ELECTROSPUN SILK SCAFFOLDS TO MIMIC ARTIFICIAL BLOOD VESSELS – HEALTHY AND OBSTRUCTED

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Introduction

In vitro models of cardiovascular disease serve as invaluable tools for unraveling disease mechanisms, evaluating new therapies, and probing physiological phenomena. A notable limitation of phantoms used in current models lies in their inherent rigidity and cytotoxicity, hindering the exploration of accurate hemodynamics and cell-to-cell interactions crucial in human physiology [1]. Integrating natural polymers like silk as the primary constituent in phantom construction offers a promising solution to this challenge. By leveraging silk's inherent compliance and biocompatibility, we can create biological *in vitro* models that more authentically replicate vessel wall properties, facilitating the investigation of essential cell interactions [2]. This project aims to develop silk-based artificial healthy and obstructed blood vessels as more physiologically relevant phantoms for *in vitro* testing of cardiac devices and pharmaceutical testing.

Methods

Silk-based blood vessel (SBBV) was fabricated by electrospinning a solution of silk [3] (8% w/v) and polyethylene oxide (5% w/v) into fibrous, porous tubular SBBV. Hydrogel-coated electrospun silk scaffolds (HCESS) were created by rotating the SBBVs in a silk hydrogel precursor solution (8% silk, 0.05mM/5mM ruthenium/SPS) and photocrosslinking under visible light for 2.5 minutes. Tensile testing of the SBBVs was conducted on day 1 and 7 of incubation in PBS. Coronary artery smooth muscle cells and NIH3T3 fibroblasts were seeded on flat ⍀5mm SBBVs samples to assess cell interactions. Tensile mechanical properties of silk hydrogels (2-6%) were tested to assess their utility in mimicking the mechanical properties of atherosclerotic plaque.

Results and Discussion

SBBV has been shown to have the modulus of atherosclerotic coronary vessels [Figure 1], but it is difficult to seed cells on porous materials under flow conditions. HCESS addresses this by seeding the vessel walls with hydrogels that support cell encapsulation and do not change the mechanical properties of the vessel.
The stiffness of the hydrogel layer can be fine-tuned through the silk concentration within the hydrogel [4]. More optimization is still required to achieve healthy artery mechanical values.

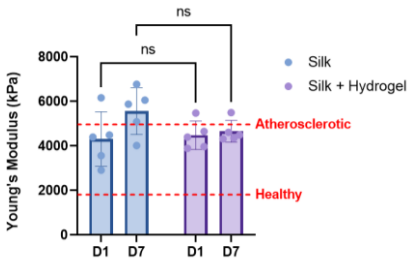

Figure 1: Young's Modulus Plot comparing electrospun silk scaffold with hydrogel-coated electrospun silk scaffolds showing no significant difference between the scaffolds at Day 1 incubation in PBS and Day 7 incubation in PBS. Stiffness of atherosclerotic coronary arteries and healthy coronary arteries were used as comparisons [5].

Hydrogels can also be used to create obstructions in the lumen, so flow through obstructed vessels can also be analyzed. The 3% silk hydrogels displayed similar mechanical properties to the fibrotic tissue in coronary plaques, and thus can be used as an obstructive mimic within the vessel. Validation of the hemodynamics experienced within the obstructed and non-obstructed vessels was done against computational fluid dynamic (CFD) studies and produced similar fractional flow reserve (FFR) and flow values.

Conclusion

Integrating silk-based scaffolds into cardiovascular *in vitro* models addresses rigidity limitations, allowing for more accurate replication of vessel properties and cell interactions. HCESS exhibits promising vessel compliance and support for cell attachment. While further optimization is needed, validation against CFD confirms their utility in mimicking physiological conditions.

References

1. Kainz, W, et al. IEE Tran. Radiat. Plasma. Med. Sci. 2019 Jan; 3(1): 1-23
2. Cui, X et al. Advanced Materials, 2020 Feb; 9(4):
3. Filipe C.E. et al. J Am Coll Cardiol Basic Trans Science. 2018 Feb, 3(1) 38-53
4. Hasturk,O. Biomaterials, 2020; 232
5. Karimi, A. Mater. Sci. Eng C. Mater. Biol. Appl. 2013 Jul. 1;33(5); 2550-4.