ORAL PRESENTATION GROUP 1 – PRESENTATION 2

Maximizing Morphology and Size Preservation of Collagen Hydrogel By External Scaffolding and Injection Molding

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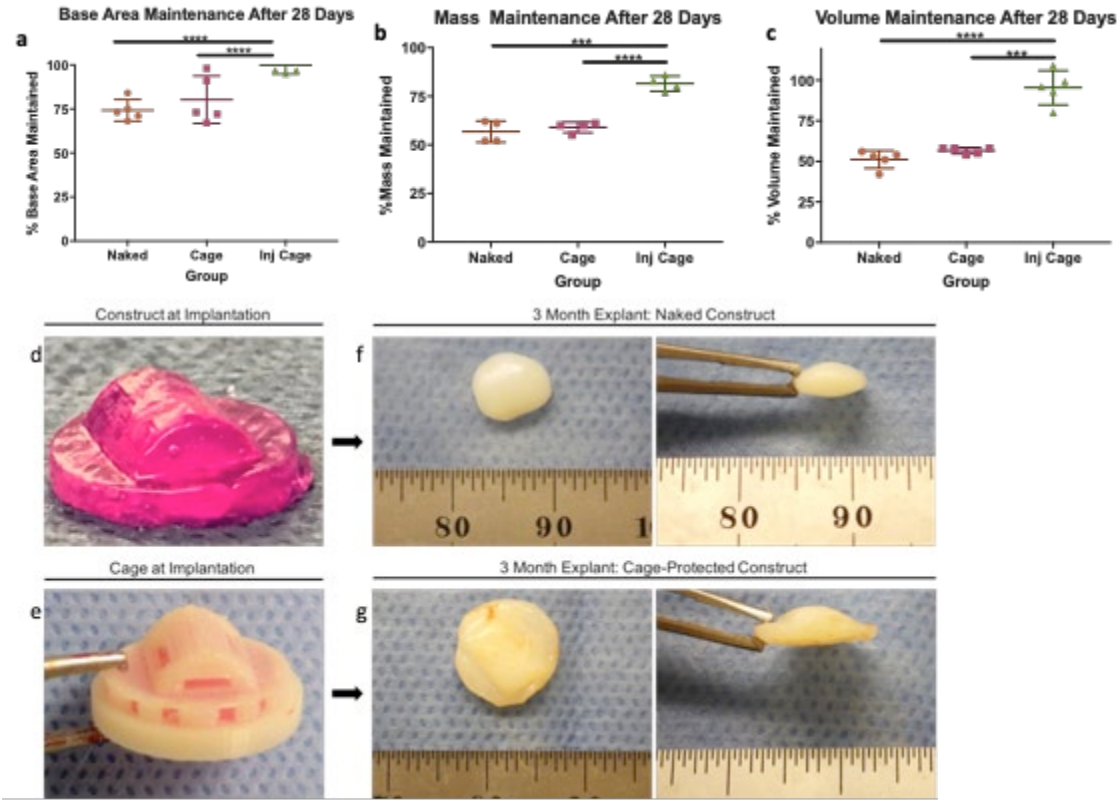
Introduction: A major obstacle to clinical utilization of autologous bioengineered auricular cartilage for microtia treatment is the significant contraction and loss of topography that occurs during maturation of the soft collagen/chondrocyte matrix into elastic cartilage. Previously, we demonstrated that an external scaffold protects chondrocyte-seeded collagen constructs from extrinsic compressive forces of the surrounding tissue. We hypothesize that by increasing the surface area contact with the external scaffold using injection molding, greater interfacial attachment between collagen and the scaffold will be achieved. We designed a hydrogel model to recapitulate and assess the maintenance of more intricate topographic features of human ear. Herein, we examine the use of injection molding in combination with external scaffolding to mitigate the intrinsic cell-mediated contractile forces of collagen hydrogels.

Methods: Custom shaped external scaffolds were designed with or without a geometric element representative of the helical rim and 3D-printed using polylactic acid (PLA). Chondrocytes were harvested from discarded otoplasty remnants, expanded to passage 3 and were then encapsulated into type I collagen. The constructs were prepared in three different groups. Demolded collagen hydrogels either without a scaffold *"naked"* or with external scaffolds *"cage"* were prepared. In *"injection-cage"* group, external scaffolds were injected with chondrocyte-seeded collagen while placed within polydimethylsiloxane molds. The constructs were either studied *in-vitro* or *in-vivo*. Following same method three control groups of acellular collagen were made. Constructs were photographed and underwent microCT for geometric measurements on day0 and at 1 and 3 months. The percentage of maintained base area, mass and volume were analyzed.

Results: ANOVA test showed significant difference in percentage of maintained base area, mass, and volume with *injection-cage* having the maximum maintenance of the mentioned measurements across all experiments. For acellular collagen constructs in the control group no significant differences were found in percentage of base area or mass maintenance but percentage of maintained volume was significantly lower in *naked* and *cage* group as compared to *injection-cage*.

Conclusions: Injection molding of chondrocyte-seeded collagen maximizes interfacial attachments to the scaffold achieving less contraction of base area, mass and volume and better preservation of topography compared to non-injection molding method, likely due to mitigation of cell-mediated intrinsic contractile forces. This technique can be used to create custom scaffolds that contour to any form, enabling the fabrication of engineered autologous cartilage tailored to individual patient anatomy, eliminating the contraction and loss of topography that has thus far impeded translation to the clinic.



Top: *In-vitro* geometrical changes of auricular chondrocyte seeded collagen constructs after 28 days. Percentages of base area (a), mass (b), and volume (c) maintenance is significantly higher in injection-cage group across all measurements. Bottom: Hydrogels with anatomical element before and after *in-vivo* implantation. *Naked* construct at implantation (d). *Cage* construct at implantation (e). Representative images of naked construct at 3-month explant demonstrating contraction and loss of topographic detail (f). Representative images of *cage* protected construct (g) from same time point showing better maintenance of volume and "helical rim" topographic element.