REVIEW ARTICLE

Treatment of knee cartilage defect in 2010

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Accepted: 16 August 2011

KEYWORDS
Knee;
Cartilage;
Osteochondritis;
Mosaicplasty;
Autologous chondrocyte culture;
Allograft

Summary  Treatment of knee cartilage defect, a true challenge, should not only reconstruct hyaline cartilage on a long-term basis, but also be able to prevent osteoarthritis. Osteochondral knee lesions occur in either traumatic lesions or in osteochondritis dissecans (OCD). These lesions can involve all the articular surfaces of the knee in its three compartments. In principle, this review article covers symptomatic ICRS grade C or D lesions, depth III and IV, excluding management of superficial lesions, asymptomatic lesions that are often discovered unexpectedly, and kissing lesions, which arise prior to or during osteoarthritis. For clarity sake, the international classifications used are reviewed, for both functional assessment (ICRS and functional IKDC for osteochondral fractures, Hughston for osteochondritis) and morphological lesion evaluations (the ICRS macroscopic evaluation for fractures, the Bedouelle or SOFCOT for osteochondritis, and MOCART for MRI). The therapeutic armamentarium to treat these lesions is vast, but accessibility varies greatly depending on the country and the legislation in effect. Many comparative studies have been conducted, but they are rarely of high scientific quality; the center effect is nearly constant because patients are often referred to certain centers for an expert opinion. The indications defined herein use algorithms that take into account the size of the cartilage defect and the patient’s functional needs for cases of fracture and the vitality, stability, and size of the fragment for cases of osteochondritis dissecans. Fractures measuring less than 2 cm\textsuperscript{2} are treated with either microfracturing or mosaic osteochondral grafting, between 2 and 4 cm\textsuperscript{2} with microfractures covered with a membrane or a culture of second- or third-generation chondrocytes, and beyond this size, giant lesions are subject to an exceptional allografting procedure, harvesting from the posterior condyle, or chondrocyte culture on a 3D matrix to restore volume. Cases of stable osteochondritis dissecans with closed articular cartilage can be simply monitored or treated with perforation in cases of questionable vitality. Cases of open joint cartilage are treated with a PLUS fixation if their vitality is preserved; if not, they are treated comparably to osteochondral fractures, with the type of filling depending on the defect size.

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doi:10.1016/j.otsr.2011.09.007
Introduction

Cartilage tissue has mechanical properties that allow movement of the joint surfaces, by combining absorption of stresses, low friction, and high resistance to wear. Despite its mechanical performance, cartilage tissue lacks blood and nerve vessels: the cells are supplied by diffusion through the extracellular matrix. This all suggests that in a complex mechanical context, the low metabolic activity of cartilage tissue protects it from excessive physical stresses. However, vascular paucity results in cartilaginous lesions having a low spontaneous repair potential. Development of surgical techniques is in full expansion with the major challenge of hyaline cartilage reconstruction on a bone base, the only long-lasting and viable solution for cartilage lesions. This is the therapeutic challenge for the coming decades.

Lesion assessment

Three factors are used to assess the initial cartilage lesion: the patient’s clinical status and the lesion’s size and type. The indication for management is based on the deterioration of the functional status measured by pain and functional limitation; these criteria are validated by a number of clinical scores [1]. The most frequently used functional scores are the International Cartilage Repair Society (ICRS) score, the International Knee Documentation Committee (IKDC) functional score, and the Hughston score. The ICRS is a validated score used to evaluate the repair of cartilage lesions, to evaluate the functional status (normal, nearly normal, abnormal, and severely abnormal), to compare the injured side with the healthy side (as a percentage of the healthy side), to evaluate pain using an analog pain scale, and to classify the sports level from normal to severely abnormal [2]. The functional IKDC has not been specifically validated for cartilage lesions, but it is a frequently used score. It evaluates, from 0 to 100, the level of activity with no pain, stiffness, effusion, locking, the patient’s sports activities, and the knee’s optimal functioning. The functional IKDC is completed by the physical IKDC, which assesses intra-articular effusion, loss of range of motion, ligament laxity, joint cracking (crepitus), disease related to grafting sites, and hopping on one foot. It is also used to analyze radiographic images. Each group of clinical and radiographic criteria is classified in grades: normal, nearly normal, normal, and severely abnormal. A final grade is given to the patient corresponding to the lowest grade [3,4]. The Hughston score is more specifically used by pediatric orthopaedic physicians and was designed to assess the treatment of osteochondritis lesions in children [5,6]. It classifies patients into five clinical categories from failure to an excellent clinical result (Table 1).

Table 1: Hughston Score.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Score</th>
<th>Functional Status</th>
</tr>
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<tbody>
<tr>
<td>Excellent</td>
<td>4</td>
<td>Normal sports activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No functional symptom</td>
</tr>
<tr>
<td>Good</td>
<td>3</td>
<td>Normal clinical examination</td>
</tr>
<tr>
<td>Fair</td>
<td>2</td>
<td>Pain on intense activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal clinical examination</td>
</tr>
<tr>
<td>Poor</td>
<td>1</td>
<td>Pain and hydrarthrosis if moderate activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal clinical examination</td>
</tr>
<tr>
<td>Failure</td>
<td>0</td>
<td>Loss of flexion less than 20°</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cessation of sports activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pain and hydrarthrosis in daily activities</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Loss of flexion greater than 20°</td>
</tr>
</tbody>
</table>

According to the ICRS guidelines, the seat of the lesion is represented by identifying the location of the cartilage involvement on drawings of the articular surfaces: a lateral view of the knee, an AP view in perspective of the femur, a superior view of the tibia in perspective, and an inferior view of the patella in perspective. There are four specific radiographic classifications for osteochondritis lesions in children (OCD). Two locate the lesions on the AP and lateral images of the knee: the Cahill and Berg [7], (Fig. 1) and Harding [8], (Fig. 2) classifications. The two other classifications evaluate the radiological signs of OCD, classifying lesions into four pathological stages: the Bedouelle [9] and Hughston et al. classifications [6].

Bedouelle classification:

- stage 1: clearly incomplete well-defined image (Ia) with more or fewer calcifications within (Ib);
- stage 2: presence of a nodule (Iia) with more or less shrinkage of the nodule in relation to the condyle (Iib);
- stage 3: sleigh-bell aspect;
- stage 4: free fragment in the joint with an empty with an empty bed.

Hughston et al. classification:

- stage 0: osteoarthritis, or impingement of the joint space greater than 50%;
Figure 1  Diagram: Cahill and Berg classification. Zone 1: medial condyle (internal half). Zone 2: medial condyle (external half). Zone 3: femoral notch. Zone 4: lateral condyle (internal half). Zone 5: lateral condyle (external half).

- stage 1: condyle irregularities, impingement of the joint space less than 50%;
- stage 2: condyle flattening;
- stage 3: healing zone with defect or sclerosis;
- stage 4: normal radiographic image.

The ICRS recommends MRI for the diagnosis and evaluation of cartilage lesion repairs, a noninvasive, reproducible exam that, when done well, is precise and informative. In the literature, there is consensus on advising two sequences that are simple to perform: the fast spin-echo (FSE) T2-weighted sequence, which shows effusion, bone edema, and alteration of the cartilage surface, and the 3D GRE T1-weighted sequence, which reveals alterations in cartilage thickness and provides very precise information on the subchondral bone. These two sequences are used to determine the lesion’s ICRS grade. To evaluate cartilage repair, the MOCART score[10,11] is used, which is based on nine criteria: filling at the edges (lateral integration), condition of the surface (lamina splendens), homogeneity of the structure, type of signal on the FSE T2-weighted sequence, type of signal on the 3D GRE FS sequence, presence of a subchondral radiolucent line, examination of the subchondral bone, presence of adherences and visualization of effusion.

Current therapeutic methods

The therapeutic tools aim to fill the cartilage loss so as to restore joint congruence, if possible to induce hyaline healing and thus prevent long-term osteoarthritic degeneration. They can be classified into subchondral stimulation repair methods, most frequently resulting in a fibrous scar (microfracturing, Pridie drilling, and abrasion), reconstruction methods contributing mature cartilage to the osteochondral unit (mosaicplasty and osteochondral allografting for massive chondral defects), and regeneration through grafting autologous chondrocyte cells aiming for hyaline repair. Nevertheless, the follow-up biopsies are often disappointing, with hyaline cartilage frequently absent even in very costly regeneration using cell culture implantation techniques.

Microfracturing

Microfracturing is a reference repair technique to which the international literature compares all emerging techniques. Initially described by Richard Steadman et al.[12] and first reported in 1997 [13], microfracturing should not be confused with Pridie drilling with a motorized drill and bit, even if this technique is widely used in France with identical histological and tissue objectives.

The principle of this technique is to obtain healing of the cartilage defect with mesenchymal stem cells contained in subchondral bone that will colonize a fibrous clot favoring creation of substitution cartilage. The technique initially described by Steadman et al. [13] consisted in débridement of the lesion’s edges, delicate ablation of the calcified plaque, or ‘’‘tidemark,’’ and then drilling microfractures to the vascularized subchondral area. These microfractures are made with a thin square nail or, better yet, with angulated punches every 3–4 mm and 3–4 mm deep. Bleeding should be present, clearly visible without or upon removing the tourniquet (Fig. 3). This bleeding will induce the creation of
a superclot, colonized by multipotent stem cells, platelets, and growth factors. After multiplication and dedifferentiation of the mesenchymal cells in this clot, a substitution filling tissue appears, which is for the most part fibrocartilaginous with type I collagen. Naturally, the properties of the fibrocartilage are different, inevitably leading to deterioration and raising the question of maintaining the results over the long term.

Even though the microfracturing technique has never been assessed in France, a survey on practices conducted by the French Arthroscopy Society (Société Française d’Arthroscopie) showed that microfracturing is only used by one-third of the surgeons who treat cartilage lesions, the majority preferring mosaicplasty and the Pridie drilling technique.

In the literature, four level 1 studies [14—17] showed that the results of microfracturing are quite good, comparable to chondrocyte culture grafting, less effective than mosaicplasty. However, the follow-up period in these studies was short. A recent powerful meta-analysis carried out by Milhoefler et al. [18] combined 28 studies with a total of 3122 patients with a mean follow-up of 41 months. It concluded that microfracturing gives good early results for good filling of cartilage defects but with fibrous tissue, explaining the secondary deterioration beginning at 2 years of follow-up. This regression is even more frequent in that the study reporting these microfracturing results has a high level of evidence and that the patients studied were very active. This technique seems to have a negative influence on secondary chondrocyte culture for cases of failure, contrary to generally accepted notions.

In conclusion, this technique currently used in all of the randomized comparative studies, except in France, is simple, can be done with arthroscopy throughout the knee, is economical, and provides good initial results. Since it produces fibrocartilage, the results deteriorate over time. It is particularly indicated for patients with a low functional demand and for lesions discovered accidentally that measure less than 4 cm².

PLUS microfracturing

This is a more recent technique whose principle is microfracturing covered by a protective membrane (periosteum or synthetic matrix). Based on the research of Breinan et al. [19,20], Behrens et al. [21], and Jakob since 2003 have developed the AMIC (autologous matrix-induced chondrogenesis) technique consisting of covering a microfracture with a collagen (I/III) membrane: the Chondro-Gide® (Fig. 4A, B). The matrix can be glued in the cartilage loss area with biological glue, with the porous side of the matrix remaining in contact with the bone surface or sutured with resorbable sutures like first-generation chondrocyte cultures. As shown by Dickhut et al., the matrix allows chondrogenic differentiation of human stem cells in vitro [22] but also the deposit of proteoglycans. This technique has a number of advantages: a procedure performed in a single intervention, low risk of hemarthrosis, protection and stabilization of the fibrous clot, absence of a donor site, and a moderate price (the price of the matrix), with no costly cell culture. Deep osteochondritis-type lesions are treated with a complement to AMIC based on a grafting technique of cancellous bone enriched with platelet-rich plasma [23]. Gille et al. [24] and Pascarella et al. [25] have reported the results of their experience, showing significant improvement in function in level 4 studies. In a series of 19 cases with a mean follow-up of 24 months, Pascarella et al. obtained 78% satisfied patients with an IKDC score improving from 30 to 83. Gille and Behrens reported a series of 32 lesions in 26 patients with a mean 36 months of follow-up: 87% of the patients seen again were satisfied, but the ICRS decreased with time, going from 31 to 59 at 12 months, 68 at 24 months, 54 at 36 months, and 37 at 48 months, a regression similar to simple microfracturing, even though this decrease in the score was not statistically significant. Benthien and Behrens [26] reported on its advantages in the treatment of patellar lesions. A recently reported small series studied by
Verdonk’s team [27] challenges the value of this technique because of the absence of signs of repair on MRI and particularly the early appearance of osteophytes in three cases out of five, despite early favorable clinical results.

3D acellular scaffolds

Three-dimensional scaffolding is an acellular filling substitute made up of multilayered biomimetics (Fig. 5; Maioregen®) alternating layers of type I collagen and layers of collagen and calcium hydroxyapatite in variable proportions. This technique, used notably at the Rizzoli Institute [28], has the major advantages of filling osteochondral loss with matrix while forgoing autologous chondrocyte culture, all within a single operation. Different cellular recruitment exists at each layer of this matrix placed on a freshened and bleeding background. The preliminary results of this new and simple method [28] are encouraging at the very short follow-up time of 6 months, showing stability and then resorption of the implant and complete filling of the defect both macroscopically and with MRI, as well as functional improvement. Histologically, no ossification has been observed; however, a mixed tissue is maturing. Clinical, morphological, and histological assessment is therefore necessary over a longer time span.

Mosaicplasty

This technique was created and then developed further by Laszlo Hangody based on an animal study on the horse begun in 1992. This widespread technique, the reference in France, has been the subject of two multicenter studies among the SFA members detailing the indications and the results at the medium term.

This demanding technique consists in a transfer of an anatomic and functional osteochondral unit harvested on the knee presenting an osteochondral lesion in a single open operation or under arthroscopy (Fig. 6A and B). The graft made is comparable on the macroscopic level to laying cobblestones, allowing the surgeon to obtain bone integration, the presence of hyaline cartilage on the pegs, but a fibrous cartilage interface. Over the short term, the mosaic graft is a validated cartilage restoration technique [29]. Different studies have taken an interest in the harvest site. In 2005, Garretson et al. demonstrated that the optimal and less restrictive site was the edges of the superomedial trochlea. As for the size and number of pegs, in a teaching session Robert [30] detailed the respective advantages of small and large pegs. The large pegs provide greater stability, less substantial fibrous interpositions, and a greater cartilage surface, at the cost of more difficult filling in cases needing multiple pegs and of probable greater morbidity with harvesting. Sgaglione [31] recommends 6- to 8-mm-wide pegs between 15 and 20 mm long. With time, a tendency to use increasingly large pegs has been observed. This harvesting comes with a certain morbidity, estimated at 0—36% in the literature [32, 33]. Following harvesting on a healthy knee for talar lesions, Reddy et al. [32] reported four painful knees out of 11 at 4 years of follow-up. On the other hand, Iwasaki et al. [33, 34] reported no complications of harvesting for humeral lesions at 2 years of follow-up. In a heterogeneous retrospective study on more than 1000 mosaic grafts, Hangody et al. [35] reported 3% morbidity with four infections and 36 cases of hemarthrosis. They also evaluated the role played by the location of the lesion, finding a positive influence of medial condylar lesions with 92% good and very good results compared to 87% for lateral condylar lesions and 79% for patellofemoral lesions.

The utility of MRI assessment is recognized by all, particularly when using ICRS sequences and the MOCART score. At 9 years of follow-up, Tetta et al. [36] studied 24 patients treated with mosaicplasty, with complete integration of the graft in 75% of the cases, correlated with the MOCART score. From the point of view of the overall result, the good and very good results reported in the literature range from 72 to 92% at more than 8 years of follow-up. The factors for the best prognosis are usually found for lesions located on the medial condyle, osteochondritis desiccans, deep, small lesions, and the shortest time to surgery possible. Large lesions have the least favorable prognosis. No correlation has been found between the size of the harvested tissue and the MOCART score.

Figure 6  A. Open mosaicplasty. B. Arthroscopic mosaicplasty.
and the development of patellofemoral osteoarthritis, often at its beginnings and only radiologically visible: 13% at a mean follow-up of 8 years for the SFA and 3% for Hangody et al. [35]. Mosaic grafting therefore seems to be a reliable technique at the short and long term. Much less expensive than the regenerative techniques, performed in a single surgical step, and providing immediate restoration of the cartilaginous surface while treating the entire osteochondral unit, mosaicplasty nevertheless remains a difficult, demanding technique not without complications. The limitation of the technique matches the size of the lesion to treat. The choice indication is a deep and small (less than 2 cm²) lesion located on the medial condyle. Beyond 2 cm², Imhoff’s team [37,38] has used 20- or 35-mm-diameter autologous grafting performed at the expense of the homolateral posterior condyle using the Mega OA TS® ancillary instrumentation (Fig. 7). The largest series reported 33 cases operated for condylar lesions that were a mean 6.2 cm² reviewed with a mean follow-up of 66 months. Thirty-one of the 33 patients had significantly improved and were willing to undergo the operation again.

Osteochondral grafting for massive chondral defects

The first use of osteochondral grafting for massive chondral defects dates from Lexer’s work in 1908. The technique consists in using a fresh or frozen epiphyseal osteochondral allograft placed in an area of voluminous osteochondral loss prepared by drilling. The graft can be positioned with press-fit technology or fixed with buried screw fixation (Fig. 8). This technique is reserved for substantial cartilage loss, usually more than 4 cm², a truly salvage treatment. Several series have reported satisfactory results in more than 75% of cases with a mean follow-up of 10 years [39–41]. These results seem less good with longer follow-up periods, decreasing from 95% at 5 years of follow-up to 66% at 20 years of follow-up [42,43]. Screw fixation seems to give better results (94% good results), improving bone fixation [44]. Jamali et al. [45] reported less satisfactory results on the knee with the appearance of signs of early patellofemoral osteoarthritis in half the cases. On the tibia, a series of post-traumatic lesions of the tibial plateau reported favorable results in 67% over the long term, comparable to femoral allografts, with failures appearing during arthroplasty. Preoperative joint impingement is a poor prognostic factor, as is allografting on kissing lesions [40].

Nonetheless, since this technique has rarely been used, no level 1 or 2 study can be found in the literature. Those available are retrospective studies with expert opinion. This technique requires a certified tissue bank and the cost is high. Yet recuperation of posterior condyle in bone banks could facilitate the dissemination of this technique.

Autologous chondrocyte culture grafting

First-generation grafts

Widely developed, used and disseminated by Lars Peterson and Matts Brittberg’s [46] Swedish school and then by Tom Minas, the principle involves placing within the trimmed and bloodless defect a culture of autologous chondrocytes that have undergone in vitro multiplication in the laboratory, implanted under a patch of periosteum harvested locally from the tibia and sutured to the edges of the cartilage loss before impermeabilization with biological glue (Fig. 9). Cell multiplication and maturation should occur and fill the defect with hyaline cartilage. This is an expensive technique, whose results remain controversial, in particular in comparative studies with mosaicplasty [47] and even microfracturing by Knutsen et al. [16]. Results have been published by a number of authors, including Brittberg and Peterson, who published the long-term results of this technique [48,49]; the histological results were not always consistent [15,47]. The results are reported for the most part on Swedish series in which the early follow-up includes few patients lost to follow-up. Biopsies were performed with confirmation of the hyaline-like phenotype. Micheli
et al. [50] reported a series of 50 patients with a minimum follow-up of 36 months, noting that a 5-point increase in the modified Cincinnati score; 84% of the patients had increased function, 2% remained the same, and 13% declared that their function had deteriorated. Peterson et al. [51] published their results on 94 patients with follow-up between 2 and 9 years. The results varied depending on the location of the defects: for the patella, the results were good in 62% of the cases and increased to 85% if medialization of the anterior tibial tuberosity was associated. For the condylar lesions, 92% good results have been announced. Biopsies show hyaline-like tissue with type II collagen in immunohistochemistry. In 10–15% of the cases, biopsies showed an exaggerated response. At the medium term, Peterson et al. [51] reported a series of 61 patients with a mean follow-up of 7.4 years. The good results were stable over time: 81% at 2 years and 83% between 5 and 11 years of follow-up. The failure rate was 16% and appeared in the first 2 years. Cole and Lee [52] reported a series of 103 cases of cartilage loss in 83 patients evaluated with the Cincinnati, IKDC, Tegner, Lysholm, and SF-12 scores. All the scores improved significantly in 30 patients with a minimum follow-up of 2 years; 79.3% of the patients declared they had improved.

Recently, Peterson et al. [53] reported the long-term results of the first 341 cases in a level 4 study (retrospective study with one-third lost to follow-up), with a mean follow-up of 12.8 years and for lesions that measured a mean 5.3 cm² in size. Seventy-four percent of the patients continued to improve beyond the 10th year and 92% were satisfied and willing to undergo the same operation if necessary. Although the initial presence of a kissing lesion worsened the long-term results, meniscectomy, age at the time of surgery, and the lesion size did not influence the results at the longest follow-up. From and medical-economic perspective, autologous chondrocyte cultures are much costlier than prostheses, and for the moment the benefit in terms of osteoarthritis prevention remains uncertain. A number of comparative studies of simple and inexpensive repair techniques such as microfracturing [16] and mosaicplasty [15,54–56] have not demonstrated the superiority of cellular cultures. Only Bentley et al. [56] found that first-generation chondrocyte grafting was better. This study examined more voluminous lesions up to 12.2 cm² and the mosaic grafting technique used small-diameter samples.

Second-generation grafting
To prevent the problems related to the periosteum patch (ossification, detachment, calcifications, leakage), matrices have been developed serving as artificial membranes. These matrices can be synthetic (carbone, polylactic or polyglycolic acid, or dacyrilen), proteic (collagen, fibrin, gelatin), or polysaccharid (alginate, agarose, hyaluronic acid). Particularly advantageous, hyaluronic acid, an extracellular matrix homeostasis drug, acts by its interaction with CD44 and ICAM 1. It also fights against chondrocyte apoptosis, oxidative stress, inhibits the catabolic interleukin IL-1 according to Fukuda, and produces metalloproteases according to Juvoli. Its chondrogenic effect occurs in stimulating differentiation, regulating the matrix structure during chondrogenesis, and influencing cellular mobility, differentiation, and development.

As early as 2002, Saris et al. [57] developed the culture of chondrocytes selected for the presence of markers of preservation of the phenotypic characteristics required for differentiation and maturation to obtain hyalin cartilage [58], a culture that is injected on a membrane (Chondroselect®) during surgery. This cell therapy can establish a "chondrogenic potential score" for the culture implanted. In a highly rigorous level 1 study comparing 57 cases undergoing this technique (Fig. 10) with 61 patients treated with microfracturing, Saris showed a significant difference in favor of chondrocyte implantation at 3 years of follow-up, both clinically using both the Knee injury and

Figure 9  Cell culture of chondrocytes with periosteal patch.

Figure 10  Chondroselect® technique (second-generation ACI).
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Osteoarthritis Outcome Score (KOOS) and the MOCART score on MRI, with 83% good results versus 62%. The best results were observed for lesions treated early and when the culture implanted had a better “chondrogenic potential score,” which argues in favor of continuing the research in this technique of improving cell therapy.

Third-generation chondrocyte grafting

These more recent techniques are still being evaluated. Their principle is culturing chondrocytes in an implantable biological matrix with ideal properties: biocompatible, biodegradable, and bioactive while preserving the phenotypic characteristics, thus favoring the cellular proliferation and synthesis of the extracellular matrix, which is permeable, easy to use, and inexpensive. Here again hyaluronic acid is often used. Beginning in 2002, Marcacci et al. [59] developed a chondrocyte culture termed “third generation,” on a matrix of esterified hyaluronic acid, Hyalograft C®; this matrix can be superimposed in several layers using a so-called mushroom technique (Fig. 11), thus filling deep cartilage loss in several thicknesses. This technique is also currently used by Brittberg. This procedure has three phases: first arthroscopic with débridement and chondrocyte harvesting, second classical cell culturing for approximately 3 weeks in presence of the matrix to obtain at least 4 million chondrocytes/cm² in presence of growth factors (TGF, BMP, IGF) and stabilizers; and third, surgery (patella) or arthroscopy (tibia, femur) for débridement, placing biological glue, and 3D cell implantation, possibly stacking several layers. Preliminary results have been reported by the precursors [60,61]. Clinical evaluation has reported no level 1 or 2 studies to date, and one level 3 non-randomized prospective study [28] with, at a mean 5 years of follow-up, a significant improvement in clinical scores, with a functional IKDC score improving from 39 to 80, and an MRI evaluation using the MOCART score showing integration of the graft in 60% of the cases. Nevertheless, the series of patients was very inhomogeneous, with half of this small series originating from relevant associated ligament or meniscus repair. From a histological perspective, 55% of the biopsies found hyaline cartilage, 18% mixed cartilage, and 27% fibrocartilage. These results seem to be improved over time with 83% hyaline cartilage beyond 18 months [62], showing the need for a long-term study of this technique.

In a level 2 study, Zeifang et al. [63] found no significant difference between first-generation chondrocyte grafting with a periosteum patch and third-generation chondrocyte grafting in a matrix foundation, with certain clinical results at 2 years of follow-up even favoring the oldest technique.

In three-dimensional regeneration methods, the Cartipatch®, from the TBF laboratory developed and assessed in France, seems to give results that are comparable with an algarose and alginate matrix (Fig. 12) during a phase II study (subjective IKDC score increasing from 36 to 85 at 18 months of follow-up), which needs to be confirmed in an upcoming prospective, randomized multicenter phase III study [64].

Surgical indications

The ideal patient who may have the best result is a patient who is less than 50 years of age, for biological and cellular reasons, but also because of lower eligibility in terms of indication for arthroplasty. The discomfort must be severe and resistant to well-conducted medical treatment. The knee must be stable, with a favorable axis, i.e., unloading the

Figure 11  Brittberg mushroom technique.

Figure 12  Culture with Cartipatch® culture.

Figure 13  Aspect of a patellar cartilaginous lesion in T2 mapping.
lesion, with no morbid obesity (BMI < 30). Smoking is unfavorable for bone healing and therefore unfavorable for deep lesions, but nothing in the literature proves that this holds true for cartilage, which is avascular. The lesion to treat must be deep (ICRS grade 3 or 4) on a single surface, and kissing lesions should not be treated surgically. The lesion’s size must be large enough, greater than 0.5 cm², without it being possible to define a maximum size, with occasionally indications for salvage surgery. We emphasize that in all cases this is not surgery for osteoarthritis. The absolute contraindications that have been recognized are obesity, joint impingement, and inflammatory diseases; others are relative because they can be dealt with at the same time, particularly for procedures in a single operation (microfracturing and mosaicplasty) or before cartilage treatment: ligament laxity stemming from ligament reconstruction, axis defect to be treated with osteotomy and weight loss. Many authors advocate nearly systematic realignment osteotomy. Previous meniscectomy does not compromise the result. However, early treatment should be pursued. Beyond clinical evaluation, MRI is now the reference examination with ICRS sequences (2D or 3D FSE T2 FS and 3D GRE T1 FS), which allow calculation of the MOCART score. In the future, T2 mapping (Fig. 13), which analyzes the deterioration of collagen fibers, will allow routine, more precise cartilage assessment. Arthroscopy can be part of the workup, notably if chondrocyte grafting is planned.

The available armamentarium is rich, but is not accessible to everyone, particularly in France where legislation is
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unfavorable to research. Palliative repair procedures using subchondral stimulation produce filling with fibrocartilage and are easy to perform under arthroscopic guidance. Practical in all the compartments of the knee, for lesions measuring less than 4 cm², these procedures give good early results, but they deteriorate over time. Several authors have reported their unfavorable effect in cases of secondary grafting, contrary to certain widely held beliefs. More recently, subchondral bone stimulation procedures have been associated with covering with a membrane or a 3D multilayer substitute, providing better filling and therefore better results. These PLUS microfractures provide good short-term results, but require long-term assessment compared to the much more expensive cell culture techniques. Mosaicplasty is part of the reconstruction techniques, bringing mature cartilage to the osteochondral unit. This is a highly demanding technique that can be done with arthroscopic guidance for a maximum of two or three pegs, or otherwise with arthroscopy. All authors agree to indicate this procedure for lesions measuring at least 2 cm², particularly for the condyles, providing 75–90% good and very good results at medium and long terms, sometimes with problems of hyaline cartilage integration. Autologous chondrocyte culture grafting has greatly progressed in the past 10 years, evolving from culture under a periosteum patch to third-generation matrices, particularly for solving the problem of filling and immediate congruence. This technique is indicated for lesions that are larger than 2 cm². However, two sizeable problems persist: cost (equivalent to at least five TKA procedures) and particularly the need for in situ alchemy, not yet sufficiently under control, but nonetheless indispensable to maturation. Although the clinical results are good and long-lasting, hyaline cartilage does not always appear. This is where the importance of research in multilayer molecular surfaces and cell selection in cultures becomes all important.

Finally, salvage procedures can turn to chondrocyte culture, but particularly to autografting procedures, an easy but expensive technique for the countries that have this available. These allografts (Fig. 14) are reserved for cases of substantial cartilage defect — greater than 4 cm² — and give good results, even though no prospective series has been reported. Other than viral transmission, bone integration remains a problem. The therapeutic choice should take several factors into account: the type of lesion (OCD or chondral fracture), location, size, depth, patient age, desired level of activity, morphotype, and finally the armamentarium available.

Overall, for cases of osteochondritis (Fig. 15), we follow the SoFCOT recommendations. When the joint cartilage is closed (SoFCOT stage I), perforation in cases of questionable vitality of the nodule on MRI will give greater certainty and satisfaction compared to screw fixation (Fig. 16). If the cartilage is open (stage II), the lesion is unstable, and the PLUS fixation proposed by Bernard Moyen, will provide a good success rate, associating revascularization through freshening of the bed and possibly mixed fixation as performed by Beaufils (Fig. 17). When the bed is empty (stage III), simple ablation of the free loose body (LB) outside the nonloadbearing areas should be abandoned; this incongruence (Fig. 18) will lead to early osteoarthritis. Filling should be preferred, with the choice depending on the size of the bed. Under 2 cm², mosaicplasty gives reliable results, particularly if the pegs are supported by an interpeg graft: between 2 and 4 cm², third-generation chondrocyte grafting is the best choice, and beyond this condylar mega-OATS® or allografting.
Adult OC fracture
ICRS 3 or 4, ICRS grade 3 or 4

For osteochondral fractures (Fig. 19), the decision will depend on the size and the patient’s activity. Mosaicplasty is a choice treatment for lesions less than 2 cm², and in the future, depending on the results, PLUS microfracturing may occupy an important place. Larger lesions are the domain of chondrocyte grafting. Finally, lesions greater than 4 cm² will be treated with either chondrocyte grafting or allograft, or mega-OATS®, with results that have not undergone as extensive scientific assessment, therefore making them less reliable. As for the choice according to the patient’s activity level, the current trend is to propose regeneration techniques to young and active patients and other repair or reconstruction techniques to less active patients.

Tibial lesions are rare. Small (less than 1 cm²) lesions accessible with the alignment guide Fig. 20) are treated with retrograde mosaicplasty, which according to Hangody provides 87% good results. Larger tibial lesions are preferentially treated with microfracturing, matrix, or 3D chondrocyte culture, but here also there has not yet been sufficient follow-up and numbers of patients for reliable results.

In 2010, trochlear-patellar lesions continue to have a poor prognosis (respectively 55% and 79% ICRS A and B in the SFA 2010 and Hangody series). Small lesions are treated with a few mosaicplasty pegs, with mediocre results: 55–75% good results [30,35]. If microfracturing is chosen here, the results are comparable. Recent articles advocate nearly
systematic realignment of the extensor system at the same time as chondrocyte grafting. Without being extremist, with these infrequent lesions (8% of the SFA series) we propose an à la carte menu depending on the usual lesions of this pathology, modifying the alignment and/or the patellar height in cases of objective instability.

Conclusions

Each osteochondral lesion of the knee is an entity in itself. Surgical management will be proposed only if the patient is symptomatic (ICRS C and D), if the lesion is deep (ICRS stage III and IV), respecting the surgical contraindications, in particular morbid obesity, axis defects, laxity, and especially osteoarthritis, which is an absolute contraindication.

The preoperative workup should be well documented: clinically according to the ICRS 2000 and morphologically on MRI with ICRS sequences for the MOCART score, well known to referent radiologists. Validated indications must be used and one must remain cautious with the emerging techniques that have not been fully validated. The established algorithms are based on the literature results and also depend on local accessibility of the different techniques.

In France, mosaicplasty is the reference technique that can treat the majority of lesions. It is a delicate technique to learn. Chondrocyte grafting should be reserved for lesions larger than 2 cm². As for isolated microfracturing, they retain their utility for patients who require a low level of functioning.

Disclosure of interest

The authors have not supplied their declaration of conflict of interest.

Acknowledgements

Acknowledgements to members of the SFA symposium: Charles Casin (Angers), Franck Chotel (Lyon-Bron pédiatrie), Guillaume Greffe (CH Lyon-Sud), David Jones (Toulouse), Benoît Lebel (CHU Caen), Elvire Servien (CHU Lyon Nord), Laurence Mainard-Simard (CHU Nancy), Didier Ollat (HIA Bégin), Mathieu Taunat (CH Versailles), and Thomas Williams (CHU Brest).

With the participation of: Fabrice Bazile (HIA Bégin), Philippe Boisrenoult (CH Versailles), Christophe Hulet (CHU Caen), Christophe Lecoq (Aubagne), Alain Mandrin (Nice), Numa Mercier (CHU Sud Grenoble), Bernard Moyen (CH Lyon-Sud), Stéphane Plaweski (CHU Sud Grenoble), Jean-François Potel (Toulouse), Henri Robert (CH Mayenne), and Cyril Mayer (CHU Lyon Nord).

References

[20] Howard A, Breinan, Scott D. Martin, Hu-Ping Hsu, and Myron

[21] Behrens P. Bitter T, Kurz B, Russiles M. Matrix-associated autolo-

gous chondrocyte transplantation/implantation (MAct/MACI),

stem cells by local transforming growth factor-beta delivery

with one step matrix-assisted technique enhanced by autolo-
gous concentrated bone marrow: in vitro characterisation of
mesenchymal stem cells from iliac crest and subchondral bone.

Chondrogenesis for treatment of focal cartilage
defects in the knee. Knee Surg Sports Traumatol Arthrosc

[25] Pascarella A, Ciatti R, Pascarella F, Latte C, Di Salvatore MG,
Liguori L, et al. Treatment of articular cartilage lesions of
the knee joint using a modified AMIC technique. Knee Surg Sports

[26] Bentlijen JP, Behrens P. Autologous matrix-induced chondroge-
nesis (AMIC) A one-step procedure for retropatellar articular

Autologous matrix-induced chondrogenesis combined with
platelet-rich plasma gel: technical description and a five
pilot patients report. Knee Surg Sports Traumatol Arthrosc
2011;19:536–42.

Grigolo, et al. A novel nano-composite muli-layered bioma-
terial for treatment of osteochondral lesions: Technique note
and an early stability pilot clinical trial. Inj Int J Care Inj
2010;41:693–701.

[29] Vasiliadis HS, Wasiak J. Autologous chondrocyte implanta-
tion for full thickness articular cartilage defects of the knee.

par plastie en mosaïque. In: Huten D, editor. Conférence
2010.

[31] Sagnolene NA, Chen E, Bert JM, Amendola A, Bugbee WD.
Curren strategies for nonsurgical, arthroscopic, and minimally
invasive surgical treatment of knee cartilage pathology. Instr

morbidity associated with osteochondral harvest from asym-
tomatic knees for the treatment of osteochondral lesions

[33] Iwasaki N, Kato H, Kamishima T, Suenaga N, Minami A. Donor
site evaluation after autologous osteochondral mosaicplasty

[34] Garretson RB, Katolik Li, Verma N, Beck PR, Bach BR, Cole BJ.
Contact pressure at osteochondral donor sites
967–74.

Bartha L, et al. Autologous osteochondral grafting—technique

et al. Knee osteochondral autologous transplantation: long-
term MR findings and clinical correlations. Eur J Radiol

[37] Brucker PU, Braun S, Imhoff AB. Mega-OACT technique—auto-
logous osteochondral transplantation as a salvage procedure for
large osteochondral defects of the femoral condyle. Oper Orthop Traumatol

[38] Braun S, Minzlaff P, Hollweck R, Wörtler K, Imhoff AB. The
5.5-year results of MegaOACT—autologous transfer of the pos-
terior femoral condyle: a case-series study. Arthritis Res Ther

[39] Aubin PP, Cheah HK, Davis AM, Gross AE. Long-term follow-up of
fresh osteochondral allografts for posttraumatic knee defects.

[40] Chu CR, Convery FR, Akeson WH, Meyers M, Amiel D. Articu-
lar cartilage transplantation—clinical results in the knee. Clin
Orthop 1999;360:159–68.

Prospective evaluation of prolonged fresh osteochondral allo-

[42] Ghazavi MT, Pritker KP, Davis AM, Gross AE. Fresh osteochondral
allografts for posttraumatic osteochondral defects of the knee.

of fresh osteochondral allografts for posttraumatic knee defects.

[44] Garrett JC. Fresh osteochondral allografts for treatment of
articular defects in osteochondritis dissecans of the lateral

[45] Jamali AA, Emmerson BC, Chung C, Convery RF, Bugbee WD.

Peterson L. Treatment of deep cartilage defects in the knee
with autologous chondrocyte transplantation. N Engl J Med
1994;331:889–95.

Autologous chondrocyte implantation and osteochondral cylin-
der transplantation in cartilage repair of the knee joint:
a prospective, comparative trial. J Bone Joint Surg Am

[48] Brittberg M. Autologous chondrocyte implantation- long-term

JB, et al. Autologous chondrocyte implantation of the knee:
multicenter experience and minimum 3-year follow-up. Clin J

[50] Peterson L, Minas T, Brittberg M, Lindahl A. Treatment of osteo-
chondritis dissecans of the knee with autologous chondrocyte
transplantation. Results at two to ten years. J Bone Joint Surg
Am 2003;85(Suppl. 2):17–22.

[51] Peterson L, Brittberg M, Kiviranta I, Akerlund EL, Lindahl A.
Autologous chondrocyte transplantation. Biomechanics and

[52] Cole BJ, Lee SJ. Complex knee reconstruction: articular car-

[53] Peterson L, Vasiliadis HS, Brittberg M, Lindahl A. Autologous

ized trial comparing autologous chondrocyte implantation with
microfracture: findings at five years. J Bone Joint Surg Am
2007;89(10):2105–12.

tion of autologous chondrocyte implantation and mosaicplasty:
A multicentered randomized clinical trial. Clin J Sport Med

[56] Bentley G, Biant LC, Carrington RW, Akmal M, Goldberg A,
Williams AM, et al. A prospective, randomized comparison of
autologous chondrocyte implantation versus mosaicplasty.
Treatment of knee cartilage defect in 2010


