

## **Tissue-engineered human heart valves: a strain-based approach**

**A. Mol<sup>1,2</sup>, C.V.C. Bouten<sup>1</sup>, M.C.M. Rutten<sup>1</sup>, S. Neuenschwander<sup>2</sup>,  
N.J.B. Driessen<sup>1</sup>, S.P. Hoerstrup<sup>2</sup>, F.P.T. Baaijens<sup>1</sup>**

- <sup>1</sup> Eindhoven University of Technology, Department of Biomedical Engineering, P.O. Box 513, 5600 MB, Eindhoven, the Netherlands
- <sup>2</sup> University Hospital Zürich, Clinic for Cardiovascular Surgery, Raemistrasse 100, CH-8091, Zürich, Switzerland

Mechanical conditioning in a bioreactor profoundly affects the composition and structure, and hence mechanical properties, of tissue engineered heart valves. Up to now, the bioreactors developed for culturing heart valves are flow-based and mimic normal heart valve opening and closing behavior. Although enhancing tissue formation and mechanical properties, the heart valves obtained with this method of conditioning are insufficient to serve as an aortic heart valve replacement. As tissue development has been shown to be largely influenced by large dynamic strains during culturing, a strain-based approach for tissue engineering of heart valves has been developed.

In a novel bioreactor system – the Pressurizer – developing heart valves are exposed to large dynamic strains by applying a dynamic pressure difference over the leaflets. The flow is kept to a minimum, serving only as a perfusion system, supplying the developing tissue with fresh nutrients. Stented heart valves were engineered based on PGA/P4HB trileaflet scaffolds seeded with cells isolated from the human saphenous vein. Tissue compaction is constrained by the stent, inducing increasing pre-strain in the tissue with culture time. In order to get insight into the strain distribution in the valve leaflets, local tissue strains are estimated using a finite element model incorporating the mechanical properties of the neo-tissue.

The strain-based approach has shown to render tissue engineered valves with superior tissue formation and organization, and hence improved mechanical properties as compared to non-strained tissue equivalents. Currently, the pressurizer is applied to engineer stented valves, but the system is very well suitable for stentless valves as well. For the latter valves, which develop less pre-strain as compared to stented valves, tissue culture under dynamic straining will be of even more importance. In conclusion, the strain-based approach using the pressurizer system is opening new possibilities to further improve tissue properties of human tissue engineered heart valves in order to serve as aortic heart valve replacements.