Annulus Fibrosus Repair Using Tough Adhesive Hydrogels

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INTRODUCTION: Low back pain and sciatica are common conditions, affecting up to two-thirds of adults at some point in their lives.[1] Up to 85% of sciatica cases result from intervertebral disc (IVD) herniations, in which the nucleus pulposus (NP) extrudes through defects in the annulus fibrosus (AF).[1] IVD herniation commonly arises from age-related proteoglycan loss in the NP or from traumatic overload, leading to structural weakening of the AF and potential nerve compression.[3] Microdiscectomy, the standard surgical treatment, effectively relieves pain but leaves the AF unrepaired, contributing to reherniation rates as high as 27% and reoperation rates up to 21%.[4] Thus, there is a critical need for an AF repair strategy that is mechanically robust, biocompatible, and technically feasible in the surgical setting.[4] Bioinspired tough adhesive (TA) hydrogels—previously shown to be strong, flexible, and non-cytotoxic in various tissue applications (tendon rupture[6], wound closure[7], dental lesions[8], and dural repair[9])—represent a promising candidate. In this study, we evaluated the adhesion strength of the TA hydrogel to AF tissue as a first step toward assessing its suitability for annular defect repair.

METHODS: *TA Synthesis:* TAs were engineered to include a tough gel dissipative matrix and chitosan-based bridging polymer that absorbs to the gel and AF surface (**Fig. 1**). Tough gels were synthesized by dissolving sodium alginate (Kimica, I-1G) and acrylamide in HBSS at 2.25% and 13.5%, respectively. This solution was mixed with N,N'-methylenebis(acrylamide) (MBAA, covalent cross-linker), TEMED (accelerator), ammonium persulfate (APS, initiator), and calcium sulfate dihydrate (ionic cross-linker) and allowed to gel overnight. Using the high positively charged amine content in slug mucus as inspiration, chitosan (HMC 54046) was selected as the bridging polymer. Chitosan was dissolved in ddH2O (1% w/w). *Functional spine unit (FSU) preparation:* FSUs were prepared from butcher-acquired oxtails. Surrounding soft tissues were dissected away. The intervertebral discs were identified under fluoroscopy, and FSUs were prepared by sawing through the superior and inferior vertebrae of each disc. *Adhesion strength measurement*: Chitosan (~100µL) was applied to the surface of the AF, and the TA was compressed onto the AF for 2 minutes, followed by a 10-minute rest period to allow for settling, with one end of the TA extending past the FSU for gripping. The opposite side of the TA was bonded to a rigid polyethylene terephthalate (PET) film. Adhesion strength was measured via lap shear testing under uniaxial tension (100mm/min) (CellScale Univert). The free end of the TA was covered on both sides by sandpaper and clamped into the upper portion of the CellScale. The FSU, with the other end of the gel adhered to it, was fixed into the lower portion of the cell scale (**Fig. 2a**). The surface area of adhesion and force at adhesion failure were recorded, with adhesion strength calculated as force over surface area. A commercially available medical adhesive fibrin sealant patch was also tested (Tachosil®). Analysis: A two-tailed, unpaired Student's t-test was used to compare adhesion strength across the two adhesives.

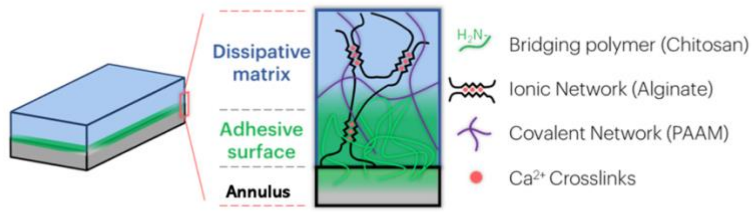

Figure 1: Synthesis of TAs for annulus tissue. TAs were engineered with two main components: a tough gel matrix and an adhesive surface layer. The gel matrix, composed of alginate and polyacrylamide, forms both ionic and covalent crosslinks that allow the material to dissipate energy. The adhesive surface was created using chitosan, an amine-rich bridging polymer, which bonds to both the gel and tissue through electrostatic interactions, covalent bonding, and physical interpenetration. Together, these features enable strong, durable adhesion to the annulus.

RESULTS: Adhesion testing demonstrated that the TA exhibited significantly greater adhesion strength compared with Tachosil®. The mean adhesion force for chitosan was 20.8 ± 9.9 kPa, while Tachosil® averaged 7.0 ± 3.1 kPa (n = 5 samples per group) (**Fig. 2b**). A two-tailed unpaired Student's t-test revealed a statistically significant difference between groups (p = 0.017). These findings indicate that TA provides stronger interfacial bonding to the test surface than Tachosil® under the same conditions, reaching adhesions strengths of up to 37 kPa.

DISCUSSION: The results of this study demonstrate that the TA , when combined with chitosan as a bridging polymer, forms significantly stronger bonds to AF tissue compared to a commercially available Tachosil®. The superior adhesion strength of the TA suggests improved mechanical integration with AF tissue, a critical property for sealing annular defects following discectomy. Given the mechanical demands of the native AF, achieving a robust and durable bond is essential to maintaining disc integrity and preventing reherniation. These findings support the TA's potential as a mechanically competent and biocompatible alternative to existing clinical adhesives. Future work will focus on long-term stability and enhancement of adhesion strength, functional validation through compression testing of FSUs to assess whether TAs can effectively prevent NP extrusion under physiological loading conditions, and in-vivo safety and effectiveness.

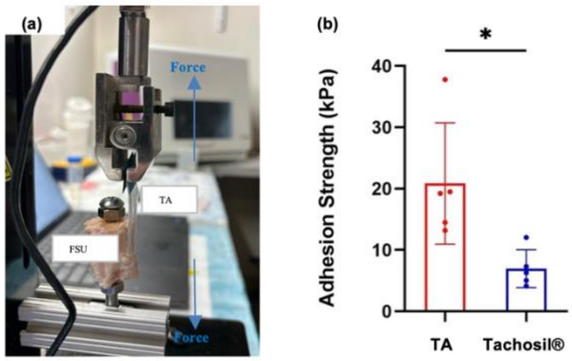

Figure 2: Lap shear testing to determine adhesion strength. (a) Testing apparatus with uniaxial lap shear force applied to TA/AF interface. (b) Adhesion to AF tissue for TA was compared to Tachosil®, analyzed via Student's t-test. *p<0.05

SIGNIFICANCE: This study provides the first evidence that tough adhesives can achieve strong, stable adhesion to annulus fibrosus tissue, highlighting their promise as a next-generation material for intervertebral disc repair. By enhancing AF repair strength, TA hydrogels may reduce postoperative reherniation and reoperation rates following microdiscectomy.

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