Development of Biodegradable Polyurethane-ureas as Gradient Scaffolds for Ligament and Tendon Repair

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Statement of Purpose: Current limitations of existing rotator cuff reconstruction strategies have generated significant interest in the development of tissue engineered tendons. Although many biomaterial scaffolds show promise as tendon grafts, current designs lack the complexity and mechanical properties of native tendons. Specifically, these scaffolds fail to mimic the innate transition of mechanical properties at the interface of tendon and bone. The supraspinatus tendon (the main tendon of the rotator cuff), ranges from ~55-175 MPa in elastic modulus and ~4–17 MPa for ultimate tensile strength depending on the spatial location[1]. Many of the current designs achieve heterogeneous properties through discrete transitions in properties, which generates stress concentrators that often lead to failure at these junctions.[2] To address these limitations, we have developed a library of biodegradable poly(ether ester urethane)ureas with highly tunable properties that can match native tissue. This library allows for appropriate selection of material by correlating tensile properties with reported tissue values. We then developed a co-electrospinning technique to form heterogeneous scaffolds with gradient properties that more accurately mimics the tendon to bone transition.

Methods: ***Biodegradable Polyurethane urea:*** The biodegradable poly(ether ester urethane)ureas (B-PURs) were synthesized under a dry nitrogen atmosphere using a two-step reaction. In the first polymerization step, a 10 wt% solution of hexamethylene diisocyante (HDI) in dimethylformamide (DMF) was continuously stirred via overhead stirrer while a 10 wt% solution of the triblock diol in DMF was added dropwise with 0.2% stannous octoate. The prepolymer solution was then cooled to room temperature. A 10 wt% solution of diaminopropane or ethylene diamine in DMF was then added dropwise while stirring for chain extension. The reaction was continued at room temperature for 1 hour, resulting in a poly(ether ester urethane)urea with a hard segment varying from 10-50%. The polymer product was then precipitated in distilled water and dried under vacuum in ambient conditions for 48 hours, then dissolved in 2,2,2-trifluoroethanol (TFE) or 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP) for further characterization and electrospinning. Films (250 µm thick) were casts and cut into microtensile bars. Chemical structure of the B-PURs was confirmed using FTIR. Mechanical properties were characterized using a uniaxial tensile appartus and tested with a 1 kN load cell in dry, ambient conditions.

Gradient Electrospinning: A glass syringe was loaded with 18 wt% B-PUR 10% HS in TFE and placed 35 cm from a copper plate collector. The solution was pumped at a rate of 0.2 mL/hr through a blunted 20 gauge needle. A voltage of 10 kV was applied to the needle tip while -10 kV was applied to the collector. Simultaneously, a second glass syringe was loaded with B-PUR 50% HS in HFIP and placed 18 cm from the collector, parallel to the B-PUR 10% HS solution. The solution was pumped through a blunted 20 gauge needle at a rate of 0.3 mL/hr. A voltage of 9 kV was applied to the needle tip. In order to produce a gradient mat, the two syringe pumps were offset by 5 cm. A sheet of PET was utilized as a shield between the two jets in order to minimize electrostatic interaction. ***Fiber mesh characterization:*** Fiber morphology was characterized with scanning electron microscopy (SEM). Mechanical properties were characterized using a uni-axial tensile tester. Electrospun mechanical properties were tested with a 100 N load cell in dry, ambient conditions.

Results: ***Biodegradable Polyurethane characterization:*** Successful B-PUR synthesis was confirmed with infrared spectroscopy, specifically focusing on the formation of the urethane and urea linkage at 1730cm^{-1} and 1640cm^{-1}, respectively. Mechanical testing of the B-PURs with varying hard segment content (10-50%) displayed a wide range in modulus ranging from 18 MPa to 233 MPa and ultimate tensile strength (17-33 MPa), **Figure 1A**.

Fiber characterization: Co-spun meshes were sectioned into 3 regions: 50% HS B-PUR, transition region, and 10% HS. As expected from film testing, the electrospun 50% HS B-PUR section had a much higher modulus and ultimate tensile strength than the 10% HS region. Samples from the transition region displayed both an intermediate modulus and ultimate tensile strength when compared to the 10% HS and 50% HS B-PUR regions, **Figure 1B**.

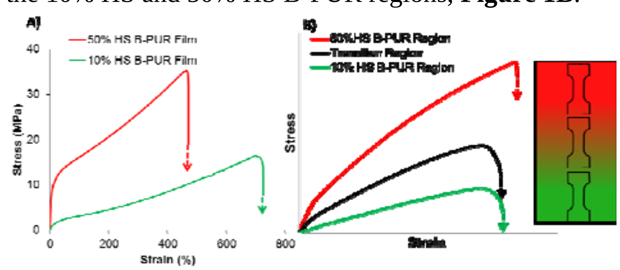

Figure 1: Stress-Strain curves of A) the typical B-PUR films and B) the gradient electrospun meshes.

Conclusions: In this study, we have demonstrated that we were able to fabricate a scaffold with gradient mechanical properties by co-electrospinning B-PURs with varying hard segment content. This scaffold shows promise in mimicking the natural gradient of properties at the tendon to bone interface. Current studies are probing these gradient properties in more detail and the effect of fiber alignment on mesh properties. Future studies will investigate cell viability, adhesion, and proliferation on these grafts. Overall, these meshes could provide improved integration at the tendon to bone interface and other musculoskeletal defects.

References:

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