(iv) Articular cartilage surgery in the knee

Oliver S Schindler

Abstract

Although articular cartilage has extraordinary mechanical properties, able to maintain almost frictionless motion over a lifetime, it is vulnerable to traumatic injury and subsequent degeneration. Poor vascularity and inability to access undifferentiated cell populations that would facilitate a response to injury, are responsible for articular cartilage’s limited ability to self-repair. The creation of cartilage repair tissue hence relies on the implantation or neosynthesis of cartilage matrix elements. This goal is achievable through a variety of repair techniques including marrow stimulation, the use of autologous or synthetic structural grafts or chondrocyte implantation. Although there are substantial differences in the complexity and technical application of each method, they are all united in the endeavour to restore joint function and prevent joint degeneration. The surgeon attempting to treat cartilage defects is required to possess not only a basic understanding of the physiology of cartilage growth, healing and repair, but also of biomechanics and kinematics of the knee, in order to appreciate the forces acting on the joint surfaces. Clinical success or failure will depend on appropriate patient selection, accurate clinical assessment, definition of the root cause and application of the right choice of treatment modality. Any therapy plan must include subsequent treatment options, which may become necessary should the first-line management fail to ameliorate symptoms.

Keywords ACI; AMIC; autologous chondrocyte implantation; cartilage; MACI; marrow stimulation; Microfracture osteoarticular autograft; repair techniques; TruFit plug

Introduction

The number of young adults suffering cartilage damage through injuries continues to grow, with estimated figures in the UK reaching 10,000 per annum. Although most of these injuries may be suitable for repair, the condition often remains undiagnosed and hence the opportunity for early treatment lost. While the natural history of localized cartilage lesions is not predictable, clinical experience suggests that, if left untreated, these defects are unlikely to heal and may progress to symptomatic degeneration of the joint.1

Not too long ago the fate of most patients with full thickness cartilage lesions was to live and suffer with the symptoms and dysfunction. The past two decades have seen orthopaedic knee surgery becoming more and more involved in seeking solutions to many new and increasingly difficult problems, with cartilage repair and regeneration technologies occupying a centre stage. Although our knowledge base of the molecular and cell biology of cartilage remains limited, a virtual explosion of information relating to the aetiology, natural history and surgical treatment of articular cartilage damage has descended on us in recent years. We may still be a long way away from the regeneration of hyaline cartilage and recreation of joint homeostasis but we are now in a position to offer remedial measures of cartilage repair to usher the restoration of joint function and prevention of joint degeneration.

Principles of cartilage function

Articular cartilage provides a bearing surface of unequalled low friction, but compared with parenchymal tissues it is a relatively primitive tissue deprived of blood vessels, lymph ducts and nerves. Although its composition, structure and performance are surprisingly complex, its relative metabolic inactivity and lack of blood supply permit only a very limited response to injury.2,3

The articulating surfaces are able to adapt to the changing surface contours, owing to the viscoelastic properties of cartilage. This allows for its deformation under load and subsequent increase in pressure transmitting area, thus minimizing peak stresses on subchondral bone. Peak stresses of up to 20 times body weight can be tolerated without causing lasting damage, as they are applied for only very short periods of time, whilst long-term application of such loads would invariably lead to cartilage break down.4 Perhaps most impressive, however, is its remarkable durability, which can survive a lifetime of use as long as joint homeostasis is maintained.5

Articular cartilage is primarily composed of extracellular matrix and tissue fluid with a sparse population of cells known as chondrocytes. All components are structurally arranged in a specific pattern, which can be divided into four distinct zones characterized by differences in composition and cell activity. Water contributes up to 80% of the volume of articular cartilage whilst chondrocytes merely contribute 1%. The structural macromolecules of the extracellular matrix consist of collagen, proteoglycans and non-collagenous protein, making up the remaining 20%. Much has been said about the importance of the collagen component of articular cartilage. Over 90% of collagen in hyaline cartilage is of type II, providing a fibrillar meshwork that gives cartilage its tensile strength and form.6 In contrast, type I collagen, commonly found in fibrocartilage, meniscus and tendons, possesses larger fibrils less able to provide a suitable scaffold for a highly hydrated matrix. Because of their ability to interact with tissue fluid, proteoglycans help to give cartilage its stiffness to compression and resilience. Proteoglycans release fluid under compression and rehydrate and expand when pressure is released. Within the matrix they are only partially hydrated, and exert a constant pressure to expand, restrained only by the collagen fibril meshwork. If this meshwork is disrupted through injury the matrix swells as proteoglycans expand, increasing the concentration of water and reducing the concentration of proteoglycans. Cartilage affected in this way will be weakened and vulnerable, not only on the surface but throughout its entire structure. If the initial insult was severe or repetitive injuries occur, cartilage may be unable to respond and a process of degradation may be initiated.8

The material properties of articular cartilage, such as stiffness, resilience and distribution of loads, are dependent on the extracellular matrix and the interaction between water and matrix molecules, whilst the existence and maintenance of the matrix
are dependent on chondrocytes. In 1860, Rudolph Virchow noted that the ‘intercellular matter is perfectly homogeneous … as clear as water’. This clear appearance of the matrix gave the tissue its name, hyaline from the Greek hyalos or glass.5

**Cartilage response to injury**

Detailed studies of articular cartilage and its composition have only been possible for the past 40–50 years.5 Its response to injury, however, has attracted scientific minds for centuries. In 1743, William Hunter noted that ‘ulcerated cartilage is a troublesome thing … once destroyed it is not repaired’.7 A little more than 100 years later James Paget reported that there are ‘no instances in which a lost portion of cartilage has been restored, or a wounded portion repaired with new and well formed cartilage’.8 Studies during the past 150 years have generally confirmed the works of Hunter and Paget by showing that cartilage may repair under certain conditions, but in most circumstances the repair tissue lacks the molecular composition and organization, material properties and durability of normal articular cartilage.3,9 Spontaneous repair of musculoskeletal tissue is based on a localized inflammatory response facilitated through the availability of appropriate blood cells. The release of mediators will stimulate migration and proliferation of mesenchymal stem cells. The occurrence of these events is critical for initiation of effective tissue repair. In the avascular articular cartilage the inflammatory response is limited and healing is unlikely to occur unless the calcific cartilage layer and subchondral bone are penetrated.

**Diagnosis of cartilage injury**

Localized damage to hyaline cartilage is often due to an acute trauma, but may also be caused by overuse, ligament instability or limb mal-alignment, or it can follow previous meniscectomy or osteochondritis dissecans. Many cartilage lesions remain undiagnosed as symptoms are often vague and mechanical problems like locking, clicking or giving way are not always present. Any delay in diagnosis may expose the lesion to further damage as appropriate measures of protection are generally not instigated. Although a clinical examination is valuable it is by no means reliable to diagnose a cartilage injury, and further investigations are often necessary. Radiolucency of cartilage prevents any radiographic investigations to act as a diagnostic modality, unless an osteochondral defect is present. MRI has been established as the gold standard due to its superiority over other imaging technologies and should be considered whenever a chondral injury is suspected (Figure 1).10

**Treatment**

The natural history of cartilage lesions is not known and the surgical treatment options are neither benign nor associated with a predictable outcome, especially with regard to the prevention of OA. Thus, surgical decision making is difficult and complex and must be taken with care, after due consideration.

The treatment of patients affected by articular cartilage lesions should be aimed at clinical pain relief, restoration of joint function, and prevention or at least delay of the onset of osteoarthritis. A conservative management approach may be suitable for some patients and may include temporary reduction in weight bearing, activity adjustment, off-loading insoles and braces, NSAIDs, oral food supplements (glucosamine and chondroitin sulphate), and intra-articular injections (corticosteroids, hyaluronic acid). The value of some of these measures, however, has been questioned. Non-operative treatment is generally more appropriate for older patients and those where osteoarthritis is already present. In view of articular cartilage’s inability to provide reliable self-repair, younger and active patients should be considered for surgical cartilage repair.

The decision on surgical management will have to take patient-specific and lesion-specific variables into account, but should never lose sight of the patient’s ambitions, concerns and goals. Other patient-specific variables include age, physical fitness, BMI, co-morbidities, and associated injuries. Lesion-specific variables include level of acuteness, size and location, containment, and previous surgical intervention. The mechanical environment of the knee often holds the key for success or failure in cartilage repair. Mechanical overload, excessive joint laxity, patellar mal-tracking and meniscal deficiency will affect the equilibrium of forces within the joint, creating an environment unfavourable for successful cartilage repair. It is hence of vital importance that the clinician who has identified an individual as suitable for cartilage repair recognises potential causes, associated injuries and abnormalities. Any significant increase in joint laxity due to ligament incompetence or rupture requires stabilization through ligament repair or reconstruction. Deviation of the mechanical leg axis towards varus or valgus may create areas of overload within the knee and should be addressed with off-loading measures (insole, brace) or axial realignment osteotomy.11,12 Patellar instability may require lateral release, medial reefing/augmentation or tibial tuberosity transfer. Only if the clinician is able to successfully identify and treat any associated abnormalities and compounding factors will his efforts to treat a cartilage lesion be rewarded with a more predictable outcome.

**Figure 1** Full thickness cartilage defect on medial femoral condyle.
Most operative procedures designed for the treatment of articular cartilage defects provide repair rather than regeneration of the lesion. However, repair of clinically significant lesions rarely restores a normal joint surface and no current replacement of articular cartilage duplicates its material properties or durability. For the purpose of definitions we should distinguish between repair and restoration. Repair involves replacement of the damaged, defective or lost tissue with functional tissue that may not be completely identical to the original structure. Regeneration on the other hand requires restoration of tissue, making it indistinguishable from normal cartilage. Although cartilage regeneration would be ideal, the question arises as to whether this is in fact necessary, or whether repair may be satisfactory. Clinicians have been striving towards the ideal of cartilage regeneration but despite the development of sophisticated cartilage repair techniques, the recreation of hyaline cartilage remains an elusive goal.

Cartilage repair techniques and treatment algorithm

Loose cartilage flaps are not amenable to re-fixation and should be sacrificed, as healing is unlikely to occur. Primary repair, however, is a suitable option for fresh osteochondral defects with a diameter of at least 10 mm, typically seen in osteochondritis dissecans, especially if the fragment has not completely dislodged. Occasionally, gentle debridement of the bony surfaces to remove fibrous tissue may be necessary to enhance healing. Fixation is facilitated with headless pins, and compression screws (e.g. Herbert® screws, Zimmer) or biodegradable pins (e.g. Smart Nail® Linvatec, Chondral Dart® Arthrex) (Figure 2).

For the treatment of full thickness surface cartilage lesions, a plethora of cartilage repair techniques have emerged since the late 1950s, with some being well established whilst others remain under clinical investigation. This article will not cover all techniques but it will outline the majority of those currently available for clinical use in the United Kingdom. The author has decided without prejudice not to include certain repair techniques (e.g. allograft transplantation, paste-graft technique, carbon fibre rods), based on the lack of supporting clinical evidence or ongoing scientific controversy.

In general, surgical options can be grouped into three categories: those that are palliative (arthroscopic wash-out & debridement), reparative (marrow stimulation) and restorative (osteochondral grafting, chondrocyte implantation, paste-graft technique). Marrow stimulation techniques are often considered first-line treatment for full thickness cartilage defects of small and moderate size (up to 4 cm²). Smaller lesions of less than 2.5 cm² that do not respond to marrow stimulation, may be suitable for osteochondral autografts or synthetic scaffolds, whilst larger lesions beyond 2.5 cm² are typically more amenable to autologous chondrocyte implantation (Table 1).

The choice of repair technique is also guided by the location of the lesion (Table 1). Structural grafts are best suited for convex areas of the anterior and inferior portion of the femoral condyles, but difficult to employ in areas relatively inaccessible to perpendicular graft placement like the posterior condylar regions. They are also relatively unsuitable for the somewhat concave tibial and trochlear regions, as the harvested plugs are typically obtained from areas of convexity on the femoral condyle or inter-condylar notch. For inaccessible lesions or those located on the tibia or patellofemoral joint, marrow stimulation or autologous chondrocyte implantation are the treatments of choice.

Osteochondral fragment on medial femoral condyle re-attached using bioabsorbable barbed fixation pins. Divergent pin placement enhances fragment compression and stability. (Illustration on the right with kind permission of Arthrocare Europe.)
Marrow stimulation techniques

Natural repair of musculoskeletal tissue begins with an inflammatory response led by the invasion of inflammatory cells that will stimulate migration and proliferation of mesenchymal cells. These inflammatory events are critical for initiation of effective tissue repair. Marrow stimulation techniques are cartilage repair methods based on this principle. They rely on the creation of blood supply and access of bone marrow cells with chondrogenic potential to the otherwise avascular joint surface. Breaching the subchondral plate will promote bleeding and local migration of undifferentiated mesenchymal stem cells and growth factors, allowing for the formation of a ‘superclot’. The pluripotential nature of mesenchymal stem cells carries the creative ability to formulate repair cartilage often rich in collagen type I. Various techniques have been described to stimulate fibrocartilage ingrowth, most of which evolved out of incidental observations and only later received clinically scientific justification.

The mechanical properties of this tissue, otherwise known as fibrocartilage, are very different to those of hyaline cartilage. Fibrocartilage is commonly present in the meniscus, annulus fibrosus and at the insertion of ligaments and tendons into bone, tissues whose principle function it is to resist tension, whereas hyaline cartilage is mainly designed to resist compressive forces. The differences in mechanical properties between the tissues have been attributed to variations in collagen make-up.

Growing fibrocartilage into areas previously occupied by hyaline cartilage will expose the new tissue to a mechanical environment characterized by compressive forces to which it is somewhat ill-equipped. It may henceforth be tempting to assume...
that such lesions may be exposed to earlier failure and subsequent degeneration. However there is no reliable scientific evidence available as yet, which is able to conclusively support this assumption. In one study biopsies taken during second-look arthroscopies following microfracture have shown that the new grown tissue may not be pure fibrocartilage but consist of a combination of fibrocartilage and hyaline-like cartilage.15 If this is true it could suggest that such tissue may potentially carry improved mechanical properties and wear resistance compared to simple fibrocartilage, making marrow stimulation an attractive alternative to other cartilage repair techniques. Microfracture has been shown to provide beneficial outcome in 75–100% of patients.12,14 Most authors agree that this technique is likely to offer satisfactory relief for at least 3–5 years, whilst long-term outcomes and benefits are still unknown.12,15

**Pridie or trans-cortical drilling**

This cartilage repair strategy involves the use of a power drill or Kirschner wire to perforate the subchondral plate. The technique was devised by Kenneth Hamden Pridie from Bristol in the late 1950s, who observed the growth of fibrous tissue on previously eburnized joint surfaces in response to trans-cortical drilling.16 Combining the Magnusson debridement with the application of numerous drill holes to areas of full thickness cartilage defects has been shown to provide most patients with an acceptable level of pain relief in the medium term.16,17 Although trans-cortical Pridie drilling can be performed arthroscopically, the technique has its limitation in that it requires perpendicular drill placement, making it unsuitable for relatively inaccessible areas like the patellofemoral joint. It has also been argued that heat generation during the drilling procedure may affect viability of bone and bone marrow, compromising its potential to provide tissue repair. However, no conclusive evidence of such detrimental effects on clinical outcome exists. The procedure continues to be performed for the treatment of osteonecrosis and as part of a patelloplasty, when retaining the patella in total knee arthroplasty (Figure 3).

**Abrasion arthroplasty**

Introduced by Magnusson in the 1940s and later popularized by Johnson, abrasion arthroplasty was initially designed for the treatment of more widespread cartilage loss in patients suffering joint degeneration.18,19 It is often combined with lavage, removal of loose bodies, resection of unstable cartilage and partial meniscectomy, and is particularly successful in those patients suffering mechanical symptoms at the outset. The superficial layer of the subchondral bone is removed using an arthroscopic burr, allowing the mesenchymal marrow cells to be released into the lesion, which will stimulate the fibrocartilage repair process (Figure 4). The technique has been shown to provide symptomatic relief in 60–70% of patients for periods of 3–5 years, with results generally better in younger patients.20 If performed in patients with mono-compartmental disease, then the results of abrasion arthroplasty are more predictable and durable when combined with off-loading osteotomy.

The technique of abrasion arthroplasty is simple and can be performed entirely arthroscopically. In smaller lesions of up to 2.5 cm², a spherical high speed burr (Sterling® 3.5 mm Spherical Burr, Linvatec) is used to create several golf ball dimple type indentations in the base of the defect (Figure 4). For larger lesions a cone shaped burr (Sterling® 6 mm Oval Burr, Linvatec) is often more appropriate. It is important that no islands of sclerotic bone are left and that just enough bone is removed to facilitate bleeding. Fluid inflow should be interrupted and intra-articular pressure reduced intermittently to ascertain the level of subchondral marrow release. In younger patients with fresh full thickness cartilage defects simple removal of the calcific layer with a sharp curette or Volkmann spoon may sometimes be sufficient to allow for subchondral bleeding. The technique is particularly useful in areas like the retro-patellar surface, where microfracture is difficult to perform.

**Microfracture**

Based on the principles of the Pridie procedure, the technique of microfracture was popularized by Steadman in the early 1990s.14,21 Certain advantages have been claimed, including the avoidance of heat generation caused by drilling and better accessibility through the use of angled instruments, allowing for microfracture to be performed in places where drilling would otherwise be unfeasible. Microfracture is an appealing option in the treatment of articular cartilage injury because it is relatively simple to perform and carries minimal morbidity. The clinical success of microfracture is age dependent. The best results are typically achieved in younger patients with well contained, relatively small mono-polar lesions of up to 4 cm², although
larger and bipolar lesions may also be treated successfully with this technique.

Critical for the success is the removal of all damaged or loose cartilage fragments from the periphery of the lesion, and creation of vertical cartilage margins to which repair tissue can bond (Figures 5 and 6). This will also help to contain the growing tissue and to protect it from being dislodged accidentally. The calcified cartilage layer at the base of the lesion is carefully removed, using a Volkmann spoon or curette, and care should be taken not to damage the subchondral plate. Using an arthroscopic awl (ChondroPicks®/C210 Arthrex), the subchondral plate is then perforated to a depth of approximately 4 mm, starting around the periphery of the lesion and working towards the centre. Microfracture holes should be kept 3–4 mm apart, which equals 3–4 holes/cm². Awls with differently angled tips are available to allow easier access to difficult areas of the knee. The choice of awl will depend on the location of the defect, as the tip should be driven into the bone at a right angle. Typically, a 30° or 45° awl is utilized for most areas and the knee should be manoeuvred in a way so as to bring the surgical field into view. The surgeon should not be afraid to create accessory portals to improve perpendicularity and to avoid iatrogenic injury through inappropriate portal placement. A metal spatula (Malleable Graft Retractor No. 232024, Mitek/DePuy) can be advantageous and will ease the introduction of sharp instruments through arthroscopy portals. Before removing the arthroscope, the irrigation fluid pump pressure is reduced or the inflow stopped altogether to judge the adequacy of the surgical preparation. Under direct visualization the surgeon can now observe whether marrow content (fat droplets and blood) is released in equal measures from the microfracture holes. Occasionally, the bleeding response may appear inadequate and holes may have to be deepened or additional ones made. At the end of the procedure the knee joint is evacuated of all fluid and no drains are used, as this may interfere with the formation of the clot.

**Autologous matrix induced chondrogenesis**

Autologous matrix induced chondrogenesis (AMIC® Geistlich Pharma) is a variation on the microfracture technique and has been developed in response to the often unpredictable results achieved with microfracture alone. The technique combines the standard microfracture procedure with the application of a cell-free collagen membrane (Chondro-Gide®) in a single-stage procedure. The membrane is placed onto the microfractured
area and either secured with sutures (Vicryl or PDS 6–0) or commercially available fibrin glue (Tisseel®, Baxter). The idea is to capture the pluripotent mesenchymal cell population in the defect and to create a protected environment for cartilage regeneration. Despite certain theoretical advantages, clinical results of matrix induced chondrogenesis have so far failed to confirm any supremacy over standard marrow stimulation techniques for the treatment of femoral lesions, although those on the retro-patellar surface have indicated more promising results.22

Post-operative rehabilitation following marrow stimulation
Key to success after any marrow stimulation technique is the patient’s willingness to adhere to a specific rehabilitation program in order to optimize outcome. Patients should use cold therapy and compression continually for the first 3–7 days (CryoCuff®, Aircast) and intermittently thereafter, as this will help to control pain and inflammation.

As with all techniques, the rehabilitation protocol varies with size and location of the treated defect. Lesions in the tibio-femoral weight bearing zone should be off-loaded with crutch assisted very limited weight bearing (VLWB) ambulation (5–15 lb) for 6–8 weeks, followed by partial weight bearing (PWB) (20–30 lb) for a further 2 weeks. For lesions smaller than 1 cm in diameter, return to normal weight bearing may commence earlier. Some surgeons consider the use of a continuous passive motion (CPM) machine beneficial, based on the understanding that it may assist in reshaping and containing blood clot or cartilage cells through gentle motion of the opposing surface across the defect. It is recommended to use CPM intermittently during the day over a period of 6–8 h in a 24-h period, and some patients tolerate its use at night. The rate is usually 1 cycle/min, with a flexion range of 0–90°. If CPM is unavailable, instructions should be given to perform passive flexion and extension with approximately 500 repetitions three times a day or to use an exercise bike with no resistance. A deep water exercise programme is begun at 2–3 weeks and should include underwater jogging and paddling with a float.23 Elastic resistance cord exercises can commence at 8 weeks whilst progressive weight training should be delayed for 4 months. Return to impact, pivoting and cutting activities will depend on the patient’s clinical presentation, but even in the absence of any intra-articular effusion is generally not recommended for at least 4–6 months.

Patients with lesions in the patellofemoral joint are allowed to fully weight bear as long as they avoid compression of the patellofemoral joint. This is best achieved by use of a hinged brace. The surgeon should, at the time of arthroscopy, determine the knee flexion angles at which the patellofemoral mechanism comes into contact with the lesion. The brace can then be adjusted to allow free flexion up to this point. Typically, the braces are locked at 20° to prevent flexion beyond the point where the centre ridge of the patella engages with the trochlear groove. Similarly, any exercise regime needs to avoid pressure in the patellofemoral joint in the contact range of the lesion for about 3–4 months. CPM is utilized in the same fashion as for tibio-femoral lesions. The brace is gradually unlocked after 4–6 weeks and can be discarded after...
8 weeks, at which point progressive strength training can be instigated.

Replacement techniques

Replacement techniques consist of osteochondral autograft (OATS®, Arthrex), osteochondral allografts, synthetic resorbable scaffolds (Trufit® CB plug, Smith&Nephew) and metallic surface arthroplasty (HemiCap®, Arthrosurface).

Osteochondral autograft

Osteochondral autograft transplantation, otherwise known as mosaicplasty, was popularized by Hangody from Hungary in the early 1990s.3,24 The method is based on the transfer of one or more cylindrical osteochondral plugs into the cartilage defect, providing instantaneous repair with hyaline cartilage (Figure 7). Although the procedure is generally performed through a miniarthrotomy, smaller lesions may be amenable to being treated entirely arthroscopically. A sizing guide is used to determine the number and size of grafts that are needed. Both the creation of the recipient socket and the harvesting of donor graft plug require the tubular cutting instruments to be placed perpendicular to the surface to avoid graft obliquity. This in itself limits this technique to areas relatively accessible, unless the surgeon is willing to expose the knee in a formal arthrotomy.

The graft is harvested from the non-weight bearing periphery of the trochlea or inter-condylar notch and measures between 2.5 and 10 mm in diameter. The graft harvester is introduced to a depth of about 12–15 mm and then twisted to disengage the base of the plug. It is recommended to undersize the depth of the recipient socket by 2 mm. The donor plug, which has remained in the harvester, is then placed over the recipient site and advanced by approximately 2 mm. The plug is then engaged with the opening. Once in-line with the socket, it can be gently driven down until it is well seated but minimally proud.

It is critical to the success that the surgeon aims to recreate normal surface congruity, which becomes particularly problematic if several plugs are used (Figure 7). The technique is limited by the amount of donor tissue available and hence is best suited for lesions up to 2–4 cm². Although fibrocartilage will grow into the donor defect within 6–8 weeks, donor site morbidity, such as anterior knee pain, has been associated with this technique. To overcome this problem some clinicians have inserted synthetic plugs for backfill of osteochondral autograft sites hoping that this may create a more physiological repair.

The ideal locations for autologous osteochondral grafting are the convexities of the femoral condyles, whilst those of the patellofemoral joint and tibia, with their varying surface geometries, make structural grafts more difficult to fit in place.

Synthetic resorbable scaffolds

Synthetic osteochondral scaffolds (Trufit® CB plug, Smith&Nephew) are off-the-shelf bioabsorbable cylinders engineered to mimic the composition of human bone and cartilage.24 Produced from biodegradable materials including calcium sulphate, polylactide–glycolide (PLG) and polyglycolide (PGA), their synthetic structure is designed to resorb within 6–18 months after implantation, leaving the cartilage repair construct behind. These bioresorbable scaffolds have the obvious advantage over permanent implants that cartilage repair or regeneration can occur without the inhibition of residual foreign material. The bilayer design of the TruFit® implant incorporates a cartilage and bone phase, each designed to provide appropriate mechanical stiffness for the adjacent tissue. The cartilage phase is relatively soft and malleable, which gives the implant the ability to be contoured to fit any joint surface geometry, making it more versatile than osteochondral plugs. They offer a mechanically stable environment with a porous nature that provides conduits for tissue ingrowth. The temporary matrix allows mesenchymal stem cells to impregnate the pores of the scaffold, guiding the formation of bone on one side and cartilage on the other (Figure 8). Preclinical studies have demonstrated restoration of hyaline-like cartilage in a goat model, with subchondral bony incorporation at 12 months. Early clinical results of patients enrolled in the Hospital for Special Surgery Cartilage Registry have been favourable, with a good safety profile and no adverse effects25,26 (Figure 9). However, concerns remain about graft stability if several plugs are placed adjacent to each other. Furthermore, the author has observed two cases out of 45 where graft involution and shrinkage were noted 3 months following surgery, even though patients remained asymptomatic.

Figure 7 Placement of osteoarticular autograft cylinders into a defect on the lateral femoral condyle. Care should be taken in recreating physiological surface geometry in order to avoid graft displacement and impingement.
The technique for implanting synthetic osteochondral scaffolds is similar to the one described for autologous osteochondral plugs, but avoids the harvesting procedure and donor site morbidity. Plugs are available in different sizes, ranging from 5 to 11 mm in diameter. Once the appropriate size is chosen, the drill/cutting sleeve is placed perpendicular to the surface incorporating the defect. One should aim to slightly oversize the plug in order to avoid leaving peripheral areas uncovered. The drill/cutting sleeve is then advanced to a depth of 8–10 mm, with small adjustments to maintain perpendicularity still being possible in the initial stage. A manual drill is introduced into the sleeve and residual tissue and bone are removed. Both sleeve and drill are retrieved together,

Surgical technique of applying cylindrical synthetic bioabsorbable scaffold. The cutting sleeve must cover the entire defect and is placed perpendicularly onto the cartilage surface. The sleeve is then driven into the cancellous bone to a depth of 8–10 mm. The inner core is removed and a synthetic biphasic plug of appropriate length is introduced to cover the defect.

**Figure 8**

MRI scan showing a full thickness cartilage defect on the medial femoral condyle (left) treated with a synthetic bioabsorbable biphasic scaffold. A follow-up scan (middle, right) obtained 3 months after implantation shows signs of graft integration.

**Figure 9**
leaving a cylindrical space behind. The length of the implant is then adjusted according to the depth of the created defect by simply cutting to bone equivalent aspect with a knife. It is advantageous to advance the implant by 1–2 mm beyond the tip of the delivery sleeve to ease engagement and alignment with the defect before insertion. The implant is press-fitted into the defect by gently tamping the piston of the delivery guide with a mallet. Once seated, final adjustments and contouring can be performed until the graft matches the surrounding surface geometry and graft margins are flush with the adjacent surface.25

**Partial re-surfacing arthroplasty**

Metallic partial re-surfacing implants, like the HemiCap® knee implant (Arthrosurface), may be appropriate for patients typically between the ages of 40 and 60 years who have focal condylar defects and who are likely to undergo knee replacement surgery in the future (Figure 10). The procedure is intended to bridge the gap between biologic procedures and conventional joint replacement, and like osteochondral plug implantation can be performed through a mini-arthrotomy. The cartilage defect is milled to a specified depth and width to receive a mushroom shaped implant with a highly polished surface that attempts to closely match the convexity and surface anatomy of the replaced area. The available implants are limited to use on distal femoral condyles only. Although the technique of partial surface replacement has been used for a few years, there are no comparative studies or medium-term outcome studies available. These implants should hence be used with utmost caution.

**Post-operative rehabilitation following osteochondral or synthetic plug implantation**

There are currently no clear guidelines on rehabilitation measures following plug implantation. Emphasis should be placed on early range-of-motion exercises, possibly augmented by CPM. Surgeons are at odds about the merits of weight bearing restrictions and whether or not this may affect the clinical outcome. Concerns that pistoning of slightly unstable plugs may lead to cyst formation and potential surface incongruencies, however, have led most surgeons to support a 4- to 8-week period of VLWB. Thereafter, patients are allowed progressive weight bearing as tolerated combined with an appropriate exercise regime, but avoiding impact activities for a minimum of 10–16 weeks. Patients are permitted to return to sports when there is minimal effusion, full range of motion and quadriceps strength has reached 80% of the contralateral leg.

**Cell based repair techniques**

In the early 1970s, Bentley and Greer were able to show that chondrocytes transplanted into articular cartilage defects enhanced healing.27 Their discovery, combined with knowledge about the limited capacity of cartilage to respond even after marrow stimulation, sparked research towards transplanting tissue with chondrogenic potential. Two principal techniques have since evolved, and it is estimated that approximately 10 000 patients have been treated with chondrocyte implantation to-date.

**Autologous chondrocyte implantation**

Autologous chondrocyte implantation (ACI) is considered to be one of the first forms of clinical tissue engineering. The first human application of this technique was performed in 1994 by Peterson and Brittberg at the University of Gothenburg in Sweden.28 The aim of this treatment is to enable the regeneration of hyaline or hyaline-like cartilage, thereby restoring normal joint function. The basic technique has undergone considerable development since its inception and has become an established form of treatment for symptomatic osteochondral defects in the knee, with lesions on the femoral trochlea and condyles being particularly suitable.29–33

The data on the relative effectiveness of ACI compared with other cartilage repair techniques such as microfracture and mosaicplasty are somewhat inconsistent. Furthermore, there is a lack of long-term follow-up, and quality of life gain following treatment with ACI compared with other alternatives remains unproven. Poor pre-operative function and a long history of symptoms with numerous earlier surgical procedures have been shown to be poor prognostic indicators. It is thus essential that these factors together with properties of the chondral lesion are taken into account during patient selection and counselling.

Chondrocyte implantation has traditionally been considered a second or third-line treatment, mainly based on its surgical complexity and cost implications. The attitude towards ACI, however, would benefit from being reassessed, as the clinical outcome of chondrocyte implantation techniques performed in patients who previously received a failed cartilage repair
procedure has shown inferior results when compared to those individuals where ACI was used primarily.

The technique of ACI is a two-stage procedure (Figures 11 and 12). At first the surgeon will perform an arthroscopic evaluation of size and depth of the lesion and obtain a small cartilage biopsy, usually from the supero-medial or supero-lateral edge of the femoral trochlea. Three to four full thickness cartilage chips of about 5 mm in length will typically provide 100–300 mg of biopsy specimen, containing approximately 250 000 cells, and will be enough to fill the bottom portion of the specimen container. The cells are kept at a constant temperature of 4 °C in a storage box and forwarded to the processing facilities within 24 h. The chondrocytes within the received tissue sample are then isolated and cultured in the laboratory over a period of 4–6 weeks. During this period the number of cells increases by 50-fold, to reach approximately 12–20 million. In a second surgical procedure, the damaged area is typically exposed through a medial para-patellar approach, as this is less likely to infringe with future surgical intervention. Previous incisions, however, should be taken into account in order not to compromise skin viability. The lesion is cleared of all remaining cartilage and debrided down to the calcified layer. Firm vertical margins of healthy surrounding cartilage are established. Bleeding into the defect is to be avoided, hence care should be taken not to break through the subchondral bone plate. Should bleeding occur, however, cotton buds soaked with epinephrine may be useful in facilitating haemostasis. In order to contain the cultured chondrocytes in the defect a watertight environment needs to be created. In the initial description of ACI a periosteum flap obtained from the medial aspect of the tibial metaphysis is sutured with the cambium layer facing down onto the defect margins using 6–0 PDS or Vicryl, with a P-1 cutting needle. During initial suture placement, the four corners of the graft are secured first and further sutures are placed in 3 mm increments. A flexible cannula is inserted under the apex of the flap to allow for cell injection and a watertight seal created though the application of commercially available fibrin glue (Tisseel®, Baxter) onto the sutured margins of the flap. The chondrocytes are then injected and the proximal opening sealed. Instead of periosteum, resorbable cell-free collagen membrane substitutes (ChondroGide®, Geistlich, Restore®/DePuy) are available. They avoid graft harvesting time and donor site morbidity, and have so far shown no adverse effects on clinical outcome compared to periosteum at short-term follow-up.

The chondrocyte implant matures over a period of 18 months. In the Proliferation Stage between weeks 0 and 6 the tissue is soft and extremely fragile. This is followed by the Transitional Stage lasting up to 6 months, during which the tissue presents putty like consistency. In the Remodelling Stage the tissue slowly matures and hardens. This final stage is estimated to take approximately 12–18 months, although some changes in matrix remodelling and maturation may continue well beyond this point.

The procedure of ACI is, however, not without its problems. Technical difficulties with fixation of the membrane and problems with graft delamination and overgrowth (hypertrophy) have been reported. The implantation of cultured chondrocytes in suspension has also led to concerns about the uneven distribution of chondrocytes within the defect and the potential for cell leakage. A limited number of long-term studies with up to 10-year follow-up have, however, confirmed good or excellent results in 82–92% of patients. Complications included superficial wound infections, post-operative haematomas, intra-articular adhesions, and periosteal hypertrophy, whilst complete graft failure was reported in up to 16% of cases. Minas reported on a group of 169 patients with large cartilage lesions of up to 12 cm² treated with ACI. Overall, 87% of patients showed significant improvement after a minimum follow-up of 24 months, whilst 13% were considered failures.

Autologous chondrocytes with matrix scaffold

Difficulties and complications associated with ACI, together with the need for a relative extensile arthrotomy to facilitate suturing, sparked the desire to create a more reliable and simplified method to deliver autologous chondrocytes into cartilage lesions. Second generation technologies have now emerged using the traditional method of chondrocyte culturing. Instead of injecting expanded autologous chondrocytes under a membrane, the chondrocytes are seeded onto a collagen matrix which is placed directly onto the lesion. As this technique is essentially ‘suture-free’, it is quicker to perform than ACI and requires less extensile exposures, which is of particular advantage when combined with other interventions such as ligamentous reconstruction, bone grafting or high tibial osteotomy. A further advantage of this method of cell delivery is that the scaffold may act as a barrier to invasion of the graft by fibroblasts, which may otherwise induce fibrous repair. Two different carriers have so far emerged. The Hyalograft C implant (Hyaff-11®, FIDIA Advanced Biomaterials) is a three-dimensional matrix graft that uses a hyaluronic acid based scaffold for the delivery of chondrocytes, whilst the Matrix Autologous Chondrocyte Implantation method (MACI®, Genzyme) utilizes a purified and cell-free porcine collagen membrane. Studies of these cell based 2nd generation
techniques have been promising, with reported good clinical medium-term results with up to 3-year follow-up. Problems of graft hypertrophy, which is a major cause of morbidity in ACI, are rarely observed when such scaffolds are utilized. Although repair tissue initially appears to show a mixture of hyaline and fibrocartilage, in vitro studies have confirmed improved histomorphometric characteristics and cartilage maturation with time. Further clinical and histological evidence will be required to validate the long-term outcome of this technique in vivo.

The MACI technique still requires a 1st stage cartilage harvesting procedure followed by a six- to eight-week culturing period. A week prior to the implantation date, chondrocytes are seeded onto the collagen membrane, which will allow for the delivery of approximately 2–5 million cells/cm². The membrane is correctly shaped to match the defect geometry and should not protrude beyond the margins. It should, however, be emphasized that the everted edge of the membrane should cover the vertical wall of the defect, presenting cells to the cartilage-graft interface to facilitate chondral union. A thin layer of fibrin glue is injected into the base and the membrane with the rough surface facing downwards placed into the lesion and evenly compressed using digital pressure for 3–5 min. The cartilage-graft interface is secured with a minimum of fibrin sealant. In uncontained defects the use of biodegradable bone anchors and

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Figure 12

Surgical technique of matrix autologous chondrocytes implantation (MACI). Defect exposure and debridement through mini arthrotomy. Precise size determination and preparation of MACI membrane. Fibrin glue application to dry defect base immediately followed by implantation of MACI membrane.

Figure 13

Large uncontained osteoarticular defect on the lateral aspect of the medial femoral condyle following osteochondritis dissecans (OCD). Bone grafting (bone graft obtained from tibial metaphysis) and autologous chondrocyte implantation performed using single-stage sandwich technique. MRI scan obtained 12 months following surgery (right) confirms consolidation of bone graft and satisfactory cartilage regeneration.
partial suture fixation may be necessary to safeguard against graft delamination.

**Post-operative rehabilitation following chondrocyte implantation**

Several rehabilitation regimes have been produced, all of which show slight variations in the timing of weight bearing and commencement of sporting activities. In general, most regimes emphasize a short period of complete immobilization in a brace or cylinder cast following surgery, ranging from 12 h to 7 days. Thereafter, CPM is initiated to provide a chondrogenic stimulus, as demonstrated by O’Driscol and Salter.41

The post-operative treatment varies depending on the location of chondrocyte implantation, but is broadly similar to the rehabilitation measures imposed following marrow stimulation, although periods of joint protection are often extended. Lesions in the tibio-femoral weight bearing zone are off-loaded with VLWB although periods of joint protection are often extended. Lesions in the patellofemoral joint are allowed to load bear for 8 weeks, typically followed by a short period of PWB, whilst those in the patellafemoral joint are allowed to load bear almost immediately, provided a motion restricting brace is worn. Physiotherapy is particularly important during the initial post-operative period and should focus on maintaining muscle function and joint flexibility.23 Hydrotherapy, including underwater jogging, has proved to be very popular at this stage. The patient is then gradually introduced back to normal daily activities and at around 4 months allowed to perform light sporting activities, e.g. cycling and swimming. At 6–9 months the activity level may be stepped-up, introducing rowing, the cross-trainer and gentle weight training. Cutting, twisting and turning activities are usually avoided until the surgeon is happy with the progress and confident that the cartilage graft has taken. Most surgeons verify cartilage integrity by obtaining an MRI scan between 4 and 9 months (Figure 13). Second-look arthroscopies are rarely necessary, especially since the introduction of collagen membranes has substantially reduced the risk of graft hypertrophy, and should be reserved for those patients complaining of mechanical symptoms such as locking or clicking. Return to full level sporting activities is not desirable much before 12–18 months following surgery. "

**REFERENCES**


FURTHER READING


