Electronic Supplementary Information (ESI) For:

Tissue-Mimetic Hybrid Bioadhesives for Intervertebral Disc Repair

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Supplementary notes

1. Materials

Sodium alginate (Kimica Corporation) was used for all the experiments with NP glues and AF sealant. For the cytocompatibility test and *in vitro* culture, 1.5 g of alginate was dissolved in 500ml of DI water, and the purified alginate was obtained by sterile filtered, frozen, and lyophilized. Calcium sulfate dihydrate was purchased from Sigma. Chitosan (DDA: 95%, medium and high molecular weights) was purchased from Lyphar Biotech and used for mechanical tests. For the cytocompatibility test, chitosan was dissolved in DI water with 0.8 % v/v acetic acid and then filtered through a 0.22 μm filter. The coupling reagents, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC) (cat. #03450) and N-hydroxysulfosuccinimide (NHS) (cat. #130672), were purchased from Sigma-Aldrich.

2. Human intervertebral disc (IVD) tissue and cell preparation

Fresh human IVD tissues (one for the mechanical test (54 years old, Male, degenerated); the other one for the 3D cytocompatibility test (19 years old, male, Thompson scale: 1)) and human primary NP cells (56 years old, male, Thompson scale: 2-3) were provided by Spinal Tissue Biobank at McGill University. All replicates n in the experiments involving human primary cells, or human tissue represent the technical replicates from one independent experiment of one donor. Specifically, isolated human discs (from a donor, 19 years old, male) are used for the 3D culture following established protocols from Spinal Tissue Biobank.{Citation} Briefly, after the removal of the muscles and ligament around the disc and vertebral, parallel axial cuts were made through the vertebral bodies close to the cartilage end plates using a handsaw. Discs isolated are rinsed in 1xPBS supplemented with 100 μg/mL gentamicin (Thermo Fisher Scientific, cat. #15710-072) and 0.5 μg/mL fungizone (amphotericin B; Thermo Fisher Scientific, cat. #15290018) for 5 minutes. Discs then received two 5 minutes of serial washes with Hank's Balanced Salt Solution (Sigma-Aldrich, cat. #H9394) supplemented with 100 μg/mL gentamicin and 0.5 μg/mL fungizone. Discs are cultured in tissue culture medium (2.25 g/L glucose DMEM, supplied with 0.5% gentamicin, 5% FBS (Sigma-Aldrich, cat. #12483020), 1% GlutaMAX (Thermo Fisher Scientific, cat. #35050-061), 50 μg/mL ascorbic acid) for pre-swelling for 48 hours. Then the NP or AF tissue is isolated separately for the 3D cytocompatibility test. Human cells were isolated from fresh non-degenerated IVD tissues from a human donor (56 years old, male); around 1.07×10^6 NP cells were harvested from 1 g of NP tissue and used in passages 2-3.

3. Bovine tissue preparation

Bovine disc tissues used for the lap shear test were isolated from the bovine tail with 18 months provided by Oligo Medic. The bovine discs for *ex vivo* biomechanics tests are isolated from bovine tails with levels cc2/3, cc3/4, and cc4/5 from healthy and skeletally mature animals, purchased from a local grocery store.

4. Rheological measurement

Strain sweep tests were performed on human NP samples or the in-situ alginate hydrogels (20 mm in diameter and 1 mm in thickness) on the stage of rheometer (TA Instruments). A 20-mm parallel plate was used, and a gap was set at ~1 mm. The strain swept from 0.05% to 50% under a constant angular rate of 10 rad/s. Time sweep tests characterized the gelation kinetics of the alginate hydrogel with an oscillation frequency of 1 Hz (~ 6.28 rad/s) and strain of 0.1% for 45 min. The storage modulus and shear modulus were recorded as a function of time. The stress relaxation profile was assessed under a step strain of 15%. The duration required to relax half of the initial stress defines the stress relaxation time, $t_{1/2}$.

5. Lap shear adhesion test

For the lap shear adhesion test, NP glue adhesion imparted by the adhesion primer was quantified using a modified lap shear configuration. Before testing, lap-shear specimens were fabricated in an acrylic mold with 3 mm thickness, 10 mm width, and 20 mm length. First, 1.5 mm thick, 10 mm width, and 20 mm length of tissues of NP, inner AF (IAF), or outer AF (OAF) were obtained from the bovine tail in coccygeal IVD levels of cc1/2, cc2/3, cc3/4, and cc4/5. Then the tissues were placed in the base of the acrylic mold. Then to apply the NP glue, the bridging adhesion primer was dropped on the top of the tissue, followed by an injection of the alginate hydrogel on the primed tissues. Next, it was covered by a glass sheet and kept in a 4^{o}C refrigerator overnight. Negative control samples were without the application of adhesion primer. Before testing, the samples were placed at room temperature for 1 hour. For the adhesive failure strength measurement, specimens were taken out from the mold and glued to a custom acrylic backing by Super Glue and then fixed on a universal testing machine (model 596; Instron, Norwood, MA, USA) with a 10 N load cell. Then, the specimen was loaded to failure at a constant loading rate of 5 mm per minute. The strain-stress at failure and the type of failure were recorded. For the adhesive energy test, a 1-mm notch was created at the interface between hydrogel and tissues before loading, and the critical strain corresponding to the ultimate stress was recorded. All data were collected on Instron software and post-processed on MATLAB (MathWorks, Natick, MA, USA) code.

6. The Congregation of Rhodamine-B isothiocyanate to chitosan polymeric chains.

To visualize the depth of chitosan, part of the adhesion primer, into the AF, Rhodamine-B isothiocyanate (Cayman Chemical, cat. #20653) was conjugated to chitosan polymeric chains with the following steps. Briefly, 1 wt% chitosan was first dissolved in 80 mM acetic acid and sterilized through 0.22 μm PES filters (Thermo Fisher Scientific, cat. #13100106). Anhydrous methanol (Thermo Fisher Scientific, cat. # A412-1) was added to the filtered chitosan solution with a volume ratio of 1:1. The mixture was stirred for 3 hours at room temperature and degassed before use. Rhodamine B was dissolved in methanol at 2 mg/ml. The staining solution was added to the chitosan/methanol mixture drop-by-drop under stirring. The final concentration of fluorescent dyes in the reaction medium was controlled to give the label to D-glucosamine residue at a ratio of 1:50. The reaction lasted for 18 hours for rhodamine B-labeled chitosan in dark at room temperature. Then, 1 N NaOH solution (Sigma-Aldrich, cat. #S2770) was used to precipitate chitosan from the solution. The precipitates were collected and dialyzed with DI water until no fluorescent signal was detectable in the water. The precipitates were freeze-dried before use.

7. Confocal imaging for primer penetration depth

The adhesion primer, which was made by conjugated chitosan, was cast over an 8 mm diameter punch of bovine AF tissue for 2 min. Following incubation, the extra solution was aspirated off the AF and applied with alginate hydrogels for 15 min or 24 hours at 4 ^{o}C. Consequently, the specimens were embedded in Tissue-Teck O.C.T. Compound for cryosectioning to produce 12 μm thick sections mounted on charged slides (Thermo Fisher Scientific, cat. #22-037-246). Sections were then stained with a 1:1000 dilution of 1 μg/mL stock solution of 4′,6-diamidino-2-phenylindole (DAPI) for 5 minutes to visualize AF cell nuclei. Slides were imaged on a Zeiss LSM 800 confocal microscope to visualize cross-sectional depth-of-penetration. The confocal images were imported into MATLAB, and the depth was analyzed.

8. Extract preparation for cytotoxicity of NP glues to 2D human NP cell

To measure the cytotoxicity of the NP glues to human primary NP cells, the monolayer culture of cells in the extracts medium of NP glues was performed following the standard protocols in International Organization for Standardization (IOS) 10993-5. Briefly, the extracts of NP glues were prepared with a 200 mg/mL concentration in 12-well cell culture-treated polystyrene microplates. A mass of 200 mg of NP glue was placed in the center of the well, and 1 mL of low glucose (2.25g/L) DMEM was added to cover the glue completely. The samples were incubated at 37^{o}C for 24 hours. The concentration of the EDC/NHS in the primer used for NP glue is in a gradient of 0, 20, 30, and 50 mg/mL. The extracts were prepared on the same day that human primary NP cells were seeded into 96-well microplates. After 24 hours of incubation, the extracts were collected into small vials and supplemented with 1% GlutaMAX, 0.5% gentamicin, and 10% FBS on the monolayer human primary NP cells. Cells were cultured in the normal complete DMEM medium for the negative control group. In the test, human primary NP monolayer cells cultured in the described extract medium (d) for 24 hours were evaluated via Live/Dead assay. The negative control group was treated with 70% methanol for 30 minutes before the Live/Dead assay (Fig. S5).

9. Human NP Cell in vitro culture in NP glues

The NP cells were encapsulated in hydrogels for in vitro experiments. As previously described, purified sodium alginate was dissolved in DMEM (2.25 g/L glucose). Then NP cells suspension was mixed with alginate hydrogel precursors at a final cell density of 1 million cells per mL to match the low cell density in native human NP (4 million cells per cm3).54 Next, cell-alginate precursors were mixed with CaSO4 slurries. The mixture was immediately injected into a customed glass model with 2 mm thickness and incubated at 37 oC for 45 minutes for full gelation. Finally, the cell-gel samples were punched out with 6 mm diameter small pieces and cultured in a 24-well plate for 21 days. 600 μL culture medium was added to each well plate and was changed every three days. The conditional medium was collected at each time point. Four formulations of alginate hydrogel of NP glues were investigated: 1 kPa–high MW, 1 kPa–low MW, 3 kPa–high MW, and 3 kPa–low MW, where the concentrations of calcium in alginate hydrogels were 14 mM,15 mM, 20 mM, and 23 mM, respectively. High and low molecular weights refer to alginate molecular weights of 1500 kDa and 92 kDa, respectively.

10. Cell viability test of NP cells encapsulated in NP glues

For human primary NP cells encapsulated in the alginate hydrogel, on days 1, 3, 7, 14, and 21, the samples were put in a serum-free medium containing calcein AM and ethidium homodimer fluorescent dyes (Live/Dead®, Thermo Fisher Scientific, cat. #L3224), according to the manufacturer's instructions. Cell viability was evaluated using an EVOS M5000 microscope. Twenty consecutive 10 μm sections were imaged. The image stacks were merged and saved as a single-color JPEG file (red and green separate), and the labeled cells were quantified through Image J code. The viability of cells was calculated from the proportion of green and total cells.

11. Metabolic activity assay

Metabolic activity was measured in the NP cell-laden hydrogel samples on day 1, day 4 and day 7. Each of the sample in the 24 well-plate was incubated in 600 μL culture medium containing 10% (v/v) alamarBlue (Invitrogen, cat. #DAL1025) for 4 hours. 3 times 100 μL of each sample were transferred to black 96 well plates (Corning, cat. #3880) and fluorescence intensity was measured at excitation 540 nm, emission 585 nm (Tecan M200 Infinity Pro). 10% alamarBlue in culture medium was used as a blank value and was subtracted from all the sample values.

12. Biochemical quantification analysis

The amount of sulfated glycosaminoglycan (sulfated GAG) synthesized by NP cells encapsulated in alginate hydrogel for 21 days was evaluated by the 1,9-dimethylmethylene blue (DMMB) assay.[1] The hydrogels containing NP cells were removed from their culture medium on day 1 or day 21. The conditional medium was collected over the culture period. Chondroitin sulfate (Sigma-Aldrich, cat. #C9819) was used to make the standard curve, and 4 M guanidine hydrochloride ($CH_5N_3 \cdot HCl$) was added to standard curves when quantifying sulfated GAG content released in the hydrogel. Reagents are added to a 96-well plate, followed by reading under a microtiter plate reader (Tecan M200 Infinity Pro) using the absorbance at 530 nm. The dry mass of hydrogel was measured as the mass of the frozen and lyophilized constructs on day 1 and day 21. Samples without dilution were fit in the middle of the linear range of the standard curve, and results were expressed per mg of the dry weight of the gel sample.

13. IVD motion segment preparation for mechanical tests

Frozen bovine tails for biomechanical loading tests were purchased from a local grocery store. Spinal motion segments (i.e., vertebrae-disc-vertebrae) were isolated from the levels C2/C3, C3/4, and C4/C5. Facet joints, transverse processes, ligaments as well as musculature were carefully removed. The motion segments were potted in two Dragon Skin (Smooth-On) molds with an acrylic resin (DenPlus, Canada) on both ends of the segments. The cured potting materials were drilled to create holes for the fixture. Afterward, the potted motion segments were wrapped in PBS-soaked gauze and–stored at - 20 ^{o}C until further use. Before testing, the potted motion segments were submerged in 1X PBS with protease inhibitor at 4 ^{o}C to allow full hydration overnight. On the day of testing, the specimens were warmed in 1X PBS at room temperature for 2 hours.

All motion segments were randomly assigned to 'Intact', 'Defect', 'Glue', 'Glue+Patch', and 'Glue+Plug' groups. Except 'Intact', all the groups underwent nucleotomy following a standard clinical procedure. Specifically, a 3-mm biopsy punch

(Integra LifeSciences) was inserted 7 mm deep into the posterolateral side of the AF, and the resulting plug of tissue was removed using a rongeur. Following the initial tissue removal, the NP was then disrupted with micro scissors, and ~ 200 mg of fragmented NP tissue (around ~25% of NP) was removed from the IVD. For the Glue condition, the injured IVD was treated with NP glue alone. To do so, the adhesion primer (Chitosan, EDC, and NHS) of ~150 μL was first injected slowly into the NP cavity using a 3-mL syringe and a 20G x 1-1/2" needle (BD PrecisionGlide™, NJ) to prime the inner tissue surface. After 2 minutes, the extra primer solution was aspirated, followed by injection of the mixture of alginate and calcium sulfate to in-situ form alginate hydrogels (~150 μL). The specimens were then covered by a parafilm and set for 15 minutes before mechanical testing. For the groups of Glue+Patch or Glue+Plug, after removal of the partial NP as mentioned for Glue groups, the AF defect was treated with the adhesion primer and sealed with the AF patch (Glue+Patch) or inserted with the AF plug (Glue+Plug). Gentle compression was applied on the AF sealant for 10 minutes to enable adhesion and covered by a parafilm until mechanical testing.

14. Biomechanical test of IVD motion segments

Cyclic loading tests: Changes in IVD motion segment biomechanical properties in the groups with/without repair after nucleotomy were characterized using axial tension-compression and stress relaxation tests on a testing device (model 596; Instron, Norwood, MA, USA). Specimens were loaded cyclically in force control at tensile 0.2 MPa and compressive 0.5 MPa loads for 20 cycles at 0.5 Hz.[2–5] Next, stress relaxation tests were performed with ramp displacement applied until the force equivalent of 0.15 MPa compression was achieved; after that, the constant displacement was held for 15 min. All biomechanical testing was performed at room temperature. A MATLAB code was used to extract defined biomechanical parameters from raw force-displacement data (Fig. 3B and Fig. S1, Fig. S4). The parameters were determined from the average value of the last 5 complete test cycles as described.[4] Compressive/tensile stiffness was defined as the slope of the force-displacement curve within 80% of the maximum/minimum displacement region. Range of motion (ROM) was the total displacement of the motion segment during a compression-tension cycle. Dissipated energy was defined as the area between loading and unloading curves in the force-displacement response. The neutral zone (NZ) length was defined as the distance between two points in the loading and unloading curves at which the load was zero and the slope of the force-displacement response in the NZ denoted the NZ stiffness.[6] Preceding parameters were determined from the average value of the last 5 test cycles.[4] In the stress relaxation test, the force-time was recorded, and the stress relaxation along with time was normalized to the initial stress. All biomechanical testing was performed at room temperature. **Failure compression tests:** To evaluate the herniation risks, we performed displacement-controlled (2mm/min; ramp-to-failure) compressive failure tests on motion segments on a 5° inclined foundation to maximize stress at the repair site (Fig. 3H).[7,8] The tests were performed on a test instrument (ElectroPuls® E10000; Instron, Norwood, MA, USA). The stress was defined as the applied force normalized to IVD cross-sectional area. The load-displacement curves showed two types of failure mechanisms (Fig. 3H): endplate fracture or disc subsidence (a direct drop of force); NP extrusion (force perturbations). The extrusion failure can also be observed during the tests, which was defined as a 2 mm protrusion of NP or implant materials from the outer radius

of the AF.[7] The failure strength for all the groups was recorded in Fig. 3I: the failure strength for Intact groups was defined as the maximum stress at the point of endplate fracture; for the defect and repaired groups, the failure strength was defined the stress of NP extrusion point.

15. Bioadhesive evaluation on living human IVD model in bioreactor

To evaluate the swelling and adhesion of the bioadhesives under physiological conditions, we tested them on human IVD loaded with an IVD bioreactor for 28 days. The isolation of human disc and the design and operation of the IVD bioreactor were described in the previous studies.[9,10] Briefly, a living human lumbar IVD of level L2/L3 (from a donor, 53 years old, male) was isolated and then conditioned in a culture medium to reach equilibrium for 48 hours. Nucleotomy was performed by creating a 4-5 mm vertical linear incision with 3 mm depth in the AF at the post-lateral position of the disc with a scalpel, followed by removal of 0.9248 g NP tissue with pituitary and curette. After applying the NP glue (~1 mL) and the AF patch, we assembled the bioreactor with the repaired IVD, and filled the culture chamber with the disc culture medium. After pre-loading of 0.1 MPa static compression for 48 hours to reach the equilibrium status, a physiologically relevant cyclic compressive loading was applied to the IVD for 26 days. The daily loading pattern contains 4 statuses: (1) 2 hours dynamic compressive loading from 0.1 – 0.6 MPa at 0.1 Hz; (2) 6 hours static compressive loading of 0.1 MPa; (3) 2 hours dynamic compressive loading from 0.1 – 0.6 MPa at 0.1 Hz; (4) 14 hours static compressive loading of 0.1MPa. The medium will be changed every 7 days. The displacement, force, and time of the mechanical data were recorded. The IVD height and diameters were recorded at the beginning and end of the culture. The TA patch dimensions pre- and post-culture were measured.

16. Swelling property of NP glue and AF patch

To evaluate the swelling properties of each component of the bioadhesive, the NP hydrogel and AF patch were prepared and shaped into disks of 3 mm in thickness and 5 mm in diameter. They were immersed and swollen freely in PBS at 37 °C. The diameter and thickness of the disks were measured using a calliper after 7 days; given the thickness of the disks, the duration is sufficient to reach equilibrium and we observed no additional change in dimension. The swelling ratio was calculated by dividing the post-value by the initial value (pre-value).

17. Fabrication and characterization of thermoplastic polyurethane (TPU) reinforced AF patch

Fabrication of TPU-AF patch: The TPU scaffold was 3D printed using Creality Ender 3 V2 (Shenzhen Creality 3D Technology Co., Ltd.) into crossed layers with 40 mm in length, 5 mm in width, and 3 mm in thickness. Note that the angle between fibers is 30^{o}, matching with that of collagen fibers of AF respecting to the transversal plane of the spine (Fig. S10A). To obtain different mechanical responses, the mesh design of the scaffold was varied for large, medium, and small sizes as shown in Fig. S10B. The distance between two TPU fibers (d) are 4 mm, 3 mm, and 2 mm respectively. After printing, the scaffold was treated with plasma to improve the hydrophilicity. When preparing the TPU-AF patch, the alginate-polyacrylamide tough hydrogel was prepared and injected into the mold (40 mm in length, 5 mm in width, and 3 mm in thickness), and the plasma-treated TPU was immediately pressed into the mold and covered with glass for gelation at room temperature overnight (Fig. S10C).

Tensile test of TPU-AF patch: To measure the tensile properties (elastic modulus and ultimate strength), the strips of TPU-AF hydrogel were tested with a tensile test machine (1000 lb force load cell). The displacement rate was 100 mm min^{-1}. The representative stress-strain curves are shown in Fig. S10D, where the nominal stress was obtained by dividing the force by the area of the cross section, and the nominal strain was obtained by dividing the change in length by the original length. The elastic modulus is extracted as the slope of the linearly fitted stress-strain curve at 5% strain. The TPU scaffold can dramatically stiffen the AF patch and the small-mesh condition resembles the modulus of human AF (Fig. S10E). Further, we examined the tensile strength of the TPU-AF patches. Consistent with the elastic modulus, the strength correlates inversely with the mesh size and the obtained range also contains a reported value of human AF (Fig. S10F).

Supplementary figures

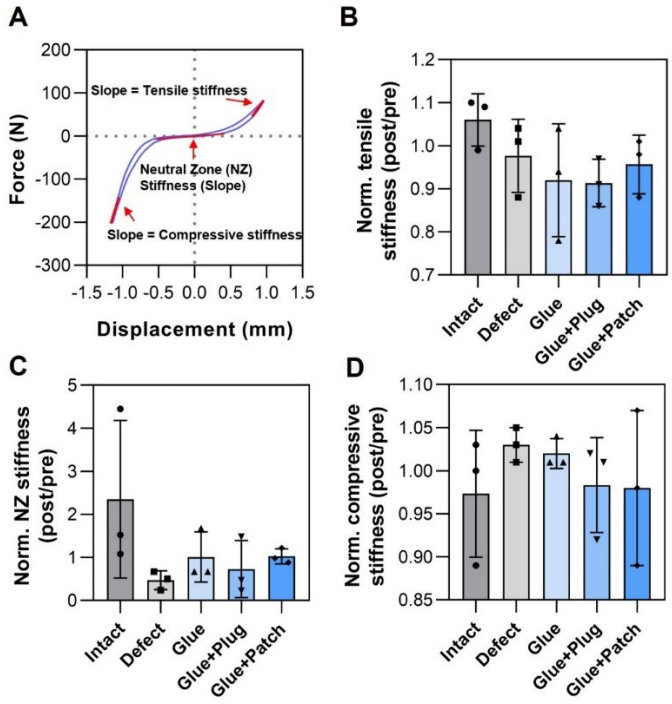

Fig. S1. Biomechanical evaluation with bovine motion segments under cyclic loading.
The analysis of additional biomechanical parameters was performed with the same data obtained from the samples as shown in Figure 3. (A) The biomechanical parameters are defined as indicated by red lines added to the force-displacement curve. The calculated parameters include tensile stiffness (B), neutral zone stiffness (C), and compressive stiffness (D). No statistical difference is found when comparing the defect group and other repair groups. The Glue+Patch group is closest to the intact group in terms of ZN stiffness and compressive stiffness. Data reported as means ± SD for n = 3 replicates per condition.

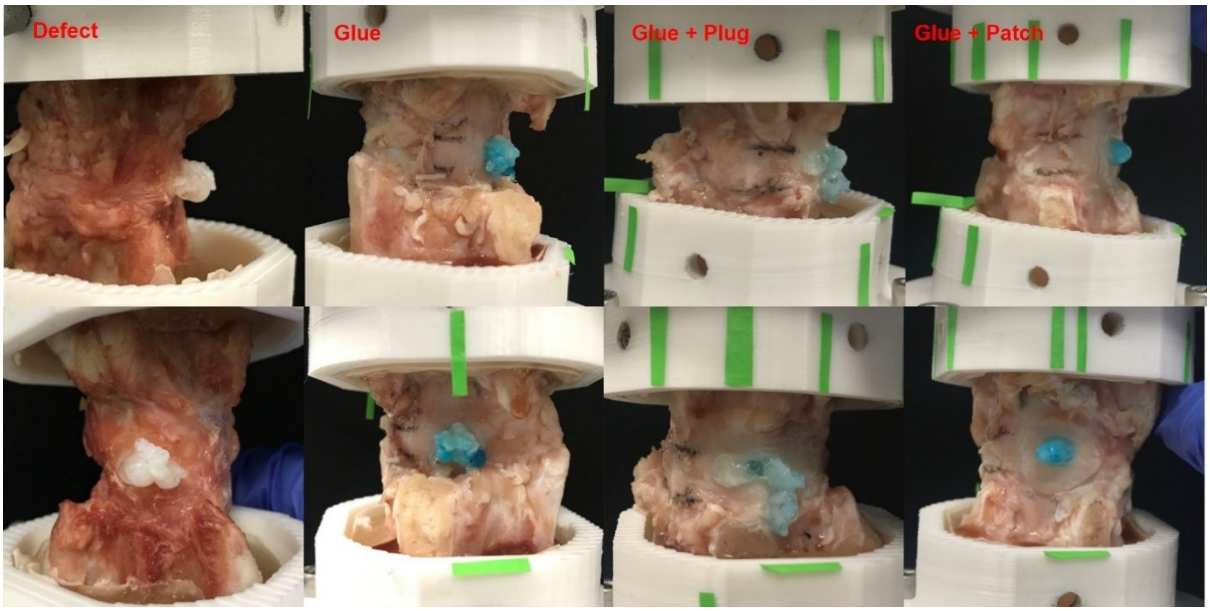

Fig. S2. Digital images of bovine spinal motion segments under extreme loading.

In extreme compressive loading tests, the herniation occurs among groups of Defect, Glue, Glue+Plug, and Glue+Patch. The NP tissue is white in color, the NP glue is blue, and the AF plug or patch is transparent.

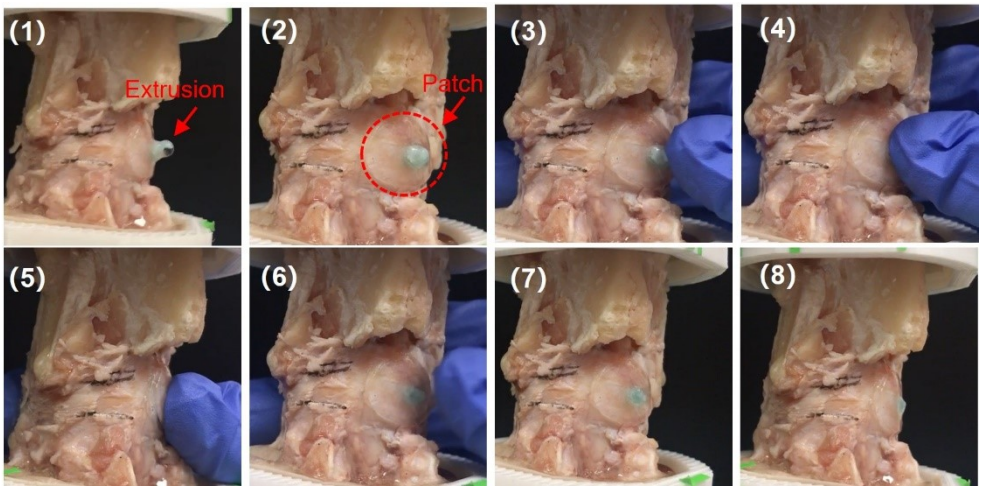

Fig. S3. Herniation recovery with the Glue+Patch treatment and gentle compression.
For the Patch+Glue group, the glue is excluded under the extreme compressive loading test (1), while the sealant patch remains adhered to the AF tissue (2). Compressing the patch gently (3)-(5) can retract the protruding volume of glue back to the disc (6)-(8).

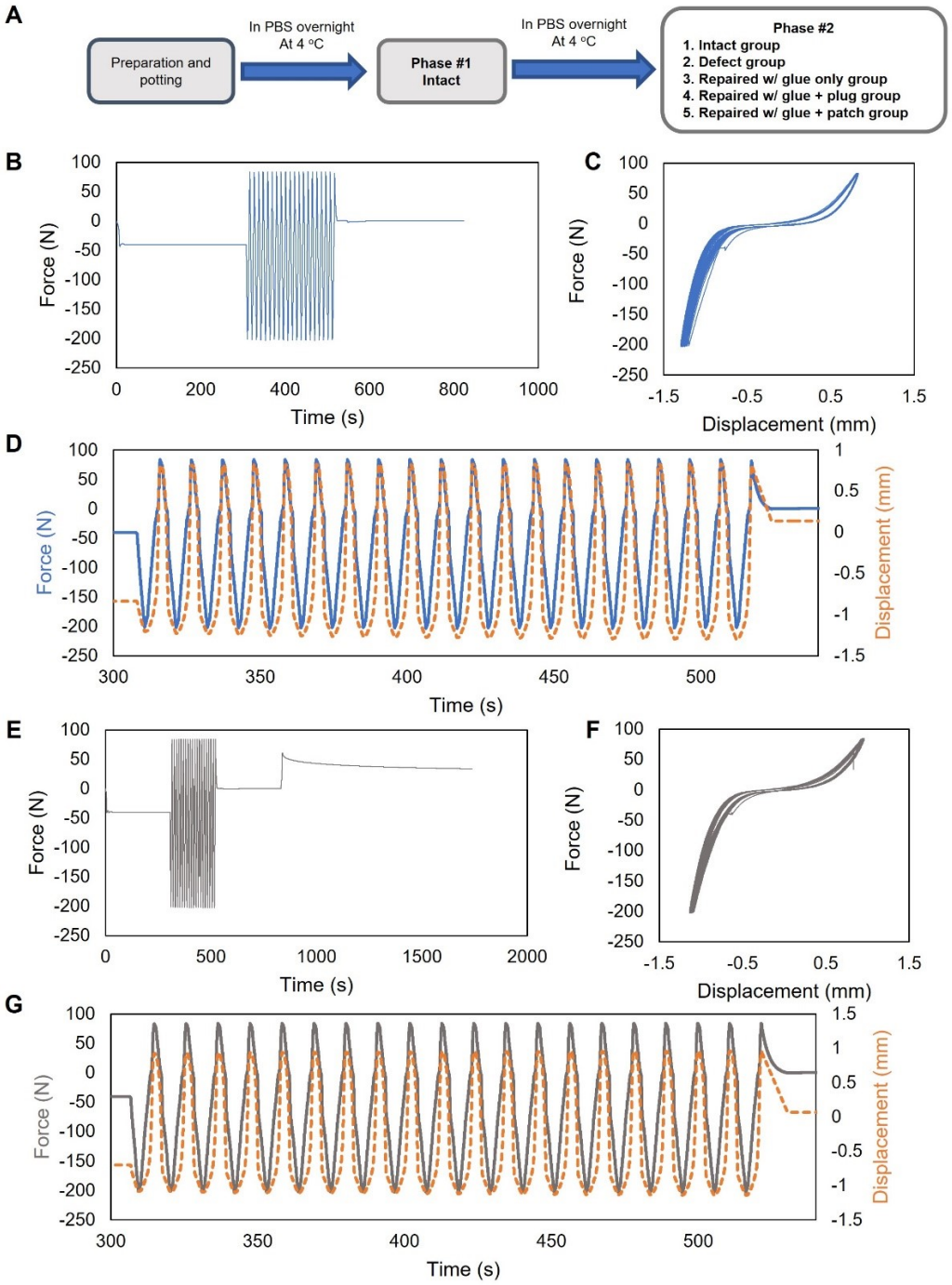

Fig. S4. Workflow and representative data of cyclic loading tests on bovine IVD.
(A) Workflow of the cyclic loading test process. For the Glue+Patch sample (phase #1), the force-time (B) and force-displacement curves (C) of the complete loading pattern, and the detailed curves of force-time (solid) and displacement-time (dashed) of 20 cycles are plotted in D. The same plots for the Glue+Patch sample (phase#2: post-repair) are presented in E-G.

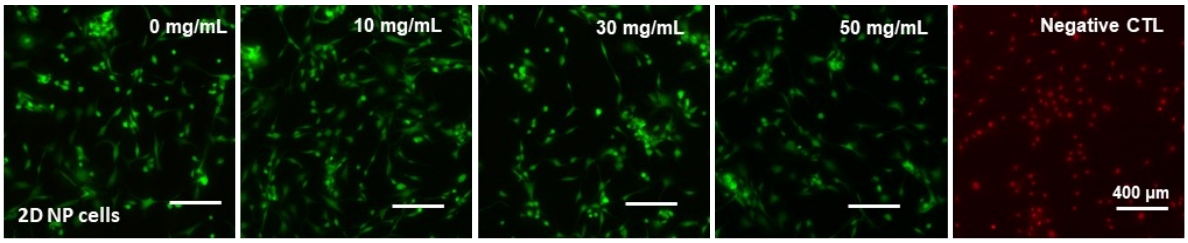

Fig. S5. Live/Dead staining of monolayer human primary NP cells cultured with conditional extract medium of the NP glue with varying EDC/NHS inputs.

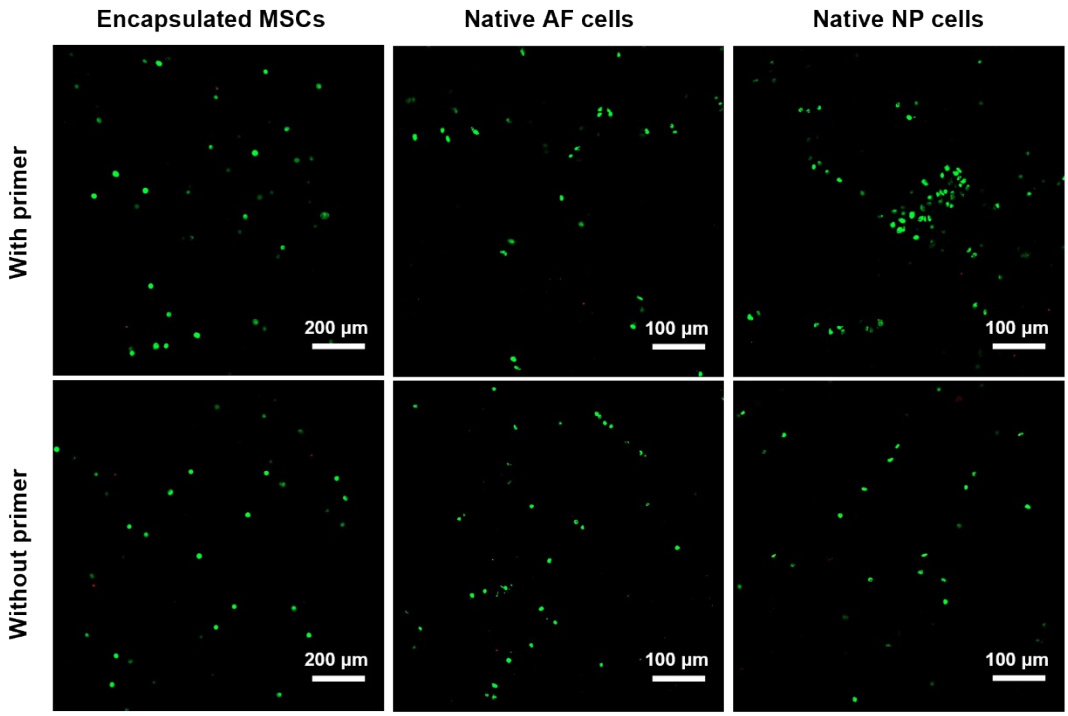

Fig. S6. Confocal imaging of Live/Dead assay of MSCs in glue, in human NP tissue, and in human AF tissue.
The MSCs-laden glues were applied to the human AF/NP tissues, the primer group showing comparable viability with no primer group.

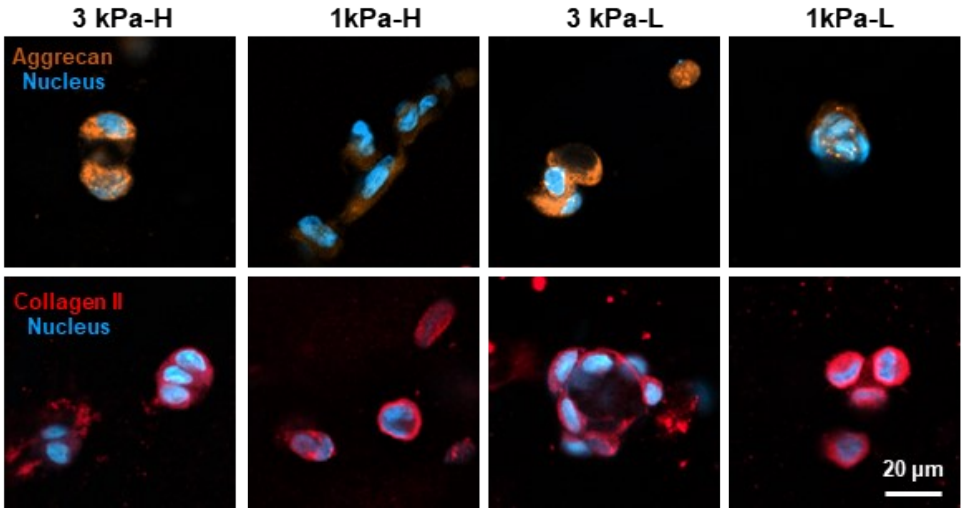

Fig. S7. Confocal images of immunofluorescence staining of aggrecan and collagen II, deposited by human primary NP cells within NP glues on day 21.

H and L refer to the high and low molecular weight of alginate used to form the NP glue.

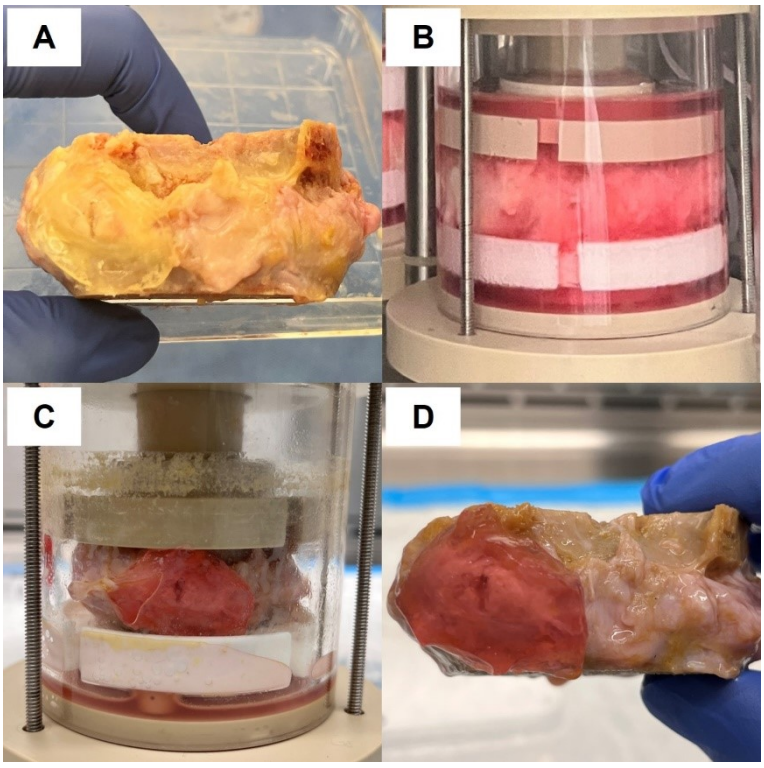

Fig. S8. Bioadhesive evaluation in human IVD tissue in an IVD bioreactor.

(A) The IVD sample repaired with Glue+Patch bioadhesives before loaded on the bioreactor. (B) The setup of the culture chamber in the bioreactor with culture medium. (C) At the end point of the culture, the medium was removed from the culture chamber. (D) The sample after 28 days of culture under dynamic loadings in the bioreactor.

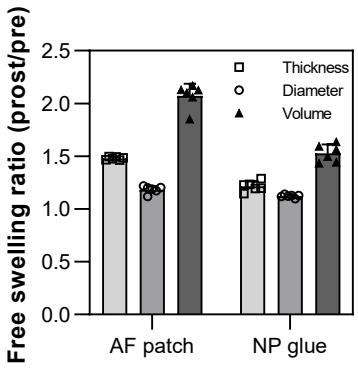

Fig. S9. The swelling ratio of NP glue and AF patch swelled in PBS for 7 days.

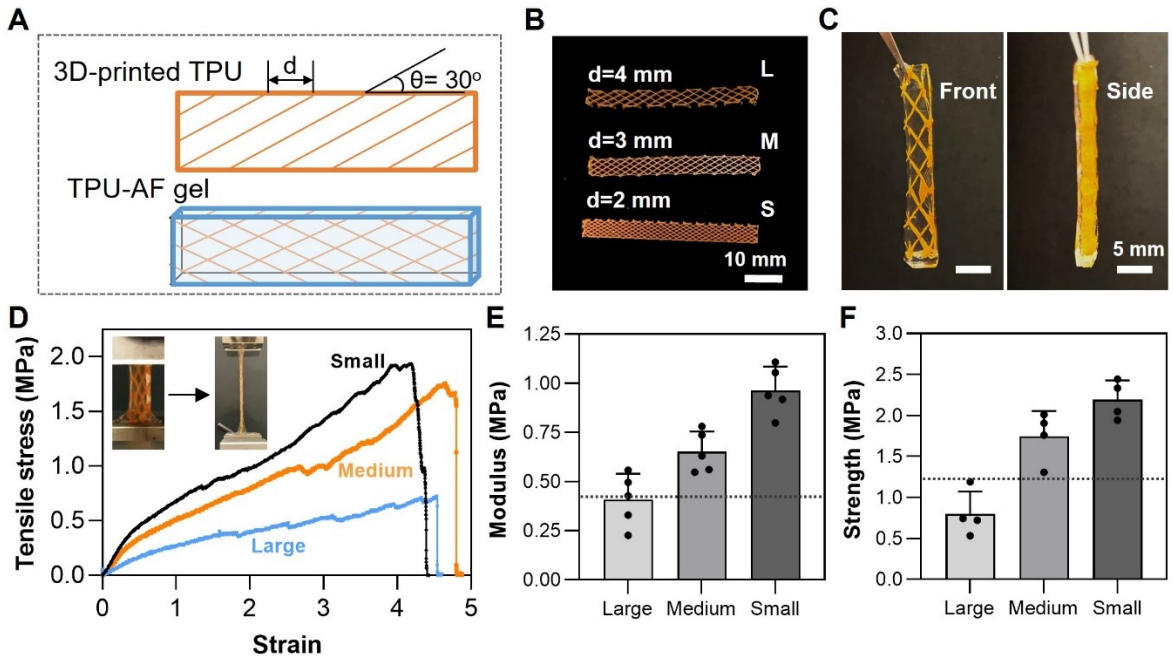

Fig. S10. Tensile test of TPU enhanced AF patch (TPU-AF patch).

The orientation of the TPU fibers is designed according to the angle to the collagen fibers in native AF tissue, that is 30° to the transverse plane of the spine (A). Then the 3D-printed TPU ply scaffolds were embedded in AF patch. Three mesh sizes were measured in the test. (B) The distance (d) of the TPU-fibers is 4mm, 3 mm, and 2 mm corresponding to large, medium, and small mesh sizes. The front and side view of the TPU-AF gel with large mesh size for tensile test is shown in C. The representative stress-strain curves of TPU-AF gels are shown in D. The linear modulus and strength were calculated as in E and F. The reported linear modulus of non-degenerated human AF by tensile test in the axial direction of the IVD is reported as 0.42 ±0.11 MPa,[11] showing in E with dash line. Similarly, the documented strength of posterolateral outer AF of non-degenerated human IVD by the tensile test is indicated by a dash line in F (~1.25 MPa).[12] TPU, thermoplastic polyurethane.

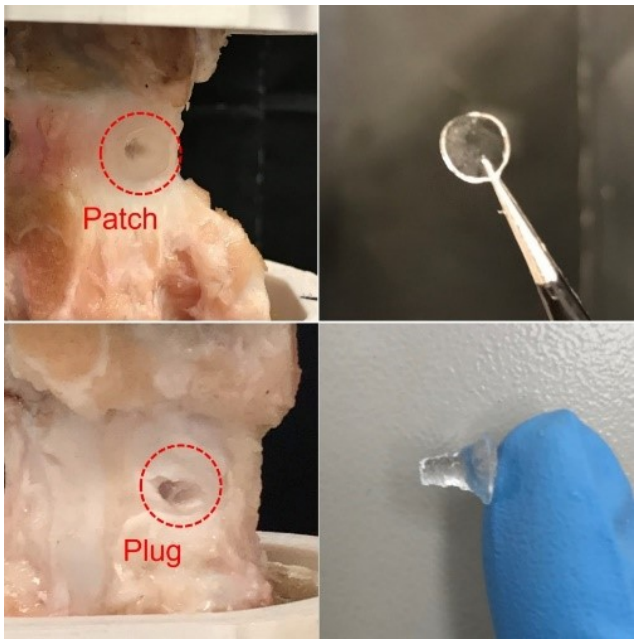

Fig. S11. Images of annulus fibrosus sealant patch (top) and plug (bottom).

Supplementary table

Table S1. The swelling ratio of human IVD and the AF patch pre- and post-culture in the bioreactor.

	Pre-culture	Post-culture	Swelling ratio (post/pre)
IVD diameter 1 (mm)	60.27	61.23	1.016
IVD diameter 2 (mm)	47.18	47.79	1.013
IVD height (mm)	27.53	24.77	0.900
IVD volume (mm^3)	62409	57805	0.926
AF Patch length (mm)	25.71	26.89	1.046
AF Patch width (mm)	17.87	19.81	1.109
AF patch thickness (mm)	3.000	4.590	1.530
AF Patch volume (mm^3)	1378	2445	1.774

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