Characterization of a Novel Bio-Inductive Biocomposite Scaffold for Tendon and Ligament Healing

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INTRODUCTION: Prolonged recovery following rotator cuff tendon repair or anterior cruciate ligament reconstruction remains a challenge for both the patient and surgeon. The ability to optimize the healing process and potentially shorten rehabilitation time would constitute a significant advancement. A novel, bio-inductive, biocomposite scaffold has been designed to participate in the healing process through tissue ingrowth and remodeling to improve tendon and ligament repair and reconstruction. This study characterized time-zero properties (strength, pore structure) and degradation kinetics. The *in vivo* response and its ability to support rapid host cell ingrowth and tissue maturation was evaluated in a sheep patella tendon defect and subcutaneous models.

METHODS: The biocomposite scaffold (BioBrace™, Biorez Inc.) is a highly-porous collagen matrix, reinforced with bioresorbable PLLA micro-filaments, to provide an open 3-D biologic scaffold with strength (**Fig 1A,B**). *Mercury Porosimetry (MIP)*: The pore structure of the biocomposite scaffold was characterized via scanning electron microscopy (SEM) and mercury porosimetry. Mercury intrusion volume was recorded as a function of pore diameter for 2.5cm long segments of 5mm wide biocomposite scaffolds; log differential was calculated to remove noise from the data. *In vitro degradation testing*: PLLA fibers were submerged in phosphate-buffered saline (PBS) at a 30:1 solution-to-polymer mass ratio and maintained at 37C ± 2C and pH 7.4 ± 0.2. Tensile testing (per ASTM D2256) was carried out on n=12 samples per timepoint at a strain rate of 2%/second. Molecular weight (MW) was measured on one sample per time point via Gel Permeation Chromatography (GPC). 5mm-wide biocomposite scaffold devices underwent tensile testing (n=6) at a strain rate of 2%/second. *In vivo response*: The central third of the patella tendon was excised and the biocomposite scaffold secured with interrupted sutures (**Fig 2D**), or the defect was left empty (**Fig 2E**) following ethics approval. Paraffin histology was performed at 3 and 12 weeks to evaluate the local cell and tissue responses.

RESULTS: SEM of the scaffold's cross section revealed a porous, interconnected matrix with polymer filaments measuring 15µm in diameter (**Fig 1C**). Mercury porosimetry data revealed a porosity of 80%, cumulative pore volume of 4.2 cm^3/gm, and a peak pore diameter of 19.7µm (**Fig 2-top**). The *in vitro* degradation profile of tenacity (ultimate tensile strength/weight of the material) and molecular weight of the PLLA fiber demonstrate near complete loss after 130 and 156 weeks, respectively (**Fig 2-bottom**). The correlation coefficient between tenacity loss and molecular weight loss was R=0.983. Ultimate tensile strength of the biocomposite scaffold was 141.0N ± 4.5N, and stiffness was 14.5N/mm ± 0.5N/mm. The biocomposite scaffold supported rapid cellular ingrowth and extracellular matrix production in both the subcutaneous and patellar tendon locations at 3 weeks (**Fig 1F**) while the empty defect collapsed on itself with some new fibrous tissue noted (**Fig 1G**). At twelve weeks tissue remodeled in the patella tendon and subcutaneous sites (**Fig 1H,I**). Scattered multinucleated cells were noted adjacent to some of the PLLA fibers at both 3 (not shown) and 12 weeks (**Fig 1H,I**). There is also increased tissue production, maturation, and alignment with no evidence of an adverse inflammatory response.

DISCUSSION: This preclinical assessment demonstrates the biocomposite scaffold architecture has a high degree of porosity that is adequate in size and volume to support bulk cellular infiltration. PLLA fibers used in the biocomposite scaffold have a reproducible degradation curve that correlates with the reduction of its tensile strength over time. Previous studies (data on file) have shown that the degradation profile of the PLLA fibers is directly related to that of the implant construct. When placed in an *in vivo* environment, the implant supports a rapid ingrowth and maturation of new tissue. Comparison of the cellular response across implant sites revealed similar responses. In a clinical setting, the initial strength of the implant and the resultant host tissue ingrowth may serve to optimize the balance between the local biomechanical and biological healing environment. Further studies are warranted and underway.

SIGNIFICANCE/CLINICAL RELEVANCE: The ability of a biocomposite scaffold to rapidly induce the formation of host generated regularly oriented connective tissue within in a tendon defect may represent a novel approach to the repair/reconstruction of severely damage tendons or ligaments.

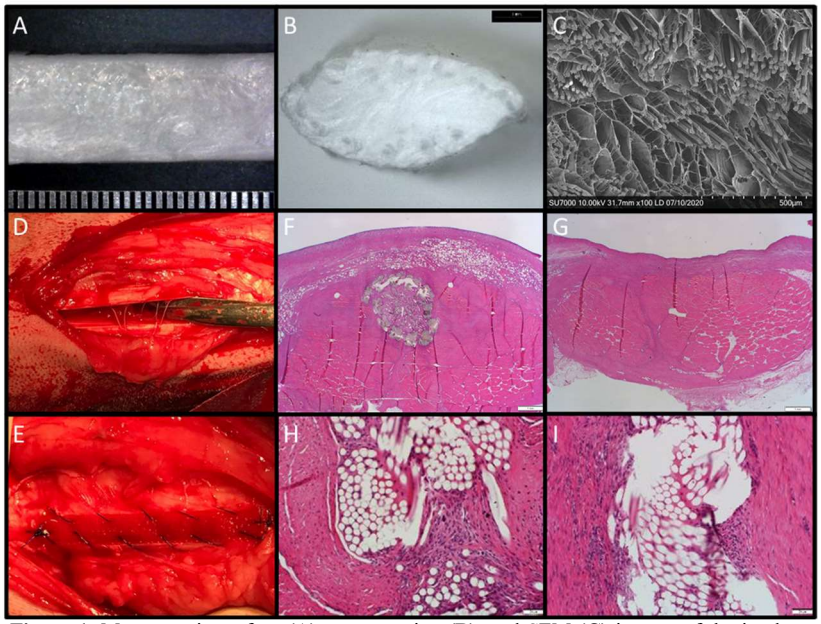

Figure 1. Macroscopic surface (**A**), cross-section (**B**), and SEM (**C**) images of the implant. Middle third patellar tendon empty defect (**D**). Biocomposite scaffold sutured in defect (**E**). H&E histology of the biocomposite scaffold (**F**) and empty defect (**G**) at 3 weeks. H&E histology of the biocomposite scaffold at 12 weeks in cross-section (**H**) and longitudinal section (**I**).

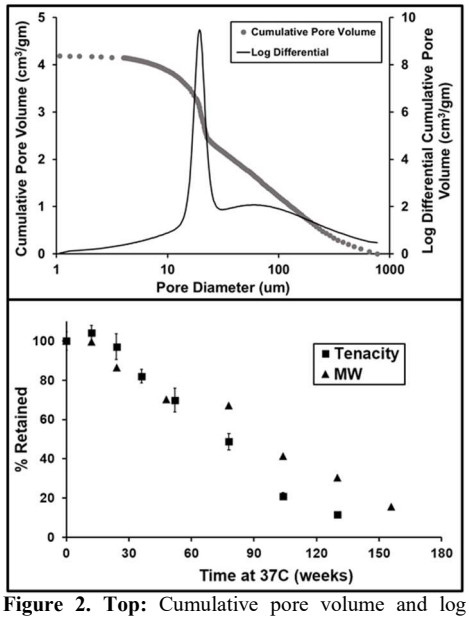

Figure 2. Top: Cumulative pore volume and log differential as a function of pore diameter in the biocomposite scaffold. **Bottom:** *In vitro* degradation of PLLA fiber fraction of scaffold over time as measured by retained molecular weight (MW) and remaining tenacity (tensile strength/weight).