Multi-Functional Molecule Release for Hernia Repair

S.D. McCullen, G.T. Hilas, M.S. Taylor, J.T. Corbett
Poly-Med, Inc., 51 Technology Drive Anderson, SC, 29625

Statement of Purpose: Hernia repair is one of the most common general surgery procedures performed with approximately 1,000,000 U.S. surgeries occurring annually. Current strategies for hernia repair require the implantation of a barrier mesh to restore the mechanics and boundary at the abdominal wall. Upon implantation of the mesh, a severe foreign body and inflammatory response is invoked as well as misdirected collagen synthesis. This results in poor tissue repair often requiring secondary corrective surgeries. To overcome the challenges associated with such implantable devices, engineered electrospun fibrous materials have emerged as a favorable platform technology to improve the wound healing response for medical device applications. Electrospun fibrous materials provide an ideal substrate for a temporary scaffolding for neo-tissue growth as well as bioactive molecule delivery based on their superior surface-area-to-volume ratio, and the ability to generate controlled release kinetics due to polymeric composition and fiber attributes. In this work, we characterize the integration and drug release profile of three electrospun fibrous coatings containing dexamethasone sodium phosphate (DSP) on an absorbable hernia mesh construct.

Methods: Absorbable bi-component hernia meshes were prepared by warp-knitting high lactide (Osteoprene®, Poly-Med, Inc.) 43-filament fibers with poly-axial high glycolide 10-filament fibers as previously described[1,2]. Electrospun fibers were deposited directly onto the mesh and constituted three different polymer compositions: (1) PLLA-PEG (16:84), (2) PGLA (90:10), and (3) PLLA to generate different release profiles. Polymers were dissolved in a solvent system of chloroform and dimethyl formamide or hexafluoroisopropanol and electrospun with or without DSP (5 wt%) at 1 kV/cm and 3 ml/hr. The mechanical properties of the electrospun fabrics were examined using an MTS Synergie 200 mechanical tester following typical surgical mesh testing protocols for suture-pull out and tensile testing. In addition, SEM imaging was performed to determine fiber size distribution as well as *in vitro* conditioned mass loss to determine approximate residence time of each material. DSP drug release was assessed via HPLC by incubating electrospun meshes in saline at 37°C throughout a 48 hour period.

Results: Polymers with varying DSP loadings were successfully prepared and integrated with an absorbable hernia mesh via electrospinning (**Figure 1**).

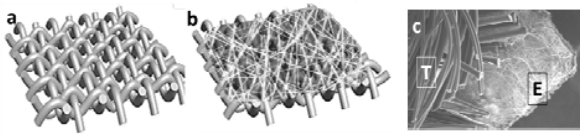

Figure 1a-c: Graphics of hernia mesh (a), medical textile coated with drug loaded electrospun fibers (b), and bilayer hernia developed at PMI (c) with medical textile (T) laminated directly to electrospun fibrous constructs (E).

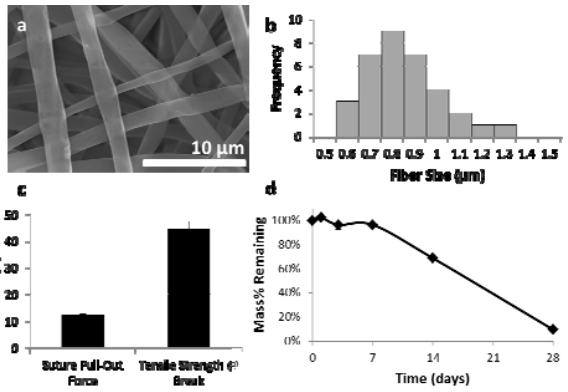

Figure 2a-d: Representative images of electrospun PGLA fibers fabricated with near uniform fiber sizes (a), displaying submicron fiber diameters (b). Macroscopic mechanics of PGLA (c) indicate that these materials have good handling properties for *in vivo* placement, while the mass degradation time frame is ~1 month (d).

Electrospinning conditions were optimized for each polymer system to yield uniform submicron fiber sizes, superior strength and handling properties. **Figure 2** shows representative data from electrospun PGLA with resulting mechanical properties of the electrospun fabric.

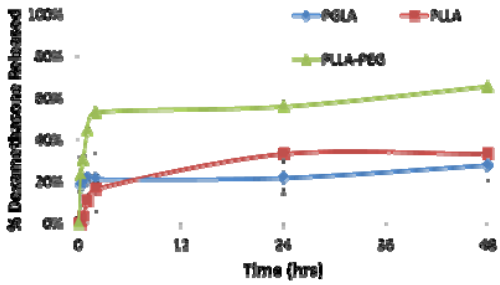

Figure 3: DSP release profiles from current polymer formulations of varying monomeric ratios of PLLA, PLGA, and PLLA-PEG.

Drug release of DSP from each electrospun system can be seen in **Figure 3** above. Release was able to be tailored over a range of profiles to provide burst and intermediate release systems based on the chosen polymer composition. Burst release is thought to be ideal as the inflammation period occurs within the first few hours after surgery. Intermediate and potentially long-term release profiles may assist in minimizing the overall chronic foreign body response to the mesh implant which occurs over an extended amount of time; possibly minimizing excessive scar tissue formation.

Conclusions: Electrospun fibrous materials with various compositions were successfully integrated into an absorbable hernia mesh, providing functionality for tailored anti-inflammatory drug release to mitigate the inflammatory and foreign body response.

References:

1. Hilas et al. Transaction of the Society for Biomaterials (2013) Abstract #395.
2. US Patent Application 11/886,370.