Tuning Bending Stiffness in Elastomeric Electrospun Scaffolds for Heart Valve Tissue Engineering

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Statement of Purpose: Biodegradable thermoplastic elastomers are attractive for application in cardiovascular tissue construct development due to their amenability to a wide variety of processing methods and the property tuning that can be achieved through processes such as electrospinning. For the function of heart valve leaflet tissues bending stiffness is a key mechanical property, yet control of this parameter has been largely neglected in the electrospinning literature. Specifically, sufficiently low bending stiffness is critical to the success of any proposed tissue engineered heart valve replacement. This study evaluated the effect of processing variables on the microstructure and bending mechanics of electrospun biodegradable polyurethane scaffolds. Further evaluation was performed to measure in-plane mechanical response in conjunction with bending stiffness The results of these studies could be utilized to optimize the mechanical response of tissue engineered heart valve constructs.

Methods: Electrospun constructs were fabricated using poly(ester urethane)urea (PEUU) in a manner similar to that reported previously [1]. A target collection mandrel was rotated at a tangential velocity of 8 cm/s and rastered at 0.3, 1.5, 3.0, or 30 cm/s along its rotational axis to putatively control scaffold architecture and bending mechanics. For further control a two-component fiber population was generated by concurrently electrospinning poly(ethylene oxide) (PEO, 900k MW) onto the target mandrel from a nozzle oriented on the opposite side of the mandrel from the PEUU nozzle. The PEO fiber population was dissolved from the formed scaffold by soaking for 3h in distilled water prior to mechanical testing.

Electrospun constructs were mechanically tested using previously defined procedures for biaxial mechanical testing [2] and three-point bending [3]. Custom structural analysis [4] was performed on electron micrographs of the scaffolds to elucidate relationships between construct microstructure and mechanical behavior.

Results: Increasing the collection mandrel translational velocity during fabrication resulted in a lower density of scaffold fiber intersections, without any significant change in fiber orientation. Interestingly, constructs that possessed lower fiber intersection densities were associated with stiffer responses to bending. (**Figure**) Further, scaffolds where the PEUU fiber network structure was interrupted by the dissolution of PEO fibers exhibited a lower bending modulus (15 vs. 20 MPa, $p<0.05$) despite the use of identical rotational and translational velocities for fiber collection.

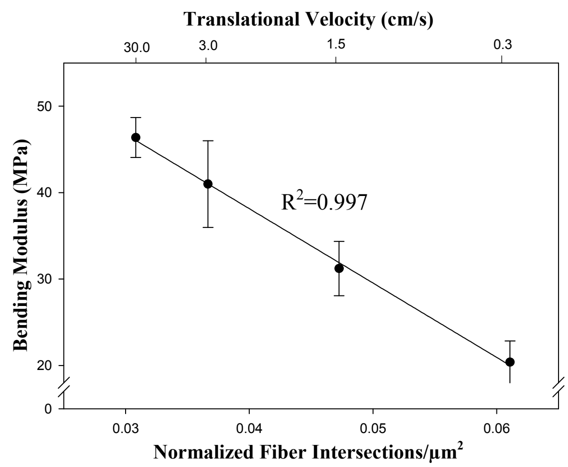

Figure. Bending modulus is inversely related to scaffold fiber intersection density and directly related to mandrel rastering speed.

Conclusions: In this work we describe, for the first time, the flexural mechanical properties of electrospun tissue engineering constructs, and how they can be tuned by altering fabrication conditions, including the utilization of a sacrificial fiber population to putatively disrupt PEUU fiber connections. As described previously [1], high mandrel translational velocities were associated with the distinct microstructural change of decreased fiber intersection densities. Further, the lowest rastering speed studied was also associated with high levels of in-plane mechanical anisotropy reminiscent of valvular tissue biaxial mechanical properties [1]. This observed trend was unexpected and outlines the need for further research, and development of a structural deterministic model to explain the full mechanical response of such constructs.

In summary, the insight gained from the described approach to relate processing parameters to microstructure and critical mechanical parameters could have immediate applications in developing more successful tissue engineering constructs for heart valve replacement.

References:

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