Enhancing Bone-Tendon Repair: A Biomimetic Strategy Utilizing Enthesis-Mimicking Suture Anchor-Tendon Hybrid Graft with Growth and Differentiation Factor-7 (GDF-7) for Multi-Cell Patterning

Chenyang Wang, Xu Zhang, Dan Wang, Patrick S.H. Yung, Rocky S. Tuan, Dai Fei Elmer Ker

1School of Biomedical Sciences, 2Institute for Tissue Engineering and Regenerative Medicine, Ministry of Education Key Laboratory for Regenerative Medicine, 3Department of Orthopaedics and Traumatology, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China. 4Center for Neuromusculoskeletal Restorative Medicine, Hong Kong Science Park, Hong Kong SAR, China.

Corresponding author: Dai Fei Elmer Ker elmerker@cuhk.edu.hk

Disclosures: DFE Ker holds a US patent for fabrication of QHM polymer. Other authors have no disclosures to declare.

INTRODUCTION: Rotator cuff repair remains challenging due to the need for addressing load bearing deficits in the mechanically compromised shoulder while simultaneously revitalizing injured fibrocartilage and tendon tissue. To address these, we designed a biomimetic bone-tendon graft (Suture Anchor-Tendon Hybrid Graft; SATHG) containing Growth and Differentiation Factor-7 (GDF-7) to reduce mechanical stress and enhance tissue healing at the repair site. To reduce mechanical stress, SATHG was designed to mimic geometric attributes of native entheses such as collagen fiber angulation, tissue geometric flaring, mechanical gradation, and tissue interdigitation1. To enhance fibrocartilage and tendon healing, we utilized GDF-7 to achieve the simultaneous differentiation of human mesenchymal stem cells (hMSCs) into fibrochondrocytes and tenocytes, enabling facile multi-cell patterning of SATHG.

METHODS: To perform FEA optimization, 3D in silico models of the SATHG and humeral bone were created in Solidworks (Dassault Systèmes, France) and arm abduction was simulated using a 100 N tensile force (Figure 1). Ex vivo tensile testing validated the design, exhibiting superior load, displacement, stiffness, and work-to-failure. Larger SATHG diameters also improved pull-out strength, indicating robust bone attachment. Immuno- and cytochemical staining assessment for tenocyte (SCX, TNC, and Picosiris Red) and fibrochondrocyte (COL2A1, Sox9, and Alcian Blue) differentiation was performed. To assess tissue response and in vivo healing, 10 rabbits underwent surgery to create a 5 mm rotator cuff defect for implantation of non-porous SATHGs followed by histological assessment (H&E and safranin-O staining) at 6 weeks post-surgery.

RESULTS: FEA showed a 43.6% reduction in peak stress concentration for the optimized SATHG design compared to the control1. Optimized SATHGs had low stress in central regions. Ex vivo tensile testing validated the design, exhibiting superior load, displacement, stiffness, and work-to-failure. Larger SATHG diameters also improved pull-out strength, indicating robust bone attachment. Immuno- and cytochemical staining assessment such as Alcian blue staining showed simultaneous fibrochondrocyte and tenocyte differentiation of hMSCs within a single construct/well when treated with GDF-7. In vivo studies showed unexpected damage in SATHG implants in the non-optimized, tendon-like regions but encouragingly, H&E and safranin-O staining revealed evidence of biocompatibility and enthesis regeneration (Figure 2).

DISCUSSION: This study demonstrated that geometric mimicry of the entheses increased the mechanical properties (e.g., ultimate load) of a bone-tendon graft and that a single growth factor (GDF-7) induced simultaneous cell fates (tenocyte and fibrocartilage) in a spatially controlled manner within a single construct for multi-cell patterning. These findings will facilitate soft-to-hard, tendon-bone tissue attachment despite their severe mechanical mismatch and promote eventual graft-host integration. However, our FEA study focused on mechanical optimization of SATHG’s soft-to-hard interface and unexpected damage was observed in the graft’s tendon-like regions. This hampered biomechanical evaluation and is a limitation of the current work. Further optimization of the SATHG’s tendon-like regions (e.g., geometric shape and thickness) will be performed in future studies to improve mechanical performance. Taken together, this biomimetic approach holds promise for musculoskeletal repair and implant durability.


ACKNOWLEDGEMENTS: This work was supported by grants from The Chinese University of Hong Kong, Health Medical Research Fund of Hong Kong, Research Grants Council of Hong Kong, and Innovation and Technology Commission of Hong Kong.

ORS 2024 Annual Meeting Paper No. 366