Bacteria-Responsive Electrospun Fibers for Wound Infection Surveillance

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Statement of Purpose: On average, around 5.7 million patients per year suffer from chronic wounds [1]. These wounds are highly susceptible to infection and biofilm formation, which can interfere with wound healing processes [2]. To further complicate this clinical need, ~50% of diabetic ulcer patients with a limb threatening infection do not show systemic infection symptoms, delaying diagnosis and treatment.[5] Despite the prevalence of chronic wound infections, there is no expert consensus on the standard of care for infection surveillance.[6] Currently, infection assessment requires wound swabbing, which is highly susceptible to misdiagnoses. Thus, there remains a critical need for chronic wound dressings that specifically respond to active infections to aid in earlier surveillance.

Our approach is to synthesize a bacteria responsive shape memory polymer (SMP) that is synthesized in a primary, circular shape and fixed into an elongated temporary shape prior to implantation. The secondary shape is stable unless bacteria are present. Bacterial enzymes can penetrate the polymer, cleaving enzyme-labile moieties and inducing shape recovery to the circular shape, alerting wound care clinicians to the presence of bacteria in the wound.

Since polymer films are not porous or easily penetrable, we hypothesized that a porous fiber mat could increase the shape change rate in these materials. Electrospinning is a process to fabricate fibrous mesh scaffolds and is compatible with our SMP chemistry. Additionally, electrospun meshes could enable a more conformable wound dressing material with more clinically-relevant handling and mechanical properties. The goal of this work is to explore the effects of pore size and fiber alignment on the shape memory properties to increase the rate of enzymatically-induced SMP shape.

Methods: A segmented polyurethane SMP was synthesized using hexamethylene diisocyanate (HDI) as a coupling agent, polypropylene glycol (PPG) as a soft segment, and triethylene glycol (TEG) as a chain extender. To enable bacteria-response, polyglutamic acid (pGlu), which is degraded by the V8 protease of *Staph. aureus* was added in the backbone. The process starts by reacting the HDI with PPG with a catalyst to create a prepolymer in tetrahydrofuran (THF), then adding in the chain extenders (TEG and pGlu). After precipitation and drying under vacuum successful synthesis was confirmed by Fourier transform infrared (FTIR) spectroscopy. For electrospinning, 1.5 g of polymer was dissolved in 4 ml chloroform and placed in a syringe with 15.89-millimeter diameter, and with a 22-gauge flat tip needle. A charge of 12.6 volts was applied to the needle, and a dispense rate of 2 ml/hour was set. Humidity was set to 50%, and electrospinning was carried out at room temperature. A sheet of aluminum foil was used on the rotating mandrel as a collector, which was 10 centimeters away from the needle. The air flow was controlled in our apparatus to guide proper charge movement and solvent vaporization. Mandel rotation rates was varied to alter fiber alignment. Electrospun fibers were characterized in terms of surface morphology using scanning electron microscopy (SEM), shape memory properties via dynamic mechanical analysis (DMA), and mechanical properties using tensile testing.

Results: A library of segmented polyurethanes with shape memory properties has been successfully synthesized, and control (non-enzymatically responsive SMPs) have been electrospun to produce fibrous meshes. SEM images (**Figure 1**) confirm that electrospinning parameters were successfully optimized, and fiber mats were achieved with bigger pores compare to the control polymer film formed by melt processing using a hot press.

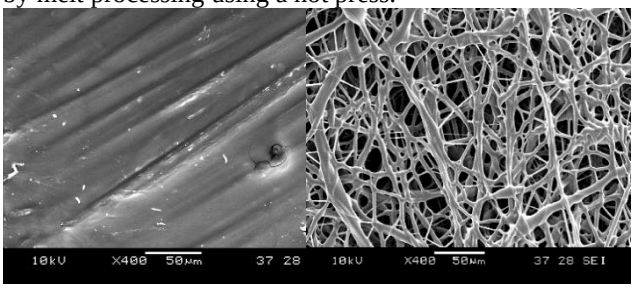

Figure 1. SEM images of (left) control polymer film and (right) electrospun mesh.

As shown in **Table 1**, even thin fibrous meshes (0.11mm) have good mechanical and shape memory properties, also fiber formation could improve shape fixity in comparison with bulk films. To improve other properties, thicker fibrous mats will be made and analyzed in the future.

Table 1. Mechanical and shape memory properties of the electrospun fibers

Measurement	SMP Film	Electrospun Mesh
Young's modulus (kPa)	160 ± 5	15 ± 4
Tensile strength (kPa)	11892 ± 103	953 ± 28
Elongation at break (%)	1234 ± 97	355 ± 28
Shape fixity (%)	74	95
Shape recovery (%)	100	84

Conclusions: Current work is focused on fiber formation with the pGlu-containing polymer to study the enzyme response of the electrospun fibers in comparison to the bulk film. Furthermore, we will study the effects of fiber alignment on mechanical and shape memory properties of fibers. Overall, this system is a promising approach to improving infection surveillance in chronic wounds.

References: [1] *Galdiero, E, (2019). Pharmaceutics.* [2] *Dreifke, M, (2015). Mater. Sci. Eng.* [3] XixiXiao,(2020). Colloids and Surfaces, [4] Lee (2018). Acta Biomaterialia. [5] Jayesh, D, (1995). Electrostatics.