IN-VITRO, IN-VIVO, AND BIOMECHANICAL EVALUATION OF THE PROPERTIES OF BIOTAPE *XM*™ TERMINALLY STERILE ACELLULAR PORCINE DERMAL MATRIX

INTRODUCTION

As the tendon quality decreases due to age or chronic damage, the importance of reliable soft tissue reinforcement during tendon repair becomes apparent. The ideal graft for such applications would be strong, safe, effective, easy to handle, sterile, and readily available while also exhibiting *in-vivo* properties such as host cell affinity and revascularization without eliciting an inflammatory or immune system response. The purpose of this evaluation was to characterize the histological and biomechanical properties of a terminally sterile acellular porcine dermal matrix, BIOTAPE *XM*™ Matrix (Wright Medical Technology, Inc, Arlington, TN) intended for use in soft tissue applications such as posterior tibial tendon repair augmentation.

IN-VITRO CELLULAR AFFINITY AND PROLIFERATION

MATERIALS & METHODS

In an effort to determine how human mesenchymal stems cells(hMSCs) interact with the BIOTAPE *XM*™ Matrix over time, hMSCs were seeded (5.0 x 106 cells/ml) onto the matrix and assessed for affinity and morphology, after incubation time periods of 30 minutes, 4 hours, and 3 days using ScanningElectron Microscopy (SEM).

RESULTS

- 30 Minutes:
  The hMSCs coated nearly the entire surface of the material although the density of the cel coating was somewhat variable. Cells that attached to the surface retained a rounded morphology with initial evidence of cell spreading. | **Figure 1A**

- 4 Hours:
  Numerous cells had assumed a flattened morphology while many hMSCs still maintained a rounded shape.| **Figure 1B**

- 3 Days:
  Uniformly flattened hMSCs were evident after 3 days of incubation on the BIOTAPE *XM*™ Matrix indicating cell viability, attraction, and attachment on a matrix conducive to growth.
  The extensive covering of the BIOTAPE *XM*™ Matrix with hMSCs at the 3 day timepoint could be indicative of cell expansion; however, since proliferation was not specifically measured, the possibility of cell spreading cannot be ruled out. | **Figure 1C**

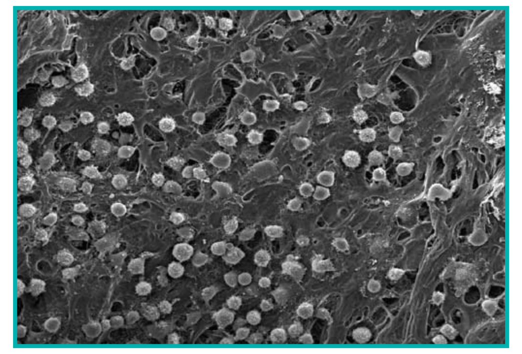

Figure 1A | 30 Minutes - 200x

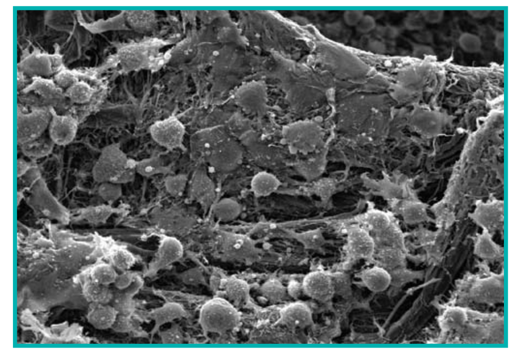

Figure 1B | 4 Hours - 350x

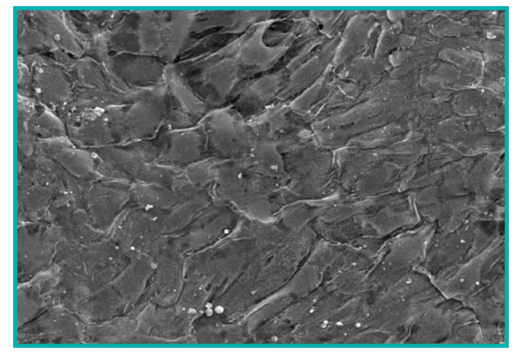

Figure 1C | 3 Days - 250x

IN-VIVO CANINE TENDON RESPONSE

MATERIALS & METHODS

Three different xenograft materials were evaluated in a canine Achilles tendon augmentation model at 6 weeks to determine differences in host tendon histological response to these materials in a tendinous application.

MODEL

- A surgically transected canine Achilles tendon was treated with end-to-end primary repair augmented with one of the three xenografts.
- To protect the repair, the joint was immobilized during the first four weeks and full activity was allowed during the remaining two weeks.
- Augmented repairs were excised at 6 weeks, fixed in 10% neutral buffered formalin, and processed for routing paraffin section staining using Hematoxylin & Eosin (H&E) (250x shown).
- Transverse and longitudinal slides were qualitatively evaluated for cellular and vascular infiltration, incorporation of the graft material and immunogenic response.

MATRICES EVALUATED: (n=3)

- Terminally sterile acellular porcine dermal matrix, BIOTAPE *XM*™ Matrix (Wright Medical Technology, Inc., Arlington, TN)
- Intentionally cross-linked equine pericardium, OrthADAPT® Bioimplant FX (Pegasus, Irvine, CA)
- Multi-layered porcine small intestine submucosa (SIS) graft, RESTORE® Orthobiologic
- Soft Tissue Implant (Depuy Orthopedics, Warsaw, IN)

RESULTS

Three distinct matrix interactions were observed.

- BIOTAPE *XM*™ Matrix
  - Gross observation compared to healthy tendon | **Figure 2A**
  - Excellent fibroblast infiltration and evidence of vascularization within the matrix. | **Figure 2B**
  - Fibroblast infiltration was apparent among matrix collagen bundles.
  - A scattered, mild inflammatory response as expected with implantation.
  - Localized areas of matrix, incorporated or attached to the native tendon, were evident.
- OrthADAPT® Bioimplant FX
  - No cellular infiltration or vascularization within the matrix.
  - Pronounced inflammatory response characterized by thick encapsulation with foreign body granulomas composed of giant cells and macrophages.
  - Hypothesized that the magnitude of encapsulation and lack of cell infiltration observed are attributable to the highly crosslinked material properties. | **Figure 2C**
- RESTORE® Orthobiologic Soft Tissue Implant
  - Material was in great part resorbed at this six week timepoint.
  - Implant fibers were associated with a resolving inflammatory reaction.
  - Degree of material resorption consistent with reported short term retention. | **Figure 2D**

Figure 2A | Explants

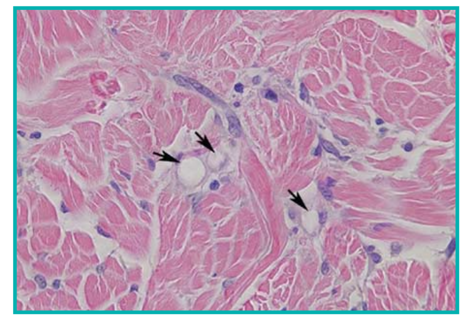

Figure 2B | BIOTAPE *XM*™

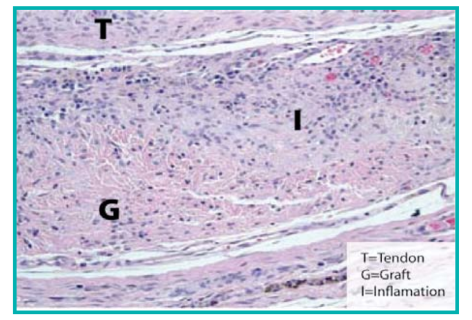

Figure 2C | RESTORE®

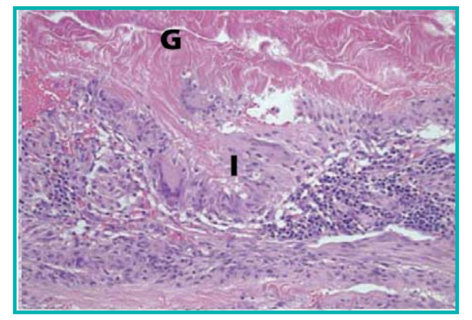

Figure 2D | OrthoADAPT®

BIOMECHANICAL TESTING

The biomechanical effects of augmented posterior tibial tendon (PTT) human tissue was evaluated in a tensile testing model compared to primary repair alone.

MODEL

- Matched human cadaver PTT tendon pairs were harvested and surgically transversely cut to simulate a mid-section tendon rupture.
- Groups:
  - Primarily repair (n=7)
  - Primarily repair augmented with a 3 x 4 cm BIOTAPE *XM*™ Matrix(n=7)
- Constructs were pre-loaded for 60 s and pre-conditioned for 30 s before loading to failure at a rate of 1 mm/s | **Figure 3A**
- Evaluated for failure load, stiffness, and creep at 10 N

RESULTS

- Average Failure Load:
  - Primary repair: 111.4 ± 32.8 N
  - BIOTAPE *XM*™ augmented repair: 190.1 ± 46.7 N.
  - Significantly higher with augmentation-(p = 0.023) | **Figure 3B**
- Average Creep Percentage at 10 N:
  - Primary repair: 2.84 ± 0.64%
  - BIOTAPE *XM*™ augmented repair: 2.34 ± 0.74%
  - Significantly less with augmentation-(p = 0.016)

DISCUSSION

- hMSC interaction with the BIOTAPE *XM*™ Matrix indicated that the matrix serves as a suitable host for cells. The uniformly flattened hMSC morphology at 3 days indicated cell viability, attraction, and attachment on a matrix conducive to growth.
- Histology from this 6 week canine Achilles augmentation model indicated that the BIOTAPE *XM*™ Matrix exhibited the greatest regenerative propensity of the three xenografts studied. The durability and beneficial incorporation of the BIOTAPE *XM*™ matrix is preferred over a rapidly dissipated or negative interaction in tendon applications where continued augmentation is desired.
- Biomechanical results show improved strength and less laxity in primary PTT repairs augmented with BIOTAPE *XM*™ Matrix compared to primary PTT repairs alone at an initial time zero timepoint.
- Collectively, the results from these three studies show that the matrix serves as a viable host for cellular attachment, undergoes cellular infiltration, revascularization, and various stages of matrix incorporation at a 6 week timepoint in a canine Achilles model, and provides biomechanical benefit to primary PTT repair alone at an initial timepoint.

CONCLUSIONS

As evidenced through in *vitro*, *in-vivo*, and biomechanical testing, the BIOTAPE *XM*™ Matrix exhibits properties desirable for use as a soft tissue augmentation material. The performance of this product in cellular, animal, and biomechanical models points to the efficacy and cell-friendly functionality of the material in tendon applications.

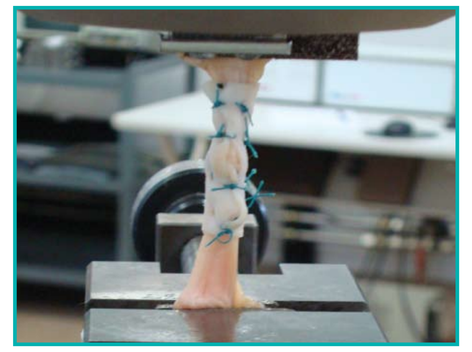

Figure 3A |

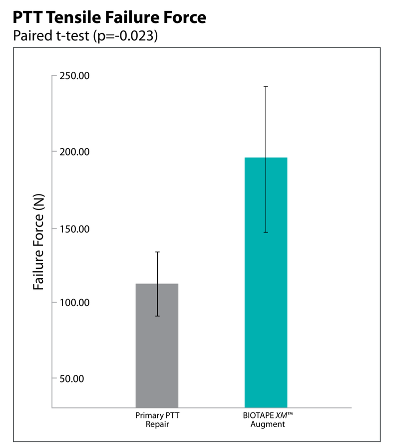

Figure 3B |