Tissue engineering of functional heart valves: A strain-based approach

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Introduction
Mechanical conditioning in a bioreactor is a prerequisite for functional tissue engineering of heart valves to enhance tissue formation [1]. Large strains have shown to be a very important mechanical stimulus for human heart valve tissue equivalents [2]. The goal of this study is to develop a strain-based approach to tissue engineer human heart valves.

Materials and methods
Stented heart valve scaffolds were prepared from a non-woven PGA mesh, coated with P4HB [Fig. 1]. Human saphenous vein cells were seeded onto the scaffolds using fibrin as a cell carrier [3]. During tissue culturing, static strains are induced due to tissue contraction constrained by the stent. Additional strains are induced by applying a dynamic pressure difference over the valve in custom-built bioreactor systems [Fig. 2].

Tissue formation and mechanical properties were analyzed after 4 weeks of culturing in non-loaded control tissue strips, valves exposed to static strain, and valves exposed to additional dynamic strains.

Results
The outcome after 4 weeks of culturing is shown in Fig. 3. Histology shows a compact tissue structure in the valves and more loosely organized tissue in the strips [Fig. 4]. Abundant collagen formation can be identified in the valves (stained blue).

Discussion
Straining of the developing heart valve tissue during culturing represents a promising approach towards living human aortic valve replacements. Strained valves contain more tissue, which is stronger and stiffer compared to tissue cultured without strains. Dynamic strains, in addition to static strains induced by the stent (∼10%), does not further improve tissue formation and mechanical properties, but represents a useful tool to obtain better organized and more homogeneous tissue.

References