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Bioreactor-manufactured cartilage grafts repair acute and chronic osteochondral defects in large animal studies

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Abstract:
Objectives: Bioreactor-based production systems have the potential to overcome limitations associated with conventional tissue engineering manufacturing methods, facilitating regulatory compliant and cost-effective production of engineered grafts for widespread clinical use. In this work, we established a bioreactor-based manufacturing system for the production of cartilage grafts.
Materials & Methods: All bioprocesses, from cartilage biopsy digestion through the generation of engineered grafts, were performed in our bioreactor-based manufacturing system. All bioreactor technologies and cartilage tissue engineering bioprocesses were transferred to an independent GMP facility, where engineered grafts were manufactured for two large animal studies.
Results: The results of these studies demonstrate the safety and feasibility of the bioreactor-based manufacturing approach. Moreover, grafts produced in the manufacturing system were first shown to accelerate the repair of acute osteochondral defects, compared to cell-free scaffold implants. We then demonstrated that grafts produced in the system also facilitated faster repair in a more clinically relevant chronic defect model. Our data also suggested that bioreactor-manufactured grafts may result in a more robust repair in the longer term.
Conclusion: By demonstrating the safety and efficacy of bioreactor-generated grafts in two large animal models, this work represents a pivotal step towards implementing the bioreactor-based manufacturing system for the production of human cartilage grafts for clinical applications.

Keywords: bioreactor-based manufacturing, cartilage tissue grafts, osteochondral defects, nasal cartilage chondrocytes, regulatory compliance, tissue engineering