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Research review paper

Weaving for heart valve tissue engineering

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ABSTRACT

Weaving is a resourceful technology which offers a large selection of solutions that are readily adaptable for tissue engineering (TE) of artificial heart valves (HV). The different ways that the yarns are interlaced in this technique could be used to produce complex architectures, such as the three-layer architecture of the leaflets. Once the assembly is complete, growth of cells in the scaffold would occur in the orientation of the yarn, enabling the deposition of extra cellular matrixes proteins in an oriented manner. Weaving technology is a rapidly evolving field that, first, needs to be understood, and then explored by tissue engineers, so that it could be used to create efficient scaffolds. Similarly, the textile engineers need to gain a basic understanding of key structural and mechanical aspects of the heart valve. The aim of this review is to provide the platform for joining these two fields and to enable cooperative research efforts. Moreover, examples of woven medical products and patents as well as related publication are discussed in this review, nevertheless due to the large, and continuously growing volume of data, only the aspects strictly associated with HVTE lay in the scope of this paper.

1. Concept of smart scaffold and general characteristic of aortic heart valve

The aortic heart valve (AHV, see Fig. 1) is responsible for the unidirectional blood flow between the left ventricle and the aorta. It is a highly demanding environment, where the valve opens over 100,000 times each day is subjected to shear stress, bending forces, strain and loading forces (Yacoub & Takkenberg, 2005; Dohmen & Konertz, 2009). While most humans will have normal function of the valve, some will need AHV replacement surgery, due to several problems, such as aortic insufficiency, stenosis and aortic aneurysm. It is estimated that the annual number of patients requiring HV replacement in 2050 will be 850,000 worldwide (Yacoub & Takkenberg, 2005).

Commonly, the valve is replaced with a mechanical or bioprosthetic valve. The problem with these substitutes is that, for mechanical valves, the patient will need to commit to a lifetime of anticoagulants and bioprosthetic valves are limited by tissue degradation. An alternative that has been widely studied is the use of a biodegradable scaffold that has a mechanical integrity close to the aortic valve, where cells can grow and remodel the structure and that the final product will be a functional autologous aortic valve (Dohmen & Konertz, 2009; Dohmen, 2012).

This scaffold must be able to mimic the complexity of the AHV. One important characteristic of the AHV is its ability to interact with its constituent parts through passive and active communication and adjust the appropriate response to the environment (Yacoub et al., 1999). A passive communication can be seen on the changes in the sinuses upon establishing the vortices that ensure valve closure, preventing blood backflow, and coronary flow during systole (Chester et al., 2014). During the cardiac cycle, active communication occurs, when the cusp, annulus, sinus and sinotubular junction change in shape, size and stiffness. An examples of active communication are changes of shape, size and stiffness of cusp, annulus, sinus, sinotubular junction, during specific parts of the cardiac cycle (Arjunon et al., 2013).

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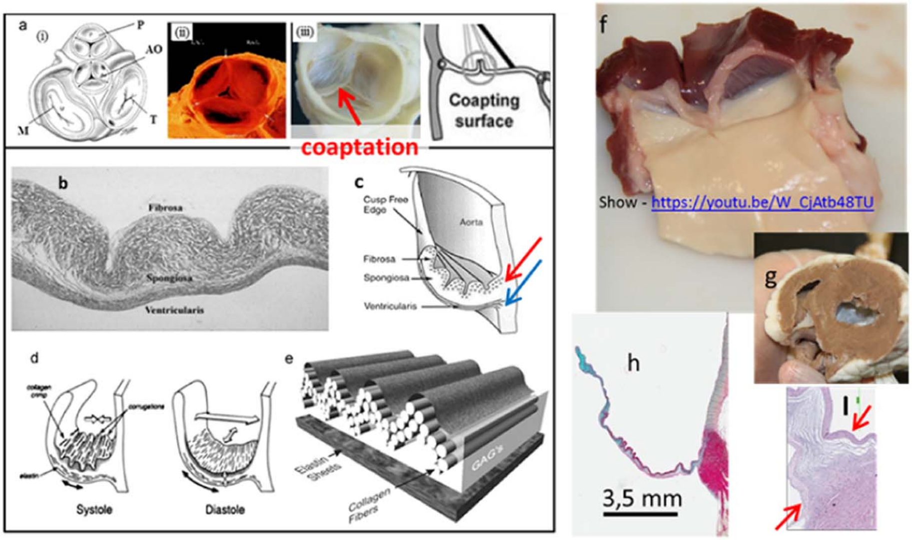

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Fig. 1. The basic structural/functional aspects of the heart valve (HV). Schematics of the 2D position of the four valves on valvular basal plane of the heart where P: pulmonary valve, AO: aortic valve, M: mitral valve, and T: tricuspid valve (a-i), porcine pulmonary heart valve (a-ii), decellularized porcine aortic heart valve (a-iii). Leaflet consist of three distinguishable layers: fibrosa, spongiosa and ventricularis (b). Each layer contains specifically oriented fibers, red arrow indicates circumferentially oriented fibers of collagen, blue arrow indicates radially oriented fibers of elastin (c).The types (collagen, fibronectin, elastin and others) and arrangement of fibers are responsible for the function of the valve (opening & closing) (d, e). The fibrosa layer is a continuation of aorta and ventricularis is a continuation of the ventricular chamber. (f) The view of sheep aortic valve from ventricular side, after dissecting the heart (g). The leaflets contain glycosaminoglycans (GAGs, mainly in spongiosa, blue color), which works as a lubricant between layers and a shock absorber (h). The hinge area (in-between the arrows) histology highlights the importance of fiber arrangement (I). The cells are housed and maintained in a highly organized network of fibers. Reprinted with permission from (Hasan et al., 2014). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Thus, to achieve this complexity, the substitutes must host cells that will be able to be expressed and produce extracellular matrix that will function in a similar way to the native valve. Despite the currently reported progress on restoring function of organs using transplanted human induced pluripotent stem cells (Imberti et al., 2015), delivering viable cells, derived from out of the patient's body is associated with to multiple risks (Vunjak-Novakovic et al., 2010). Therefore, the smart scaffold is the best alternative for clinically relevant Tissue Engineered Heart Valve (TEHV) (Zafar et al., 2015a; Yacoub, 2015).

The role of the scaffold is to provide a temporary 3-dimensional structure for cellular attachment, infiltration, and proliferation. The materials should possess biomimetic properties and should be highly porous, thereby facilitating cellular infiltration, stimulation of neo-tissue formation, and integration with native tissue (Tara et al., 2014).

The smart scaffold should be resorbable, non immunogenic, capable of attracting, housing and instructing cells to produce the particular phenotype (Yacoub, 2015). It must also reproduce the performance and mechanical properties of the native valve in the short and long term. Scaffolds based on synthetic polymers and biological scaffolds are the two major categories of scaffolds suitable for smart applications. The first category includes scaffolds made out of synthetic polymers (El-Sherbiny & Yacoub, 2013), decorated (with peptides (Li et al., 2013; Ji et al., 2013), antibody (Kang et al., 2013; Lim et al., 2011), aptamers (Esposito et al., 2014) and enzymes (Kalsi et al., 2002) in the way that enables attracting and instructing the host cells (either from surrounding tissue or form blood) to differentiate to a tissue specific phenotype. The second type of intelligent scaffolds is made out of decellularised organs, for example valves (Khan et al., 2014), decellularised non cross linked ECM (Zafar et al., 2015b), amniotic membrane (Hodde, 2002), and scaffolds made out of alginate manufactured from sea weed (Liberski et al., 2016a), or chitin/chitosan derived from shrimp and crabs shells (Muzzarelli, 2011).

The logic behind applying textile technologies to create grafts for HVTE is to utilize its advantages that have already showed up in a shape of textile medical vascular graft used widely in clinical practice. The major advantage of textile techniques is that they enable reproducing the anisotropic properties of the valve (Sohier et al., 2014; Hwang et al., 2009), therefore the textile-based scaffold would be able to have the required functionality and characteristic (see Fig. 2. In the area of tissue engineered vascular grafts various studies demonstrate the viability of these scaffolds (Thomas et al., 2013).

As target geometry of the aortic HV, tissue engineers use a simplified model of native valve (See Fig. 2 medium panel). The personalization of such model would require artistic skills of the computer graphic, who intuitively would draw the structure matching the target geometry. To perform the customization in the controllable, computing based manner, the parametric model of HV is required. This is not an easy task to accomplish since valve consists complex geometrical features including curvatures; nevertheless, the model was successfully generated and the output is shown in Fig. 2. By changing the parameters listed in the software's dialog-box, the model can be resized according to Magnetic resonance imaging (MRI) or Computed Tomography (CT) indication by personnel without any artistic inclinations. The model reflects the real shape of HV of a human body and can be easily adjusted to suit the various cases such as age and disease. The model is defined by numbers of parameters such as thicknesses, diameters and lengths of the tubes, height and depth of the sinuses. The remaining parameters are set as a factor of the above and are driven by them. This makes the parametric model flexible and at the same time, it reflects the shape of a human HV throughout the whole range of sizes and other variables. The additional parameter defines the opening of the leaflets. This feature allows for further analyzing the strength, fatigue and flow through the model. This helps to validate the HV grafts before weaving. Therefore, it shortens the production time, prevent from any inaccuracy and reduce the need and cost of physical prototypes.

2. Basics of weaving and its applications

2.1. Types of woven fabrics

Weaving is the process in which two sets of yarns are interlaced to lie at right angles to each other. These two sets consist of the warp ends (or ends) – threads that run along the length of the fabric – and the weft picks (or picks) – threads that run from selvedge to selvedge (see Fig. 3A). However, for more complex fabrics, such as three-dimensional and tri-axial fabrics, the yarns' categorization as ends and picks does not apply (Horrocks & Anand, 2000a).

Among textiles with interlaced yarns, the woven fabrics usually have higher strengths and greater stability (Horrocks & Anand, 2000a). Properties, such as thickness, strength, porosity, extensibility and durability, depend on the weave used and the thread spacing (number of threads per cm). The structures in woven fabrics can also be modified to achieve largely different properties in the weft and warp directions. The raw material used will also influence the overall properties of the final fabric. The critical parameters for yarns are the yarn count (or linear