

Corporate Medical Policy

Autologous Chondrocyte Transplantation

Description of Procedure or Service

Autologous chondrocyte implantation (ACI) or transplantation is a form of tissue engineering that creates a graft from a patient's own cartilage cells to repair defects in articular cartilage. The procedure involves the collection of cartilage cells, which are grown in a laboratory to create new cartilage tissue. This new tissue is then implanted into the defect, with the goal of improving the quality of cartilage repair.

Background

Hyaline cartilage, the naturally occurring cartilage which covers the weight-bearing surfaces of bones in mobile joints, is very durable but has a low capacity for regeneration because of its avascular and relatively acellular composition. Osteochondral (OC) surfaces that are damaged by trauma or degenerative processes usually fill in with fibrocartilage, which is less suitable for absorbing stress than hyaline cartilage, making the joint susceptible to further damage and development of arthritis.

Nonsurgical treatments for damage to articular cartilage include weight reduction, physical therapy, braces and orthotics, intraarticular injection of hyaluronic acid derivatives, and nonsteroidal anti-inflammatory agents. Many surgical options are available, including cartilage debridement or repair, subchondral drilling, abrasion, spongialization, microfracture, implants, OC grafting, autologous chondrocyte implantation (ACI), and total joint replacement.

There is no standard approach to the treatment of hyaline cartilage defects in the knee. Results from these conventional methods can be suboptimal or short-lasting, except in individuals with very low activity demands. If defects progress to severe osteoarthritis, total knee replacement (TKR) may become necessary.

ACI involves surgical removal of a small piece of articular cartilage, harvesting of cells from the cartilage, growth of these cells in a specialized laboratory, and implanting the cultured cells over the cartilage lesion, with the goal of restoring resilient, durable cartilage at the site of injury. In first-generation ACI, the cultured cells are injected under a periosteal membrane that is usually taken from the tibia of the patient and sutured over the knee lesion. In second- and third-generation ACI, the cultured cells are injected under or grown attached to a synthetic membrane or scaffold that is sutured over or adhered to the knee lesion. ACI was first performed in 1994 in Sweden, at the University of Göteborg (Brittberg et al., 1994) and has been performed on more than 55,000 patients worldwide since its introduction.

Current National Institute for Health and Care Excellence (NICE) guidelines recommend Autologous chondrocyte implantation (ACI) is recommended as an option for treating symptomatic articular cartilage defects of the knee, only if:

- the person has not had previous surgery to repair articular cartilage defects
- there is minimal osteoarthritic damage to the knee (as assessed by clinicians experienced in investigating knee cartilage damage using a validated measure for knee osteoarthritis)
- the defect is over 2 cm² and
- the procedure is done at a tertiary referral center. (NICE, 2017).

The SUMMIT (Superiority of Matrix-induced autologous chondrocyte implant versus Microfracture for Treatment of symptomatic articular cartilage defects) trial compared matrix-applied chondrocyte implantation (MACI[®]) against MF. The TIG/ACT/01/2000 (TIG/ACT) trial compared ACI with characterized chondrocytes against MF. The ACTIVE trial compared several forms of ACI against standard treatments, mainly MF. In the SUMMIT trial, improvements in knee injury and osteoarthritis outcome scores (KOOSs), and the proportion of responders, were greater in the MACI group than in the MF group. In the TIG/ACT trial there was improvement in the KOOS at 60 months, but no difference between ACI and MF overall. Patients with onset of symptoms < 3 years' duration did better with ACI. Results from ACTIVE have not yet been published. Survival analysis suggests that long-term results are better with ACI than with MF. Economic modelling suggested that ACI was cost-effective compared with MF across a range of scenarios.

From the Mistry et al. analysis, the main limitation was the lack of randomized controlled trial data beyond 5 years of follow-up. A second was that the techniques of ACI are evolving, so long-term data come from trials using forms of ACI that are now superseded. In the modelling, they assumed that durability of cartilage repair as seen in studies of older forms of ACI could be applied in modelling of newer forms. A third was that the high list prices of chondrocytes are reduced by confidential discounting. The main research needs are for longer-term follow-up and for trials of the next generation of ACI.

Twelve month studies have shown positive results, predictable outcomes of ACI. Researchers continue to investigate the clinical outcomes to yield new insights into mechanisms of cartilage repair over a long term.

Matrix-induced Autologous Chondrocyte Implantation (MACI)

The purpose of the MACI procedure is to help regenerate health articular cartilage in the knee to reduce the inflammatory response that often leads to pain, swelling and loss of motion.

The Matrix-induced autologous chondrocyte implantation (MACI) procedure is a 2 stage procedure consisting of 4 steps: 1. Arthroscopy for diagnosing and sizing the defect, obtaining a chondral biopsy and harvesting hyaline cartilage. 2. Seeding the cultivated autologous chondrocytes on an absorbable collagen membrane; up to 1 million cells per square centimeter. This process could take several weeks to accomplish. 3. An open arthrotomy is used to prepare the defect site, size and shape the implant and attach the implant to the lesion site. 4. Postoperative rehabilitation.

Regulatory Status

Implantation of autologous chondrocytes is a surgical procedure and, as such, is not subject to regulation by the FDA. However, the FDA does license biological products such as: Carticel (Vericel Corp., formerly manufactured by Genzyme Biosurgery) and ACI-Matrix collagen membrane (Vericel Corp.).

Several other products have been considered or tested for the purpose of ACI but have not yet received FDA clearance.

Benefit Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits.

Related policy with specific coverage: refer to Osteochondral Grafting of Articular Lesions policy.

Policy Statement

GEHA will provide coverage for autologous chondrocyte implantation/transplantation when it is determined to be medically necessary because the medical criteria and guidelines as documented below have been demonstrated.

When Autologous Chondrocyte Transplantation is covered

GEHA considers Autologous Chondrocyte Implantation (ACI) medically necessary for the treatment of disabling full-thickness articular cartilage defects of the knee caused by acute or repetitive trauma **and** when there are symptoms of disabling knee pain related to a full thickness, focal chondral defect **and all** of the following criteria are met:

- A. Body mass index (BMI) less than or equal to 35; **and**
- B. Failure of conservative therapy (minimum of 2 months of physical therapy) as well as established surgical interventions (i.e., microfracture, drilling, abrasion, or osteochondral autograft). *Please note: neither diagnostic arthroscopy, lavage, or debridement are considered adequate to meet this criterion;* **and**
- C. Focal articular cartilage defect down to but not through the subchondral bone on a load bearing surface of the femoral condyle (medial, lateral, trochlear) or the patella); **and/or**
- D. Focal, full-thickness (grade III or IV) unipolar lesions of the patella or the weight bearing surface of the femoral condyles or trochlea at least 1.5 cm² in size; **and**
- E. Documented minimal to absent degenerative changes in the surrounding articular cartilage (Outerbridge Grade II or less), and normal-appearing hyaline cartilage surrounding the border of the defect; **and**
- F. Normal knee biomechanics, or alignment and stability achieved concurrently with autologous chondrocyte implantation; **and**
- G. Adolescent patients should be skeletally mature with documented closure of growth plates (e.g., 15 years or older). Adult patients should be too young to be considered an appropriate candidate for total knee arthroplasty or other reconstructive knee surgery (e.g., younger than 55 years)

When Autologous Chondrocyte Transplantation is not covered

Autologous chondrocyte transplantation is considered experimental/investigational for all other indications, including but not limited:

- A. Talar lesions, or lesions of other joints (e.g., hip and shoulder)
- B. For individuals with a prior total meniscectomy
- C. Osteochondritis dissecans lesions
- D. Initial or first line surgery
- E. Patients with an unstable knee
- F. Osteoarthritis or other inflammatory disease of the joint (where an osteoarthritic or inflammatory process significantly and adversely affects the quality of the peri-lesional cartilage)
- G. Kissing lesions
- H. Previous cancer in the bones, cartilage, fat, or muscle of the treated limb.
- I. Combined meniscal allograft and autologous chondrocyte implantation of the knee
- J. Combined autologous chondrocyte implantation and osteochondral autograft transfer system for surgical repair of cartilage defects of the knee

Policy Guidelines

This procedure is generally considered contraindicated in individuals with a known history of an allergy to gentamicin and for individuals with sensitivities to materials of bovine origin.

Physician documentation

Completed GEHA Osteochondral Procedure form (This can be found on the geha.com website).

Results of Arthroscopic assessment or MRI History and Physical performed with the last 12 months including height and weight.

Documentation of conservative treatment and results of conservative treatment.

Any other such documentation to provide evidence that member meets the coverage criteria set forth in this policy.

Applicable Codes include but are not limited to:

CPT/HCPCS Code	Description
27412	Autologous chondrocyte implantation, knee
29870	Arthroscopy, knee, diagnostic; with or without synovial biopsy (separate procedure)
29874	Arthroscopy, for removal of loose body or foreign body (e.g., osteochondritis dissecans fragmentation, chondral fragmentation)
29877	Arthroscopy, debridement/shaving of articular cartilage (chondroplasty)
29879	Arthroscopy, abrasion arthroplasty (includes chondroplasty where necessary) or multiple drilling or microfracture
J7330	Autologous cultured chondrocytes, implant
S2112	Arthroscopy, knee, surgical, for harvesting of cartilage (chondrocyte cells)

Scientific References

American Academy of Orthopaedic Surgeons (AAOS). The Diagnosis and Treatment of Osteochondritis Dissecans. Guideline and Evidence Report. December 4, 2010. Available at: http://www.aaos.org/research/guidelines/OCD_guideline.pdf.

Brittberg M. Autologous chondrocyte implantation--technique and long-term follow-up. *Injury*. 2008;39 Suppl 1:S40-S49.

Brittberg M, Lindahl A, Nilsson A, Ohlsson C, Isaksson O, Peterson L. Treatment of deep cartilage defects in the knee with autologous chondrocyte transplantation. *N Engl J Med*. 1994;331(14):889-895.

Brittberg M, Recker D, Ilgenfritz J, Saris DB, SUMMIT Extension Study Group. Matrix-Applied Characterized Autologous Cultured Chondrocytes Versus Microfracture: Five-Year Follow-up of a Prospective Randomized Trial. *The American journal of sports medicine*. 2018 May;46(6):1343-51.

Centers for Disease Control and Prevention (CDC). Osteoarthritis Fact Sheet. Updated February 2, 2017. Available at: <http://www.cdc.gov/arthritis/basics/osteoarthritis.htm#2>

Deng Z1, Jin J1, Zhao J1, Xu H1. Cartilage Defect Treatments: With or without Cells? Mesenchymal Stem Cells or Chondrocytes? Traditional or Matrix-Assisted? A Systematic Review and Meta-Analyses. *Stem Cells Int*. 2016;2016:9201492. doi: 10.1155/2016/9201492. Epub 2015 Dec 29.

Ebert JR, Schneider A, Fallon M, Wood DJ, Janes GC. A comparison of 2-year outcomes in patients undergoing tibiofemoral or patellofemoral matrix-induced autologous chondrocyte implantation. *The American journal of sports medicine*. 2017 Dec;45(14):3243-53.

Gille J1, Behrens P2, Schulz AP1, Oheim R3, Kienast B3. Matrix-Associated Autologous Chondrocyte Implantation: A Clinical Follow-Up at 15 Years. *Cartilage*. 2016 Oct;7(4):309-15. doi: 10.1177/1947603516638901. Epub 2016 Apr 6.

Gomoll AH, Gillogly SD, Cole BJ, Farr J, Arnold R, Hussey K, Minas T. Autologous chondrocyte implantation in the patella: a multicenter experience. *The American journal of sports medicine*. 2014 May;42(5):1074-81.

Knutsen G1, Drogset JO2, Engebretsen L3, Grøntvedt T2, Ludvigsen TC3, Løken S3, Solheim E4, Strand T4, Johansen O5. A Randomized Multicenter Trial Comparing Autologous Chondrocyte Implantation with Microfracture: Long-Term Follow-up at 14 to 15 Years. *J Bone Joint Surg Am*. 2016 Aug 17;98(16):1332-9. doi: 10.2106/JBJS.15.01208.

MACI FDA approval: MACI (Autologous Cultured Chondrocytes on a Porcine Collagen Membrane) retrieved from <https://www.fda.gov/biologicsbloodvaccines/cellulargenetherapyproducts/approvedproducts/ucm533177.htm>

McCarthy, Helen S., et al. "Magnetic Resonance Imaging Parameters at 1 Year Correlate With Clinical Outcomes Up to 17 Years After Autologous Chondrocyte Implantation." *Orthopaedic Journal of Sports Medicine*, Aug. 2018, doi:10.1177/2325967118788280.

Minas T1, Von Keudell A, Bryant T, Gomoll AH. The John Insall Award: A minimum 10year outcome study of autologous chondrocyte implantation. *Clin Orthop Relat Res*. 2014 Jan;472(1):41-51. doi: 10.1007/s11999-013-3146-9.

Mistry H, Connock M, Pink J, et al. Autologous chondrocyte implantation in the knee: systematic review and economic evaluation. *Health Technol Assess*. 2017;21(6):1-294.

National Institute for Health and Care Excellence (NICE). *Autologous chondrocyte implantation (ACI) for treating cartilage damage in the knee*. London, UK: National Institute for Health and Care Excellence; 2017. NICE Clinical Guidelines No. TA477.

Shaikh N1, Seah MKT1, Khan WS1. Systematic review on the use of autologous matrix-induced chondrogenesis for the repair of articular cartilage defects in patients. *World J Orthop*. 2017 Jul 18;8(7):588-601. doi: 10.5312/wjo.v8.i7.588. eCollection 2017 Jul 18.

Policy implementation and updates

June 2018 Complete reformatting and updates to policy content; clarification and expansion of covered vs non-covered indications.

May 2019 Formatting updates. Updated policy content. Clarification and expansion of covered indications