Straining-mode dependent collagen remodeling in engineered heart valve tissue
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Introduction
Tissue engineered heart valves often lack sufficient amounts of functionally organized collagen fibers and consequently do not meet in vivo mechanical demands. To improve collagen remodeling, and hence mechanical properties, the effects of two modes of mechanical conditioning, being either static or dynamic, were quantified for several indices of collagen remodeling.

Material and methods
Rectangular strips (35x5x1 mm) of PGA/P4HB were seeded with human venous myofibroblasts and constrained at the outer ends (static strain). The effect of uniaxial dynamic straining (4%, 1Hz) (fig. A) was investigated on 1) the secretion of collagen remodeling markers for synthesis and degradation, differences in 2) collagen and 3) cross-links on gene expression and protein levels and 4) tissue mechanical properties.

Results
1) Dynamic conditioning enhanced both collagen synthesis and degradation compared to static conditioning (fig. 1).

2) Dynamic conditioning downregulated collagen mRNA expression and collagen content (fig. 2), but 3) enhanced both cross-link mRNA expression and content (fig. 3).

4) Dynamic conditioning for 4 weeks increased cross-link densities, correlated to higher moduli. No difference in the amount of collagen was found (fig. 4).

Conclusions
• Gene expression results correspond to protein data.
• Compared to static conditioning, dynamic conditioning resulted in:
  1) higher collagen remodeling activities, 2) lower collagen expression and content, but 3) enhanced collagen cross-link expression and density, correlated to 4) improved mechanical properties.
• Straining-mode dependent remodeling responses can be used to balance collagen and cross-link production and, thus, to fine-tune tissue mechanical properties via mechanical conditioning protocols.