Small Animal Model to Measure Collagen Deposition Using a Knit Construct: A Preliminary Study

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Statement of Purpose: When implanted in living tissues, meshes elicit a cellular response that triggers a tissue reaction that results in the encapsulation of the implant. The thickness and amount of collagen deposition is variable and largely dependent on the mesh design variables of yarn chemistry, yarn form, yarn size, and knit construction. Accordingly, a simple, knit construct was developed which had a high aspect ratio with respect to the length, for the preliminary *in vivo* evaluation of a new mesh design. As such, the novel construct could be implanted using a known rat gluteal muscle model typically used for sutures.[1,2] Previously, an absorbable bicomponent mesh (ABM) comprised of a fast-degrading and slow-degrading yarn was shown to temporally modulate mesh physical and biomechanical properties for application in hernia repair.[3] Using the two absorbable yarns which comprise the ABM, an absorbable biocomponent construct (ABC) was knit to evaluate the tissue integration response during the transition phase, when the biomechanical properties modulate from high stiffness to high compliance. Although the ABC does not modulate properties, the integration of the ABC was evaluated with respect to yarn chemistry, form, and size. Changes in the collagen deposition with time were quantitatively measured using the thickness of the fibrotic capsule and the collagen/total protein ratio. For comparison, a polyethylene terephthalate construct (PETC) comprised of yarn with similar form and size was used as a clinically-relevant control.

Methods: ABC Preparation: A polyaxial segmented copolyester, P17, was prepared by end grafting a polyaxial poly(trimethylene carbonate) with glycolide and caprolactone. P7 was polymerized by end grafting linear poly(trimethylene carbonate) with l-lactide and trimethylene carbonate. P17 and P7 were melt extruded into a 10- and 43-filament yarn, respectively. The ABC was warp knit using a plied-construction of the two yarns around a single needle on an 18 gauge raschel knitting machine followed by a heat setting process. The resultant weight-ratio of P17 to P7 was 30/70. The PETC was plied and knit in the same manner as that of the ABC to isolate the variable of yarn chemistry.

Study Design and Surgical Procedure: Four adult female Sprague-Dawley rats were used for the tissue response study. The study design consisted of 2 rats for each time period (3 and 6 weeks) with one sterilized (EtO) knit construct (ABC and PETC) implanted, as described previously[1], in each gluteal muscle of two rats. Effects due to implant type and implantation time were determined using a split plot design analyzed by two-factor analysis of variance (SAS, v9.2) to compare means.

Characterization Methods: Capsule thickness measurements were obtained using Masson's trichrome stained histological images (400x), using a Leica DME microscope and digital image-analysis software (Motic IP, 2.0). The procedure for determining the collagen/protein ratio is described in detail elsewhere.[4]

Results: The effect of implant type was significant for each time period (Fig. 1); however, the capsule thickness of the ABC group was more substantial at 3 weeks with no change at 6 weeks. In contrast, the thickness of the capsule increased significantly between 3 and 6 weeks for the PETC. Figure 2 indicates that the effect of implant type on the collagen/total protein ratio was significant for each time period, but not significant between time periods. At 6 weeks, the ABC sections had lower collagen content and capsule thickness compared to PETC.

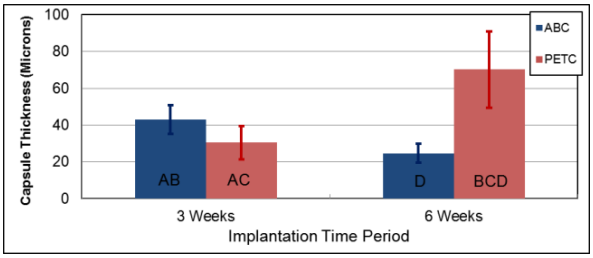

Figure 1. The capsule thickness for the ABC and PETC implants at the implantation periods of 3 and 6 weeks. Corresponding letters indicate a significant difference ($p < .05$).

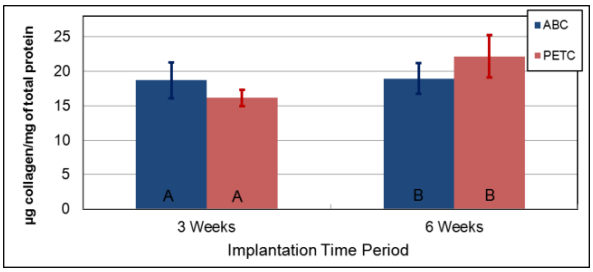

Figure 2. The collagen/total protein ratio for the ABC and PETC implants at the implantation periods of 3 and 6 weeks. Corresponding letters indicate a significant difference ($p < .05$).

Conclusion: A simple animal model for the evaluation of new mesh materials with respect to tissue integration was developed. Preliminary data indicates that the ABC showed collagen deposition that was greater at 3 weeks and denser at 6 weeks compared to that of the PETC.

References:

1. Bezwada, R. et al., *Biomaterials*, 16, 1141 (1995).
2. Im, J. et al., *Poly Degr Stab*, 92, 667 (2007).
3. Shalaby, S.W., Peniston, S.J., U.S. Pat. Appl. 11/866,370 (2006).
4. Gascon-Barre, M. et al., *J Histochem Cytochem*, 37, 377 (1989).