

Piezoelectric and Magnetically Aligned Hydrogel Scaffold Enhances Tendon-to-Bone Interface Regeneration via SDF-1 Delivery and Stem Cell Modulation

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INTRODUCTION: Functional regeneration of the tendon-to-bone interface in chronic rotator cuff injuries remains challenging due to poor tissue integration and fatty infiltration. This study develops a multifunctional hydrogel scaffold to mimic the complex enthesis microenvironment and promote targeted healing.

METHODS:

A novel injectable hydrogel system (nMag/SDF-1/PVDF-TrFE) was fabricated by integrating piezoelectric PVDF-TrFE core-shell nanofibers loaded with SDF-1 into a magnetically responsive matrix. Magnetic alignment created a gradient-oriented structure, simulating native enthesis architecture. Nanofiber parameters (core-shell diameter, length, SDF-1 load) were optimized to enhance piezoelectric output and bioactivity. In vitro assays evaluated ADSC proliferation, migration, tenogenic differentiation, and activation of AMPK and PI3K/Akt pathways.

For in vivo evaluation, 24 New Zealand white rabbits were randomly assigned to four groups: (1) blank control, (2) scaffold without SDF-1, (3) non-aligned SDF-1/PVDF-TrFE hydrogel, and (4) magnetically aligned nMag/SDF-1/PVDF-TrFE hydrogel. A standardized supraspinatus tendon-to-bone repair model was established. At 8 weeks post-surgery, specimens were analyzed via histology, immunofluorescence, qPCR, and biomechanical testing.

RESULTS: Rabbits treated with nMag/SDF-1/PVDF-TrFE hydrogel showed superior tendon-bone integration, significantly higher biomechanical strength (load-to-failure: 32.5 ± 3.1 N) compared to control (18.9 ± 2.7 N, $p < 0.01$), improved collagen alignment, and reduced fatty infiltration (oil red O area ratio \downarrow 46%). Immunostaining revealed elevated expression of tenogenic markers (Scx, Tnmd), and qPCR confirmed upregulation of AMPK and Akt pathway components.

DISCUSSION AND CONCLUSION: This piezoelectric and magnetically aligned hydrogel scaffold enhances enthesis regeneration by promoting stem cell homing, modulating key signaling pathways, and suppressing fatty degeneration. The system offers a promising therapeutic approach for functional rotator cuff repair.

