



Medical Policy: Carticel Autologous Cultured Chondrocytes			
Prepared By:	Leela Rangaswamy, M.D.	Reviewed Date:	07/06/2017
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POLICY

- The procedure is recommended as second line therapy after failure of conservative care and typically surgery.
- In the procedure cartilage is removed from a less weight-bearing area and the chondrocytes are isolated. The chondrocytes are then grown in vitro until there are enough to reimplant in the damaged area.
- There are no long-term studies to show that the graft in fact produces cartilage similar to natural cartilage covering the weight bearing surfaces. Therefore, there are no studies to show that the procedure is in fact beneficial and delays progression of degenerative arthritis.
- Not indicated for repetitive trauma, as there is no scientific study to show that this in fact causes the development of a single osteochondral defect with an otherwise pristine joint.
- There should be objective evidence that the individual will follow postoperative rehabilitation program.
- The patient should not participate in sports with twisting, turning and torqueing motions, as this will cause the transplant to fail.

CRITERIA

ALL THE FOLLOWING CRITERIA MUST BE MET PRIOR TO CONSIDERATION:

1. **Conservative Care:** Failure of conservative therapy (minimum of 2 months of physical therapy).
2. **Subjective Clinical Findings:** Presence of disabling pain and/or knee locking.
3. **Objective Clinical Findings:**
 - A. Failure of established surgical interventions (i.e., microfraction, drilling, abrasion) (diagnostic arthroscopy, lavage, or debridement is not considered adequate to meet this criterion). Note: The procedure may be reasonable prior to other surgery for larger lesions (>1.5-2.0 sq cm). AND
 - B. Focal articular cartilage defect down to but not through the subchondral bone on a load bearing surface of the femoral condyle (medial, lateral, trochlear) (not in the patella). AND
 - C. Single, clinically significant, lesion that measures between 1 to 10 sq cm in area that affects a weight-bearing surface of the medial femoral condyle or the lateral femoral condyle. AND
 - D. Procedure is not being done for treatment of degenerative arthritis (osteoarthritis). AND
 - E. Stable knee with intact meniscus and normal joint space on X-ray. AND
 - F. Full-thickness lesion [*Modified Outerbridge Grade III-IV] that involves only cartilage. AND
 - G. Knee is stable with intact, fully functional menisci and ligaments. AND
 - H. Normal knee alignment. AND
 - I. Patient is less than 60 years old. AND
 - J. Body Mass Index of less than 35.
4. **Imaging Clinical Findings:** Chondral defect on the weight-bearing surface of the medial or lateral femoral condyle on: MRI OR Arthroscopy.

ACI Exclusion Criteria: ACI is definitely not recommended in the following circumstances: Lesion that involves any portion of the patellofemoral articular cartilage, bone, or is due to osteochondritis dissecans; A "kissing lesion" or Modified Outerbridge Grade II, III, or IV exists on the opposite tibial surface; Mild to severe localized or diffuse arthritic condition that appears on standing x-ray as joint space narrowing, osteophytes, or changes in the underlying bone; Unhealthy cartilage border; the synovial membrane in the joint may be used as a substitute border for up to 1/4 of the total circumference; Prior total meniscectomy of either compartment in the affected knee (Must have at least 1/3 of the posterior meniscal rim.); History of anaphylaxis to gentamycin or sensitivity to materials of bovine origin; Chondrocalcinosis is diagnosed during the cell culture process.

SUPPORTING DOCUMENTATION

ODG Knee and Leg (updated 06/27/17)-Online Version

Autologous chondrocyte implantation (ACI)

Recommended as a second-line surgical option either after failure of initial arthroscopic repair or when a full-thickness articular cartilage defect is very large (3 cm² or greater).

See also Microfracture surgery; Osteochondral autograft transplant system (OATS).

ODG Indications for Surgery -- Autologous chondrocyte implantation (ACI):

Criteria for ACI requires all of the following:

1. Conservative Care: patient has failed to respond after a minimum 2 months to conservative treatment such as physical therapy, bracing, and nonsteroidal anti-inflammatory drugs.
2. Subjective Clinical Findings: Patient is capable and willing to strictly follow the rehabilitation protocol and post-operative weight bearing restrictions; AND has disabling pain and/or knee locking.
3. Objective Clinical Findings:
 - A) Defect was caused by acute or repetitive trauma; AND
 - B) Patient has had an inadequate response to a prior arthroscopic or other surgical repair procedure (e.g., debridement, microfracture/drilling/abrasion chondroplasty, or osteochondral allograft/autograft), OR has full-thickness articular cartilage defects 3 cm² or larger; AND
 - C) Presence of focal, full thickness (grade III or IV) unipolar lesions involving only cartilage on the weight bearing surface of the femoral condyles or trochlea that are a minimum of 1.5 cm² in size; AND
 - D) Documented minimal to absent degenerative change in the surrounding articular cartilage (Outerbridge Grade II or less) with normal appearing hyaline cartilage surrounding the border of the defect; AND
 - E) Normal knee biomechanics, or alignment and stability will be achieved concurrently with ACI; AND
 - F) Individual is skeletally mature with documented closure of growth plate and is too young to be considered an appropriate candidate for total knee arthroplasty or other reconstructive knee surgery (less than 55 years); AND
 - G) Body Mass Index (BMI) is no greater than 30.
4. Imaging and/or Surgical Findings: Sizable chondral defect on the weight-bearing surface of the medial, lateral femoral condyle or trochlea on MRI or documented at arthroscopy.

ACI Exclusion Criteria: Not recommended in the following circumstances:

Any lesion that involves patella articular cartilage, any involvement of underlying subchondral bone, or due to osteochondritis dissecans; "kissing lesion" on the opposite tibial or patellar surface; mild to severe arthritic conditions with joint space narrowing on standing x-rays and/or presence of osteophytes; unhealthy cartilage border; prior total meniscectomy (must have at least 1/3 of the posterior meniscal rim); chondrocalcinosis. (Bentley, 2003) (Wasiak, 2002) (UHC, 2014) (BlueCross, 2016c)

For average hospital LOS if criteria are met, see Hospital length of stay (LOS).

Risk versus benefit: While some argue that ACI has slightly better results than other options as the primary surgical treatment of larger femoral articular traumatic defects (75% or better outcomes), its downside is the increased surgical risk of a second surgery open procedure (infection 1-2%, scarring, stiffness, atrophy), time loss and expense. Long-term RCTs and systematic reviews have yet to demonstrate superiority of ACI versus other arthroscopic regenerative procedures. Perhaps more compelling are reports of 70% good results with delayed ACI following previous failed arthroscopic techniques. Risk vs. benefit outcomes analysis supports treating only the 25% failed previous arthroscopic group with open ACI [75% + (25% x 70%) = 92.5% relative surgical success compared to 75-80% with primary ACI]. For full thickness articular cartilage defects 3 cm² or greater, where other arthroscopic techniques are not recommended, ACI is a reasonable primary surgical option.

Several studies confirmed some short- to intermediate-term success with this technically demanding technique when performed by experienced surgeons. (Zaslav, 2009) (Schindler, 2009) (Saris, 2009) However, systematic reviews performed in 2006 concluded that while the use of ACI and other chondral resurfacing techniques was becoming increasingly widespread, there was no evidence of significant outcome differences between ACI and other interventions. (Wasiak-Cochrane, 2006) (Ruano-Ravina, 2005) (Ruano-Ravina, 2006) Surgical implantation of

healthy cartilage cells (autologous chondrocyte implantation) is an alternative option for the treatment of large articular cartilage defects. ACI is primarily used to treat full-thickness cartilaginous defects of the distal femur by arthroscopically extracting healthy chondrocyte cells from the patient's knee, culturing the cells through a process termed Carticel (Genzyme), and implanting them back into an articular defect via an open surgical procedure. Revised FDA labeling suggests a more restricted use of autologous chondrocytes: as a second-line therapy after failure of initial arthroscopic repair; when no improvement has been achieved using all available alternative treatments that can be performed arthroscopically, only alternatives requiring open arthrotomy remain available. (1) ACI is at least as effective as other treatments in the short to mid-term; (2) it is the only treatment with true potential for tissue regeneration; and (3) if long-term results turn out to be good, that could counterbalance the higher initial morbidity and cost. ACI was compared with osteochondral allograft in 4 studies, subchondral marrow stimulation in 5 studies, and with abrasion in the remaining study. Outcomes with the various approaches were similar. (Vavken, 2010) A large case series (224 patients) with a 10- to 20-year follow-up noted 92% satisfaction, but bipolar lesions had worse outcomes. Age, lesion size, prior meniscal injuries or marrow stimulation procedures did not appear to affect the final outcome. (Peterson, 2010) The benefits of ACI last well into the second decade, and in over three-fourths of patients 10-20 years after the implantation it appears to provide reduced pain and increased function. General consensus favors osteoarticular allograft transplants (OATs) and marrow stimulation techniques for relatively small lesions and ACI or osteochondral allografts for larger ones. ACI may be more appropriate for young, active individuals who participate in "cut-and-run" sports such as football, soccer, and tennis. Patience on the part of the patient is required, since there are two surgeries involved followed by non-weight bearing for an extended period. (Vasiliadis, 2010) ACI provides potentially more durable results, but microfracture offers a faster recovery. (Kon, 2011) Young patients with osteoarthritic knees have generally poor outcomes from alternative matrix-assisted autologous chondrocyte implantation (MACI) as a salvage procedure in cartilage lesions, with significantly poorer outcomes in knees with previous meniscectomy procedures. (Filardo, 2012) Limited case-series reports of moderate success with ACI treatment of trochlear (not patellar) lesions, and also combination ACI/high tibial osteotomy have not been further verified with higher level research. (Mandelbaum, 2007) (Bode, 2015)

Recent research:

The longest clinical trial follow-up to date (14-15 years) involved 80 patients who were randomized at arthroscopy to either microfracture or ACI for focal femoral cartilage defects. No significant differences in functional outcomes were seen, but twice as many ACI failures went on to total knee arthroplasty (6 vs. 3) and radiographic osteoarthritic progression was slightly higher following ACI (57% vs. 48%). (Knutsen, 2016) Other higher quality longer-term outcome studies have shown relatively good durability of ACI procedures. A prospective cohort of 210 patients followed over 10 years had 25% graft failure but improved function in 75%, with some increased risk of failure with very large defects and with prior marrow stimulation. (Minas, 2014) A large case-series of 827 patients using several different ACI techniques noted no differences in outcomes between techniques, with 78% graft survival at 5 years. Worse results were seen with presence of degenerative changes or prior regenerative procedures. (Nawaz, 2014) A prospective case-series of 104 younger patients treated with ACI for large chronic lesions (7.8 years mean duration before ACI) had good results in over 70%, past 5 years. Most had undergone previous marrow stimulation surgeries, suggesting reasonably good salvage results in that difficult-to-treat group. (Biant, 2014) A meta-analysis of 12 RCTs comparing ACI with marrow stimulation and osteochondral allografts showed no differences in intermediate-term outcomes with the differing techniques, or between generations of ACI. (Mundi, 2015) Three other concurrent meta-analyses reached the same conclusions that there is insufficient data regarding any superiority of ACI and that it may be appropriate to reserve ACI for larger defects and failure of other repair procedures. (Li, 2015) (Samsudin, 2015) (Oussedik, 2015) ACI should also be avoided in obese (BMI over 30) patients who have been shown to have no sustained improvement at 2 years. (Jaiswal, 2012) Worse outcomes have also been reported in females with ACI, especially so with patellar defects. (Kreuz, 2013) Weak evidence (case-series only) has suggested some success with patellar ACI, which remains off-label, but quality RCTs are lacking. (Gomoll, 2014) Similarly, a systematic review of level 3 and 4 studies has noted statistically significant improvements with combined ACI/patella-femoral osteotomy over patellar ACI alone. (Trinh, 2013)

Other insurance guidelines:

Washington worker's compensation guidelines no longer cover ACI since it is argued that prior indications have only been for failed chondral procedures, but that those procedures themselves decrease the odds of ACI salvage success. (Washington, 2016) Other carriers continue to cover ACI for limited indications. (BlueCross, 2016c) (UHC, 2014)

REFERENCE(S)

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