Articular cartilage provides a vital function in the homeostasis of the joint environment. It possesses unique mechanical properties, allowing for the maintenance of almost frictionless motion over a lifetime. However, cartilage is vulnerable to traumatic injury and due to its poor vascularity and inability to access mesenchymal stem cells, unable to facilitate a satisfactory healing response. Untreated chondral defects are thus likely to predispose patients to the development of osteoarthritis.

Reconstitution and repair of articular cartilage is dependent on the neosynthesis or implantation of cartilage matrix elements, a goal which can be achieved through a variety of surgical means. Commonly used repair techniques include marrow stimulation, structural osteo-articular autografts or chondrocyte implantation. Despite substantial differences in the complexity and technical application of each method, all are united in the endeavour to restore joint function and prevent joint degeneration. Anyone attempting to treat cartilage defects must possess a basic understanding of the physiology of cartilage growth, and relevant factors affecting cartilage healing and repair. Furthermore, knowledge of the biomechanics and kinematics of the knee are essential in order to appreciate the forces acting on joint surfaces and repair tissues. Although clinical success is dependent on appropriate patient selection, accurate clinical assessment, definition of root causes and application of the right choice of treatment modality, the ultimate outcome of any intervention remains heavily reliant on the surgeon’s proficiency in the technical aspects of the chosen surgical procedure.

Keywords: cartilage; repair; chondrocyte implantation; marrow stimulation, MACI.

INTRODUCTION

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 [19]. Although its composition, structure and performance is surprisingly complex, its relative metabolic inactivity and lack of blood supply permit for only a very limited response to injury [7,14, 29,42,53]. While the natural history of localised 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 [15,40].

The numbers of young adults suffering cartilage damage through injuries continues to grow, with estimated figures reaching 10,000 per annum in the UK alone (Fig. 1) [50]. Although most of these injuries may be suitable for repair, the condition often remains undiagnosed and the opportunity for early treatment is subsequently lost.
A plethora of cartilage repair techniques have emerged for the treatment of full thickness surface cartilage lesions since the late 1950s (2,14). Emulating the sophisticated structure of hyaline cartilage is a tall order and although most repair technologies rarely restore a normal joint surface or duplicate material properties or durability of native cartilage, they have shown to provide effective pain relief, and restoration of joint function, at least in the short to medium term. Their ability to prevent or delay the onset of osteoarthritis however remains unclear, which in part is due to the ethical dilemma of conducting appropriate comparative studies (14,15,17).

This article will not cover all techniques but the majority of those currently available for clinical use. The author has decided without prejudice not to include certain procedures (e.g. allograft transplantation, paste-graft technique, carbon fibre rods), based on the lack of supporting clinical evidence or ongoing scientific controversy.

WHO IS THE IDEAL CANDIDATE FOR CARTILAGE REPAIR?

The decision on the surgical management will have to take patient-specific and lesion-specific variables into account, without losing sight of the patient’s physical ambitions, concerns and goals. Patient-specific variables focus on age, physical fitness, body mass index (BMI), co-morbidities, leg alignment, and associated injuries (36). Lesion-specific variables include level of acuteness, size and location, containment, and history of previous surgical interventions. The mechanical environment of the knee often holds the key for success or failure in cartilage repair. Mechanical overload through malalignment, excessive joint laxity, patellar maltracking and meniscal deficiency will affect the equilibrium of forces within the joint, creating an environment unfavourable for successful cartilage repair. Only if the clinician is able to identify and address any of these compounding factors will his efforts of treating cartilage defects be leading to a more predictable and durable outcome (18,68).

Loose cartilage flaps are generally not amenable to re-fixation and should be sacrificed as healing is unlikely to occur. Primary repair, however, is a suitable option for fresh osteo-chondral defects with a diameter of at least 10mm typically seen in osteochondritis dissecans (Fig. 2) (62). Occasionally, gentle debridement of the bony surfaces to remove fibrous tissue may be necessary to stimulate marrow access and to enhance healing. Fixation is facilitated with headless nails, compression screws or barbed biodegradable darts or pins (62).

Surgical options can be grouped into three basic categories; those which are palliative (e.g. arthroscopic wash-out & debridement), reparative (e.g. marrow stimulation) and restorative (e.g. osteochondral grafting, chondrocyte implantation). Marrow stimulation techniques are often deemed most appropriate as first line treatment for full thickness cartilage defects of small and moderate size (up to 4 cm²). Smaller lesions of less than 2 cm², which do not respond to marrow stimulation, may be suitable for osteochondral autografts or synthetic scaffolds, whilst larger lesions beyond 2 cm² are typically considered for autologous chondrocyte implantation (Table I) (17).

The choice of repair technique is also guided by the location of the lesion (Table I). 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 region. They are also relatively unsuitable for areas of surface concavity e.g. tibia and trochlea, as the harvested plugs are typically obtained from areas of convexity on the femoral condyle or intercondylar notch. For inaccessible lesions or those located on tibia or patello-femoral joint, marrow stimulation or autologous chondrocyte implantation are often considered treatments of choice (11,17,36,41,47,66).

**Marrow Stimulation**

Spontaneous repair of musculoskeletal tissue is based on a localised inflammatory response led by the invasion of inflammatory cells that will stimulate migration and proliferation of mesenchymal stem cells. These inflammatory events are critical to initiate 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 together with local migration of undifferentiated mesenchymal stem cells and growth factors, allowing for the formation of a so called 'super-clot' (47,66). The pluripotent nature of mesenchymal stem cells carries the creative ability to formulate repair cartilage.

The mechanical properties of this tissue, otherwise known as fibro-cartilage, are very different to those of hyaline cartilage. This is attributed to variations in collagen make-up which is characterised by a predominance of collagen type I. Collagen type I is also commonly found in menisci, annulus fibrosus and at the insertion of ligaments and tendons into bone, tissues whose principle function it is to resist tension. Hyaline cartilage there against is rich in collagen type II and mainly designed to resist compressive forces.

Consequently, growing fibro-cartilage into areas previously occupied by hyaline cartilage will expose the new tissue to a mechanical environment characterised 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 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 fibro-cartilage but consist of a combination of

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*Fig. 2. — MRI (left) showing a classic osteochondritis dissecans lesion on the lateral aspect of the medial femoral condyle in a 14-year-old child. The osteochondral fragment was stabilised through cross pin fixation using biodegradable barbed arrows. Follow-up MRI obtained 12 months later (right) demonstrates osseous integration and maintenance of joint surface congruity (Author’s case).*
fibro-cartilage and hyaline-like cartilage (32). If this is true, it could suggest that such tissue may potentially carry improved mechanical properties and wear resistance compared to simple fibro-cartilage.

**Transcortical Pridie 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 Pridie of Bristol (1906-1963) in the late 1950s, following his observation that growth of fibrous tissue occurred on previously eburnised joint surfaces in response to focal breaching of the subchondral bone plate (56). Combining surface debridement with the application of numerous trans-cortical 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 (30,39,56). 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 patello-femoral joint unless an arthrotomy is performed (Fig. 3). 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 currently exists. The procedure continues to be performed for the treatment of osteonecrosis and as part of a patelloplasty when retaining the patella during total knee replacement surgery (Fig. 3) (64).

**Abrasion arthroplasty**

Introduced by Paul Magnuson of Chicago (1884-1968) in the 1940s and later popularised by Lanny Johnson of Lansing, abrasion arthroplasty was initially designed for the treatment of more widespread cartilage loss in patients suffering joint degeneration (31,39). It is often combined with lavage, removal of loose bodies, resection of unstable cartilage and partial meniscectomy and 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 fibro-cartilage repair process. The technique has shown to provide symptomatic relief in 60 to 70% of patients for periods of 3 to 5 years. The outcome is generally age dependent and best results are often observed in younger patients (57). If performed in cases of mono-compartmental disease the results of abrasion arthroplasty are more predictable and durable especially when combined with off-loading measures (e.g. off-loading osteotomy) (68).

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 is used to create several ‘golf-ball-dimple’ type indentations in the base of the defect. For larger lesions a cone shaped burr 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, as overzealous abrasion may otherwise weaken and compromise the subchondral bone plate. Fluid inflow should be interrupted and intra-articular pressure reduced.
intermittently to ascertain the level of subchondral marrow release (Fig. 4). 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 inaccessible areas such as the retro-patellar surface where microfracture is sometimes difficult to perform.

Microfracture

Based on the principles of the Pridie procedure, the technique of microfracture was popularised by Richard Steadman of Vail in the early 1990s (22,59,66). 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 infeasible. 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 (35). Best outcomes are typically achieved in younger patients with well contained, relatively small monopolar lesions of up to 4 cm², although larger and bipolar lesions may be treated with this technique but carry less predictable results. Microfracture has been shown to provide satisfactory outcome in 75% to 100% of patients (47,66,68). Most authors agree that this technique is likely to offer good pain relief for at least 3 to 5 years, whilst long-term outcome and benefits are still unknown (22,32,68).

Critical for the success is the removal of all damaged or loose cartilage fragments from the

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Fig. 5. — Surgical technique of microfracture : Creation of vertical margins and removal of the calcific cartilage layer with curette or Volkmann spoon. Perforation of subchondral bone plate with microfracture awl to facilitate mesenchymal clot formation. Awl tip should be driven perpendicularly into subchondral bone. Gradual conversion of ‘super-clot’ into fibrocartilage over a period of 8 to 12 weeks (Copyrights of illustration remain with author).
periphery of the lesion and to create healthy vertical cartilage margins to which repair tissue can bond (Fig. 5, 6). This will also help to contain the blood clot and protect the regenerating tissue 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 (47). Using an arthroscopic awl, the subchondral plate is then perforated to a depth of approximately 4 mm, starting around the periphery of the lesion working toward the centre. Microfracture holes should be kept 3 to 4 mm apart which equals 3 to 4 holes per square centimetre. Awls of 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 approximately at right angle. Typically a 30° or 45° awl is utilised for most areas and the knee should be manoeuvred in a way 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 or trough can be advantageous and will ease the introduction of sharp instruments through arthroscopy portals. Before removing the arthroscopic irrigation fluid pump pressure is reduced or the inflow stopped altogether to judge upon the adequacy of the surgical preparation. Under direct visualisation the surgeon can now observe whether marrow content (fat droplets and blood) is released in equal measures from the microfracture holes. One should be aware that this process may take several minutes and that bleeding may be slow at first. Occasionally, however, 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 drains are to be avoided as this may interfere with the formation of the ‘super-clot’.

**Autologous Matrix Induced Chondrogenesis**

Autologous matrix induced chondrogenesis (AMIC® Geistlich Pharma) is a variation to 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 in a single stage procedure (8). This membrane is placed onto the microfractured area through a mini-arthrotomy and secured with either degradable 6-0 sutures or commercially available fibrin glue. The idea is to capture the pluripotent mesenchymal cell population in the defect and to create a protected environment for cartilage regeneration. The technique bears certain theoretical advantages over standard marrow stimulation. However, clinical results for the treatment of femoral lesions have so far failed to confirm definitive supremacy over standard marrow stimulation techniques, whilst those on the retro-patellar surface have indicated more promising results (23,37).

**REPLACEMENT TECHNIQUES**

**Osteochondral autograft**

Osteochondral autograft transplantation, otherwise known as mosaicplasty, was popularised by...
Lázló Hangody of Budapest in the early 1990s (26,27). The method is based on the transfer of one or more cylindrical osteochondral plugs into the cartilage defect, providing instantaneous repair through structural reconstitution. Although the procedure is generally performed through a miniarthrotomy, smaller lesions may be amenable to be 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 itself limits this technique to areas relatively accessible, unless the surgeon is willing to expose the knee to a formal arthrotomy.

Grafts are harvested from the non-weight bearing periphery of the trochlea or inter-condylar notch and usually measure between 2.5 to 10 mm in diameter. A graft-harvester is introduced to a depth of about 12 to 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 (27). Using a sizing guide or tamp that overlaps the plug by 1-2 mm will avoid rim damage and allow the plug to be advanced further until it is flush with the surrounding articular surface.

It is critical to the success that the surgeon aims to recreate normal surface congruity, which becomes particularly problematic if several plugs are used (33). The technique is limited by the amount of donor tissue available and hence best suited for lesions of less than 4 cm². Although fibro-cartilage will grow into the donor defect within 6 to 8 weeks, donor site morbidity such as anterior knee pain has been associated with this technique (38,58). To overcome this problem some clinicians have inserted synthetic plugs (e.g. Calcium Sulfate, TruFit®) to backfill osteochondral autograft sites, hoping that this may create a more physiological repair (1).

The ideal locations for autologous osteochondral grafting are the convexities of the femoral condyles, whilst those of the patello-femoral joint and tibia with their varying surface geometries make structural grafts more difficult to fit in place (10). Clinical results have been variable especially in cases of multiple plug application, and as donor site morbidity has remained problematic, it is not surprising that enthusiasm for this technique has waned in recent years (1,38,38).

**Synthetic resorbable scaffolds**

Synthetic osteochondral scaffolds like the Trufit® plug (Smith&Nephew, Andover, USA) and the BioMatrix® Cartilage Repair Device (Arthrex, Karlsfeld, Germany) are off-the-shelf bioabsorbable cylinders engineered to mimic the composition of human bone and cartilage (20,69,70). Produced from biodegradable materials including calcium sulphate, polylactide-glycolide (PLG) and polyglycolide (PGA), their synthetic structure is designed to resorb within 6 to 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 bi-layer design of the TruFit® implant incorporates a cartilage and bone phase, each designed to provide appropriate mechanical stiffness in keeping with 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 of a porous nature that provides conduits for tissue in-growth. 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. Preclinical studies have shown restoration of hyaline-like cartilage in a goat model with subchondral bony incorporation at 12 months (51). Early clinical results have been favourable, demonstrating a good safety profile of the implant after follow-up periods of up to 3 years (5,61,69,70). Some investigators however, observed signs of surface depression, interface resorption and poor incorporation on MR scanning during the intermediate post-
operative interval (6-12 months) (Fig. 7) (1,71). These findings were thought to reflect part of the natural history of graft incorporation, as plug appearance substantially improved with longer follow-up. At 16 months Bedi and associates were able to demonstrate flush surface morphology in 70% of plugs and complete or near complete fill in 90% (5). However some concerns about the safety profile and the plugs ability to fully integrate into the host bone remain (1,71).

The technique is similar to the one described for autologous osteochondral plugs but avoids 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 fully incorporating the defect (Fig. 8, 9). 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 to 10 mm, with small adjustments to maintain perpendicularity still 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 leaving a cylindrical space behind. The length of the implant is then adjusted according to the depth of the created defect by simply cutting the bone-equivalent aspect of the plug with a knife. It is advantageous to advance the implant by 1 to 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 small 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 (70). Following the reduction of the intra-articular fluid pressure the plug will become saturated with bone marrow cells and blood, a process which may take several minutes and which should be monitored arthroscopically.

Partial re-surfacing arthroplasty

Metallic partial resurfacing implants like the HemiCap® knee implant (Arthrosurface, Franklin, Mass., USA) targeting patients typically between the ages of 40 and 60 years, who have focal condylar defects and are likely to undergo partial or total knee replacement surgery in the future. 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 arthroscopy. 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 primarily designed to

Fig. 7. — MRI scan (proton density coronal sequence) showing a full thickness cartilage defect on the medial femoral condyle (left) treated with a synthetic bioabsorbable biphasic scaffold (True-Fit® plug). Follow-up scan obtained 3 ½ months after implantation shows early signs of graft integration (middle & right) (Author’s case).
be used on medial and lateral femoral condyle (Fig. 10). Although the technique of partial surface replacement has been available for some time no comparative or medium-term out-come studies are yet available to verify its clinical performance. These implants should hence be used with utmost caution.

**CELL BASED REPAIR TECHNIQUES**

In the early 1970s George Bentley and Robert Greer were able to demonstrate the chondrogenetic potential of transplanted cartilage cells (9). This sparked the development of autologous chondrocyte implantation (ACI), considered to be one of the first forms of clinical tissue engineering (12). Two principal techniques have since evolved and it is estimated that approximately 10,000 patients have been treated with chondrocyte implantation to date (17).

The first human application of this technique was performed in 1994 by Lars Peterson and Matts Brittberg of Stockholm (12). The treatment aims at the regeneration of hyaline or hyaline-like cartilage rich in collagen type II, 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 femoral trochlea and condyles being particularly suitable (Fig. 11) (10,25,44,49,63). Data on the relative effectiveness of chondrocyte implantation compared with other cartilage repair techniques is emerging, including some longer-term
follow-up studies (4,10,28,32,34,60). Although most cartilage repair techniques provide satisfactory short-term clinical outcome making them almost indistinguishable, both microfracture and mosaic-plasty have shown to deteriorate with time, whilst chondrocyte implantation have demonstrated time dependent long-term improvements (35,41,48). Superiority regarding quality of life gain following chondrocyte implantation compared with alternative repair technologies however has yet to be established. Poor pre-operative function, previous surgical procedures, and long history of symptoms have all shown to be poor prognostic indicators (10,46). It is thus essential that these factors

Fig. 10. — Antero-posterior and lateral radiographs showing a metallic surface replacement implant (Hemi-Cap®) in situ on the weight bearing surface of the medial femoral condyle.

Fig. 11. — Intra-operative, MRI (proton density sequence) and arthroscopic images (top) showing a large uncontained osteoarticular defect on the lateral aspect of the medial femoral condyle due to end-stage osteochondritis dissecans in a 24-year-old before and after reconstructive surgery. Defect treated with debridement, bone grafting (bone graft obtained from tibial metaphysis) and matrix autologous chondrocyte implantation using a sandwich technique. MRI scan and arthroscopic image (bottom middle and right) obtained one year following surgery confirmed consolidation of bone graft and satisfactory cartilage regeneration (Author’s case).
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 clinical outcome of chondrocyte implantation techniques performed in patients following a failed cartilage repair procedure revealed inferior results when compared to those individuals where ACI was used initially (3,28,36).

**Autologous Chondrocyte Implantation (ACI)**

The technique of ACI is a two-stage procedure. 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. In acute cases however, or where there is little visual degeneration, it may be permissible to utilise loose cartilage flaps from the periphery of the lesion itself. 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 need to be kept in a designated storage box at a constant temperature of 4°C and forwarded to the processing facilities within 24 hours. The chondrocytes within the received tissue sample are then isolated and cultured in the laboratory over a period of 4 to 6 weeks. During this period the number of cells increases by 50 fold to reach approximately 10 to 20 million (12). 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 interventions. 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 should 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 prior to implantation.

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 was 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 is created though the application of commercially available fibrin glue (e.g. Tisseel® Baxter, Newbury, United Kingdom) onto the sutured margins of flap. The chondrocytes are then injected and the membrane checked for any cell leakage. The cannula is then withdrawn and the proximal opening sealed. Second generation techniques utilise off-the-shelf resorbable, cell-free collagen membranes (e.g. Chondro-Gide® Geistlich, Wolhusen, Switzerland; Restore® DePuy Orthopaedics, Warsaw, USA) (25,37). These membranes avoid graft harvesting time and donor site morbidity, and have so far shown no adverse effects on clinical outcome compared to periosteum (24,67).

The chondrocyte implant matures over a period of 18-24 months. In the *Proliferation Stage* between week 0 to 6 the tissue is soft and extremely vulnerable. This is followed by the *Transitional Stage* lasting up to 6 months, during which the tissue presents putty like consistency. The *Remodelling Stage* during which the cartilage hardens is thought to take 12 to 18 months, although some changes in matrix composition and maturation may continue 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 (24). 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 (65).
A limited number of long-term studies with up to 10 year follow-up, have confirmed good or excellent results in 82% to 92% of patients (10,13,45, 49,54). Reported complication rates were low and included superficial wound infections, postoperative haematomas, intra-articular adhesions, periosteal hypertrophy, and graft failure.

**Autologous chondrocyte scaffolds**

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 the cartilage defect. Third generation technologies have therefore been developed. They utilise the traditional method of chondrocytes culturing, but instead of injecting expanded autologous chondrocytes under a membrane, cells are seeded onto a collagen matrix which is placed directly onto the lesion (Fig. 12). As this technique is essentially ‘suture-free’, it is quicker to perform than ACi and requires a less extensile exposure. This is of particular advantage when the procedure is combined with other interventions such as ligamentous reconstruction, bone grafting, or high tibial osteotomy (63). A further advantage of this method of cell delivery is that the scaffold may act as a barrier to the invasion of fibroblasts, which may otherwise compromise the creation of hyaline cartilage by inducing fibrous repair. Several different carriers have so far emerged. Most widely used are Hyalograft®C (Anika Therapeutics, Bedford, USA), a three-dimensional matrix graft, which uses a hyaluronic acid based scaffold for the delivery of chondrocytes, Matrix Autologous Chondrocyte Implantation method (MACI® Genzyme, Cambridge, USA),
which utilises a purified and cell-free porcine collagen membrane, and Novocart® 3D (B Braun, Melsungen, Germany), a bovine based bi-phasic foam composed of collagen and chondroitin-sulphate.

Study results of these cell based 3rd generation techniques have been promising and are at least equivalent to those achieved with ACI, with reported good clinical medium-term results (32,34). Problems of graft hypertrophy, a recognised cause of morbidity of 1st generation ACI, is rarely observed when such scaffolds are utilised (3,11,24,43,67). Although repair tissue initially appears to show a mixture of hyaline and fibro-cartilage, in vitro studies have confirmed improved histomorphometric characteristics with cartilage maturation over time (21). 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 five to eight week culturing period. A week prior to the implantation date chondrocytes are seeded onto the collagen membrane, which will allow for a concentration of approximately 2 to 5 million cells per square centimetre. Surgical preparation prior to implantation is identical to the ACI technique, with emphasis placed on the creation of vertical defect edges. The membrane is correctly shaped to match the defect geometry and should not protrude beyond its margins. To best achieve this, it is recommended to create a template using foil from a suture pack which is pressed into the lesion to adopt the shape of the defect and then cut with a pair of fine scissors (Fig. 13). The everted edge of the membrane must 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 of the defect and the membrane, with the rough surface (cambium equivalent layer) facing downwards, is placed into the lesion and evenly compressed using continuous digital (thumb) pressure for 3 to 5 minutes. The graft margin interface is then secured with a minimum of fibrin sealant. In uncontained defects the use of biodegradable bone anchors and partial suture fixation may be necessary to safeguard against graft delamination. The knee is then put through a full range of motion once or twice to assess for membrane stability and impingement. Complete immobilisation in a brace or plaster of Paris for 1 to 7 days, depending on size and location of the lesion,
is generally recommended to safeguard against graft delamination in the immediate post-operative period.

**POST-OPERATIVE REHABILITATION**

Regardless of the type of cartilage repair the principles of post-operative rehabilitation measures are surprisingly similar. Key to success is the patient’s willingness to adhere to a specific rehabilitation programme in order to optimise outcome. All patients should use cold therapy and compression continually for the first 3 to 7 days and intermittently thereafter to control pain and inflammation. Non-steroidal anti-inflammatory drugs (NSAIDs) should be used with caution, especially following marrow stimulation, due to concerns that they may suppress the inflammatory response and with it cartilage regeneration.

**Following marrow stimulation & structural grafting**

Lesions in the tibio-femoral weight bearing zone should be off-loaded with limited weight bearing (5-15 lb) for 6 to 8 weeks, followed by partial weight bearing (20-30 lb) for a further 2 weeks. For well contained lesions smaller than 1 cm in diameter return to normal weight bearing may commence earlier. Some surgeons consider intermittent use of a continuous passive motion (CPM) machine for 4 to 8 hours per day beneficial, based on the understanding that it may assist in reshaping and containing the blood clot and enhancing chondrogenesis (52). The rate is usually one cycle per minute with a flexion range of 0° to 90°. If a 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 week 3 to 4 and should include gentle under water jogging and paddling with a float (16). Elastic band resistance exercises may commence at weeks 8 whilst progressive weight training should be delayed for approximately 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 to 6 months. The time frames for off loading and joint protection may be considerably reduced when structural grafts are utilised (61).

Patients with lesions in the patello-femoral joint may fully weight bear as long as knee flexion is restricted. This is best achieved by using a hinged brace, typically locked at 20° to 30° to prevent flexion beyond the point where the centre ridge of the patella engages with the trochlea groove. Similarly, any exercise regime should aim to avoid patello-femoral compression for about 3 to 4 months. Braces may be discarded after 6 to 8 weeks, when progressive strength training can be commenced upon.

**Following cell based cartilage repair**

Most protocols recommend a short period of complete immobilisation in a brace or cylinder cast for 1 to 7 days, followed by CPM (52). The post-operative treatment is broadly similar to the measures mentioned above whilst time periods are generally extended. Joint compression in the treated area is to be avoided for 8 to 12 weeks, whilst physiotherapy should focus on maintaining muscle function and joint flexibility (16). Hydrotherapy, including underwater jogging, has proved to be very popular at this stage. The use of a walking stick or walking poles might be advisable in the transitional period, particularly if the patient is ambulating outside the home environment. 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 to 9 months the activity level may be stepped-up introducing rowing, cross-trainer and gentle weight training. Cutting, twisting and turning activities are usually avoided until the surgeon is satisfied with the progress and confident that the cartilage graft has taken. Most surgeons verify cartilage integrity by obtaining MRI scans at 6-12 months (55). Second-look arthroscopies are rarely necessary with modern techniques unless significant mechanical symptoms develop, especially if associated with pain. Return to full level sporting activities is not desirable much before 12 to 18 months following surgery. A review of 1363 patients treated with
different surgical techniques revealed that continued sports participation at pre-injury level was possible in 65%, with the best durability being achieved after chondrocyte implantation (48).

CONCLUSION

The desire to overcome the inability of cartilage to provide a self-healing response following injury has engaged scientific minds over the past decades and has led to the emergence of various cartilage repair technologies. These may be classified into palliative (e.g. debridement), reparative (e.g. marrow stimulation) and restorative (e.g. chondrocyte implantation) procedures. The choice of treatment, which may best suit the patient, is dependent on a number of variables and pertain to those relating to the patient (e.g. biological age, physical demands) and the defect (e.g. response to previous surgery, location, size). A blanket approach should hence be avoided and treatment of cartilage lesions individualised. Currently available surgical procedures have enabled us to provide a satisfactory solution to a problem whose natural history would otherwise suggest the development of progressive joint degeneration if left untreated. The technical application of these measures can be difficult and require not only an understanding of root causes and cartilage biology but a high level of surgical finesse and the application of appropriate post-operative measures in order to achieve the desired out-come.

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