Functional tissue-engineered human heart valves for systemic applications

Funtional tissue-engineered human heart valves for systemic applications

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Introduction

The capacity of growth and regeneration of tissue-engineered (TE) heart valves may overcome the limitations of contemporary heart valve prostheses. So far, the proof of principle has only been demonstrated in low pressure applications in lambs [1,2], leaving the demanding challenge to engineer valves from human cells suitable for systemic application.

Methods

Stented trileaflet heart valve scaffolds are fabricated from PGA/P4HB. The scaffolds are seeded with human saphenous vein cells using fibrin as a cell carrier [3] and placed in custom-built bioreactors systems, referred to as the Diastolic Pulse Duplicator (DPD; Fig. 1).

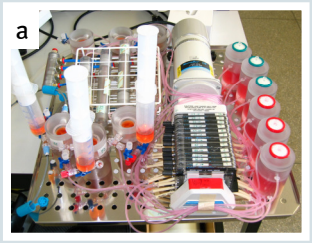

Figure 1 *Photograph of six DPDs in use simultaneously (a) and a schematic drawing of its components (b).*

The valves are conditioned by mimicking solely the diastolic phase of the cardiac cycle [4]. Tissue composition, strength, and functionality are analyzed after four weeks of culture.

Results

The stented heart valves are intact after culture (Fig. 2) and show dense and homogeneous tissue formation throughout the full thickness of the leaflet (Fig. 3). The tissue consists for a large part of collagen, the load-bearing protein in tissues (Fig. 3 and 4).

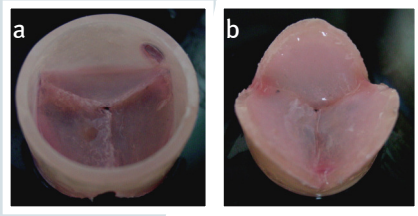

Figure 2 *Photographs of TE valves after 4 weeks of culture: (a) view from aortic side, and (b) view from ventricular side.*

Anisotropic behavior is observed with larger stiffness in the circumferential direction compared to the radial direction. This anisotropic behavior is considered to contribute to the functionality of the leaflets to a large extent. The mechanical properties of the TE human heart valves show high resemblance to native human aortic valve leaflets, with minimal contribution of the initial scaffold (Fig. 5).

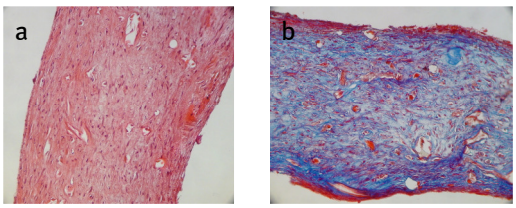

Figure 3 *Tissue composition throughout the thickness of a leaflet. (a) H&E staining for general tissue morphology, and (b) Masson Trichrome staining for collagen (100X magnification).*

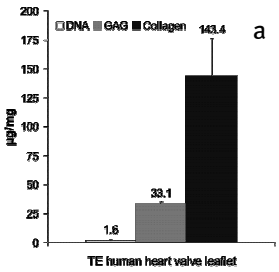

Figure 4 *Tissue composition of a TE human heart valve leaflet.*

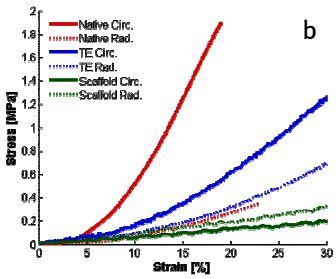

Figure 5 *Mechanical behavior of TE human heart valve leaflets, native human heart valve leaflets (data provided by [5]), and the initial scaffold.*

The TE human valves show proper opening and closing behavior when exposed to physiologic aortic valve flow conditions (Fig. 6). Coaptation is, however, minimal and prolapse (*) of the leaflets is observed after several hours of testing.

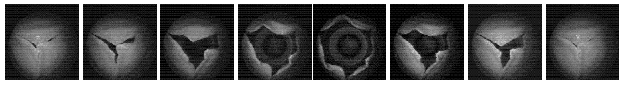

Figure 6 *Opening and closing behavior of a TE human heart valve when exposed to human aortic valve flow conditions.*

Discussion

Tissue-engineered human heart valves, seeded using fibrin as a cell carrier and conditioned in the DPD, show excellent tissue properties with large amounts of collagen present throughout the full thickness of the leaflets. Mechanical properties approximate those of native human aortic valve leaflets. This study demonstrates the feasibility of tissue engineering human heart valves suitable for systemic application.

References

[1] Hoerstrup SP et al. Circulation 2000;102:III44-III49.
[2] Sodian R et al. Circulation 2000;102:III22-III29.
[3] Mol A et al. Biomater. 2005;26:3113-3121.
[4] Mol A et al. Ann. Biomed. Eng. 2005 – in press.
[5] Stradins P et al. Eur. J. Cardiothorac. Surg. 2004;26:634-639.