Title: Safety and Early Clinical Performance of High-Purity Type I Collagen Augmentation in Arthroscopic Meniscal Repair: A Prospective Feasibility Study

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INTRODUCTION

Meniscal tears are among the most frequently encountered intra-articular knee injuries and represent a significant cause of pain, functional limitation, and early degenerative change in active adults. Contemporary orthopaedic practice increasingly favors meniscus-preserving arthroscopic repair techniques over partial meniscectomy, given the well-established role of the meniscus in load transmission, joint stability, and long-term cartilage protection [1,2]. Despite improvements in arthroscopic instrumentation and suture constructs, healing rates following meniscal repair remain variable, particularly in tears extending into avascular zones or those with complex morphology [3,4].

Failure of meniscal repair is multifactorial and influenced by tear pattern, vascularity, mechanical stability, biological milieu, and patient-related factors. Even under optimal mechanical conditions, biologic healing remains a limiting factor, especially in the inner two-thirds of the meniscus where vascular supply is poor [5]. Reported failure rates for arthroscopic meniscal repair range from 10% to 30%, with higher rates observed in isolated repairs and degenerative tear patterns [6,7]. These limitations have driven interest in biologic augmentation strategies aimed at enhancing intrinsic healing potential.

Collagen-based scaffolds and biologic matrices have emerged as promising adjuncts in meniscal surgery. These materials are designed to provide a biocompatible framework that supports cell migration, extracellular matrix deposition, angiogenesis, and tissue remodelling at the repair site [8]. Experimental and early clinical studies have suggested that collagen augmentation may improve meniscal healing, reduce pain, and enhance functional recovery, particularly in tears with limited intrinsic healing capacity [9,10]. However, heterogeneity in collagen processing, scaffold architecture, and clinical application techniques has limited the generalizability of existing evidence.

High-purity type I collagen is a bioengineered collagen matrix composed of more than 97% native type I collagen, manufactured to remove immunogenic proteins, elastin, and lipids while preserving the native triple-helical structure. Unlike cross-linked or chemically modified scaffolds, high-purity type I collagen remains un-crosslinked, allowing controlled enzymatic degradation and progressive replacement by organized host tissue [11]. Its phosphorylated collagen structure has been shown to enhance bioactivity, angiogenesis, and early granulation, properties that are advantageous in environments with limited intrinsic vascularity such as the meniscus.

The clinical performance of high-purity type I collagen has been demonstrated across multiple surgical disciplines, including chronic wound management, reconstructive surgery, scar modulation, and tissue regeneration [12, 13]. Prospective studies and randomized trials have consistently reported favourable safety profiles, improved tissue quality, reduced inflammation, and enhanced functional outcomes with its use [14, 15]. These reproducible biological effects provide a strong rationale for exploring its application in meniscal repair, where biologic failure remains a major challenge.

Before undertaking large randomized controlled trials, feasibility studies play a critical role in evaluating procedural practicality, safety, early clinical signals, and variability of outcomes. Such studies are particularly important when introducing biologic adjuncts into technically demanding procedures such as arthroscopic meniscal repair [16]. Feasibility data inform study design, sample size estimation, outcome selection, and refinement of surgical technique for subsequent trials.

The present prospective single-arm feasibility study was therefore designed to evaluate the safety, handling characteristics, and early clinical performance of high-purity type I collagen augmentation in arthroscopic meniscal repair of the knee. Secondary objectives included exploratory assessment of pain reduction, functional improvement, and early radiological healing trends. The findings of this study are intended to generate preliminary clinical signals and inform the design of a future randomized controlled trial comparing high-purity type I collagen augmentation with standard meniscal repair.

MATERIALS AND METHODS

Study Design and Setting

This study was designed as a prospective, single-arm feasibility study evaluating the safety, procedural practicality, and early clinical outcomes of high-purity type I collagen augmentation in arthroscopic meniscal repair of the knee. The study was conducted at a tertiary care orthopaedic centre with expertise in sports medicine and arthroscopic knee surgery. The primary intent of the study was exploratory, aimed at generating preliminary clinical signals and feasibility data to inform the design of a future randomized controlled trial [17].

The study was approved by the Institutional Ethics Committee prior to patient enrolment and was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was obtained from all participants after detailed explanation of the study objectives, procedures, potential benefits, and risks.

Patient Selection

Adult patients aged 18 to 45 years presenting with symptomatic, repairable meniscal tears of the knee were screened for eligibility. Inclusion criteria comprised longitudinal, vertical, or bucket-handle meniscal tears involving the red-red or red-white zones, deemed suitable for arthroscopic repair based on preoperative magnetic resonance imaging and intraoperative assessment. Both medial and lateral meniscal tears were included.

Exclusion criteria included complex degenerative meniscal tears, root tears, radial tears extending into the avascular zone, advanced osteoarthritis (Kellgren–Lawrence grade ≥ 2) [18], inflammatory arthropathy, active infection, prior surgery on the index knee, concurrent ligament reconstruction, systemic illness affecting wound healing, known hypersensitivity to collagen, pregnancy, or inability to comply with postoperative rehabilitation and follow-up.

Arthroscopic Surgical Technique

All procedures were performed under spinal or general anaesthesia with the patient positioned supine and a pneumatic tourniquet applied to the proximal thigh. Standard anterolateral and anteromedial arthroscopic portals were established. Diagnostic arthroscopy was performed to confirm tear morphology, location, and reparability.

Meniscal tears were carefully debrided at the margins using a shaver or rasp to promote vascular ingress and enhance healing potential. Care was taken to preserve meniscal tissue

and avoid excessive removal of fibrocartilaginous material. Meniscal repair was performed using an all-inside, inside-out, or hybrid suture technique based on tear location and surgeon preference, ensuring stable fixation and restoration of meniscal contour.

Application of High-Purity Type I Collagen Augmentation

Following completion of meniscal suturing, high-purity type I collagen was prepared according to manufacturer instructions. The collagen matrix was rehydrated in sterile normal saline and trimmed into thin strips suitable for arthroscopic delivery. Using a grasping instrument or cannula-assisted technique, the collagen matrix was placed directly over the repaired meniscal tear site, ensuring intimate contact with the repair interface.

The collagen was gently moulded to conform to the meniscal surface and secured through inherent adherence and contact pressure from the surrounding synovial fluid environment. No additional fixation devices were used. Care was taken to avoid displacement during final inspection and joint lavage. The arthroscopic portals were closed in standard fashion.

Postoperative Rehabilitation Protocol

All patients followed a standardized postoperative rehabilitation protocol. Partial weight-bearing with crutches was initiated immediately after surgery and continued for four weeks. Knee range of motion was restricted to 0–90 degrees for the first four weeks, followed by gradual progression to full range of motion by six weeks.

Closed-chain strengthening exercises were initiated at six weeks, with gradual return to low-impact activities by three months. Return to pivoting or high-impact sports was deferred until after six months, based on clinical and imaging assessment.

Outcome Measures

The primary feasibility outcomes included procedural safety, absence of collagen-related adverse events, and completion of the surgical technique without technical difficulty. Secondary exploratory clinical outcomes included pain assessed using the Visual Analog Scale [19], knee function assessed using the Lysholm Knee Scoring Scale [20] and the International Knee Documentation Committee (IKDC) subjective score [21], and patient satisfaction. Outcomes were assessed preoperatively and at six weeks, three months, and six months postoperatively.

Radiological assessment of meniscal healing was performed using magnetic resonance imaging at six months. Healing was graded using a modified MRI meniscal healing score based on signal intensity, continuity, and tear morphology.

Data Collection and Management

All clinical data were collected prospectively using standardized case report forms. Data were anonymized using unique study identifiers and entered into a secure electronic database. Data quality checks were performed periodically to ensure completeness and accuracy. Radiological assessments were performed by a musculoskeletal radiologist blinded to clinical outcomes.

Statistical Analysis Plan

Given the feasibility nature of the study, no formal hypothesis testing or sample size calculation for efficacy was performed. The sample size was determined pragmatically to allow assessment of safety, procedural feasibility, and variability of outcomes [22]. Continuous variables were summarized as mean ± standard deviation or median with interquartile range, depending on distribution. Changes in clinical outcome scores over time were analysed using paired t-tests for normally distributed variables or Wilcoxon signed-rank tests for non-normally distributed variables. Ninety-five percent confidence intervals were calculated for mean changes to provide estimation of effect size rather than definitive efficacy.

REFERENCES

1. Fairbank TJ. Knee joint changes after meniscectomy. J Bone Joint Surg Br. 1948 Nov;30B(4):664-70. https://pubmed.ncbi.nlm.nih.gov/18894618/
2. Papalia R, Del Buono A, Osti L, Denaro V, Maffulli N. Meniscectomy as a risk factor for knee osteoarthritis: a systematic review. Br Med Bull. 2011;99:89-106. doi: 10.1093/bmb/ldq043.
3. Barrett GR, Field MH, Treacy SH, Ruff CG. Clinical results of meniscus repair in patients 40 years and older. Arthroscopy. 1998 Nov-Dec;14(8):824-9. doi: 10.1016/s0749-8063(98)70018-0.
4. Noyes FR, Barber-Westin SD. Arthroscopic repair of meniscal tears extending into the avascular zone in patients younger than twenty years of age. Am J Sports Med. 2002 Jul-Aug;30(4):589-600. doi: 10.1177/03635465020300042001.
5. Arnoczky SP, Warren RF. Microvasculature of the human meniscus. Am J Sports Med. 1982 Mar-Apr;10(2):90-5. doi: 10.1177/036354658201000205.
6. Grant JA, Wilde J, Miller BS, Bedi A. Comparison of inside-out and all-inside techniques for the repair of isolated meniscal tears: a systematic review. Am J Sports Med. 2012 Feb;40(2):459-68. doi: 10.1177/0363546511411701.
7. Pujol N, Tardy N, Boisrenoult P, Beaufils P. Long-term outcomes of all-inside meniscal repair. Knee Surg Sports Traumatol Arthrosc. 2015 Jan;23(1):219-24. doi: 10.1007/s00167-013-2553-5.
8. Stone KR, Rodkey WG, Webber R, McKinney L, Steadman JR. Meniscal regeneration with copolymeric collagen scaffolds. In vitro and in vivo studies evaluated clinically, histologically, and biochemically. Am J Sports Med. 1992 Mar-Apr;20(2):104-11. doi: 10.1177/036354659202000202.
9. Zaffagnini S, Giordano G, Vascellari A, Bruni D, Neri MP, Iacono F, Kon E, Presti ML, Marcacci M. Arthroscopic collagen meniscus implant results at 6 to 8 years follow up. Knee Surg Sports Traumatol Arthrosc. 2007 Feb;15(2):175-83. doi: 10.1007/s00167-006-0144-4.
10. Verdonk R, Madry H, Shabshin N, Dirisamer F, Peretti GM, Pujol N, Spalding T, Verdonk P, Seil R, Condello V, Di Matteo B, Zellner J, Angele P. The role of meniscal tissue in joint protection in early osteoarthritis. Knee Surg Sports Traumatol Arthrosc. 2016 Jun;24(6):1763-74. doi: 10.1007/s00167-016-4069-2.

11. Shoulders MD, Raines RT. Collagen structure and stability. Annu Rev Biochem. 2009;78:929-58. doi: 10.1146/annurev.biochem.77.032207.120833.
12. Frantz C, Stewart KM, Weaver VM. The extracellular matrix at a glance. J Cell Sci. 2010 Dec 15;123(Pt 24):4195-200. doi: 10.1242/jcs.023820.
13. Narayan N, Nareddula U, Nanjundaiah RK, Manakchand KK. Clinical and Histopathological Outcomes of High-Purity Type I Collagen in Chronic Wounds: A Systematic Review of Four Randomized Controlled Trials. Cureus. 2026 Jan 3;18(1):e100717. doi: 10.7759/cureus.100717.
14. Narayan N, Shivannaiah C, Gowda S. Evaluating the Efficacy of High-Purity Type I Collagen-Based Skin Substitute Versus Dehydrated Human Amnion/Chorion Membrane in the Treatment of Venous Leg Ulcers: A Randomized Controlled Clinical Trial. Cureus. 2025 Jul 30;17(7):e89031. doi: 10.7759/cureus.89031.
15. Narayan N, Gowda S, Shivannaiah C. A Randomized Controlled Clinical Trial Comparing the Use of High Purity Type-I Collagen-Based Skin Substitute vs. Dehydrated Human Amnion/Chorion Membrane in the Treatment of Diabetic Foot Ulcers. Cureus. 2024 Dec 5;16(12):e75182. doi: 10.7759/cureus.75182.
16. Thabane L, Ma J, Chu R, Cheng J, Ismaila A, Rios LP, Robson R, Thabane M, Giangregorio L, Goldsmith CH. A tutorial on pilot studies: the what, why and how. BMC Med Res Methodol. 2010 Jan 6;10:1. doi: 10.1186/1471-2288-10-1. Erratum in: BMC Med Res Methodol. 2023 Mar 11;23(1):59. doi: 10.1186/s12874-023-01880-1.
17. Leon AC, Davis LL, Kraemer HC. The role and interpretation of pilot studies in clinical research. J Psychiatr Res. 2011 May;45(5):626-9. doi: 10.1016/j.jpsychires.2010.10.008.
18. Kohn MD, Sassoon AA, Fernando ND. Classifications in Brief: Kellgren-Lawrence Classification of Osteoarthritis. Clin Orthop Relat Res. 2016 Aug;474(8):1886-93. doi: 10.1007/s11999-016-4732-4.
19. Koo M, Yang S-W. Visual Analogue Scale. Encyclopedia. 2025; 5(4):190. doi:10.3390/encyclopedia5040190
20. Peccin MN, Ciconelli R, Cohen M. Specific questionnaire for knee symptoms-The Lysholm knee scoring scale- Translation and validation into Portuguese. Acta Ortop Bras. 2006;14(5):268–272.
21. Anderson AF, Irrgang JJ, Kocher MS, Mann BJ, Harrast JJ; International Knee Documentation Committee. The International Knee Documentation Committee

Subjective Knee Evaluation Form: normative data. Am J Sports Med. 2006 Jan;34(1):128-35. doi: 10.1177/0363546505280214.

22. Julious SA. Sample size of 12 per group rule of thumb. Pharm Stat. 2005;4(4):287–291. doi:10.1002/pst.185