Deformation controlled load application in heart valve tissue-engineering

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Introduction

Mechanical behavior of tissue-engineered heart valves still needs improvement when native aortic valves are considered as a benchmark [1]. Although it is known that cyclic straining enhances tissue formation, optimal loading protocols have not been defined yet.

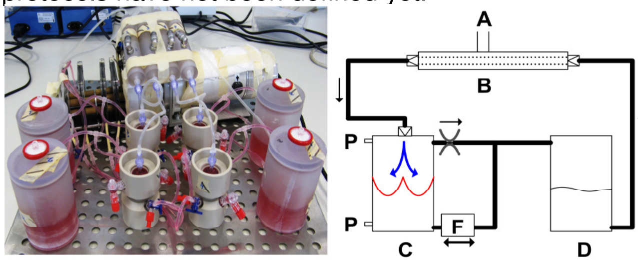

Figure 1: (a) Picture of 4 bioreactor systems. (b) Schematic drawing of a single bioreactor system, consisting of a pneumatic-air valve (A), a pulsatile pump (B), a bioreactor (C), including two pressure sensors (P) and a flow sensor (F), and a medium container (D).

To study the effect of mechanical conditioning on tissue development, it is desired to monitor and control induced deformations during load application.

Objective

To develop a bioreactor system for heart valve culture in which leaflet deformation is assessed and controlled in real time and non-invasively.

Materials & Methods

A combined experimental-numerical approach [2] was developed to assess volumetric and local leaflet deformation of the cultured heart valve in diastolic configuration (Fig. 1).

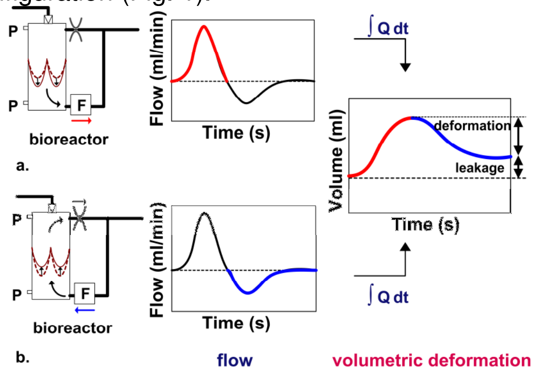

Figure 2: Flow-based deformation measurement principle. (a) A pressure difference over the heart valve causes the leaflets to bulge down; fluid exits the bioreactor (in red). (b) After deformation, the leaflets return to their undeformed state; fluid reenters the bioreactor (in blue). By time-integration of the flow signals, volumetric deformation is distinguished from leakage.

Volumetric deformation of the heart valve was measured using a non-contact measurement method based on flow monitoring (Fig. 2).

A numerical model was employed to relate volumetric deformation to local tissue strains in the valve leaflets. This approach was further developed and a PID controller to regulate deformation was incorporated into the bioreactor system.

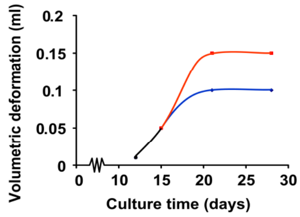

Figure 3: The protocols applied to the tissue-engineered heart valves.

To evaluate the functionality of the bioreactor system, 8 heart valves was tissue-engineered in 2 experiments. In each experiment 4 valves (A, B, C and D) were cultured by applying 2 different conditioning protocols (Fig. 3).

Results & Discussion

Good correspondence between the measured and the prescribed deformation values was found in both experiments (Fig. 4a ,b). Mean relative error values of all valves did not exceed 5%. However, controlled load application was not possible for heart valves having leak flows larger than ~10 ml/min (Fig. 4c,d).

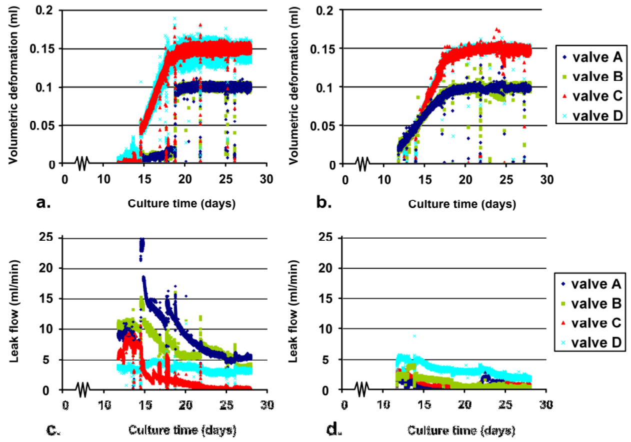

Figure 4: Measured volumetric deformation values (a, b) and leak flows (c, d) of tissue-engineered heart valves, given as a function of the culture time for (a, c) experiment I and (b, d) experiment II.

Conclusion

This bioreactor system has promising possibilities to systematically elucidate the effects of temporal loading patterns on tissue properties, and to develop an optimal conditioning protocol for tissue-engineering of aortic heart valves.

References

1.Mol A et al., Circulation 2006; 114(19):152-158.

2. Kortsmit et al., Submitted for publication.

/ department of biomedical engineering