CHAPTER

61

Autologous Chondrocyte Implantation in the Knee

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AUTOLOGOUS CHONDROCYTE IMPLANTATION IN THE KNEE IN A NUTSHELL

History:
Pain in ipsilateral compartment; recurrent effusions; prior cartilage treatment common

Physical Examination:
Pain in ipsilateral compartment of lesion; rule out coexisting pathology

Imaging:
Standing radiographs, including 45-degree posteroanterior and mechanical axis views; magnetic resonance imaging commonly shows articular cartilage lesion

Indications:
Grade III or IV lesions, 2 to 10 cm^2

Contraindications:
Diffuse degenerative lesions; bipolar lesions

Surgical Technique:
Diagnostic arthroscopy: evaluate lesion for size and depth; evaluate and treat concomitant pathology
Articular cartilage biopsy: full-thickness biopsy from superomedial trochlea, superolateral trochlea, or intercondylar notch; can be stored up to 18 months
Implantation: surgical exposure; parapatellar arthrotomy; can use mini-arthrotomy for condyle lesions
Defect preparation: debride to subchondral bone; vertically oriented walls; hemostasis; size defect
Periosteum harvest: 3-cm medial incision, 5 fingerbreadths below joint line; #15 blade to incise periosteum; oversize 2-mm sharp periosteal elevator, smooth forceps
Securing of the patch: 6-0 Vicryl sutures, 3 to 4 mm apart; leave small opening
Watertightness testing: saline-filled tuberculin syringe; look for leakage around periphery; seal with fibrin glue and retest; aspirate saline from defect
Chondrocyte injection: sterile aspiration and resuspension; slowly inject through opening, filling entire defect; sew defect in patch and seal with fibrin glue

Postoperative Management:
Continuous passive motion beginning after 6 to 8 hours; touch-down weight bearing for 4 to 6 weeks, then advance; return to activities at 8 to 12 months

Symptomatic chondral lesions are likely to lead to diminished knee function and progressive deterioration over time. Owing to the inability of cartilage lesions to heal, several technologies have emerged for the replacement of articular cartilage defects. Many techniques to treat articular cartilage injuries are palliative or reparative and therefore have a limited capacity to restore hyaline or hyaline-like tissue to the defect. Autologous chondrocyte implantation attempts to replace the articular cartilage defect with hyaline-like cartilage tissue. This process involves taking a biopsy of healthy articular cartilage, which then undergoes enzymatic degradation to proliferate chondrocytes. The chondrocytes are subsequently reimplanted into the knee under a periosteal patch, with the goal of restoring normal articular cartilage to the defect. Autologous chondrocyte implantation can lead to good or excellent results in appropriate candidates provided there is strict adherence to the surgical technique and rehabilitation protocol.

History

Patients with symptomatic chondral lesions typically complain of pain localized to the compartment affected by the lesion. Patients may also complain of swelling after activities, locking, catching, and crepitation. For lesions in the medial and lateral femoral condyles, weight-bearing activities typically aggravate the symptoms. Lesions in the patella or trochlea are aggravated by sitting, stair climbing, and squatting activities. In patients who are candidates for autologous chondrocyte implantation, it is important to review previous operative notes and arthroscopic pictures, because many patients have undergone prior surgical treatment.

Physical Examination

Patients with symptomatic chrondral lesions are typically tender on the ipsilateral joint line or over the affected portion of the condyle. They may also have an effusion. Particular attention should be paid to lower limb malalignment for medial or lateral femoral condyle injuries. For patella or trochlea lesions, the patellar grind test may be positive. In addition, the patient should be evaluated for lateral retinacular tightness, patellar apprehension, and abnormal Q angle. A thorough ligament examination should also be performed to rule out any ligamentous laxity.

Imaging

Diagnostic imaging should include a standard weight-bearing anteroposterior radiograph of both knees in full extension, a 45-degree-flexion posteroanterior weight-bearing radiograph, and non–weight-bearing lateral and Merchant or skyline views. The evaluation should be performed to rule out global osteoarthritis and any bony involvement of the lesion (e.g., osteochondritis dissecans) and to evaluate alignment. If malalignment is a concern, a full-length mechanical axis view should be obtained. Magnetic resonance imaging can be helpful for delineating the extent of articular cartilage lesions, assessing subchondral bone, and detecting any associated ligament or meniscal injures.

Indications and Contraindications

The indications for autologous chondrocyte implantation are symptomatic, unipolar, full-thickness (Outerbridge[6] grade III or IV) articular cartilage lesions. Lesions of the medial or lateral femoral condyles are most common, but patellar and trochlear lesions are also amenable to autologous chondrocyte implantation. Commonly, patients have failed previous treatments, including debridement, marrow stimulation, and osteochondral autograft techniques. Osteochondritis dissecans is not a contraindication for autologous chondrocyte implantation, provided the bone loss is less than 6 to 8 mm. If the bone loss is greater than 8 mm, advanced techniques for autologous chondrocyte implantation with single- or two-stage bone grafting can be performed. Bipolar lesions (greater than grade II chondral lesion on the opposing surface) are considered a contraindication to the procedure. Malalignment and ligament instability are not contraindications, but they must be addressed concomitantly with bony realignment or ligament reconstruction.[2] In addition, menisical deficiency in the affected compartment must be addressed with allograft meniscal transplantation. Patellofemoral lesions are commonly treated with simultaneously performed anteromedialization of the tibial tubercle.

Surgical Technique

Arthroscopic Assessment and Biopsy

Positioning

Depending on the surgeon's preference, the limb may be placed in a standard leg holder or maintained in the unsupported supine position.

Examination under Anesthesia

An examination under anesthesia should be performed to confirm full range of motion and the absence of concomitant ligamentous laxity or malalignment.

Diagnostic Arthroscopy

A careful and systematic assessment of the entire joint must be performed. Once the chondral defect is identified, a probe is used to assess the quality of the articular surface. Surrounding areas of softening and fissuring must be noted as well. The defect assessment includes measuring its dimensions (both anterior and posterior and medial and lateral) as well as noting the lesion location, depth, quality of surrounding tissue, and condition

of the opposing surface. All these factors determine whether the lesion is amenable to autologous chondrocyte implantation (Fig. 61–1).

Articular Cartilage Biopsy

When there is an intention to treat a cartilage lesion with autologous chondrocyte implantation, an articular cartilage biopsy is performed with either a gouge or a sharp curet. The preferred technique of the senior author is to perform the biopsy in the lateral intercondylar notch (Fig. 61–2). This is the region where anterior cruciate ligament notchplasty is regularly performed. Alternative sites include the lateral, medial, or proximal aspects of the trochlea. The biopsy specimen should be a full-thickness area of articular cartilage measuring approximately 5 by 10 mm. This biopsy represents 200 to 300 mg in total weight, containing between 200,000 and 300,000 cells. The specimen should cover the bottom of the biopsy specimen container (Fig. 61–3). The specimen is placed via sterile technique into the vial containing the culture medium and sent for next-day delivery at 4°C to Genzyme Biosurgery Corporation (Cambridge, MA) for processing. The cellular expansion process takes 3 to 5 weeks. The specimen can be stored for up to 18 months before expiration. Once processed, the suspension of autologous chondrocytes contains 12 million cells per 0.4 mL of culture medium. For larger or multiple lesions, two or more vials of chondrocytes can be requested.

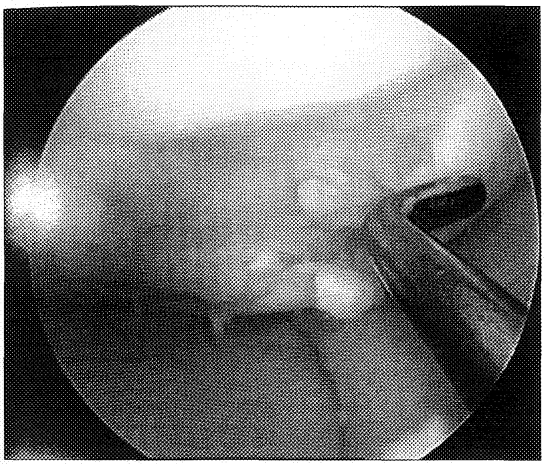


Figure 61–1 Arthroscopic photograph of a 20- by 25-mm grade IV symptomatic chondral lesion of the medial femoral condyle as measured with an arthroscopic probe.

Implantation of Autologous Chondrocyte Cells

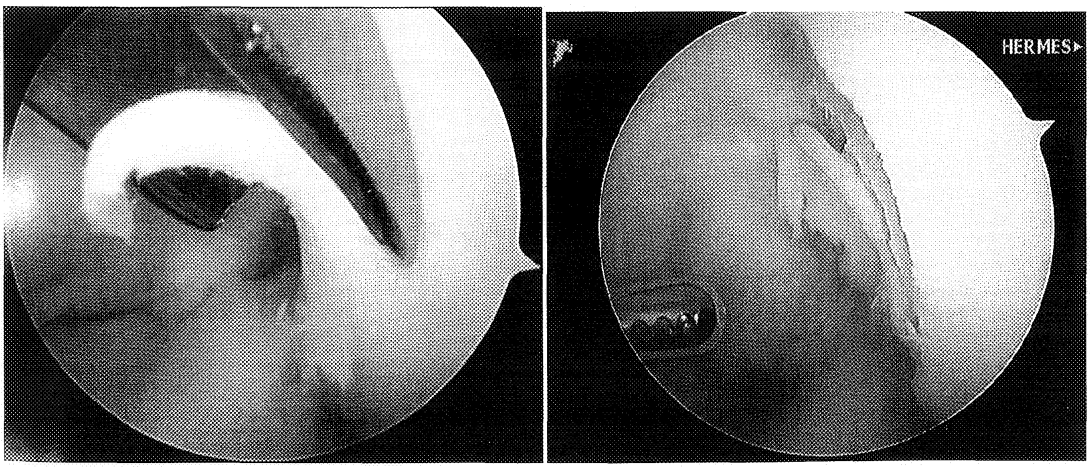
Positioning

The patient is positioned supine on a standard operating table. Access to the entire lower extremity is necessary. A tourniquet should be placed on the thigh. A lower extremity positioning device can be helpful as well.

Specific Surgical Steps

Surgical Exposure

A standard midline incision with a medial parapatellar arthrotomy can provide access to medial and lateral femoral condyle lesions, as well as patella and trochlea lesions. Smaller incisions are often possible with certain



A B

Figure 61–2 *A*, Arthroscopic photograph showing the lateral intercondylar notch during arthroscopic biopsy using a gouge. Care is taken to avoid the weight-bearing area of the lateral femoral condyle. *B*, Arthroscopic photograph of the intercondylar notch following biopsy.

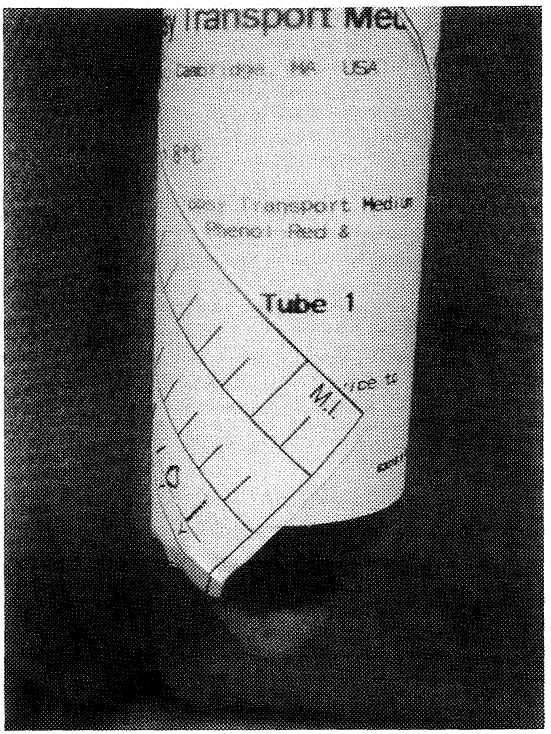


Figure 61–3 The cartilage biopsy specimen fills the bottom of the specimen container.

defect locations. Laterally based lesions are often approached through a lateral retinacular release only. Medially based lesions are often approached through a mini-arthrotomy. The patella can then be subluxated using a Z-type retractor in the intercondylar notch.

Defect Preparation

Once the defect has been identified, it must be prepared. Defect preparation requires that the surrounding cartilage walls be healthy, full thickness, and firmly attached (Fig. 61–4). Using a fresh number 15 scalpel blade, the defect is outlined, and a sharp ring curet is used to excise the cartilage down to the level of the subchondral bone. Care is taken not to penetrate the subchondral bone to prevent bleeding into the defect. The walls of the remaining cartilage are prepared so that they are vertically oriented. It is important to keep the lesion contained so that there is a rim for the periosteum to be sewn. Once the defect is prepared, adequate hemostasis must be achieved. Neuropatties soaked with a dilute 1:1000 epinephrine and saline solution can be applied using thumb pressure. If bleeding is difficult to control, hemostasis can be obtained with a needle-tip electrocautery device; this should be used with caution, however. Bleeding may be especially problematic in patients who have previously undergone a marrow stimulating technique.

Once the defect is prepared, it must be accurately sized using a sterile ruler. A piece of paper from the sterile surgical glove wrapping can be used to trace the outline of the defect and create a template for the appropriate periosteal patch configuration.

Periosteal Patch Harvest

A 3-cm incision is made on the medial border of the proximal tibia, approximately 5 fingerbreadths distal to the joint line, 2 cm distal to the pes anserinus tendon attachments. Blunt dissection is used to develop the plane between the periosteum and the overlying subcutaneous fat and fascia. Electrocautery should not be used on the periosteum. Using the defect template and a fresh number 15 scalpel blade, the periosteum is incised down to the underlying bone on the medial, lateral, and distal borders. The proximal border can be left intact until the harvest is nearly complete. A sharp, curve-tipped periosteal elevator is used to perform the subperiosteal dissection from distal to proximal (Fig. 61–5). Smooth forceps are used to provide gentle traction on the periosteal edges. Once an adequate piece of periosteum is obtained, it is amputated at its proximal portion. Owing to the tendency for the periosteum to shrink slightly after harvest, the patch should be oversized by 2 mm in each dimension. If the periosteum tears during harvest, it can be repaired during suturing, although this is not ideal. The periosteum should be kept moist at all times. In addition, the outer surface of the periosteum should be marked to distinguish it from the inner cambium layer, which will face the implanted cells. If a tourniquet was used up to this point, it should be deflated, and hemostasis should be obtained at the site of the periosteal harvest as well as at the area of defect preparation.

Securing of the Periosteal Patch

At this point, the periosteum is laid over the defect and trimmed to the appropriate size. The periosteum is secured with a 6-0 absorbable Vicryl suture on a P-1 cutting needle (Fig. 61–6). Sterile mineral oil or glycerin should be used to lubricate the suture for smooth passage. The periosteum is secured so that there is no overlap of the overlying cartilage. In addition, the periosteum is tented over the defect to allow adequate filling with the injected cells. Particular attention must be paid to contouring trochlear defects, ensuring that the periosteum is not tented beyond the normal contour of the articular surface. It is usually most efficient to start by placing the sutures at the four corners of the defect. The suturing technique involves passing the needle through the periosteum from outside to inside approximately 2 mm from the tissue edge. The needle then enters the cartilage perpendicular to the inside wall of the defect 2 mm below the articular surface and exits the articular surface a minimum of 3 mm from the edge of the defect. The sutures are then tied, with the knot placed over the periosteal patch at the junction of the patch and the articular cartilage. The sutures are placed approximately 3 to 4 mm apart to provide a watertight seal. A small

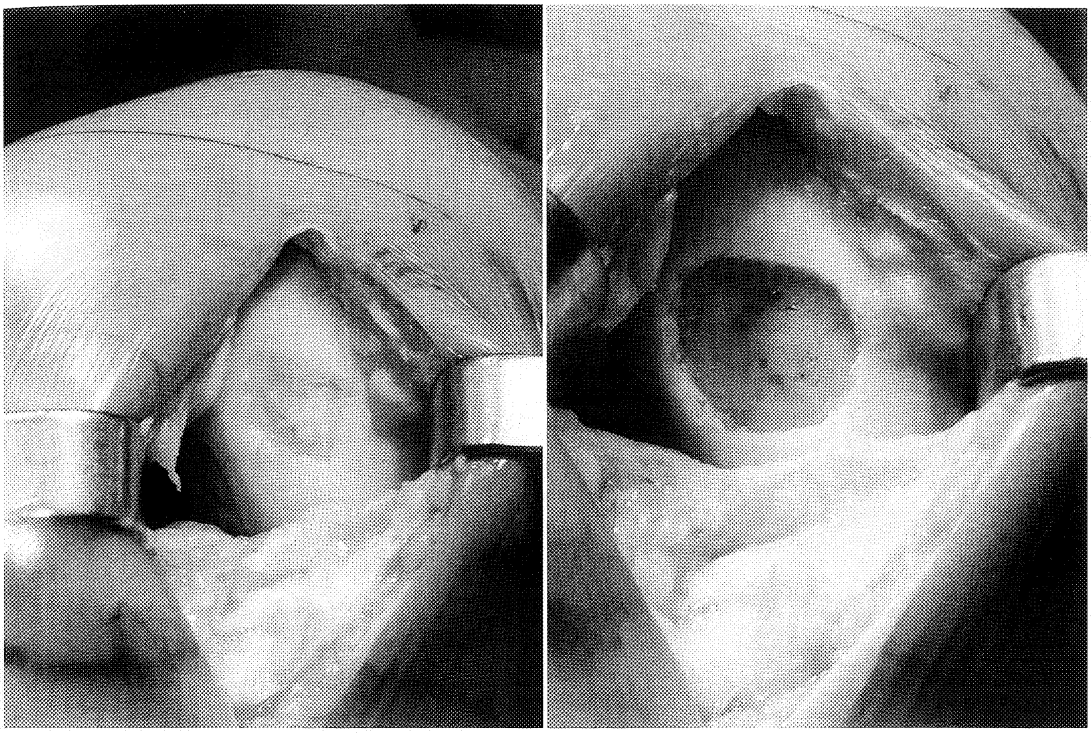


Figure 61-4 *A*, Lesion of the medial femoral condyle exposed through a mini-arthrotomy before preparation. *B*, The same lesion after defect preparation, with vertical walls at the transition zone.

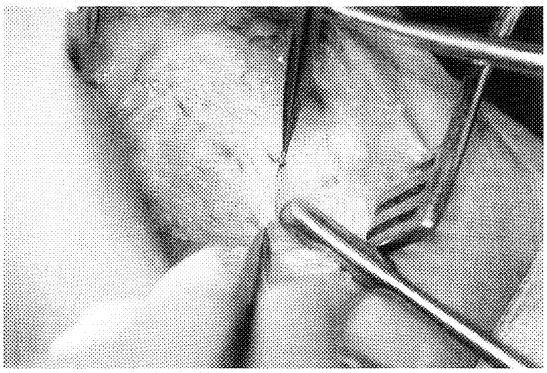


Figure 61-5 Periosteum is harvested from a small incision on the medial aspect of the tibia below the pes anserinus tendons. Smooth forceps are used to provide gentle traction on the periosteum while a periosteal elevator is used to lift the flap.

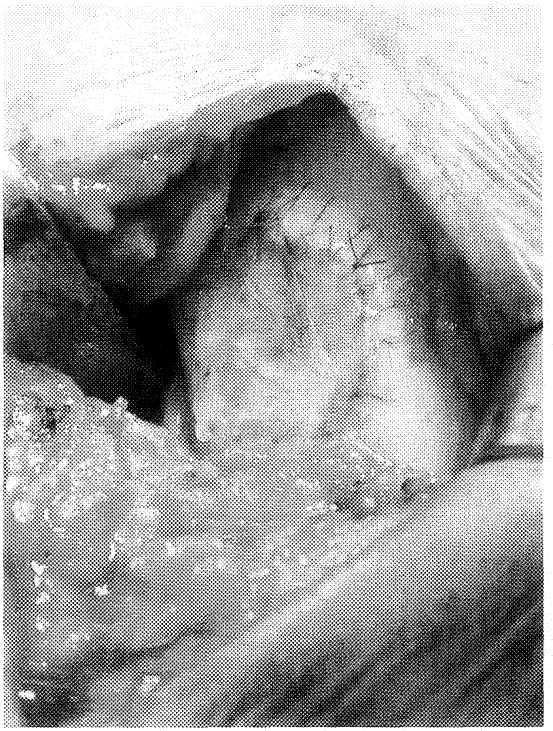


Figure 61–6 The periosteal patch is sewn into place over the defect using 6-0 Vicryl interrupted sutures.

opening approximately 5 mm wide is left at the proximal end of the defect to allow insertion of the cells. If the defect is uncontained, one may need to suture to the surrounding synovium or through small drill holes made with a Kirschner wire. Alternatively, mini bone anchors can be placed, preloaded with the suture material.

Watertightness testing is performed with a saline-filled tuberculin syringe and an 18-gauge catheter. The catheter is placed in the opening in the patch, and the saline is injected. Any leakage seen around the periphery of the defect should be sealed with additional sutures. After the test, the saline should be aspirated from the defect to prevent cellular dilution. Once the defect is deemed watertight, the periosteal patch is sealed with fibrin glue. Commercially available fibrin glue (Tisseel, Baxter Health Care, Glendale, CA) is preferred by the senior author. The fibrin glue is applied along the edges of the defect, and a second watertightness test is performed.

Chondrocyte Handling and Injection

The autologous chondrocyte cells are delivered in a small vial. The exterior of the vial is not sterile, and careful handling is required to ensure that the cells remain sterile during resuspension, aspiration, and implantation. The vial should be held in the vertical position with the plastic cap removed. The top of the vial is wiped with alcohol, and a sterile 18-gauge catheter with the metal needle in place is inserted into the vial and advanced until the tip is just above the fluid level. The metal needle is withdrawn, and a sterile tuberculin syringe is attached to the plastic catheter, which remains in the vial. The fluid is then aspirated in the syringe, leaving the cells behind. The fluid is gently ejected back into the vial to resuspend the cells. This is performed approximately three times to achieve a uniform suspension. The catheter with the cells is then carefully withdrawn from the vial.

The catheter with the cells is placed at the opening at the top of the prepared defect (Fig. 61–7). It is advanced to the distal end of the lesion, and the cells are slowly injected into the bed with a side-to-side motion. The catheter is slowly withdrawn, and the opening at the proximal end of the defect is closed with additional sutures and sealed with fibrin glue.

Wound Closure

Once the defect is sealed, the knee is extended, and no further motion of the knee is allowed for the next 6 to 8 hours. This permits the cells to adhere before the initia-

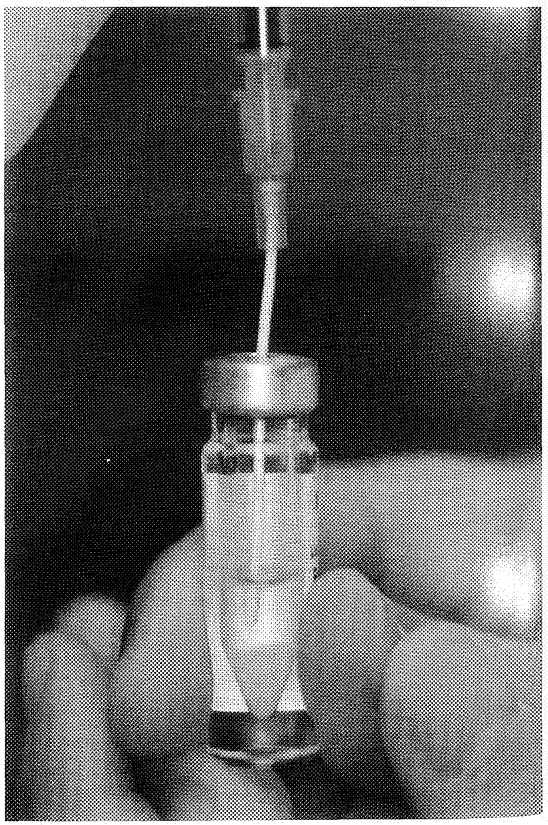


Figure 61–7 The nonsterile vial containing the cells following cellular expansion. The cells are aspirated using a tuberculin syringe.

tion of continuous passive motion. Standard wound closure is performed in layers by closing the arthrotomy, subcutaneous tissue, and skin. A soft sterile dressing is applied to the knee, and the use of drains is avoided to prevent damage to the periosteal patch.

Postoperative Management

Early Phase (0 to 6 Weeks)

Continuous passive motion is initiated 8 hours after surgery, once cell adherence has occurred. This is performed 6 to 8 hours a day at 1 cycle/minute for 2-hour increments. We begin continuous passive motion at 0 to 45 degrees of flexion and increase it as tolerated. Currently, we allow only touch-down weight-bearing for the first 4 weeks to protect the implantation site. However, clinical results suggest that earlier weight bearing may be tolerated, depending on lesion containment. Therapy focuses primarily on quadriceps reactivation with isometric contraction and modalities to limit pain and effusions. Patellofemoral lesions are limited to about 45 degrees of flexion when using continuous passive motion, but patients are permitted to flex to 90 degrees several times a day to prevent motion loss.

Transition Phase (6 to 12 Weeks)

At this stage, full motion should be achieved, and weight bearing is progressed as tolerated to full. Strengthening and exercises can include closed chain activities and functional training.

Maturation and Final Phase (3 to 18 Months)

After 3 months, full motion should be maintained, and strengthening and functional training can start to progress. Resumption of full activities should be delayed at least 8 months to protect the lesion while it continues to mature. It may take up to 18 months for the lesion to mature to a level at which full activities can be tolerated.

Results

The results of autologous chondrocyte implantation were initially reported from Sweden in 1994 (Table 61–1).[1] The first 23 patients treated consisted of 16 with femoral condyle lesions and 7 with patella lesions, with an average follow-up of 39 months. Fourteen of the 16 patients with femoral condyle lesions had good or excellent results, whereas only 2 of the 7 with patella defects achieved good or excellent results.[1] The poor results in the latter group were explained by the failure to address patellar malalignment at the time of implantation.

Two studies with longer follow-up were subsequently published on the Swedish experience with autologous chondroctye implantation.[7,8] Peterson et al.[8] published the results in 94 patients with a 2- to 9-year follow-up.[8] Ninety-two percent of patients with isolated femoral condyle lesions had good or excellent results. Again, the results for patella lesions were not as good, with only 65% achieving good or excellent results. Histologic analysis of biopsy specimens from 37 knees showed a correlation between hyaline-like tissue in the defect and good to excellent clinical results. Another follow-up study by Peterson et al.[7] demonstrated the durability of the results at a mean of 7.4 years. Of 50 patients who had achieved good or excellent result at 2 years, all continued to have good or excellent results at 5 to 11 years after implantation.

The senior author's experience includes 103 chondral defects treated in 83 patients between September 1997 and September 2002. Thirty patients had a minimum follow-up period of 24 months (mean, 33.9 months; range, 24 to 60 months). Significant improvements were seen in all patients using the Modified Cincinnati, International Knee Documentation Committee (IKDC),

TABLE 61–1
Results of Autologous Chondrocyte Implantation

Author (Date)	Lesion Location	No. of Patients	Mean Follow-up	Significant Improvement (%)	Good or Excellent Results (%)
Peterson et al. (2002)[7]	F	18	>5 yr		89
	OCD	14	>5 yr		86
	P	17	>5 yr		65
	F, ACL	11	>5 yr		91
Minas (2001)[5]	F, Tr, P, T	169	>1 yr	85	
Micheli et al. (2001)[4]	F, Tr, P	50	>3 yr	84	
Peterson et al. (2000)[8]	F	25	>2 yr		92
	P	19	>2 yr		65
	F, ACL	16	>2 yr		75
	Multiple	16	>2 yr		67
Gillogly et al. (1998)[3]	F, P, T	25	>1 yr	88	88
Brittberg et al. (1994)[1]	F, P	16	39 mo		88
	P	7	36 mo		29

ACL, anterior cruciate ligament; F, femur; OCD, osteochondritis dissecans; P, patella; T, tibia; Tr, trochlea.

Tegner, Lysholm, Knee Injury and Osteoarthritis Outcome Score (KOOS), and Short Form-12 (SF-12) scoring systems. Despite the inclusion of patellofemoral lesions and complex pathology (e.g., multiple defects, combined meniscus transplantation and autologous chondrocyte implantation), improvements were 40% to 80% above baseline, depending on the group analyzed and the scoring systems used. Additional series have also been reported from the United States, with patients achieving an 85% success rate at short to medium follow-up.[3-5]

Complications

The most common complications following autologous chondrocyte implantation are periosteal graft hypertrophy and arthrofibrosis. Graft hypertrophy typically occurs between 3 and 7 months postoperatively. This may be related to abrasion of the periosteal patch with motion, especially with patch overlap at the host cartilage edge. This can be treated with careful arthroscopic debridement of the hypertrophic tissue. Arthrofibrosis following autologous chondrocyte implantation is possible, especially with patella and trochlea lesions and when combined with distal realignment. For this reason, range of motion must be initiated early in physical therapy.

Graft failure with delamination or degeneration of the repaired tissue is another possible complication. The patient may be a candidate for repeat autologous chondrocyte implantation or may require an alternative procedure such as osteochondral allograft transplantation.

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