

P41

Towards an optimal mechanical conditioning strategy for tissue engineered heart valves

Mirjam Rubbens¹, Anita Mol¹, Ralf Boerboom¹, Ruud Bank², Frank Baaijens¹, Carlijn Bouten¹

¹*Eindhoven University of Technology, Eindhoven, Netherlands*, ²*TNO Quality of Life, Leiden, Netherlands*

Objectives:

Tissue engineered heart valves often lack sufficient amounts of functionally organized collagen fibres and consequently do not meet in vivo mechanical demands. Various mechanical conditioning protocols were applied to engineered human heart valve tissue to optimize collagen architecture (collagen amount, cross-links, and orientation) and thus improve mechanical properties.

Method:

Rectangular strips (35x5x1 mm) of PGA/P4HB were seeded with human venous myofibroblasts and constrained at the outer ends (0% static strain). Different uniaxial straining protocols were applied, including continuous cyclic straining (4%, 1Hz, for 10 days and 4 weeks) and intermittent cyclic straining (3h on/off, 4%, 1Hz, for 2, 3, and 4 weeks).

Results:

Compared to constrained controls, continuous cyclic straining downregulated collagen expression, but enhanced cross-link density and collagen remodelling after 10 days of culture. Importantly, the enhanced cross-link density due to cyclic straining correlated with improved mechanical properties after 4 weeks of culture. Intermittent straining resulted in increased collagen production, cross-link densities, collagen organization and mechanical properties at faster rates, as compared to constrained controls.

Conclusions:

Cyclic straining is relevant to enhance cross-link formation and collagen remodelling, but continuous straining is unfavourable for collagen production. Therefore, intermittent straining is the most promising mechanical conditioning protocol to create stronger tissues in shorter culture periods. These results are of utmost importance for heart valve tissue engineering, where insufficient mechanical properties are the main limiting factor for systemic application. Current studies concentrate on optimizing intermittent straining protocols and/or combination with other cues to further improve mechanical properties.