Meniscal Regeneration using a Bovine Dermal Collagen Matrix

Mark A. Randolph¹, Sanford C. Edwards, BS², Amanda M. Meppelink, BS², Thomas J. Gill, M.D.³.
¹Harvard Medical School, Massachusetts General Hospital, Boston, MA, USA, ²Massachusetts General Hospital, Boston, MA, USA, ³Harvard Medical School, Boston, MA, USA.


Introduction: Total and partial meniscectomy secondary to injury have been common treatments for injured menisci; however, such therapies are strongly associated with the development of articular cartilage degeneration leading to osteoarthritis. Animal studies and clinical experiences have shown that the development of arthritis is proportional to the amount of meniscus removed. In cases where the inner portion has to be excised, there are no FDA approved approaches to replace or regenerate the inner meniscus in order to prevent joint degeneration. Strategies where the inner meniscus can be repaired or regenerated could prevent the adverse consequences involved with whole or partial meniscectomy. SurgiMend® (TEI Biosciences, Inc.) is an FDA-approved collagen matrix manufactured from fetal and neonatal bovine dermis using a process that preserves the collagen molecules and extracellular matrix fiber architecture in an undamaged, native state. When implanted, SurgiMend does not initiate a foreign body reaction; rather, it is able to bind cells and cell products, and become revascularized to generate a metabolically active tissue having the capacity to be remodeled. The purpose of this study was to investigate the reparative and regenerative capacity of a bovine acellular dermal collagen matrix placed into a meniscal defect in swine.

Methods: The medial meniscus was exposed in the left stifle joint in twelve MGH miniature swine (40-45kg). Three, 4 mm full-thickness cylindrical defects were made; in the anterior horn, posterior horn, and the central body of the meniscus (Figure 1). In the experimental group (randomized by site), SurgiMend (TEI Biosciences, Boston, MA) cylindrical Type I/III collagen fiber implants measuring 3 mm thick and 5 mm in diameter were press fit into the defects and secured with a single 3-0 Ethibond suture. One control site was untreated without any implant. The other control site was treated with a cylinder of meniscus removed when making the defects and sutured. Three animals were euthanized at 3 weeks, three at 8-10 weeks, while the remaining three were followed for 6 months. Tissues were harvested and studied grossly, immunohistochemically, and histologically using polarized light and the following stains: H&E, Trichrome, and Safranin-O.

Results: At all time points the autologous meniscus implants were not healed nor integrated into the defects (Figure 2). At three weeks the dermal collagen implants were still apparent in the defect and populated with cells. Immunofluorescence with an antibody against bovine collagen demonstrated the presence of the implant and invading cells. By 8-10 weeks, the implants were integrated with the meniscus with evidence of healing. In some implants the regenerated tissue had the normal geometry of the native meniscus (Figure 3). The implants were revascularized and repopulated by cells that resembled fibrochondrocytes typical of meniscal tissue (Figure 3). Healing of the scaffold to native meniscus was always observed at peripheral contact site and frequently at the interface with the white zone. No evidence of inflammatory cells was present indicating the implants did not cause an immune response. The results at 6 months mirrored those seen at the 3 month time point with regeneration of
the defect in which the implant was placed. In many of the 6-month animals it was difficult to identify the implant site. There did not appear to be any gross changes in the articular cartilage.

**Discussion:** The bovine dermal collagen scaffolds integrated seamlessly into the meniscal defects. Cell migration into the scaffold material occurs by three weeks and vascularization was noted. The scaffolds were undergoing remodeling by eight weeks, being populated by fibrochondrocytes, and integrating into the defects. These results show that the bovine dermal matrix is capable of permitting repair and regeneration of meniscal lesions in swine. Whereas weight bearing is generally restricted in human patients following meniscus repair, this swine model is rigorous in that the animals are immediately weight bearing postoperatively. This model was effective for evaluating the biocompatibility and regenerative capacity of the material, but future testing should focus on replacing the inner rim of the meniscus to simulate repair in humans.

**Significance:** The results from this study demonstrate that implants made from bovine dermal collagen placed into meniscal defects can permit regeneration of the swine meniscus. This scaffold material could be used to promote meniscus repair and regeneration following partial or whole meniscectomy.
Figure 3. Histological results from pig 20721 (Left) showing the area (dotted line box) of the collagen implant at 8 weeks. Polarized light shows the birefringence of the collagen fibers in the regenerated implant and the section stained with trichrome shows the vessels in that regenerated area. A high magnification field from an implant in pig 20734 shows the fibrochondroctyes and the arrows indicate the vessels in the regenerated meniscal tissue.