arteries for children. In vivo evaluation revealed that the braided structure had adequate properties and acceptable biocompatibilities. Zhang et al. engineered a tri-layer scaffold of an inner and middle layer from electrospun silk fibroin (SF) and poly(l-lactide-co-ε-caprolactone) (PLCL) and an outer layer of braided SF yarn, to mimic the structure of native blood vessels. The results demonstrated that the braided outer layer significantly increased the suture retention strength, bursting strength, compliance, and added mechanical stability.[25] Besides good mechanical properties and biocompatibility, the prototype sample also exhibited appropriate anticoagulation properties because of the heparin coating.

3. Anatomy of Tubular Soft Tissues Determining the Requirements of Tubular Textile-Scaffold

According to the ASTM Standard F2312-11, a TE scaffold is defined as "a support, delivery vehicle, or matrix for facilitating the migration, binding, or transport of cells or bioactive molecules used to replace, repair, or regenerate tissues". Hence, essential design requirements of scaffolds include both, temporary structural and mechanical support as well as providing an adequate environment to promote cellular activity and viability. A well-designed scaffold matches the structural, morphological, and physiological characteristics of the target tissue and is consistent with the surrounding macro-and microstructure. As previously outlined the scaffold structure does not only define the mechanical properties but also has a significant influence on the cell behavior.[65] The ECM supplies the cells with nutrients as well as growth factors and promotes cell differentiation which results in the formation of various tissues.[32,65] Morphological characteristics can be controlled by the material as well as the fiber and yarn properties, while mechanical properties can be balanced by the textile technique used. The various requirements, not only structural and functional but also biomechanical and biochemical, differ considerably among the different tissue types. For example, connective tissues such as tendons and ligaments require a significantly higher tensile strength compared to tubular tissues such as blood vessels, aorta, esophagus, or trachea.[27] A thorough understanding of the functionality, structure, and physiology of the specific tissue is needed to identify requirements for the scaffold design.

In the field of regenerative medicine, many potential applications require tubular structures. Especially the intent to replace nerves and cardiovascular vessels, but also whole organs such as trachea, esophagus, or other gastrointestinal organs call for complex tubular scaffolds.[66] The primary function of these tubes is the supply of nutrients and the removal of waste products. For example, blood vessels provide oxygen and nutrients and discharge metabolic waste; the esophagus transports food to the gastrointestinal system; the trachea connects the larynx and the bronchi for breathing.

3.1. Macro- and Microstructure

Tubular tissues range in size from the smallest, for example, capillaries or blood vessels, to medium-sized, such as the urethra, or large tubes, such as the esophagus, trachea, or arteries. Although hollow tubular tissues appear to be simple tubes, in fact, they constitute complex structural and compositional features challenging to replicate. In order to develop scaffolds as substitutes for tubular tissues that replicate physiological form and function, the diverse biological and anatomical characteristics must be understood, including cellular function, mechanical properties, and vascularization.[67]

Generally, they comprise multiple layers, each with specific features that add to the function of the tissue to perform cyclical contracting motions, allowing permeability and additional functions. The tissues vary in size, form, wall thickness, wall microstructure, number of layers, composition, etc. depending on the intended application Moreover, most tubular tissues vary intrinsically in radius and symmetry, which challenges precise reconstruction.[68] The typical structure of native tubular tissue of an artery and trachea is illustrated in **Figure 9**.

The design of tubular scaffolds should consider properties such as high surface-area-to-volume ratio, porosity, pore size, pore design, pore interconnectivity, mechanical resilience, and durability to repeated expansion and contraction, permeability, and degradation.[69,70]

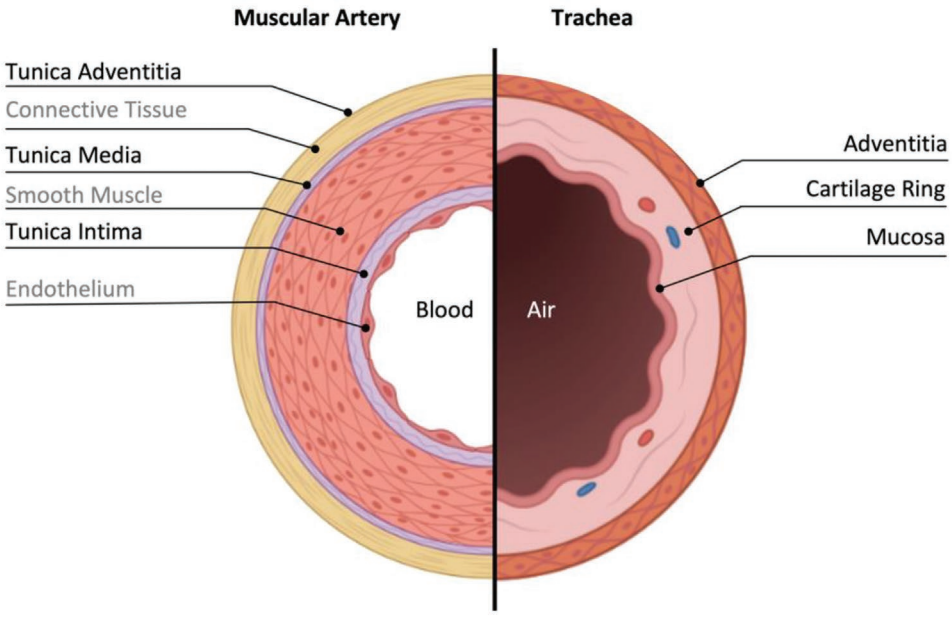

Figure 9. Schematic Diagram of structures of native hollow tubular tissues; specifically highlighting a cross-section of the vasculature (arteries, veins, and capillaries) and respiratory (trachea) systems.

3.2. Blood Vessels

In the vascular system, the arteries carry the oxygenated blood from the heart to the organs. Capillaries irrigate these organs' cells, and the veins return the hypoxic blood to the heart for a new cycle of circulation.[71] The structure of arteries and veins is essentially the same, composed of a three-layer wall: tunica intima, tunica media, and tunica externa (Figure 9).[64,71] The inner layer (tunica intima) consists of a smooth layer of endothelial cells. They form a barrier and prevent permeability between the wall of the blood vessel and the blood. The tunica intima prevents clumping of blood platelets. Damage to the cell layer increases the risk of thrombose. The middle layer (tunica media) primarily consists of smooth muscle cells, collagen- and elastin fibers. Contracting motions create a cyclic pulsatile blood flow. The outer layer (tunica adventitia or externa) mainly consists of ECM rich in collagen fibers to secure it in the surrounding tissue and ensure the vessel's mechanical resistance.[71]

Depending on the blood vessel type, the specific composition of these vascular layers varies.[71] Arteries, for example, have a thicker muscular media and a small inner lumen to withstand high arterial blood pressure.[64] Veins, however, have to withstand low venous blood pressure, which is why their walls are overall thinner and they are less elastic.[71] In particular, their media layer contains fewer muscle cells, and the lumen is larger compared to arteries for passive blood flow. In addition to the cellular organization within the wall structure, the ECM, which mainly contains elastic fibers, provides elasticity to the blood vessel for it to expand with increased blood pressure and contract and narrow the lumen, again.[71] Therefore, a TE blood vessel needs to be biocompatible, have good mechanical properties and compliance, be suture-able, be durable, have prolonged patency, and be anti-thrombogenic and vasoactive.[71]

3.3. Esophagus

The esophagus is a hollow tubular organ about 25–28 cm long.[72] It runs between the trachea and aorta and connects the pharynx and stomach to transport food through muscle contraction. The tissue is a tri-layered muscular with a nanoscale fibrous architecture.[14] The inner layer (mucosa) is made of endothelial cells and is subject to. The middle layer (submucosa) is a dense connective tissue, rich in collagen, and elastin to provide elasticity and flexibility. The outer layer (muscularis externa/ adventitia) forms the muscular wall of the esophagus and consists of circumferential and longitudinal aligned muscle cells.[72]

3.4. Trachea

The trachea connects the larynx to the two main bronchi and creates an airway for breathing. It is about 10–12 cm long and on average 2.5 cm in diameter, with dimensions slightly varying between men and women.[67] The tube is connected to 15 to 20 horseshoe-shaped cartilages arranged longitudinally along the trachea, which is joined together by a ligament. The cartilages reinforce the wall and prevent the trachea from collapsing during in- and exhalation.[73] The tissue is comprised of the mucosa (inner), submucosa (middle), cartilaginous layer, and adventive (outer) (Figure 9). The inner lumen is lined with an endothelial layer (mucosa), which protects the airway from dust and other foreign particles.[67] The submucosa is formed by loose connective tissue that consists of elastic fibers, proliferated cells, and secretion. On the exterior is the adventive, a loose connective tissue rich in collagen and elastin fibers that connect it to surrounding tissues and organs, such as the esophagus.[73]

In summary, tubular tissues generally have a similar structure of three distinct tissue layers. They are composed of a multicellular multi-layered wall system with an inner lumen. The innermost layer has a smooth morphology to ensure the passage of the medium and prevent clotting. The middle layer is made up of fibrous muscle cells, arranged to facilitate mechanical movement. The outermost layer provides support and embeds and connects it to the surrounding tissue. Nevertheless, these tubular tissues have a different specific complex microstructure and composition of the ECM, cells, and other primary components.

The scaffold should closely mimic the architectural and hierarchical parameters of the principal tissue layers and their characteristics, to reproduce the macro-and microstructure and provide a 3D environment . The scaffold design approach largely determines the macrostructure. The fabrication of multiple layers can be achieved by utilizing one or a combination of textile techniques.

Besides the morphological, and architectural dimensions and organization, microstructural aspects of the scaffold facilitate cell attachment, tissue formation, and function as well as consistency to the native tissue. Microstructural requirements include porosity and surface topography. Porosity is characterized by the ratio of hollow volume to a total volume of a substrate and is dependent on pore size, pore size distribution, interconnectivity, and reproducibility of pores.[74] Particularly noteworthy are pore size and interconnectivity of the pores for enhanced cell attachment and cell-material interaction.[39,74] Essentially, porosity determines the infiltration rate, and cell distribution and provides optimum space for the transport of biological substrates, such as nutrients, growth factors, and metabolic waste.[75] The reproducibility of the pores is critical as it relates to the mechanical and structural stability of the scaffold. Based on the cell size, migration requirements, and transportation properties, scaffolds need a minimum pore size.[39] In textiles, the porosity of fibrous scaffolds can be controlled on three levels. The inter-fiber gap represents the first level. The pore size is characterized by the gap between neighboring fibers and can be adjusted by fiber diameter, size, cross-sectional shape, distribution, and orientation. The electrospinning parameters control the porosity of nonwoven structures; however, the shape and distribution are somewhat irregular and challenging to predefine, which also impacts pore connectivity resulting in low reproducibility. In yarn-based structures, the inter-fiber porosity can be changed by the number of fibers in the yarn and the yarn-packing density.[39,74] The second level is governed by the inter-yarn gap, which is controlled by the pattern and manufacturing parameters. Depending on the type of textile structure, the porosity can be manipulated by the density of yarn crossings, yarn fineness, twist, texture, and crimp.[39] Regardless of the textile formation, knitted, woven, and braided scaffolds provide uniform pore distribution, excellent reproducibility, pore connectivity, and processability. In the case of knitted scaffolds, the porosity can be varied selectively by changing the stitch density and the stitch pattern.

In the case of braided scaffolds, porosity can be varied by controlling the bias angle of the interlacing yarns. In the case of woven scaffolds, it is possible to change the porosity by controlling the inter-yarn gaps through a beating action.[74] It may be noted that woven and braided scaffolds share similar surface topographies formed by the interlacing yarns. Knitted scaffolds, however, comprise curved yarns, which have a significant effect not only on the elastic behavior of the textile structure but also on cell attachment depending on the cell size and cell type.[74]

3.5. Mechanical Properties

Mechanical properties significantly influence the success of the scaffold as a substitute. They must match those of the native tissue to ensure its functionality and affect cell behavior. Noteworthy is that the mechanical properties of the scaffold change as tissue regeneration proceeds, due to cell growth and material degradation, for both in vivo as well as in vitro regeneration.[27] For specific tubular structures, the mechanical properties are also different. However, general mechanical performance characteristics of tubular tissues are longitudinal strength and circumferential non-linear elasticity, compliance (i.e., adjustable volume expansion of respiratory and vascular systems) to withstand physiological pulsatile pressure without bursting, suture retention strength, fatigue resistance, and anisotropy.[39,72,74–76] Tubular tissues, such as the aorta, trachea, or esophagus, are subject to biomechanics, that is, exponential cyclical loading, in order to allow the flow of blood or air and transport food. Cardiovascular tissues have both non-linear elastic and non-linear viscoelastic behavior.[27] The ability to deform elastically without bursting, even under high forces, such as with the rise of blood pressure, is crucial for their purpose and depends largely on the high proportion of elastin and collagen fibers and the arrangement of the different cell types.[46] "Collagen fibrils of high modulus reinforce the matrix anisotropic and decrease the flexibility along its axis".[72] Thus, tubular scaffolds require sufficient stress-strain properties in the longitudinal and circumferential directions. This is particularly challenging as compliance and elasticity are inversely related. The non-linear behavior of blood vessel scaffolds is a common issue in the development of scaffolds. Dimensional stability and mechanical strength are crucial to prevent collapsing of the trachea. Besides, the trachea elongates to bridge the movement of the chest due to breathing. Hence, the scaffold needs to provide absolute flexibility. The anatomical dimensions of blood vessels, esophagus, and trachea and their mechanical properties are compared in **Table 2**.

The properties of the scaffold should not outperform but rather be in the range of those of the native tissue.[27] A superior stiffness would suppress the contracting and relaxing movement. However, too low mechanical strength will cause low patency and result in consequent failure.[3] Resistance to suture retention in the axial direction to withstand forces resulting after implantation for in vivo viability are also an essential mechanical characteristic of tubular scaffolds.[75]

The anisotropic behavior is another critical characteristic attributed to the differential structural organization of the cells and fibers. As discussed by Singh et al., arterial tissue is 40% stiffer in circumferential compared to the axial direction and approximately 100% stiffer when inflated to physiological pressures.[64]

Table 2. Structural and mechanical properties of vasculature, esophagus, and trachea.

	Blood Vessel[64,71]			Esophagus[14,72]	Trachea[67,73]
	Large	Medium	Small		
Diameter [mm]	>10	6–10	1–6	>20	13–22
Total length [mm]	400	8000	160 00	200–250	100–120
Wall thickness [μm]	1500	1000	125–800	4300–5500	1000–3000
Mechanical properties	High compliance at low pressure and low compliance at high pressure (average compliance of artery: 7.4 mmHg × 10^{-2}, average compliance of vein: 2.7 mmHg × 10^{-2}), physiological pressure (60–250 mmHg), viscoelasticity (determined by elastic components: elastic modulus of elastin = 0.6–1 MPa, collagen = 1 GPa, smooth muscle = 0.1 MPa)			Highly elastic tissue exhibiting anisotropic behavior; non-linear mechanical feature of mucosa–submucosa layer; ultimate strength (axial: 2.19 MPa and radial: 1.41 MPa), elastic modulus (axial: 2.30 MPa and radial: 1.44 MPa), ultimate strain (axial: 70.0% and radial: 82.5%)	Displays higher strength in compression than in extension, non-linear viscoelastic; elastic modulus (2.5–7.7 MPa) tracheal muscle is stiffer in the longitudinal direction than circumferential, anisotropic behavior

Among the textile scaffolds, woven structures possess a limited elasticity and are commonly stiff due to the tight interlacement. The orthogonal arrangement of weft and warp yarn results in low axial elongation and poor radial compliance properties.[64] The structure of braids is similar to woven structures in that the yarns are interlaced. Thus, possessing equivalently high mechanical stiffness and strength. The angled interlacement and low yarn density allow for radial expansion. However, circumferential elasticity is at the expense of a longitudinal shortening.[64] Another limitation of braids is low elastic recovery. Knitted and nonwoven structures have somewhat lower mechanical properties. On account of their loop construction, knits are highly elastic and flexible, with low bending rigidity. Hence, demonstrate good compliance and considerable deformability.[74] Compared to weft knitted structures, warp knits are stiffer and inherently more dimensional stable. Disadvantages of knitted structures for the construction of tubular substrates are the insufficiently small pores and lack of structural instability.[64] Nevertheless, they are most prominent and suitable for engineering flexible tubular substrates, for example, blood vessel applications.[74] Electrospun nonwoven structural designs are usually multi-layered structures to provide sufficient strength and mimic anisotropic behavior. The use of different polymeric components in individual layers provides more flexibility in controlling the mechanical scaffold response from each structural layer.[64]

Moreover, the scaffolds' mechanical features can be tailored by adjusting the microstructural aspects stated earlier. Both mechanical and microstructural aspects are interrelated and need to be considered mutually.

3.6. Biological Properties

Implantable medical devices, such as scaffold engineered tissues, have to comply with individual biological requirements such as biocompatibility, biodegradability, and biomechanical interaction, irrespective of in vitro or in vivo TE. The concept of biocompatibility is defined by the ISO 10 993 standard and specifies materials that are in direct contact with living tissues, should not negatively interfere with their metabolism, including all reactions of the body. Given that scaffolds interact with the surrounding tissue, they should not provoke any negative immune response, which may cause inflammation or infection, resulting in failure of the engineered tissue. Thus, implantable medical devices are subject to rigorous testing, for example, hemocompatibility, cytocompatibility, toxicity, and carcinogenicity. By this means, it will be ensured that both functionality and adequate behavior in its surrounding environment are warranted. However, as pointed out by Durand and Marchand, ISO 10 993 standard helps to assess potential damaging consequences rather than advance tissue growth. The biocompatibility of fibrous scaffolds is assessed by the nanostructure (material–cell interaction), microstructure (fiber surface chemistry–cell interaction), macrostructure (scaffold structure–cell interaction),[77] behaving as closely as possible to the native tissue. A rapid interaction between the cells and the scaffold demonstrates a good material selection.[38] The material should be selected by a combination of its chemical, physical, mechanical, or other specific properties. For one, due to its required biocompatibility (pure and non-toxic) and second to be suitable for easy processability of the respective textile technology.[38] In addition to the material properties, the morphological and topographical features, in particular the enlarged surface area of nanofibers, have an enhancing effect on the biocompatibility of the scaffold for cell migration.[77] As tissue growth proceeds, the temporary support structure of the tissue is absorbed by the body and creates a biological structure without the need for revision surgery to remove the graft.[10]

The material's biodegradation rate should be adjusted to tissue growth, which can be done by the choice and mixture of materials. Ideally, the cells metabolize the scaffold for their nutritional needs and convert non-usable substances into non-toxic by-products that can be removed.[10,74] In addition, the biomechanical and biochemical interaction of scaffold–cell or cell-cell interaction profoundly influences cell growth, proliferation, and differentiation.[78] Biomechanics entail mechanical, anatomical, and physiological requirements of the scaffold under consideration of physics, chemistry, and biology of the material. It has recently surfaced that by combining both hydrophilic and hydrophobic materials in scaffold engineering of blood vessels, deposition of proteins on the fiber surface can be avoided and can prevent thrombosis.[75] Biochemical cues, such as growth factors or other factors, facilitate cell growth, while biomechanical stimulation by bioreactors facilitates cell differentiation,

which ultimately will also promote tissue growth. These requirements should also be considered for scaffold engineering.

4. Key Principles of the Hierarchical Architecture of Textile Structures for Tissue Engineering

The hierarchical structure of biological tissues causes multiple characteristics to interact and additional functions to emerge that go beyond the properties of the individual levels. The structural design, in which molecular features interact with those on the nano-, micro-, and macro-scale results in the functionality of the tissue. Due to their unique structural and mechanical performance characteristics, fiber-based scaffolds can mimic the structure of the biological tissue.

The precise control over spatial pore distribution and pore size by adjusting fabrication parameters and changing design features or fabric patterns are important advantages of textile-based scaffolds.[51] Pore size and interconnectivity are critical for cell attachment and viability, also determining the mechanical properties and ultimately the success of tissue regeneration.

Third, textile-based scaffolds can replicate the biomechanical properties of human tissue. Many human tissues, including the blood vessel, nerve, muscle, and heart wall, exhibit anisotropic mechanical behavior that could be mainly attributed to the variations in the distribution of collagen fibers in these tissues.[33] Knitted scaffolds have intrinsic anisotropic properties. Woven scaffolds can also have anisotropic properties by using different wefts and warps. Moreover, conventional textile techniques open up the infinite possibilities to engineer complex 3D scaffolds with a high degree of manufacturing precision, reproducibility, and potential industrial scale-up.[10] Compared to 2D structures, that is, non-woven membranes, 3D scaffolds allow for more complex microarchitecture and provide greater structural integrity and a more favorable microenvironment for cell differentiation, proliferation, and growth.[79] Understanding the variety of structural designs of textiles and their premises greatly broadens scaffold design approaches. By researching the structure- structure-property relations and 3D architectures, the scaffold design increasingly resembles the native tissue in its construction as well as in its mechanical properties.

The scaffold design is an essential aspect of the regeneration of neo-tissues or organs.[10] The multi-scale approach—material selection, fiber engineering, yarn fabrication, and textile processing allows superior control over the macro-and microstructure of the scaffold design as well as its performance characteristics. The individual levels inevitably impact each other and predetermine the structural and morphological as well as physical, chemical, and biological properties of the final construct.

The performance characteristics including biocompatibility, dimensional and structural support, mechanical, biological, and chemical compliance, and a cell-favorable environment of textile-based scaffolds are closely related to material selection, fiber, yarn, and fabric properties. Altering specific parameters of material, fiber, yarn, or structural design controls the overall performance characteristics of the scaffold.[74] The textile structure should be designed for the targeted tissue type due to the various structural and functional diversity. The specifications of the design aspects are predetermined by the native tissue type, its anatomy, and physiology. The fabrication of a uniform model that is suitable for several tissue types is not possible, since cell types and size, as well as tissue structure and function, vary greatly even within the individual tissue.[80] However, essential architectural scaffolding requirements include dimensional stability, elasticity, strength, porosity, and morphology.

In general, textile structures offer superior mechanical properties, including high strength, tear-resistance, and fatigue resistance to withstand physical and biomechanical constraints, high surface area and interconnectivity, great flexibility, and low bending stiffness.[29,39] Textile structures offer a unique potential in their variety of designs, patterns, and affiliated properties. The broad designs of textile structures can range from highly elastic large open pores to non-flexible very dense small porous structures. The pore size, distribution, reproducibility, and connectivity of the scaffold are directly related to successful cell attachment and infiltration.[10] Textile architecture exhibits three levels of porosity that can be selectively controlled through fiber spacing, yarn spacing, and subjecting the textile structures to secondary operations.[39] Furthermore, the large volume to surface ratio of the fibers facilitates cells to adhere and migrate into the structures,[66] while the physical anisotropy of the textile structure promotes cell distribution.[39]

The three levels of textile technologies, that is, fiber, yarn, and fabric, allow precise size-to-scale recreation of the native tissue structure and its ECM. Fibrous scaffolds create an ECM, providing a favorable environment for cell adhesion, growth, and differentiation.[28] The geometry and design of the scaffold, as well as its biological, chemical, and physical requirements, depend on the targeted application, that is, the native tissues.[51] The viability of the physiological system results both from the material properties and from the complexity of the biological micro-and macrostructure, which in turn determine the biomechanical behavior of the tissue. Specific characteristic properties of the scaffold can be assigned to individual textile structures.

4.1. Fiber Characteristics

Fibers create the smallest unit in textile structures, yet are closely linked to the overall performance of the final fabric structure.[39] Their chemical, physical, mechanical, and biological properties as well as their structure are closely related to the structural, physical, and mechanical properties of the scaffold.[29] Fibers are categorized to their dimensions of length to diameter ratio (fineness), in nano- and microfibers as well as in staple fibers or filaments. Unlike filaments, staple fibers are limited in length. In addition, fibers vary in geometry, for example, in size, diameter, fineness, cross-sectional shape, as well as in morphology and structure. Based on their parameters, fibers possess superior mechanical properties, including high surface area per unit volume, high mechanical strength, great flexibility, low-bending stiffness, and low basic weight.[77]

4.1.1. Fiber Diameter

Nanofibers ranging from 100nm to 1µm are primarily used in the construction of scaffolds due to their high surface area,

which facilitates cell response. The reduced fiber diameter increases cell-cell interaction and reduces the areas that cells are unable to attach to.[39] Hence, the fiber diameter has a significant impact on cell adhesion, cell arrangement, and cell behavior. As outlined by Jiao et al.,[32] the fiber size influences cell behavior with cell size:

- If the fiber diameter is larger than the cell, the cells elongate along with the fiber.
- If the fiber diameter is smaller than the cell, the cells interact with the fiber.

Wang et al. compared the effect of thinner and thicker fiber diameters on cell infiltration and vascularization.[81] The different fiber diameters were generated by changing the electrospinning conditions. The scaffold formed of thicker fibers sized 5–6 µm, had macropores sized of about 40 µm and 83% porosity, whereas the scaffold formed of thinner fibers, sized 0.7 µm, had micropores sized of about 4.6 µm and 66% porosity. It was found that the thicker fiber scaffold remarkably enhanced the infiltration of smooth muscle cells of the tunica media, and the middle layer of arteries, and the cells were homogeneously distributed (**Figure 10**). The microporous structure of thinner fibers could not facilitate cell infiltration. However, this is also may be attributed to the pore size and cell size. Studies into the effects of pore size on textile-based scaffolds have shown, that the pore size of 30–40 µm is most favorable for vascularization and efficient regeneration of a functional tunica media.[77]

4.1.2. Fiber Orientation

Moreover, fiber orientation, as well as their biological and chemical properties, affects the fiber-cell and the scaffold-cell interaction.[82] The orientation of the fiber in the microstructure, that is, aligned or randomly oriented, affects cell proliferation and differentiation (**Figure 11**). Several studies have investigated the effect of fiber alignment on cell behavior and activity. Niu et al. prepared three different types of tubular scaffolds with different fiber orientation directions, random, circumferential, and axial to mimic the intima layer, the inner layer, of blood vessels.[13] The native structure of the intima consists of longitudinally aligned cells. The cells were cultured onto the different structures and assessed. The cell proliferation of the cells did not differ significantly. However, cell differentiation was inevitable. Circumferentially and axially aligned fiber arrangement showed spindle-like shaped cells along the direction of the fiber. Zhu et al. also evaluated the guidance of cell proliferation and infiltration along with the fiber arrangement.[83] They prepared a bi-layer scaffold, of which, the internal layer comprised of circumferentially aligned microfibers and the outer layer of randomly oriented nanofibers. It was found that the inner layer provided topographic guidance for the cells to elongate, while the outer layer offered mechanical stability. Hu et al. also found that fiber alignment enhanced cellular proliferation and aligned nanofiber surface topography promoted cellular response, adhesion, and proliferation.[12] They developed a four-layered tubular scaffold mimicking the structure of native blood vessels. Each layer showed a different fiber orientation: an inner longitudinal aligned, an inner middle layer of stable oblique direction, an inner middle layer in 45-degree circumferential aligned fibers, and an outer layer of random fiber orientation.

4.1.3. Fiber Topography

The third aspect that needs consideration in the scaffold design is the cross-sectional shape and structure of the fiber. The

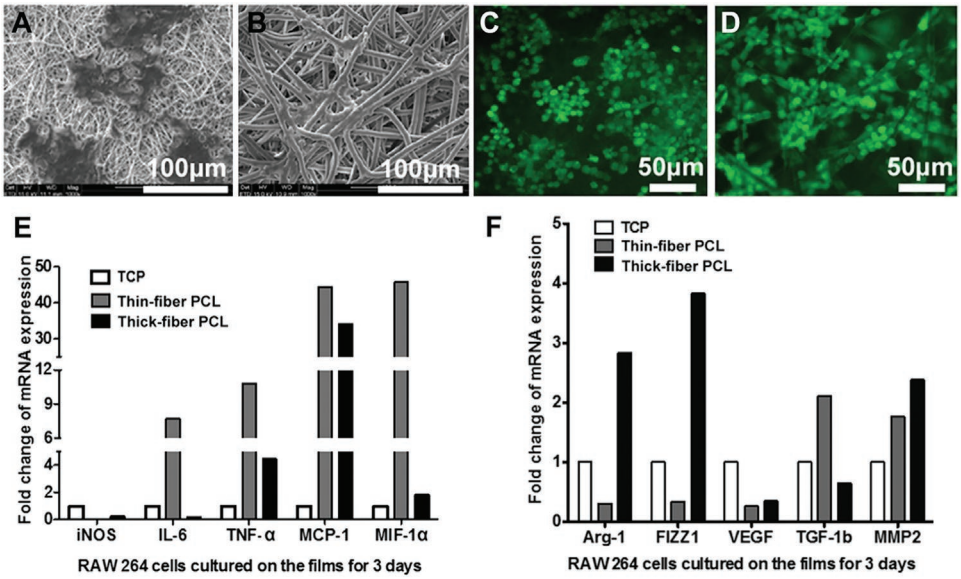

Figure 10. Evaluation of cell infiltration and macrophage polarization by in vitro culture of Raw264 cells. SEM images show the attachment on the A) thinner-fiber PCL mat and the B) thicker-fiber PCL mat. Fluorescent images show the infiltration and distribution of the cells within the C) thinner-fiber mat and the D) thicker-fiber mat. The gene expression of macrophages was detected using real-time PCR. E) The expression of M1 macrophage-related genes; F) The expression of M2 macrophage-related genes. Reproduced with permission.[81] Copyright 2014, Elsevier.

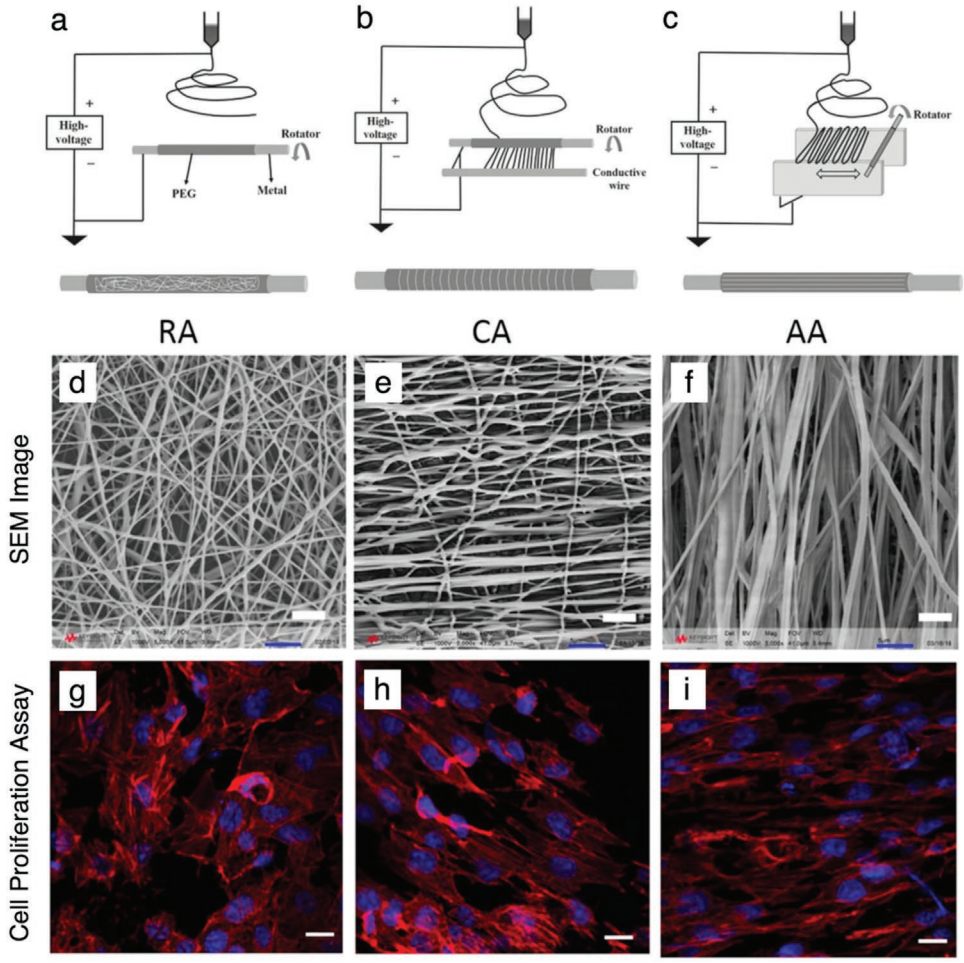

Figure 11. Schematic diagram showing the fabrication of tubular scaffolds with different structures: a) RA scaffolds, b) CA scaffolds, and c) AA scaffolds. SEM images of fiber morphology d) RA, e) CA, and f) AA; the scale bar is 5 µm. Results of assay of cell proliferation on the scaffolds at different time points of cell culture. Stained cytoskeleton of cells on samples of g) RA, h) CA, and i) AA. The scale bar is 20 µm. Reproduced with permission.[23] Copyright 2019, SAGE Publishing.

cross-sectional shape influences the properties of the material, including morphology and adsorption, and therefore controls cell behavior.[32] Profiled fibers are commonly used to achieve specific functionalities or properties of the structures. They exhibit a larger surface area compared to regular circular fibers, potentially enhancing cell adhesion and growth. The prospective cell cultivation is related to focal adhesion, the contact points between the cell membrane and fiber, which are characterized by the fiber shape and cell size.[39] Hence, cross-sections that enlarge the fiber's surface area, for example, fibers with longitudinal grooves, can inhibit cell adhesion. On the other hand, shaped fibers potentially favor cell proliferation.[77] Nevertheless, profiled fibers are currently primarily used in nerve reconstruction. Nevertheless, there are few studies on the effect of fiber shapes and cell interaction, but it is a considerable approach that improves the functions of scaffolds. Core-shell structured fibers were produced by Duan et al.[84] to improve biocompatibility for enhanced cell adhesion and proliferation while maintaining sufficient mechanical strength. The co-axial electrospinning technique was used to obtain fibers with a PCL core and outer collagen surface. The PCL provides good mechanical properties, whereas collagen is necessary for its biocompatibility. It was found that this is a promising approach as the fibers not only improved tensile strength, stitching strength, and bursting pressure, but also supported the cells to adhere, grow, and infiltrate into the interior. Fibers can be produced by various technologies, including melt-spinning, wet-spinning, and electrospinning. Due to its simple, cost-effective, and versatile setup,[85] the latter has evolved as a predominant technique to manufacture nanofibers from a polymeric solution. In addition to this, electrospinning provides the ability to produce fibers from a wide range of materials, both synthetic and natural, making this technique highly versatile and resourceful. The tailoring of the polymer solution enables the creation of fibers with tunable properties and novel functionalities, by adjusting the characteristics of the solution, for example, viscosity.[86] Another reason nanofibers are of great interest for Biomedical Textiles is the ability to create highly porous random oriented (isotropic) or aligned (anisotropic) structures.[51] The technique enables fibred fabrication with refined morphology, diameter, or porosity by optimizing the solution concentration or process parameters, such as the rotation speed of the

collector, voltage, or flow rate. A detailed review of the electrospinning production parameters of polymeric nanofibers has been published by Ibrahim and Klingner.[85]

Fibers and filaments with larger microchannels, deep grooves, as well as hollow fibers induce improved capillary action that, in addition to the adsorption phenomenon onto the fiber surface, encourages cell adhesion but also cell infiltration and migration compared to round section fibers. Fiber topography is a tunable parameter to control cell migration, either to promote or impede it.

4.1.4. Natural Fibers and Fiber-Forming Polymers

While several materials can be used in fiber processing, material selection for fiber engineering entails the careful consideration of the cytocompatibility and mechanical properties as well as biodegradability. For once, to promote cell attachment and proliferation, but also to not provoke negative immune reactions.[4,29,30] Biological human tissue consists of considerable amounts of natural polymers, such as structural proteins, enzymes, or polysaccharides.[82] Hence, long-chain biopolymer fibers ensure a high similarity with the native ECM, thus readily interacting with the biological system.[82] In recent studies, a wide variety of biopolymers have been used to construct scaffolds, including silk,[23,24,87] collagen/PCL,[84,88] gelatin composites,[26,89,90] PCL,[79,91,92] PCL composites[11,21,93–95] PGA,[16] PVA[18] and others. Biopolymers can be of natural or synthetic origin. While naturally derived polymers are superior in biocompatibility compared to synthetic polymers, promoting cell adhesion and proliferation, they exhibit limitations in their mechanical performance, such as low stiffness and strength.[82,96]

Natural biopolymers, such as collagen, are components of cell membranes and account for a substantial amount of the ECM of human vascular musculature. Collagen is often used with other materials to form composite scaffolds for TE.[84,88,97] Other natural biopolymers, which have been used, include silk and gelatin. Their superior biodegradability and biocompatibility compared to synthetic polymers in terms of cell viability and interaction is a major advantage for their application. SF has been used to develop a suitable implant and matrix material that promotes tissue regeneration, as SF offers several advantages over other biomaterials. It shows very high strength and corresponding great mechanical properties. Because of the ability to manipulate the protein structure and composition during production and thus precisely control the properties, SF has been extensively studied for scaffolding.

Synthetic biopolymers provide better mechanical strength and controlled biodegradability in comparison with natural polymers. They allow greater flexibility in the design and development of new products but challenge minimizing cytotoxicity in such products. As part of their favorable mechanical properties, synthetic biopolymers currently used in TE have proven to be very challenging for a successful application. For example, cell adhesion on untreated polymers has been assessed as insufficient.[48] Moreover, the hydrophobic surfaces prevent the spatial growth of the cells. Biopolymers that have been used in scaffold engineered tissues include PLA, PCL, and PLCL which combine the desirable mechanical properties of PCL with the increased degradation and biocompatibility of PLA, PVA, PET, PGA, and its copolymers PLGA, PEG, etc. and their copolymers. It is essential to note that not all synthetic biopolymers are biodegradable and thus not suitable for TE. Among those, PET, ePTFE, and PU/TPU offer excellent properties but do not degrade.[98] PCL is among the most frequently used biomaterials and has also found applications in a wide range of medical devices outside of TE. In existing in vivo applications, the use of PCL is limited to long-lasting implants and implants with controlled drug delivery, due to the slow degradation of several months to 2 years.[69] As PCL and PLCL have proven to contain acceptable but not excellent cytocompatibility, it is ideal to combine them with a natural biopolymer, thus providing sufficient mechanical support while improving biocompatibility and shortening degradation time. Composite materials combine favorable properties of the individual components and allow them to affiliate their characteristics. In other words, they are designed to augment the complementary properties of the respective materials and offset the prevailing disadvantages. Numerous reports investigate material blends that improve the physical or chemical characteristics of the scaffold.[11,38,87,89,99] From the scan of the literature, the most prevalent materials were PCL, PLA, PLGA, PEG, and their co-polymers as well as SF and collagen. Nevertheless, they all incorporate some component of slow-degrading polymer that persists with signs of surrounding inflammation and walling off by the host tissue.[16] Another study investigated a polytrimethyl carbonate (PTMC)/Gelatin blend to fabricate tubular scaffolds.[89] The strength and tuneable degradability of the synthetic polymer and the biocompatibility rendered by gelatin can be compounded together to fabricate a biomaterial to complement each other's properties and conceal their limitations.

However, the choice of material depends primarily on the type of fabric and its requirements. In the case of blood vessel regeneration, hydrophilic materials are considered ideal for blood-contacting applications.[21] A summary of data on fiber diameters of electrospun nanofibers in regard to specific biopolymers is listed in **Table 3**. The studies summarized in Table 2 researched the influence of material selection for electrospinning fibers on fiber diameter and cellular response.

4.2. Yarn Characteristics

Yarn is a long, thin, and continuous structure of mono- or multifilament or twisted bundles of fibers. It is an intermediate textile product that is further processed into woven, knitted, or braided most commonly 2D textile structures. It is, therefore, an important aspect to be considered in the multi-scale architecture of textiles. Yarn-based scaffold designs compared to electrospun nonwoven designs allow better control over pore size, fiber density, anisotropic or isotropic behavior, and mechanical stability—aspects, which have been identified as essential criteria to successfully fabricate functional tissues.[102] In addition, the yarn arrangement has superior control over the order of spatial design, material deposition, and internal continuity.[9] Yarn characteristics influence the overall performance of the structure, in particular surface morphology as well as the

Table 3. Polymers used for electrospun nanofibers and cells for engineering tubular scaffolds of vascular, trachea, or esophageal tissues.

Polymer	Cell type	Fiber diameter [nm]	Remarks on material selection	Ref.
PET/PCL	HUVECs	433	Biocompatible, enhance elasticity and compliance	[11]
PLCL	HUVECs	466–600	Copolymer of PLA and PCL, more elastic and flexible, adjustable biodegradability, and good biocompatibility	[13]
PU	EpCs, SMCs	360–440	slow degradation rate	[14]
PVA	ECs		biodegradable	[18]
SF/TPU	HUVECs	609–657		[22]
SF	HCAECs, HASMCs, HAAF	400–600 nm	degree of crystallinity strongly impacts in vivo biodegradation	[15]
PGA/ PCL,	-	190–260 nm	Hydrophilic (PGA), hydrophobic (PCL)	[26]
PTMC, Gelatin	BALB/c3T3	6–8 μm	biocompatible enzymatic degradation, excellent Bioreceptivity	[89]
PCL/ Collagen	ECs		Mechanical properties (tensile strength, suture strength, burst pressure, and good compliance) (PCL), good biocompatibility (collagen)	[84]
PLA/PCL	Esophageal	300–500	Long degradation time and elasticity	[93]
PCL/ PLGA	SMCs, ECs	609–657 nm	Accelerating degradation (PLGA), superior mechanical properties, and hydrophobic (PCL)	[94]
TPU/PCL/PEG	HUVECs	-	adjustable chemical and unique mechanical properties, and bio-degradability	[100]
PHBV/ PVA/ Elastin	HUVECs, SMCs and MSC	500–800 nm/1–2 μm (PHBV) 200–250 nm (PVA)	withstand cyclic loading (PHBV), improve elasticity, regulate cell proliferation (elastin), hydrophilic (PVA)	[101]

biomechanical behavior of the scaffold.[102] The differential organization of the different cell types determines the physiological function of the tissue. The precise control over the fiber alignment of fibrous yarn architectures produces anisotropic spatial structures. Mitchell and Tojeira studied the interdependence of the anisotropy of the structure and the facilitation of cell adhesion, proliferation, and differentiation for tissue formation.[103] Essentially, the fabrication of aligned fibers generates highly anisotropic yarns or structures. However, by creating woven, knits or braids, the overall scaffold is isotropic, the desired feature. Thus, even if fiber and yarn are highly anisotropic, the external structure can still be isotropic.[103] The key yarn parameters include geometry, mechanical and microstructural properties, such as diameter, linear density, tensile strength, rigidity, and flexibility are controlled during the manufacturing process and by the properties of the selected material and fiber. The surface morphology and internal yarn structure are closely related to the fiber size, fiber properties, fiber alignment, and fiber bonding.

Yarn fabrication considerations entail the material characteristics of the fibers that tune the structure and properties of the yarn. Composite or hybrid yarns are a simple approach to combining desirable properties by mixing different fibers. Aghaei-Ghareh-Bolagh et al. produced a highly twisted protein-based tropoelastin-silk nanofiber yarn to combine the physical strength of SF with fibers of tropoelastin for enhanced cellular activity.[104] The combination of physical and biological benefits values this as a promising approach for TE applications.

Additional aspects which influence the yarn structure and properties include crimp, texture, and twist. Local-specific mechanical properties of the scaffold may be achieved by implementing yarns of different mechanical properties, twist factors, structures, or textures.[9]

4.2.1. Nano-Yarn Structures

Conventional yarn is commonly in micro to millimeter scale and therefore not suitable for scaffold engineering, due to inhibited cell-cell interaction.[39] Nanoyarns manufactured of electrospun nanofibers may pave the way for higher performance scaffolds. Recently, transforming nanofibers into yarn that is processed into woven, knitted, or braided textiles suitable for tissue scaffolds are emerging.[21,105,106]

Recently, many modified electrospinning methods have been reported to develop long-length nanofibrous yarns.[107] The overall aim is to create robust nanofiber yarns with good structural and mechanical properties for textile engineering. Conventional spinning techniques refer to the assembly of fibers or filaments using drawing and twisting processes to align fibers and impart strength. Collectors used in electrospinning set-ups have been mostly developed for producing nanofiber membranes.[47] The engineering of nanofiber bundles assembled into long-length yarns require a dynamic collector with a continuous uptake, such as a rotating disk, funnel, or water bath.

In terms of yarn structure, nanofiber yarns can be categorized into pure nanofiber yarns and micro/nanofiber composite yarns. Based on the spinning principle, pure nanofiber yarns are divided into orientation type and twist type, and micro/nanofiber composite yarns are divided into core-spun yarn, wrapped yarn, and blended yarn.[107] Different hybrid nanofiber yarn formation techniques, such as an integrated twisting and winding device within the electrospinning process, a rotating ring twisting method, coating yarn with nanofibers by un- and rewinding yarn between discs and blended yarn through spinning nanofibers on sliver, are shown in **Figure 12**.

Teo and Ramakrishna[108] reviewed the electrospun nanofiber assembling techniques to develop a nanoyarn. Significant drawbacks of nanoyarn are its relatively poor mechanical tensile strength, limited length, and low production speed compared to microfiber yarn.[108] The former are fundamental properties necessary to withstand the stresses and strain subject to the yarn in textile manufacturing. Wu et al. developed a continuous fabrication of uniaxial highly aligned nano-yarn via electrospinning, which can be processed from various polymers. The highly hierarchical nano-yarn structure featured anisotropic characteristics and enhanced mechanical properties of the textile architecture. Greater strength can be imparted by twist and fiber density which increases fiber friction. Joseph et al. fabricated a tubular plain-woven nanotextile of low-strength nanoyarn in the size of 70–200 µm made of hierarchically aligned nanofibers.[21] The fabricated scaffold had superior mechanical properties and increased wettability compared to nonwoven fibrous scaffolds. The enhanced wettability of nanotextiles for blood-contacting applications, by developing hybrid micro-nanofibers yarns to fully exploit the benefits of textile technologies, is a promising approach.[21,105]

Liu et al. developed a core-shell yarn with a PGA multifilament core and a shell of aligned PCL nanofibers. The hybrid microfiber- nanofiber yarn had both the desired surface morphology of PCL nanofibers that promote cellular response and the mechanical properties of PGA microfiber yarn to meet the requirements of weaving, knitting, and braiding processes. The surface morphology and corresponding fiber alignment were controlled by the speed of the rotating disk, which ultimately affects the hydrophilicity, a key characteristic of cell adhesion and proliferation.[109]

4.3. Fabric Characteristics

Textile technologies enable infinite structural designs with a wide variety of adjustable morphological properties. Traditionally, textile structures are single-layer, plane interloped, or interlaced yarns in 2D structure, which are assembled into 3D architectures during additive manufacturing processes, such as sewing, gluing, or welding. In comparison to 2D textiles, 3D textiles have a spatial yarn architecture. It is worth defining the difference between 3D fabrics and 3D structures:

- 3D fabrics are 2D structures with a 3D geometry, for example, thick-walled multilayer structures, which have no yarn system in the thickness (z-direction) or spacer fabrics,
- 3D structures have yarn systems in all three spatial directions and thus ensure a corresponding effect. In general, 3D structures require a 3D geometry based on a volume-forming textile architecture.

2D or 3D fabrics require assembling processes, commonly known as a cut-and-sew approach. The seams create inherent regions of weakness, which impact the structural characteristics and overall mechanical performance of the textile. Also, seams are error-prone variables that damage the original structure during assembly caused by needle and yarn and can cause ruptures during stress-strain impacts, for example, during the expansion and relaxation of tubular tissue, such as pulsating blood flow of the aorta.

4.3.1. 3D Fabrics

The advantages of integral 3D structures are the significant improvement of structural homogeneity, the mechanical properties in the z-direction, and the reduction of the risk of delamination.[49] Engineering textile-based seamless 3D shaped scaffolds are a critical approach in TE and especially challenging. Tissue substitutes aim to replace the 3D ECM of the native tissue. 3D biomimetic designs regenerate the in vivo environment and allow cells to influence their microenvironment. They typically serve at least one of the following purposes: to allow cell attachment and migration; to release and store cells and biochemical factors; to allow diffusion of vital cell nutrients and metabolic waste; to provide certain mechanical and biological stimuli to manipulate cellular behavior. Thus, due to the necessary resemblance of structural dimension to the native tissue, a 3D seamless design can promote and guide tissue regeneration.[39,51] Such architectures can mimic the hierarchically porous macro-and microstructure of the native ECM and support 3D cellular growth as they "provide optimal spatial and nutritional conditions for the cells, also determining the successful integration with surrounding tissue".[111] Compared with 2D substrates, cells loaded within a 3D matrix display enhanced biological activities, and cells are more likely to proliferate and have a lower requirement of integrin usage for cell attachment.[39]

3D scaffold structures shaped similarly to the native tissue can be fabricated using conventional textile technologies. Some of the multiple textile engineering methods may be more suitable than others depending on the structural and mechanical requirements of the biomimetic design.

5. Design and Application of Textile Structures for Tubular Soft Tissue Engineering Scaffolds

Blood vessels, including arteries, capillaries, veins, and aorta range in their diameter but also slightly differ in their structure. From the scan of the literature, it is apparent that small-diameter blood vessels are of paramount interest since they are prone to occlusion, causing cardiovascular diseases, such as thrombosis, atherosclerosis, intimal hyperplasia, or other diseases. These scaffolds require specific mechanical and morphological aspects in compliance, blood flow rates, and blood pressure compared to large diameter conduits. The development of textile-based tubular scaffolds with a large diameter, such as esophagus or trachea, has been researched to a limited extent. The formation techniques, targeted tissue type, material, and the scaffold design with remarks on the number of layers and fiber alignment are summarized in **Table 4**.

5.1. Single-Layer Tubular Textile Structures

For vascular substitutes in TE, single-layer scaffolds of nonwoven tubular structures have been fabricated. A large proportion of studies developed single-layer scaffolds reporting novel electrospinning techniques to control nanofiber orientation that benefits cell responses. The approach was to investigate and

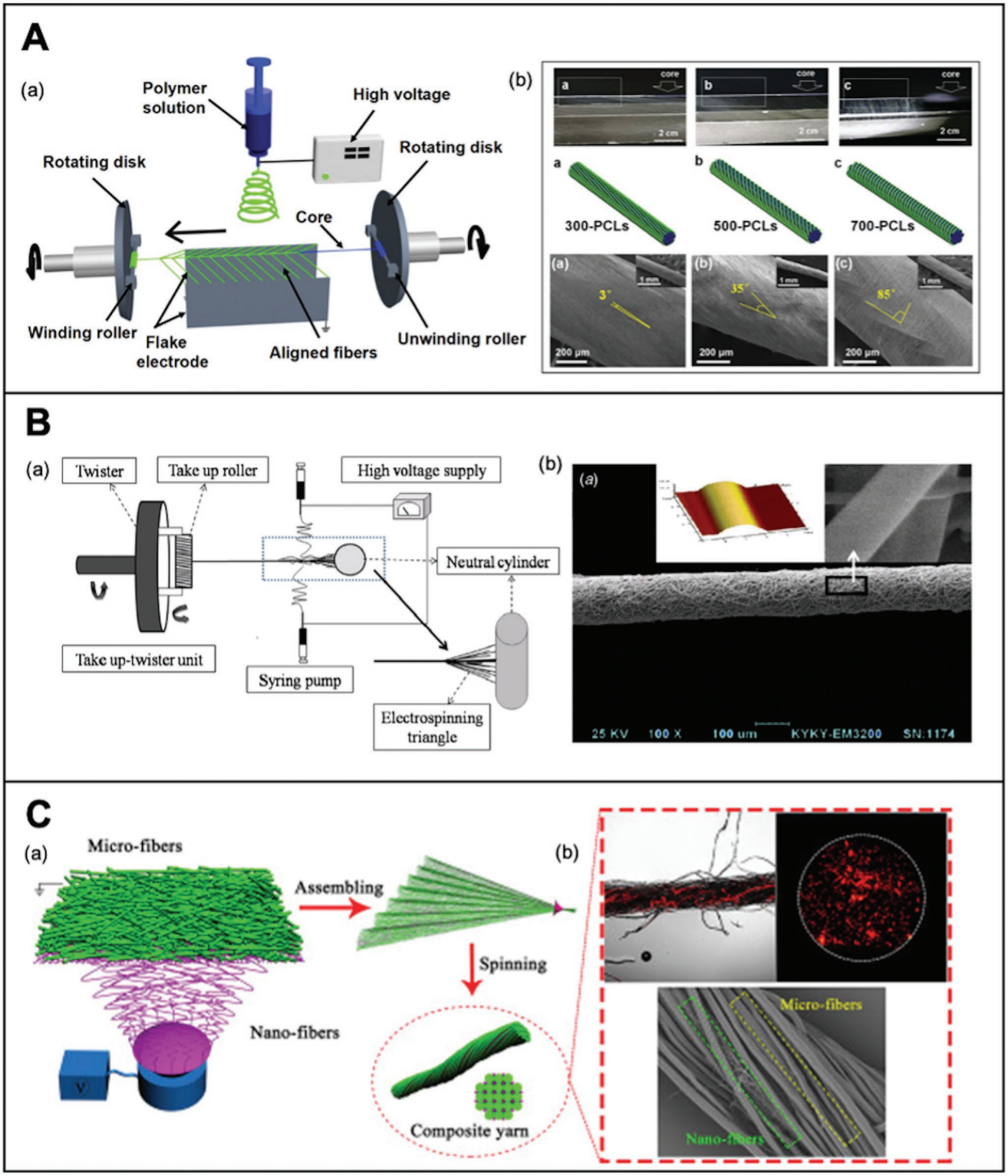

Figure 12. Different Nanofiber Yarns Formation Techniques A) Schematic of the device used to prepare A-PCLs. (a) Schematic illustration of the fabrication process and (b) surface morphology and SEM Images of PCL yarn with different unwinding roller speeds (a) 300-PCLs, (b) 500-PCLs, and (c) 700 PCLs. Reproduced with permission.[109] Copyrights 2019, Wiley-VCH. B) Schematic illustration of the electrospinning setup to produce nanofiber yarns (top view of the set-up) with twisting and winding integrated device, (b) SEM and AFM image of PLLA electrospun nanofiber yarn from TFE solution. Reproduced with permission.[110] Copyright 2013, IOP Publishing. C) Schematic illustration of the formation process of composite yarn (b) SEM image and optical images of fluorescent PAN nanofiber/ viscose micro-fiber hybrid yarn. Reproduced with permission.[105] Copyright 2019, Elsevier.

enhance mechanical biomechanical and morphological properties to improve physical characteristics and cellular interaction. The emphasis is on changing and optimizing process and/ or material parameters rather than the structural design. The fiber alignment is a key parameter that influences the mechanical properties and cellular response.[13,79,89,90] The electrospinning process parameters, in turn, control fiber alignment.[93,94] Further primary considerations entail the material properties to enhance the biomechanical and biochemical characteristics for better dimensional stability, elasticity or faster degradation rate, and increased biocompatibility.

5.2. Multi-Layer Tubular Textile Structures

Recently, it has been acknowledged that multi-layer structures could regulate macroscopic mechanical properties and benefit cell differentiation, proliferation, and functional longevity in TE scaffolds. Chung et al. successfully engineered a three-layered sandwich design made of an inner and outer electrospun PCL nanofiber structure with a middle layer modified with SF, for esophagus replacement assessed in vivo regeneration on a rat model.[114] The development of an esophagus substitute has also been researched by Wu et al. and Yekrang et al., who developed a novel biodegradable tubular hybrid scaffold with a multi-layer architecture by combining knitting and electrospinning.[14,15,26,79,88,97,106,116] The plain weft-knitted tubular fabric made of braided yarns was coated with PCL nanofibers and gelatin, for enhanced biocompatibility. Studies on tracheal reconstruction also designed a multi-layer structure. However, non-textile techniques are generally used in TE of the trachea.

Li and Zhao developed a braided tube reinforced electrospun SF/PLCL scaffold for small-diameter blood vessel application to improve the mechanical properties of the graft.[23] Alessandrino et al. constructed a tri-layer reinforced electrospun SF scaffold for small-diameter blood vessel application, using an intermediate braided structure to enhance the mechanical performance of the scaffold.[24] Tubular tissues constitute a multi-layer wall structure concept. Hence, about half of the publications use a multi-layer architecture design approach, which offers an effective strategy to mimic the structure and functions of native tubular tissues. Single-layer scaffolds commonly do not provide sufficient structural and functional support for regeneration. Therefore, the attempt is the full reconstruction of the native tissue, including its multiple layers to impart specific mechanical properties to fulfill physiological requirements. The structure of the individual layers differs in the fiber orientation and/ or the fabrication method.[12]

Another important finding is that the multi-layer structures possess superior mechanical properties, despite the otherwise relatively low strength, stability, and compliance of electrospun scaffolds. Aligned multi-layer scaffolds have good mechanical properties with high tensile strength in circumferential and longitudinal directions compared to only layered randomly oriented fibers.[12] Though, in this study, the viability and proliferation of cells on the inner layer of the structure were low. In comparison, Wu et al. developed a three-layered structure composed of complete random oriented fiber layers. The inner and outer nanofiber layer of pure natural polymers were to mimic the structure and components of the native ECM, whereas the microfiber middle layer was to regulate pore size and prevent delamination. The results indicate that the fibers of the middle layer enhanced the mechanical properties and suture retention strength. Moreover, the symmetrical structure of natural and synthetic polymers effectively facilitated cellular behavior. However, this is mainly attributed to the biocompatibility of the natural polymer. On the effect of combining different fiber diameters and/or nano yarns, the results of a study by Wu et al. show that each layer and the entire scaffold had good mechanical properties to support tensile and compressive strength. In a three-step approach, they fabricated an electrospun scaffold of axial aligned dense nanofibers in the inner layer, loose yarns in the middle layer, and random oriented dense nanofibers in the outer layer. While the inner layer maintained structural support, and the outer layer adhered the yarn of the middle layer to the inner layer, the yarn layer promoted cell proliferation and orientation along the fiber direction and into the interior of the scaffold. This suggests that the porous structure of the yarn overcomes the lack of insufficient cell infiltration. The control over fiber orientation is reported as the principal topographical control of nonwoven structures. However, limited cell infiltration is associated with nonwoven structures due to the dense nanofibers that impede homogeneous pore distribution and pore size. Substantial challenges remain in fiber alignment as well as harmonizing the layers to prevent delamination. Furthermore, mimicry of the biomechanical properties, specifically burst pressure, suture retention force, and compliance, of the native ECM and adequate cell infiltration, represent challenges.

Another approach to biomimicking the mechanical property of the native tissue is the design of hybrid structures, reinforcing electrospun layers with either knitted or braided structures to create a multi-layer architecture. There are similarities between the findings of electrospun multi-layer structures and hybrid structures. The detailed architecture confers higher mechanical performance and resistance as well as cell interaction. In the study, Alessandrino et al. developed a tri-layer sandwich structure consisting of an inner and outer electrospun nanofiber layer and a middle warp braided textile layer to overcome the lack of mechanical properties of the electrospun layers.[24] The results of mechanical testing confirmed the significant contribution of the micro-yarns to the burst and tensile strength of the scaffold. In vitro and in vivo studies showed that the electrospun layers exhibited high biocompatibility. In order to prevent delamination issues, Alessandrino et al. used a patented coupling technology, bonding the crossing points between the layers, thus responding as a single structure to physical impacts.[24] Following the present results, the study by Zhang et al. braided on top of the inner and middle layer electrospun structures to add mechanical stability and non-linear elasticity.[25] In addition, the large pores of the braided structure allowed for SMC cells to adhere. This warrants further studies on a tubular, three-layered scaffold of composite structures, tailoring the mechanical properties of each layer to match those of the native tissue. Interestingly, coating strategies were also adopted to link electrospun and textile structures effectively. Furthermore, coatings of fibers or scaffold surfaces, or hydrogel layers were incorporated to overcome the issue of leakage due to exceedingly high porosity when expanded due to pressure.[22]

Table 4. An overview of current fiber-based formation techniques for hollow tubular scaffolds in soft TE.

Formation Technique	Tissue	Material	Tubular scaffold design	Ref.
Electrospinning	Small-diameter blood vessel	PET/PCL	Single layer	[11]
Electrospinning	Esophagus	PLA/PCL	Single layer	[93]
Electrospinning	Blood vessels (tunica media)	PTMC, Gelatin	Single layer	[89]
Electrospinning	Small-diameter blood vessel	TPU/PCL/PEG	Multi-layer	[12]
Electrospinning	Small-diameter blood vessel	PCL/PLGA	Bi-layer	[94]
Braiding, Electrospinning	Blood vessel	SF/PAM/ TPU	Tri-layer	[22]
Braiding, Electrospinning	Small-diameter blood vessel	SF/PLCL	Bi-layer	[23]
Electrospinning, Braiding	Small-diameter blood vessel	SF	Tri-layer	
Electrospinning	Esophagus	PU	Bi-layer	[14]
Braiding	Vascular tissue	PGA	Single layer	[16]
Weaving	Vascular tissue	n.a.	Tapered single layer	[20]
Electrospinning	Small-diameter blood vessel	PLCL	Single layer with controlled fibre alignment	[13]
Braiding	Aorta, Large-diameter vessel	PCL/PPDO	Single layer, composite filament	[17]
Knitting	Blood vessel	PVA	Single layer	[18]
Electrospinning	Vascular tissue	PLCL/COL	Tri-layer	[15]
Weaving	Vascular tissue	PLLA, PCL	Single layer, Nanoyarn fabrication	[21]
Electrospinning	Artery	PHBV/ Elastin	Tri-layer with bi-directional architecture	[101]
Braiding, Electrospinning	Small-diameter blood vessel	SF/PLCL	Tri-layer	[25]
Electrospinning	Trachea	P(LLA-CL)/ Collagen	Bi-layer	[97]
Knitting, Electrospinning	Esophagus	PGA/PCL, Gelatin	Multi-layer	[26]
Knitting	Artery	PVA	Single layer, coated	[112]
Knitting, Electrospinning	Small-diameter blood vessel	PLA/PLCL	Bi-layer	[95]
Electrospinning	Esophagus	PVBH/ Gelatin	Single layer with dual oriented fiber alignment	[90]
Electrospinning	Medium-diameter blood vessel	ELR	Bi-layer	[113]
Electrospinning	Small-diameter blood vessel	PCL/ Collagen	Single layer, core-shell fibers	[84]
Electrospinning	Vascular tissue	P(LLA-CL)/ Collagen	Multi-layer	[88]
Electrospinning	Esophagus	PCL/SF	Tri-layer	[114]
Knitting	Small-diameter blood vessel	PEG/SF	Single layer, coated	[19]
Electrospinning	Vascular tissue	PCL	Single layer	[92]
Electrospinning	Vascular tissue	Biosyn	Single layer	[115]
Electrospinning	Small-diameter blood vessel	PCL	Single layer with controlled fiber alignment	[79]

6. Perspectives and Summary

This paper has outlined the necessary considerations in scaffold construction from a textile technological perspective and discussed the current status and potential of textile engineering in resembling the multi-layer tubular soft tissue. As a consequence of the challenging interdisciplinary complexity and the many aspects that determine the success of TE, research has increased exponentially over the last ten years. It has broadened the understanding of how the multi-scale architecture of fibers, yarn, and textile structures interact in textile-based scaffold engineering. An ideal scaffold should be readily available, of low cost, with a long shelf life, biocompatible, with an appropriate degradation rate, non-toxic, and non-immunogenic. Moreover, it must support tissue formation and have similar mechanical and physiological properties as the native tissue. The scaffold must support cell-specific growth and differentiation, respectively.

6.1. Challenges and Future Perspectives of Textile Technologies for Tubular Scaffolds

Textile technologies develop a variety of nonwoven, knitted, woven, or braided hollow tubular scaffolds suitable for TE. The precise control over macro-and microstructure and mechanical properties holds great promise in engineering complex multi-layer tubular scaffolds.

However, various limitations and challenges remain in the design and construction of the scaffold. Textile-based scaffold design limitations include 1) tubular structures that do not sufficiently meet the properties of the native tissue and its environment. In particular, the non-linear elongation/viscoelastic behavior and radial compliance of blood vessels and the esophagus mismatch between native tubular tissue and scaffold. In addition, the regional specific mechanical properties (suture retention strength), and accumulation of high stress

at the connective tissue interface, challenge the structural approach.

2) Replicating the 3D multi-layer wall structure each with differentiating in cell types, microstructure, and functions, in its entirety. The challenge of mimicking the differentiating layer-specific requirements remain. 3) Technical limitation of textile machines to construct complex patterns with high efficiency. Currently, most textile-based scaffolds are fabricated manually or on modified miniature textile machines, limiting the scaffold design. The development of advanced textile machines will have a positive impact on the design and manufacture of textile-based scaffolds.

Textile-based scaffold designs potentially overcome some of these challenges. The elastic structure of knits is useful where structures have to adapt to different circumferential changes. Adjusting the stitch density can optimize circumferential elasticity and longitudinal strength. The increase or decrease in knitted loops contributes to the tensile strength of the fabric. Due to the greater elasticity of knitted structures, a high burst strength may result in fluid leakage. Braiding is like knitting often used for elastic tissues but has higher axial strength. Nevertheless, leaking issues are also among braided structures, potentially fatal for in vivo applications. A promising prospect in this respect is combining different manufacturing techniques. Knit or braid reinforced electrospun scaffolds level the excellent mechanical properties, and the superior biocompatibility and cell behavior of nonwoven ECM-like structures can lead to favorable results. On the one hand, nanofibers can resemble the native tissue and have unique properties, on the other hand, they can only be formed in 2D fabrics. Hybrid structures incorporating hydrogels, coatings, or freeze-drying have also exhibited great results in both considerations.

Strategies of textile-based tubular scaffolds emphasize appropriate material selection or fine-tuning of key process parameters in electrospinning. Potential directions that need further research are profiled fibers. Compared to regular circular cross-sectional fibers, profiled fibers add features, such as wettability, due to the differences in surface area and topography, for example, grooved fibers possibly improve cell proliferation and ease transport of components along the fiber channels. Another potential research direction includes different yarn structures, for example, core-sheath yarns may show different flexibility and elongation properties between the core and the sheath; double-covered yarns exhibit high abrasion resistance; false twist textured top layer of yarn with lower stretch properties produce smoother yarn.[30]

More complex patterns feature a variety of morphologies and versatile properties. Exploring different pattern designs and yarn arrangements possibly enhances the performance of the scaffold. Moreover, advanced fabric structures such as different knitted spacer fabrics (vertical spacer yarn configuration, knitted walls spacer structure, diagonal spacer yarn configuration) have not yet been adapted for engineering tubular scaffolds.[52] The 3D fabric structure potentially promotes cell migration, proliferation, and differentiation and better match the properties of the tissue.

6.2. Summary

Scaffold-based TE has to match multiple requirements, such as biocompatibility, biodegradability, load-bearing mechanical properties, an ECM-like structure, and a tailored 3D shape mimicking the native tissue. A variety of natural and synthetic polymers are used as scaffold materials, which can be processed to form fibers in nanoscale via electrospinning. The morphology, diameter, and porosity of the nanofibers, as well as nanofiber alignment, can be optimized by changing the process parameters or process setup. Nanofibers facilitate, due to their extraordinary surface-to-volume ratio, cell adhesion, proliferation, infiltration, and differentiation.

Textile technology holds great promise in functional engineering scaffolds. The versatility of manufacturing techniques allows the control over mechanical and porous properties of the scaffold to provide temporary structural support, facilitate cell activity and provide consistency with the native tissue. Moreover, textile engineering allows the reconstruction of the complex multi-layer tissue structure with a wide range of mechanical and morphological characteristics. However, the appropriate method needs to be chosen based on the demands of the targeted tissue.

Multiple textile-based TE strategies have emerged over the past years predominantly electrospinning nanofiber nonwoven and yarn-based woven, knitted, or braided scaffolds with the aim to develop functional scaffolds suitable for regenerating small to large blood vessels, trachea, or esophagus. Textile technologies enable the fabrication of versatile multi-layer tubular structures and complex patterns.

Among different textile technologies, electrospinning has been widely used for developing tubular scaffolds owing to its relative simplicity and ease of control over the key process parameter. Despite the benefits, electrospun structures often lack mechanical strength and porosity due to dense fiber spacing which can impact cell migration. Moreover, electrospinning is limited to fabricating small-diameter layered tubes rather than 3D fabric structures. Compared to nonwovens, yarn-based textile techniques enable greater control over mechanical and micro-and macrostructural properties, for example, pore size and pore distribution. Knitted structures are superior in adapting to circumferential changes. An increase or decrease in stitch density controls circumferential elasticity and longitudinal strength. Similarly, braids are elastic structures but with higher axial strength. Nonetheless, the high burst strength of knitted and braided tubes possibly causes fluid leakage, which is fatal for in vivo applications.

A promising approach is hybrid tubular designs, for example, knit or braid reinforced electrospun scaffolds. The yarn-based design improves the mechanical properties while the electrospun nanofibers enhance biocompatibility and cell response. The highly hierarchical nanotextile features improved mechanical compliance and equally promote biological interaction. Hybrid scaffold designs, for example, multi-layer structures (nanofiber coated textile tubes; hydrogel coated textiles) improve mechanical properties and biocompatibility equally. Additionally, these strategies overcome fluid leakage issues and permeability requirements. The recent developments in nanoyarn engineering substantially enhance the performance of the scaffold. In particular, the development of pure or hybrid nanoyarn structures with sufficient mechanical properties for weaving, knitting, or braiding, demonstrates great potential in engineering different 3D tubular scaffolds. The highly hierarchical nanotextile

features improved mechanical compliance and equally promote biological interaction. Nevertheless, the low strength and limited length of pure nanoyarn challenge its application in textile engineering. Although electrospun nanoyarn opens a wide range of applications, it still needs further improvement in terms of productivity output and mechanical features.

Apart from the versatile techniques, originating from their ability to create tissue-specific architectures and biomimetic the natural tubular structure, an understanding of the structural and biomechanical properties of the native tubular tissue is crucial. Although the multicellular wall structure of arteries and their unique mechanical properties (anisotropy, non-linearity, compliance, viscoelasticity) have been extensively researched, the consideration of all these characteristics mostly remains incompatible.

With the growing interest in tubular textile-based scaffolds, significant advances were made, illustrating the potential in this research field. The exponential increase in this area has broadened the understanding of how key principles of textile engineering (fiber, yarn, fabric) control and guide tissue formation. However, studies in this field limited scaffold design to plain fabric patterns, ignoring the wide variety of more advanced textile designs and their unique features. Moreover, the sole consideration of the scaffold material is insufficient for achieving successful outcomes.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords

braiding, fiber-based techniques, knitting, textile technology, tubular tissue engineering, weaving, yarn-based scaffolds

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