Translation of Engineered Cartilage: In Vitro Evaluation of Integration Capacity of MSC-Based Constructs

The limited endogenous healing capacity of articular cartilage has motivated tissue engineering efforts aimed at restoring function and averting the onset of osteoarthritis. When interest centers on restoring focal defects, consideration must be given to both construct properties as well as integration with native tissue. We have recently shown that mesenchymal stem cells (MSCs) seeded in photo-polymerizable hyaluronic acid (HA) hydrogels undergo chondrogenic differentiation and synthesize a cartilage-like matrix with increasing properties over time[1,2]. To extend this work towards *in vivo* implantation, the ability of these constructs to integrate to native tissue is of paramount importance. In many *in vitro* integration models, a testing regime is employed where a cylindrical defect is filled with the engineered material and the integration strength is measured[3]. Utilizing this push-out testing modality, we analyzed the effect of initial HA macromer density on the functional integration of MSC-seeded hydrogels to native tissue (Fig. 1). Consistent with our previous findings of enhanced matrix distribution in constructs of lower density, we found that lower density constructs integrate with native tissue to a greater extent than higher density HA constructs (Fig. 2)[4]. Ongoing work is employing the application of compressive dynamic loading of *in vitro* repaired constructs to determine the durability of this repair as well as load transmission through this interface. Further, we are employing novel imaging modalities to provide quantitative assessment of integration quality (Fig. 3). This work will further our goal of clinical translation of engineered cartilage constructs for therapeutic applications.

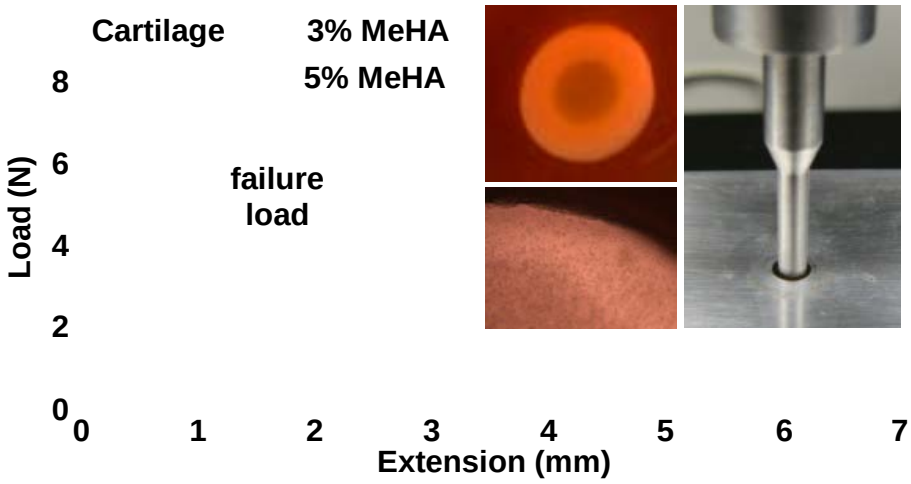

Figure 1. Representative load-extension plots from push-out tests on day 28. Note the high failure load for the autologous cartilage repaired sample. Insets: MSC-seeded 5% MeHA cultured within cartilage annulus at low (top left) and high (bottom left) magnification. Push-out indenter and testing platform (right).

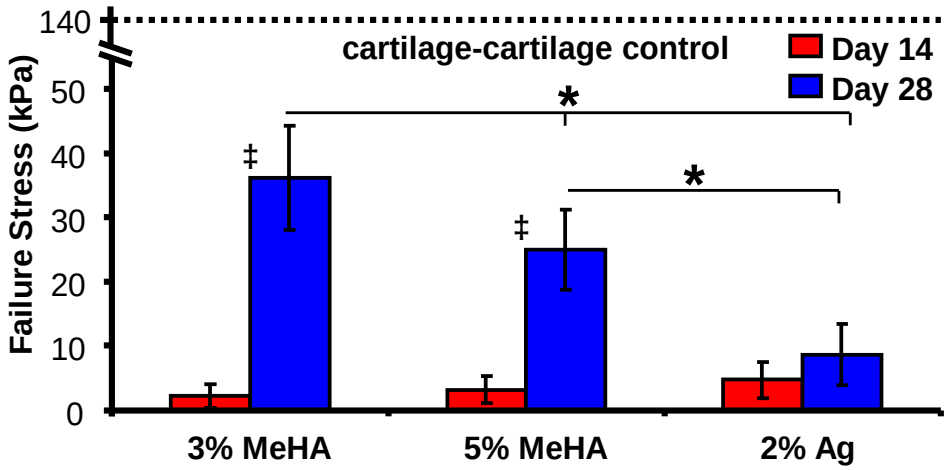

Figure 2. Failure stress values (mean ± standard deviation; n=4) for MeHA and agarose constructs. Note dotted line represents cartilage-cartilage control at day 28. (*p<0.05; ‡p<0.05 from day 14 to 28)

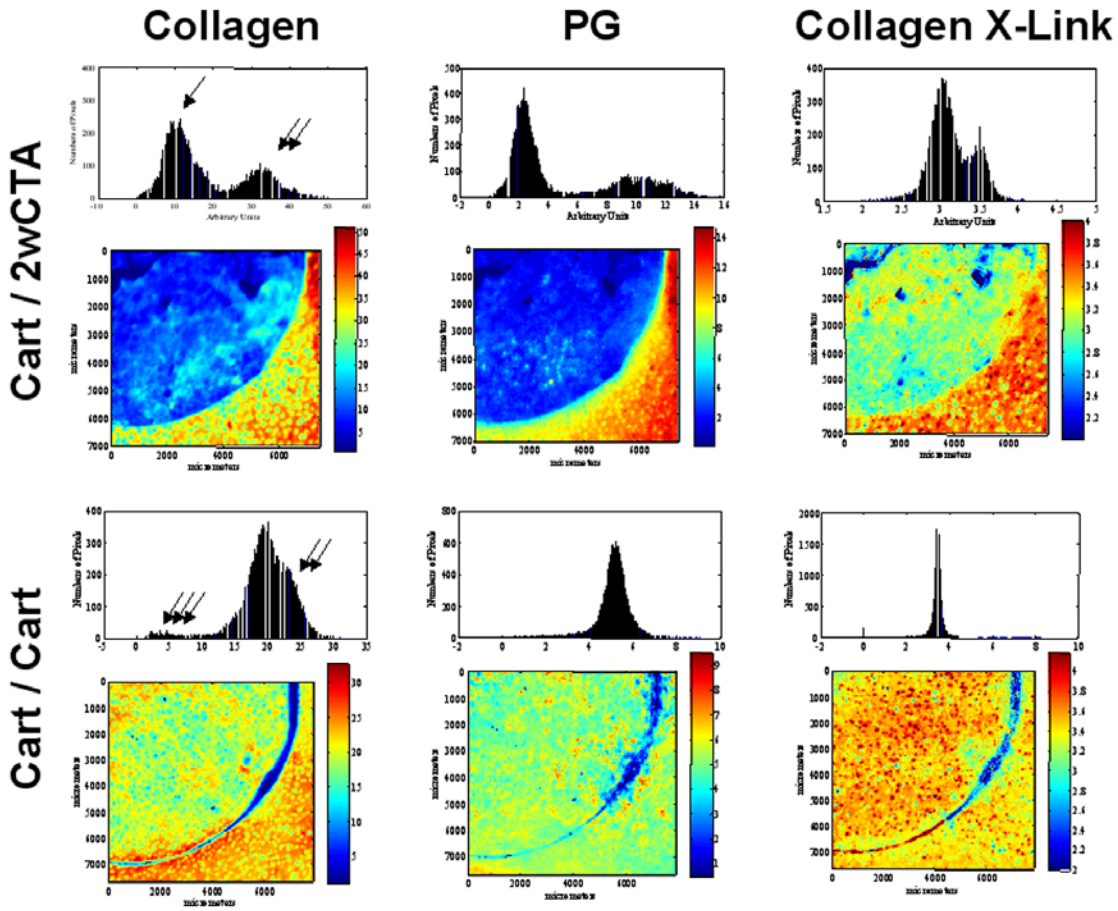

Figure 3. FT-IRIS-determined qualitative evaluation by histogram and compositional distribution of cartilage-to-engineered construct and cartilage-to-cartilage interfaces at 4 weeks (↑: 2wCTA, ↑↑: Natural cartilage, ↑↑↑: Interface).

Recent Publications:

1. Erickson IE, Huang AH, Chung C, Li RT, Burdick JA, Mauck RL. Differential Maturation and Structure-Function Relationships in Mesenchymal Stem Cell- and Chondrocyte-Seeded Hydrogels. Tissue Engineering Part A 2009;15(5):1041-1052.
2. Kim M, Erickson IE, Mauck RL, Dodge GR. Evaluation of Cartilage Integration using Tissue Engineered Cartilage in an in vitro Model of Cartilage Repair. Osteoarthritis Research Society International World Congress, Montreal, Quebec; 2009
3. Erickson IE, Huang AH, Sengupta S, Kestle S, Burdick JA, Mauck RL. Macromer density influences mesenchymal stem cell chondrogenesis and maturation in photocrosslinked hyaluronic acid hydrogels. Osteoarthritis and Cartilage 2009;17(12):1639-1648.
3. Kim M, Erickson IE, Yoder J, Mauck RL, Witschey W, Fenty M, Reddy R, Dodge GR. Evaluation of Integrative Cartilage Repair with Scaffold-Free Constructs. The 56th Annual Meeting of the Orthopaedic Research Society. New Orleans, Louisiana; 2010.
4. Erickson IE, Kestle S, Burdick JA, Mauck RL. In Vitro Cartilage Integration of MSC-Seeded Hyaluronic Acid Constructs. The 56th Annual Meeting of the Orthopaedic Research Society. New Orleans, Louisiana; 2010.

Personnel:

Isaac Erickson
Minwook Kim
Sydney Kestle
George Dodge, PhD
Jason Burdick, PhD

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