Technical Note

Single-Stage Combined Autologous-Allogenic Cartilage Restoration: Surgical Technique

Brendan Swift, M.D., Ting Zhang, M.D., Fauzan Akhter, and Brian J. Chilelli, M.D.

Abstract: Articular cartilage injuries in young patients pose a notable treatment dilemma. Multiple reported techniques exist, although some of the most prominent methods currently rely on multiple procedures for chondrocyte harvest and colony expansion prior to implantation. The associated cost and effort this requires limits availability on a global basis, which creates a need for a more widely available cartilage procedure. This Technical Note describes a method for cartilage restoration that incorporates autologous chondrocytes in allogenic extracellular matrix, along with biologic augmentation all performed in a single stage.

Articular cartilage injuries of the knee have long posed a treatment dilemma in young, active individuals. Procedures to repair or restore articular cartilage have continued to evolve, with significant advancements in techniques and outcomes over the past 2 decades. There is a growing body of literature demonstrating improved clinical outcomes following various cartilage restoring techniques at mid- to long-term follow-up.[1,2] Common surgical techniques include matrix-associated autologous chondrocyte implantation (MACI), osteochondral allograft transplantation, osteochondral autograft transfer, marrow stimulation, and other newer procedures utilizing synthetic scaffolds and/or biologic augmentation. Fresh osteochondral allografts have been successfully used to treat chondral and osteochondral defects for decades, but cost and access to these tissues vary globally. Osteochondral autograft transfer has also been a popular cartilage restoring procedure but is best served for small lesions (1-2 cm^2) that are amenable to 1 or 2 osteochondral plugs. Deterioration of results and increased donor site morbidity have been associated with larger lesions requiring multiple plugs (mosaicplasty).[3-6] Increasing evidence has emerged to support the superiority of autologous chondrocyte implantation (ACI) over microfracture techniques with lower failure rates and improved patient-reported outcome measures.[1,7,8] Despite encouraging results, use of ACI remains limited globally, secondary to associated cost, which, depending on system design, may be prohibitively expensive.[9-11]

In recent years, additional techniques have been described that utilize autologous chondrocytes, orthobiologics, or biologic-based implants with reimplantation in the same setting, eliminating the requirement for a second-stage surgery and frequently reducing the costs associated. Gobbi et al.[12] have described a 1-stage technique that utilizes a biologic scaffold (collagen or hyaluronic acid [HA] based), activated with multipotent cells obtained from bone marrow aspirate concentrate (BMAC). Most recently, they demonstrated good to excellent outcomes at a mean of 8 years following HA-BMAC repair of full-thickness cartilage lesions with median area of 6.5 cm^2 with regeneration of hyaline-like tissue.[13]

Additionally, the BioCartilage study group has described the use of a cartilage allograft extracellular matrix, mixed with platelet-rich plasma, applied over a microfractured defect bed and sealed with fibrin glue.[14] They found significantly improved patient-reported outcomes of clinical significance and low failure rates at 2 years postoperatively.[15] Recent reports have further suggested encouraging results in the use of micronized cartilage allograft augmented with an autologous source of mesenchymal stem cells via

From Mercy Health-Cincinnati Sports Medicine and Orthopaedic Center, Cincinnati SportsMedicine Research and Education Foundation, Cincinnati, Ohio, U.S.A.

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Address correspondence to Brian Chilelli, M.D., Mercy Health-Cincinnati SportsMedicine and Orthopaedic Center, 4700 E. Galbraith Road, Suite 300A, Cincinnati, OH 45236, U.S.A. E-mail: brianchilelli@gmail.com

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platelet-rich plasma or locally through microfracture.[16,17]

Early studies by Albrecht et al.[18] demonstrated the regeneration of hyaline cartilage in full-thickness chondral lesions treated with minced autologous cartilage fixated with fibrin glue in an animal model. Salzmann and colleagues[19] carried out a recent review of autologous minced cartilage and outlined the growing body of evidence to support its use, through demonstrable cartilage outgrowth in vivo with histologically similar appearance to adjacent, healthy cartilage[20-23] comparable to ACI methods but achievable in a single-stage procedure.

The present technique article builds on these innovative advances in the treatment of full-thickness cartilage lesions. Using techniques and products that are already cleared by the US Food and Drug Administration and available in market, we describe a single-stage repair technique applicable in small to large cartilage defects that combines the implantation of minced autologous and allogenic cartilage fragments augmented with a BMAC-embedded HA scaffold.

Surgical Technique

A full technique description can be found in Video 1. After induction of anesthesia, the patient is positioned supine as typical for an arthroscopic knee procedure. To enable access for harvest, the operative knee and the ipsilateral iliac crest are included in the sterile field preparation. Following ligamentous examination under anesthesia, a diagnostic arthroscopy can be performed to examine all areas of chondral injury. Associated procedures such as ligamentous repair or periarticular osteotomy can be performed as indicated prior to proceeding with the present cartilage repair technique (Fig 1).

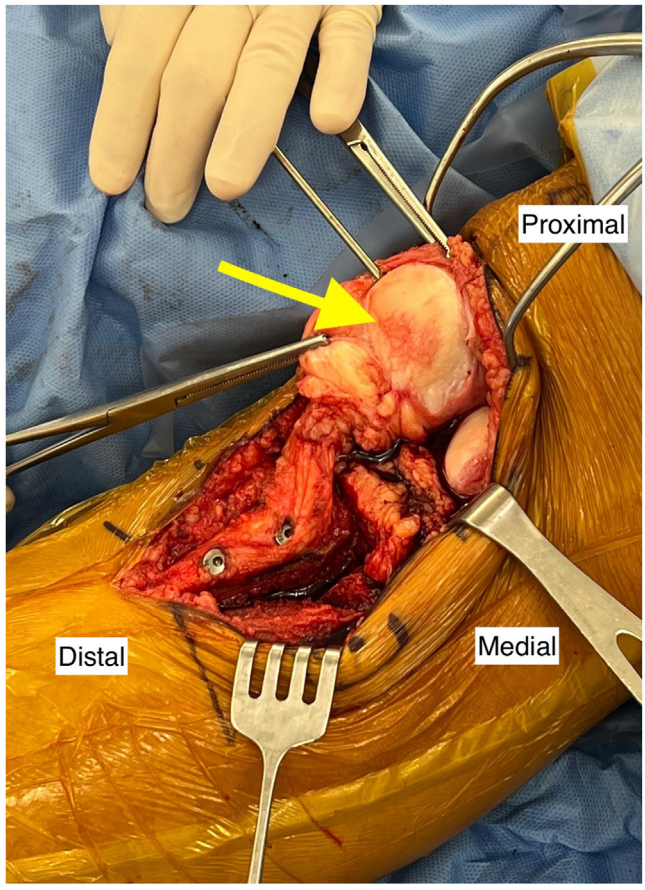

Fig 1. To reduce the risk of failed cartilage restoration, concomitant procedures should be completed to address any concurrent knee malalignment or instability. A right knee patellar cartilage injury is demonstrated here (arrow) after a tibial tubercle anteromedialization to address extensor mechanism alignment and to offload the repair site.

BMAC Harvest and Preparation

A 5-mm incision is made over the anterior superior iliac crest. Subsequently, a Jamshidi needle is centered on the iliac crest and directed between the inner and outer tables of the ilium, whereby a 60-mL volume of bone marrow can then be aspirated. This volume is then processed in a commercially available system (Angel Bone Marrow Aspirate Processing System; Arthrex) to isolate bone marrow concentrate.

Autograft Cartilage Harvest and Preparation

As the BMAC is processed, attention is then turned to the approach to the cartilage defect. An open approach is utilized to incorporate any adjunctive procedures and centered over the region of concern. Typically, we will utilize a standard medial parapatellar approach for medial tibiofemoral or patellofemoral defects and a lateral subvastus approach for lateral tibiofemoral defects. A biopsy gouge is then used to harvest a cartilage biopsy from the lateral intercondylar notch, which is then placed in a specimen cup with saline, subsequently minced using an arthroscopic shaver, and collected in an attached GraftNet tissue collector (Arthrex) (Fig 2). The autologous minced cartilage is then set to the side in a sterile specimen cup on the back table for later reimplantation.

Defect Preparation

Ring curettes are used to remove all unviable cartilage back to stable margins. The calcified layer is removed with care taken not to violate the subchondral bone. Hemostasis can then be achieved at the subchondral region of the defect using thrombin-soaked gel foam.

Graft Preparation

Once prepared, the defect is sized using the foil sizing sheet provided in the HA matrix membrane (Hyalofast; Anika Therapeutics). The foil is pressed into the base of the defect, cut to size, and then placed over the membrane to cut a shape- and size-matched portion. This membrane is then seeded with 1 to 2 cc of BMAC and set aside.

Fig 2. As a source of autologous chondrocytes, autograft cartilage is harvested from the intercondylar notch using a biopsy gouge. This graft material is minced using an arthroscopic shaver and captured using a Graftnet (Arthrex) tissue collector (arrow). This minced cartilage is incorporated along with BioCartilage allograft extracellular matrix (Arthrex) to create a paste used to fill the area of cartilage defect.

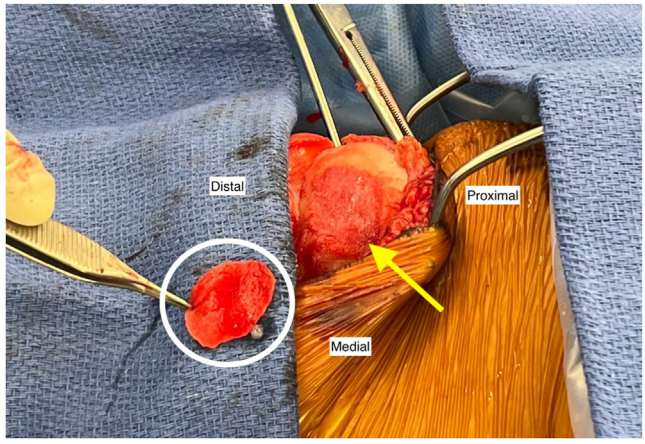

Fig 3. A right knee patellar cartilage defect is identified (arrow) after filling with mixed autologous-allogenic putty. A hyaluronic acid membrane can be seen here (circled) after it was trimmed to fit the cartilage defect and was seeded with bone marrow aspirate concentrate. This membrane will later be stitched over the packed defect site to protect the graft material.

The graft putty is then prepared using BioCartilage allograft extracellular matrix (Arthrex) along with the minced autograft cartilage and BMAC for the delivery of progenitor cells. This mixture is then placed within the base of the prepared defect and packed to a level where the graft height is recessed by 1 mm from the surrounding healthy native articular cartilage (Fig 3). Subsequently, a light layer of Tisseal fibrin glue (Baxter) is placed over the graft and left to rest for 3 minutes to allow setting of the adhesive. The previously sized HA membrane is then placed over the graft tissue and secured with interrupted 6-0 Vicryl sutures along the margins of the membrane to secure it to the surrounding healthy articular cartilage surface (Fig 4). A second application of fibrin glue is then placed over the membrane and allowed to set before taking the knee through a gentle range of motion to ensure security of the implanted construct.

Postoperative Rehabilitation

A postoperative rehabilitation protocol is administered to all patients. For femoral condyle or tibial plateau lesions, the knee is locked in extension initially with patients instructed to dangle from a chair or table, allowing the operative knee to come to 90° of flexion 3 to 5 times a day. Continuous passive motion (CPM) is initiated 72 hours following surgery for 6 to 8 hours per day, initially from 0° to 30°. Flexion is then increased by 5° to 10° daily to a maximum of 90°. CPM is used daily for 6 weeks. Patients are kept touch-down weightbearing for 6 weeks before progressing to weightbearing as tolerated by 8 weeks.

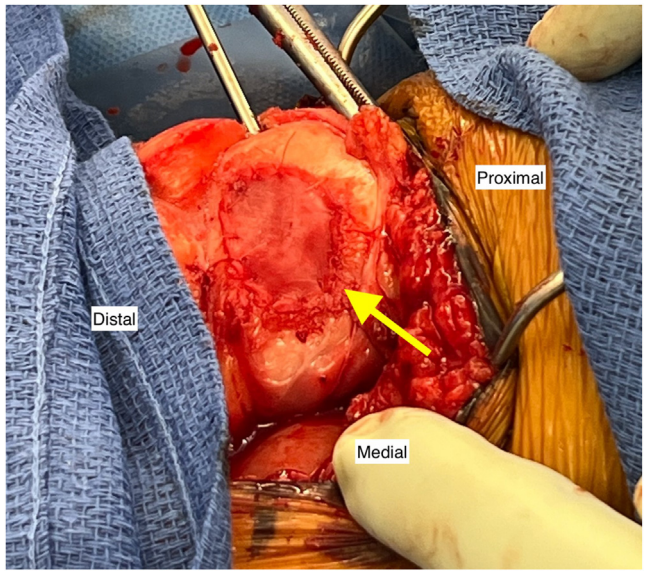

Fig 4. A right knee patellar cartilage defect is identified here after placement of a mixed autologous-allogenic graft and subsequently covered with hyaluronic acid membrane for protection of the graft site. The membrane is stitched into adjacent healthy cartilage with 6-0 monofilament suture.

Table 1. Pearls and Pitfalls of the Described Single-Stage Combined Autologous-Allogenic Cartilage Restoration Technique

Pearls	Pitfalls
Cartilage defect can be prepared with standard ring curettes; subsequently, hemostasis can be achieved with thrombin-soaked gelfoam and/or epinephrine-soaked patties.	Plan ahead for bone marrow aspirate, in terms of both separate site prep and case sequence to allow for concurrent aspirate processing while preparing cartilage lesion.
Foil from the collagen membrane packaging is pressed into the base of the defect and trimmed to create a template that can then be used to cut out the shape- and size-matched membrane prior to implantation.	Neglecting malignment, meniscal deficiency, or ligamentous laxity will place the cartilage restoration at greater risk of failure.
A biopsy gouge can be used to obtain a cartilage specimen from the intercondylar notch of periphery of the trochlea. It is then cut into small pieces with a scalpel or scissors prior to placing into a saline-filled specimen cup to be minced by the Graftnet device.	Take care not to violate subchondral bone in the preparation of the defect; microfracture of the lesion bed is not performed to avoid potential future negative effects of violating the subchondral bone.
	Inadequate fixation of the membrane places the construct at increased risk of failure secondary to shear stresses. Ensure adequate use of fibrin glue and perimeter suture, and confirm stability with range of motion under direct visualization surface.

For patellar and trochlear lesions, the knee is locked in extension initially with patients instructed to dangle from a chair or table, allowing the operative knee to come to 90° of flexion 3 to 5 times a day. CPM is initiated 72 hours from surgery 6 to 8 hours per day, initially from 0° to 30° of flexion. After 2 weeks, this is increased to 0° to 60°, followed by 0° to 90° at 4 weeks. CPM is used daily for 6 weeks. These patients may be full weightbearing as tolerated (while locked in extension in brace) immediately following surgery. Patients undergoing concomitant tibial tubercle osteotomy are made touch-down weightbearing for 6 weeks followed by progressing weightbearing, with a goal of full weightbearing without crutches at 10 weeks.

Discussion

The primary advantage of the present technique surrounds its single-stage nature. Further pros and cons, advantages and disadvantages can be found in Tables 1 and 2 respectively. Although a formal cost comparison is beyond the scope of the present report, by removing the need for chondrocyte culture expansion and a second procedure, we notably reduce resource requirement, presumably reducing associated cost as compared with current-generation MACI techniques. Additionally, we feel that this procedure may be more cost-effective than osteochondral allograft transplantation while avoiding delays in obtaining a fresh allograft or difficulty with access to such grafts. The materials and techniques used in the present description have support in their use in isolation. In a multicenter prospective cohort study by Cole et al.[15] assessing short-term outcomes following the Bio-Cartilage technique, clinically significant improvements in patient-reported outcomes were observed in patients treated with microfracture augmented with allograft cartilage at a 2-year follow-up. Furthermore, they demonstrated fair cartilage integration with the restoration of hyaline cartilage on assessment with post-operative magnetic resonance imaging. However, opponents of this technique may raise concerns about the microfracture portion of the procedure. Microfracture has been shown in select cases to alter the subchondral bone architecture and biomechanics with the potential to compromise the results associated with future revision cartilage surgery in the form of ACI/MACI.[24-28] Therefore, our proposed technique relies upon BMAC to provide the mesenchymal cells as opposed to the marrow elements from microfracture, thus avoiding the potential pitfalls associated with violating the subchondral bone.

Minced autologous cartilage has demonstrated promise over the years in treating full-thickness articular cartilage defects of the knee. Christensen et al.[29] discovered hyaline cartilage integration using minced autologous cartilage fixed with fibrin glue alone.

Table 2. Advantages and Disadvantages of the Described Single-Stage Combined Autologous-Allogenic Cartilage Restoration Technique

Advantages	Disadvantages
Single-stage procedure	Involves a secondary surgical site for bone marrow aspirate concentrate harvest and associated risks
No requirement for chondrocyte culture expansion, thus less resource requirement	Requires an open approach to adequately suture the membrane into position
Provides mesenchymal stem cell source for graft without the need for intralesional microfracture	Requires coordination or availability of centrifuge for processing of bone marrow aspirate concentrate

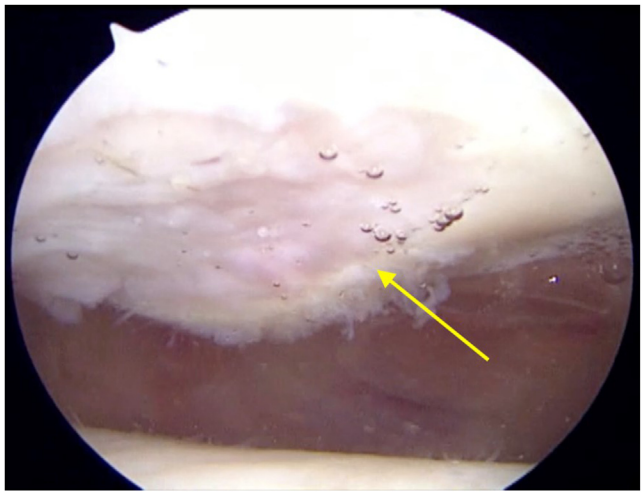

Fig 5. Arthroscopic view of a patellar cartilage defect (arrow) 5 months after combined autologous-allogenic restoration; a right knee patellofemoral space is viewed through an anterolateral portal. The patient in question returned to the operating room for removal of tibial tubercle osteotomy screws and denied any patellofemoral symptoms at that time.

Moreover, Salzmann et al.[30] published good results with their technique involving minced autologous cartilage covered by a collagen membrane that was secured using a 6.0 monofilament suture, creating a biologic seal and protecting the graft site from mechanical stress. Furthermore, Gobbi et al.[13] achieved good 6-year clinical outcomes in patients treated with HA-BMAC, combining cell-based repair and structural scaffolding. Although an assessment of patient outcomes was not within the scope of the present report, we are currently collecting patient-reported outcome measures and looking forward to reporting our results in the future. Our single-stage technique combines the key elements of the abovementioned techniques, notably providing cartilage tissue, cell-signaling growth factors, and structural scaffolding to facilitate the regeneration and integration of hyaline-like tissue. As demonstrated in Figure 5, we achieved good integration and fill at follow-up with macroscopic evidence of hyaline-appearing tissue.

The risks of this surgical technique are similar to those previously described and include infection, donor site morbidity related to BMAC harvest, failure of hyaline cartilage restoration or integration, and potential graft hypertrophy. Certainly, these risks are always present in attempts to restore hyaline cartilage in vivo, and our technique does not pose additional risks compared to previously mentioned studies or techniques.

To maximize success with the procedure, we urge surgeons to comprehensively evaluate patients by obtaining a thorough history, physical examination, and interpretation of imaging modalities. This requires a detailed assessment to evaluate for ligamentous instability, meniscal deficiency, or limb malalignment. We recommend addressing malalignment with staged or concomitant osteotomy in an attempt to increase the longevity of the cartilage-restoring tissue and increase the success with patient-reported outcomes, which has been demonstrated with other cartilage repair techniques following realignment procedures.[31-34] A similar approach is recommended for ligamentous instability or meniscal deficiency.

The present technique capitalizes on combining established cartilage-restoring techniques supported by clinically significant improvements in patient-reported outcomes and radiographic evidence of healing. Furthermore, by maintaining a single-stage procedure, we eliminate many of the costs that would be associated with ex vivo chondrocyte culture expansion. Further studies are required to assess long-term outcomes of the present technique.

Disclosures

All authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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