Tissue Engineered Rotator Cuff Tendon Using Swine Small Intestinal Submucosa

Introduction: Acute tear or chronic overuse injury of rotator cuff tendons (RCT) is a common pathology encountered in overhead athletes and the elderly. While primary repair of acute tears may be possible, chronic injuries often result in extensive tendon degeneration requiring tendon mobilization or replacement techniques. Previous studies have demonstrated that swine small intestinal submucosa (SIS) acts as a biological scaffold promoting a reconstructive healing response rather than formation of non-specific scar tissue. Indeed, SIS xenografts have been successfully used in animal models to regenerate ligaments and repair large fascial defects. The purpose of this study was to determine the efficacy of SIS in stimulating the regeneration of a RCT in a canine model. The hypotheses were: H1 - The use of a SIS xenograft will induce complete regeneration of a fully resected rotator cuff tendon, with gross and histological appearances similar to those of the native tendon, and H2 - The mechanical strength of the SIS-regenerated bone-tendon-muscle construct (BMT) will be similar to that of the contralateral sham-operated structure over a 6 month time period.

Materials and Methods:

Surgical Procedures: The infraspinatus tendon (IST) was bilaterally elevated from its musculotendinous junction and replaced by a 15 x 50 x 1mm, 10-ply SIS implant. One end of the SIS implant was sutured to the infraspinatus muscle (ISM), and the other end to a bleeding bone trough created over the IST insertion on the humerus. The free end of the contralateral IST (sham) was sutured back to its original position within a similar bony trough. Gross and Histology Procedures: Eight dogs were euthanized 3 and 6 months postoperatively and all ISTs grossly examined. In 3 dogs the ISTs were harvested to include the musculotendinous junction and greater tubercle, and fixed in 10% buffered formalin. Sagittal sections were cut and prepared for histology. Sections were stained with hematoxylin-eosin and examined under light and polarized light microscopy. Mechanical Testing Procedures: In 5 dogs per time period, both shoulders were harvested en bloc, wrapped in saline soaked sponges and frozen at -20°C until testing. The right shoulders from 6 additional dogs were used to evaluate the structural properties of the native IST. Prior to testing, soft tissues were dissected so that each specimen was composed of the scapula, ISM, IST (native, SIS-regenerated or sham-operated), and humerus. Specimens were orthotopically oriented in a custom-designed fixture and tested in a saline bath. To mimic clinical conditions of tendon rupture due to humeral head instability, the IST was displaced laterally by a probe at 25 mm/s until failure. Recorded parameters included: tendon cross sectional area, failure mode, and peak tendon load at failure. Paired t-tests were used to compare SIS-regenerated and sham-operated BMT constructs at 3 and 6 months. One way ANOVA and Tukey’s post-hoc tests were used to evaluate the properties of each construct over time and in comparison to those of the native IST. Significance level was set at p < 0.05.

Results: Gross Anatomy and Histology: At 3 months the gross appearance of both BMT constructs demonstrated a smooth continuity from the musculotendinous junction to the humeral insertion (Fig.1). Histologically, both constructs showed mild fibroplasia with an abundant collagenous extracellular matrix regularly oriented along the longitudinal axis of the tendon. The SIS-regenerated tissue was well integrated to the humerus with evidence of endochondral ossification and occasional Sharpey’s fibers anchored to the bone. The muscular interface appeared as a fibrous interdigitation between regenerated tissue and adjacent muscle. There was no evidence of residual SIS in any specimens. At 6 months both BMT constructs had a gross appearance similar to that observed at 3 months, completely spanning the original defects and showing good continuity with ISMs and greater tubercles without adhesions to peripheral tissues. Histologically, both constructs showed a decrease in cellularity and fibroplasia indicative of tissue remodeling. The extracellular matrix remained oriented with the long axes of the tendons, the regenerated tissue, well anchored to the bone by a mature transition zone, was classified as dense, regularly oriented connective tissue.

Discussion: The results of this study suggest that a SIS scaffold can be used to create a tissue engineered replacement of a RCT in a canine model. The gross appearance, histological continuity and failure mode of the SIS-regenerated constructs mimicked those of sham-operated and native ISTs, thus suggesting host tissue ingrowth and implant remodeling with solid integration of the regenerated tissue to muscular and bony interfaces. Importantly, tissue ingrowth occurred without histological evidence of foreign body or immune-mediated reactions. Sham operations were intended to simulate tendon mobilization and re-implantation procedures routinely performed to treat chronic RCT injuries. Although the ultimate strength of SIS-regenerated tendons was significantly smaller than that of native ISTs, it was similar to that of re-implanted tendons. Therefore, SIS implants could represent a potential alternative to tendon mobilization procedures, especially in the presence of degenerative tissues or large rotator cuff defects.

References:

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