

C56. Optimization Of The Collagen Architecture In Engineered Human Heart Valve Tissue

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OBJECTIVES: The load-bearing capacity of heart valves is mainly determined by its collagen architecture (collagen amount, cross-links, and orientation). Thus, our protocols for tissue-engineered heart valves aim to optimize and control this collagen architecture using mechanical conditioning strategies. Here, the relevance of different straining-modes for use in heart valve tissue engineering is studied.

METHODS: A model system was developed that enables strictly controlled application of static, dynamic and alternated straining (3h on/off) to heart valve tissue strips consisting of fast degrading PGA-based scaffolds seeded with human vascular cells. Collagen amount, cross-links, and orientation were quantified using qPCR, HPLC, and 3D vital imaging using multiphoton microscopy combined with image analysis.

RESULTS: Continuous dynamic straining downregulated collagen expression compared to static controls but enhanced cross-link densities after 10 days of culture. Importantly, the enhanced cross-link density correlated with improved mechanical properties after 4 weeks of culture. Dynamic straining alternated with periods of rest improved and accelerated the alignment of the collagen fibers in the straining direction, as compared to statically cultured tissues.

CONCLUSIONS: Despite a lower collagen amount, the quality and structural integrity of the tissue is improved at a faster rate by dynamic straining via an increase in collagen cross-link densities and more aligned collagen fibers. Straining-mode dependent responses will allow balancing collagen and cross-link production and thus to fine-tune tissue properties with a well organized collagen network. This is of utmost importance for cardiovascular tissue engineering, where a functional load-bearing capacity is a prerequisite for in-vivo application.