ARTICULAR CARTILAGE LESIONS: PREVALENCE AND SOCIETAL IMPACT

Articular cartilage defects are common, with almost two-thirds of 31516 knee arthroscopies having cartilage lesions. However, of those, only 59% were in young patients under 40 years with grade IV defects which would be potential targets for cartilage restoration.1 Aetiologies of articular cartilage injury include repetitive microtrauma due to predisposing background factors such as malalignment, or damage to the cartilage in acute traumatic events. Osteochondral lesions in a young population are most commonly secondary to osteochondritis dissecans (OCD).2 The growth in incidence of knee articular cartilage injury in young patients has been implicated with increased participation in athletic activities. Frequently, cartilage injuries can occur with ligament injuries, such as anterior cruciate ligament tears.1 Over time, individuals can progress to degenerative joint disease due to the inability of the chondral defect to heal, leading to significantly reduced physical activity and substantial lifestyle modifications. It has been reported that focal cartilage defects impair quality of life in a similar fashion to severe osteoarthritis, causing long-term deficits in knee function.3 Articular cartilage restoration surgery has been shown to improve quality of life and be cost-effective.4

HISTORY OF ARTICULAR CARTILAGE RESTORATION

Hunter is historically given credit for first describing cartilage injury as ‘a troublesome thing and that when once destroyed it is not repaired’.5 This concept of cartilage not being able to heal was highlighted by Landells6 on necropsy 3–10 years from original injury in which no appreciable healing of the cartilage occurred. Pridie7 introduced the first technique of cartilage repair with subchondral drilling to treat osteoarthritis in 1959. In 1997, Steadman et al8 refined this technique into the modern microfracture marrow stimulation procedure. Hangody et al9 described autologous mosaicplasty with 5-year follow-up in 1997. The scientific work on the periosseum playing a critical role in bone growth and fracture repair led to the use of the cambium layer as a source of undifferentiated mesenchymal cells to assist with cartilage regeneration. The first case series of autologous chondrocyte transplant was published by Lars Peterson in 1994 (box 1).10

ARTICULAR CARTILAGE SURGICAL TREATMENT

The goal of cartilage restoration is to relieve present symptoms, as well as to demonstrate long-term durability and prevent or delay the need for future surgery. Unfortunately, biomechanical features of hyaline cartilage have been difficult to replicate with available surgical procedures resulting in fibrocartilage or hyaline-like cartilage formation.18-20 Still, techniques such as marrow stimulation or microfracture (MFX), osteochondral autograft transfer (OAT) or osteochondral allograft (OCA), synthetic cell-free scaffolds, and cell therapy options such as autologous chondrocyte implantation (ACI) have shown favourable results in clinical outcomes at short-term follow-up.18-20 However, few studies have compared long-term survivorship and functional outcomes of cartilage repair procedures due to insufficiency of patients, and variation in defect size, number and location. Therefore, it is difficult to state definitively which techniques are best in absolute terms; rather, we favour an individualised approach depending on the geographic availability of cartilage restoration techniques, the chondral lesion and patient characteristics, and economic considerations. In this review, we evaluate the current knowledge, practice, evidence, surgical techniques and patient management strategies for available cartilage restoration options. In addition, we discuss future strategies to manage articular cartilage injuries and improve the biological quality of the repair tissue to improve clinical outcomes.
In our opinion, the most fundamental aspect of treating articular cartilage defects is in recognition and understanding of the pathology leading to or associated with the defect. It is critical to determine if this is simply an acute injury, or a chronic lesion from abnormal contact pressures. In the femorotibial joint, assessing for ligament status, coronal alignment and meniscus status will determine if concomitant ligament reconstruction, osteotomy or restoration of meniscus function is necessary in addition to cartilage restoration. In the patellofemoral joint, the most commonly associated factors encountered with cartilage lesions include medial patellofemoral ligament (MPFL) insufficiency addressed with MPFL reconstruction, distal malalignment with tibial tubercle osteotomy, and tight lateral retinaculum with lateral retinacular lengthening. It is essential to recognise that any successful cartilage restoration procedure requires concomitant pathology correction.

Varus or valgus malalignment has been demonstrated to correlate strongly with medial and lateral cartilage overload and loss, respectively. In addition, unloading the compartment has a reduced risk of subsequent cartilage loss in that compartment. With cartilage procedures, there clearly has been demonstrated a positive effect of unloading a maligned knee with osteotomy in addition to performing the cartilage restoration technique. We consider osteotomy in any case where the affected compartment has five degrees or greater malalignment. The role of the meniscus in increasing the contact area and decreasing contact stresses in the medial and lateral femorotibial compartments has been well established. Certain types of meniscus tears can be similar to removal of the entire meniscus, such as a radial tear, or a root tear of the posterior horn. If significant meniscus deficiency is present, then meniscus allograft transplantation has been shown to normalise increased contact pressures.

Microfracture and augmentation
Microfracture has been studied as a treatment for articular cartilage injury for over a century and has distinct advantages and disadvantages as a treatment for cartilage lesions (box 2). One strategy to augment a microfracture is to utilise a scaffold. The first reported series of scaffold-augmented microfracture demonstrated good preliminary results. Of the five patients who were treated with a cell-free polymer-based matrix, three demonstrated adequate defect fill at 12 months, but subchondral cysts and osteophytes developed in a majority of the patients. A retrospective review of 40 patients treated with autologous matrix-induced chondrogenesis plus microfracture showed variable results, as magnetic resonance observation of cartilage repair tissue analysis at 12 months revealed inconsistent defect filling. A recent study by Siclari et al used a polyglycolic acid-hyaluronic bioabsorbable implant immersed in platelet-rich plasma along with drilling. Although the results are influenced by the combination of the scaffold, biomediators and the drilling technique, the patients showed improved Knee injury and Osteoarthritis Outcome Scores and hyaline-like cartilage restoration.

In 1997, Steadman et al described arthroscopic marrow stimulation, or modern microfracture. Hangody advanced the autologous osteochondral transfer technique to mosaicplasty to treat larger lesions with multiple smaller osteochondral cylinder plugs. Brittbeg and Peterson were the first to publish a case series of cell transplant with autologous chondrocyte implantation (ACI). Peterson et al and Minas et al report the first long-term results of ACI for large chondral defects. Gross et al and Bugbee report the long-term results of fresh osteochondral allograft for treatment of cartilage defects with similar results.

In a comparative trial of MFX and ACI, Saris reports superior results for ACI at 5 years. Saris et al also reported in a prospective randomised controlled trial (SUMMIT trial) that M-ACI was superior for treating defects greater than 3 cm² in size at 2 years compared to MFX.
microfracture compared to microfracture alone. A small pilot study evaluated a combination treatment utilising microfracture with a polyglycolic acid-byaluronan matrix augmented with autologous bone marrow concentrate. The results supported integration of marrow stem cells into the cartilaginous defect to produce adequate defect filling.

Current research supports the use of microfracture for specific indications. Small lesions (≤2–3 cm²) in younger, active patients and older, more sedentary patients may be treated with this technique. Additionally, larger lesions (≥2.5–3 cm²) in older, low-demand patients may benefit from microfracture. The optimal indication for microfracture is a small, full-thickness lesion in a young, high-demand patient with <12 months of symptoms. Beyond these specific indications, microfracture has shown inferior results compared to other cartilage restoration techniques. Multiple authors indicated worse outcomes when lesions were >2–4 cm². Patients over 35–43 years of age demonstrated worse results compared to younger patients when treated with microfracture. Additionally, a body mass index >25–30 kg/m² predicted worse outcomes at a minimum follow-up of 2 years. There are limited data on microfracture in the patellofemoral joint; however, available studies indicate either inconsistent results or a high failure rate.

Surgical technique
Mithoefer and Steadman have comprehensively described the technique of microfracture. The cartilage lesion must be identified and debrided to stable peripheral margins using a ring curette or arthroscopic shaver (figure 1A). The calcified cartilage layer, located between the deep cartilage and subchondral bone, is then carefully removed. Following removal of the calcified cartilage layer, micropenetration of the subchondral bone using commercially available pick instruments or drills creates microfracture holes. The holes are created homogeneously, starting at the periphery of the defect and then moving towards the centre. After microfracture, the inflow is turned off to confirm influx of blood and marrow products (figure 1B). The released blood and marrow elements are necessary for MSC stimulation and repair tissue formation. If the microfracture is to be augmented with the cartilage allograft extracellular matrix, the arthroscopic fluid must be turned off. The particles can be added to the defect base, and then fibrin glue can be added to stabilise the repair site. Alternatively, this can be done in an open fashion for difficult anatomic areas such as the patella (figure 1C).

Reported outcomes of microfracture are predominantly positive; however, there are patient-specific and injury-specific factors that can greatly influence outcome. Table 1 summarises the outcome for microfracture techniques reported in the literature.

Osteochondral autograft and allograft
OAT and OCA have the advantage of replacing injured cartilage, or a bone and cartilage defect, with mature hyaline cartilage and subchondral bone architecture (boxes 3 and 4). Tissue replacement, in contrast to cell therapy, allows an immediate restoration of the joint surface.

OCA is a reasonable option for the treatment of large osteochondral lesions of the femoral condyle, trochlea or patella in young patients and older, high-demand patients. Preoperatively, donor tissues must be matched on the basis of the geometry of the patient’s knee. Once a potential donor is identified, the allograft tissue undergoes a short period (typically 2 weeks) of microbiological testing. Transplant must be performed after testing is complete, but prior to chondrocyte demise. While chondrocytes have been shown to be viable for up to 42 days after harvest, it is recommended that implantation occurs 14 to 28 days following tissue procurement to ensure optimal cell viability. Given the limited window of chondrocyte viability, the logistics of this surgery are often challenging for both the patient and surgeon. Basic science research has demonstrated the viability of chondrocytes in fresh allograft implants at the time of transplant and in long-term follow-up. Long-term follow-up retrieval studies have shown survival of allograft chondrocytes at 23 years after implantation.

Surgical technique
OAT can be performed with a number of different approaches including formal arthrotomy, mini-open or arthroscopically assisted techniques. It should be noted that in our experience, mosaicplasty is best performed with a small open arthrotomy

Figure 1 (A) Arthroscopic photo demonstrating a 2 cm full-thickness cartilage lesion in the lateral femoral condyle following lesion preparation. (B) Following placement of microfracture holes spaced 3–4 mm apart to maintain integrity of subchondral bone plate and arthroscopy pump turned off to demonstrate egress of marrow elements. (C) Open microfracture augmentation with allograft cartilage extracellular matrix in a patellar lesion.
After identifying a donor site, the osteochondral lesion should be thoroughly debrided of all non-healthy tissue using curettes and shavers. Once the debridement is complete, accurate size measurement must be performed using a guide to determine the lesion diameter. This recipient site is then prepared to receive the donor grafts using one of the commercially available systems. Attention should then be directed towards the harvesting of donor plugs to determine the number and arrangement of plugs needed in order to completely fill the lesion. It is crucial that the donor plugs be harvested perpendicular to the articular surface to ensure that they are congruent with the recipient site articular surface. It should also be noted that when transferring multiple plugs, our preference is to harvest and implant each plug in succession. The plugs are placed into the defects gently using ‘thumb’ pressure only and achieving press fit stability.

The two methods in which OCA is performed are the osteoarticular shell method and the more common osteochondral dowel technique. When using the osteoarticular shell technique, a custom geometrically matched graft must be constructed to fit precisely into the footprint of the defect. This is a technically demanding procedure that requires additional fixation. On the contrary, the osteochondral dowel method utilises commercially produced instrumentation to achieve press-fit fixation of single or multiple grafts. The approach used in both of these techniques is generally a small medial or lateral parapatellar arthrotomy depending on the location of the lesion. A circular template is then utilised to define the size and geometric shape of the lesion. If the lesion is non-circular, a larger diameter dowel, multiple dowels or the shell technique may be required. This constrained geometry is a limitation of this technique as it may require removal of healthy surrounding cartilage in order to cover the lesion being treated.

The recipient site must be prepared by reaming the subchondral bone to a depth between 3 and 5 mm. Additionally, subchondral osteochondral dowel technique.

**Table 1** Outcomes of microfracture for articular cartilage lesions

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Mean age (years)</th>
<th>Mean size of lesion (cm²)</th>
<th>Mean follow-up (years)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bae et al&lt;sup&gt;31&lt;/sup&gt;</td>
<td>124</td>
<td>61.3</td>
<td>Femoral: 3.5</td>
<td>11.2</td>
<td>5 years survival: 88.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tibial: 2.3</td>
<td></td>
<td>10 years survival: 67.9%</td>
</tr>
<tr>
<td>Steadman et al&lt;sup&gt;38&lt;/sup&gt;</td>
<td>72</td>
<td>30.4</td>
<td>2.77</td>
<td>11.3</td>
<td>Lysholm: 59—89&lt;br&gt;Tegner: 3—6&lt;br&gt;Improved SF-36 and WOMAC</td>
</tr>
<tr>
<td>Gobbi et al&lt;sup&gt;42&lt;/sup&gt;</td>
<td>53</td>
<td>38</td>
<td>4.00</td>
<td>6</td>
<td>Lysholm: 56.8—87.2&lt;br&gt;Tegner (at 2 years): 3.2—6&lt;br&gt;Tegner (final follow-up): 6—5&lt;br&gt;Improved IKDC and subjective scores</td>
</tr>
<tr>
<td>Miller et al&lt;sup&gt;43&lt;/sup&gt;</td>
<td>81</td>
<td>49</td>
<td>2.29</td>
<td>2.6</td>
<td>Lysholm: 53.8—83.1&lt;br&gt;Tegner: 2.9—4.5</td>
</tr>
<tr>
<td>Mitrofeuer et al&lt;sup&gt;45&lt;/sup&gt;</td>
<td>48</td>
<td>41</td>
<td>4.82</td>
<td>3.5</td>
<td>Good or excellent: 67%&lt;br&gt;Improved ADL, IKDC and SF-36 scores</td>
</tr>
<tr>
<td>Mitrofeuer et al&lt;sup&gt;44&lt;/sup&gt;</td>
<td>32</td>
<td>38</td>
<td>4.92</td>
<td>3.4</td>
<td>Good or excellent: 66%&lt;br&gt;Improved ADL, Marx activity rating scale and Tegner scores Decline after improvement in 47%</td>
</tr>
<tr>
<td>Steadman et al&lt;sup&gt;46&lt;/sup&gt;</td>
<td>20</td>
<td>23</td>
<td>1.55</td>
<td>6.4</td>
<td>Mean return to competition 13.4 months&lt;br&gt;Tegner (post-op): 10&lt;br&gt;Lysholm(post-op): 86</td>
</tr>
<tr>
<td>Gobbi et al&lt;sup&gt;46&lt;/sup&gt;</td>
<td>67</td>
<td>31.4</td>
<td>4.01</td>
<td>Minimum: 2</td>
<td>Lysholm (2 years): 45.4—90.4&lt;br&gt;Lysholm (final f/u): 77.2&lt;br&gt;Tegner (2 years): 3—5&lt;br&gt;Tegner (final f/u): 4&lt;br&gt;IKDC scores declined after improvement</td>
</tr>
<tr>
<td>Mitrofeuer et al&lt;sup&gt;47&lt;/sup&gt; (Review of 28 studies)</td>
<td>3122</td>
<td>39</td>
<td>3</td>
<td>3.4</td>
<td>Short-term improvement (&lt;24 months): 75–100%&lt;br&gt;Long-term improvement (&gt;24 months): 67–86%</td>
</tr>
</tbody>
</table>

ADL, activity of daily living; f/u, follow-up; IKDC, International Knee Documentation Committee; post-op, postoperative; SF-36, Short Form 36.

**Box 3** Osteochondral autograft transfer advantages and disadvantages

- **Advantages**
  - Whole tissue transfer (bone and cartilage)
  - Single stage surgery
  - Hyaline cartilage
  - Inexpensive

- **Disadvantages**
  - Technically challenging
  - Small lesions
  - Donor site morbidity

**Box 4** Osteochondral allograft advantages and disadvantages

- **Advantages**
  - Whole tissue transfer (bone and cartilage)
  - Single stage surgery
  - Hyaline cartilage
  - Can treat large lesions

- **Disadvantages**
  - Limited graft availability
  - Possible infection risk
  - Possible immune reaction
  - Expensive

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cysts are filled with bone graft so that a stable base is achieved for transplant. Once the recipient site has been fully prepared, the depths of the superior, inferior, medial and lateral poles of the site should be measured. The size-matched osteochondral donor plug should be harvested from the same anatomic location on the corresponding allograft condyle. The graft is then placed in the defect by applying gentle uniform pressure across the articular surface. Dental picks can be used to guide the graft into the correct perpendicular position. Generally, stable fixation may be obtained utilising the press-fit technique. If the graft is unstable, however, metal or bioabsorbable compression screws should be used to supplement graft fixation.

Overall, the outcomes of OAT procedures have been promising in appropriately selected patients (table 2). Histological analysis has shown that the transferred hyaline cartilage has a high rate of survival of transferred chondrocytes with fibrocartilage ingrowth at the bony base and chondral matrix integration along the perimeter of the transplanted plug. The donor sites, however, tend to fill with fibrocartilage and approximately 3% of patients may develop symptoms of fibrocartilaginous prominence and overgrowth.56 Despite this drawback, good to excellent clinical outcomes have been achieved in approximately 92% of femoral condyle lesions.46 The results of this study have since been replicated in series published by Karataglis et al51 and Dozin et al.49 Karataglis et al51 found that 87% of patients demonstrated functional improvement after OAT while Dozin et al.49 found that 88% of patients with OCD lesions demonstrated significant improvement after mosaicplasty. Krych et al57 performed a study of 96 patients comparing outcomes of OAT to microfracture for articular cartilage defects. They demonstrated the OAT group to maintain a higher level of athletic activity when compared to the microfracture group.57 This outcome most likely suggests that patients who were treated with microfracture were modifying their activities to decrease symptoms in their knee.

**Table 2 Outcomes of osteochondral autograft transfer**

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Procedures</th>
<th>Number of knees</th>
<th>Mean defect size (cm²)</th>
<th>Defect location</th>
<th>Patient age (years)</th>
<th>Mean follow-up (years)</th>
<th>Results/conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gudas et al, 2005</td>
<td>OAT vs MF</td>
<td>57 (28 OAT vs 29 MF)</td>
<td>2.8±0.7 vs 2.8±0.7</td>
<td>OAT: 25 MFC, 3 LFC, 23 MFC, 6 LFC</td>
<td>24.3 (15–40)</td>
<td>3</td>
<td>96% good and excellent outcomes in OAT vs 52% for MF; OAT superior in young, active athletes &lt;40 years at 3 years follow-up</td>
</tr>
<tr>
<td>Dozin et al, 2005</td>
<td>OAT vs ACI</td>
<td>44 (22 in each group)</td>
<td>1.9±0.6</td>
<td>26 MFC, 5 LFC, 13 P</td>
<td>27.7</td>
<td>3</td>
<td>Complete recovery in 88% of the OAT group and 68% of the ACI group (p&lt;0.09)</td>
</tr>
<tr>
<td>Hangody et al, 2008</td>
<td>OAT</td>
<td>977</td>
<td>Not reported</td>
<td>798 MFC/LFC, 147 PF, 31 TG</td>
<td>Not reported</td>
<td>14</td>
<td>92% good/excellent results in femoral condyles, 87% for tibia, 74% for patellar and trochlear lesions</td>
</tr>
<tr>
<td>Karataglis et al, 2006</td>
<td>OAT</td>
<td>37</td>
<td>2.73 (0.8–12)</td>
<td>26 MFC/LFC, 11 PF</td>
<td>31.9 (18–48)</td>
<td>3</td>
<td>32 of 37 patients (86.5%) reported improvement of their preoperative symptoms</td>
</tr>
<tr>
<td>Marcacci et al, 2007</td>
<td>OAT</td>
<td>30</td>
<td>&lt;2.5</td>
<td>MFC/LFC</td>
<td>29.3</td>
<td>7</td>
<td>IKDC grade 1/2 77% good/excellent results; IKDC subjective score significantly improved from preoperative (34.8) to 7-year follow-up (71.8)</td>
</tr>
<tr>
<td>Gudas et al, 2009</td>
<td>OAT vs MF</td>
<td>47 (25 OAT vs 22 MF)</td>
<td>3.2±0.44 vs 3.17±0.38</td>
<td>OAT: 21 MFC, 5 LFC, 20 MFC, 2 LFC</td>
<td>23.5</td>
<td>10</td>
<td>IKDC grade 92% good/excellent in OAT vs 86% in MF, IKDC grade 1/2 100% in OAT vs 19% MF, 83% OAT vs 63% after MF maintained excellent or good results after 4.2 years</td>
</tr>
<tr>
<td>Lim et al, 2012</td>
<td>OAT vs ACI</td>
<td>70 (22 OAT vs 30 MFX vs 18 ACI)</td>
<td>2.77 vs 2.74 vs 2.84</td>
<td>OAT: 19 MFC, 3 LFC, 23 MFC, 7 LFC</td>
<td>28.5</td>
<td>5.7</td>
<td>IKDC grade 1/2 82% in OAT, 80% in ACI, and 80% in MFX, no difference in Tegner, Lysholm or HSS scores between interventions</td>
</tr>
<tr>
<td>Ulstein et al, 2014</td>
<td>OAT vs MF</td>
<td>25 (14 OAT vs 11 MF)</td>
<td>3 vs 2.6</td>
<td>OAT: 10 MFC, 2 LFC, 2 TG MFX: 10 MFC, 1 LFC</td>
<td>32.3</td>
<td>9.8 (median)</td>
<td>Change over time for Lysholm and KOOS scores was similar between the MF and OAT groups. No difference between isokinetic muscle strength</td>
</tr>
</tbody>
</table>

ACI, autologous chondrocyte implant; ADL, activity of daily living; HSS, Hospital of Special Surgery; ICRS, International Cartilage Repair Society; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; LFC, lateral femoral condyle; MFC, medial femoral condyle; MF, microfracture; OAT, osteochondral autograft transfer; P, patella; PF, patellofemoral; TG, trochlear groove; TP, tibial plateau.

For larger lesions in appropriately selected patients, OCA has shown relatively consistent results, especially when treating lesions of the femoral condyles (table 3). Five-year and 10-year survival rates of 95% and 85% were obtained for femoral condyle osteochondral defects treated with OCA. Williams et al. have demonstrated improved SF-36 scores and activity of daily living scales at a mean follow-up of 4 years in patients with isolated femoral condyle osteochondral defects who were treated with OCA. Additionally, they found MRI evidence of osseous graft integration in 78% of patients. A study published by Emmerson et al. showed that 72% of patients with a mean lesion area of 7.5 cm² achieved good to excellent results with only a 15% reoperation rate in a long-term follow-up (mean of 7.8 years) study.

There are now proprietary cryopreserved viable OCAs available (Cartiform, Osiris Therapeutics, Inc.). This allograft is currently available in a 2 cm² size to treat smaller lesions. The main advantage is that the cells remain viable, up to 70%, at 2 years. This can facilitate surgical planning and elective scheduling, rather than waiting for a fresh stored graft in the traditional manner. Currently, there are no clinical data for review, but several hundred cases have been performed in the USA (figure 2D). Additional strategies may evaluate methods to improve incorporation into the host bone, such as augmentation with bone marrow aspirate concentrate (BMAC) or PRP. Some efforts are being made to utilise living donor transplants as structural grafts, which may significantly increase graft availability across the world where currently living grafts are not available.

**Synthetic cell-free scaffold**

Biomaterial scaffolds have been proposed to support the articular cartilage and subchondral bone structure. The advantages of this approach to cartilage restoration is that there is no donor site morbidity, it allows for a single-stage off the shelf procedure, it would be relatively low cost, have no potential immune response, and can re-establish the cartilage-subchondral bone structure. These materials also allow progenitor cells to seed the defect, enhance the production of cartilaginous matrix, and may support differentiation of progenitor cells to hyaline-producing chondrocytes. Additionally, these materials are typically degradable and provide temporary protection to the repair site as well as subchondral bone. The majority of these scaffolds have been developed as biphasic implants to restore the zonal restoration of cartilage and to regenerate the subchondral bone.

A variety of materials continues to be studied, and many commercial products are available. This concept has been applied to the design of several degradable biphasic scaffolds. The TruFit OBI plug (Smith & Nephew Endoscopy, USA) is a synthetic scaffold with 3 mm of polylactide-co-glycolide to simulate the matrix of articular cartilage and a calcium sulfate trabecular network similar to cancellous bone. The scaffold bilayer undergoes staged resorption with the calcium sulfate phase resorbing over the first several months and the remaining polymer over a period of 1–3 years. This controlled resorption facilitates bone and soft tissue remodelling and allows subchondral bone replacement in the bony phase and fibrocartilage tissue at the surface. The main clinical drawback of this technique is the delayed biological incorporation of the plug, associated with reported failures in which patients have reported persistent symptoms and joint effusion at 6 months. The symptoms of persistent bony oedema may be quite severe, necessitating removal of the plug with relief of symptoms in several cases. As a result, this scaffold has been removed from clinical use in the USA and Europe.

Clinical outcomes of cell-free scaffolds for cartilage repair have been encouraging (table 4). The MaioRegen scaffold (FinCeramica Faenza, Italy) is a multilayered biomaterial consisting of collagen type I and magnesium-hydroxyapatite. It had reported good preclinical results in an animal model, and therefore clinical trials were conducted. A larger clinical trial was conducted in humans consisting of 49 patients who were treated for large osteochondral lesions and followed for 2 years. Clinical outcomes were overall good and MRI findings in 30 patients demonstrated that 70% had complete filling of the lesion. A mid-term trial from a different centre including 27 patients treated for chondral or osteochondral lesions confirmed these results and demonstrated good potential at 5-year follow-up. However, a recent study of six knees demonstrated incomplete regeneration of the cartilage and poor subchondral bone repair, with the authors urging caution for future use. Clearly, further studies are needed, perhaps in a comparative study design.

**Cell-based treatment strategies**

While cell-based treatments previously applied almost exclusively to ACI, today there are many more options available.

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**Table 3 Results of osteochondral allograft transplant**

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Type of osteochondral allograft</th>
<th>Number of knees</th>
<th>Mean defect size (cm²)</th>
<th>Defect location</th>
<th>Patient age (years)</th>
<th>Mean follow-up (years)</th>
<th>Results/conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross et al., 2005</td>
<td>Fresh</td>
<td>125</td>
<td>&gt;3</td>
<td>60 MFC/LFC, 65 TP</td>
<td>27</td>
<td>10</td>
<td>Femoral condyles: KM survivorship 95% at 5 years, 85% at 10 years; tibia KM survivorship 95% at 5 years, 80% at 10 years</td>
</tr>
<tr>
<td>Williams et al., 2007</td>
<td>Fresh</td>
<td>19</td>
<td>6</td>
<td>14 MFC, 5 LFC</td>
<td>34</td>
<td>4</td>
<td>Significant improvement in ADLs, SF-36 scores; MRI osseous trabecular incorporation in 78%, correlated with SF-36 scores</td>
</tr>
<tr>
<td>Emmerson et al., 2007</td>
<td>Fresh</td>
<td>66</td>
<td>7.5</td>
<td>41 MFC, 25 LFC</td>
<td>28.6 (15–54)</td>
<td>7.7</td>
<td>72% good/excellent results, 15% reoperation, subjective improvement 3.4–8.4</td>
</tr>
<tr>
<td>McCulloch et al., 2007</td>
<td>Prolonged fresh (avg. 24 days)</td>
<td>25</td>
<td>&gt;2</td>
<td>17 MFC, 7 LFC, 1 MFC and LFC</td>
<td>35</td>
<td>3</td>
<td>84% patient satisfaction; 88% radiographic incorporation; significant improvements in Lysholm, IKDC, ADLs, SF-12</td>
</tr>
<tr>
<td>Levy et al., 2013</td>
<td>Fresh</td>
<td>129</td>
<td>8.1</td>
<td>77 MFC, 45 LFC, 7 both</td>
<td>33</td>
<td>13.5</td>
<td>Survivorship 66% at 20 years; age &gt;30 risk factor for failure</td>
</tr>
<tr>
<td>Raz et al., 2014</td>
<td>Fresh</td>
<td>63</td>
<td>&gt;3 cm in diameter</td>
<td>29 LFC, 29 MFC</td>
<td>28</td>
<td>21.8</td>
<td>Survivorship 69% at 20 years; patients with surviving grafts had good function</td>
</tr>
</tbody>
</table>

ADL, activity of daily living; IKDC, International Knee Documentation Committee; KM, Kaplan-Meier; LFC, lateral femoral condyle; MFC, medial femoral condyle; SF-12/36, Short Form-12/36; TP, tibial plateau.
They can be characterised as one-stage or two-stage procedures, with utilisation of autograft or allograft chondrocytes or stem cells. ACI was originally described by Peterson and colleagues, as reported in 1994.10 This technique using periosteum covering (P-ACI) has provided good long-term results as reported by Peterson et al.71 Complications of ACI include symptomatic hypertrophy, delamination and graft failure.72 Hypertrophy of the graft is the most common complication with an incidence of 15–36%.72 In an attempt to decrease this complication as well as donor site morbidity, second-generation and third-generation techniques have been developed. Collagen-covered ACI (C-ACI) replaces the periosteal flap with a porcine collagen membrane as a graft covering. Clinical success with this technique demonstrates that the periosteal covering is not essential for cartilage regeneration and can significantly reduce the incidence of subsequent surgeries due to graft hypertrophy.73 Matrix-induced ACI (M-ACI) is a third-generation technique that was developed to utilise tissue engineering to provide a scaffold and even cell distribution in the final graft. In this technique, cultured cells are seeded onto a collagen membrane matrix in the laboratory.74 In contrast, both P-ACI and M-ACI require the chondrocyte suspension to be injected under a membrane at the time of surgery, which can cause uneven distribution in the lesion due to the effects of gravity.72 M-ACI is technically attractive because it is a simplified surgical procedure that can be performed with a limited open approach or even arthroscopically, thereby avoiding the morbidity and delayed rehabilitation associated with an arthrotomy. In a prospective randomised study, Bartlett et al.75 concluded that the clinical, arthroscopic and histological outcomes are comparable for both C-ACI and M-ACI. Similarly, a second randomised clinical trial demonstrated similar outcomes between P-ACI and M-ACI at 2-year follow-up.76 A recent RCT of M-ACI versus MFX demonstrated superior results in the M-ACI-treated patients in lesions over 3 cm².77

The ideal candidate for this procedure is a youthful, healthy patient with a symptomatic, unipolar, full-thickness cartilage defect in an otherwise normal knee. A contraindication to ACI would include concomitant bone loss of greater than 6–8 mm, such as an unstable OCD lesion that has failed fixation. In this scenario, a bone graft or sandwich technique would be indicated. A 2009 study by Minas et al.77 suggested that ACI following failed marrow-stimulation procedures may have a failure rate three times that of non-treated defects due to violation of the subchondral bone. This work suggests that marrow-stimulation techniques be used judiciously for larger cartilage defects that may require ACI as a future treatment.77 In cases where ACI is performed for failed microfracture, the intrarticular osteophytes must be removed.77

### Surgical technique
ACI is a two-stage procedure.10 The first stage allows for thorough arthroscopic evaluation of the knee to determine the appropriateness of this cartilage restoration technique, as well as to assess the lesion for size and depth. Cartilage biopsies are then taken from the lateral trochlea or intercondylar notch (minimal-weightbearing areas), from which the chondrocytes are cultured. After an interval of 6 weeks, the second stage consists of implantation of the chondrocytes. This typically involves an open arthrotomy, subluxation of the patella, and thorough debridement of the defect down to the underlying calcified layer. Since 2007, we have used a synthetic type I/III collagen patch for ACI cases in place of the periosteum and have not had difficulty with hypertrophy, as with the periosteum.73 It is important to note that this is also an off-label, surgeon directed use in the USA and must be discussed with the patient during the informed consent process. The defect is measured and templated with sterile tracing paper, placed over the synthetic membrane, and cut to size. We have found that removing 1–2 mm circumferentially to the collagen membrane helps to accommodate for the inevitable swelling and expansion that the patch undergoes once the cells are added. While the membrane and cells are prepared, a thin layer of fibrin glue is applied to the

![Figure 3 Injection of autologous cells under collagen membrane in patellar cartilage defect (collagen-covered autologous chondrocyte implantation).](image-url)
bed of the defect and direct pressure is maintained in order to obtain haemostasis. The collagen membrane is then sutured to the adjacent articular margin with a 6–0 Vicryl on a cutting needle immersed in sterile glycerin or mineral oil to allow suture passage easily through the patch and articular surface (note: there should be no overlapping). A small opening is maintained to inject the cells with an angiocath and a single cutting needle immersed in sterile glycerin or mineral oil to provide haemostasis. The collagen membrane is then sutured to the defect size (cm²) and direct pressure is maintained in order to obtain a water-tight seal (figure 3).

Early results of ACI were promising, with 84–90% excellent and good outcomes at 3 years for lesions treated on the femoral condyles. In one long-term study, Peterson et al. reported good or excellent clinical results in 50 of 61 patients after 2 years, which persisted in all 50 patients 5–11 years later. This suggests that if patients have a good early result, this should be maintained with good durability over time. There have been several randomised controlled trials comparing ACI with other cartilage reparative and restorative procedures (table 5).

Gradually, since background factors have been increasingly recognised and appropriately treated, ACI has become a reliable treatment option for patellofemoral cartilage lesions. Recently, Gillogly et al. demonstrated good to excellent results in 83% of cases with ACI of the patella after a mean follow-up of 7.6 years. Mandelbaum et al. reported that ACI of isolated trochlear lesions has both functional and symptomatic benefits. The theoretical benefit of ACI over microfracture is the amount and percentage of hyaline cartilage present in lesions treated with ACI. Two years following ACI, Peterson et al. found 80% hyaline cartilage after biopsy. It is important to note that ACI is not Food and Drug Administration (FDA) approved currently in the USA for treatment of patellar lesions, or for treatment of bipolar patellofemoral lesions, despite its excellent clinical benefits.

### Table 5 Results of ACI

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Type of ACI</th>
<th>Number of knees</th>
<th>Mean defect size (cm²)</th>
<th>Defect location</th>
<th>Patient age (years)</th>
<th>Mean follow-up (years)</th>
<th>Results/conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gooding et al., 2006</td>
<td>ACI-P vs ACI-C</td>
<td>68 (33 ACI-P, 35 ACI-C)</td>
<td>4.54</td>
<td>26 MFC, 11 LFC, 4 trochlea, 27 patella</td>
<td>30.5</td>
<td>2</td>
<td>Good/excellent 75% ACI-C vs 67% ACI-P (not significant), 36% ACI-P maintained with good durability over time. There have been no complications reported.</td>
</tr>
<tr>
<td>Knutsen et al., 2004</td>
<td>ACI-P vs MF</td>
<td>80 (40 MF, 40ACI-P)</td>
<td>4.5 MF, 5.1 ACI-P</td>
<td>71 MFC, 29 LFC</td>
<td>MF: 31.1 ACI-P: 33.3</td>
<td>2</td>
<td>SF-36 functional component score: MF superior to ACI-P at 2 years with preop score difference taken into account (p=0.01). No difference in Lysholm or VAS pain score at 2 years. Younger patients (≤30 years) did better (p=0.007) and more active patients (preop Tegner &gt;4) did better (p=0.0005)</td>
</tr>
<tr>
<td>Kon et al., 2009</td>
<td>ACI-C vs MF</td>
<td>80 (40 MF, 40 ACI-C)</td>
<td>2.5 MF, 2.2 ACI-C</td>
<td>MF: 28 MFC, 10 LFC, 2 trochlea ACI-C: 26 MFC, 12 LFC, 2 trochlea</td>
<td>29.8 (MF: 30.6 ACI-C: 29.0)</td>
<td>5 (min)</td>
<td>ACI-C was superior compared to MF for improvement in IKDC objective (MF 2.5–75% normal/near normal, OAT 15—90% normal/near normal; p&lt;0.001) and subjective scores (MF 41.1–70.2, OAT 40.5–80.2; p=0.003) at 5 years</td>
</tr>
<tr>
<td>Lim et al., 2012</td>
<td>OAT vs MF vs ACI</td>
<td>70 (22 OAT vs 30 MF vs 18 ACI)</td>
<td>2.77 vs 2.74 vs 2.84</td>
<td>OAT: 19 MFC, 3 LFC MF: 23 MFC, 7 LFC ACI: 13 MFC, 5 LFC</td>
<td>28.5</td>
<td>5.7</td>
<td>ICRS grade 1/2 82% in OAT, 80% in ACI, and 80% in MF; no difference in Tegner, Lysholm or HSS scores between interventions at any time points</td>
</tr>
<tr>
<td>Minas et al., 2014</td>
<td>ACI</td>
<td>210</td>
<td>118 (118 MF, 57 CCI) 2.4 MF, 2.6 CCI</td>
<td>All MFC/LFC</td>
<td>33.9 (same mean age in each group)</td>
<td>3</td>
<td>Improvement in over KiOS score was greater in CCI at 36 months (21.25 CCI vs 15.83 MF; p=0.048). More responded to treatment in CCI (83% CCI vs 62% MF). Superiority of CCI over MF increased with increased duration of symptoms (&gt;3 years, CCI 25.8 vs 14.7; p=0.03)</td>
</tr>
<tr>
<td>Niemeyer et al., 2010</td>
<td>ACI-C (matched by age)</td>
<td>74 (37 in each group)</td>
<td>Not reported, but matched</td>
<td>Each group: 12 MFC, 2 LFC, 15 patella, 8 trochlea</td>
<td>Group 1: 47.8 Group 2: 31</td>
<td>2</td>
<td>Better clinical outcome in younger patients (IKDC at 24 months: group 1: 72.2; group 2: 76.1; p=0.26; Cincinnati at 24 months: group 1: 82.7; group 2: 76.8; p=0.09)</td>
</tr>
<tr>
<td>Saris et al., 2009</td>
<td>CCI vs MF</td>
<td>118 (61 MF, 57 CCI)</td>
<td>2.4 MF, 2.6 CCI</td>
<td>All MFC/LFC</td>
<td>33.9 (same mean age in each group)</td>
<td>3</td>
<td>Improvement in over KiOS score was greater in CCI at 36 months (21.25 CCI vs 15.83 MF; p=0.048). More responded to treatment in CCI (83% CCI vs 62% MF). Superiority of CCI over MF increased with increased duration of symptoms (&gt;3 years, CCI 25.8 vs 14.7; p=0.03)</td>
</tr>
<tr>
<td>Zefafang et al., 2010</td>
<td>ACI-P vs MACI</td>
<td>21 (10 ACI-P, 11 MACI)</td>
<td>4.1 ACI-P, 4.3 MACI</td>
<td>85.7% MFC</td>
<td>ACI-P: 29.1 MACI: 29.5</td>
<td>2</td>
<td>At 24 months, change in scores ACI-P vs MACI: Tegner 1.7 to 6.6 (p=0.104), IKDC 25.2 vs 19.0 (p=0.499), Lysholm 22.7 vs 1.2 (p=0.048). Only Lysholm showed significant difference with ACI-P being superior to MACI</td>
</tr>
</tbody>
</table>

ACI, autologous chondrocyte implant; CCI, characterised chondrocyte implantation; HSS, Hospital of Special Surgery; HTO, high tibial osteotomy; ICRS, International Cartilage Repair Society; IKDC, International Knee Documentation Committee; KODOS, Knee Injury and Osteoarthritis Outcome Score; KSS, Knee Society Score; LFC, lateral femoral condyle; MACI, matrix-associated autologous chondrocyte implantation; MF, microfracture; MFC, medial femoral condyle; MFX, microfracture; OAT, osteochondral autograft transfer; preop, preoperative; SF-36, Short Form (36) Health Survey; VAS, visual analogue scale.
results in a recent multicentre trial. In comparison to MFX, Saris et al. found characterised chondrocyte implantation to result in better structural repair at 12–18 months, better clinical results at 3 years and reported that at 5 years patients treated early for their symptoms with characterised chondrocyte implantation obtained superior clinical results to MFX. Saris also reported in a prospective RCT (SUMMIT trial) that M-ACI was superior for treating defects greater than 3 cm² in size at 2 years compared to MFX.

Recently, a phase III trial is currently underway in the USA for NeoCart (Histogenics). This strategy transitions from implanting cells to the implantation of neocartilaginous tissue. It utilises a tissue engineered implant that combines a bovine type I collagen matrix scaffold with autogenous chondrocytes and bioreactor treatment to promote the chondrocyte phenotype. Phase I and II results have been promising, with superior outcomes compared to MFX in RCT at 2-year follow-up. An advantage of this procedure technically is that the implant can be fixed to the defect using fibrin glue rather than suturing, which allows surgery to be performed through a smaller exposure and saves operative time (figure 4A–C). Novocart 3D is another MACI technology that has demonstrated good results at short-term follow-up (Aesculap Biologics, LLC, Center Valley, PA, USA). Similar to NeoCart, this scaffold can also be glued into the cartilage defect.

One-stage cell-based procedures

The use of particulated juvenile allograft cartilage (PJAC) for chondral defects is an evolving treatment consideration. The most commonly used product currently consists of allograft articular cartilage from donors aged <13 years (DeNovo NT Natural Tissue Graft, Zimmer Inc). PJAC transplantation for the treatment of full-thickness cartilage defects is performed in a manner very similar to ACI. Lesion preparation is completed with removal of damaged cartilage, creation of stable vertical walls, and removal of the calcified cartilage layer, limiting any bleeding of the subchondral bone, and then application of fibrin glue to secure the cartilage cubes into the defect. When the defect is uncontained, a collagen membrane cover can be used to enclose the allograft (figure 5). A large advantage to this technique is single-stage surgery. A limitation to the use of PJAC is the lack of published outcome data. The few studies that do exist regarding their use have demonstrated promising results. Tompkins et al. reviewed 13 patients in whom PJAC was used for patellar cartilage defects averaging 2.4±1.2 cm². At an average of 33 months of follow-up, they found good clinical results overall with excellent defect filling on repeat MRI. In a recent case series published by Farr et al., the authors reported similar results with good clinical outcomes.

Another promising single-stage treatment option is a cell-based cartilage regeneration technique reported by Saris and colleagues. With this procedure, the authors prepare the cartilage defect in the standard fashion. The cartilage is then partially digested to its building blocks of chondrons, or cartilage cells in their surrounding matrix. These are then combined with a very specific ratio of allogeneic MSCs. Clinical trials are currently underway.

GEOGRAPHICAL DIFFERENCES

There are significant differences in what options are available to surgeons depending on their geographic location. For example, fresh-stored OCAs are only available in the USA and parts of Australia. The absence of fresh osteochondral or composite grafts means that other options have to be employed for bone and cartilage lesions. For example, to treat an OCD lesion with bone loss, a sandwich technique can be utilised where an autograft is used to restore the bone loss and then a cartilage treatment, such as ACI, can be used to restore the articular cartilage phase. In Europe, the MaioRegen scaffold is available to treat this problem. Regulatory bodies and biological availability are continually changing in each country and each region of the

Table 6 Validated outcome measures and classifications

<table>
<thead>
<tr>
<th>Outcome measures</th>
<th>KOOS</th>
<th>SF-36*</th>
<th>IKDC Subjective Assessment Test</th>
<th>Marx Activity Rating Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICRS Classification System</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cartilage Defects</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1 (nearly normal)</td>
<td>(A)</td>
<td></td>
<td>(A) soft indentation</td>
<td></td>
</tr>
<tr>
<td>Grade 2 (abnormal)</td>
<td>(B)</td>
<td></td>
<td>(B) superficial fissures and cracks</td>
<td></td>
</tr>
<tr>
<td>Grade 3 (severely abnormal)</td>
<td>(C)</td>
<td></td>
<td>(C) cartilage defects extending down &gt;50% of cartilage depth</td>
<td></td>
</tr>
<tr>
<td>Grade 4 (severely abnormal)</td>
<td>(D)</td>
<td></td>
<td>(D) penetration of subchondral bone but not across entire diameter of defect</td>
<td></td>
</tr>
</tbody>
</table>


Figure 4 (A) Arthroscopic view of a cartilage defect of the lateral femoral condyle. (B) Open arthrotomy demonstrating placement of Novocart (Histogenics) implant placed into defect with fibrin membrane to contain defect.

Figure 5 Juvenile particulated chondral allograft (deNovo, Zimmer) placed into uncontained patellar cartilage lesion with collagen membrane to contain defect.
world. Therefore, it is important for the cartilage surgeon to have several options available when treating specific lesions in the knee.

**FUTURE DIRECTIONS**

Stem cell treatment has enormous potential for cartilage repair. Bone marrow-derived (BMSC), adipose-derived (ASC) and synovial membrane-derived stem cells (SMSC) possess the ability to produce hyaline cartilage. Adipose tissue is easily obtained from the infrapatellar fat pad, but its differentiation is more laborious than BMSC. Although both show promise, BMSC may be superior to ASC at forming hyaline cartilage. In a rabbit model, SMSC (when embedded with PRP) exhibited the ability to promote hyaline cartilage synthesis.92 Clinical trials utilising stem cells have shown encouraging results. An RCT using peripheral blood stem cells to hyaluronic acid showed superior MRI and International Cartilage Repair Society (ICRS) scores (table 6).35

A one-stage procedure combining a favourable scaffold with autogenous BMAC could be an effective alternative to the two-stage MACI process. In this technique described by Gobbi et al.,93 a one-stage approach is taken by utilising a Hyaff 11 scaffold (Hyalofast scaffold, Anika Therapeutics Srl), which is a derivative of hyaluronic acid. This is loaded with BMAC (BMAC Harvest Smart PreP2 System, Harvest Technologies) harvested from the ipsilateral iliac crest at the time of surgery (figure 6). The BMAC is activated with the use of Baxtroxobin enzyme (Patelex Act, Plateltex SRO, Slovakia) to create a sticky clot. The stabilised clot is then placed into the full-thickness cartilage defect that has been previously prepared with stable vertical walls and intact subchondral bone. It is covered with a cut-to-size Hyaff 11 scaffold that is fixed with suture and sealed with fibrin glue. In a 2-year follow-up, this has compared favourably with the MACI technique in clinical outcomes, MRI follow-up and second look arthroscopy with histological hyaline-like features.93 This stabilised clot technique has also demonstrated good results with a collagen type VIII membrane at a minimum of a 3-year follow-up in large lesions with an average size of 8 cm².94 This has also been used for very large lesions, up to 20 cm², so-called biological arthroplasty.95

Another option of the one-step approach may be the use of a scaffold-free cell delivery system utilising MSCs from the synovium. This concept was first demonstrated by Nakamura and colleagues in 2007 when they cultured porcine synovial MSCs to develop a tissue-engineered construct (TEC) that was implanted into cartilage defects. The repair tissue was chondrogenic-like, and exhibited good histological and biomechanical characteristics.96 That group further suggested the feasibility of an allogeneic MSC-based cartilage repair model in a porcine study of immature and mature pigs in which they demonstrated equivalent repair tissue, regardless of donor age.97 In addition, this scaffold-free TEC, composed synovial MSCs, attached firmly to the surface of the cartilage defect, thereby maintaining the integrity of the subchondral plate and allowing for a suture-free construct. The encouraging preclinical work led to the ‘first-in-men’ clinical trial that began in 2013 and was completed in 2015 with results pending.98 In this trial, isolated chondral lesions <5 cm² are treated in a two-stage process. First, 1 g of the synovial membrane is harvested from the knee joint, grown in culture for expansion of MSCs, and implanted by arthroscopy or open arthrotomy 3–5 weeks later. The joint is immobilised for 2 weeks, partial weight-bearing for 6–8 weeks, and return to full activity at 12 months.98

To summarise, the field of articular cartilage restoration is rapidly evolving. While we have learnt that pathological background factors such as malalignment, meniscus deficiency or ligament laxity have to be addressed in order to provide an optimal environment for cartilage repair, we are still optimising other aspects of cartilage repair. Future work may allow testing of the inflammatory and degradatory environment of a joint in order to better estimate survival and success of cartilage repair based on biological or imaging biomarkers. Additional questions remain about return to high demand activity and a durable joint surface restoration that can match normal articular hyaline cartilage and subchondral bone in the active patient population. Existing cartilage treatment options have advantages and disadvantages, allowing for an individualised approach based on the patient’s goals and surgeon’s preferences. There is a need to improve available options, with an ideal single-stage, minimally invasive, durable and cost-effective approach yet to be defined.

**Key messages**

- Identify and address malalignment, meniscus deficiency or ligament laxity to provide an optimal environment for cartilage restoration.
- Many cartilage repair and restoration options are available, with advantages and disadvantages for each surgical technique.
- An individualized approach based on the lesion characteristics, patient’s goals, and surgeon preferences should be made.
- The future single stage, minimally invasive, durable and cost-effective cartilage procedure has yet to be defined.

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