

## Hyaluronic Acid-Based Hydrogels for Scar-Free Tendon Repair

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**Statement of Purpose:** Peritendinous adhesions are a common and detrimental complication following flexor tendon injury and surgery. We evaluated post-surgical anti-adhesion properties of three hyaluronic acid-based hydrogels histologically and mechanically in a rabbit tendon model.

**Methods:** We developed a thiolated hyaluronic acid (HA) and poly (ethyleneglycol) diacrylate (PEGDA) hydrogel network called CMHA-SX (also referred to as Carbylan™-SX) that could be dried down into a film or left as a gel.

Rabbits (n = 4) were divided into three groups of eight. In each group, the fourth and third toes from both hindpaws were randomly assigned one of four treatments. In each toe we made incisions into the flexor profundus tendon through the tendon sheath. The 4 treatment groups were: (i) a control with no treatment, (ii) SeptraFilm®, an industry standard, (iii) our *in situ*-crosslinked HA gel, and (iv) our pre-formed HA films.

At 3 weeks animals were sacrificed and rabbit toe samples containing the tendon were harvested. We looked at the tissue anatomy and histology, and evaluated the samples mechanically. We performed one-dimensional tensile tests to determine the maximum force and total energy needed to break any adhesion and pull the tendon free from the sheath.

**Results/Discussion:** Our anatomical and histological results showed that all three treated groups showed less inflammation and connective tissue formation than the untreated control. The HA film group showed the least amount of newly formed connective tissue. Mechanically, as hypothesized, the HA film performed the best, requiring the least maximum force or total energy to remove the tendon (4.03 N, 1.55E-2 J), followed by the HA gel (5.29 N, 2.79E-2 J), SeptraFilm® (5.52 N, 3.58E-2 J), and control (9.71 N, 6.54E-2 J). The necessary force in the film group was statistically no different than that necessary to pull out an unoperated tendon, further indicating the post-surgical effectiveness of the HA film.

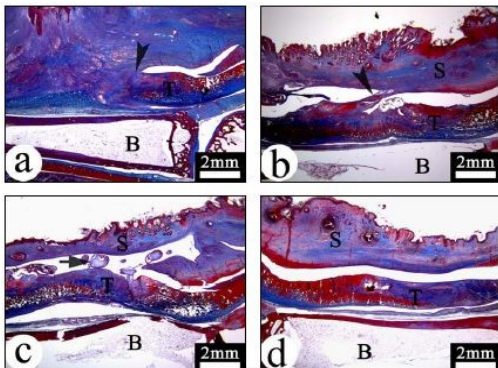


Figure 1. Histological results. A – No treatment. B – SeptraFilm®. C – Carbylan-SX gel. D – Carbylan-SX film. B = Bone; T = Tendon; S = Skin; arrow head indicates adhesion. Arrow indicates residual of Carbylan-SX gel.

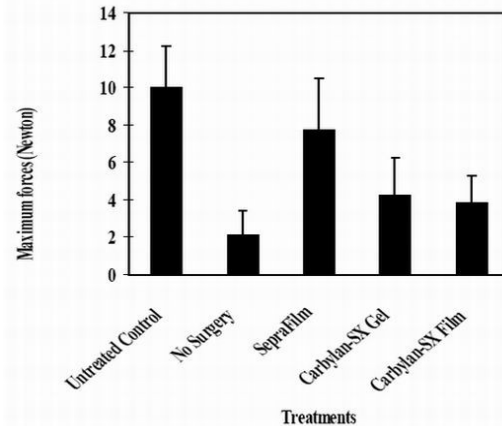


Figure 2. Forces necessary to remove tendon from tendon sheath 3 weeks post-surgery.

**Conclusions:** Our easily handleable Carbylan™-SX films and gels provide a biocompatible barrier that prevented post-surgical peritendinous adhesion better than the current industry standard, SeptraFilm®.

### References:

- Duflo, S. "Vocal Fold Tissue Repair in Vivo Using a Synthetic Extracellular Matrix." *Tissue Eng.* 2006;12(8):1271-1280.
- Hansen, JK. "In Vivo Engineering of the Vocal Fold Extracellular Matrix With Injectable Hyaluronic Acid Hydrogels: Early Effects on Tissue Repair and Biomechanics in a Rabbit Model." *Ann Otol Rhinol Laryngol* 2006;114(9): 662 – 670.
- Y. Liu, H. Li, X.Z. Shu, S.D. Gray, G.D. Prestwich, "Crosslinked Hyaluronan Hydrogels Containing Mitomycin C Reduce Post-operative Abdominal Adhesions", *Fertil. & Steril.* 2005;83:1275-1283.
- Liu, Y. "Reduced Post-operative Intra-abdominal Adhesions Using Carbylan-SX, a Semisynthetic Glycosaminoglycan Hydrogel." 2006.
- Prestwich, GD. "Injectable Synthetic Extracellular Matrices for Tissue Engineering and Repair." *Tissue Engineering* (J. Fisher, Ed). 2006;125-134.
- Sondrup, C. "Cross-linked Hyaluronan-Coated Stents in the Prevention of Airway Stenosis." *Otolaryngol Head Neck Surg.* 2006;135(1):28-35.