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Tissue engineered heart valves develop native-like collagen architecture

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Introduction
To meet \textit{in vivo} demands, native heart valves have developed an inhomogenous and anisotropic collagen network [Fig 1].

Figure 1: The native collagen fiber architecture (left) has parallel bundles running from the commissures (green) towards a more branched circumferential network in the belly (red). Adapted from [1]. This is represented (right) by a narrow fiber distribution (high alignment) in the commissures and a wider distribution in the belly.

In tissue engineering we hypothesize that: \textit{mimicking hemodynamic loads in a bioreactor will result in native-like tissue development.}

Although this approach resulted in strong human tissue engineered heart valves (TEHV) [2] several questions remain:

• Do TEHV develop local native-like fiber architecture?
• Can we optimize protocols for this goal?

Results
TEHV (n=10) were cultured for 4 weeks using 3 different loading protocols. Indentation tests were performed in the belly and commissure region of each leaflet. In 7 out of 10 valves circumferential alignment ($0^\circ$) was found in the belly region and commissural fiber direction was between 0 and $45^\circ$. The exact commissural fiber direction varied between protocols.

Figure 3: Top left: loading protocols applied during culture. Top right & bottom row: Estimated fiber distributions demonstrate increasing fiber alignment with increasing load during culture.

In 5 out of 10 valves commissural alignment was higher (narrower distribution) than in the belly; the other 5 valves did not reveal differences. Interestingly overall fiber alignment increased with applied load [Fig 3], which is consistent with theoretical predictions [4].

Conclusions
• Yes, TEHV do develop native-like fiber architecture:
  – circumferential orientation in belly region ($0^\circ$)
  – orientation between 0 and $45^\circ$ in commissure region
• Yes, we can optimize protocols for this goal:
  – Increased loading leads to increased collagen alignment

References