Modeling cell-mediated compaction and collagen remodeling in tissue-engineered heart valves

Citation for published version (APA):

Document status and date:
Published: 01/01/2013

Document Version:
Accepted manuscript including changes made at the peer-review stage

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher’s website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

Link to publication

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license above, please follow below link for the End User Agreement:
www.tue.nl/taverne

Take down policy
If you believe that this document breaches copyright please contact us at:
openaccess@tue.nl
providing details and we will investigate your claim.

Download date: 18. Oct. 2019
Modeling cell-mediated compaction and collagen remodeling in tissue-engineered heart valves

Sandra Loerakker, Christine Obbink-Huizer, Frank P.T. Baaijens

Introduction
When tissue-engineered heart valves (TEHVs) are implanted in the pulmonary position, the in vivo functionality is compromised by cell-mediated leaflet compaction/retraction (Fig. 1), which leads to valvular insufficiency if the blood pressure is too low to cancel out retraction. It is hypothesized that the diastolic aortic pressure is sufficiently high to counteract the cell-mediated leaflet retraction.

Fig. 1: TEHVs remodel after implantation such that severe leaflet retraction occurs (indicated by the arrows).

Objective
The goal of this study was to develop a theoretical framework and finite element (FE) model to predict tissue compaction/retraction and collagen remodeling in TEHVs, to answer the following question:

Are the pulmonary (2 kPa) and aortic (10 kPa) diastolic pressure high enough to counteract leaflet retraction in TEHVs?

Methods
Compaction was modeled by including contractile stresses exerted by the cells [1] and cell-mediated crimp of the collagen fibers (Fig. 2). Collagen remodeling consisted of strain-dependent degradation and oriented production [2].

For validation, the model was first applied to simulate compaction and collagen remodeling in engineered strips, where compaction and collagen alignment have been quantified. Next, remodeling of TEHVs was simulated under applied pressures of 0, 2, and 10 kPa.

Results
Tissue-engineered strips (validation)
Rectangular tissue-engineered constructs compact half in width and show a strong collagen alignment in the constrained direction (Fig. 3) [3, 4]. The model results correspond with the experimental results.

Fig. 3: Tissue compaction and collagen alignment in strips observed from experiments (top) and predicted by the FE model (bottom).

TEHVs remodeling at different pressure levels
At aortic pressure, the model indeed predicts that cell traction and collagen remodeling result in valvular insufficiency (Fig. 4). At aortic pressure, retraction is sufficiently counteracted by the blood pressure to ensure full closure of the valve.

Fig. 4: Initial geometry (left) of TEHVs and their loaded configuration (middle and right) after remodeling at different pressures.

Discussion
The FE model successfully predicted compaction and collagen remodeling in engineered strips. For TEHVs, the model predicted a decrease of the leaflet retraction with the applied pressure. However, complete valve closure was only present at aortic pressure conditions, which may explain the regurgitation issues in pre-clinical studies where TEHVs are implanted in the pulmonary position.

References