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Autologous Chondrocyte Implantation: Current Surgery and Rehabilitation

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ABSTRACT

RIEGGER-KRUGH, C. L., E. C. MCCARTY, M. S. ROBINSON, and D. A. WEGZYN. Autologous Chondrocyte Implantation: Current Surgery and Rehabilitation. *Med. Sci. Sports Exerc.*, Vol. 40, No. 2, pp. 206–214, 2008. Autologous chondrocyte implantation (ACI) is a treatment option for full-thickness chondral, or osteochondral injuries that are painful, debilitating, and progressive. Goals of surgery and rehabilitation include replacement of damaged cartilage with hyaline or hyaline-like structure, maintained durability to withstand knee intraarticular forces over time with a productive level of function, and restoration of the normal surface congruity of the joint. Intermediate and long-term results are promising in terms of clinical improvement and durability using ACI. This article outlines the surgical technique, the histological and biomechanical principles on which the surgery and rehabilitation process are based, and a recommended rehabilitation protocol. **Key Words:** CARTILAGE DEFECTS, CHONDRAL INJURIES, CARTILAGE REGENERATION, CARTILAGE LESIONS

Injuries to the articular cartilage of the knee have long been recognized as painful, progressive, and debilitating. Autologous chondrocyte implantation (ACI), which was initiated during the 1980s in Sweden, is a treatment option for full-thickness chondral or osteochondral injuries (26). Brittberg et al. (1) reported on ACI in a group of patients with full-thickness cartilage defects treated with ACI. In this 1994 study, ACI was performed in 23 patients with isolated defects of knee cartilage as a result of either trauma or osteochondritis dissecans. The authors reported that 14/16 patients with femoral lesions had restored considerable knee function at the 3-yr follow-up (1). The success was attributed to the formation of new cartilage that was histologically similar to normal cartilage in that it had type II collagen (1). The current article outlines the surgical technique, histological, and biomechanical concepts on which the surgery and rehabilitation process are based, and the rehabilitation protocol used at our institution.

ACI SURGICAL TECHNIQUE

Definition/indications/contraindications of ACI. Chondral injuries are unique in that the repair process of articular cartilage is limited (27), and, in addition, chondrocytes have limited migratory abilities (16). Full-thickness lesions larger than a few millimeters in diameter do not heal (27). Typically, chondral injuries are caused by repetitive shear, torsional loads, or high-impact stress (16). The reported prevalence of isolated, focal articular cartilage defects is approximately 5% (16).

Several well-described techniques are used to treat chondral lesions by stimulating the marrow to produce a fibrin clot overlying the lesion. These techniques include abrasion, drilling, and microfracture (27). Acceptable results occur using marrow stimulation techniques as an initial procedure for lesions smaller than 2 cm^2 (16). Clinically, these treatment options may have limited durability in terms of long-term outcomes (27). Long-term outcomes for ACI are not yet known.

Indications for ACI include symptomatic lesions located in the femoral condyles, femoral trochlea, or patella (26). Ideally, the lesions are between 10 and 40 mm in diameter, with a depth of bony defect between 6 and 8 mm (26). Age range is usually between 15 and 55 yr old, with body mass index ideally less than 30 $kg{\cdot}m^3$ (16,26). Contraindications include knee joint skeletal malalignment, ligamentous instability, meniscal deficiency (5,20), bipolar lesions (grade II or higher on the opposing surface), and lesions involving significant bone loss (20). Goals of the surgery and rehabilitation are to

- control the patient's symptoms (5,20);
- maintain the durability to withstand knee intraarticular forces over time, with a productive level of function (5,20);
- restore the normal surface congruity of the joint (5);

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- prevent the progression of focal chondral injuries to full-blown osteoarthritis (5);
- replace damaged cartilage with hyaline or hyaline-like structure (20); and
- allow for future treatment options (20).

Preoperative evaluation. A proper preoperative evaluation includes a full history and physical examination to understand the mechanism of injury and to potentially identify risk factors for future lesions. Patients with focal chondral or osteochondral lesions are typically young, active individuals. A specific traumatic episode is frequently absent from the history. Patients with chondral lesions often will complain of pain during high-impact loading activities. Interference with daily activities due to pain and postoperative expectations by patients are important to note.

Typical physical examination findings can include effusion, decreased range of motion, joint line tenderness, patellar instability, and apprehension, as well as crepitation and other mechanical symptoms. Presentation can be subtle and may mimic more common pathology, including meniscal tears and patellofemoral maltracking. Standard radiographic evaluation should include posteroanterior weight-bearing views to assess for medial and/or lateral compartment narrowing, and bilateral merchant views to assess patellar facet wear, subluxation, and tilt (16). Additionally, bilateral long-leg standing radiographs are obtained to evaluate possible malalignment that could potentially compromise cartilage implantation (16). MRI may be beneficial for a more thorough evaluation of other intra-articular derangements, such as cruciate and collateral ligament injuries and meniscal pathology. A systematic and thorough evaluation is essential to address any pathology that may compromise the ACI. Depending on the pathology identified, staged or concomitant procedures, such as anterior cruciate ligament reconstruction, osteotomies, and meniscal repair or transplantation, may be indicated (16).

Surgical procedure. ACI is a two-staged procedure. Before definitive management, a detailed and well-documented arthroscopic examination should be performed. If the patient is an optimal candidate, surgical intervention is recommended. Under general anesthesia, a bloodless field is obtained through the use of a tourniquet (1). Autologous cartilage is harvested from the unloaded proximal, medial edge of the trochlea during initial arthroscopy (26). The harvested cartilage should ideally contain the entire cartilaginous surface with underlying subchondral bone (2). The weight of the harvested cells is usually 200–300 mg and includes between 200,000 and 300,000 cells (16). Once harvested, the cartilage is placed in a chilled, sterile, sodium chloride solution, with the goal of isolating the cells within 2–5 h (1). The cartilage specimen is then minced and washed three times in a specific culture medium, followed by an enzymatic digestion process that lasts 16 h (1). The isolated cells are then filtered through a nylon mesh, washed three times, counted, and suspended again in a culture medium supplemented with a small percentage of the patient's serum (1). The culture medium is changed twice weekly and tested for bacterial growth (1). This process enables the chondrocytes to be cultured for several weeks, thereby increasing the number of cells by a factor of 20–30 (26). The transplantation of the chondrocytes can occur no sooner than 2 wk after the harvesting and culturing of the cells (26).

At the second operation, the patient receives either general anesthesia or a spinal block, as well as prophylactic intravenous antibiotics (1). The patient is positioned supine on the operating table, and a midline skin incision is performed, followed by a medial or lateral parapatellar arthrotomy, depending on the location of the lesion. The next step is debridement of the lesion, which includes sharp dissection to the level of subchondral bone (26). The lesion is measured to allow proper sizing of the periosteal flap to be harvested from the ipsilateral medial tibia (1,26). The periosteal flap is carefully sutured over the defect, using a small 6.0 nonabsorbable suture, leaving a small opening for injection of the chondrocytes (26). The periosteal flap can have no defects or leaks, which ensures maximal containment of the chondrocytes. The repair often is augmented with fibrin glue (26). The implantation of the chondrocytes is now performed using an angiocath to inject the cells through the superior opening (26). Once completed, the remaining sutures and additional fibrin glue are placed in the periosteal flap. If performed correctly, the periosteal flap not only contains the chondrocytes, but also allows the cells to receive nutrition via diffusion (26). The wound is closed sequentially in layers, and a standard postoperative compressive dressing is applied. Postoperative cryotherapy is used to help control swelling and pain. An intraarticular drain is not advised, because it may physically remove the transplanted cartilage (26).

Outcomes of ACI. There is no conclusive evidence in the literature that ACI technique has superior results compared with other surgical techniques for full-thickness cartilage defects (9,18). Outcomes have been reported as similar to microfracture (18) and osteochondral cylinder transplantation (9). Because different patient populations may be advised to select different surgical procedures, comparison of outcomes among the different surgical procedures is difficult. Both positive effects and disadvantages/risks of ACI have been reported, with the positive outcomes seeming to outweigh the negative outcomes.

Overall results of ACI have been encouraging through the years. Brittberg et al. (1), in 1994, reported outcomes after 36 months following transplantation of femoral condylar and patellar lesions. He categorized ratings as excellent (no pain, swelling, or locking with strenuous activity), good (mild aching with strenuous activity but no swelling or locking), fair (moderate pain with strenuous activity and occasional swelling but no locking), or poor (pain at rest, swelling, and locking). Patients with femoral condylar transplants had decreased knee pain, swelling, and crepitation, and knee locking was completely gone. Biopsy results indicated that 11 of the 15 femoral transplants had the appearance of hyaline cartilage. He also categorized gross appearance as biologically acceptable if the cartilage defect was filled with cartilaginous tissue that was in contact with, as well as level with, the surrounding articular cartilage. At 3 months, the initial arthroscopy showed regenerated areas of cartilage with visible borders that were level with the surrounding articular surface. Two years after transplantation, 14 of his 16 patients with femoral condylar transplants had good-to-excellent results (1). The two patients followed for the longest period had excellent results at 55 and 59 months after transplantation. For seven patients with patellar transplants, outcomes were graded excellent or good in two, fair in three, and poor in only two at a mean follow-up of 36 months after transplantation. Five of seven patients with patellar transplants had improved knee function, as indicated by an absence of locking. In 1996, Peterson (25) presented results of ACI in 219 patients with a minimum follow-up of 2 yr, which demonstrated an 85% success rate in isolated femoral lesions (25). Peterson et al. (27) evaluated the durability of ACI grafts in either the femoral condyle or patella in 61 patients, with a mean follow-up of 7.4 yr. At 2 yr, 50 of the 61 patients had good or excellent results, and at 5–11 yr, 51 of the 61 had good or excellent results (27).

Other positive outcomes were reported in the years after 1994. In 2001, Micheli et al. (22) reported a 94% success rate in a multicenter cohort study involving 50 patients treated with ACI, with a minimum of a 36-month follow-up. In 2003, Peterson et al. (28) evaluated ACI for the treatment of osteochondral dissecans in 58 patients at follow-up times of 2 and 10 yr, with a 90% successful clinical result. Also in 2003, with 40 patients with lesions on the weight-bearing area of the femoral condyle, Horas et al. (9) reported that at 2 yr after surgery, defects in all patients showed complete and mechanically stable surfaces. In 2004, Knutsen et al. (18), with 40 patients with single defect in the femoral condyle, stated that at 2 yr after surgery, his patients had significantly reduced pain and had significant clinical improvement overall. He noted that younger patients had better outcomes than older patients.

By 2005, Fu et al. (4) reported their superior results of ACI over debridement in a cohort study conducted during a 3-yr period with 54 and 42 patients, respectively. Also in 2005, Mithofer et al. (23) investigated ACI for use in high-level athletes. A total of 45 soccer players underwent ACI, with a 41-month follow-up. Of these players, 72% had good to excellent results (23). The number of good to excellent results improved to 85% of players with single cartilage lesions and 93% in players with lesions isolated to the medial femoral condyle (23). Again in 2005, Browne et al. (2) reported a 71% improvement at the 5-yr mark in a difficult group of patients with prior surgical procedures, large lesions, and poor function at baseline. By 2006, Henderson et al. (8) had outcomes on 230 patients with either femoral, trochlear, or patellar lesions. He expressed that the ACI provided a durable long-term option for articular cartilage repair. He had experienced good to excellent results in 84% of cases as long as 11 yr after surgery. His outcome scores were based on the IKDC (International Knee Documentation Committee) clinical outcome questionnaire, modified Cincinnati knee score, and SF-36 physical component of the SF-36 score.

Whereas many studies have demonstrated positive outcomes for the ACI, some risks, disadvantages, and poor outcomes have occurred. Brittberg et al. (1), in 1994, noted the negative clinical outcomes of ACI, including continued knee locking and pain and poor capacity for cartilage to repair. Poor transplantation results were reported in patients with severe chondromalacia, with biopsy results indicating that only one of seven patellar transplants had the appearance of hyaline cartilage. Only one of the seven patients with patellar transplants had a biopsy specimen with an intact articular surface and a hyaline appearance comparable with that of the surrounding cartilage. Brittberg et al. (1) noted that patients with patellar transplants could develop other future pathology, such as osteoarthritis, and require other procedures, additional surgery because of severe central wear in the transplants and the possibility of a total knee replacement. By 2002, Peterson et al. (27) reported the timeline that if graft failure occurred, the graft usually would fail within the first 2 yr. By 2003, Horas et al. (9) reported that in one patient with a very large patellofemoral defect, there was increased pain and deterioration in function. In 2004, Knutsen et al. (18) reported 2 failures out of 40 patients with a single defect in the femoral condyle. By 2006, Henderson et al. (8) reported a reoperation rate after ACI of 30.9% of his 230 repairs and a general reoperation rate from him and others from 5.1 to 51%. Most of these reoperations were a result of the periosteal patch, such as adhesions, extrusion, and delamination, or a result of graft hypertrophy, which is overfilling of the lesion site, with a loss of continuous cartilage-surface thickness. Graft hypertrophy occurred mostly in small lesions and seemed to be a problem of the implanted cells, and not the patch (8).

Current recommendations are to perform marrow-stimulation techniques, such as microfracture, for lesions less than 2 cm^2, and ACI for lesions larger than 2 cm^2 (16). Proper patient selection and education are important to the success of ACI. Intermediate and long-term results are promising in terms of clinical improvement and durability using ACI (16). Although ACI continues to be the most widely researched clinical cartilage-repair technique, other investigators are studying alternative methods to treat osteochondral injuries (7). In 2006, Kim et al. (17) discussed the use of gene therapy to repair articular cartilage lesions. In 2007, Kuroda et al. (19) reported the successful use of autologous bone marrow stromal cells harvested from the iliac crest, cultured in the lab, and subsequently implanted into a 20 × 30-mm full-thickness articular cartilage defect of the weight-bearing medial femoral condyle in a 31-yr-old active judo competitor with a defect in the medial femoral condyle. These cells (which are mesenchymal stromal cells) in adult bone marrow are multipotent and can develop into bone, cartilage, and other connective tissue structures, depending on the stimulus imposed on these cells. Seven months after surgery, the defect was filled with a hyaline-like type of cartilage tissue, and clinical symptoms had improved significantly. The patient had regained his previous activity level and experienced no pain or other complications.

HISTOLOGICAL AND BIOMECHANICAL PRINCIPLES OF ACI SURGERY AND REHABILITATION

The two main goals for the ACI rehabilitation program are 1) local adaptation and remodeling of the repair and, and 2) return to function (7). The entire rehabilitation team must have expertise in the anatomy and biomechanics of the knee and associated lower-limb joints, rehabilitation progression based on histological and biomechanical principles, and the effects of surgery and progressive rehabilitation on graft integrity and healing tissues.

Rehabilitation methods include proper use of exercise equipment, manual therapy, techniques and modalities to reduce pain and effusion; restoration of soft-tissue balance; open– versus closed–kinetic chain exercises; braces and orthoses; and restoration of proprioceptive and neuromuscular function (7,30). All of the aspects of rehabilitation apply to the patient's overall physical activity—that is, to monitored and structured exercise and to daily functional mobility. Expertise of the rehabilitation specialist is particularly needed in the ways described below.

Healing and remodeling of articular cartilage. Structure and function of articular cartilage in healthy, degenerated, and healing states (20) is a primary consideration for the development of the surgical technique as well as the rehabilitation protocol. The primary components of healthy articular hyaline cartilage are water, glycosaminoglycans, collagen fibers, and relatively few chondrocyte cells. The collagen is principally type II, with significantly less of the seven other types. The proteoglycan of interest is aggrecan, which has a protein backbone with both chondroitin sulfate and keratin sulfate attached to it. Large molecules of aggrecan are formed when aggrecan interacts with a hyaluronic acid chain. Collagen traps the large proteoglycan aggregates, and water interacts with the proteoglycans to make hyaline cartilage hydrophilic. Negatively charged proteoglycans push the matrix toward the surface semipermeable membrane, all of which provides a firm substance that resists deformation of the cartilage. These complex components result in superior loading characteristics and extremely low friction at the cartilage surface (20). In addition, all of these events occur without our awareness in healthy cartilage, which is aneural.

Collagen fiber orientation is aligned as a result of tensile loading. There are four layers of articular, hyaline cartilage. The fibers in the superficial zone are parallel to the articular cartilage surface. Collagen protects the deeper layers from shear stress during joint loading (20) and maintains an intact articular surface as they are stretched (and strengthened) with deformation from weight bearing and muscle activity. The fibers of the deep zone are perpendicular to the subchondral bone and serve to secure the cartilage to the bone. The collagen fibers of the deepest portion, the tidemark, are parallel to the articular cartilage surface, and provide a final resistance to shear deformation at the surface. Chondrocyte viability depends on physical stress and electrostatic forces. The effect of overload, underload, and optimal load is significant and follows the same principles, although with different magnitudes, as other structures of the musculoskeletal system (24).

Hyaline cartilage is able to withstand normal function, whereas fibrocartilage is less able. With optimal ACI and rehabilitation, the injected chondrocytes gradually remodel and form tissue that is mostly composed of type II hyaline-like cartilage (27), which may include some fibrocartilage (32).

Rehabilitation progression based on biomechanical principles related to tibiofemoral and patellofemoral joint anatomy. An understanding of the forces and loads that will be exerted on the graft are essential in the design of an ACI rehabilitation program. The contact pressure ([contact area/contact load (distribution and magnitude)]) should be considered to minimize the danger of damaging the graft and to support the healing process by stimulating the graft physiologically in positions, which lead to no harm to the graft (7).

The repair site is most vulnerable for the first 3 months after surgery. During this time, impact loading, excessive loading, and shear must be avoided, which requires precise location of the lesion and knowledge of areas of contact on the lesion site (7). For knee joint ACI, shear and excessive loading must be avoided initially and added gradually and progressively. Warning signs must be sought, and the program should be altered accordingly.

At the patellofemoral joint (PFJ), adaptation and remodeling of the repair are achieved by optimizing the PFJ contact pressure, which occurs by altering the contact force or the contact area or both. The patella glides on the distal femur during tibiofemoral flexion and extension, which produces shear stress on the contacting surfaces (7). The contact area and contact location on the retropatellar surface changes with knee motion, with increased contact area with weight bearing and increasing knee flexion (10). Demand moments or torques (resisting moment/torque) with physical activity must incorporate these mechanical effects of joint loading.

At the tibiofemoral joint, physiologic motion includes significant accessory motion, glides in particular, which produce shear and compressive stress. An example of lesion specific rehabilitation would be the cautious loading of a lesion area on the posterior aspect of the medial femoral condyle from 90 to 120° of knee flexion (15) when this area is in contact with the tibia. Knee joint loading from 0 to 80° might be carried out safely without damage to the graft site.

Progression of difficulty of an exercise program or functional activity can occur by changing the demand moment by muscle shortening (concentric contraction), muscle holding (isometric contraction), or muscle lengthening or control (eccentric contraction). The demand moment is composed of an external moment, produced by an external load, push, pull, etc., acting through a moment arm + a passive constraint moment, which occurs when a body structure (tendon, ligament, etc.) is actively stretched and acts at the same joint through its own moment arm. The internal response moment, often a muscle moment, occurs in response to the demand moment. For example, during a squat exercise, little demand moment produced near standing would require little quadriceps muscle moment, and greater demand moment with greater knee flexion would require greater quadriceps muscle moment.

Within the constraints of loading the graft site, the demand moment of the physical activity should match the variation of a muscle group throughout the joint range of motion (14,36), so that the muscle can be overloaded appropriately throughout the joint range of motion. For example, while avoiding shear and excessive compression at the lesion site, the demand moment of an exercise to strengthen the quadriceps should be the greatest at 45–60°, when the quadriceps muscle group is the strongest (14,36). Exercise produced by exercise equipment may or may not provide a demand moment that follows the strength variation curve of the targeted muscles. The demand moment progression for each device needs to be analyzed to assess this relationship.

Manual therapy can be beneficial as part of the intervention program, if the clinician is a rehabilitation specialist with a high level of expertise. This expertise requires expert clinical decision making in patient selection, hypothesis formation related to goals and outcomes, knowledge of the level of force that will be helpful to progress joint motion and provide optimal stimulation without harm to the graft tissue; delivery of the joint mobilizations; and assessment of the outcomes. The delivery requires precise location of anatomical structures, the ability to judge and provide accurate levels of force, and the ability to provide the mobilization force at accurate angles of application. Gentle manual mobilization of the parapatellar joint and surrounding soft tissue is particularly important in preventing adhesions/arthrofibrosis after ACI (7).

Many factors contribute to presurgical deterioration of cartilage, such as advanced age, obesity, poor nutrition, knee joint malalignment, ligamentous or meniscal injury, and repetitive impact loading (3). Each could contribute to deterioration of the graft site postsurgically if these factors still exist (7).

Restoration of soft-tissue balance. Soft-tissue balance includes normal passive and active joint range of motion, including mobilization the patella. The balance involves achievement of soft-tissue flexibility of the lower limb (7,30).

Continuous passive motion (CPM) is used early on to prevent soft-tissue restrictions, stiffness, and adhesions after surgery, and to promote the healing process (7,33). Positive effects of CPM include greater differentiation of mesenchymal cells to hyaline articular cartilage with use of CPM than with immobilization or intermittent active motion (33). Specific outcomes related to use of CPM on joint range and graft healing after ACI have not been reported (7).

Partial immobilization, with use of braces or orthoses, is needed in the early postoperative time to protect the graft, while prolonged immobilization is avoided. Early introduction of graded intermittent pressures occurring with joint motion can increase synovial fluid flow, which enhances articular cartilage nutrition (7) and stimulates chondrocyte activity (35). Because active joint range of motion involves higher joint-contact pressures than passive motion, active motion is increased more gradually and cautiously than passive motion (7). Restored soft-tissue balance also is important in helping prevent abnormal correlated motion—that is, abnormal linking of joint motions that alter lower-limb alignment and function (31).

Open– versus closed–kinetic chain exercises. Controversy exists as to whether open–kinetic chain (OKC) or closed–kinetic chain (CKC) exercise leads to better rehabilitation after ACI (6). Specific location of load bearing on the joint, joint contact pressures at different joint range, and control of joint shear are critical to monitor with use of either type of exercise (6,21,29). For the knee joint, in CKC exercise, lower joint-contact pressures occur from 0 to 45° of knee flexion and are highest at 90°, with this relationship determined by the changing demand moment of the ground-reaction force. In OKC exercise, joint contact pressures are lowest near knee extension. Greater patellar lateral displacement occurs with OKC exercise (29). Tibiofemoral shear force decreases with CKC exercise (21). Whereas OKC exercise targets specific muscles, CKC exercise activates multiple muscle groups and is more functional (6).

Restoration of proprioceptive and neuromuscular function. After even minor injuries, loss of fine motor function has been shown to result (11–13). If this is the case, then loss of these fine motor functions can result from ACI surgery. Intentional quadriceps and gastrocnemius muscle activity can improve lower-limb and, in particular, genu varus alignment (34). Whereas significant malalignment is corrected concomitant with the ACI

TABLE 1. Guidelines for autologous chondrocyte implantation (ACI) rehabilitation.

Phase 1. Early Protection Phase (Weeks 0–6)

Goals
- Protect healing tissue from load and shear forces
- Decrease pain and effusion
- Restoration of full passive knee extension
- Gradually improve knee flexion
- Regain quadriceps (Q) control

Brace
- Locked at 0° during weight-bearing (WB) activities
- Sleep in locked brace for 2–4 wk

WB
- WB status varies based on lesion location and size, and other variables related to the individual patient

For femoral condyle lesions
- Non-WB for 1–6 wk; may begin toe-touch WB immediately per physician if lesion < 2.0 cm^2
- Begin toe-touch WB (approximately 9–14 kg) at weeks 2–3; progress to partial WB (approximately one-fourth body weight) at weeks 4–5

For patellofemoral lesions
- Immediate toe-touch WB of approximately 25% body weight, with brace locked in full extension
- Progress to 50% WB at week 2 and 75% WB at weeks 3–4, with brace locked in full extension

Range of motion (ROM)
- Immediate motion exercise day 1
- Full passive knee extension immediately
- Initiate continuous passive motion (CPM) day 1 for a total of 8–12 $h \cdot d^{-1}$ (0–60°; if patellofemoral lesion > 6.0 cm^2, 0–40°)
- Progress CPM ROM as tolerated 5–10$° \cdot d^{-1}$
- May continue CPM for total of 6–8 $h \cdot d^{-1}$ for up to 6 wk
- Patellar mobilization (four to six times per day)
- Passive knee flexion ROM at least two to three times daily
- Passive knee ROM as tolerated
- 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
- For patellofemoral lesions, knee flexion ROM goal is 90° by weeks 2–3, 105° by weeks 3–4, and 120° by week 6
- Stretch hamstrings (H) and calf

Strengthening program
- Ankle pump, using rubber tubing
- Quadriceps (Q) setting
- Multiangle isometrics (cocontractions Q/H)
- Active knee extension 90–40° for femoral condyle lesions (no additional resistance)
- Straight-leg raises (four directions)
- Stationary bicycle when ROM allows; low resistance
- Electrical muscle stimulation and/or biofeedback during quadriceps exercises
- Isometric leg press at week 4 (multiangle)
- May begin use of pool for gait training and exercises week 4
- Initiate weight-shifting exercises with knee in extension by weeks 2–3 for patellofemoral lesions
- No active knee extension exercises for patellofemoral lesions

Functional activities
- Gradual return to daily activities
- If symptoms occur, reduce activities to reduce pain and inflammation
- Extended standing should be avoided

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: one-half body weight with crutches at 6 wk; progress to full WB at 8–9 wk; discontinue crutches

TABLE 1. (Continued).

Phase 2. Transition Phase (Weeks 6–12)

- 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

Strengthening exercises
- Progress WB exercises
- Initiate weight shifts week 6 for femoral condyle lesions
- Leg press at weeks 7–8
- Minisquats 0– 45° week 8
- Toe-calf raises week 6 for patellofemoral lesions, week 8 for femoral condyle lesions
- Progress balance and proprioception drills
- Initiate front lunges, wall squats, and front and lateral step-ups at weeks 8–10
- For femoral condyle lesions, progress non-WB knee extension (0.45 $kg \cdot wk^{-1}$)
- 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 to 40°, or avoid angle where lesion articulates
  Progress 0.45 kg every 2 wk, beginning at week 20 if no pain or crepitation; must monitor symptoms
- Continue progressing balance and proprioception
- Bicycle
- Stairmaster
- Swimming
- Nordic-Trak/elliptical

Functional activities
- As patient improves, increase walking (distance, cadence, incline, etc.)

Maintenance program
- Initiate at weeks 16–20
- Bicycle: low resistance, increase time
- Progressive walking program
- Pool exercises for entire lower extremity
- Straight-leg raises
- Leg press
- Wall squats
- Hip abduction/adduction
- Front lunges
- Step-ups
- Stretch quadriceps, hamstrings, calf

Criteria to progress to phase 4
- Full, nonpainful ROM
- Strength within 80–90% of contralateral extremity
- Balance and/or stability within 75–80% of contralateral extremity
- No pain, inflammation, or swelling

(*continued on next page*)

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TABLE 1. (Continued).

Phase 4. Maturation Phase (Weeks 26–52)

Goals
- Gradual return to full unrestricted functional activities

Exercises
- Continue maintenance program progression 3–4 times per week
- Progress resistance as tolerated
- Emphasis on entire lower-extremity strength and flexibility
- Progress agility and balance drills
- Impact-loading program should be specialized to the patient's demands
- Progress sport programs depending on patient variables

Functional activities

The patient may return to various sport activities as progression in rehabilitation and cartilage healing allows. Generally, low-impact sports, such as swimming, skating, rollerblading, and cycling, are permitted at about 6 months; higher-impact sports, such as jogging, running, and aerobics, at 8–9 months for small lesions, and at 9–12 months for larger lesions; and high-impact sports, such as tennis, basketball, football, and baseball, at 12–18 months

ACI Rehabilitation Variations Based on Concomitant Surgical Procedures and Lesion Variation

Meniscal allograft
- Rehabilitation is altered to allow healing of meniscus allograft
- WB similar to isolated femoral condyle lesion
- 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 it may be delayed on the basis 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
- Dependent on graft selection (patellar tendon, hamstring, allograft)
- 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 to 90° for up to the first 4 wk
- WB is similar to isolated trochlea 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 because of 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 trochlea lesions, ROM, and the initiation of active knee extension, exercises are slightly decelerated, and aggressive knee-extension resistance exercises are avoided for up to 9–12 months

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

Recommended rehabilitation protocol for ACI surgery, including modified protocol for concomitant surgery. CPM, continuous passive motion; Q/H, quadriceps/hamstring.

surgery, skeletal malignment from muscle imbalance and correlated postures from habitual weight-bearing patterns before surgery and at adjacent joints could result in return of functional skeletal malalignment.

Two distinct points regarding rehabilitation after ACI surgery are brought to the forefront in a review of the recent literature. First, proper rehabilitation is vital to the success and long-term outcomes of patients (5). Second, development of an appropriate rehabilitation program is challenging and must be highly individualized to ensure successful outcomes (30).

There is minimal evidence on which to base a properly designed rehabilitation program (5,7,30). Consequently, to date, guidance for ACI rehabilitation has been predominantly based on a combination of expert opinion, animal studies, basic science, and clinical biomechanics (7). Practicing clinicians must note that when these factors exist, the fears of graft failure increase and usually result in an overcautious approach to ACI rehabilitation (7).

Important factors that could affect the clinical outcome of ACI surgery include the compressive and shear forces at the affected joint. Rehabilitation of lesions on a weight-bearing surface of a femoral condyle must attempt to avoid excessive compressive forces, whereas rehabilitation of lesions located within the trochlea or retrosurface of the patella should minimize excessive shear forces (30). To assist the rehabilitation professional, guidelines based on a timeline of graft healing have been developed to direct patient care (5,7,30). The graft healing timeline has been reported in three stages or phases.

The proliferative stage, which lasts up to 6 wk, is characterized by a primitive cell response, with tissue fill of the defect (7). Proliferation of the chondrocytes occurs in the first 6 wk after cell implantation. At this time, PROM and controlled partial weight bearing help to promote cellular nutrition through synovial fluid diffusion as well as provide the proper stimulus for the cells to produce specific matrix markers (30). Strengthening exercises during this stage focus on neuromuscular control, proprioception, and functional gait. There is a consensus of opinion that weight bearing and ROM should be restricted in early rehabilitation, but there is considerable variation across cartilage-repair centers as to the extent and duration of these restrictions (7). Communication between the surgeon and the rehabilitation professional is vital regarding these issues.

The transition or matrix production stage varies in its length, but it seems to be complete by 3–6 months. At this stage, a type II collagen framework is produced along with the proteoglycans that form the cartilage matrix. The graft tissue has a gelatin-like consistency, and it is well integrated to subchondral bone and adjacent articular cartilage (7). During this phase, the patient achieves full ROM and progresses from partial weight bearing to full weight bearing. Progression from partial to full weight bearing varies by factors, such as lesion location, surgical technique, and clinical decision making by the surgeon. Variance of initiation can be compared by the reporting by Horas et al. (9) of partial weight bearing beginning at weeks 3–4, with full weight bearing by 3 months. By 6–9 months, the cartilage is the consistency of putty (7). Patients will start to experience good symptom relief during this period (7). Continued maturation of the repair tissue is fostered through higher-level functional and motion exercises (30). Low-impact activities are initiated by months 5 to 6 and are progressed to moderate-impact activities for months 7 to 9.5 (5).

The remodeling and maturation stage has been reported to last as long as 2 yr. During this stage, matrix proteins cross-link and stabilize in large aggregates, and the collagen framework reorganizes further to integrate into the subchondral bone (7). Fully mature repair tissue, which may take 12–24 months, can show stiffness very close to the surrounding articular cartilage (5).

The development and progression of an individualized rehabilitation program depend on the above stages of graft healing and several other variables, including specifics regarding the patient, lesion, and surgery. Patient age, body mass index, general health, nutrition, quality of articular cartilage, previous activity level, specific goals, and motivation level must all be considered. The lesion location, size, depth, containment, and quality of surrounding tissue significantly affect rehabilitation. Regarding the surgery, the procedure, the amount of tissue involvement, and any concomitant procedures all affect the rehabilitation program (5,30). 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 1).

REHABILITATION PROTOCOL

The guidelines developed by Gillogly et al. (5) follow the above-stated stages and special precautions after ACI surgery and are used at our institution, with one exception. At our institution, the patient is non–weight bearing for the first 6 wk, especially for lesions with contact near knee extension. These guidelines divide the remodeling and maturation stage into separate sections to allow for specific exercise breakdown. Guidelines are altered on the basis of concomitant surgeries (Table 1).

In summary, ACI is an advanced surgical technique with demonstrated and promising outcomes for people with full-thickness chondral or osteochondral injuries. Both surgical technique and rehabilitation protocol are developed from sound histological response to tissue healing and mechanical loading, to promote optimal recovery and function. Future directions include the use of bioengineering techniques, such as in the development of a cartilage patch, composed of a matrix instead of chondrocytes alone (20).

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