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Sports Medicine

Augmented Marrow Stimulation: Drilling Techniques and Scaffold Options

"Next Generation Cartilage Repair and the Pre-Arthroplasty Patient" Operative Techniques in Sports Medicine

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Marrow stimulation is a commonly used surgical adjunct in the treatment of knee cartilage injuries. While initial studies on traditional microfracture demonstrated favorable short-term results, survivorship and clinical outcomes at medium- and long-term follow-up were subsequently shown to be inferior as compared to cell- and graft-based treatment options. As a result, numerous technical modifications and biologic augmentation approaches have been developed with the goal of improving the efficacy and the durability of marrow stimulation procedures. This chapter presents an overview of the basic and clinical science of marrow stimulation, its evolution over the past 25 years, and preliminary outcomes of treatment augmentation with biologic, scaffold, and cartilage-based approaches.

KEYWORDS marrow stimulation, articular cartilage, microfracture, orthobiologics

Introduction

Articular knee cartilage injuries are a common source of pain and dysfunction, with a reported prevalence between 4% and 6% in the general population.[1,2] While smaller, partial-thickness chondral defects are often asymptomatic, full-thickness defects extending to the subchondral bone are symptomatic, limiting conditions. Given limited autologous healing capacity and post-traumatic inflammatory response, chondral injury can predispose patients to the development of osteoarthritis if not addressed.[3,4]

Arthroscopic microfracture for the treatment of articular cartilage defects was popularized by Steadman in the 1990s.[5] The technique involves creating small perforations in the subchondral bone at the site of a cartilage defect to release bone marrow contents including mesenchymal stem cells (MSCs) into the defect that can promote cartilage healing and restoration. While initial short-term clinical outcomes demonstrated encouraging improvements in pain and function,[6,7] survivorship deteriorated at long-term follow-up[8,9] and outcomes have been proven to be inferior to reparative cartilage treatment techniques such as osteochondral allograft (OCA), osteochondral autograft transfer (OAT), and both traditional and matrix-associated autologous chondrocyte implantation (ACI and MACI, respectively).[9-12] Microfracture treatment failure has been most often attributed to osseous overgrowth, subchondral cyst formation, and healing with a fibrocartilaginous scar that is mechanically inferior to native hyaline articular cartilage.[13-15]

As a result, there has been an increased focus on refining traditional marrow-stimulation techniques in order to improve clinical efficacy and durability.[16,17] This paper presents an overview of the basic and the clinical science of marrow stimulation, the approach's evolution over the past 25 years, and the preliminary outcomes of treatment augmentation with orthobiologic, scaffold, and cell-based products.

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Indications and Contraindications

Marrow stimulation procedures can be considered in a symptomatic patient with an isolated, contained, full-thickness (International Cartilage Repair Society [ICRS] Grades III or IV) chondral injury of the knee.[18] It is typically reserved for use in younger patients with smaller chondral injuries, generally less than 2-4 cm^2 that do not extensively violate the subchondral bone.[13,19] In athletes, the threshold for treatment with microfracture is generally reduced to <2 cm^2 as previous investigations have associated poorer outcomes with the treatment of larger defects.[6]

Contraindications to microfracture include large chondral lesions (>4 cm2), lesions of the patella, the presence of uncontained or bipolar lesions, or diffuse degenerative cartilage disease.[14,17] Relative contraindications include extensive injury of the subchondral bone, which may be more amenable to restorative treatment options like OCA that replace the entire diseased cartilage and subchondral unit, as well as older age and elevated BMI (>30).[18] Patients with diffuse osteoarthritis, inflammatory arthritis, AVN, infection, or neoplasm or those who cannot adequately complete post-operative rehabilitation are not considered suitable surgical candidates.[20,21]

If concomitant knee pathology such as meniscal injury, lower extremity malalignment, or ligamentous instability is also identified during clinical work-up or at the time of diagnostic arthroscopy, it should be addressed either at the time of index surgery or shortly thereafter in a staged manner.[22] Assessment of alignment is of substantial importance as unaddressed malalignment was seen as the underlying cause for failure of up to 56% of patients presenting with a failed previous cartilage surgery.[23]

Marrow Stimulation Drilling Technique

Diagnostic Arthroscopy

While X-ray and magnetic resonance imaging (MRI) are valuable clinical tools for identifying focal cartilage defects and concomitant knee pathology (Fig. 1), diagnostic arthroscopy remains the gold standard of diagnosis because it allows for direct visualization, manipulation, sizing, and grading of the defect according to either Outerbridge or ICRS classifications.

The patient is positioned supine on a standard operating table, and a non-sterile tourniquet is placed on the thigh, which is used at the surgeon's discretion. An examination under anesthesia should be performed to evaluate range of motion and the presence of ligamentous patholaxity. Following examination, the leg is prepped and draped in a sterile fashion. An 11-blade is used to make standard anteromedial and anterolateral portal incisions. If needed, an accessory portal can be made with the assistance of a spinal needle to increase visualization. A comprehensive diagnostic arthroscopy is then conducted to evaluate for loose bodies, additional cartilage defects, and other concomitant pathology. Once the isolated lesion is identified, it should be probed and measured to allow for grading based on ICRS or Outerbridge criteria and to determine the optimal treatment course.

Arthroscopic Preparation of Defect

Before proceeding with microfracture, diseased cartilage surrounding the defect is carefully debrided with the use of either an arthroscopic curette or shaver. The end product of debridement should be a perimeter of healthy tissue with

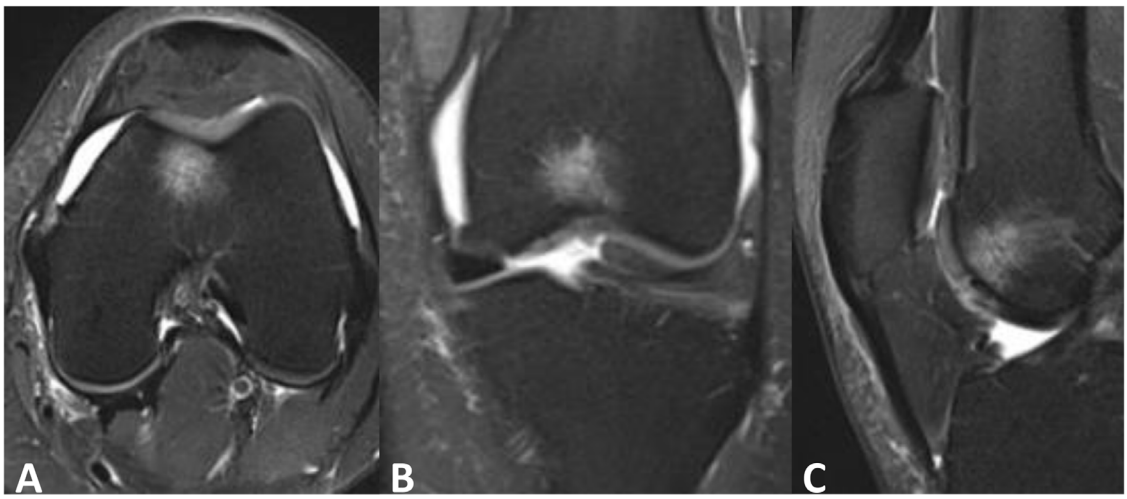

Figure 1 T2-weighted MRI with A) axial, B) coronal, and C) sagittal slices demonstrating a focal chondral defect of the medial femoral trochlea with underlying subchondral edema.

stable, vertical walls encircling the defect, which both optimizes fibrin clot formation and creates a flush load-bearing zone.[24] A curette is used to remove the calcified cartilage layer, keeping the underlying subchondral plate intact. This is a vital step in the procedure because while the calcified cartilage must be sufficiently removed to promote nutrition diffusion and clot stabilization, violation of the subchondral bone has been associated with subchondral cyst and intralesional osteophyte formation.[25,26]

Microdrilling

Microdrilling has largely replaced traditional awl microfracture as the technique of choice for the senior author when performing marrow stimulation procedures. Initial microfracture technique descriptions preferred the use of an awl to bone drilling because of concerns of local osteocyte death secondary to thermal necrosis.[5] However, such assumptions have largely proven to be incorrect,[27] and furthermore, awl microfracture has been found to produce more trabecular compaction, cyst formation, and sclerosis of the subchondral bone than microdrilling.[28-33]

Traditional awl microfracture involves creating approximately 2.5 mm wide by 2 mm deep perforations in the exposed subchondral bone. Holes are made 3-4 mm apart to avoid convergence, starting first at the periphery of the defect before working centrally to cover the entire lesion surface. Subchondral microdrilling utilizes the same tenets of spacing and working peripherally to centrally, but holes are deeper and have a smaller diameter. (Fig. 2) The preferred device of the senior author (PowerPick, Arthrex Inc., Naples, FL) is a microdrilling system that drills at a width of 1.5 mm and a depth of either 4 mm or 6 mm depending on device specifications. The device is also outfitted with an angled tip that can be adjusted to 30° or 45° depending on lesion accessibility. The senior author's technique has been described previously.[17,34,35] Once drilling is complete, the arthroscopic fluid should be turned off and tourniquet let down in order to confirm egress of marrow contents into the defect.

Aside from the advantages of decreased bone remodeling when compared to awl microfracture, the deeper, smaller holes are generated by microdrilling leads to improved marrow stromal access and increased subchondral hematoma volume, which may result in superior cartilage repair based on preclinical models.[36-39] Clinically, drilling has been shown to significantly improve patient-reported outcome scores and lower revision rates when compared to traditional awl-based techniques at 3-year follow-up.[40] In the study, Beletsky et al. reported that patients who underwent microdilling were significantly more likely reach the minimal clinically important difference (MCID) thresholds established for the International Knee Documentation Committee (IKDC) (72% vs 33%, $P = 0.002$), Knee Injury and Osteoarthritis Outcome Score (KOOS) Pain (42.9% vs 11.1%, $P = 0.02$), and KOOS Sport (55.6% vs 18.2%, $P = 0.04$) subscales at 6 months postoperatively. At 1-year, patients who underwent microdrilling also demonstrated higher rates of reaching the MCID on the KOOS Quality of Life (83.3% vs 56.5%, $P = 0.04$) and Short-Form 12 Physical Component Score (PCS) (90.9% vs 60.0%, $P < 0.01$). Additionally, 41% of

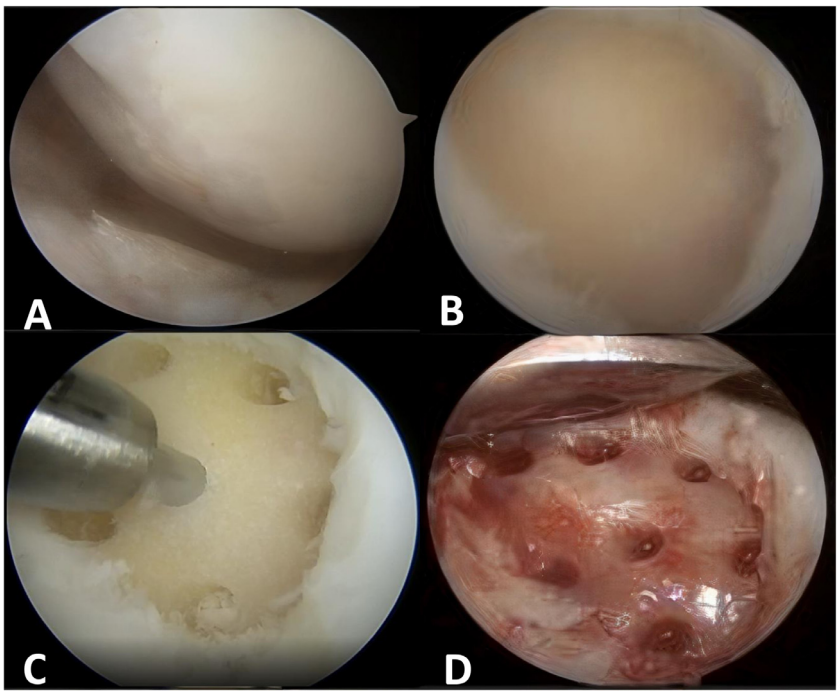

Figure 2 Arthroscopic microdrilling of a focal chondral defect. A) Focal cartilage defect of the medial femoral condyle visualized during arthroscopy. B) First, debridement is performed to the subchondral plate, creating stable defect edges. C) Using a PowerPick (Arthrex Inc., Naples, FL), microdrilling is performed to promote marrow stimulation. D) Arthroscopic visualization demonstrates a debrided lesion, stable edges, and access to the marrow elements once the tourniquet is let down.

patients treated awl microfracture patients required revision surgery by 3-year follow-up, compared to 18% of patients treated with microdrilling ($P = 0.03$).[40]

Biologic Augmentation

Given historically inferior outcomes to structural grafts and ACI/MACI, biologic augmentation has become an attractive adjunct to marrow stimulation procedures. Biologic augmentation has the potential to harness emerging autologous cell-based therapies in order to improve the quality of repair while limiting the unwanted production of subchondral cysts and biologically inferior fibrocartilage. While these products remain investigational to date due to a lack of large-scale clinical data, a 2018 review of biologic augmentation literature has demonstrated positive patient-reported outcomes compared to patients treated with marrow stimulation alone.[41]

Platelet-Rich Plasma (PRP)

Platelet-rich plasma (PRP) utilizes autologous venous blood processed to generate a product rich in platelets and chondrogenic growth factors, such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth factor-beta (TGF- β). Autologous blood collected is collected peripherally and concentrated via centrifugation to increase platelet concentration from a range of 150,000-350,000 platelets/μL in whole blood up to roughly 1,000,000 platelets/μL, a level shown to promote bone and soft tissue healing.[42] While PRP is used across many settings within orthopaedics to promote soft tissue healing with varying levels of success, it is theorized that when used as an adjunct to marrow stimulation, the concentration of platelets and growth factors can stimulate MSC differentiation into chondrocytes, resulting in chondrocyte proliferation and type II collagen and proteoglycan synthesis.[41,43]

Preparations and protocols for the collection and use of PRP vary based on the commercial system being used to generate the product. The senior author prefers the Angel System (Arthrex Inc, Naples, FL). Peripheral blood is collected at the time of the procedure and is centrifuged into separate components to generate an isolated PRP concentrate with adjustable leukocyte concentration. Multiple investigations and reviews have demonstrated that the use of leukocyte-poor PRP (LR-PRP) formulations have been associated with generally improved functional and pain outcomes when compared to leukocyte-rich PRP (LR-PRP) compositions, secondary to a reduction in the number of catabolic and pro-inflammatory markers such as tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), interleukin-six (IL-6), and interferon-gamma (IFN-γ).[44-46] After arthroscopic microfracture, all fluid is drained from the joint, the prepared defect is thoroughly dried, and PRP is injected into the area of the microfractured defect under direct, dry arthroscopic visualization.

Clinical outcomes following PRP-augmented microfracture have yielded mixed results when compared to traditional microfracture. While some comparative studies have failed to identify any improvement in outcomes following augmentation, a meta-analysis of 7 studies by Boffa et al. demonstrated that PRP-augmented microfracture of the knee and ankle led to statistically significant improvements in patient-reported outcomes at short-term follow-up.[47-49] Overall, the body of current literature supports the use of PRP as a safe, viable adjunctive to marrow stimulation procedures, though further long-term study is warranted to better understand the indications and efficacy of PRP augmentation as well as the ideal PRP preparation in order to maximize treatment outcomes.

Bone Marrow Aspirate Concentrate (BMAC)

BMAC is an autologous concentrate of bone marrow aspirate, a source of mesenchymal stromal cells (MSCs) plus immunomodulatory growth factors and cytokines that may help to promote the proliferation of chondrocytes and hyaline cartilage regeneration. The aspirate can be harvested from multiple sources, but in knee procedures, the proximal tibia is often the most directly accessible harvest site. Before the initiation of arthroscopy, the anteromedial aspect of the tibia is palpated at roughly 5-6 cm distal from the medial joint line. A trocar is then introduced through the skin at an angle directed superolateral toward the fibular head. The trocar should then be advanced through the bone cortex to the intramedullary canal with the use of a mallet; a noticeable loss of resistance will be felt between 1 and 2 cm once the trocar has entered the canal. The central portion of the trocar is removed and a syringe prefilled with heparin is attached. Aspiration is accomplished by combining quarter rotations of the trocar with slight withdraws and reinsertions to disrupt the medullary trabeculae. This maneuvering is performed until 60 cc of aspirate is collected. The aspirate is processed according to the specifications of the centrifuge processor, and similarly to the administration of PRP, is injected over the prepared microfractured defect surface after evacuating the joint of arthroscopic fluid.

Centrifugation concentrates MSCs as well as vital cytokines and androgenic growth factors such as interleukin-1 receptor antagonist (IL-1RA), IL-8, PDGF, TGF- β, and bone morphogenetic protein- 2 (BMP-2) and bone morphogenic protein-7 (BMP-7).[50-52] While the concentration of MSCs only represents 0.001%-0.01% of the total number of mononuclear cells following centrifugation and processing, BMAC can deliver the vital chondrogenic growth factors and cytokines at a concentration far greater than PRP.[51]

To our knowledge, there are no prospective studies that directly compare outcomes of microfracture augmented with BMAC to microfracture alone for the treatment of chondral injuries in the knee. However, direct comparison studies have been carried out for chondral injuries of the talus, with encouraging results. Murphy et al. completed a prospective evaluation of 101 microfracture cases of the talus with and without augmentation and found that while there were no statically significant differences in patient-reported outcome metrics (PROMs), the revision rate in the augmentation group was 12% compared to 29% in the microfracture group at 36-month follow-up

($P = 0.015$).[53] Similarly, Gobbi and colleagues compared outcomes following implantation of BMAC-soaked hyaluronic acid construct following microfracture to both traditional microfracture and MACI for the treatment of cartilage injuries.[54,55] When compared to traditional microfracture at 5-year follow-up, clinical outcomes were significantly superior in those treated with microfracture + BMAC. Patients treated with microfracture showed significant postoperative improvements in IKDC objective scores compared to baseline, but scores deteriorated as the length of follow-up increased. Meanwhile, no long-term deterioration in IKDC outcome scores was observed in the microfracture + BMAC cohort.[54,55]

Scaffold-Based Repair Augmentation

In recent years, the use of scaffold augmentation following microfracture repair has emerged in the clinical setting. Like traditional microfracture or drilling, scaffold augmentation is a treatment option in patients with focal defects <2 cm2 seeking a single-stage, cost-effective, autologous procedure without the risks of autologous donor site morbidity, allograft donor availability, or substantial resource burden that may be required in other reparative and restorative cartilage treatment options. Scaffold techniques were developed as a means to provide additional stability to the defect site during primary healing while also providing a base or medium that promotes autologous repair. The approach has demonstrated the ability to improve marrow clot stabilization which in turn promotes MSC containment and organization.[56-58] Furthermore, the added stability conferred allows for accelerated return to loading of the knee, which is critical from MSC differentiation and chondrocyte proliferation within the scaffold medium.[59-61]

Autologous Matrix-Induced Chondrogenesis (AMIC)

AMIC is a one-step marrow augmentation technique that combines traditional marrow stimulation with fixation of a two-layer membrane composed of porcine type I and III collagen. The technique was first introduced by Benthiens and Behrens, though new generations have refined the procedure which has resulted in improved quality of cartilage regeneration and clinical outcomes.[62-64]

Following standard diagnostic arthroscopy and arthroscopic marrow stimulation of a chondral defect, the lesion is measured with a sterile paper or aluminum guide plate so that the collagen matrix (Chondro-Gide, Geistlich Pharma AG) can be cut according to exact lesion dimensions. The matrix is then introduced into the joint and affixed with fibrin glue. After allowing 5 minutes for the thrombin glue to properly set, the knee is then fully flexed and extended multiple times to ensure scaffold positioning and stability.

A systematic review of all AMIC literature was conducted in 2017 by Gao et al.[65] The review identified 12 studies of AMIC being used in the knee. Overall, the studies demonstrated that patients treated with AMIC reported improved functional knee scores at short-, medium-, and long-term follow-up. However, eleven of these studies were case series with no comparison cohort of microfracture or other restorative/reparative cartilage treatment. There was, however, one randomized trial compared patients treated with AMIC to traditional microfracture.[66] The study demonstrated that AMIC was superior to microfracture alone in the modified Cincinnati score at 5-year follow-up, but no differences were observed in any other pain, functional, and defect fill analyses.[66]

Injectable Scaffolds

Advancements in tissue engineering have led to the development of cell-free scaffolds made from synthetic or natural materials that can be utilized in single-stage augmentation repair of cartilage defects. These scaffolds act similarly to products such as AMIC but confer the additional advantages of being (1) highly conformable to lesion size and depth because of their liquid state, (2) engineered to promote MSC recruitment and differentiation, and (3) biodegradable to allow for robust healing and hyaline chondrogenesis and tissue substitution / remodeling within the defect site.[67,68]

Gelrin C (Regentis Biomaterials Ltd., Haifa, Israel) is an acellular hydrogel injectable composed of crosslinked polyethylene glycol diacrylate and fibrinogen.[69-71] The biochemical components of Gelrin C stabilize the marrow clot that forms following marrow stimulation, reinforcing the defect site to allow for autologous repair. Following lesion debridement and marrow stimulation, Gelrin C is injected into the defect and allowed to fill the repair site. Once sufficiently spread within the lesion, the product is converted from hydrogel to semi-solid using ultraviolet light applied directly to the defect site for 90 seconds.[67] When the hydrogel is sufficiently cured, all instrumentation is removed, and the joint is then moved through the full range of motion to ensure the implant is secure.

The semi-solid product is designed to degrade over 6 -12 months as autologous tissue fills the repair site. Using a rat model, Peled et al. demonstrated that rats subjected to a 7-mm segmental tibial defect that were treated with with external fixation plus implantation of a with fibrinogen hydrogel demonstrated increased type II collagen and proteoglycan content at the healing lesion site compared to rats treated with external fixation stabilization alone.[70] While clinical trials of Gelrin C are still in early stages, a preclinical prospective cohort study of 21 patients treated with Gelrin C microfracture augmentation for the repair of femoral condyle lesions was published by Trattnig et al. in 2015.[67] The study found that both patient-reported outcomes and cartilage regeneration as defined by the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) score were statistically superior as compared to baseline. Additionally, the average signal intensity on MRI at 2-year post-operative was found to approach that of normal, healthy cartilage, suggesting good tissue quality and fill following repair.[67] Gelrin C has received European CE mark approval but is in the midst of a phase III FDA clinical trial (ClinicalTrials.gov identifier:

NCT03262909) and is not currently approved nor available for clinical use outside of the clinical trial in the United States.

Cellular-Based Repair Augmentation

Cellular-based scaffold repair is another emerging frontier of augmented marrow stimulation procedures. The promise of cellular-based repair methods lies in the ability to augment marrow stimulation repair techniques with either native hyaline chondrocytes or extracellular matrix to promote natural hyaline cartilage regeneration. Multiple potential allogenic and autologous cell-based products exist in clinical practice. These products vary in their cost and availability, as some are shelf-stable while others are freshly harvested near or at the time of implantation. Additionally, in regards to composition and form, some products are injectable while others take the form of solid implants.

Allogeneic Cartilage

While the use of allogenic tissue is made challenging by high costs and limited donor availability, it confers the advantage of providing native cartilage without the donor site morbidity associated with autologous procedures such as ACI, MACI, and OATs. Another potential advantage of [structural] allogeneic cartilage products is their ability to repair lesions with hyaline cartilage rather than the fibrocartilage associated with marrow stimulation.[72-75]

DeNovo Natural Tissue (DeNovo NT) (Zimmer, Warsaw, IN) is a particulated juvenile articular cartilage (PJAC) product that has been available for commercial use since 2007.[76] PJAC is collected from fresh cadaveric femoral condyles of donors aged 13 years or younger and contains live cells within their native extracellular matrix that has been processed into blister packs of 1-mm3 explants.[76,77] In vitro analyses that have estimated matrix synthesis by juvenile chondrocytes to be 100 times greater than that of adult cartilage cells.[78-80] In vivo studies have also demonstrated that juvenile chondrocytes do not stimulate an allogeneic lymphocytic response.[80] However, PJAC products are not without limitations. De Novo NT is designed to be used in a single-stage procedure, but high cost and a limited shelf-life of approximately 40 days makes off-the-shelf use of this product logistically challenging.[78] Nonetheless, the use of PJAC in the repair of cartilage defects of the knee has demonstrated encouraging short-term clinical results, with the most optimal outcomes occurring with patellofemoral defect treatment.[81-83] However, no prospective, randomized trials against a control group of microfracture or similar procedure have been performed to date, limiting available data to isolated cohort studies.

PJAC implantation has been described previously by the senior author.[77] Following diagnostic arthroscopy, an arthrotomy is performed to expose to relevant joint space where the cartilage defect is located. The defect is then thoroughly debrided to the level of the subchondral bone with a curette and/or careful use of a scalpel. Unlike most other cell-based augmentation methods, marrow stimulation is not performed when implanting PJAC, and any subchondral bleeding should be mitigated with direct pressure or the use of fibrin sealant. Following debridement, the defect space should be measured with a sterile ruler or sterile foil that is pressed into the defect space to create a form-fitting imprint. Surgeon preference varies in preparing the cartilage for implantation, but the overall technique remains the same. PJAC is removed from its packaging and loaded into the foil implant or alternatively, directly into the defect. Adhesive fibrin clue is then used to secure the cartilage within the implant, and allowed to dry to ensure proper fixation.

Biocartilage (Arthrex, Naples, FL) is another source of allogeneic cartilage that can be used in the augmentation of microfracture repair. The product is a micronized scaffold comprised of dehydrated cartilage extracellular matrix components including type II collagen, proteoglycans, and growth factors derived from an allogeneic source.[72,73] At the time of implantation, the product is rehydrated with a blood-derived biologic agent, either PRP or BMAC, in a 1:1 ratio. The biologic agents provide additional growth factors that function synergistically with MSCs released during marrow stimulation to promote hyaline chondrogenesis.[84,85] In an equine model, micronized cartilage augmentation proved superior in promoting autologous cartilage formation when compared to microfracture alone.[75] Clinically, the use of micronized cartilage has only been investigated in short term studies, though results have been favorable. Brusalis and colleagues published outcomes of BioCartilage augmentation in 10 patients, which demonstrated significant improvements in PROMs at 2-year follow-up.[86] Meanwhile, a recent multicenter cohort investigation of 48 patients reported clinically significant improvements in 90% of patients at 2 years status post procedure.[87]

BioCartilage can be used concomitantly following any arthroscopic marrow stimulation procedure.[73,88] After debridement and subchondral microfracture or drilling, arthroscopic fluid is drained from the knee and the defect is dried thoroughly. The cartilage-biologic mixture is prepared and made to be homogenous and is then loaded into a Tuohy needle and introduced into the joint under arthroscopic visualization. The mixture is then spread across the defect and compacted with a freer elevator to be flush and slightly recessed with respect to the surrounding healthy chondral borders. Fibrin glue is then applied and smoothed to match the contour of the surrounding surface and allowed to dry.

Cryopreserved tissue such as Cartiform (Arthrex, Naples, FL) is another allogenic cartilage product that can be utilized to augment marrow stimulation repair. In comparison to PJAC and BioCartilage, cryopreserved allogeneic cartilage products confer a handful of advantages. Namely, cryopreserved cartilage is shelf-stable for up to 2 years,[89,90] includes a layer of full-thickness articular cartilage replete with live chondrocytes on top of a thin osseous layer,[89] and can be easily trimmed to match the defect's size.[91] Both basic science and clinical investigations have demonstrated early promise.

Geraghty et al. compared isolated microfracture to microfracture augmented cryopreserved cartilage in a goat model.[90] A difference in quality and the depth of hyaline tissue regrowth was identified as early as 3 months postoperatively and was maintained until the study's conclusion at 1 year postoperatively.[90] Bennett et al. published a retrospective case study of 12 patients treated with microfracture augmented with Cartiform which found statistically significant improvements in multiple PROMs and no clinical failures at 2-year follow-up.[92]

Cartiform is most commonly implanted during an open procedure. Following diagnostic arthroscopy, an arthrotomy is performed to expose to the injured articular surface. Sharp dissection and debridement of the chondral lesion is performed with a scalpel or curette, and then bone marrow stimulation is performed to stimulate repair. Once the defect is sufficiently prepared, the cryopreserved implant is introduced to the surgical field and marked for cutting based on lesion size. Once matched to the defect, the graft is cut and secured to the defect periphery using suture anchors. Additional fixation can be achieved with suturing to the healthy cartilage rim, if needed.

Autologous Cartilage

In comparison to allogeneic products which are limited by donor availability, autologous cartilage implantation involves harvesting a small portion of a patient's own articular cartilage from a non-weight-bearing region of the knee that is then re-applied to the site of focal injury. This can be performed in a single stage following point of care preparation (ie mincing) or as part of a 2-stage procedure with culture-based expansion, such as in MACI.

Multiple preclinical studies have been performed to assess the efficacy of reimplanting minced autologous cartilage. While minced autologous cartilage has been shown to be inferior with regards to tissue expansion in vitro when compared to juvenile chondrocytes,[79] it has been demonstrated that autologous minced cartilage is an effective source of tissue for cartilage repair[85] and that chondral fragmentation increases extracellular matrix production.[93] In a clinical trial comparing microfracture alone to microfracture augmented with a single-stage minced autologous cartilage scaffold, patient-reported outcomes were superior in patients treated with autologous minced cartilage augmentation compared to isolated microfracture at 2 years of follow-up.[94] Additionally, on 1-year postoperative MRI, patients treated with isolated microfracture were significantly more likely to develop intralesional osteophytes when compared to those treated with microfracture + augmentation (25% vs 70%, respectively; $P = 0.015$).[94] In their 2015 study, Christensen et al. treated 8 patients with osteochondritis dissecans of the knee with a scaffold of combined autologous bone and cartilage chips embedded in fibrin glue. At 1-year postoperatively, all patient reported outcome measures were significantly improved and

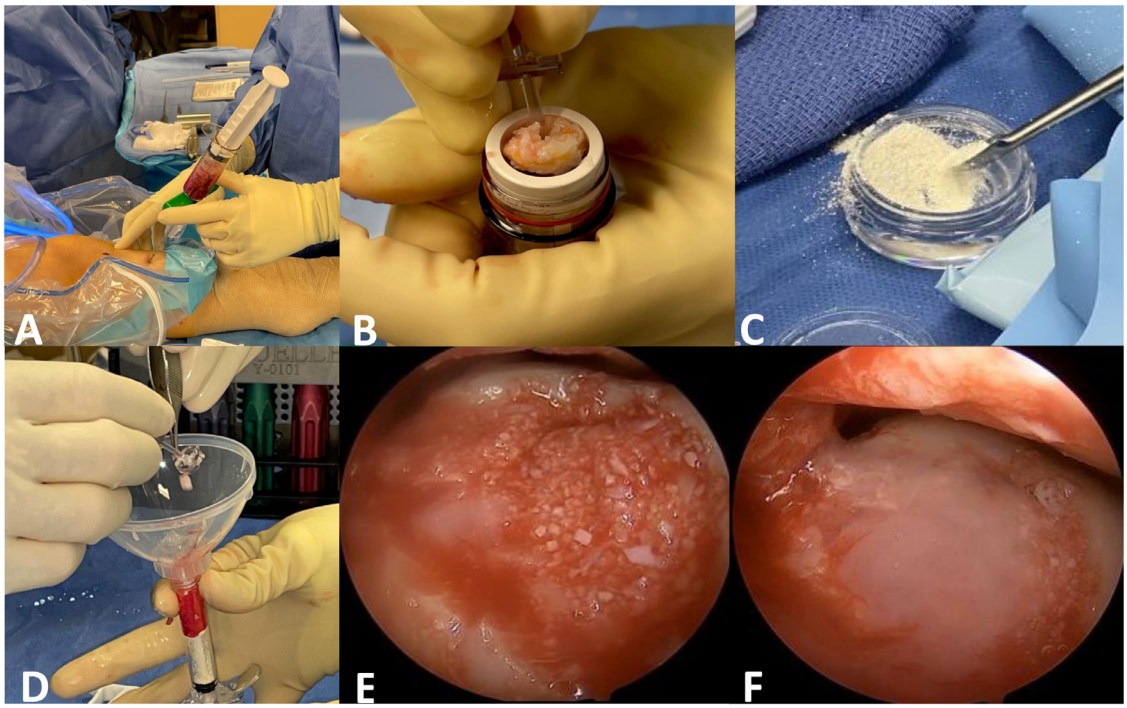

Figure 3 AutoCart (Arthrex Inc., Naples, FL) procedure to repair a focal chondral defect of the knee. A) Bone marrow aspirate is harvested from the proximal tibia. B) Autologous hyaline cartilage is collected arthroscopically using a GraftNet (Arthrex Inc., Naples, FL) collection device connected in line to the arthroscopic shaver. C) BioCartilage (Arthrex Inc., Naples, FL) is transferred from original packaging to a sterile specimen cup containing the harvested autologous cartilage and bone marrow aspirate concentrate. D) The AutoCart preparation is loaded into a syringe and connected to a Tuohy needle to allow for arthroscopic deployment. E) The AutoCart mixture is injected at the defect repair site. F) Final defect visualization following fibrin glue application.

CT demonstrated bone filling of greater than 80% in all eight patients.[95] Similarly, a recent prospective study by Massen et al. demonstrated significant improvements in pain and function at 24-month post operatively in 27 patients treated with a second-generation autologous minced cartilage augmentation.[96]

The current preferred technique of the senior author has been outlined in previous publications.[17,97] At the conclusion of diagnostic arthroscopy, lesion debridement, and marrow stimulation, a GraftNet (Arthrex Inc., Naples FL) collection device is connected in-line with the arthroscopic shaver and suction device. Viable cartilage may be collected from loose bodies found within the joint during arthroscopy, or harvested unstable cartilage flaps, or non-weight bearing areas of the knee such as the lateral intercondylar notch.[98] The collection device is then disconnected so that the collected fragmented cartilage can be added to a Tuohy needle for implantation. If additional biologic augmentation is being performed, BMAC or PRP can be mixed with the cartilage fragments before being loaded to the needle. The joint is then drained of arthroscopic fluid and the defect bed is dried thoroughly. The needle is inserted into the joint under direct visualization and the cartilage fragments are spread across the lesion surface until even defect fill to a level just below the surrounding cartilage surface is attained. A layer of fibrin glue is applied and allowed to dry before moving the joint through a full range of motion to ensure fixation.

Combined Allogeneic and Autologous Cartilage

The continued evolution of biologic marrow stimulation augmentation has resulted in the combination of allogeneic and autologous cartilage products into one single-stage scaffold-based procedure. AutoCart (Arthrex Inc, Naples, FL) is a novel augmentation procedure that combines autologous mixed cartilage, BioCartilage allogeneic cartilage, and a biologic rehydrating agent into a single repair mixture(Fig. 3). The technique has been described previously by the senior author and is similar to the technique described for autologous minced cartilage implantation.[99,100] Following defect debridement and microdrilling, a suction-activated GraftNet device is used to capture healthy hyaline cartilage from unstable flaps, loose bodies, or from non-weight bearing regions of the knee. The collected autologous cartilage is then extracted from the device and mixed in a 1:1:1 ratio with BioCartilage and either PRP or BMAC on the sterile back table of the operating room. The resultant mixture is transferred to a syringe and then advanced through a Tuohy needle that is reintroduced to the joint. Following adequate hemostasis and sufficient drying of the prepared defect, the AutoCart mixture is ejected from the needle and spread within the defect to a level that is just below the surface of the surrounding native cartilage surface. A layer of PRP and activated autologous fibrin serum generated using the Thrombinator system (Arthrex Inc, Naples, FL) is then applied in a 1:1 ratio over the defect using a Y syringe and then smoothed over in order to ensure a flush surface with the surrounding joint surface. Commercially available allogeneic fibrin sealant may also be used for fixation. While no clinical efficacy studies have been published to date, investigations are currently ongoing and the biologic components of AutoCart have individually demonstrated promising early results.

Conclusion

Marrow stimulation remains a viable treatment option for the repair of small articular cartilage knee injuries. While first-generation microfracture has been found to be inferior at mid- to long-term follow-up when compared to other surgical interventions, refined subchondral drilling techniques and the advent of orthobiologic augmentation offers the promise of enhanced cartilage repair and improved long-term clinical outcomes. Preliminary studies have demonstrated many of these advances to be efficacious; however, further long-term evaluation is needed to determine the durability of these emerging therapies.

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