Semi-degradable Multifunctional Hydrogel Constructs for the Repair of Cartilage Defects

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Statement of Purpose. Currently no clinically successful technique exists to halt the degeneration of articular cartilage due to a cartilage defect. Biodegradable hydrogel scaffolds, elastic and porous cross-linked polymers, have been investigated for cartilage replacement, providing an attractive matrix through which chondrocytes can grow. However, fully degradable scaffolds are unable to support tissue generation with cartilage-like mechanical properties (1). A solution may be the use of non-degradable hydrogels containing degradable microparticles, loaded with growth factors, to encourage cell growth into the matrix. The result is the integration of cartilage tissue with the mechanically stable hydrogel scaffold, resulting in a composite hydrogel/cartilage construct, capable of functioning like healthy cartilage. Chondrocyte migration will be dependent on microstructure of the scaffold and growth factor type, dose, and release rate.

Hydrogels fabricated from two different methods were developed and characterized in terms of their morphology and mechanical properties.

Experimental Methods. Hydrogels were prepared from two different methods. In the Suspension Method, microparticles were prepared from poly(lactic-co-glycolic acid) using a water/oil/water double emulsion technique, and with growth factor suspended in phosphate buffered saline in the internal aqueous phase. Microparticles were collected by centrifugation and physically incorporated into the hydrogel solution by stirring prior to cryotropic gelation. In the Direct Incorporation Method, microparticles were made directly into the hydrogel solution with growth factor in PBS as the internal aqueous phase and the hydrogel solution as the external aqueous phase, and subsequently subjected to freeze-thaw cycling.

Insulin, used as a model for insulin-like growth factor-1, was added in varying doses to PBS in the internal aqueous phase. The particles were added in the amounts of 16, 23, 33, and 46 wt%. The hydrogel solutions were then physically cross-linked by using 5 cycles of the freeze-thaw technique.

Hydrogels prepared from the Suspension Method were analyzed over the course of 8 weeks of swelling in PBS at 37 °C. The scaffold morphology was analyzed by scanning electron microscopy. An Instron load cell was used to determine compressive moduli in unconfined compression (n=6).

Results and Discussion. SEM analysis showed that the particles were spherical in shape with a smooth surface, with an average diameter of 29.98 ± 17 µm. Figure 1 shows the microparticles embedded within the hydrogel matrix using the Suspension method (a) and the Direct Incorporation Method (b). The large pores seen in hydrogels made using the Direct Incorporation method are attributed to the evaporating solvent during hydrogel formation.

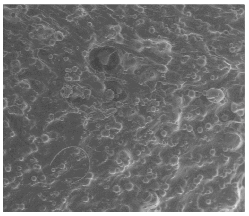
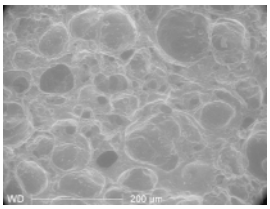
(a)  (b) 

Figure 1: Microparticle size distribution (a); microparticles embedded in hydrogel matrix (b).

Figure 2 shows the average compressive moduli of the hydrogels increased over the first four weeks and decreased thereafter. The increase in modulus is attributed to the hydrogels reaching equilibrium and the reduction in modulus to the microparticles degrading and leaving pores in the matrix.

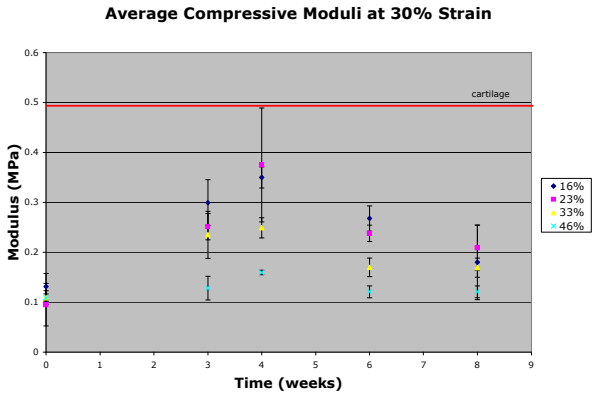


Figure 2: Average compressive moduli of Suspension Method hydrogels loaded with increasing amounts of microparticles, over an 8 week period of swelling in PBS at 37 °C.

Hydrogels have mechanical properties approaching that of healthy cartilage. Growth factors have been successfully incorporated into the microparticles. Preliminary cell culture studies show that chondrocytes are able to grow on the gels.

References.

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