

Repair of Chondral Thickness Defects Using Cartilage Allograft Matrix in a Goat Model

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INTRODUCTION & BACKGROUND

Articular cartilage lesions generally do not heal, or heal only partially under certain biological conditions due to the lack of nerves, blood vessels and a lymphatic system¹. The limited reparative capability of hyaline cartilage results in the generation of repair tissue that lacks the structure and biomechanical properties of normal cartilage².

MTF's Cartilage Allograft Matrix (CAM) was developed to treat full thickness chondral lesions. It contains endogenous growth factors and extracellular matrix key components that are found in native articular cartilage. Cartilage Allograft Matrix can be used to augment the microfracture technique to help improve outcomes of microfracture procedures.

Efficacy of the Cartilage Allograft Matrix (CAM) has been demonstrated in a goat osteochondral defect model at 6 months. The purpose of this study was to evaluate the effect of the CAM implant on the healing potential of full thickness chondral defects in an in vivo medial femoral condyle and trochlear groove goat model in comparison with Microfracture.

MATERIALS & METHODS

Design:

Three female Spanish goats were enrolled in this study to represent the CAM group. The goat was chosen as the in vivo model because of the large relative stifle joint size, ease of handling, and use in other published cartilage repair studies³. The CAM samples used for this study were prepared from articular cartilage portions of goat long bones at the Musculoskeletal Transplant Foundation (MTF – Edison, NJ) using procedures analogous to those used to prepare human CAM. CAM samples were aliquoted such that preparation would yield enough tissue to correspond with filling a 6mm defect, the critical size defect in the goat model⁴. Two animals were enrolled to represent the microfracture group.

Surgical Implantation:

For animals assigned to the CAM group, one implant was placed in the medial femoral condyle, representing a weight-bearing site, and the other in the lateral trochlear sulcus, representing a non-weight bearing or backfill site. The placement of the medial femoral condyle defect (MFC) was defined as 10mm distal to the condyle groove junction and aligned with the medial crest of the trochlear groove. The placement of the lateral trochlear sulcus was defined as approximately 5-10mm distal to the top of the lateral trochlear ridge and aligned with the middle of the lateral trochlear groove. The defects were filled with the test material to approximately 0.1 mm below the surface. Fibrin sealant was applied over the surface of the carefully packed Cartilage Allograft Matrix. For animals assigned to the microfracture group, full thickness cartilage defects were created 6mm in diameter with 6 circumferential holes and 1 central hole created using a custom awl with a tapering tip approximately 0.5 to 0.9mm diameter. All animals were placed in a modified Thomas splint for 7 days post-operatively.

Post-Operative Treatment and Euthanasia:

All animals were housed at Thomas D. Morris, Inc. (Reistertown, MD) for the duration of the study. The goats were maintained in large indoor runs (pens) or outdoor runs following surgery having unrestricted access at all times. Animals were observed daily for general health concerns throughout the course of the study. On day 168 ± 5 after surgery, animals were humanely euthanized according to the AVMA Panel on Euthanasia guidelines (JAVMA, 2007) and prepared for evaluation.

Histology:

All specimens were sent to Premier Labs (Longmont, CO) for histological processing. Decalcified histology was performed

on the repaired defect sites by processing center cuts of the medial femoral condyle and the lateral trochlear sulcus, both in the proximal-distal orientation. Safranin-O staining was performed to demonstrate the presence of proteoglycan content, an important component in the extracellular matrix region of hyaline cartilage. Histology of Safranin-O stains positive (red) for proteoglycans and the bone region is stained green. Immunohistochemical staining was performed to demonstrate the presence of Collagen Type II, the primary collagen component in hyaline cartilage. Brown stains positive for Collagen Type II; the counter stain is purple.

Modified O'Driscoll Scoring:

All histology slides were sent for pathological scoring using the Modified O'Driscoll scoring method. This scoring system evaluates the nature of the predominant tissue, structural characteristics, freedom from cellular changes of degeneration, freedom from cellular changes of degeneration in adjacent cartilage, reconstitution of subchondral bone, inflammatory response in subchondral bone region, and Safranin-O staining.

RESULTS

The efficacy of CAM has been demonstrated in a goat chondral defect model at 6 months. Histology showed that implantation of CAM resulted in hyaline or hyaline-like cartilage that was integrated with the host tissue, with preliminary establishment of a tidemark. Positive staining for Safranin-O (indicating the presence of proteoglycan) (Figures 1A & 1B) and Collagen Type II was observed in the cartilage region (Figures 1C & 1D).

Cartilage Allograft Matrix:

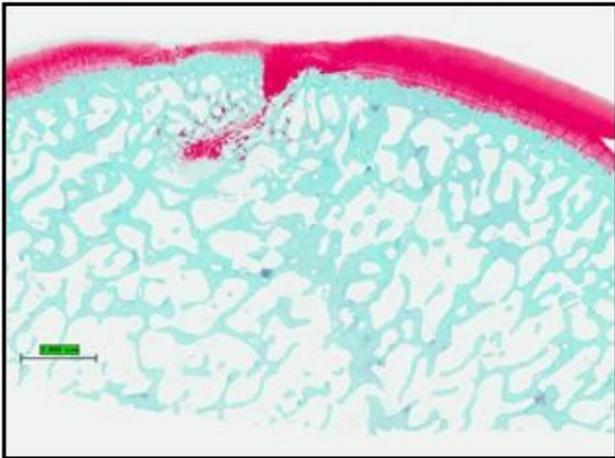


Figure 1A: Cartilage Allograft Matrix, Medial femoral condyle, Safranin-O stain

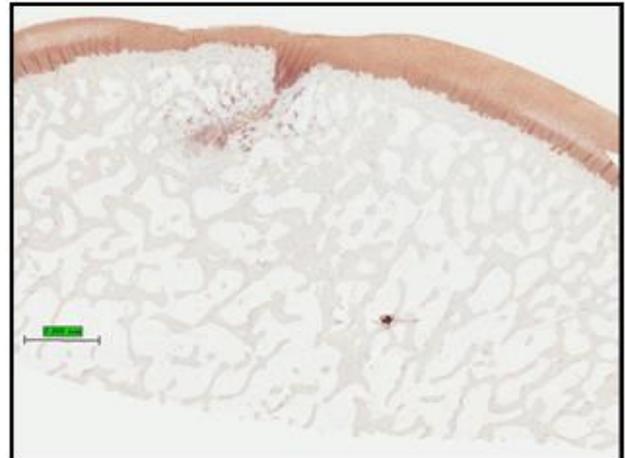


Figure 1B: Cartilage Allograft Matrix, Medial femoral condyle, Collagen Type II stain

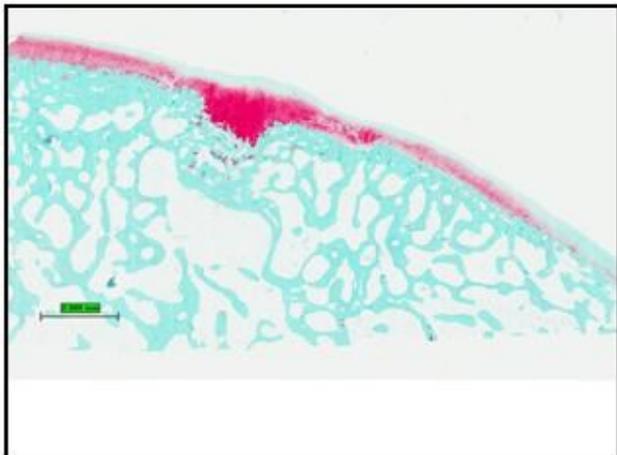


Figure 1C: Cartilage Allograft Matrix, Lateral proximal trochlear sulcus, Safranin-O stain

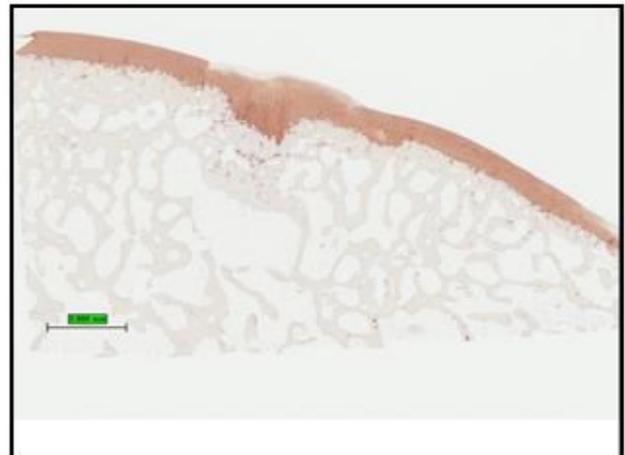


Figure 1D: Cartilage Allograft matrix, Lateral proximal trochlear sulcus, Collagen Type II stain

After 6 months, Microfracture resulted in only partial filling of the defect with reduced Safranin-O staining in the repair tissue where present (Figures 2A & 2B).

Microfracture:

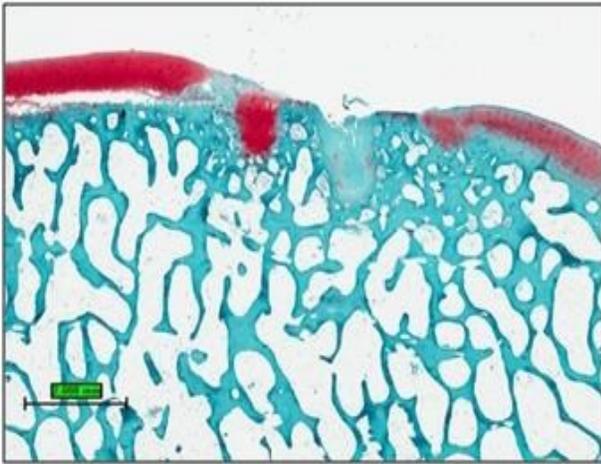


Figure 2A: Mfx, Medial femoral condyle, Safranin-O stain

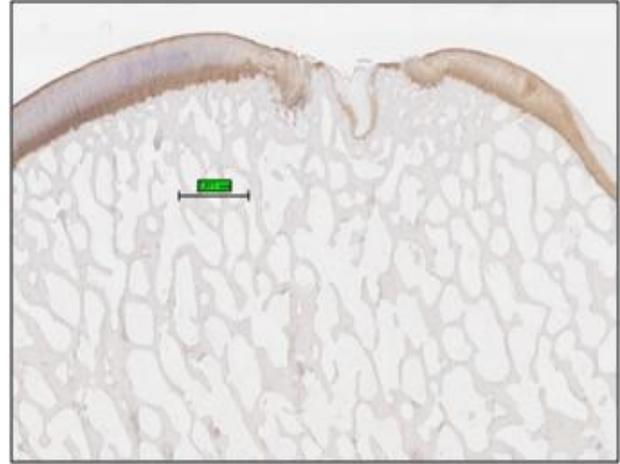


Figure 2B: Mfx, Medial femoral condyle, Collagen Type II stain

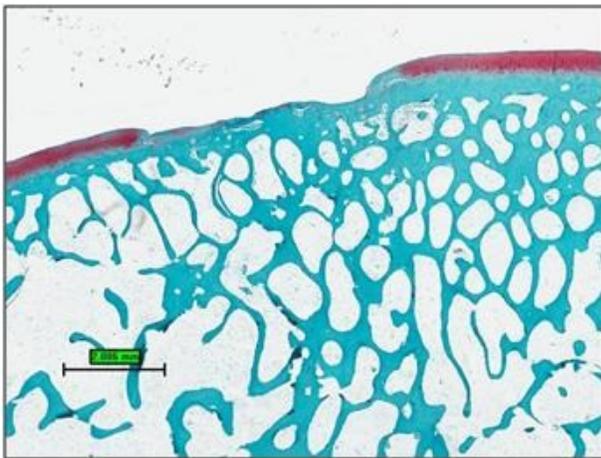


Figure 2C: Mfx, lateral proximal trochlear sulcus, Safranin-O stain

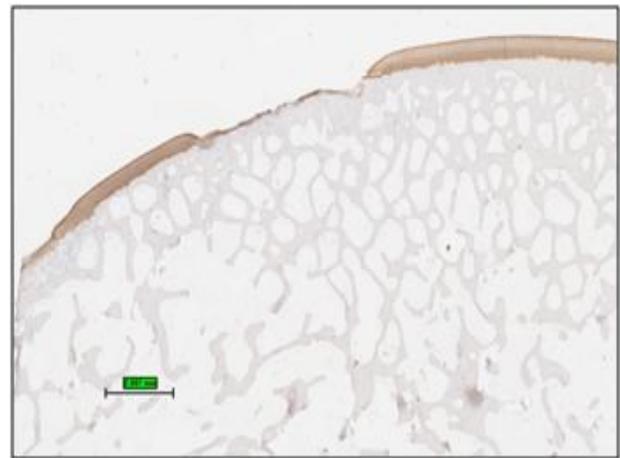
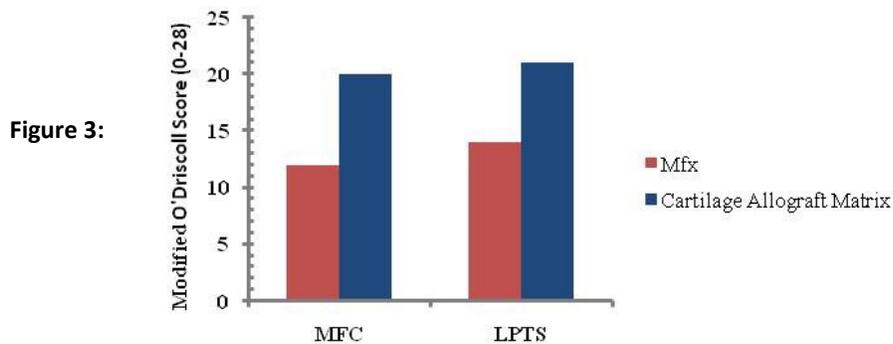


Figure 2D: Mfx, lateral proximal trochlear sulcus, Safranin-O stain

Histological scoring of the Cartilage Allograft Matrix was compared to Microfracture at 6 months. Cartilage Allograft Matrix performed 67% better in the MFC site and 50% better in the LPTS site (Figure 3).

**Modified O'Driscoll Scores:
6 month time point**



Photomicrograph of Cartilage Allograft Matrix-treated defect (Figure 4) in the medial femoral condyle (MFC) showed that most of defect is filled with hyaline cartilage (black arrows), a very small amount of which is degenerate. The hyaline cartilage is present across the entire defect, and is bonded to both lateral margins and the deep margin. The lateral margins of the defect are denoted by short blue arrows.

Photomicrograph of Microfracture-treated defect (Figure 5) in the medial femoral condyle (MFC) showed that most of the defect is empty, and there is only a small amount of hyaline cartilage at the lateral margins of the defect (black arrows). This hyaline cartilage is partially degenerated. The lateral margins of the defect are denoted by short blue arrow.

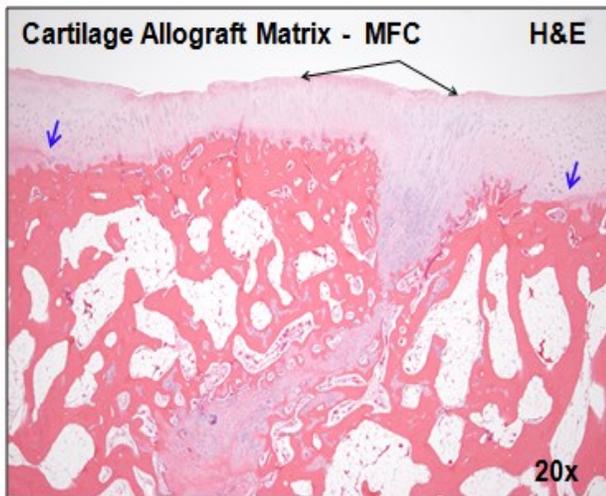


Figure 4: Photomicrograph of Cartilage Allograft Matrix, Medial femoral condyle, Hematoxylin and eosin stain (H&E)

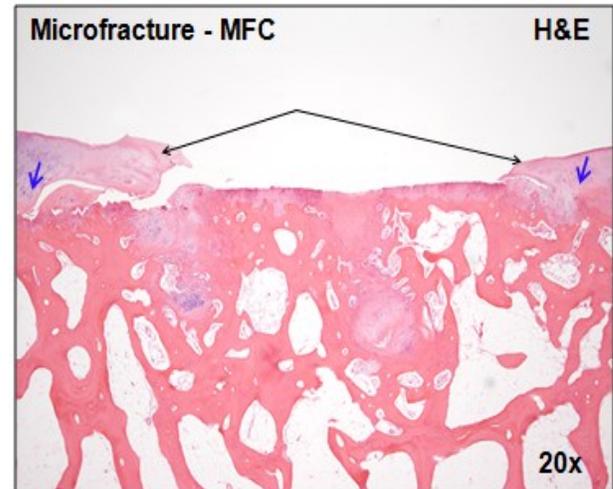


Figure 5: Photomicrograph of Microfracture, Medial femoral condyle, Hematoxylin and eosin stain (H&E)

DISCUSSION

Cartilage Allograft Matrix provides surgeons with an off-the-shelf alternative to treating full thickness cartilage lesions that has demonstrated to be superior to the Microfracture procedure. Efficacy of the Cartilage Allograft Matrix prepared from goat tissue has been demonstrated in a clinically relevant animal model of a critical sized, surgically created chondral defect. Histological scoring of the Cartilage Allograft Matrix has proven to be significantly better than Microfracture in both the medial femoral condyle and the trochlear sulcus in-vivo at 6 months.

REFERENCES

1. Hunziker E.B. Articular cartilage repair: basic science and clinical progress. A review of the current status and prospects. *Osteoarthritis and Cartilage* 2001; 10: 432-463.
2. Chen F.S., Frekel S.R., DeCesare P.E. Repair of Articular Cartilage Defects: Part I. Basic Science of Cartilage Healing. *American Journal of Orthopedics* 1999; Jan: 31-33.
3. Shahgaldi BF, Amis AA, Healey FW, McDowell J and Bentley G. Repair of cartilage lesions using biological implants. A comparative histological and biomechanical study in goats. *J Bone Joint Surg [Br]*,1991 Jan, 73:1, 57-64.
4. Jackson DW, Lalor PA, Aberman HM, Simon TM. Spontaneous Repair of Full-Thickness Defects of Articular Cartilage in a Goat Model: A Preliminary Study. *J Bone Joint Surg Am*, 2001 Jan, 83:53-64.