Treatment of Full-Thickness Cartilage Lesions with a 3D-Printed Implant in an Equine Preclinical Model

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INTRODUCTION:

Articular cartilage is a highly specialized connective tissue, which plays a critical role in providing a surface with minimal friction for joint motion as well as absorbing biomechanical forces. However, due to the low cellularity as well as poor vascularity and innervation, articular cartilage has a limited ability to repair following damage. The development of a treatment for cartilage lesions that enables restoration of the joint surface with tissue biomechanically identical to articular cartilage is highly sought after. To date, no treatment exists that is capable of achieving this.

Chondrograft™ is a 3D printed porous implant composed of nanomaterials with robust mechanical stiffness that fosters host integration designed for use in cartilage repair. The objective of this study was to validate the use of the Chondrograft™ Implant for the treatment of full thickness cartilage lesions, assessing its ability to fill the defect and support the engraftment of repair tissue to the underlying subchondral bone. The first hypothesis was that the Chondrograft™ will fill the full thickness cartilage defect and induce repair tissue that is superior to the untreated control. Our second hypothesis was that the Chondrograft™ will perform better in biomechanical testing compared to untreated controls.

METHODS: Bilateral 15mm diameter cartilage defects were created on the lateral trochlear ridge of the femur in 12 mature horses (IACUC approval 3171). One defect was implanted with Chondrograft™, which was positioned flush with the cartilage surface, and held in place with fibrin glue and a single PLLA dart (Arthrex Trimit Pin). The contralateral limb was an untreated (empty/full thickness) control defect. Horses were exercised starting day 28 and end points were at 36-weeks (4 horses) and 52-weeks (8 horses). Lameness examinations were performed every 4 weeks and recheck arthroscopic evaluation was performed at 12 weeks. Post-mortem evaluation included arthroscopic and macroscopic appearance scoring, MRI, histological assessment and biomechanical testing. Lameness, MRI scores and data relating to ICRS scores were assessed for normality, following which a t-test (parametric) or Mann-Whitney test (non-parametric) was performed. Mechanical testing data was assessed with a two-way ANOVA with Tukey's post-hoc test to determine statistical significance for stiffness comparing treatment groups and location.

RESULTS: Lameness scores were not statistically different between Chondrograft™ and control limbs at any time points. The 12-week follow-up arthroscopy revealed the Chondrograft™ treated defects had a mean repair tissue fill of 99.17 ± 1.946% compared to 45.83±33.70% in the control group ($P < 0.0001$)(Figure 1). The total ICRS scores for the Chondrograft™treated defect was 11.25±1.13 compared to 4.08±3.09 in the control defects ($P<0.0001$). Post-mortem ICRS scores for defect fill and border attachment to surrounding cartilage were improved in the Chondrograft™ treated defects (3.5 ± 0.67 and 3.25 ± 0.97 respectively) compared to the control defects (2 ± 1.13 and 1.83 ± 1.19) ($P = 0.0016$ and $P = 0.0068$). The overall ICRS score of the Chondrograft™ treated defects were 9.67 ± 2.31 compared to controls 4.83 ± 2.7 ($p = 0.0001$) (Figure 1). MRI MOCART scores were significantly higher (better) for Chondrograft™ treated defects compared to empty/debrided controls (74.58 vs 47.08, $P=0.0008$). Biomechanical testing revealed significantly higher repair tissue stiffness in Chondrograft™ treated defects compared to controls ($P<0.0001$)(Figure 2).

DISCUSSION AND CONCLUSION:

In concordance with our hypothesis, Chondrograft™ successfully filled a full thickness cartilage defect and provided repair tissue that was more similar to healthy articular cartilage than controls. Our second hypothesis that the Chondrograft™ will be biomechanically superior to control defects was also confirmed. The Chondrograft™ treated defect had improved defect fill compared to the control group, as well as a much smaller standard deviation representing reduced individual variability in the repair tissue fill. The overall ICRS score in the Chondrograft™ treated defects at the 12-week arthroscopic follow-up was 11.25, a significant improvement compared to control defects (4.08, $P<0.0001$). A further benefit of Chondrograft™ is its improved ability to become incorporated with the surrounding cartilage. This is evidenced by the MOCART MRI scores and the ICRS scores. The border attachment to surrounding cartilage was improved in the Chondrograft™ treated group at 3.25 compared to 1.83 in the control group. This incorporation is important to help reduce biomechanical and structural deterioration of the repair tissue over time due to exposure to shear forces. A limitation of this study is the potential role of the fibrin glue in providing growth factors encouraging repair in the Chondrograft™ treated group may have contributed (to a small degree) to the improved healing as fibrin glue was not used within control defects.

Chondrograft™ results in excellent defect filling and integration to the surrounding cartilage, with biomechanical function similar to normal healthy articular cartilage. The Chondrograft™ implant appears to be a viable option to improve cartilage defect healing and sustaining articular surface congruency, which persisted for 12 months after implantation.