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EXPERIMENTAL AND THEORETICAL EVALUATION OF FAILURE PROPERTIES FOR IMMATURE TISSUE ENGINEERED CARTILAGE

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INTRODUCTION

Articular cartilage functions as a low friction load bearing soft tissue. The contact area and load distribution is highly location dependent in the knee joint [1]. Regeneration and repair strategies for osteoarthritis include tissue-engineered cartilage, which will need to bear high mechanical stresses and strains. There has been variable success in developing tissue-engineered cartilage with compressive mechanical properties comparable to native tissue (modulus = 40kPa – 1000kPa) [2-4]. There has also been some debate on the costs and benefits of implanting immature constructs and allowing them to elaborate their properties in situ, or culturing them in vitro and implanting them only after they have elaborated sufficiently functional properties. The former strategy may benefit from using the body as a bioreactor and might promote better construct integration, though constructs may bee to frail to sustain the physiological loading environment. The failure properties of engineered cartilage have not been widely evaluated, and may greatly affect the successful implantation of engineered cartilage as a repair strategy for the knee joint. The objective of this study was twofold: 1) to evaluate the failure properties of agarose hydrogels used as scaffolds in our tissue engineering studies, and 2) to evaluate whether joint congruence might sufficiently shield immature constructs to prevent their early failure. The long-term hypothesis of this study is that engineering analyses, based on an informed failure criterion for tissue constructs, might allow proper pre-assessment of failure risk for a given set of construct properties, dimensions, and joint congruence.

MATERIALS AND METHODS

The failure mechanics of agarose was evaluated experimentally using contact loading with a cylindrical indenter (radius = 3 mm). Agarose samples were prepared as 2% weight by volume (w/v) with 10μm spheres to provide texture for strain analysis. Samples were cut into half cylinders (radius = 3mm, thickness = 2.4mm) and placed into a cored cartilage half-cylinder (inner radius = 3mm, outer radius = 9mm, thickness = 3mm; Figure 1) to mimic in situ implantation. Samples were tested in a saline bath and loaded at a rate of 1%/s until failure. A high-resolution camera was used to acquire images for strain analysis using digital image correlation (Vic2D, Correlated Solutions Inc.). The maximum and minimum principal strains and the maximum shear strain were determined up to the failure point.

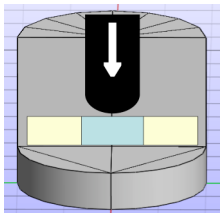

Figure 1. Schematic of confined compression apparatus used to load half-cylinder agarose samples (light blue) in cartilage (yellow boxes). The diameter of the indenter (black piece) was equivalent to the diameter of the construct. The front face was flat to acquire images for strain analysis.

To perform finite element analyses, previously reported measurements of the compressive modulus of immature constructs were employed [3], while the hydraulic permeability of 2% w/v agarose was determined from a permeation experiment using saline under a prescribed column of fluid (10 kPa). A finite element model of articulating cartilage layers was created using FEBio (http://mrl.sci.utah.edu/software/febio). A biphasic plane strain contact analysis was used with 1 mm thick opposing articulating layers. The model included a tissue construct in the bottom flat layer (curvature = 0.0 mm^{-1}), surrounded by healthy cartilage tissue. The top layer was cylindrical and the contact congruence was altered by adjusting its curvature (0, 0.05, 0.1, and 0.2 mm^{-1}). Contact analyses of intact articular layers (no construct) were also performed. The cartilage

properties were taken from [5] and the compressive modulus of immature constructs was set at 0.04 MPa. A 0.5N load was applied over a 2 s ramp. The peak principal strains, stresses and fluid pressure were examined in the construct at the peak applied load.

RESULTS

Just before failure, agarose samples subjected to contact with a cylinder exhibited a maximum principal strain of 0.10 ± 0.02 and a minimum principal strain of -0.22 ± 0.06. The peak strains were located below the indenter along the centerline of contact (Figure 2). The maximum shear strain was 0.16 ± 0.04.

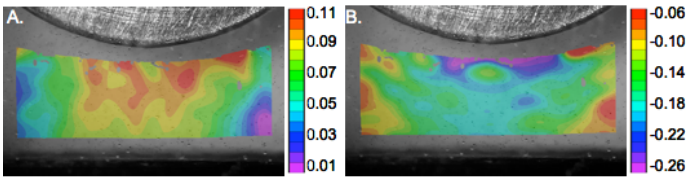

Figure 2: A) Maximum and B) minimum principal strains of agarose just prior to failure.

The hydraulic permeability of 2% agarose was 7.5×10^{-13} ± 2.5×10^{-13} $m^4/N\cdot s$. The average load at failure was 0.5N and the contact stress at failure was estimated at 23.2 ± 0.6 kPa.

In the finite element analysis, the peak compressive stress ranged from 0.2MPa for a fully congruent surface (0 mm^{-1}) to 0.3 MPa for a curvature of 0.2 mm^{-1}. The largest principal strains in the construct were located along the contacting surfaces with the top cartilage layer (Figure 3). The magnitude of the principal strains and the maximum shear strain increased with increasing curvature for the agarose and control conditions (Figure 4). The magnitude of the principal strains and maximum shear strain decreased in the control condition (Figure 4 – red line).

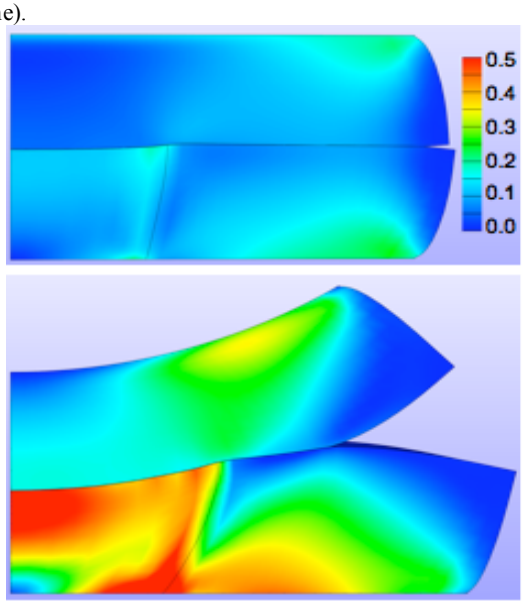

Figure 3: Contour map of the maximum principal strain for a curvature of 0.0 mm^{-1} (top) and 0.2 mm^{-1} (bottom). The agarose implant is represented by the left piece on the bottom surface.

DISCUSSION

The finite element model used in this study provides an initial assessment of the state of strain in engineered constructs implanted into joints of various congruences during low to moderate loading. The location in the peak maximum and minimum strains in the finite element analyses was consistent with the location of crack initiation in the experimental contact studies. As expected, the principal strains were greater for constructs whose mechanical properties are inferior to those of native cartilage. For all cases except perfect congruence, the maximum principal strains predicted by the FE models exceeded the threshold for failure observed in the experimental studies. These findings suggest that implantation of engineered cartilage with inferior mechanical properties will likely lead to failure under *in vivo* loading, unless high joint congruence provides sufficient stress shielding of the construct.

The increase in magnitude of the principal strains with increasing curvature was similarly observed in the control condition, where two intact articular layers are modeled. However, the strain magnitudes were significantly smaller than in the construct. These findings confirm that implanting more mature engineered cartilage into high load bearing regions should have better chances of survival.

The current study represents a first iteration toward the long-term goal of developing engineering-based criteria for assessing failure risk of implanted constructs. The models used in the current analyses did not account for the disparity between tensile and compressive properties of cartilage or tissue constructs. Failure criteria for tissue constructs have not yet been identified, though the experimental results of this study indicate that agarose is more susceptible to failure in tension. Future work will focus on improving the agreement between finite element models and experimental measurements of strain in tissue constructs, to help formulate a validated failure criterion that can be employed in the assessment of construct failure risk under a variety of in situ loading environments.

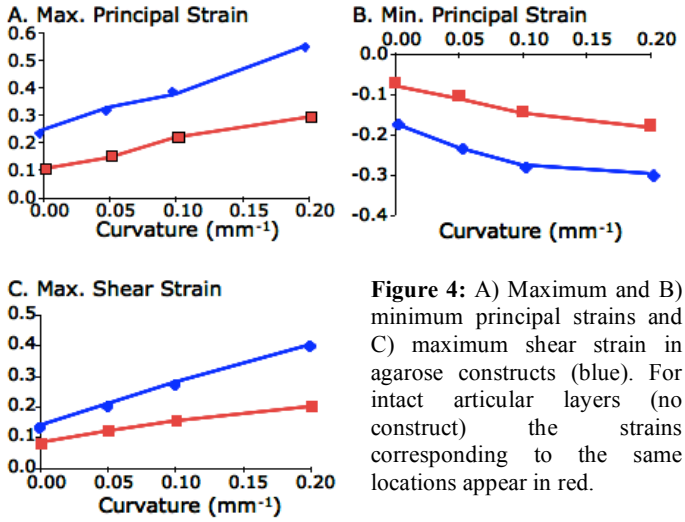

Figure 4: A) Maximum and B) minimum principal strains and C) maximum shear strain in agarose constructs (blue). For intact articular layers (no construct) the strains corresponding to the same locations appear in red.

ACKNOWLEDGMENTS

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