


ESR 8

Project title and research strand:	Bio-based fibre-reinforced aortic heart valve. Strand 2: Fibres for medical application.	
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Abstract

Current heart valve replacements meet only partially the clinical demands for patients in need of such a device. Low functionality span, calcification, hemocompatibility issues, and in particular, the need of life-long surgeries for pediatric patients are commonly encountered issues. Therefore, there is a pressing need for advanced replacement solutions. In this study, we tackle this necessity by designing aortic heart valves endowed with customized fiber reinforcements and hydrogel matrix, both purely fabricated from native-like silk fibroin. To predict the mechanical behavior of these innovative scaffolds, a mathematical model is employed, utilizing the properties of the scaffolds' constituent materials, and experimentally validated through tensile testing. Valve hemodynamics of biomimetic rational-designed configurations were thoroughly assessed mechanically, and hemodynamically in accordance to ISO 5840 guidelines. Valves demonstrated compliant acute hemodynamic performance under aortic, as well as favorable biocompatibility based on in vitro cytocompatibility studies. The developed silk fibroin-based aortic heart valve shows promise as a novel replacement solution to address the limitations of current surgical standards.

BIOMIMETIC AORTIC HEART VALVE MADE OF NATIVE-LIKE SILK FIBROIN FOR IN-SITU TISSUE ENGINEERING

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INTRODUCTION

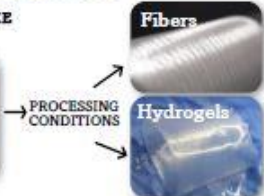


Valvular disease globally affects millions of patients. Issues like stenosis and regurgitation impairs proper valve function (1). Valvular replacement is most often seen as treatment of choice. However no commercially available substitute is regarded as an ideal solution. Tissue

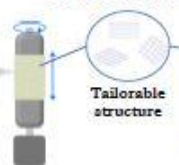
engineering offers promise, focusing on relying in the own's body regeneration capabilities. These implants must ensure full functionality and stability at the time of implantation. Silk fibroin emerges as a potential solution due to its biological compliance and mechanical strength. This study explores using native-like silk fibroin (NLSF) scaffolds for aortic valve replacement, evaluating hemodynamic functionality, mechanical properties, and biological response for clinical suitability

RESULTS AND DISCUSSION

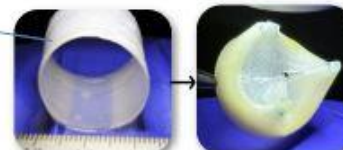
LIQUID NATIVE-LIKE SILK FIBROIN



COMPOSITE DEVELOPMENT



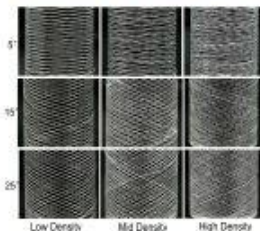
AORTIC VALVE REPLACEMENT



- ✓ Biomimetic mechanical properties
- ✓ Withstands autoclave sterilization

Figure 1. From the NLSF solution developed by Spintex Engineering, different processing conditions lead to different material forms. From NLSF fibers and hydrogels, using bespoke methodology inspired by filament winding techniques, a fiber reinforced composite was produced, with adaptable reinforcement structure. This tubular structure was developed into an aortic heart valve implant, using a polymeric stent.

Tuning of fiber structure



The filament winding fabrication technique developed allows for high levels of accuracy and repeatability. The composites' rule of mixture can be used for the prediction of mechanical of the scaffold to be fabricated.

Figure 2. Tubular scaffold and various fiber pattern structures, achieved by adapting the rotational and translational speeds of the fabrication mandrel

Biomimetic Properties

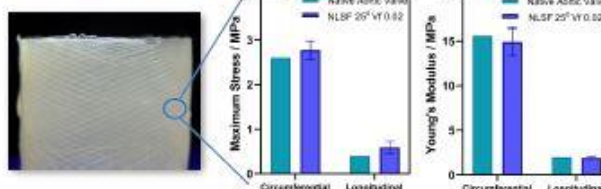


Figure 3. Tensile test values for maximum strength and Young's Modulus of scaffold, fabricated with rule of mixtures prediction, and native aortic valve (2).

Acute Hemodynamic Assessment

All measured values are compliant with ISO 5840 guidelines for a 23 mm diameter valve., with regurgitation factor of $9 \pm 0.06\%$ and EOA of $2.35 \pm 0.06 \text{ cm}^2$. Mean transvalvular pressure gradients were adequately small.

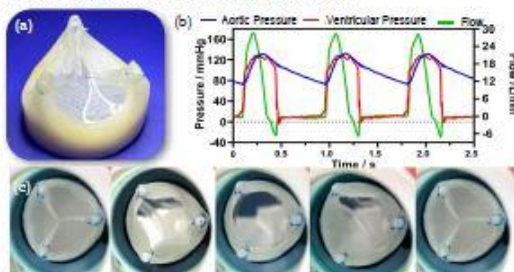
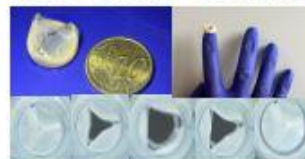


Figure 4. (a) Valve assembly (b) Pressure and flow measurements during flow loop assessment. (c) Opening and closing under aortic conditions.

Proof of concept – pediatrics patients



A 14 mm diameter valve was fabricated and acutely assessed at pediatric aortic conditions (150 bpm and 1 L/min) cardiac output, demonstrating good valve opening and closure behavior.

CONCLUSIONS

The methodologies presented here demonstrated the fabrication of native-like silk fibroin scaffolds with native-like tunable mechanical properties. The fashioned valve presented great hemodynamic behavior at aortic conditions, demonstrating the potential of this manufacturing methodology for an aortic heart valve implant.

Acknowledgements

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References

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