The collagen organization in heart valves: a target for tissue engineered valves

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The collagen organization in heart valves
A target for tissue engineered valves

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Introduction
The main challenge in tissue engineering of heart valves is mimicking the complex structure of native tissue. This structure ensures the functional integrity of the valve under high-pressure conditions. Since collagen is the main load-bearing component in tissue, the aim in this study is to investigate the function-collagen structure relationship in native human and porcine heart valves.

Materials and Methods
Function
The mechanical properties of the valve leaflets (Young’s modulus (E), maximum stress and strain) were assessed by uniaxial tensile experiments in two directions.

Structure
Local collagen amount and the number of collagen cross-links were measured using reversed phase HPLC. Collagen fibril structure was analyzed in TEM images at different locations in the valve (fig.1). The correlation of collagen fibril thickness and tissue stress [1,2] was investigated using a numerical model of the heart valve [3] and TEM images.

Results and Discussion
Function

<table>
<thead>
<tr>
<th></th>
<th>E-modulus [MPa]</th>
<th>max. stress [MPa]</th>
<th>max. strain [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circumferential</td>
<td>20.9 ± 6.6</td>
<td>3.1 ± 1.7</td>
<td>21.6 ± 8.1</td>
</tr>
<tr>
<td>Radial</td>
<td>2.1 ± 1.1</td>
<td>0.45 ± 0.14</td>
<td>30.9 ± 9.8</td>
</tr>
</tbody>
</table>

Table 1. Mechanical properties averaged for three human heart valves.

Human heart valve leaflets clearly showed anisotropic properties. The values are within the range of the limited available data from literature [4].

Structure – Biochemical analysis

Human leaflets (age 47-53 years, n=6)

Porcine leaflets (age 6 months, n=3)

The relative collagen amount in human vs. porcine valves was significantly higher (p<0.05). Conversely, porcine valves showed more cross-links per triple helix than human valves. Furthermore, the inner segments (within red frame) of the porcine valve leaflets showed significantly more collagen compared to the outer segments. This was not observed in human valves (fig.2). The difference in local collagen distribution between human and porcine native valves might be age- or species-related.

Structure – Fibris

Porcine

Figure 3: a. Cauchy stress prediction of a heart valve leaflet under high pressure conditions [3]; b. cross-section of collagen fibrils at the fixed edge (blue star) and in the belly (red star) of a porcine valve leaflet.

Future Research
The differences in collagen structure found between porcine and human valves inspire to further investigate different age groups of both human and porcine valves. This will elucidate the pathways of collagen fibrillogenesis in the developing heart valve. Evaluation of the collagen structure-function relationship of a native human valve will be used to improve the design of tissue-engineered heart valves.

References