Biomimetic Adhesive Enhances Enthesis Repair in Rats

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INTRODUCTION

The tendon–bone enthesis is a highly specialized interface tissue that provides graded structural and mechanical transitions between tendon and bone, enabling efficient load transfer during movement. When injured, however, the enthesis rarely regenerates its native architecture and instead heals with disorganized fibrocartilaginous scar tissue, predisposing patients to chronic pain, impaired function, and high rates of re-injury [1,2]. Restoring scarless enthesis healing is therefore a central challenge in orthopedic repair. We recently developed a biomimetic polymer adhesive that can be applied at the tendon–bone interface prior to surgical suturing. This adhesive mimics natural extracellular matrix chemistry and promotes integration at the repair site. Our previous work demonstrated that the application of adhesive leads to formation of enthesis – like tissue in the healing site whereas suture only group was presented by disorganized fibrocartilage tissue [3]. The present study sought to determine whether adhesive treatment also improves repair-site morphology and biomechanical function in a rat enthesis injury model. We hypothesized that adhesive application would reduce excessive scar tissue formation, restore organized morphology, and enhance biomechanical recovery.

METHODS

The polymer adhesive was synthesized using lysine diisocyanate (LDI) and amino acids to mimic native matrix properties. An Achilles tendon–calcaneus enthesis injury was created in 10-week-old female rats (**Fig.1**). In the suture-only group (n=11), the transected tendon was reattached to the calcaneus by transossal suturing. In the adhesive + suture group (n=11), polymer adhesive was applied at the tendon–bone interface prior to suturing. Left ankles served as intact controls (n=8). At 8 weeks post-surgery, healing was evaluated by the following methods: 1) µCT analysis for cross-sectional area and repair site volume; 2) histological imaging for tissue organization; and 3) mechanical testing for ultimate load, stiffness, displacement, ultimate stress, and elastic modulus. Female rats were chosen to minimize variability due to sex-related differences in tendon–bone healing. All procedures were approved by IACUC. Statistical analysis performed by Mann-Whitney method.

RESULTS

Adhesive-treated repairs exhibited a more compact and organized tissue morphology resembling native enthesis, while the suture-only group displayed enlarged cross-sectional areas and increased repair site volumes, consistent with scar overgrowth (**Fig. 2**). Mechanical testing showed no significant differences among groups in ultimate load, displacement, or stiffness (**Fig. 3B–D**). However, adhesive treatment produced a positive trend towards improved material properties, with higher ultimate stress and elastic modulus compared to suture-only, though values remained below those of intact controls (**Fig. 3E-F**).

DISCUSSION

Application of the biomimetic polymer adhesive reduced scar formation and restored more physiological enthesis architecture. These findings are consistent with our prior work showing adhesive-mediated scarless healing [3], and further demonstrate that structural improvements may contribute to enhanced mechanical quality of the repair tissue. Although ultimate load and stiffness were not significantly increased at 8 weeks, the upward trend in stress and elastic modulus indicates early improvements at the tissue level. It is possible that longer healing durations, optimized dosing, or combination therapies (e.g., growth factors or stem cells) will be necessary to achieve full restoration of enthesis biomechanics. Importantly, the adhesive strategy integrates seamlessly with current surgical repair techniques, suggesting strong translational potential.

SIGNIFICANCE

This study demonstrates that a biomimetic polymer adhesive improves enthesis structural repair and partially restores biomechanical properties. Such adhesives could serve as a valuable adjunct to surgical repair, potentially enhancing functional recovery and reducing long-term complications following enthesis injuries.

REFERENCES:

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ACKNOWLEDGEMENTS

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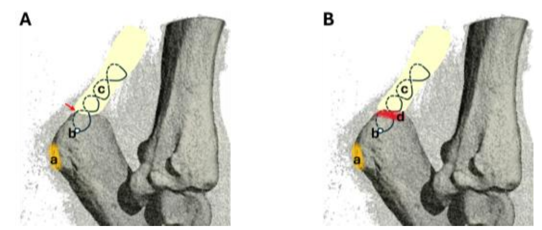

Fig. 1 Achilles tendon(AT) enthesis injury model.
Transected original AT enthesis (**A,B,a**). Transossal suture of AT (**A,b,c**) in suture only group. Transossal suture of AT following by polymer adhesive application (**B,b,d,c**) in adhesive plus suture group.

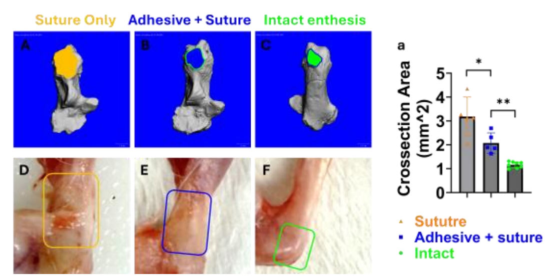

Fig. 2 Biomimetic polymer adhesive application reduces the cross-sectional area and tissue volume of newly formed enthesis at the healing site. The enthesis cross-sectional area was increased in the suture-only group compared to the adhesive-plus-suture group and normal enthesis (**A–C**), with quantification shown in panel (**a**). Healing site volume was visually greater in the suture-only group compared to the adhesive-plus-suture group and normal enthesis (**D–F**). n = 4 - 8. *,** $p < 0.05$.

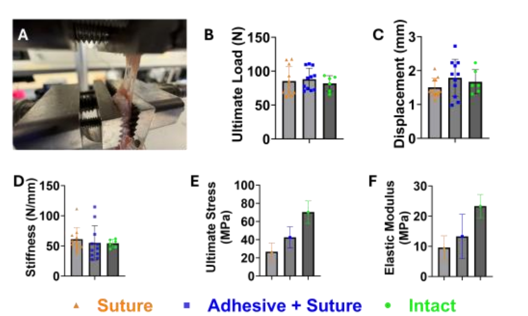

Fig. 3 Biomechanical testing of the Achilles tendon enthesis. Samples were clamped, and tensile load was applied until failure (**A**). No significant differences were observed among groups in ultimate load, displacement, and stiffness (**B-D**). A trend toward increased ultimate stress and elastic modulus was detected in the adhesive-plus-suture group compared with the suture-only group, although values remained below those of the normal group (**E**, **F**). n = 6-11.