A Next-Generation, Suture-Free Cartilage Repair Strategy Using a Col II Patch Graft and hPDA Fueled Bioglue

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INTRODUCTION: Articular cartilage is a crucial tissue that provides frictionless joint movement and shock absorption. However, its avascular nature severely limits its intrinsic ability to heal after injury, often resulting in progressive degeneration and osteoarthritis. In the United States, nearly 900,000 individuals are affected by cartilage injuries each year, with approximately 200,000 requiring surgical intervention. Current clinical approaches, such as microfracture surgery and autologous chondrocyte implantation, are limited by the formation of mechanically inferior fibrocartilage, high revision rates, and prolonged rehabilitation. Consequently, there is a critical unmet need for a cost-effective, single-stage, and “off-the-shelf” cartilage repair strategy that enables consistent regeneration of hyaline-like cartilage while eliminating the need for sutures to achieve stable fixation. To address this challenge, the objective of this study was to develop a type II collagen (Col II) patch graft scaffold integrated with a hydrophilic polydopamine (hPDA)-fueled Col II bioglue, engineered to enable suture-free fixation and provide mechanically stable cartilage repair.

METHODS: Type II collagen (Col II) was isolated from bovine articular cartilage (BAC) using sequential extraction and purification to remove non-collagenous proteins, lipids, and proteoglycans. The purified collagen was neutralized, washed, and freeze-dried for scaffold and gel preparation. Water-soluble hydrophilic polydopamine (hPDA) was synthesized from insoluble polydopamine (PDA) particles. Dopamine was polymerized in TRIS/HCl buffer (pH 8.5) under stirring condition to form PDA. The resulting PDA particles were dissolved in NaOH and subjected to ethanol-induced crystallization. The precipitate was thoroughly washed, dried, and collected as a hPDA powder for subsequent bioglue preparation. Scaffold molds were designed in SolidWorks and 3D-printed with PLA. Homogenized Col II solution was cast, dehydrated, freeze-dried, and crosslinked with EDC/NHS to improve mechanical stability. Scaffold characterization was performed to evaluate degradation, swelling behavior, and mechanical properties. For enzymatic degradation studies, native bovine articular cartilage (BAC), crosslinked scaffolds, and non-crosslinked scaffolds (5 mg each) were incubated in collagenase solution at 37 °C. Samples were retrieved at 4, 8, and 12 hours, washed, freeze-dried, and their weight change was measured to determine degradation. Mechanical testing was carried out using a uniaxial testing system (CellScale UniVert, Canada). Tensile and lap-shear properties were evaluated at a loading rate of 5 mm/min, while compressive properties were tested at 1.3 mm/min under hydrated conditions. For adhesive strength assessment of the hPDA fueled Col II bioglue, 20 µL of hPDA-fueled Col II bioglue was applied between cartilage tissue strips (5 × 10 × 2 mm) harvested from skeletally mature bovine articular cartilage. The bonded constructs were incubated under controlled conditions, followed by lap-shear testing until failure to quantify adhesive strength. For swelling analysis, crosslinked and non-crosslinked scaffold samples (10–20 mg) were placed in microcentrifuge tubes and immersed in PBS at 37 °C. At predetermined time points (4, 8, 16, 24, and 48 hours), the samples were removed, gently blotted to eliminate excess surface fluid, and weighed. The swelling ratio (%) was calculated as the percentage increase in mass relative to the initial dry weight of each sample.

RESULTS: Our Col II patch graft scaffolds (**Fig. 1A**) demonstrated key structural and mechanical properties essential for cartilage repair. SEM imaging confirmed that crosslinked Col II scaffolds possessed a highly porous and interconnected architecture (**Fig. 1B & 1C**), favorable for cell infiltration and nutrient transport. FTIR analysis further verified the chemical composition and successful crosslinking of the scaffolds (data not shown). Degradation studies revealed stark differences between groups. Native cartilage and non-crosslinked scaffolds degraded rapidly, showing ~95–100% mass loss by 12 hours (**Fig. 1D**). In contrast, crosslinked patch graft scaffolds exhibited significantly improved stability, with only ~40% degradation at 12 hours ($p < 0.001$ vs. native and non-crosslinked). Mechanical testing confirmed substantial reinforcement of the patch graft scaffold properties following crosslinking. The tensile modulus increased from ~1.7 MPa to ~6.8 MPa (**Fig. 1E**), and tensile strength rose from ~0.25 MPa to ~1.1 MPa (**Fig. 1F**). Similarly, the compressive modulus increased from ~0.2 MPa to ~1.2 MPa (**Fig. 1G**), while compressive strength improved from ~0.25 MPa to ~1.25 MPa (**Fig. 1H**). The most significant enhancement was observed in adhesive performance of col II bioglue with hPDA incorporation. Lap-shear testing showed that the Col II + hPDA group achieved a modulus of ~0.57 MPa compared to ~0.18 MPa in Col II alone (**Fig. 1I**). Similarly, lap-shear strength was ~0.045 MPa in the Col II + hPDA group, over threefold greater than the ~0.015 MPa observed in Col II alone (**Fig. 1J**). These results underscore the robust adhesive capacity of hPDA, attributed to catechol and primary amine functional groups that form strong bonds with cartilage matrix proteins. Swelling studies showed that both crosslinked and non-crosslinked scaffolds absorbed fluid rapidly, reaching ~650–700% within 4 hours. Non-crosslinked scaffolds continued swelling up to ~900% by 48 hours, while crosslinked scaffolds plateaued at ~730% after 24 hours, maintaining equilibrium thereafter (**Fig. 1K**).

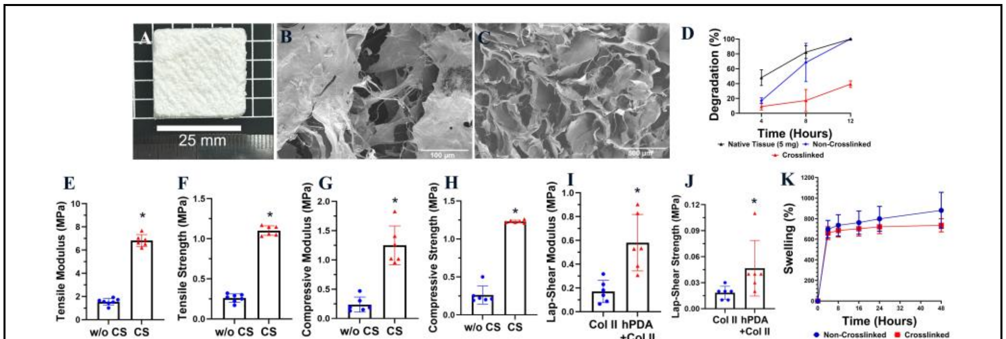

Fig.1. Physico-mechanical properties of Col II patch graft and Col II bioglue: (A) Photograph of the Col II patch graft scaffold, (B) SEM image showing the porous structure of a crosslinked Col II scaffold (top surface view), (C) SEM image showing the porous structure of a crosslinked Col II scaffold (cross-sectional view), (D) Degradation percentage of native BAC (bovine articular cartilage) tissue, non-crosslinked (w/o CS) Col II scaffold and cross-linked (CS) Col II scaffold, (E) Tensile Modulus, (F) Tensile Strength, (G) Compressive Modulus, and (H) Compressive Strength for Col II scaffolds before and after crosslinking, (I) Lap-Shear Modulus for Col II and Col II with hPDA bioglue, (J) Lap-Shear Strength for Col II and Col II with hPDA bioglue, (L) Swelling percentage of non-crosslinked and cross-linked Col II patch graft scaffold (n=4-6 per group; p*<0.05).

DISCUSSION: We have developed a single-stage, “off-the-shelf” cartilage repair strategy by integrating a porous type II collagen (Col II) patch graft scaffold with a hydrophilic polydopamine (hPDA) fueled Col II bioglue. The Col II scaffold exhibited an interconnected porous architecture, confirmed by SEM, that is essential for facilitating cell infiltration and nutrient transport during tissue regeneration. Crosslinking markedly enhanced scaffold mechanics, with the tensile modulus reaching approximately 7 MPa. Most notably, the incorporation of hPDA-fueled Col II bioglue significantly improved adhesive performance. Lap-shear testing revealed that the Col II + hPDA group achieved more than a threefold increase in adhesion strength compared to Col II alone. This strong adhesion is attributed to the catechol and primary amine functional groups of hPDA, which form stable covalent and noncovalent interactions with tissue matrix proteins. These results demonstrate the potential of the Col II patch graft integrated with hPDA fueled Col II bioglue as a next-generation, suture-free solution for cartilage repair. In vitro studies on cartilage regeneration, along with an explant culture repair model, are currently in progress.

SIGNIFICANCE: Our single-stage, “off-the-shelf” cartilage repair strategy offers a suture-free fixation and enhanced mechanical stability for effective cartilage repair.

ACKNOWLEDGEMENT: The authors acknowledge the support from the National Science Foundation (NSF) under the award # 2347673 to Dr. Solaiman Tarafder.