Tissue engineered heart valves develop native-like collagen architecture

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Martijn Cox, Jeroen Kortsmit, Carlijn Bouten, Frank Baaijens

Eindhoven University of Technology, Department of Biomedical Engineering, The Netherlands

Introduction

To meet *in vivo* demands, native heart valves have developed an inhomogenous and anisotropic collagen network [Fig 1].

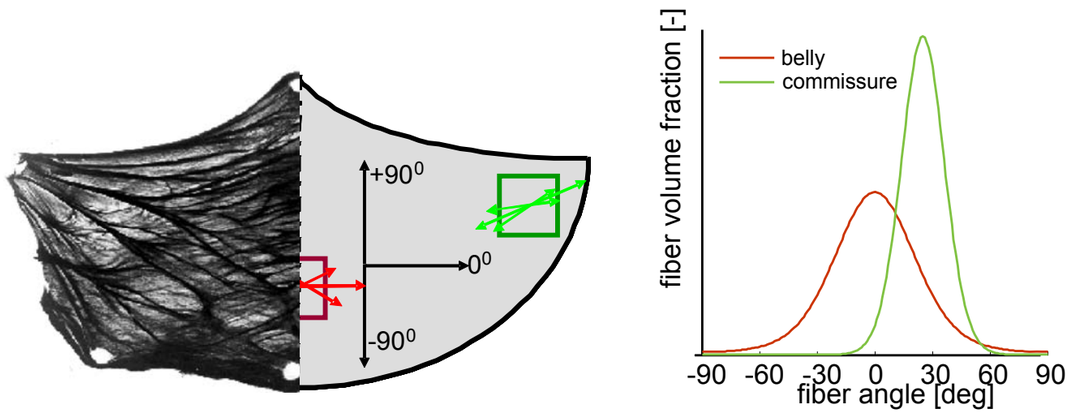

Figure 1: The native collagen fiber architecture (left) has parallel bundles running from the commissures (green) towards a more branched circumferential network in the belly (red). Adapted from [1]. This is represented (right) by a narrow fiber distribution (high alignment) in the commissures and a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

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

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

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

Method

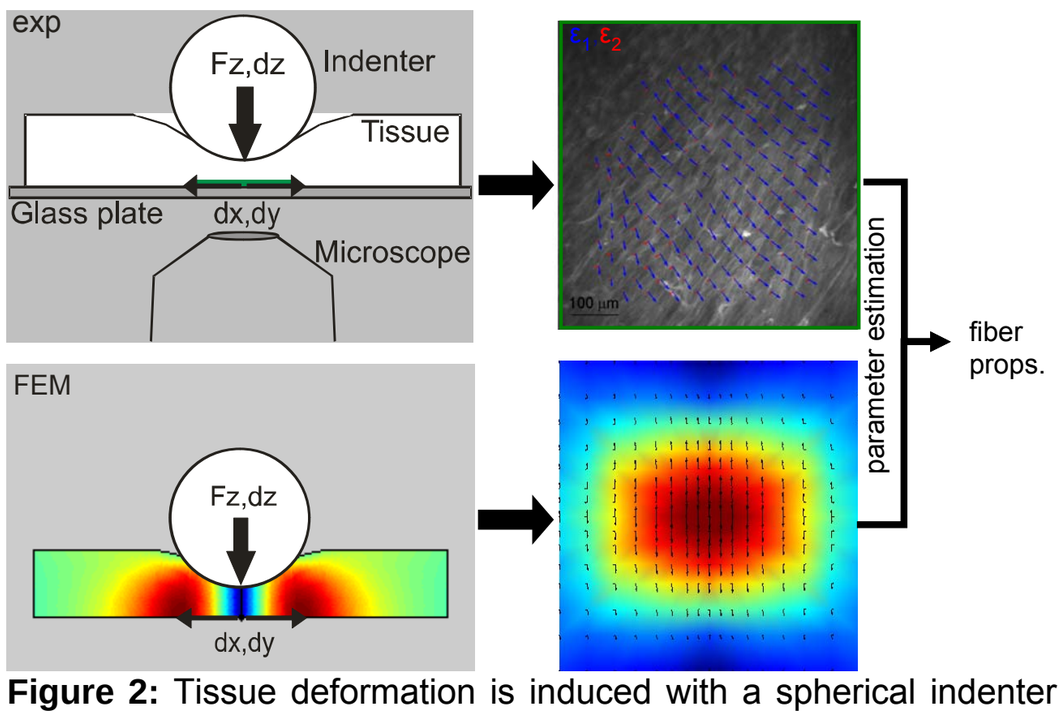

Figure 2: Tissue deformation is induced with a spherical indenter and measured using inverse confocal microscpoy. Digital Image Correlation shows that tissue deforms mainly perpendicular to the main fiber direction. An inverse Finite Element (FEM) analysis is used to estimate fiber distribution and mechanics [3].

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 (0º) was found in the belly region and commissural fiber direction was between 0 and 45º. The exact commissural fiber direction varied between protocols.

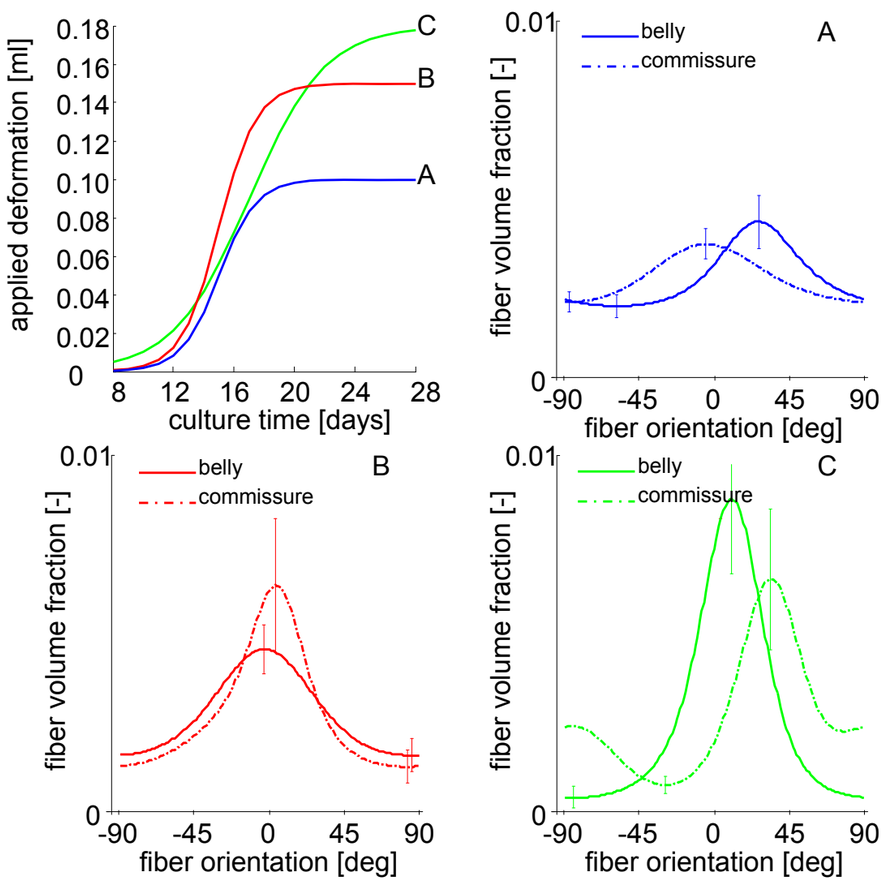

Figure 3: Top left: loading protocols applied during culture. Top right & bottom row: Estimated fiber distributions demonstrate increasing fiber alginment with increasing load during culture.

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 (0º)
  - orientation between 0 and 45º in commissure region
- **Yes, we can optimize protocols for this goal:**
  - Increased loading leads to increased collagen alignment

References

[1] Sauren AAHJ: *PhD Thesis*, *1981*
[2] Mol A et al.: *Circulation 114(I), 2006*
[3] Cox MAJ et al,: *JBiomech 41(2), 2008*
[4] Driessen NJB et al.: *BMMB 7, 2008*