Autologous chondrocyte implantation (ACI) has now been performed for over a decade in the United States. ACI has been demonstrated as a reproducible treatment option for large, full-thickness, symptomatic chondral injuries of the knee. As clinical experience has expanded and indications broadened to more complex cartilage defects, it has become evident that aggressive treatment of coexisting knee pathology is essential for optimal results. This includes management of malalignment, ligamentous, and/or meniscal deficiency, and subchondral bone loss to make the intra-articular environment as ideal as possible for successful cartilage restoration. Additionally, refinements in the rehabilitation necessary for biologic cartilage repair have been made, based on better understanding of the maturation process of the repair cartilage, allowing for earlier initiation of knee range of motion, strengthening exercises, and weight bearing. These changes have enhanced the recovery for the patient and decreased the risk of motion deficits. This article will discuss patient selection for ACI, review ACI surgical technique, including management of coexisting knee pathology, present postoperative ACI rehabilitation guidelines, and summarize clinical outcomes after ACI.

Key Words: cartilage, cartilage transplantation, chondrocyte transplantation, tibiofemoral joint

With the introduction of new treatment methods for cartilage repair over the past 10 to 15 years, a corresponding interest has developed in gaining a better understanding of the scope of the clinical problem and classification of cartilage injuries. Certainly all cartilage defects do not produce the same degree of clinical symptoms, progress at the same rate toward osteoarthritis, or require uniform treatment. Consideration must be given to the size, depth of involvement, location, and number of defects. Additionally, individual patient parameters, such as age, body mass, activity demands, and perhaps most importantly the condition of the remainder of the knee, all influence treatment decision making. We have learned that failure to address any copathologies of the knee, such as mechanical malalignment, ligamentous instability, or deficient meniscal function, will expose any cartilage repair process to a continued overload environment and often doom the clinical outcome. Therefore, not all cartilaginous injuries require the same treatment, and treatment must be tailored to the individual patient and cartilage lesion.

As with any new and innovative treatment method, there have been constant refinements in technique, indications, and clinical expectations for cartilage repair with autologous chondrocyte implantation (ACI). While no treatment option is universally ideal for all full-thickness cartilage defects, the goal remains a repair that can restore the normal surface congruity of the joint, control the patient’s symptoms, maintain the durability to withstand the intra-articular forces of the knee over time, and prevent the progression of focal chondral injuries to full-blown osteoarthritis. These newer treatment methods continue to be evaluated as to their consistency and reproducibility of outcomes, durability of repair, and cost effectiveness.
The technique of autologous chondrocyte implantation (ACI), first reported by Peterson and colleagues in 1994, has gained a major role in the treatment of large, full-thickness chondral injuries. The initial stage in this technique involves taking a small biopsy of healthy chondral tissue at the time of arthroscopic evaluation. The biopsy tissue is then sent to the lab (Genzyme Biosurgery, Cambridge, MA), where in vitro chondrocyte cell culture returns a 12-fold increase in the number of chondrocytes available for implantation into the defect at the second stage of the procedure. The principle behind using autologous chondrocytes is to produce a repair tissue that more closely resembles the morphologic characteristics of hyaline cartilage and is therefore better able to restore the durability and natural function of the knee joint. As worldwide experience with this technique has grown, good clinical outcomes beyond a decade postoperatively have been demonstrated.

**Patient Selection for Autologous Chondrocyte Implantation**

The primary indications for ACI are symptomatic, large, full-thickness chondral lesions located on the femoral condyles and trochlear groove in patients ranging in age from adolescence to their fifties. These patients must also be willing and able to comply with the postoperative rehabilitation protocol. ACI is not indicated as a treatment option for severe osteoarthritis, as defined by the presence of bipolar bone-on-bone lesions. If a large lesion is present on the reciprocal surface (kissing lesions), with exposed bone, the opposing surface is not suitable for this technique. This is particularly true when secondary bony deformity exists as a result of the arthritic process.

Results of treatment for isolated chondral injuries of the patella and tibia with ACI have not been as consistent as treating those of the femoral condyles and trochlea. However, with greater understanding of the importance of patellar alignment, the results of patellar ACI have improved. The indications for ACI treatment of the tibia include a traumatic, substantial-sized defect in a younger patient. Degenerative lesions on the tibia are rarely indicated for this technique of chondral resurfacing. ACI is contraindicated in active inflammatory arthritis or infection. Prerequisites for a successful outcome with ACI also include appropriate bony alignment, ligamentous stability, meniscal function, adequate motion, and muscle strength, in addition to a focal chondral injury in a knee without significant bony arthritic changes. In general, the defects treated by this technique are larger than 2 cm² and the average size in the authors’ series has been well over 5 cm².

As experience with biologic resurfacing of cartilage injuries has grown, it is apparent that the assessment of the condition of the overall knee is as important as the assessment of the chondral defect itself. The presence of coexisting knee pathology, such as ongoing ligamentous instability, bony malalignment, or complete meniscal deficiency will prevent an environment conducive for cartilage repair. Any abnormalities in these factors must be addressed prior to, or concomitant with, treatment of the cartilage defect with ACI. Failure to recognize and treat these coexisting factors will result in poorer patient outcomes or complete failure of the resurfacing procedure.

**Preoperative Evaluation**

A detailed patient history is important to confirm that symptoms are indeed coming from the chondral injury. This is particularly relevant to patients that have undergone prior repair techniques, such as marrow stimulation, for the cartilage defect. Perhaps the repair has been adequate and further symptoms are from incomplete rehabilitation of the patellofemoral joint with corresponding anterior knee complaints and not symptoms from a previously treated femoral condyle lesion. Typically patients with condyle lesions have pain with weight-bearing or increased loading circumstances, complaints of catching or partial locking, and recurrent swelling and pain localized to the area of the defect. The presence of a trochlea or patellar lesion will have similar findings, but with aggravation of pain complaints with stairs, getting in and out of a chair or car, and anterior knee pain.

Physical examination should include evaluation of meniscal function, ligamentous stability, patellar tracking, gait, and overall clinical alignment. In order to adequately evaluate a patient for ACI, it is essential that weight-bearing anterior-posterior and 45° posterior-anterior and patellar alignment radiographs be obtained. This allows initial assessment of the alignment of the tibiofemoral and patellofemoral portions of the joint and gives an indication of any underlying bone involvement associated with the defect from osteochondritis dissecans (OCD) or a traumatic osteochondral defect. A long leg limb alignment view to assess the mechanical axis is used to definitively determine the potential need for realignment osteotomy.

MRI can then be used to assess both the ligament and meniscal status as well as defining the degree of subchondral bone involvement. Increased signal and edema in the subchondral bone by MRI, may indicate persistent overload of the involved compartment, making realignment an essential and possibly more important adjunct to cartilage resurfacing. Additional information is often available on patients...
with known articular cartilage lesions through previous operative reports, previous studies, and intraoperative video photographs of prior procedures. Taking advantage of any available information will help in determining the suitability of the defect for ACI.

The most definitive step in assessing the suitability of a chondral lesion for ACI comes at the time of arthroscopic evaluation. The size, location, and depth of the defect, the status of the surrounding articular cartilage and underlying bone, as well as the status of the opposing chondral surfaces, are all evaluated. Containment of the defect is also assessed. In other words, does the bordering rim of healthy articular cartilage fully surround the defect or do the margins of the defect fade into the intercondylar notch or perimeter of the condyle or trochlea? This assessment is important as it may indicate that special techniques will be necessary to secure the periosteal patch to hold the autologous chondrocytes during implantation. The basic question to answer when assessing the cartilage status is: will the joint be improved with resurfacing of the defect or is the degenerative process too advanced diffusely within the joint with multiple involved bipolar surfaces, in which case, ACI or any other biologic resurfacing procedure will be inadequate in improving the patient’s symptoms? The ideal chondral lesion to repair with autologous chondrocyte implantation is a full-thickness defect surrounded by healthy, normal-appearing cartilage in an otherwise healthy knee. Any deviation from the ideal may require specific variations in technique or concomitant procedures to address additional pathology. Arthroscopic assessment also gives an opportunity for exam under anesthesia to confirm ligament stability and allows evaluation of the meniscal function and patellofemoral tracking.

**ACI Surgical Technique**

The surgical technique for autologous chondrocyte implantation includes 2 stages: the first involves an arthroscopic procedure to obtain a chondral biopsy for growing the autologous chondrocytes and the second is an open procedure for implantation of the cells within the chondral defect. The biopsy is obtained from the superior peripheral edges of the lateral or medial femoral condyles superior to the sulcus terminalis or from the inner edge of the intercondylar notch. The total volume of the several slivers of chondral tissue is about the size of a pencil eraser. The time between the biopsy and the implantation can be as short as 3 to 6 weeks or as long as months until the optimal time as determined by the patient and surgeon, based on return of motion and strength and other individual patient or family factors.

**Surgical Exposure**

The amount of exposure necessary for the implant procedure is determined by the size and location of the defect. A midline incision is generally recommended, followed by a medial or lateral parapatellar arthrotomy, exposing the corresponding chondral injury. As with any surgical procedure, it is essential that the full extent of the defect be exposed, facilitating all the technical aspects of the implantation. Inadequate exposure can lead to the incomplete securing of the periosteal patch to the defect, possibly resulting in cell leakage or graft delamination. Multiple, complex or hard-to-reach chondral injuries often require a larger midline incision with a medial parapatellar arthrotomy or mini-midvastus approach to sublux the patella for exposure.

**Defect Debridement**

During debridement of the defect, all damaged and unhealthy-appearing cartilage and fibrocartilage is removed using small curettes, leaving exposed subchondral bone with a rim of stable cartilage. This provides a stable nonmobile edge to affix the periosteal patch and decreases the risk of micromotion of the patch during rehabilitation, with incipient increased risk of graft delamination or hypertrophy. Overly aggressive debridement is avoided so as not to enter the cancellous portion of the bone, which would create excessive bleeding within the defect. The goal of adequate debridement of the defect is to have a dry defect with clean subchondral bone and a healthy surrounding cartilage border at the periphery (Figure 1). The best method for obtaining the correct size for the periosteal graft is to create a template from the sterile paper that comes with surgical gloves. A template can be made by placing a slightly larger piece of the paper over the defect and outlining the defect with a marking pen (Figure 2).

**Periosteal Harvest**

The next step is to obtain a periosteal graft to be transferred to the defect and secured to contain the cells. The periosteum harvest is from the proximal medial tibia. A separate incision is made just anterior to the posterior border of the tibia. The periosteum is easily accessible at this location. Obesity, inactivity, smoking, and increased age may lead to atrophy of the periosteum. In the event that the proximal medial tibia periosteum is thin and inadequate, an alternate site for periosteal procurement is the distal femur. Regardless of which periosteal harvest site is used, the final graft should be a clean contiguous layer, without holes or excessive fat or fascia on its outer surface (Figure 3). Although the medial femoral metaphysis serve as a good backup source, usually
the proximal tibia serves as the best and most consistent source for periosteal graft harvest.

**Securing Periosteal Graft**

The periosteal graft is then aligned over the defect in the orientation matching the template with the cambium layer of the peristeum facing the defect. The periosteum is next sutured to the cartilage rim. Then the suture line at the periosteal graft-defect interface is sealed with fibrin glue, using any of the commercial preparations of fibrin glue available in most operating rooms to assure a watertight seal of the chondral edges and the peristeum by acting as a rapidly setting sealant.

**Implantation of Autologous Chondrocytes**

The autologous chondrocytes are then sterilely injected under the periosteal graft into the defect.

![Figure 1](image1.png)

**FIGURE 1.** (A) This defect of the trochlea show scant fibrous tissue covering the exposed bone and irregular edges of damaged cartilage at the periphery (arrows). (B) The same defect has now been debrided back to a margin of healthy cartilage and the fibrous tissue has been removed exposing the subchondral bone. The defect is now ready for ACI.

![Figure 2](image2.png)

**FIGURE 2.** This defect of the lateral femoral condyle in a collegiate softball player (A) is covered with sterile glove paper to allow a template of the defect to be outlined and (B) used to obtain an exact size-matched periosteal graft from the anteromedial tibia just distal to the Pes insertion.

Each vial contains about 10 to 12 million chondrocytes and provides more than adequate cells for defects up to 10 cm² (Figure 4). The injection site is then closed with 1 or 2 additional sutures and sealed with fibrin glue. At this point the ACI is complete. Any concomitant procedures should be completed prior to implanting the chondrocytes and no additional manipulation of the joint should follow the implantation. The arthroscopy and wound is then closed in a layered fashion, and a soft sterile dressing.
and knee immobilizer applied to the knee. A drain is not routinely used due to the potential for damage to the graft by contact or from the suction effect of the drain. The postoperative course and rehabilitation will be covered in a later section.

COMPLEX DEFECTS

Uncontained Chondral Lesions

In cases where the defect is not fully contained by a rim of healthy cartilage, special techniques may be necessary to secure the periosteum and still establish a watertight seal. Locations where defects not infrequently involve at least 1 uncontained border include those extending to the intercondylar notch, such as OCD defects of the medial femoral condyle, the proximal margin of the patella, the lateral margin of trochlear defects from patellar dislocations, and the posterior lateral femoral condyle in lateral OCD. If a synovial fringe of tissue exists and is still well attached to the margin of the bone, the periosteum can be attached securely to the synovium. More frequently, there is no appropriate soft tissue for fixation and only bone surface remains at the margin. In these cases, absorbable microanchors loaded with 5 to 0 absorbable suture and the smallest free needle available work very well in securing the periosteum directly to the bone in the uncontained portion of the defect.

Multiple Chondral Lesions

Despite more extensive involvement in knees with multiple chondral lesions, good to excellent functional outcomes scores are still very possible. Provided the remaining knee is free of significant bony arthritic changes and coexisting knee pathology conditions are corrected, excellent outcomes comparable to those of smaller lesions can be achieved with ACI. The main factors to consider when undertaking multiple lesions treated with ACI are extensile exposure, insuring that multiple vials of cells will be available, and a plan to obtain sufficient periostium. In general, it is feasible to obtain 2 typical-sized grafts from the usual proximal tibia site. Both templates should be placed on the periosteum to achieve the best orientation and utilization of available periostium before cutting the grafts. If there has been previous surgery at the tibia and there is concern about adequate periostium, we have used the contralateral tibia in several cases. The distal femur, as described above under periostial harvest, should also be used when necessary for multiple defects.

Massive Chondral Lesions

A massive chondral defect is defined as a lesion greater than 8 cm². We have used ACI on defects over 20 cm², with outcomes similar to more usual-sized defects. Provided that the knee is nonarthritic and coexisting pathologic conditions are addressed, excellent outcomes can be expected when massive chondral defects are treated with ACI. One significant difference, however, is the time required for healing of the maturing repair tissue. It will take longer for maturation and therefore the rehabilitation process is controlled accordingly. We have also used an unloader brace during the first 6 months postoperatively in cases where an osteotomy was not

FIGURE 3. The periostium is harvested from the proximal medial tibia just distal to the pes insertion. (A) Through this small separate incision, the paper template is used to guide the size of the periostial graft. (B) Any excess fat is removed from the periostium prior to it being sutured over the defect.
FIGURE 4. (A) The suture line is sealed with fibrin glue applied through a syringe insuring a watertight seal for the cells. Note at the arrow a small opening left to inject the cells under the periosteal graft. (B) Cells are injected through a plastic catheter under the periosteal graft. The injection site is then closed with suture and also sealed with fibrin glue.

necessary. These massive-sized chondral lesions are also more likely to have uncontained cartilage borders and the technique of securing the periosteum with microanchors is frequently used.

Copathology and Concomitant Procedures

Good results with ACI, like any method of cartilage repair, should not be expected if coexisting knee pathology is not addressed. As we have developed a greater understanding of the clinical presentation of articular cartilage lesions, it appears that there are multiple factors that contribute to intra-articular knee problems. It is therefore predictable that there will often be coexisting knee pathology accompanying large chondral defects. Regardless of whether or not any coexisting knee pathology contributed to or occurred simultaneous with the chondral injury, the presence of continued knee pathology is clearly detrimental to restoring articular cartilage function and durability. Therefore, it is critical that associated knee pathology, including mechanical malalignment (both of the tibiofemoral joint as well as the patellofemoral articulation), ligamentous instability, and meniscal deficiency be corrected prior to, or in conjunction with, the cells being implanted. Another issue to be assessed is the degree of underlying bone damage to the subchondral bone, especially in OCD lesions or traumatic osteochondral injuries. Failure to recognize coexistent knee pathology prior to autologous chondrocyte implantation will dramatically reduce the chances of a good outcome.

When deficiencies are present in any of these areas, treatment needs to be planned to maximize the recovery of the patient, while still addressing the various co-pathologies. Many factors, such as the degree or severity of the deficiency, total number of problems, age of the patient, and the patient’s ability to comply with postoperative restrictions go into determining the best approach to each individual patient situation. In the authors’ experience, performing only 1 additional procedure at the same time as the ACI is preferred. This would include performing an ACL reconstruction or osteotomy, or meniscal transplantation or anteromedialization of the tibial tubercle, in addition to the ACI. However, when more extensive coexisting knee pathology exists to where 3 or more definitive reconstructive procedures may be indicated, staging may be more prudent. This is intended to cut down on the effect of cumulative potential complications. While there is no absolute answer as to when to include a concomitant procedure, versus staging, the author has not found increased risk of complications when combining ACI with 1 additional procedure. Of the initial 200 patients undergoing ACI, 55% underwent the following concomitant procedures in descending order of frequency: anteromedialization of the tibial tubercle, ACL reconstruction, high tibial osteotomy (HTO), and meniscal transplant. An additional 12% underwent a staged procedure, usually bone grafting of an osteochondral defect or HTO.

Tibiofemoral Malalignment

Biomechanical malalignment is typically addressed at the time of ACI. The type and location of the osteotomy depends on the type and degree of deformity. The traditional recommendations for osteotomy
correction of knee malalignment calls for overcorrecting the deformity to shift the mechanical axis to the opposite compartment.\textsuperscript{15,34} While that may be appropriate for treatment of osteoarthritis, the purpose of osteotomy associated with cartilage resurfacing is to decrease the forces in the overloaded compartment and balance the forces across the joint. As many of these patients are younger in age, they would not tolerate overcorrection, which they view as a deformity.

**Ligamentous Insufficiency**

Persistent ligamentous insufficiency produces excessive shear forces across the chondral surfaces in the knee. Even subtle laxity or giving way of the knee can result in unacceptable forces across the maturing cells, resulting in damage to the maturing repair tissue produced by autologous chondrocyte implantation. Anterior cruciate ligament (ACL) tears have been the most common ligamentous injury we have seen with full thickness chondral injuries.\textsuperscript{7} Posterior cruciate ligament (PCL) reconstruction also can accompany ACI. Typically performed concomitantly, ACL reconstruction should be completed prior to proceeding with ACI. Arthroscopic ACL reconstruction should be completed prior to proceeding with the arthrotomy for the autologous chondrocyte implantation. In cases where exposure may be a problem, such as very posterior condylar or any tibial defect, it may be beneficial to wait for final fixation of the tibial side of the ACL graft until the ACI procedure is completed.

**Meniscal Deficiency**

Meniscus transplantation should be considered in knees that have had a total meniscectomy performed in the same compartment as the chondral injury.\textsuperscript{7,35,36} A meniscal allograft will help to reduce the concentrated forces in the involved compartment and help protect the newly formed repair tissue.\textsuperscript{7,36} We tend to favor meniscal transplantation in younger patients and adolescents with complete absent menisci, and certainly if early tibial articular wear is present. The older patients with longstanding meniscectomy may be better served with osteotomy. It is interesting to note that of all the patients reported from the extensive Swedish series, with its high percentage of good and excellent results at long term follow-up, no patients underwent meniscal transplantation as that procedure is unavailable in that country.\textsuperscript{36} One could logically conclude that meniscal transplantation is the least essential component to a successful clinical outcome.

**Patellofemoral Malalignment**

Abnormal patellar tracking is not only the likely source of the patellar or trochlear injuries, but also would preclude an environment conducive for the maturation of the implanted chondrocytes into hyaline-like repair tissue. In addition to the concerns of lateral maltracking of the patella, decreasing the patellofemoral contact forces also is desirable. Depending on the degree of lateral maltracking, the amount of medialization can be adjusted accordingly. In some cases without lateral maltracking, anterior transfer of the tibial tubercle alone may be sufficient to reduce the contact pressure of the patellofemoral articulation.

In the vast majority of cases of patellar or trochlear chondral injuries, a distal patellar realignment procedure should be performed in combination with ACI. In our series of 92 patella and/or trochlea ACI procedures, 94% (88/94 patients) underwent concomitant anteromedialization of the tibial tubercle. While the patellar realignment can be performed with the initial arthroscopy, we have found it more prudent to almost always combine the distal realignment with the ACI for patellar or trochlear defects, allowing the osteotomized tubercle to be turned up proximally, giving extensile exposure to the knee. After the implantation, the tubercle is replaced to the modified position and held with screw fixation.

**Bone Deficiency**

One situation that routinely requires staging is the treatment of bone deficiency. In cases where the bony deficiency of the defect exceeds 7 to 8 mm in depth, a separate staged bone grafting procedure is performed. With further experience, the initial technique of open bone grafting has been replaced with an arthroscopic technique. After arthroscopic debridement of any necrotic bone in the base of the defect, autologous bone is harvested from the proximal tibia or distal femur through a cortical window and then a core harvest instrument from an osteochondral graft set. The harvest sites are backfilled with off-the-shelf bone graft plugs. The ACI procedure can then be performed at least 4 to 6 months later after the bone graft has incorporated.

Bone grafting allows restoration of the level of the subchondral bone and gives a healthy base for the chondrocytes to attach and grow.\textsuperscript{4} Staged bone grafting is usually done at the time of arthroscopic evaluation and chondral biopsy.

Another newer technique is the so-called “sandwich” bone-grafting technique, which allows single-stage bone grafting of a bony defect in combination with ACI. In this procedure, the defect is exposed with an arthrotomy, as described above, and the base of the defect debrided of necrotic bone. Bone graft is then obtained either from the iliac crest or from the distal femur or proximal tibia, as described above. We have favored taking local bone from around the knee and backfilling the donor site rather than expose the patient to the morbidity of an iliac crest harvest. The
bone graft is then impacted into the defect up to the level of the subchondral bone. First a periosteal graft is placed in the defect with the cambium side up toward the joint and secured with sutures either into the base of the rim of articular cartilage or with absorbable suture anchors into the bone. Then a second graft is secured to the chondral surface with the cambium side down toward the defect, again in an identical fashion to the basic ACI procedure. The cells are then injected below the outer layer of periosteum thus sandwiching the cells between the 2 layers of periosteum, both with their cambium layers facing the cells. The bone graft then consolidates concurrently with the maturation of the chondrocytes. This procedure is technically very demanding.

Rehabilitation Following ACI

The rehabilitation program following chondrocyte implantation is vital to the success and long-term outcomes of patients (Table 1). The protocol is based on the maturation process of the chondrocytes, size of the defect, and location of the defect. The concept of a slow, gradual maturation of the repair tissue is crucial to understanding the rehabilitation following ACI. The biologic nature of the hyaline-like repair tissue must be both protected and stimulated to allow the maturation and remodeling of the tissue. Premature overload of the repair tissue will increase the likelihood of failure.

<table>
<thead>
<tr>
<th>TABLE 1. Rehabilitation following autologous chondrocyte implantation.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1. Early protection phase (weeks 0-6)</td>
</tr>
<tr>
<td>Goals</td>
</tr>
<tr>
<td>• Protect healing tissue from load and shear forces</td>
</tr>
<tr>
<td>• Decrease pain and effusion</td>
</tr>
<tr>
<td>• Restoration of full passive knee extension</td>
</tr>
<tr>
<td>• Gradually improve knee flexion</td>
</tr>
<tr>
<td>• Regain quadriceps control</td>
</tr>
<tr>
<td>Brace</td>
</tr>
<tr>
<td>• Locked at 0° during weight-bearing (WB) activities</td>
</tr>
<tr>
<td>• Sleep in locked brace for 2-4 wk</td>
</tr>
<tr>
<td>WB</td>
</tr>
<tr>
<td>• WB status varies based on lesion location and size</td>
</tr>
<tr>
<td>For femoral condyle lesions</td>
</tr>
<tr>
<td>• Non-WB for 1-2 wk, may begin toe-touch WB immediately per physician if lesion &lt;2.0 cm²</td>
</tr>
<tr>
<td>• Begin toe-touch WB (approximately 9-14 kg) at weeks 2-3; progress to partial WB (approximately ¼ body weight) at weeks 4-5</td>
</tr>
<tr>
<td>For patellofemoral lesions</td>
</tr>
<tr>
<td>• Immediate toe-touch WB of approximately 25% body weight, with brace locked in full extension</td>
</tr>
<tr>
<td>• Progress to 50% WB at week 2 and 75% WB at weeks 3-4, with brace locked in full extension</td>
</tr>
<tr>
<td>Range of motion (ROM)</td>
</tr>
<tr>
<td>• Immediate motion exercise day 1</td>
</tr>
<tr>
<td>• Full passive knee extension immediately</td>
</tr>
<tr>
<td>• Initiate CPM day 1 for total of 8-12 h/d (0°-60°; if patellofemoral lesion &gt;6.0 cm², 0°-40°)</td>
</tr>
<tr>
<td>• Progress CPM ROM as tolerated 5°-10° per day</td>
</tr>
<tr>
<td>• May continue CPM for total of 6-8 h/d for up to 6 wk</td>
</tr>
<tr>
<td>• Patellar mobilization (4-6 times per d)</td>
</tr>
<tr>
<td>• Passive knee flexion ROM at least 2-3 times daily</td>
</tr>
<tr>
<td>• Passive knee ROM as tolerated</td>
</tr>
<tr>
<td>• For femoral condyle lesions, knee flexion ROM goal is 90° by weeks 1-2, 105° by week 3, 115° by week 4, and 120°-125° by week 6</td>
</tr>
<tr>
<td>• For patellofemoral lesions, knee flexion ROM goal is 90° by weeks 2-3, 105° by weeks 3-4, and 120° by week 6</td>
</tr>
<tr>
<td>• Stretch hamstrings and calf</td>
</tr>
<tr>
<td>Strengthening program</td>
</tr>
<tr>
<td>• Ankle pump using rubber tubing</td>
</tr>
<tr>
<td>• Quadriceps setting</td>
</tr>
<tr>
<td>• Multantia isometrics (cocontractions Q/H)</td>
</tr>
<tr>
<td>• Active knee extension 90°–40° for femoral condyle lesions (no resistance)</td>
</tr>
<tr>
<td>• Straight leg raises (4 directions)</td>
</tr>
<tr>
<td>• Stationary bicycle when ROM allows; low resistance</td>
</tr>
<tr>
<td>• Electrical muscle stimulation and/or biofeedback during quadriceps exercises</td>
</tr>
<tr>
<td>• Isometric leg press at week 4 (multantia)</td>
</tr>
<tr>
<td>• May begin use of pool for gait training and exercises week 4</td>
</tr>
<tr>
<td>• Initiate weight-shifting exercises with knee in extension by weeks 2-3 for patellofemoral lesions</td>
</tr>
<tr>
<td>• No active knee extension exercises for patellofemoral lesions</td>
</tr>
<tr>
<td>Functional activities</td>
</tr>
<tr>
<td>• Gradual return to daily activities</td>
</tr>
<tr>
<td>• If symptoms occur, reduce activities to reduce pain and inflammation</td>
</tr>
<tr>
<td>• Extended standing should be avoided</td>
</tr>
</tbody>
</table>

758 J Orthop Sports Phys Ther • Volume 36 • Number 10 • October 2006
TABLE 1 (continued)

Swelling control
- Ice, elevation, compression, and modalities as needed to decrease swelling

Criteria to progress to phase 2
- Full passive knee extension
- Knee flexion to 120°
- Minimal pain and swelling
- Voluntary quadriceps activity

Phase 2. Transition phase (weeks 6-12)

Goals
- Gradually increase ROM
- Gradually improve quadriceps strength/endurance
- Gradual increase in functional activities

Brace
- Discontinue brace at week 6
- Consider unloading knee brace for femoral condyle lesions

WB
- Progress WB as tolerated
  - For femoral condyle lesions: ½ body weight with crutches at 6 wk; progress to full WB at 8-9 wk, discontinue crutches
  - For patellofemoral lesions: progress to full WB at weeks 6-8, discontinue crutches

ROM
- Gradual increase in ROM
- Maintain full passive knee extension
- Progress knee flexion to 125°-135° by week 8
- Continue patellar mobilization and soft tissue mobilization, as needed
- Continue stretching program
- Progress WB exercises
- Initiate weight shifts week 6 for femoral condyle lesions
- Leg press at weeks 7-8
- Mini-squats 0°-45° week 8
- Toe-call raises week 6 for patellofemoral lesions, week 8 for femoral condyle lesions
- Progress balance and proprioception drills
- Initiate front lunges, wall squats, front and lateral step-ups at weeks 8-10
- For femoral condyle lesions, progress non-WB knee extension (0.45 kg/wk)
- For patellofemoral lesion, may begin non-WB knee extension without resistance in a ROM that does not allow for articulation of the lesion
- Stationary bicycle, low resistance (gradually increase time)
- Treadmill walking program at weeks 10-12
- Continue use of electrical muscle stimulation and or biofeedback as needed
- Continue use of pool for gait training and exercise

Functional activities
- As pain and swelling (symptoms) diminish, the patient may gradually increase functional activities
- Gradually increase standing and walking

Criteria to progress to phase 3
- Full ROM
- Acceptable strength level
- Hamstrings within 20% of contralateral extremity
- Quadriceps within 30% of contralateral extremity
- Balance testing within 30% of contralateral extremity
- Able to walk 1.6-3.2 km or bike for 30 min

Phase 3. Remodeling phase (weeks 12-26)

Goals
- Improve muscular strength and endurance
- Increase functional activities

ROM
- Patient should exhibit 125°-135° flexion

Exercise program
- Leg press (0°-90°)
- Bilateral squats (0°-60°)
- Unilateral step-ups, progressing from 5 to 20 cm
- Forward lunges
- Walking program
- Progress non-WB extension (0°-90°), for patellofemoral lesions perform from 90°-40°, or avoid angle where lesion articulates
  - Progress 0.45 kg every 2 wk beginning week 20 if no pain or crepitation; must monitor symptoms

J Orthop Sports Phys Ther  Volume 36  Number 10  October 2006  759
There are 3 basic phases associated with this healing process: the proliferative phase, the matrix production phase, and the maturation phase. Each successive phase can accommodate greater degrees of load, allowing the addition of sequential weight bearing, exercise, and impact. Fully mature repair tissue, which may take 12 to 24 months, can show stiffness very close to the surrounding articular cartilage. During the initial phase of rehabilitation, the critical elements are range of motion, protection of the graft from mechanical overload, and strengthening exercises to allow for a functional gait.

Early controlled ROM and weight bearing are necessary to stimulate cellular orientation and chondrocyte development. Continuous passive motion is started 6 to 12 hours after surgery. The CPM is used for 8 to 12 hours per day for 2 to 3 weeks, although CPM use is recommended for up to 6 to 8 weeks. Because the surgical procedure involves an open approach and subsequent soft tissue trauma, passive ROM is performed cautiously so as not to facilitate swelling. However, caution must be placed on avoiding loss of motion from soft tissue adhesions. Therefore, a gradual restoration of motion is utilized. Typical goals include 90° of flexion at 1 week postoperative, 105° at week 2, 115° at week 3, 125° at week 4, and gradual progression to 135+° following week 6. Soft tissue mobilization and patellar mobilization are also performed as needed.

Unless the lesion is excessively large, deep, or uncontained, immediate toe-touch weight bearing is performed, progressing to 25% body weight at week 2, 50% at weeks 4 to 5, and finally to full weight bearing by 6 to 8 weeks. Progression of weight bearing is guided by the size of the defect; smaller well-contained defects are progressed more rapidly than larger uncontained defects (Figure 5). Exercises are initially limited by the weight-bearing status, and subsequent soft tissue trauma, passive ROM is performed cautiously so as not to facilitate swelling. However, caution must be placed on avoiding loss of motion from soft tissue adhesions. Therefore, a gradual restoration of motion is utilized. Typical goals include 90° of flexion at 1 week postoperative, 105° at week 2, 115° at week 3, 125° at week 4, and gradual progression to 135+° following week 6. Soft tissue mobilization and patellar mobilization are also performed as needed.

Unless the lesion is excessively large, deep, or uncontained, immediate toe-touch weight bearing is performed, progressing to 25% body weight at week 2, 50% at weeks 4 to 5, and finally to full weight bearing by 6 to 8 weeks. Progression of weight bearing is guided by the size of the defect; smaller well-contained defects are progressed more rapidly than larger uncontained defects (Figure 5). Exercises are initially limited by the weight-bearing status, and subsequent soft tissue trauma, passive ROM is performed cautiously so as not to facilitate swelling. However, caution must be placed on avoiding loss of motion from soft tissue adhesions. Therefore, a gradual restoration of motion is utilized. Typical goals include 90° of flexion at 1 week postoperative, 105° at week 2, 115° at week 3, 125° at week 4, and gradual progression to 135+° following week 6. Soft tissue mobilization and patellar mobilization are also performed as needed.

Unless the lesion is excessively large, deep, or uncontained, immediate toe-touch weight bearing is performed, progressing to 25% body weight at week 2, 50% at weeks 4 to 5, and finally to full weight bearing by 6 to 8 weeks. Progression of weight bearing is guided by the size of the defect; smaller well-contained defects are progressed more rapidly than larger uncontained defects (Figure 5). Exercises are initially limited by the weight-bearing status, and subsequent soft tissue trauma, passive ROM is performed cautiously so as not to facilitate swelling. However, caution must be placed on avoiding loss of motion from soft tissue adhesions. Therefore, a gradual restoration of motion is utilized. Typical goals include 90° of flexion at 1 week postoperative, 105° at week 2, 115° at week 3, 125° at week 4, and gradual progression to 135+° following week 6. Soft tissue mobilization and patellar mobilization are also performed as needed.
beginning with quadriceps setting and straight leg raise exercises, and progressing to lower extremity exercises in weight bearing and on exercise machines. Emphasis is placed on restoring quadriceps strength initially and then progressed to maximize strength of the entire lower extremity. Addition of further exercises should be based upon the size, location, and amount of containment of the lesion by normal surrounding cartilage.

Basic science studies have shown that it may take up to 6 months for the graft site to become firm and at least 9 months to become as durable as the surrounding healthy articular cartilage. Thus, low-impact activities, such as swimming, biking, golfing, and skating, are initiated by months 5 to 6 and progressed to moderate-impact activities, such as jogging, from months 7 to 9. The patella and trochlea are protected from open-chain exercises and shear loading for at least the first 3 months. Following these principles during the repair, maturation continuum will provide an optimum environment for the tissue to grow and mature.

The inclusion of concomitant surgical procedures to address issues with tibiofemoral alignment, patellofemoral alignment, ligamentous stability, and meniscal pathology will alter the rehabilitation approach (Table 2). The rehabilitation specialist must consider the healing constraints of the ACI procedure as well as the concomitant surgery.

**Clinical Results**

ACI has been performed for over a decade in the United States and Europe and almost 2 decade in Sweden. Peterson et al. have reported a retrospective analysis on the first 100 patients treated with ACI, with follow-up ranging between 2 to 9 years. Twenty-three of 25 (92%) patients with isolated femoral condyle chondral lesions had successful outcomes, while 16 of 18 (89%) patients with osteochondral defects had good to excellent results. Multiple rating scales, including the Modified Cincinnati Score, Tegner Score, and Lysholm Score, were used to assess the clinical and functional outcomes. Additionally, they reported a 96% durability of good to excellent results initially at 2-year follow-up, with 30 of 31 patients maintaining those results at 7.5-year follow-up. The overall clinical outcomes remained constant (80% good to excellent results at 2 years, and 78% at 7.5 years) and second-look arthroscopies did not show signs of tissue breakdown. Additionally, experience has grown rapidly in the US and Europe, further documenting and defining the clinical applicability of this technique.

Other international centers with at least 2-year follow-up have reported comparable outcomes to the Swedish series. Spalding from the United Kingdom and Bahuard from France both reported good to excellent clinical outcome of 75% and 84%, respectively, with military personnel, showing that the majority of these patients were able to return to active military duty. Further series from Norway and the United Kingdom show similar clinical results and also show histologic data on biopsies with 75% of the specimens showing hyaline-like repair tissue. Bentley et al. reported on a prospective randomized

---

**FIGURE 5.** Both of these defects are in the medial femoral condyle; however, the defect in A is smaller, well contained, and surrounded with normal articular cartilage and will allow for more rapid advancement of weight bearing. The defect in B is massive and involves the entire weight-bearing area of the condyle, causing weight bearing to proceed in a slower, more controlled fashion.
TABLE 2. Autologous chondrocyte implantation rehabilitation variations based on concomitant surgical procedures and lesion variation.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Rehabilitation Variations</th>
</tr>
</thead>
</table>
| Meniscal allograft | - Rehabilitation is altered to allow healing of meniscus allograft  
- Weight bearing (WB) similar to isolated femoral condyle lesion  
- Range of motion (ROM) progression is slightly slower  
- No active knee flexion is allowed past 90° for the first 6-8 wk  
- Resisted hamstring exercises are avoided for the first 12 wk  |
| High tibial osteotomy | - Rehabilitation is altered to allow healing of the tibial osteotomy  
- WB is progressed similar to an isolated femoral condyle lesion, although may be delayed based on radiographic evidence of bone healing  
- ROM progression is slightly accelerated to minimize loss of knee motion  
- The use of heel wedges, orthotics, and/or unloading knee braces is recommended when WB is progressed |
| Anterior cruciate ligament reconstruction | - Rehabilitation is altered to prevent healing of the ACL  
- WB similar to isolated femoral condyle lesion  
- ROM progression is slightly accelerated to minimize arthrofibrosis, prevention is key |
| Distal realignment | - Rehabilitation is altered to minimize strain on tibial tubercle  
- ROM is slower, from 0°-90° for up to the first 4 weeks  
- WB is similar to isolated trochea lesion, with immediate partial WB in a knee brace locked in extension  
- Active knee extension exercises are avoided for the first 6-8 wk |
| Osteochondritis dissecans | - Rehabilitation is similar to isolated guidelines initially  
- Return to functional and impact activities is slightly decelerated  
- WB may also be delayed up to 4 wk in the presence of concomitant bone-grafting procedures |
| Large, deep, uncontained, and multiple lesions | - Rehabilitation program is highly individualized and is decelerated due to more extensive lesion and more tenuous repair  
- For femoral condyle lesions, WB progression is delayed for 2-4 wk, with an initial period of non-WB for up to 2-4 wk  
- For trochea lesions, ROM, and the initiation of active knee extension exercises are slightly decelerated, aggressive knee extension resisted exercises are avoided for up to 9-12 mo |
| Combined femoral condyle and trochlea lesions | - Rehabilitation is altered to address healing constraints of both lesion locations  
- WB progression follows the isolated femoral condyle lesion guidelines  
- ROM and exercise progression follows the isolated trochlea lesion guidelines |

The study comparing ACI and mosaicplasty found that 88% excellent and good results with ACI, versus 69% in the mosaicplasty group at 19 months follow-up. One-year, second-look arthroscopies showed 82% excellent and good repairs in the ACI group, versus only 34% in the mosaicplasty group. 

Horas et al reported on 40 patients randomly assigned to ACI or mosaicplasty for chondral injuries. At 2 years, both groups had improved pain, although the ACI group lagged behind the mosaicplasty group on Lysholm scores. Histologically, the ACI group showed fibrocartilage superficially and hyaline-like repair tissue closer to the subchondral bone. 

Knutsen et al reported a randomized controlled study of 40 patients treated with microfracture and 40 patients treated with ACI at 4 centers, with 2-year follow-up. Both methods showed acceptable outcomes at this early follow-up and there were no significant differences on macroscopic appearance or histologic findings. 

Minas and Chiu reported results on 235 patients treated with autologous chondrocyte implantation and found an 87% success rate over a 6-year period. The majority of his patients had complex lesions with coexistent knee pathology or salvage patients with early degenerative changes, such as osteophytes or some joint space narrowing. The authors have also noted that salvage patients with early degenerative changes do not attain as high of activity scores after ACI, however, they have the highest patient satisfaction ratings, perhaps because they were starting at very difficult baseline levels.

The author’s clinical results with the initial 112 patients treated with ACI have shown a 91% good to excellent success rate over a five-year period (Figure 6). Of the 54 patients with a 2-year or greater follow-up, significant improvements from the baseline scores were noted in each of the assessment tools utilized (Modified Cincinnati Rating Scale, Knee Society Clinical Rating, and Sports Score) with a consistent progression over time. The average clinician and patient evaluations of overall knee function showed significant improvement from baseline, and showed an improvement on an annual basis. The baseline scores for clinician and patients were scores of 3.9 out of 10, consistent with poor levels of function. The 24-month follow-up showed improvement in knee function, with a significant increase in average score to 8.3 and 7.9, consistent with good to excellent outcomes. At 36, 48, and 60 months, the clinician and patient scores continued to show improvement over baseline without decline in function over time. Additional subgroup analysis has shown no statistical difference in outcomes for gender, size of the defect, location of the defect on the femur, isolated versus multiple defects or ACI with concomitant procedure or alone. There was, however, a statistical difference, with better results with lesions treated within 1 year from injury or onset of symptoms than in chronic defects present for greater than 1 year.
FIGURE 6. This 39-year-old female had persistent pain about her medial compartment. (A) Medial femoral condyle defect after debridement and (B) after periosteal graft and implantation of cells. (C) Second-look arthroscopy at 12 months after autologous chondrocyte implantation, showing excellent restoration of articular cartilage surface.

The Cartilage Registry Report, an international multicenter observational assessment of patients treated with ACI, has revealed that 78% of all defects treated with ACI had improvement by patient assessment, while 81% of isolated femoral condyle defects had improved. Clinician evaluations have shown a 79% improvement for all lesions and an 85% improvement in femoral condyle lesions. The most common adverse event reported with ACI is intra-articular adhesions (2%). The next most common adverse events include detachment/delamination (less than 1%).

CONCLUSION

Autologous chondrocyte implantation is a reproducible treatment option for large, full-thickness symptomatic chondral injuries with appropriate knowledge of technique and patient selection. It provides a cellular repair that offers a high percentage of good to excellent clinical results over a long follow-up period. It is applicable over a wide range of chondral injuries from simple to more complex lesions. It is essential that the intra-articular environment be as close to normal as possible for successful cartilage repair. Coexisting knee pathology must be aggressively treated. ACI does have a prolonged postoperative rehabilitation course necessitated by the biologic nature of the repair and patients must be able to comply with the rehabilitation and temporary restrictions required for a successful outcome. Within these guidelines, ACI has proven to be very beneficial for patients with difficult articular cartilage injuries. With further basic science and clinical research, the reproducibility, ease of surgical delivery of the autologous cells, and results can only be anticipated to improve.

REFERENCES