Instructional Course 102

Complex Knee Reconstruction: Articular Cartilage Treatment Options

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Physicians have known for over 250 years that articular cartilage damage is a "troublesome thing and once destroyed, it is not repaired."[1] Although chondral lesions that penetrate to or through the subchondral bone may fill with fibrocartilage, the biomechanical and biochemical features remain inferior to hyaline cartilage.[2-4] Unlike the recognized poor prognosis of the meniscectomized knee, the natural history of chondral lesions remains far more speculative. At this juncture, treatment recommendations are for those lesions believed to be contributing to a patient's symptoms and are not generally directed toward asymptomatic lesions. Clinical experience has taught us that after these lesions become symptomatic (a cause of pain, swelling, mechanical symptoms), they tend to persist or inexorably progress over an indeterminate time course.

On one end of the spectrum, small full-thickness cartilage lesions in low-demand patients can fill in with fibrocartilage and may render a patient asymptomatic. On the other end, large osteochondral lesions in higher-demand patients are less likely to develop a clinically significant fibrocartilagenous healing response and more frequently result in pain and disability.[3,5] The treatment algorithm is evolving and may be construed as a spectrum of options ranging from those that are considered palliative (arthroscopic debridement and lavage), reparative (marrow stimulation techniques), and restorative (osteochondral grafting and autologous chondrocyte implantation) (Fig 1).

Whichever treatment is chosen, it is critical that the surgeon at least consider what subsequent treatment option might be required should the index cartilage treatment fail to relieve the patient's symptoms. Therefore, we often choose to implement the least destructive and invasive treatment options first so as to avoid "burning a bridge" for future options.

DECISION MAKING

The basic principles of decision making are patient- and defect-specific. Patient-specific variables include patient age, demand level, response to previous treatment, and the presence of cofactors such as malalignment, ligament insufficiency, and meniscal deficiency. Defect-specific variables include defect location, number, size, depth, geometry, and degree of containment.

Patient-Specific Variables

Age remains a primary determinate in the decision making and treatment algorithm for symptomatic chondral disease. For example, relatively young patients (those younger than 25) with large chondral defects (greater than 4 to 5 cm^2) that do not violate the subchondral bone may be more amenable to treatment with autologous chondroctye implantation (ACI) than with osteochondral (OC) allograft transplantation simply because it may be advantageous to avoid violation of the subchondral bone. This violation can potentially compromise future treatment options or introduce additional problems not present before treatment. Additionally, although the risk of disease transmission is considered an important deterrent for some patients, it is particularly disconcerting to a teenage patient, for

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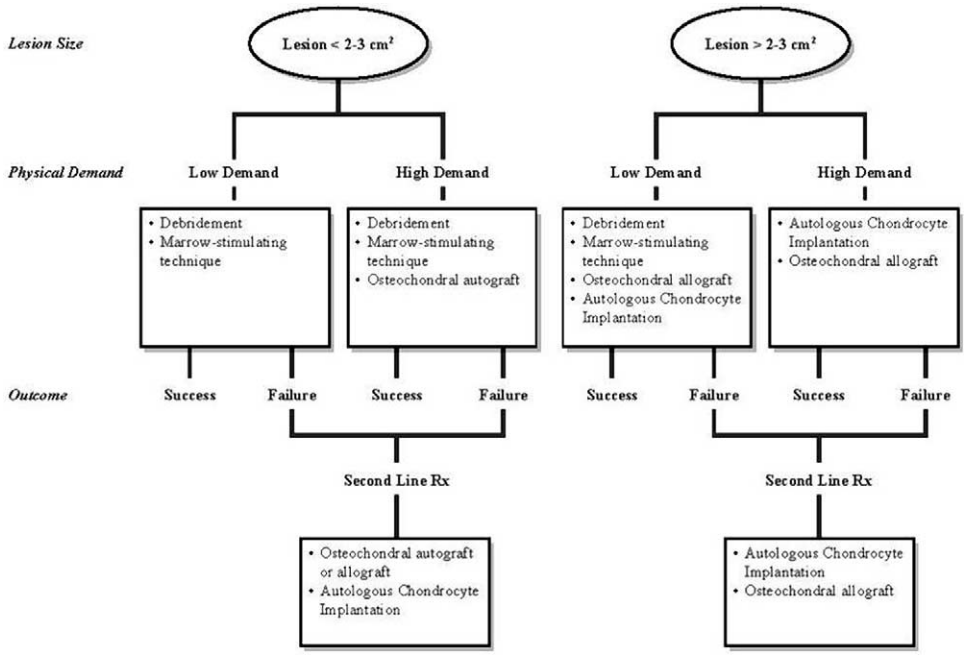

FIGURE 1. Treatment algorithm showing the decision variables considered for the treatment of chondral defects of the femoral condyle. A hierarchy of decision nodes begins with considerations for defect size, patient demand level, and the various treatment options available, including those that are implemented should the first-line treatment fail. Working in the background are additional patient-specific and defect-specific variables.

example, with a symptomatic focal chondral defect. In the event that ACI fails to relieve a patient's symptoms, OC grafting remains a suitable option for revision. Alternatively, older patients (older than 40 years) with larger defects that involve the subchondral bone may be more ideally suited for OC allograft transplantation because of age-related biologic deterioration of donor chondrocytes required for ACI and a desire to rapidly return to activities of daily living without a prolonged period of time required to achieve symptom relief.

The concept of procedure demand-matching may be analogous to the treatment of the nonagenarian with a relatively inexpensive bipolar hemiarthroplasty prosthesis in the setting of a displaced femoral neck fracture. As our understanding of the level of symptom relief and success rates associated with each treatment option improves, we can theoretically begin to match the treatment to the patient's expectations and level of physical, chronologic, physiologic, and emotional demand. For example, competitive athletes experiencing limitations because of the chondral disease may respond less favorably to marrow stimulation techniques compared with lower-demand patients who otherwise become symptomatic with low impact or activities of daily living. In addition, the prolonged time to achieve symptom relief with ACI in some patients may be untenable because of lifestyle considerations and job-related issues. Therefore, they may be more appropriately treated with OC grafting as an alternative to ACI.

Determining the patient's previous treatment and postoperative course before recommending additional treatment for chondral disease is critical to the success of the subsequent option chosen. For example, a lesion initially treated with debridement and lavage is often considered most similar to a virgin lesion. Several options remain available depending on how they flow through the treatment algorithm. A patient treated with marrow stimulation and appropriate postoperative rehabilitation may be advanced readily through the treatment algorithm to a restorative option. Finally, patients treated with one restorative option (ACI) who do not respond favorably have few alternatives other than revising the ACI with another ACI or with OC grafting. To date, there are very little data describing the indications and results for revision with the same procedure that initially failed to alleviate patient symptoms.

Cofactors must be addressed either concomitantly or in a staged fashion. Even small degrees of physiologic varus or valgus are often corrected when treating defects in the medial or lateral compartment, respectively. Unlike osteotomies performed for advanced bipolar arthrosis of a single compartment, these osteotomies are generally designed to neutralize or slightly overcorrect deformity to protect the cartilage procedure (Fig 2). Most commonly, osteotomies are

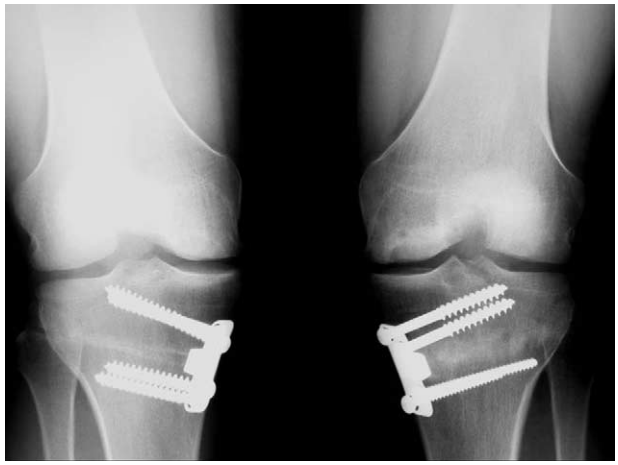

FIGURE 2. One year postoperative radiographs in an 18-year-old patient with bilateral OCD lesions of the medial femoral condyles treated with fresh OC allograft transplantation and simultaneously performed medial opening wedge osteotomies. The threshold to perform osteotomy to realign deformity to neutral or just beyond neutral is considerably reduced because of our understanding of the necessity to unload the cartilage restoration procedure.

performed simultaneously with cartilage restoration procedures in younger patients (younger than 35) and in a staged fashion in older patients. Occasionally, patients who undergo osteotomy first do not require subsequent treatment of the chondral lesions. Techniques such as opening wedge osteotomy with allograft bone graft have considerably lessened the morbidity of this procedure, and unlike the use of osteotomy in the advanced arthritic knee, the frequency of this procedure seems to be rising in the relatively young patient with chondral disease associated with deformity.

It is notable that often less-invasive cartilage procedures such as microfracture, when used as an index operation, are less commonly performed in association with an osteotomy. This is in contrast to patients who require more advanced restorative options such as ACI or OC grafting, who commonly undergo simultaneously performed realignment procedures. This dichotomy obviously confounds our ability to clearly interpret the results of cartilage restoration procedures in these patients.

Some of these patients will have ligament insufficiency associated with chondral defects. In the acute or subacute setting, we will generally avoid treating chondral disease with anything other than benign neglect, debridement, or rarely, microfracture. The basis for this decision making is that not all of these lesions will become symptomatic, and it is believed that observation of these known lesions will help guide future treatment recommendations based on the onset and severity of symptoms.

In chronic ligament-deficient patients with symptomatic chondral lesions, the timing of ligament reconstruction is based on surgeon preference. Because stiffness is not uncommon after ACL reconstruction performed in isolation, we prefer to perform the ACL reconstruction first when treatment of the chondral defect will involve OC allograft transplantation or ACI. Alternatively, when defects are appropriate for treatment with marrow stimulation or OC autograft transplantation, we consider performing these procedures simultaneously. PCL insufficiency is generally rare in combination with symptomatic chondral defects and is treated accordingly.

The extent of ipsilateral meniscal deficiency that can be tolerated when treating chondral defects remains unknown. Although the subject of current investigation in our laboratory, even small meniscal defects (less than 30% of the meniscus is missing) that extend to the periphery are theoretically no different biomechanically than the completely meniscectomized knee. Therefore, with a high degree of discretion, we will perform simultaneous meniscus transplantation and chondral treatment when we believe that the chondral repair would otherwise be compromised because of increased tibiofemoral contact force. At no time do we intentionally stage these procedures because of the implicit interdependence and the relative protection provided by each procedure.

Defect-Specific Variables

Defect location and number will influence the pool of available treatment options. In general, most of the experience with cartilage procedures of the knee is with the femoral condyle because these are the most common lesions encountered in appropriately selected patients. Several options are available for these lesions, and decisions are predicated on the defect- and lesion-specific factors described here.

Some sites remain problematic and modify the decision-making process. For example, the tibia remains a particularly difficult area to treat. Fortunately, most patients appropriately selected for treatment of femoral or patellar lesions have minimal involvement of the tibia because of the relative contraindication of bipolar disease and the implementation of most options. Nevertheless, when relatively small tibial lesions are present during cartilage restoration of the femur, we

commonly use the microfracture technique for the tibia and formally treat the femoral lesion with a cartilage restoration technique. Other options for lesions of the tibia may include the use of OC autografts placed antegrade in an open or arthroscopically in a retrograde fashion (Fig 3), but experience is limited to anecdotal reports at this time.

Lesions of the patellofemoral (PF) joint are less commonly treated with OC grafting, although experience is growing in this area. Similarly, although the results of microfracture of the PF joint are encouraging, our experience has shown us that PF lesions do not seem to fare as well as those of the weight-bearing portion of the femoral condyle. Thus, definitive treatment of the patellofemoral joint in our practice is ACI with a concomitantly performed anteromedialization procedure. End-stage isolated bipolar disease of the PF joint in very young and severely symptomatic patients have occasionally been treated with fresh OC grafting of both the patella and trochlea because these patients have few alternatives other than PF resurfacing or total knee arthroplasty. However, the results of bipolar OC grafting of any knee compartment remain guarded and should be considered a 50-50 proposition by the surgeon and patient.

The number of defects may influence the decision to perform one treatment over another. For example, although several options are available to treat the femoral condyle, with multiple defects in other compartments, the options become substantially more limited. One strategy is to only treat defects believed to be contributing to the patient's symptoms. Alternatively, an option may be chosen that facilitates treatment of all defects. Thus, a large defect of the femoral condyle that is otherwise amenable to treatment with a fresh OC graft may be better treated with ACI in the presence of a second or third defect in other compartments.

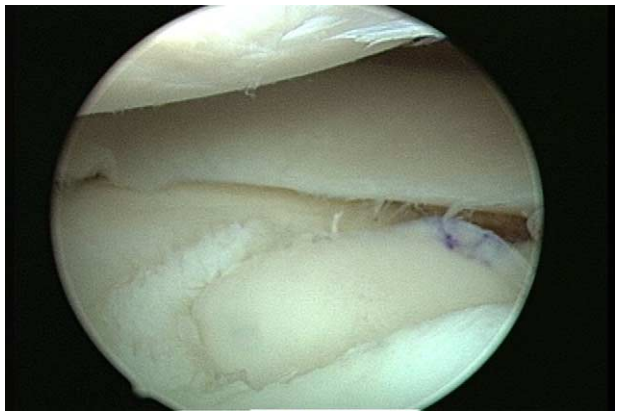

Figure 3. Arthroscopic picture of a focal chondral defect of the tibial plateau treated with a retrograde osteochondral autograft plug performed entirely arthroscopically (Courtesy of Arthrex, Naples, FL).

The size of the defect will help determine which options are appropriately indicated because of technical and biomechanical limitations. Defects less than 2 to 3 cm^2 respond more favorably than larger defects to microfracture but can alternatively be completely replaced with OC autografting techniques.

On the other end of the spectrum, extremely large defects such as those associated with high-energy trauma may best be reconstructed with fresh OC grafts using nearly an entire hemicondyle if necessary. Intermediate-sized defects that range between 2 and 10 cm^2 often are amenable to several treatment options, and the decision is predicated on the defect- and lesion-specific factors described.

Superficial defects involving only the chondral surface, especially those in young patients, are often treated definitively with nondestructive techniques such as ACI. Alternatively, very deep lesions, especially in older individuals, may more appropriately be treated with fresh OC grafting. Deep lesions in young patients can still be treated with ACI, but bone grafting is required if more than 6 to 8 mm of the subchondral bone is involved.

The techniques required to restore the subchondral surface to enable the implementation of ACI include staged bone grafting followed by ACI or the use of a single-stage technique using a periosteal "sandwich." In the first technique, we use 5.0-mm osteochondral plugs harvested from the intercondylar notch to obtain sufficient bone graft to graft the bed of the defect (Fig 4). Typically, this is done in an arthroscopically assisted fashion without the need for a periosteum containment cover. Postoperatively, patients are not allowed to bear weight for 6 to 8 weeks, followed by implantation with standard ACI techniques no sooner than 4 to 6 months after the subchondral bone grafting procedure.

Alternatively, a periosteal "sandwich" technique can be implemented without the need to stage the implantation of the autologous chondrocytes. A layer of periosteum sealed against the bone graft with fibrin glue is placed with the cambium layer facing into the joint over the bone grafted bed and fixed with a few 6-0 vicryl sutures. A second layer of periosteum with the cambium layer facing the first layer is sewn with 6-0 vicryl suture. The cells are then injected between the 2 layers of periosteum. This technique is ideal for

FIGURE 4. Arthroscopic picture of a deep OCD lesion of the medial femoral condyle treated with locally obtained bone graft harvested using 5.0-mm osteochondral autograft plugs procured from the intercondylar notch. This 16-year-old patient undergoing staging for definitive treatment with autologous chondrocyte implantation after consolidation of the bone graft for 4 to 6 months.

the recently biopsied young patient with symptomatic OCD of the femoral condyle for whom ACI is preferred over fresh OC grafting by some surgeons. In this instance, should the ACI fail to incorporate, the subchondral bed would remain restored and able to support a revision with ACI should that become necessary.

Lesion geometry is another consideration that might lead to the decision to implement one cartilage procedure over another. The instrumentation widely used for fresh OC grafting (Arthrex, Naples, FL) is predicated on a circular recipient socket prepared to receive a size-matched "dowel" of cartilage and bone with a very small tolerance between the donor and recipient. Many surgeons remain uncomfortable preparing fresh OC grafts by hand to accommodate a noncircular lesion of the femoral condyle. Considering this, large, irregularly shaped lesions may be more amenable to treatment with ACI (Fig 5).

Similarly, microfracture may be more successful for ordinary geometrically shaped (circular) lesions that have vertical "shoulders" compared with long narrow lesions in which the juxta-articular regions of normal cartilage less efficiently shields the defect from loads. Thus, defect shape may help a surgeon decide who should undergo microfracture first or who should proceed directly to other more definitive cartilage restoration techniques, such as fresh OC grafting or ACI.

Finally, some lesions may be completely uncontained and less amenable to ACI techniques and more amenable to OC grafting. There are methods, however, to manage these defects if ACI remains an otherwise ideal treatment option, including the use of mini-suture anchors loaded with 6-0 vicryl suture, small trans-osseous drill hole suture repair made with a .045 K wire, and direct periosteal patch repair to the juxta-articular synovium. Using the same logic regarding the ability for a defect to efficiently be protected from load by the intact surrounding articular cartilage, uncontained defects may be less successfully treated with marrow stimulation techniques.

PATIENT EVALUATION

Before ascribing symptoms to a known chondral defect, it is absolutely critical that the patient be

FIGURE 5. Clinical example of a long and narrow focal chondral defect of nearly the entire convexity of the medial femoral condyle. Because of the geometry of this lesion and the available instrumentation, autologous chondrocyte implantation was chosen rather than fresh OC allografting.

questioned about the nature and location of symptoms. In our experience, many patients are initially referred for definitive treatment for a chondral defect when the symptoms presumably associated with that defect are largely asynchronous. For example, patients with posteromedial weightbearing pain who have a known single lateral compartment or PF defect may have symptoms for reasons other than the defect. Thus, treatment predicated solely on the presence of a known defect may lead to a very dissatisfied patient exposed to unnecessary surgical risk and morbidity. Therefore, we encourage surgeons to avoid "linear thinking" to prevent inadvertent treatment of clinically silent lesions where symptoms do not correspond with defect location.

Imaging

Radiographs should include anteroposterior, lateral, Merchant, and 45° flexion posteroanterior weightbearing films.[6,7] Limb alignment is assessed with full leg-length films. This series of films will show joint space narrowing, osteophytes, cyst formation, and subchondral sclerosis, which are all consistent with osteoarthritis. When present, they are generally considered contraindications for these procedures.

A magnetic resonance image is valuable to assess the status of the knee ligaments and menisci if it is unknown. The magnetic resonance imaging generally tends to underestimate the degree of cartilage abnormalities seen at the time of arthroscopy. There is no uniform consensus regarding the optimal pulse sequence for cartilage imaging.[8] Fat-suppressed imaging is more sensitive than standard magnetic resonance imaging for the detection of abnormalities of the hyaline cartilage in the knee.[9] More recently, specialized fast-spin-echo magnetic resonance imaging sequences with a high-resolution matrix allowed for an accurate assessment of articular cartilage in the knee, with little interobserver variability.[10]

The role of bone scan is still being defined. Joint overload can initiate the increased osseous metabolic activity of bone that is detectable by scintigraphic methods.[11,12] We occasionally use scintigraphy in difficult cases in which the source and clinical importance of periarticular symptoms remain in doubt. In instances in which the pain is out of proportion to the clinical presentation, a bone scan can confirm the existence of increased osseous metabolic activity (which is not shown by other imaging modalities) that could be consistent with subchondral activity in the region of a chondral or osteochondral defect.[13]

SURGICAL OPTIONS

Overview

Some generalizations exist regarding the indications for different procedures. Arthroscopic debridement can be used effectively to remove debris, cytokines, and proteases that may contribute to cartilage breakdown. It is a first line treatment that is frequently employed or it may be the definitive treatment in the low-demand patient or a patient who does not want a long rehabilitation with altered weight-bearing status. Marrow-stimulating techniques are used in low-demand patients with larger lesions or as a first-line treatment in higher-demand patients with smaller lesions. Generally, the marrow-stimulating techniques are recommended for lesions less than 2 to 3 cm^2.[14,15] OC autografts are used as a first- or second-line treatment for smaller lesions and can be performed arthroscopically or open. OC allografts are used as a first- or second-line treatment in older patients with large lesions and as a second-line treatment in younger patients. ACI can be used for small and large lesions as a primary or secondary procedure depending on many variables described in the decision-making section.

Marrow Stimulation Techniques

Abrasion arthroplasty, drilling, and microfracture are the 3 most common methods used to violate the subchondral bone. We prefer the microfracture technique. Microfracture involves using a small pick to penetrate the subchondral bone, but still leaves the majority of the subchondral architecture intact. A well-shouldered lesion is created that will allow the formation of a stable fibrocartilagenous base. All unstable cartilage should be removed. Animal studies suggest that removing the calcified cartilage with a curette greatly enhances the percentage of defect fill.[16] A surgical awl is then used to create holes placed 2 to 3 mm apart, beginning first at the periphery of the lesion. The holes should not be confluent. When fat droplets can be seen coming from the marrow cavity, the approximate depth (2-4 mm) has been reached.[17] Once the procedure is completed, the tourniquet (if inflated) should be released, and the pump pressure reduced. One should see blood and marrow fat droplets coming from each hole (Fig 6).

The postoperative rehabilitation program is paramount to the success of this procedure and requires a period of non-weight bearing for femoral condyle lesions and the use of continuous passive motion for up to 6 weeks postoperatively. Steadman et al.[14] re-

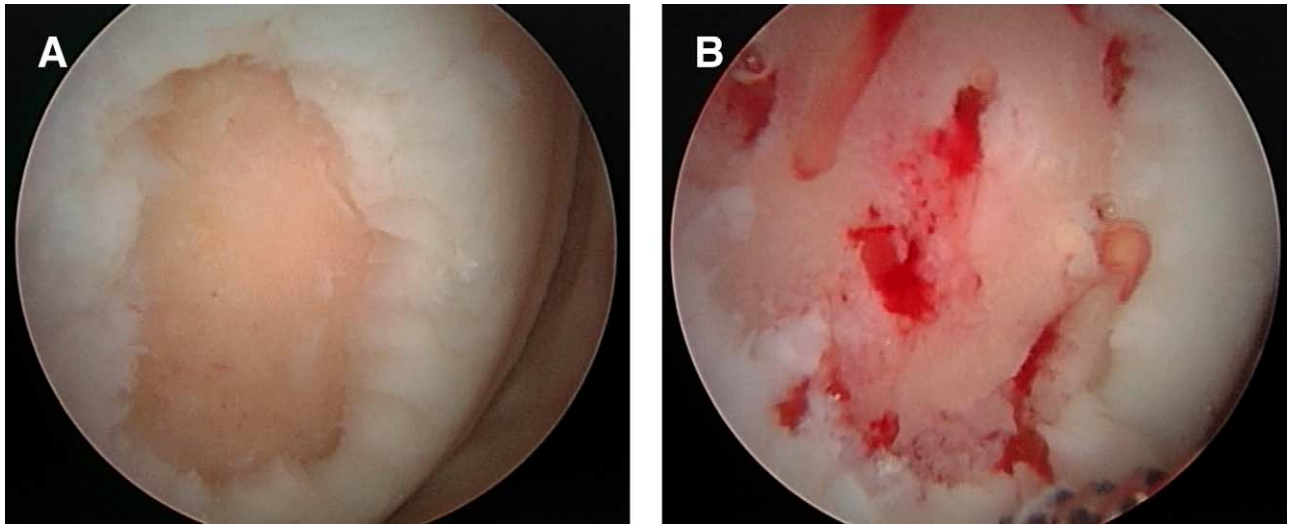

FIGURE 6. Arthroscopic pictures of (A) focal chondral defect prepared with debridement and removal of the calcified layer, and (B) microfracture with blood and marrow elements returning into the defect.

cently reported on 71 knees with 7 to 17 year follow-up times. Significant improvements were noted for both Lysholm and Tegner scores. The majority of patients indicated good to excellent results on SF-36 and WOMAC scoring systems at final follow-up, with 80% of patients rating themselves as "improved." Most of the improvement took place within the first year, with maximal improvement occurring 2 to 3 years postoperatively. Age was found to be an independent predictor of improvement in Lysholm scores; patients younger than 35 years had greater improvement those 35 to 45 years.

Osteochondral Autograft Transplantation

This technique involves transplantation of an OC graft from one region of a joint to another in an effort to restore the damaged articular surface. It is limited by the amount of donor tissue available in the knee. If considering this technique, it is generally recommended that the lesions are less than 2 cm in diameter.[18] The risk of donor site morbidity increases as more tissue is harvested. The typical site of harvest is the femoral intercondylar notch and the periphery of the lateral femoral condyle near the sulcus terminalis. The procedure can be performed through a small arthrotomy or entirely arthroscopically. We prefer to harvest donor plugs through a small lateral arthrotomy and prepare for and implant these plugs arthroscopically. Several commercial systems are available to perform this procedure. We presently use the Osteochondral Autograft Transfer System (OATS; Arthrex), which provides a series of donor and recipient harvesting tubes used to create a press-fit implant of up to 10 mm in diameter (Fig 7).

Postoperatively, patients are protected from weight

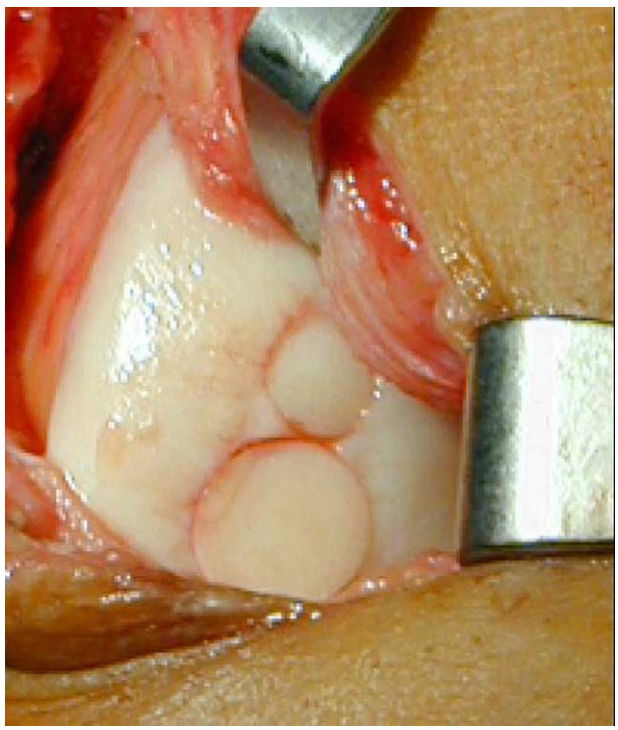

FIGURE 7. Clinical example of a focal chondral defect treated with 2 osteochondral autograft plugs (10 mm and 7 mm).

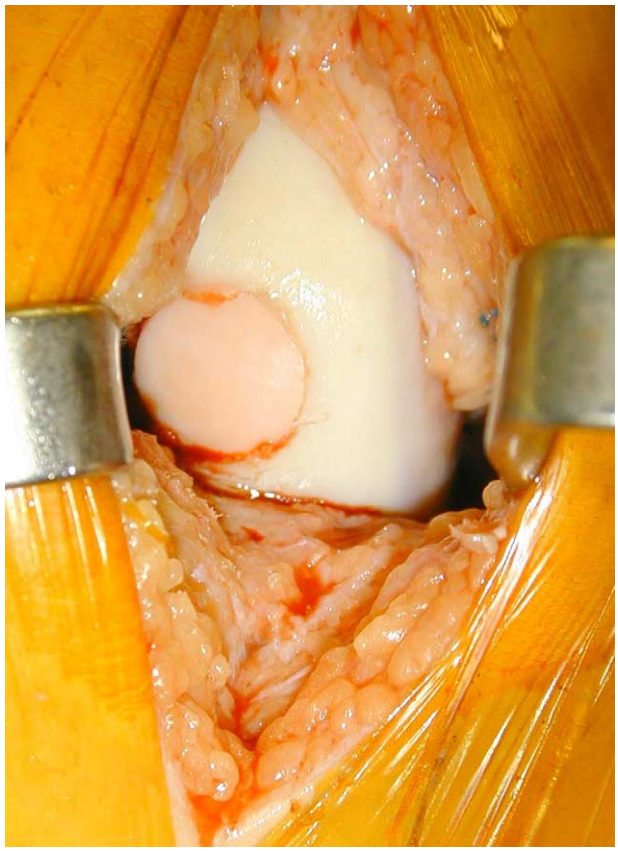

FIGURE 8. Clinical example of larger focal chondral defect treated with a single fresh osteochondral allograft.

bearing and often use continuous passive motion. A multicenter prospective study was performed comparing marrow-stimulating techniques to osteochondral allografts in 413 patients.[19] Osteochondral autograft resulted in significantly better outcomes at 3, 4, and 5 years. Although we remain encouraged by the results in our practice, we continue to use this treatment option only for relatively small lesions that require a few number of larger plugs to resurface the lesion.

Osteochondral Allograft Transplantation

Fresh size-matched OC allograft transplantation is performed through a relatively small arthrotomy using specialized instrumentation (Arthrex) designed to create an osteochondral dowel of bone and cartilage that is press-fit into a recipient socket (Fig 8). If the lesion is not amendable to a circular graft, a shell graft can be fashioned freehand typically in a trapezoidal configuration that matches a hand-prepared defect bed using a motorized burr and oscillating saw with cold irrigation. Freehand sizing of a graft is more time consuming and often requires fixation, because the fit is less precise. Bone depth is intentionally minimized because the subchondral bone is known to be the most immunologic component of the composite graft. We typically favor the use of grafts that are refrigerated and implanted before 28 days because our data suggest that beyond this time point, cell viability and sulfate uptake tend to deteriorate.

Postoperatively, patients are made non-weight bearing for up to 8 weeks and often use continuous passive motion. Gross[20] reported an 85% success rate in 126 knees followed up for a mean of 7.5 years. In 122 patients treated for femoral condyle lesions, Bugbee[21] reported a success rate of 91%. At 10-year follow-up, the clinical success was 75%. Several studies have evaluated long-term survivorship to determine the durability of osteochondral allografts.[22-26] The treatment of bipolar disease is considerably less successful than unipolar disease.[27] Garrett et al.[28] reviewed a group treated for OCD lesions in adults and found excellent results.

Autologous Chondrocyte Implantation

ACI can be used for lesions measuring roughly 2 to 10 cm^2. This is a 2-stage procedure. A biopsy specimen must be taken first from either the superomedial edge of the trochlea[29] or our preferred site, the lateral side of the intercondylar notch (the same location where an ACL notchplasty is performed). The biopsy is sent to Genzyme Biosurgery Corporation (Cambridge, MA) for processing. The biopsy specimen can be maintained for 18 months until it is processed and undergoes cellular expansion and after 3 to 5 weeks is ready for implantation. Defect preparation involves removing the remnant cartilage and leaving the healthy hyaline cartilage to form vertical walls shouldering the lesion. The periosteal patch is harvested through a 3-cm incision on the subcutaneous border of the proximal tibia, 2 finger-widths distal to the pes anserine tendon attachments. The periosteum is secured with a 6-0 absorbable vicryl suture on a P-1 cutting needle. The edges of the patch should be sealed with fibrin glue (Tisseel; Baxter Healthcare, Glendale, CA) and a water-tightness test should be performed to assure that no leakage of cells will occur. The cells are resuspended, aspirated into a small syringe, and injected under sterile conditions beneath the periosteal patch. The patch is finally sealed with additional sutures and fibrin glue (Fig 9).

Postoperatively, lesions of the femoral condyle are treated initially with minimal weight bearing and con-

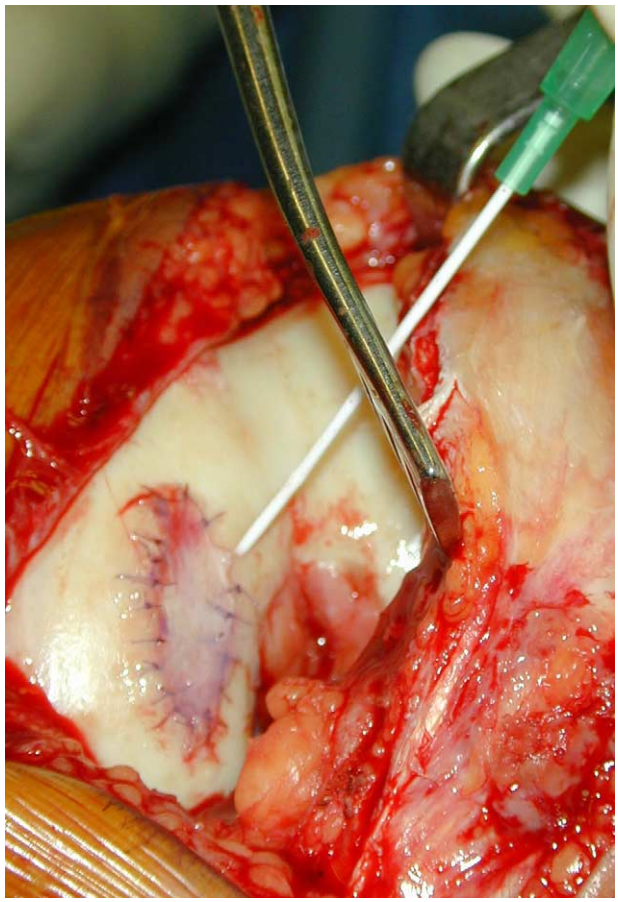

FIGURE 9. Defect of the medial femoral condyle treated with autologous chondrocyte implantation with cells being injected beneath the watertight periosteal patch sealed with fibrin glue.

tinuous passive motion. Lesions of the patellofemoral joint are often allowed to weight bear as tolerated in extension. The published results of ACI now have follow-up extending to 9 years.[29-33] Micheli et al.[30] published a multicenter study of the first 50 patients treated outside of Sweden. The patients were prospectively followed up for a minimum of 36 months. Seventy-eight percent of the patients had a previous cartilage procedure. The patients' Modified Cincinnati Score revealed a significant improvement of 5 points (10 point scale). Eighty-four percent of patients had an improvement in their condition, 2% were unchanged, and 13% declined. One third of these patients had failed a previous marrow-stimulating procedure. Peterson et al.[31] published his results on 94 patients with 2- to 9-year follow-up. He found that the results varied considerably based on location. The results of ACI for treating the patella initially were 62% good to excellent. However, later in the series, the authors began performing a distal realignment, and the results improved to 85% good to excellent, comparable to the treatment of lesions located on the femoral condyle. Our results evaluated at a minimum 2-year follow-up essentially mirror that which is reported in the literature.

FUTURE CONSIDERATIONS

Genetic engineering is another potential strategy for treating chondral injuries. This involves a combination of gene transfer techniques and tissue engineering.[33] In gene therapy, specific genes for growth factors are transferred into the chondrocyte or progenitor cells. Once treated, these cells have the potential to produce the growth factors that are conducive to chondrocyte proliferation. Tissue engineering is based on the creation of biologic substitutes for the repair or regeneration of damaged tissue. The application of this process for chondral defects involves the transplantation of viable cells into an appropriate supportive vehicle. Autologous chondrocyte implantation is an example of this technique, although the ideal scaffold for cartilage engineering has not yet been identified.[33] Probably, future considerations will focus on these scaffolds, reductions in the expenses associated with the production of these technologies, and less-invasive means to implement cartilage restoration procedures.

REFERENCES

1. Hunter W. On the structure and diseases of articulating cartilage. *Philos Trans R Soc Lond B Biol Sci* 1743;9:267.
2. Mandelbaum BR, Browne JE, Fu F, Micheli L, et al. Articular cartilage lesions of the knee. *Am J Sports Med* 1998;26:853-861.
3. Mankin HJ. The response of articular cartilage to mechanical injury. *J Bone Joint Surg Am* 1982;64:460-466.
4. Furukawa T, Eyre DR, Koide S, Glimcher MJ. Biochemical studies on repair cartilage resurfacing experimental defects in the rabbit knee. *J Bone Joint Surg Am* 1980;62:79-89.
5. Convery FR, Akeson WH, Keown GH. The repair of large osteochondral defects: An experimental study in horses. *Clin Orthop* 1972;82:253-262.
6. Mason RB, Horne JG. The posteroanterior 45 degrees flexion weightbearing radiograph of the knee. *J Arthroplasty* 1995;10:790-792.
7. Rosenberg TD, Paulos LE, Parker RD, et al. The forty-five-degree posteroanterior flexion weightbearing radiograph of the knee. *J Bone Joint Surg Am* 1988;70:1479-1483.
8. Khanna BAJ, Cosgarea AJ, Mont MA, et al. Magnetic resonance imaging of the knee: Current techniques and spectrum of disease. *J Bone Joint Surg Am* 2001;83(Suppl 2):128-141.
9. Disler DG, McCauley TR, Wirth CR, Fuchs MD. Detection of knee hyaline cartilage defects using fat-suppressed three-dimensional spoiled gradient-echo MR imaging: comparison

with standard MR imaging and correlation with arthroscopy. *AJR Am J Roentgenol* 1995;165:377-382.
10. Potter HG, Linklater JM, Allen AA, et al. Magnetic resonance imaging of articular cartilage in the knee: An evaluation with use of fast-spin-echo imaging. *J Bone Joint Surg Am* 1998;80: 1276-1284.
11. Brill DR. Sports nuclear medicine: Bone imaging for lower extremity pain in athletes. *Clin Nucl Med* 1983;8:101-106.
12. Rosenthall L, Hill RO, Chuang S. Observation of the use of 99mTc-phosphate imaging in peripheral bone trauma. *Radiology* 1976;119:637.
13. Dye SF, Chew MH. The use of scintigraphy to detect increased osseous metabolic activity about the knee. *Instr Course Lect* 1994;43:453-469.
14. Steadman JR, Briggs KK, Rodrigo JJ, et al. Outcomes of microfracture for traumatic chondral defects of the knee: Average 11-year follow-up. *Arthroscopy* 2003;19:477-484.
15. Cole BJ, Cohen B. Chondral injuries of the knee: a contemporary view of cartilage restroation. *Orthop Special Ed* 2000; 6:71-76.
16. Frisbie DD, Trotter GW, Powers BE, et al. Arthroscopic subchondral bone plate microfracture technique augments healing of large chondral defects in the radial carpal bone and medial femoral condyle of horses. *Vet Surg* 1999;28:242-255.
17. Steadman JR, Rodkey WG, Rodrigo JJ. Microfracture: surgical technique and rehabilitation to treat chondral defects. *Clin Orthop* 2001;391(Suppl):S362-369.
18. Hangody L, Kish G, Karpati Z, et al. Arthroscopic autogenous osteochondral mosaicplasty for the treatment of femoral condylar articular defects: A preliminary report. *Knee Surg Sports Traumatol Arthrosc* 1997;5:262-267.
19. Hangody GETL, Kish G, Karpati Z. Arthroscopic autogenous osteochondral mosaicplasty: A multicentric, comparative, prospective study. *Index Traumat Sport* 1998;5:3-9.
20. Gross AE. Fresh osteochondral allgorafts for post-traumatic knee defects: Surgical technique. *Oper Tech Orthop* 1997;7: 334.
21. Bugbee WD. Fresh osteochondral allografting. *Oper Tech Sports Med* 2000;8:158-162.
22. Gross AE, Aubin P, Cheah HK, et al. A fresh osteochondral allograft alternative. *J Arthroplasty* 2002;17(Suppl 1):50-53.
23. Ghazavi MT, Pritzker KP, Davis AM, Gross AE. Fresh osteochondral allografts for post-traumatic osteochondral defects of the knee. *J Bone Joint Surg Br* 1997;79:1008-1013.
24. Beaver RJ, Mahomed M, Backstein D, Davis A, et al. Fresh osteochondral allografts for post-traumatic defects in the knee. A survivorship analysis. *J Bone Joint Surg Br* 1992;74:105-110.
25. Mahomed M. The long-term success of fresh, small fragment osteochondral allografts used for intraarticular post-traumatic defects in the knee joint. *Orthopedics* 1992;15:1191-1199.
26. McDermott AG, Langer F, Pritzker KP, Gross AE. Fresh small-fragment osteochondral allografts: Long-term follow-up study on first 100 cases. *Clin Orthop* 1985;197:96-102.
27. Bugbee WD, Convery FR. Osteochondral allograft transplantation. *Clin Sports Med* 1999;18:67-75.
28. Garrett JC. Fresh osteochondral allografts for treatment of articular defects in osteochondritis dissecans of the lateral femoral condyle in adults. *Clin Orthop* 1994;303:33-37.
29. Minas T. Autologous chondrocyte implantation for focal chondral defects of the knee. *Clin Orthop* 2001;391(Suppl):S349-361.
30. Micheli LJ, Browne JE, Erggelet C, et al. Autologous chondrocyte implantation of the knee: Multicenter experience and minimum 3-year follow-up. *Clin J Sport Med* 2001;11:223-228.
31. Peterson L, Minas T, Brittberg M, et al. Two- to 9-year outcome after autologous chondrocyte transplantation of the knee. *Clin Orthop* 2000;374:212-234.
32. Gillogly SD, Voight M, Blackburn T. Treatment of articular cartilage defects of the knee with autologous chondrocyte implantation. *J Orthop Sports Phys Ther* 1998;28:241-251.
33. Brittberg M, Lindahl A, Nilsson A, et al. Treatment of deep cartilage defects in the knee with autologous chondrocyte transplantation. *N Engl J Med* 1994;331:889-895.