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Integration Strength of Engineered Cartilage to Native Cartilage and Bone and Synthetic Substrate

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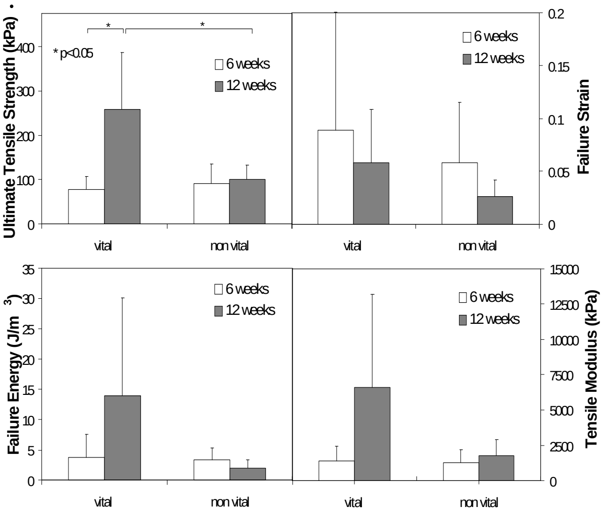
INTRODUCTION: The success of tissue engineering approaches for articular cartilage repair and regeneration relies not only on the ability of the chondrocytes to form new extracellular cartilage matrix, but also on the capacity of the new matrix to integrate with the existing cartilage surrounding the lesion and bone at the base of the lesion. The objective of this study was to investigate the integrative strength of engineered cartilage to: 1) native cartilage, 2) bone; and 3) and a synthetic porous polyethylene (PPE) substrate that could be used as part of a replacement osteochondral plug.

METHODS: Cartilage and bone discs (6mm) were made from swine tissues and PPE was commercially available. Swine chondrocytes were suspended in fibrinogen at a concentration of 80×10^6 cells/cc and mixed with the same amount of thrombin forming a slowly polymerizing fibrin glue mixture. 150 μL of the fibrin glue-cell mixture was placed on one disc. Another disc was placed on top of the fibrin glue-cell mixture and allowed to gel. Control constructs were made using acellular fibrin glue or fibroblasts in the middle. The constructs were implanted into subcutaneous pouches in the backs of nude mice for 6 and 12 weeks. Randomly selected specimens were processed for histology, and the remaining specimens were stored at –80°C prior to biomechanical testing.

The mechanical integrity of the bonding of the new cartilage to the substrate was evaluated on an Enduratech spectrometer. The constructs were attached to plexiglass rods using quick-setting cyanoacrylate glue and mounted in the actuator of the Enduratech. Tensile displacements were applied at a rate of 10 μm/s to failure and the resultant loads were recorded. Sample displacements and loads were normalized to strain and stress by sample geometry and intergration (ultimate tensile) strength (σ_{UTS}), failure strain (ε_f), failure energy (E_f), and tensile modulus (M) were calculated from the resultant stress-strain curves.

RESULTS: Histology showed new cartilage matrix formed between the discs when chondrocytes were incorporated in the fibrin glue. No cartilage formed between discs when chondrocytes were omitted or using fibroblasts. For brevity, data using bone discs are shown (Figure). Integration strength (σ_{UTS}) was highest in 12 weeks samples as demonstrated vital bone. At 12 weeks, ultimate tensile strength was ~260 kPa, a 3-fold increase over that at 6 weeks ($p<0.05$) and 2.5 fold higher than in samples using devitalized bone ($p<0.05$). Similar trends were observed in failure energy and tensile modulus, with 12 weeks samples from vital bone larger than all other groups. There was no difference in failure strain between groups. The integration strength of neocartilage with native cartilage at 12 weeks was ~90 kPa and that with PPE was ~140 kPa.



DISCUSSION & CONCLUSIONS: The integration of an engineered cartilage implant to the existing bone and cartilage surrounding a lesion is critical for a stable and successful repair. These data demonstrate that engineered cartilage has the capacity to integrate with native cartilage and bone, as well as a synthetic nondegradable material. This model could simulate the integration of cartilage with the bone and cartilage surrounding a lesion and promote regeneration of the articular surface. Further studies will focus on understanding mechanisms that control process of integrative bone and cartilage repair employing tissue engineering strategies.

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