Evaluation of a Novel Absorbable Copolymer for Tissue Separation Film Applications

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Statement of Purpose: Post-operative adhesions are a significant problem, especially in the case of gastrointestinal surgery where they can lead to complications such as bowel obstruction. A limited number of products exist to prevent adhesions, usually in the form of barrier films or gels[1]. Lactide copolymers, such as 70:30 poly (L-lactide-co-D, ø L-lactide) (PLDL), have been approved for use as separation films. However, these polymers remain in the body a substantial amount of time after the wound has healed and offer moderate conformance around soft tissue. This prompted Poly-Med to further investigate the use of high compliance, faster-absorbing materials as a barrier film.

The novel absorbable polymer Glycoprene® RD7, a 25:20:55 poly (TMC-co-caprolactone-co-glycolide) copolymer, shows promise as a more compliant, faster absorbing alternative.

Methods: Films were created from RD7 and PLDL (Poly-Med, Inc) using a custom built ¾" single screw extruder (Alex James and Associates) with a cast film die to an approximate thickness of 25 µm. *In vitro* performance of the films was characterized by conditioning test specimens in 7.4 pH phosphate buffer at 37°C. Mass loss was determined by removing samples at predetermined time points, drying to a constant weight, and comparing to initial weight according to ASTM F1635-11[2]. Tensile strength retention was measured by removing sample from the buffer and immediate testing to failure on an MTS Synergie according to ASTM D882-10[3]. Sterilized films (n=1) were implanted in a porcine model along the abdominal wall where they were secured by a central anchoring suture. Prior to implantation, the tissue surface of the sites was slightly abraded by 30 manual strokes with surgical gauze. Following a 1 month implantation period, samples were explanted. Representative tissue specimens from each implant site were collected in 10% neutral-buffered formalin and subsequently processed into hematoxylin and eosin-stained microslides for evaluation of histology.

Results: Tensile testing of film at the time zero point revealed RD7 films to have roughly a tenth the modulus of PLDL (**149.2 MPa** versus **1943 MPa** for PLDL). *In vitro* analysis shown the absorption profile of RD7 showed 20% strength retention at 30 days and over 40% mass loss at 4 months. Histological evaluation of explanted films is exhibited in Table 1 and demonstrated similar composite scores. RD7 a higher degree of encapsulation compared to PLDL and was explanted as a balled mass, mostly likely related to the use of a single anchoring suture. RD7 had a lower score for neovascularity, macrophage presence, and necrotic debris.

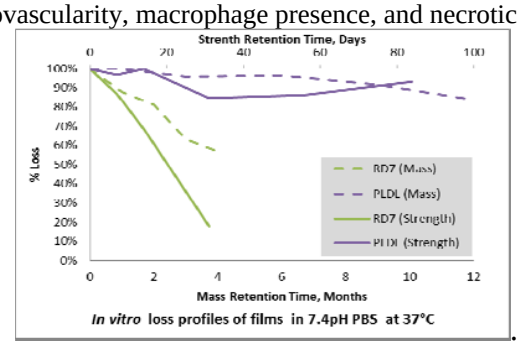

Figure 1: ***In vitro*** **strength retention and mass retentions profiles of films in 7.4pH PBS at 37°C.**

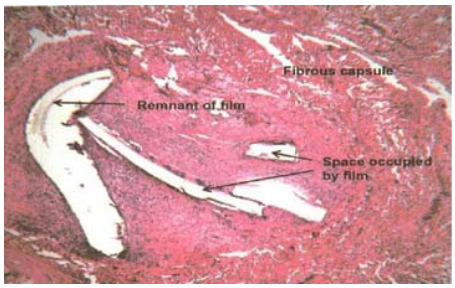

Figure 2: Histological examination of RD7 film after 1 month implantation in porcine abdomen. Image is H&E stained at 40X magnification.

Table 1: Histological evaluation of implanted films. Severity scores: 0 = not observed, 1 = minimal, 2 = mild, 3 = moderate, 4 = severe

Test article	Glycoprene™ RD7	PLDL
Fibrosis, capsule	4	2
Fibrosis, matrix	3	3
Neovascularity	0	1
Hemorrhage	2	2
Macrophages	1	2
Lymphocytes	0	0
Neutrophils	0	0
Eosinophils	0	0
Foreign Body Giant Cells	2	2
Necrotic Debris	0	1
Composite Score	**12**	**13**

Conclusion: The data suggests that Glycoprene™ RD7 exhibits beneficial materials properties to the PLDL control, such as **faster degradation** and **lower modulus** allowing for better compliance at the wound site. Since both materials produced similar histological results, RD7 is a likely candidate for continued research as a tissue separation film.

References:

1. Yoon Yeo, Daniel S Kohane. "Polymers in the prevention of peritoneal adhesions". Eur J Pharm Biopharm. Author manuscript; available in PMC 2009 January 1.
2. ASTM F1635-11 "Standard Test Method for in vitro Degradation Testing of Hydrolytically Degradable Polymer Resins and Fabricated Forms for Surgical Implants".
3. ASTM D882-10 "Standard Test Method for Tensile Properties of Thin Plastic Sheeting".
4. Shalaby, S.W. US Patent 6,462,169 (2000).