Autologous Chondrocyte Implantation

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Indications

- Symptomatic unipolar full-thickness Outerbridge grade III or IV lesions measuring in general between 2 and 10 cm² that have failed prior treatment
- Examples of suitable lesions include shallow osteochondritis dissecans (OCD) and defects that have failed cartilage repair procedures, including marrow stimulation and osteochondral grafting.
- A thorough evaluation must be performed to evaluate for associated pathology that must be addressed at the time of or prior to autologous chondrocyte implantation (ACI) surgery:
  - Ligamentous injuries: anterior cruciate ligament (ACL), posterior cruciate ligament, posterolateral corner
  - Meniscus deficiencies
  - Mechanical axis malalignment
  - Patellofemoral maltracking

Examination/Imaging

- A thorough review of existing documentation related to articular cartilage defect, including arthroscopic photos, videos, and operative notes, is necessary to determine eligibility for ACI.
- Radiographs
  - Standing anteroposterior, 45° flexion posteroanterior, lateral, and Merchant’s views.
  - If mechanical axis malalignment is suspected, full-length alignment views must also be obtained.
- Magnetic resonance imaging (MRI)
  - High-resolution, fast spin echo sequences and cartilage sequences are useful to predict the lesion location, size, and depth.
  - MRI is also useful to rule out concomitant ligamentous injuries and meniscus deficiencies (Fig. 1).
- Diagnostic arthroscopy
  - The “gold standard” for assessing for concomitant comorbidities and to evaluate the characteristics of the lesion
  - Biopsy obtained with the intention to treat the lesion with ACI

Pearls

- ACI is contraindicated for diffuse or bipolar lesions.
- If subchondral bone loss is greater than 6–8 mm, bone grafting is required at the time of or prior to ACI.

Treatment Options

- Nonoperative treatment: relative rest, anti-inflammatories, nutricueticals, physical therapy, cortisone and viscosupplementation injections, and/or unloader braces.
- Operative treatment: chondroplasty, débridement, marrow stimulation, or osteochondral grafting.
Positioning

- For both stages of the procedure (cartilage biopsy and implantation), either the patient can be positioned in the supine position or the limb may be placed in a standard leg holder.
- A tourniquet is always applied for the diagnostic arthroscopy but only used if necessary. The tourniquet is also placed prior to the implantation procedure and is inflated for the initial exposure and deflated during the suturing of the periosteal patch to assess for bleeding.
- A leg positioner is very useful to facilitate static exposure of femoral condyle lesions.
**Instrumentation**

- **Stage 1: Cartilage biopsy**
  - Standard arthroscopy instruments are sufficient.
  - In addition, a curved gouge typically used during iliac crest harvesting is used to obtain the biopsy from the intercondylar notch, where an ACL notchplasty is performed.
- **Stage 2: Cartilage implantation**
  - Micro/hand tray with fine needle holders and jeweler forceps.
  - Z-retractors
  - Ring curette
  - Curved periosteal elevator (Fig. 3)
  - Neuro-patties soaked with epinephrine
  - Angiocatheters (18 gauge)
  - Fibrin glue sealant
  - Sterile mineral oil
  - 6–0 Vicryl sutures on a P-1 cutting needle
  - 3-cc tuberculin syringe

**Pearls**

- If other procedures such as distal realignment or meniscus transplantation are planned, the arthrotomy incision should be planned to accommodate multiple procedures when possible.
- Care must be taken to avoid making parallel incisions separated by less than a 7-cm bridge.
- Performing a meticulous dissection and avoiding the fat pad or patellar tendon dissection will reduce the incidence of postoperative hemarthrosis and stiffness.
- Hemostasis should be achieved prior to suturing the periosteal patch. “Neuro-patties” soaked with 1:100,000 epinephrine solution can be used to obtain hemostasis.

**Portals/Exposure**

- **Stage 1: Cartilage biopsy**
  - Standard anteromedial and anterolateral arthroscopy portals are placed.
- **Stage 2: Cartilage implantation**
  - Femoral condyle lesions:
    - Medial: standard ipsilateral medial vastus-sparing approach
    - Lateral: lateral parapatellar approach
    - The incision avoids transection of the patellar and quadriceps tendons and is extended proximally or distally as needed to perform a comfortable exposure (Fig. 2).
  - Patellofemoral (PF) lesions
    - A midline incision with a lateral retinacular arthrotomy is made to allow for unloading the PF joint with a lateral release and extending the incision to perform a distal realignment.

![FIGURE 2](image2)

![FIGURE 3](image3)
Stage 2: Harvesting the periosteal patch
• A small (3-cm) incision is made on the anteromedial tibia about 3–5 cm distal to the pes anserine.
• If multiple lesions need to be covered, a larger piece is harvested and then divided.

Procedure 1: Cartilage Biopsy
• An examination under anesthesia is performed in every case to confirm full range of motion and the absence of any ligamentous, meniscal, or additional articular cartilage injury.
• A careful and thorough arthroscopic examination of the entire knee is documented. A probe is used to assess the lesion’s location, depth, and extent (Fig. 4). A measuring device is used to determine the size of the lesion. It is important to inspect the opposing surface to rule out bipolar disease.
Once the decision is made to proceed with cartilage biopsy, a curved gouge is introduced into the joint and carefully manipulated to remove cartilage pieces from the intercondylar notch (Fig. 5A–C). Alternative sites include the medial, lateral, or proximal trochlea. If a biopsy is taken from the trochlea, we recommend using a ring curette instead of the gouge in order to readily visualize the harvesting.
A grasper is used to remove the cartilage piece from the joint and place it in a specimen container with culture medium (Fig. 6).

- The specimen is sent via next-day-delivery to the Genzyme Corporation (Cambridge, MA) for cellular expansion.
- The cellular expansion takes about 3–5 weeks.
- The initial specimen can be stored for up to 5 years.

**Pearls**

- The biopsy should be a full-thickness area of articular cartilage. It is preferable to penetrate the subchondral bone to ensure that the deep chondrocytes are included in the biopsy.

- The total weight of the biopsy should be about 200–300 mg and contain about 200,000–300,000 cells. As a rough guide, the biopsy should cover the bottom of the specimen container and should be equal in size to three “Tic-Tacs” (Fig. 7).

- For large or multiple lesions, multiple vials can be prepared and sent at the time of implantation.
P e a r l s

• Prior to proceeding with anesthesia, the surgeon has to verify that the appropriate cells for the patient are available and not damaged.

• A circular or oval lesion is more biomechanically stable than a rectangular one.

• In preparing the lesion, avoiding subchondral bone penetration will decrease unnecessary bleeding.

• If the lesion is at the border of the articular cartilage, it may be preferable to leave mildly injured cartilage and maintain a contained lesion rather than remove it and be left with an uncontained lesion.

Procedure 2: Cartilage Implantation

STEP 1: LESION PREPARATION

• Arthroscopy is not usually performed for this stage unless other concomitant procedures are performed at the same time.

• The tourniquet is inflated at the beginning of the case.

• The arthrotomy is made to expose the lesion, allowing the borders to be marked (Fig. 8).

• Using a #15 blade, loose cartilage flaps are removed, leaving healthy vertical walls of hyaline cartilage surrounding the lesion (Fig. 9).

• Next, a ring curette is used to remove the remaining bed of cartilage down to the subchondral bone (Fig. 10A and 10B).

• Using a translucent surface (e.g., the wrapping of a surgical glove) and a marking pen, a template is created of the lesion that is used to obtain the correct periosteal patch size (Fig. 11).
Autologous Chondrocyte Implantation

FIGURE 10

FIGURE 11
Periosteal Patch Harvest

- A small incision is made on the medial border of the tibia, distal to the pes anserine insertion.
- Blunt dissection is used to avoid dividing the periosteum with the knife. The plane between the periosteum and the subcutaneous fat is developed.
- The template obtained previously is placed over the periosteum, and a marking pen is used to outline it. The periosteal patch should be oversized by about 2 mm along the entire perimeter.
- Using a fresh #15 blade, the outline is incised down to the level of the bone on the medial, lateral, and distal borders. The proximal border is left intact until the periosteal harvest is complete.
- A curved periosteal elevator is used to gently elevate the periosteum off the underlying bone (Fig. 12). An assistant uses two jeweler forceps to hold the two distal edges of the flap vertically, away from the bone (Fig. 13).
- When the patch is completely harvested, a #15 blade is used to amputate the proximal edge.
- The superficial surface of the periosteum should be marked to distinguish it from the inner cambium layer, which will face the implanted cells.
- The tourniquet is then deflated and neuro-patties soaked with a saline/epinephrine solution are used to achieve hemostasis within the lesion bed.

**PEARLS**

- If the periosteum tears during harvesting, it can be repaired in a side-to-side manner when suturing it to the lesion.
- The periosteal patch should be kept moist and flat at all times.
- Older patients and smokers tend to have thinner and more fragile periosteal sleeves. Other sources of periosteum include the distal femur or the contralateral leg.

**FIGURE 12**

**FIGURE 13**
Electrocautery set to “cutting mode” can be performed at the base of the lesion if the epinephrine-soaked sponges are not able to achieve adequate hemostasis. Thrombin may have detrimental effects on chondrocytes and, if used, should be washed away thoroughly after the bleeding stops.

**Step 3: Suturing the Periosteal Patch**
- The periosteal patch is placed over the defect and trimmed to the appropriate size.
- The periosteum is secured to the vertical walls of the lesion using 6–0 Vicryl sutures with a P-1 cutting needle. Sterile mineral oil is used to lubricate the sutures to allow smooth passage through the periosteum and cartilage.
- The sutures are first passed through the periosteum edge and advanced perpendicular to the vertical cartilage wall, following the curve of the needle and exiting about 3 mm from the edge of the defect.
- The suture knots are placed over the periosteal patch at the junction of the patch and the articular cartilage (Fig. 14A and 14B).
- A small (6-mm) opening is left at the proximal edge of the lesion to perform the waterseal test and to inject the chondrocytes.
PEARLS

• The periosteum is secured so that there is no overlap at the articular cartilage edge.

• The periosteum should first be tethered to the four “corners” of the defect. Then sutures are placed circumferentially spaced about 2–3 mm from one another.

• When suturing a trochlear lesion, care must be taken to avoid overtightening the patch, which may lead to loss of concavity.

• If the suture pulls out of the cartilage or if an uncontained lesion is encountered, two options are available:
  ■ Micro-suture anchors loaded with 6–0 Vicryl can be placed at the uncontained border and used to secure the periosteum to the underlying bone.
  ■ If the lesion is near soft tissue (synovium), the periosteum can alternatively be sewn to the soft tissue (Fig. 15).

PEARLS

• Do not prime the fibrin glue syringe needle prior to injection because the needle bore will become clogged and need replacement.

STEP 4: TESTING FOR A WATERTIGHT SEAL

■ Test for a watertight seal using a saline-filled tuberculin syringe attached to the soft tip of an 18-gauge angiocatheter (Fig. 16).
  • If leakage is noted, add more sutures and repeat testing until the saline is contained.
  • Once sealed, aspirate the saline out of the defect using the same syringe.

■ After gentle irrigation, the periosteal patch is now sealed using fibrin glue. This can be done with autologous blood or using a commercial allogeneic glue (Tisseal; Baxter Healthcare Corp. Glendale, CA) (Fig. 17). The surrounding articular cartilage is gently dried, and the glue is applied along the edges of the defect.
  ■ Reconfirm the watertight seal.
**Step 5: Chondrocyte Preparation and Injection**

- The chondrocytes arrive in small vials, each containing enough cells to fill a defect measuring less than 10 cm². Larger or multiple lesions require multiple vials, which should be planned at the time of biopsy.
- The suspension medium should be clear and the cells should appear as an off-white pellet at the bottom of the vial (Fig. 18). If the solution is cloudy, the vial should be discarded.
- The exterior of the vial is not sterile and should be carefully held upright by a circulating nurse.
- The lid is removed and the top is wiped with alcohol.

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**Pearls**

- Maintain negative pressure on the syringe during angiocath removal to prevent inadvertent cell loss back into the vial.
- A sterile 18-gauge angiocatheter with a tuberculin syringe is advanced into the vial, and the needle is removed, leaving the soft tip within the medium just above the cells.
- The medium is aspirated into the syringe, leaving the cells behind. The fluid is then gently injected back into the vial to resuspend the cells. This is repeated several times to achieve a uniform cell suspension.
- The entire contents of the vial are then aspirated into the syringe and the catheter is detached. The syringe is kept vertical in order to maintain the air bubble above the suspension.
- A new 18-gauge soft catheter is attached to the syringe and carefully placed in the residual opening in the periosteal patch. The cells are slowly injected into the defect using a side-to-side motion to coat the entire surface of the lesion (Fig. 19). The syringe and catheter are slowly withdrawn as the cells are injected.
- The patch opening is then sutured and finally sealed with more fibrin glue.

**STEP 6: CLOSURE**

- Closure of the arthrotomy is performed in layers. We do not recommend using a drain as it may damage the periosteal patch.
■ Sterile dressings are applied along with a cryotherapy device.
■ The leg is placed in a hinged knee brace locked in full extension. No further motion is allowed for at least 6 hours. This allows time for the chondrocytes to adhere to the bone before initiating continuous passive motion (CPM).

Postoperative Care and Expected Outcomes

■ Early Phase (0–6 weeks)
  • CPM is initiated no less than 6 hours after surgery and is continued for 6 hr/day for 6 weeks.
  • Therapy concentrates on quadriceps activation and isometric straight leg raises.
  • Touch-down weight bearing is allowed initially, with advancement to full weight bearing at 6 weeks. In PF lesions, patients are permitted to be weight bearing as tolerated with their knees locked in extension. However, if a distal realignment is performed at the same time, protected touch-down weight bearing is instituted.

■ Transition Phase (6–12 weeks)
  • Full weight bearing and full range of motion are achieved.
  • Closed-chain exercises and functional training are started.

■ Maturation Phase (12 weeks to 18 months)
  • Strengthening and functional training are progressed.
  • Return to full activities is delayed for at least 8 months to protect the lesion as it matures.
  • In some cases, it may take up to 18 months for the lesion to mature enough to allow full unrestricted activities.

■ Expected Outcomes
  • Overall success rates have been promising, with over 80% of patients achieving good to excellent results.

Evidence


One hundred patients with isolated focal defects were randomized to either ACI or mosaicplasty. Good to excellent results were achieved in 88% of the ACI patients and 69% of the mosaicplasty patients. Arthroscopy at 1 year showed 82% healing in the ACI group and 34% in the mosaicplasty group.

Sixty-one patients were followed for a mean of 7.4 years after ACI. Good to excellent results were found in 81% at 2 years and 83% at 5- to 11-year evaluation. The 16% failures occurred in the first 2 years.


This study compared ACI to osteochondral autograft transplantation at 2 years in 40 patients with a single femoral condyle defect. While both groups experienced decreased symptoms, the improvements provided by ACI fell behind on the Lysholm scale. No information on the inclusion/exclusion criteria or the method of randomization was available.


In this study, 80 patients with focal defects were randomized to either ACI or microfracture. Both groups showed significant improvement, with results favoring microfracture. Both groups of patients were allowed full weight bearing, which may have contributed negatively to the fragile ACI periosteal patch. Furthermore, multiple surgeons were included in the study, all of whom included their early ACI patients.


Fifty patients were followed for a minimum of 36 months after ACI. Patients demonstrated a significant improvement of 5 points on the Modified Cincinnati Scale. Eighty-four percent had an improvement in their condition.


Fifty-eight patients with documented OCD lesions underwent ACI. The patients had a mean follow-up of 5.6 years. Good to excellent results were achieved in 91%.


Ninety-four patients were followed for between 2 and 9 years. Isolated patellar ACI procedures had 62% good to excellent outcomes. When combined with a tibial tubercle osteotomy, the results improved to 85% good and excellent. Of the femoral condyle lesions, 96% had good to excellent results. In the OCD group, 89% of the patients had good to excellent results. About 15% of patients had required treatment for hypertrophic periostea.