Technical Note

Single-Stage Arthroscopic Cartilage Repair With Injectable Scaffold and BMAC

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Abstract: Injectable scaffold augmentation is a promising modality for single-stage cartilage repair. According to published studies, cartilage repair with scaffold augmentation has improved clinical outcomes, radiological fill, and histological repair compared with microfracture alone. Injectable scaffolds have the versatility to be used in large and irregularly shaped lesions. With correct preparation, they can be applied to lesions on the femoral condyle that may be vertical, or even inverted lesions such as those in the patella. They can be combined with bone marrow aspirate concentrate (BMAC) to provide mesenchymal stem cells (MSCs), thereby avoiding the need for microfracture. This protects the subchondral plate, preventing biomechanical alteration and potentially resulting in improved long-term outcomes. In this article, we demonstrate the utility of injectable scaffolds and their combination with BMAC.

The quest to repair cartilage in a single-stage arthroscopic surgery is one of the holy grails in orthopaedic surgery. Because of the avascular, aneural, and immunoprivileged nature of hyaline cartilage, the regenerative potential of cartilage after injury is limited.

The ideal indication for cartilage repair is an isolated, symptomatic lesion in a well-aligned, stable knee with an intact meniscus. It has been proposed that microfracture is indicated for cartilage defects <4 cm.[1] Long-term follow-up has demonstrated increasing failure over time, particularly in lesions >4 cm.[1,2] Autologous chondrocyte implantation (ACI) and osteochondral allograft have shown excellent results for larger lesions[3,4]; however, access to both techniques is limited by economic and regulatory restrictions.

Microfracture creates perforations in the subchondral plate to allow mesenchymal stem cells (MSCs) from the bone marrow to form an intralesional clot; this matures to form predominantly fibrocartilage to cover the defect. Proposed limitations of microfracture include failure of bone marrow MSCs to remain at the defect site (if the clot is dislodged) and biomechanically inferior fibrocartilage regeneration. Microfracture also results in stiffening of the subchondral bone and can induce bone overgrowth in ≤80% of cases. Intralesional osteophytes increase the failure rate by ≤ 10-fold.[5]

Autologous matrix-induced chondrogenesis (AMIC) is a 1-step procedure that combines microfracture with a scaffold to aid in clot stabilization and maturation. The scaffold provides a matrix to assist with MSC retention and potential differentiation along a chondrogenic lineage. Significant improvement in clinical and radiological outcomes have been reported using a number of different scaffolds.[4,6]

Injectable or hydrogel scaffolds allow for easy application via arthroscopy, even into irregular defects. They potentially provide better MSC retention after microfracture, given their reduced porosity, and some can be combined with bone marrow aspirate concentrate (BMAC). Seeding a scaffold with BMAC opens the possibility of negating the need for microfracture[5] and avoiding the subsequent bone complications.

This Technical Note describes a technique to produce an injectable scaffold that has the versatility to be applied to a vertical or inverted surface, such as the patella. The scaffold can be delivered in a single-stage

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Table 1. Steps for arthroscopic AMIC injectable Scaffold

1. Prepare the injectable scaffold according to the manufacturer's guide.
2. Arthroscopy and prepare cartilage defect.
3. Microfracture.
4. Drain water from the knee.
5. Dry the lesion.
6. Under dry arthroscopy, apply injectable scaffold to prepared defect.
7. Wait for scaffold to set.

arthroscopic procedure. Practical advice is provided for scaffold production and delivery, including the possibility of adding BMAC to increase cell content at the repair site.

Technique

Patient Positioning and Anesthesia

The patient is positioned supine on the operating table, and a thigh tourniquet is applied. Arthroscopy is performed using normal saline with use of a 4-lead gravity bag. The foot attachment of the table is removed so that the knee is flexed 90° off the table, allowing easy access to front and back of the knee.

Diagnostic Arthroscopy

Standard anterolateral (AL) and anteromedial (AM) portals are created adjacent to the patellar tendon. The knee joint is inspected arthroscopically with a 30° scope through the anterolateral portal. Cartilage injuries are probed to assess for severity and graded according to the Outerbridge grading system. Concomitant soft tissue injuries, such as meniscus tears and ligamentous injuries, are noted.

We perform this technique arthroscopically with the use of a 4-lead gravity fluid bag. We do not use dry arthroscopy with CO_2 insufflation.[7] This increases the procedure's versatility, without the need for specialized equipment.

Preparation of Injectable AMIC Mixture: CarGel and CartiFill

CarGel (Smith & Nephew, London, UK) AMIC is performed according to the techniques described in the manufacturer's product guide. The buffer solution is mixed with the chitosan solution and left for 10 minutes. Autologous blood (5 ml) is drawn via venipuncture and injected into the prepared buffer-chitosan mixture. This CarGel blood-buffer-chitosan mix is drawn into an application syringe ready to be applied to the cartilage lesion.

A critical technical tip is to keep the mixture close to body temperature. Storage of the buffer and scaffold is in a refrigerated environment of 4°C, and the operating theater is commonly cold. Early warming of both the buffer and the scaffold is important; the buffer and scaffold are warmed in a water bath at room temperature once use of the scaffold is confirmed. The scaffold mixture is also placed in the water bath until it is used, making for a consistent viscous scaffold, which is easier to apply.

For a CartiFill (Sewon Cellontech, Seoul, Korea) scaffold, 3 ml of CartiFill collagen implant is mixed with 1 ml of thrombin solution to yield the atelocollagen material; this mixture is drawn into a syringe. Another syringe with fibrinogen is prepared. Both syringes are attached to a 20-gauge application needle using a Y-shaped connector. This allows the CartiFill and fibrin glue to be delivered simultaneously during application. Table 1 summarizes the technique for AMIC with scaffold.

Scaffold BMAC Technique

BMAC can be used to increase MSCs at the repair site. BMAC can be harvested from the ipsilateral iliac crest. For such cases, the choice may be made to not perform microfracture after lesion preparation, to protect the subchondral bone plate.[5,8]

We use a centrifuge-free BMAC system, Marrow Cellution (Aspire Medical, Munich, Germany). To facilitate application and quick setting in the lesion, when using CarGel with BMAC, we do not add heparin to the syringes that are used to draw the BMAC. The cartilage lesion is first prepared, and fluid is drained from the knee. This is followed by the harvesting of BMAC. Once BMAC is obtained, 5 ml of BMAC is immediately mixed with the CarGel (instead of using blood) and applied to the lesion when appropriately viscous.

For CartiFill, we use the Harvest BMAC device (Terumo BCT, Lakewood, CO). We add 2 ml of centrifuged BMAC, 2 ml of CartiFill, and 1 ml of thrombin into a syringe for application. As described previously, this syringe and a syringe with fibrinogen are attached to an application needle using a Y-shaped connector for the CartiFill/BMAC mixture and fibrin glue, to be applied together. Table 2 summarizes the steps for cartilage repair with BMAC and scaffold.

Table 2. Steps for arthroscopic cartilage Repair With injectable Scaffold and BMAC

1. Prepare the injectable scaffold according to the manufacturer's guide.
2. Arthroscopy and prepare cartilage defect (microfracture optional).
3. Drain water from the knee.
4. Dry the lesion.
5. Harvest BMAC from the iliac crest.
6. Mix BMAC with scaffold.
7. Under dry arthroscopy, apply injectable scaffold with BMAC mixture to prepared defect.
8. Wait for scaffold to set.

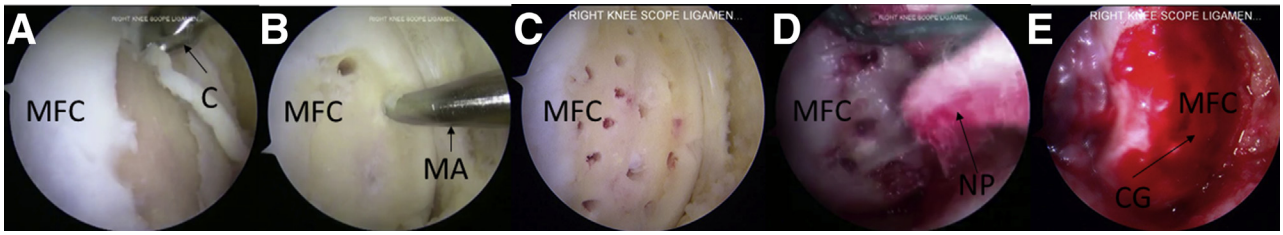

Fig 1. Arthroscopic image of right knee viewing from AL portal and working from the AM portal. Full-thickness chondral defect, measuring 3 by 2 cm in the medial femoral condyle. (A) Preparation of the defect bed using a ring curette. (B) Microfracture of the chondral defect using a microfracture awl. (C) Completion of microfracture. (D) Fluid is drained out of the knee, and dry arthroscopy is performed. Neuropatties are used to dry the defect. (E) CarGel scaffold is applied onto the dried vertical surface. Abbreviations: AL, anterolateral; AM, anteromedial; C, curette; CG, CarGel scaffold; MA, microfracture awl; MFC, medial femoral condyle; NP, neuropattie.

Cartilage Repair

Cartilage Defect Preparation

The cartilage defect site is debrided and prepared for the cartilage repair procedure. With shavers and curettes, the chondral lesion is debrided to vertical stable margins. The bed of the defect is prepared by removing the calcified cartilage, preserving the subchondral plate.[3] This can be done viewing or working from either AL or AM portal, depending on which gives the best access to the lesion.

For the AMIC technique, microfracture is performed with arthroscopic microfracture awls to a depth of ~4 mm. Microfracture lesions are created at a width of 3 or 4 mm apart throughout the surface of the cartilage defect.[3]

Application of Scaffold

Once the lesion has been prepared, the fluid is drained from the joint, and dry arthroscopy is performed. The cartilage lesion is dried using suction and patties. The scaffold is then applied to the defect (Fig 1; Video segment 1).

After application, the scaffold is allowed to solidify in the defect for 10 minutes. In the Video, we take the knee through range of motion to show stability of the scaffold applied to the lesion (Fig 2; Video segment 2). We also turn on the arthroscopy fluid and show that the scaffold applied remains stable in a fluid-filled environment (Fig 3; Video segment 3). We make use of adjuncts such as the MacDonald probe to help mold the applied scaffold in the defect and ensure it is not proud of the native chondral surface (Fig 4; Video segment 4).

The intuitive lesion to treat would be one with a horizontal surface such as a trochlear lesion. However, when prepared correctly, the injectable scaffold can be delivered as a viscous gel that can be applied on a vertical surface such as the medial femoral condyle or on an inverted surface such as the patella (Fig 5; Video segment 5). In Table 3, we share tips on how to prepare

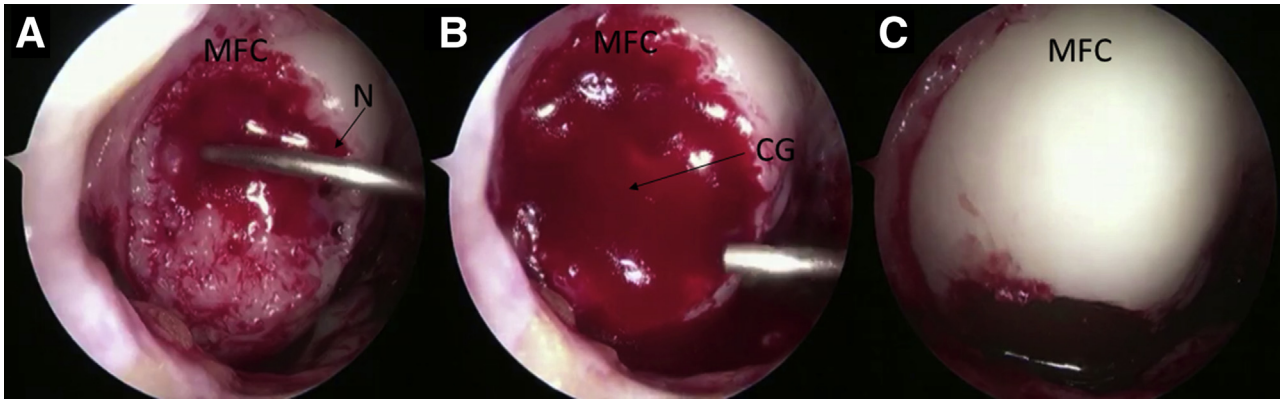

Fig 2. Arthroscopic image in a left knee viewing from the AL portal and working from the AM portal. Full-thickness chondral defect, measuring 2 by 2 cm in the medial femoral condyle. (A) Upon completion of preparation and drying the chondral defect, CarGel scaffold is applied onto the vertical medial femoral condyle. (B) After adequate warming, the scaffold can be applied onto the entire defect, with a gel-like consistency. (C) The CarGel scaffold remains stable on intraoperative full range of motion of the knee. Abbreviations: AL, anterolateral; AM, anteromedial; CG, CarGel scaffold; MFC, medial femoral condyle; N, needle.

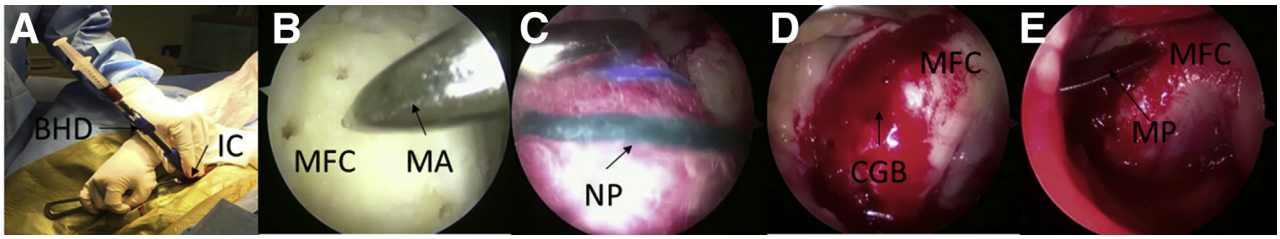

Fig 3. (A) Intraoperative photograph of BMAC harvesting from the ipsilateral iliac crest. (B) Arthroscopic image of a right knee from AL viewing portal, showing microfracture of a 3.5- by 2-cm medial femoral condyle chondral defect. (C) Dry arthroscopy and drying of the prepared defect with neuropatties. (D) CarGel seeded with BMAC is applied to the knee. (E) MacDonald probe is used, working from the AM portal, to mold the scaffold in the defect as it sets. Abbreviations: AL, anterolateral; BHD, BMAC harvesting device; CGB, CarGel scaffold plus BMAC; IC, iliac crest; MA, microfracture awl; MFC, medial femoral condyle; NP, neuropattie.

the injectable scaffold such that application can be optimized.

Postoperative Protocol

After cartilage repair, the range of motion prescribed depends on the location of the lesion and is controlled by a hinged knee brace. For patellofemoral lesions, knee flexion is initially limited to 30° in the first 3 weeks and gradually increased to 90° flexion by 6 weeks. Full range of knee motion is allowed after 6 weeks. Patients are allowed protected weightbearing (50% of body weight) for the first 6 weeks after surgery and full weightbearing after 6 weeks.

For lesions in the tibiofemoral joint, motion is restricted from 0° to 90° for 6 weeks. Patients are kept nonweightbearing for the first 3 weeks and gradually progressed to protected weightbearing (50% of body weight) over the next 3 weeks. Full weightbearing is allowed after 6 weeks.

Discussion

AMIC or "microfracture plus" techniques for cartilage repair are attractive options, as they are single-stage surgeries. There is evidence from radiological and histological studies to suggest superior tissue repair, as well as improved clinical outcomes compared with isolated microfracture.[9,10] Chondral lesions treated with the AMIC technique also have a nearly normal morphologic appearance.[11]

However, arthroscopic AMIC techniques can pose significant technical challenges, such as difficulty of placing the scaffold on irregular lesions and the need to be proficient at dry arthroscopy.[12,13] In this Technical Note we describe techniques to make this surgery more replicable. We have shared technical tips to help make these scaffolds more viscous and have also shown that injectable scaffolds can be applied to vertical and inverted surfaces.

CarGel is a chitosan-based scaffold that has been reported to prevent clot retraction, increase clot adhesivity, and maintain critical blood components within

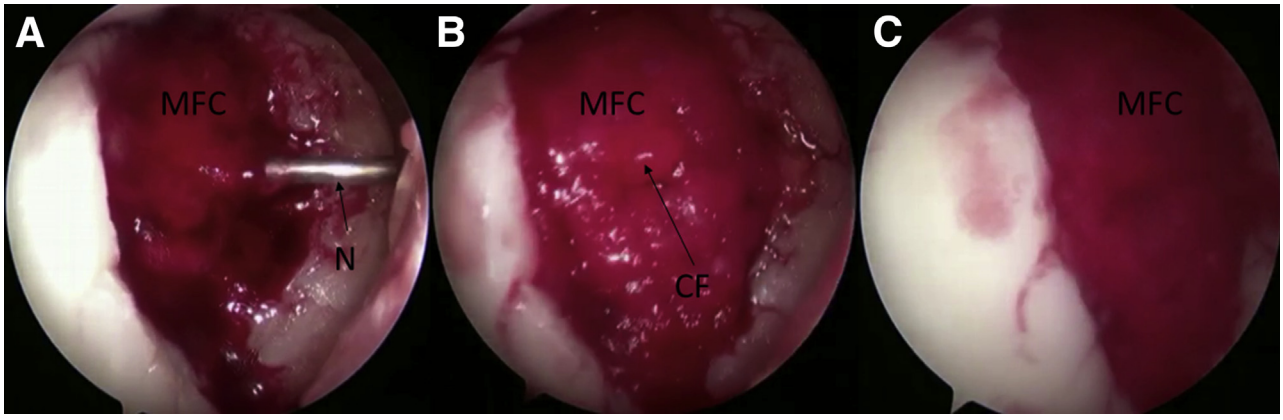

Fig 4. Arthroscopic image of the right knee from the AL portal. Full-thickness chondral defect measuring 2.5 by 1.5 cm in the superior part of the medial femoral condyle. (A) After preparation of the chondral defect, CartiFill seeded with BMAC is applied on dry arthroscopy. (B) The CartiFill scaffold has been applied fully on the defect and is left to set. (C) The scaffold remains stable on wet arthroscopy with fluid irrigation. Abbreviations: AL, anterolateral; CF, CartiFill scaffold; MFC, medial femoral condyle; N, needle.

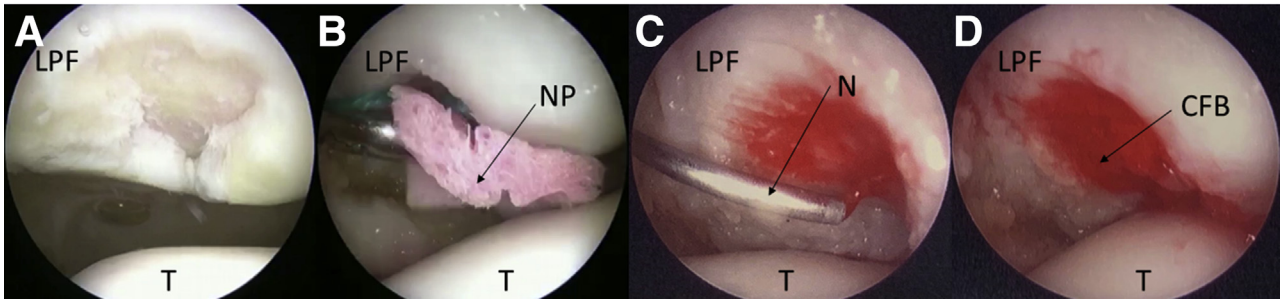

Fig 5. Arthroscopic image in a left knee from the AM viewing portal, showing the undersurface of the patella. There is a 1.5- by 1.2-cm lateral patella facet chondral defect. (A) The patella chondral defect is prepared with all loose cartilage flaps removed. (B) The defect is dried using neuropatties, working from the AL portal. (C) The CartiFill scaffold seeded with BMAC is applied onto the patella defect in an inverted position. (D) There is good stability as the gel scaffold BMAC fills the patella defect. It remains stable on knee range of motion. Abbreviations: AL, anterolateral; AM, anteromedial; CFB, CartiFill scaffold plus BMAC; LPF, lateral patella facet; N, needle; NP, neuropattie; T, trochlea.

cartilage defects to promote cartilage healing.[10] Animal studies comparing microfracture alone to microfracture with CarGel have reported significantly more lesion fill, less fibrous tissue, and superior histological assessment with regard to collagen type 2 content.[14] Shive et al.,[10] in a randomized controlled trial, compared microfracture alone to microfracture with CarGel augmentation. Magnetic resonance imaging analysis 5 years postintervention showed greater amounts of lesion fill and repair tissue T2 relaxation times that were closer to the native cartilage in the CarGel group. Clinical improvement, measured by higher Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores, was similar in both groups.[10]

CartiFill is a porcine-derived type 1 collagen scaffold developed to provide matrix stability and maintain the blood clot and bone marrow MSCs for improved healing at the repair site.[15] Kim et al.[15] conducted a randomized controlled trial comparing CartiFill with microfracture. Superior magnetic resonance observation of cartilage repair tissue (MOCART) scores were found in the CartiFill group, indicating better defect repair and filling, integration with the border zone, and effusion. The CartiFill group also had better visual analogue scale (VAS), Knee Injury and Osteoarthritis Outcome Score (KOOS) and International Knee Documentation Committee (IKDC) scores. These improvements were statistically significant at 12 and 24 months postintervention.[15] One important downside of CartiFill is that it is a porcine-derived, which can be a barrier to its use in populations with religious concerns about the use of porcine tissue.

An alternative to obtaining MSCs from microfracture is the use of BMAC to provide the pluripotent MSCs that are required for repair. This technique avoids the need to violate the subchondral plate and consequently does not result in mechanical changes to the underlying bone or bone overgrowth. Snow et al.[5] have shown that BMAC with CarGel scaffold (and without microfracture) provides an injectable gel scaffold that has macroscopic properties, clot contraction, and histological appearance similar to standard CarGel with whole blood. We share tips on using BMAC for injectable scaffold cartilage repair in Table 4.

Several authors have described techniques for the use of scaffold augmentation. Steinwachs et al.[13] described the use of CarGel scaffold augmentation of a microfracture procedure. The technique included the use of dry arthroscopy when applying the injectable gel scaffold becaue of to fears that the gel may be washed away by the irrigation fluid and recommended positioning the knee such that the lesion was in a horizontal position before application to avoid the gel scaffold dripping off the surface. In contrast, we demonstrate that

Table 3. Tips for use of injectable Scaffolds in cartilage Repair

1. Application onto a dry defect surface.
2. Vertical surface to allow gravity to drain the fluid.
3. Use small suction in the joint, which can be left in the medial or lateral gutter. Keep an arthroscopic trocar tap open to the air to prevent joint collapse.
4. Use a switching stick or probe as soft tissue retractor.
5. Use traction sutures to keep wet soft tissue from the lesion.
6. Use patties to dry the surface adequately.
7. Use a Mayo table to keep the knee at the desired flexion during application.
8. Keep the scaffold mixture warmed for optimum application and setting.
9. Use a MacDonald probe to aid in molding the scaffold on the defect surface.
10. Check the stability of the applied scaffold with range of motion of the knee.

Table 4. Tips on the use of BMAC With injectable Scaffold

1. Choose the BMAC kit that gives the highest concentration of cells.
2. Avoid the use of heparin to allow quick setting of the scaffold.
3. Perform immediate mixing of BMAC with scaffold after harvest and quick application onto the defect.

injectable gel scaffolds can be applied during dry arthroscopy in vertical or even inverted lesions, as long as the injectable gel scaffold is of the right viscosity when applied. The meticulous practice of keeping the scaffold warm allows us to achieve the viscosity for stable application onto vertical or inverted lesions.

Whyte et al.[12] described the use of Hyalofast (Anika Therapeutics, Abano Terme, Italy), a hyaluronic acid–based solid scaffold, and BMAC, without the use of microfracture. The Hyalofast solid scaffold was first cut to the appropriate size and seeded with BMAC externally, before being folded and delivered through the arthroscopic working portal and applied to the defect under dry arthroscopy; fibrin glue was recommended as an adjunct should more stability be required. Our technique allows us to treat larger and irregular shaped lesions without the need for fibrin glue.

The microfracture, injectable scaffold augmentation, and BMAC harvesting techniques discussed above are relatively safe procedures, but they do have potential limitations. When performing microfracture, excessive debridement of the calcified cartilage can result in excessive removal of subchondral bone. This may overstimulate subchondral bone growth, causing intralesional osteophytes and thinning of the overlying repair cartilage layer, with resultant adverse biologic and biomechanical implications. With injectable scaffold augmentation, there is the risk of an allergic reaction to the constituents of the scaffold material, although this occurrence is rare and difficult to anticipate. BMAC harvesting involves a separate incision at the iliac crest, which will lead to a separate scar, pain at the harvest site, possible iatrogenic nerve injury, and the risk of surgical site infection at the iliac crest.

Conclusion

Scaffold augmentation holds significant promise for improving the results of cartilage repair. Lesions traditionally considered hard to treat arthroscopically can now be addressed with an injectable scaffold arthroscopically. The addition of BMAC to these scaffolds as a source of pluripotent MSCs can avoid the potential downsides of microfracture.

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