Medical Policy Manual Surgery, Policy No. 87

Autologous Chondrocyte Implantation for Focal Articular Cartilage Lesions

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Autologous chondrocyte implantation (ACI) involves harvesting chondrocytes from healthy tissue, expanding the cells in vitro, and implanting the expanded cells to resurface articular cartilage defects.

MEDICAL POLICY CRITERIA

Note: Clinical documentation to support criteria is required (See Required Documentation).

Medically Necessary

I. Autologous chondrocyte implantation (See Policy Guidelines) may be considered **medically necessary** for the treatment of disabling full-thickness articular cartilage defects of the knee caused by acute or repetitive trauma, when all of the following criteria are met (A. – E.):

A. 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); and

B. Focal, full-thickness (grade III or IV) unipolar lesions of the patella or on the weight-bearing surface of the femoral condyles or trochlea at least 1.5 centimeters squared in size; and

C. Documented Outerbridge grade II or less degenerative changes in the surrounding articular cartilage and normal-appearing hyaline cartilage surrounding the border of the defect; and

D. Normal knee mechanics, alignment, and stability are present before or are planned to be restored simultaneously with the autologous chondrocyte implantation procedure; and

E. Body mass index (BMI) < 35.

Investigational

II. Autologous chondrocyte implantation when Criterion I. is not met and for all other joints, including talar, and any indications other than those listed above is considered investigational.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

- MACI® is a next-generation matrix-induced autologous chondrocyte implantation (ACI), and is the only ACI therapy on the market currently approved by the FDA.
- For smaller lesions (e.g., smaller than 4 cm^2), if debridement is the only prior surgical treatment, then consideration should be given to marrow-stimulating techniques before autologous chondrocyte implantation (ACI) is performed.
- The average defect size reported in the literature is about 5 cm^2; however, many studies treated lesions as large as 15 cm^2.
- Severe obesity, e.g., body mass index greater than 35 kg/m^2, may affect outcomes due to the increased stress on weight-bearing surfaces of the joint.
- Misalignment and instability of the joint are contraindications. Therefore, additional procedures, such as repair of ligaments or tendons or creation of an osteotomy for realignment of the joint, may be performed at the same time. In addition, meniscal allograft transplantation may be performed in combination, either concurrently or sequentially, with ACI.

REQUIRED DOCUMENTATION

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History and Physical/Chart Notes including BMI

- Documentation of symptoms, associated diagnoses and treatments
- Name of FDA approved therapy
- For adolescent, documentation of growth plate closure
- Imaging to support patella lesion and degenerative changes
- Documentation of knee biomechanics or alignment and stability will be achieved concurrently with request

CROSS REFERENCES

1. Orthopedic Applications of Stem-Cell Therapy, Including Bone Substitutes Used with Autologous Bone Marrow, Medicine, Policy No. 142

BACKGROUND

A variety of procedures are being developed to resurface articular cartilage defects. Autologous chondrocyte implantation (ACI) involves harvesting chondrocytes from healthy tissue, expanding the cells in vitro, and implanting the expanded cells into the chondral defect under a periosteal or fibrin patch. Second- and third-generation techniques include combinations of autologous chondrocytes, scaffolds, and growth factors.

Damaged articular cartilage typically fails to heal on its own and can be associated with pain, loss of function, and disability and may lead to debilitating osteoarthritis over time. These manifestations can severely impair a patient's activities of daily living and adversely affect quality of life. Conventional treatment options include débridement, subchondral drilling, microfracture, and abrasion arthroplasty. Debridement involves the removal of synovial membrane, osteophytes, loose articular debris, and diseased cartilage and is capable of producing symptomatic relief. Subchondral drilling, microfracture, and abrasion arthroplasty attempt to restore the articular surface by inducing the growth of fibrocartilage into the chondral defect. Compared with the original hyaline cartilage, fibrocartilage has less capability to withstand shock or shearing force and can degenerate over time, often resulting in the return of clinical symptoms. Osteochondral grafts and ACI attempt to regenerate hyaline-like cartilage and thereby restore durable function.

With ACI, a region of healthy articular cartilage is identified and biopsied through arthroscopy. The tissue is sent to a facility licensed by the Food and Drug Administration (FDA) where it is minced and enzymatically digested, and the chondrocytes are separated by filtration. The isolated chondrocytes are cultured for 11 to 21 days to expand the cell population, tested, and then shipped back for implantation. With the patient under general anesthesia, an arthrotomy is performed, and the chondral lesion is excised up to the normal surrounding cartilage. A periosteal flap is removed from the proximal medial tibia and sutured to the surrounding rim of normal cartilage. The cultured chondrocytes are then injected beneath the periosteal flap. ACI may be considered more effective for larger lesions than microfracture or osteochondral grafts, but it is technically difficult, requiring two procedures and harvesting of periosteum. In addition, use of the FDA-indicated periosteal cover may result in hypertrophy, as well as donor-site morbidity.

The ACI procedure consists of four steps:

1. Initial arthroscopy and biopsy of normal cartilage,
2. Culturing of chondrocytes,
3. A separate arthrotomy to create a periosteal flap and implant the chondrocytes, and

4. Postsurgical rehabilitation.

The initial arthroscopy may be scheduled as a diagnostic procedure and as part of this procedure, a cartilage defect may be identified, prompting biopsy of normal cartilage in anticipation of a possible chondrocyte transplant. The biopsied material is then sent for culturing and returned to the hospital when the implantation procedure (i.e., arthrotomy) is scheduled.

Methods to improve the ACI procedure are being investigated, including the use of a scaffold or matrix-induced ACI (MACI) composed of biocompatible carbohydrates, protein polymers, or synthetics. Desired features of articular cartilage repair procedures are the ability to:

1. Implant easily,
2. Reduce surgical morbidity,
3. Not to require harvesting of other tissues,
4. Enhance cell proliferation and maturation,
5. Maintain the phenotype, and
6. Integrate with the surrounding articular tissue.

In addition to the potential to improve the formation and distribution of hyaline cartilage, use of a scaffold with MACI eliminates the need for harvesting and suture of a periosteal patch. A scaffold without cells may also support chondrocyte growth.

REGULATORY STATUS

First-generation Autologous Chondrocyte Implantation

The culturing of chondrocytes is considered by FDA to fall into the category of manipulated autologous structural (MAS) cells, which are subject to a biologic licensing requirement. At the present time, only Carticel™ (Vericel Corporation) has received FDA approval for the culturing of chondrocytes through a biologics license. In 1997, Carticel received FDA approval for the repair of clinically significant, "...symptomatic cartilaginous defects of the femoral condyle (medial lateral or trochlear) caused by acute or repetitive trauma.…"

In December 2016, MACI® (Vericel) received FDA approval for "the repair of symptomatic, single or multiple full-thickness cartilage defects of the knee with or without bone involvement in adults." MACI consists of autologous chondrocytes that are cultured onto a bioresorbable porcine-derived collagen membrane. In 2017, production of Carticel was phased out, and MACI is the only autologous chondrocyte implantation product available in the United States.Second- and Third-generation Autologous Chondrocyte Implantation.

Second-generation ACI procedures have focused on developing three-dimensional constructs using native and synthetic biomaterials. Third-generation ACI products are now being engineered to deliver biofactors in sufficient quantities and in a temporally specific manner to induce a favorable chondrogenic response in the seeded cells and in cells of the host tissue, and to inhibit local or systemic tissue degenerative activities.

Several second- and third-generation methods for implanting autologous chondrocytes in a biodegradable matrix are currently in development/testing or are available only outside of the United States. These include:

- Atelocollagen (collagen gel; Koken)

- BioCart II (ProChon Biotech)
- Bioseed C (polymer scaffold; BioTissue Technologies)
- CaReS (collagen gel; Ars Arthro)
- Cartilix (polymer hydrogel; Biomet)
- Cartipatch® (agarose-alginate matrix, TBF Tissue Engineering)
- ChondroCelect® (characterized chondrocyte implantation; TiGenix)
- Chondron (fibrin gel; Sewon Cellontech)
- Hyalograft C (hyaluronic acid-based scaffold; Fidia Advanced Polymers)
- NeoCart (ACI with a 3-dimensional chondromatrix; Histogenics)
- NOVOCART®3D (collagen-chondroitin sulfate scaffold; Aesculap Biologics)

Although clinical use of these second- and third-generation ACI products has been reported in Europe and Asia, MACI® is the only one approved for use in the United States at this time.

EVIDENCE SUMMARY

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

AUTOLOGOUS CHONDROCYTE IMPLANTATION OF THE KNEE

Systematic Reviews

There have been several systematic reviews (SRs) on autologous chondrocyte implantation (ACI) of the knee. Some of these studies used Carticel™, while others have evaluated next-generation ACI products. The long-term efficacy of marrow stimulation techniques, as well as the evidence for ACI in the treatment of osteochondritis dissecans also is reviewed.

Wang (2024) published a SR reporting 10-year patient-reported and clinical outcomes after undergoing MACI of the knee.[1] A total of 168 patients representing 188 treated chondral defects with a minimum of 10 years follow-up were included. Significant and durable long-term improvements were observed across multiple PRO measures. Follow-up magnetic resonance imaging (MRI), when performed, also demonstrated satisfactory defect fill and an intact graft in the majority of patients. The all-cause reoperation rate was 9.0%, with an overall 7.4% rate of progression to total knee arthroplasty (TKA) at 10 to 17 years of follow-up. There were significant conflict of interest declarations from the authors of this study. Including several authors who receive royalties for consultation for medical device companies related to MACI.

Colombini (2023) published a SR evaluating mid and long-term efficacy of ACI and MACI in patients with knee cartilage defects related to osteoarthritis.[2] Only five studies were included; two focused on ACI and three on MACI. ACI was used for patients with a lower Kellgren-Lawrence (KL) score. MACI was used mostly in patients with a KL of >1 (II-IV). The data

obtained from 235 patients (161 ACI, 74 MACI) showed that ACI and MACI sustained stable clinical improvements up to 11 and 15 years, respectively, with a failure rate of about 10% up to 11 years. Scarce biological details regarding chondrocyte implantation were reported. The authors conclude that ACI and MACI procedures for the treatment of knee cartilage lesions associated to OA showed long-term success and allowed delaying arthroplasty. Additional trials reporting homogenous data and precise patient characterization are needed to conduct an effective literature meta-analysis and identify the clinical relevance of these procedures.

Ginesin (2023) published a SR evaluating various patellar cartilage restoration techniques including ACI.[3] A total of 24 studies which with six different surgical techniques were included; ACI was used in eight of the studies. Other techniques included osteochondral autograft transplantation (9 studies), advanced microfracture/autologous matrix-induced chondrogenesis (3 studies); osteochondral allograft transplantation (OAT; 1 study) and synthetic osteochondral graft (2 studies). The OAT procedure was used for smaller lesions (<2 cm^2) and demonstrated minimal complication rates and satisfactory outcome scores. Advanced microfracture techniques showed promise, with improvement in outcome scores and zero complications. Matrix-induced ACI consistently exhibited higher mean improvement in the measured outcome scores and resulted in fewer complications when compared with previous generations of ACI. The authors note that further prospective studies comparing OCA and matrix-induced ACI for larger patellar defects are necessary to determine the superior technique.

Migliorini (2023) published a SR evaluating the safety and efficacy of ACI for chondral defects of the knee is skeletally immature patients.[4] A total of nine studies (251 procedures) were included in the analysis. The mean age of the patients was 16.4 ± 0.7 (range, 15-17) years. The Knee injury and Osteoarthritis Outcome Score (KOOS) and International Knee Document Committee (IKDC) increased of + 41.9/100 (P = 0.003) and + 33.2/100 (P = < 0.0001) points, respectively. The Lysholm Knee Score improved of + 20.6/100 (P = 0.02) points. The Visual Analogue Scale (VAS) for pain reduced of - 3.6/10 (P = 0.004) points. The rate of graft hypertrophy was 12.5% (5 of 40 patients), and the rate of failure 5.6% (8 of 142 patients). The authors concluded that ACI for chondral defects of the knee is effective to improve PROMs in skeletally immature patients. However, the safety profile of ACI still remains controversial.

Migliorini (2022) reported findings from 47 publications that described outcomes in at least 5 patients who underwent matrix-induced autologous chondrocyte implantation (MACI) or cell-free autologous matrix-induced chondrogenesis (AMIC) for chondral defects of the knee, including 38 prospective studies and 9 retrospective studies.[5] The proportion of studies at unclear or high risk of bias ranged from approximately 20% to more than 75% in each bias domain. The authors reported significantly higher Lysholm Knee Questionnaire scores and International Knee Documentation Committee scores with AMIC relative to MACI, and significantly higher rates of treatment failure with MACI relative to AMIC. The nature of the statistical analysis limits interpretation of these findings; the authors pooled data from all studies for analysis without weighting, using simple statistical tests to compare distributions of continuous values (via t-tests) or proportions (via Chi-square); differences in baseline characteristics and various patient-reported outcome and complication measures were tested without adjustment for multiple comparisons. The time at which the outcomes were assessed was not reported, and several reported outcomes were not defined (such as hypertrophy and treatment failure).

Angele (2022) published a SR reporting on outcomes of randomized trials (RCT) of cartilage repair techniques for localized cartilage defects of the knee with minimum 5-year follow-up.[6]

The six included RCTs comprised 520 patients, with mean follow-up ranging from 5 to 16 years; 1 trial (SUMMIT, discussed in the section below detailing RCTs) compared matrix-induced autologous chondrocyte implantation (MACI) to microfracture (MF), and three compared other autologous chondrocyte implantation techniques to either MF or osteochondral autograft transplantation. All trials were considered to be at high risk of bias due to lack of blinding. The trial comparing MACI to MF indicated superior outcomes in the Knee Injury and Osteoarthritis Outcome Score (KOOS) pain, function, and activities of daily living subscales with MACI; trials of other autologous chondrocyte implantation modalities produces mixed results, with 2 trials indicating no difference relative to MF in overall KOOS or other patient-reported outcome measures, 1 trial indicating significant improvement in overall KOOS relative to MF in a subgroup of patients with symptom onset within 3 years prior to intervention, and 1 trial indicating superior Cincinatti Knee Rating System scores at 10-year follow-up relative to osteochondral autograft transfer.

Dhillon (2022) published a SR of randomized controlled trials (RCTs) comparing clinical outcomes of microfracture to third generation ACI (cells cultured within a collagen membrane, MACI) for the treatment of focal chondral defects of the knee.[7] Six studies (5 Level I, 1 Level II) met inclusion criteria, including a total of 238 patients undergoing microfracture and 274 undergoing MACI, however, two studies had an overlapping cohort and therefore the study with longer follow-up was used in all analyses. Average follow-up time ranged from 2.0 years to 6.0 years and lesion size ranged from 1.8 cm^2 to 5.0 $cm^{2.}$ Treatment failure ranged from 0% to 1.8% in the MACI group and 2.5% to 8.3% in the microfracture group. Significantly greater improvement in multiple Knee Injury and Osteoarthritis Outcome Score subscores was found in the MACI group compared with microfracture in four studies. No pooled analyses were reported. No long-term outcomes were reported.

Colombini (2022) published a SR of mid- and long-term efficacy of ACI and MACI in patients with knee cartilage defects in the presence of osteoarthritis (OA).[8] Inclusion criteria were; clear presence of osteoarthritis (KL >/= 1), ACI or MACI to treat knee cartilage defects, and minimum follow-up of 36 months. Data from five studies met inclusion/exclusion criteria (two on ACI and three on MACI) for a total of 235 patients (161 ACI, 74 MACI). The authors reported stable clinical improvements following ACI and MACI at up to 11 and 15 years, respectively. A failure rate, defined as revision with re-operation or arthroplasty, of 8% for ACI and 10% for MACI was observed at three and four years, respectively. Long-term failure rates of 9.6% at 9 years was found for ACI. The study with the longest follow-up reported a failure rate of 58.5% after 15 years for MACI. There were several limitations to the available data noted by the review authors, including the small sample size of studies and lack of biological details such as cell isolation, preservation, expansion, number, and implantation techniques.

Abraamyan (2022) completed a SR with meta-analysis that evaluated cartilage repair techniques, including microfracture, augmented microfracture, and ACI/MACI.[9] The authors included a total of 14 RCTs (N=775), and changes from baseline in the five Knee injury and Osteoarthritis Outcome Score (KOOS) subscales, including KOOS Sport, KOOS Quality of Life, KOOS Symptoms, KOOS Pain, and KOOS Activities of Daily Living, were measured. Only in the KOOS Sport subscale was statistically significant benefit with ACI/MACI procedures found compared to microfracture (p=0.02). The mean delta KOOS Sport after ACI/MACI procedures was 9.9 points greater than after microfracture and 11.7 points greater than after augmented microfracture. Comparisons between surgical techniques for the other subscales did not reach statistical significance.

A SR by Su (2021) evaluated long-term (at least two years post-treatment) clinical and radiographic outcomes of patients receiving cartilage restoration procedures including ACI and matrix-induced ACI (MACI) for the treatment of patellar chondral defects.[10] The analysis included 10 studies (N= 293) that provided patient-reported functional outcome data, six of which also provided postoperative MRI with a mean time to postoperative time to MRI of 19 months (range 8-28.8 months). All studies were retrospective, and the mean sample size was 29 (range 10-49). Four studies evaluated ACI with or without TTO procedures, one evaluated ACI alone. Among the five studies on ACI, the range of defect size was 2.92 to 6.4 cm^2 (one study did not report defect size). Two studies evaluated the MACI procedure with or without TTO for cartilage defects of the patella, and among these studies, the mean defect size was 3.75 cm^2. All studies on ACI and MACI found statistically significant improvements in functional outcomes at least two years post-procedure. With respect to MRI findings, moderate-to-complete infill of patellar cartilage lesions was seen in the majority of patients regardless of treatment type. Reoperation was common, with rates ranging from 40% to 60% in studies reporting this variable after ACI. Limitations in the available data include the retrospective study design, small sample size, and considerable variability in the outcomes reported, which precluded pooled analysis.

Zamborsky (2020) completed a SR and network meta-analysis that evaluated surgical interventions for patients with knee articular cartilage defects.[11] The authors included a total of 21 articles (from 12 RCTs) in their analysis with a total population of 891 patients. Follow-up varied widely among the included studies, ranging from 12 months to 15 years. Of the surgical interventions evaluated, microfracture was associated with significantly higher failure rates compared to ACI at 10 years of follow-up (relative risk [RR], 0.12; 95% confidence interval [CI]; 0.04 to 0.39). No significant differences in failure rates were seen between microfracture and osteochondral autograft transplantation, MACI, or characterized chondrocyte implantation at two, five, and 10 years of follow-up. No significant differences between the interventions were noted regarding reintervention, biopsy types, or adverse events. Based on efficacy and safety, ACI was ranked as the best intervention for failure outcome at 10 years of follow-up, followed by osteochondral autograft transplantation, then microfracture. Microfracture was consistently ranked worse than cartilage repair techniques for other outcomes including quality of tissue repair and return-to-activity rates.

In 2020, Gou published a SR of clinical outcomes among patients with fractures of knee cartilage who were treated with ACI (n=332) or microfracture (n=327) from 12 RCTs.[12] Patient age ranged from 25 to 41 years, with the majority of patients male. Treatment follow-up ranged from 1.5 to 15 years. There were diverse types of autologous chondrocyte implantation performed among the studies including MACI®, NeoCart, ACI with periosteum, and ChondroCelect. Outcomes included an overall clinical score, Knee Injury and Osteoarthritis Outcome Score subdomains of activities of daily living and function, quality of life, pain relief score, and failure/operation rate. No significant difference was found between the interventions in improvement in International Knee Documentation Committee and Lysholm scores or overall Knee Injury and Osteoarthritis Outcome Score measures at one, two, or five years of follow-up. There was also no difference in failure rate between the groups at two, three, or five years. ACI was associated with significant improvements in activities of daily living up to five years follow-up compared to microfracture as well as greater improvement in quality of life and pain relief at five and two-year follow-up examinations, respectively. Major limitations of this SR and meta-analysis include the small number of eligible RCTs in the final analysis and heterogeneity in ACI techniques, scales and scores for outcome measures, and lesion sizes. Blinding of the

patients or surgeons was difficult to perform given the two-step procedure of autologous chondrocyte implantation.

Migliorini (2020) published a SR evaluating the clinical outcomes of ACI and Mesenchymal Stem Cell (MSC) injections for the treatment of focal chondral defects of the knee.[13] Forty-three publications were included in the analysis of which 11 were RCTs and 32 were cohort studies, and pooled analyses were conducted in data from 3340 procedures. ACI procedures were analyzed as either first-generation (p-ACI) in which a periosteal patch is harvested from the proximal tibia is utilized, second-generation (c-ACI) in which a graft containing type I/III collagen membrane is utilized, or third generation (m-ACI), in which autologous chondrocytes are seeded and cultured on type I and III collagen membranes is utilized. Twelve studies reported on p-ACI procedure, eight studies reported on c-ACI procedures, and 13 studies reported on m-ACI procedures. In the p-ACI group (987 knees), the Cincinnati Score improved by 18.94% (p=0.1), VAS by 38% (p=0.01), Tegner score by 19.11% (p=0.03), Lysholm score by 22.40% (p=0.01), International Knee Documentation Committee (IKDC) by 27.36% (p=0.003). In the c-ACI group (444 knees), the Cincinnati Score improved by 23.80% (p=0.08), KOOS by 23.48% (p=0.03), VAS by 33.2% (p=0.005), IKDC by 33.30% (p=0.005). In the m-ACI group (599 knees), the Cincinnati Score improved by 26.80% (p=0.08), KOOS by 31.59% (p=0.1), VAS by 30.43% (p=0.4), Tegner score by 23.1% (p=0.002), Lysholm score by 31.14% (p=0.004), IKCD by 30.57% (p<0.001). The authors conclude that ACI techniques are considered a concrete solution to treat focal chondral defects of the knee, and significant improvements from first- to third-generation techniques has been observed.

Gou (2020) published a SR of trials of articular cartilage lesions of the knee treated with either ACI or microfracture (MF). The SR included 12 RCTs (N=659; 332 ACI, 327 MF).[12] Patients treated with ACI had a significant benefit in activities of daily living at follow-up up to five years post-procedure compared with patients treated with MF. ACI treatment also was found to provide greater improvement in quality of life (QoL) and pain relief than MF at 5-year and 2-year follow-up examinations, respectively. However, no significant difference in the improvement in International Knee Documentation Committee (IKDC) and Lysholm scores or overall Knee Injury and Osteoarthritis Outcome Score (KOOS) measures were found between patients in the ACI and MF groups at 1-year, 2-year, or 5-year follow-up examinations. No significant group differences in failure rate were found at 2-year, 3-year, or 5-year follow-up timepoints.

A SR and network meta-analysis published by Zamborsky (2020) on level 1 RCTs evaluating long-term outcomes from surgical interventions for patients with knee articular cartilage defects included 891 patients from 21 publications.[11] The authors found that at 10-year follow-up, there was a significantly higher failure rate in patients treated with MF compared to those treated with ACI. At three-year follow-up, KOOS was higher in patients who underwent chondrocyte implantation or MACI compared to MF. No significant differences were found between groups with respect to reintervention, biopsy types, or adverse events.

Andrade (2019) published a SR of clinical studies that assessed surgical outcomes of patellofemoral cartilage restoration surgeries, including ACI.[14] Forty-two studies were included in the review (N= 1,311 knees and 1,309 patellofemoral defects). The mean follow-up evaluated was 59.2 months. Among the restoration techniques included in the review, 56% were ACI. Significant improvement in at least one outcome was observed in almost all studies and these surpassed the minimal clinically important difference (MCID) threshold. The authors

concluded, however, that no definitive conclusions could be made regarding the best surgical technique across all evaluated given the lack of comparative studies.

The effectiveness of cartilage repair procedures including ACI for the treatment of symptomatic knee chondral defects was evaluated in a SR with meta-analysis published by Jones (2019).[15] Weighted mean improvements in IKDC, Lysholm, and visual analog scale for pain (VAS pain) scores were calculated from preoperative to short- (1-4 years), mid- (5-9 years), and long-term (≥10 years) postoperative follow-up. The meta-analysis included a total of 89 studies with 3894 unique patients. All cartilage repair procedures met MCID values at short- and midterm follow-up for IKDC and Lysholm scores; ACI/MACI additionally met minimal clinically important difference values at the long-term follow-up. This led the authors to conclude the procedure provides extended maintenance of clinical benefits for patients undergoing these surgical interventions as compared with microfracture.

Coughlin (2019) published a SR of outcomes of cartilage restoration techniques for grades I - IV cartilage defects in the adolescent knee, including ACI.[16] Eleven studies (N=307) were included in the review, with 98 of these subjects having had ACI (mean age 16.0), which was the most common procedure included in the review. ACI was among the procedures observed to have the most positive postoperative functional outcomes and lowest complication rates.

A SR by Sacolick (2019) examined the patient-reported outcomes, complication rates, and failure rates of ACI and MACI for osteochondritis dissecans in adults.[17] Nine clinical studies were assessed (type not specified), with 179 (>200 lesions) patients aged 18-49 years (mean=27.6 y). Follow-up ranged from 6.5 months to 10 years. Results of patient-reported outcomes showed that 85% of patients reported excellent or good outcomes. Statistically significant improvements from preoperative to final follow-up were reported for all patient-reported outcome measures used across the studies including the IKDC, Lysholm Knee Questionnaire, EuroQol Visual Analog Scale, Cincinnati Rating System, and the Tegner Activity Scale. Of the studies that reported complication and failure rates for ACI/MACI, 23 (15.7%) of 146 patients reported complications, and failure rate was 8.2%. Unplanned reoperations were necessary for 20.5% of patients. The study results showed that ACI/MACI had the best outcomes for active young males with small lesions. Older adults and less active individuals, as well as those with lesions >6 cm2, did not fare as well. A limitation of this review was its lack of randomized trials with controls to compare to ACI/MACI.

In 2017, the National Institute for Health Research (NIHR) reported on a SR assessing the clinical effectiveness ACI in the knee[18]. The NIHR review focused on reports from previous SRs including adults with symptomatic articular cartilage defects in the knee published between 2004 and 2014. Twelve SRs including 19 studies (11 RCTs) were selected. The main comparator of interest was microfracture and four trials (n=712) were identified that compared second- and third-generation ACI with microfracture. One of the trials (ACTIVE, N=390) shared selected results with the NIHR reviewers but no results have been published. In summary, both MACI and ChondroCelect were more clinically effective than microfracture for the outcomes of reductions in pain and improvements in function on the KOOS over two to five years. Limited long-term data were available on the failure rates of both ACI and microfracture after five years; data were available from six observational studies. The conclusions regarding follow-up after five years were primarily based on one of the observational studies judged to be the highest quality (Nawaz [2014], N=827), For ACI, failure rates were lower in patients who had no previous knee repair and in people with minimal evidence of osteoarthritis. Larger defect size was not associated with poorer outcomes in these patients.

In 2016, DiBartola reported a SR of clinical outcomes after ACI in the knees of adolescents ranging from 11 to 21 years (mean age 16.2), including five case series (N=115).[19] No RCTs or comparative studies were included in this review. Overall, 99 patients (83%) underwent ACI with periosteal cover, six (5%) with type I/type III collagen cover, and 14 (12%) with matrix-induced ACI. Follow-up ranged from 12 to 74 months (mean, 52.3 months). Mean defect size was 5.3 cm^2 (range, 0.96 to 14 cm2). All studies reported significant improvement in clinical outcomes scores. Graft hypertrophy was the most common complication (7.0%). The overall percentage increase in clinical outcome scores was 35.7% (SD, 14.2%). Limitations of this review include the fact that no RCT's or comparative studies were included in this review, and all of the studies were considered to be of fair, not good quality in terms of their methodology.

In 2016, DiBartola also published a SR with meta-analysis on the use of different surgical treatments for cartilage lesions of the knee, focusing on histological outcomes including the degree of defect repair, integration to boarder zone, and macroscopic appearance (to calculate the IRCS score), as well as histological appearance such as hyaline-like cartilage, fibrocartilage, fibrous tissue, or mixed fibrocartilage and hyaline-like cartilage.[20] Grades included normal/excellent (ICRS score = 12), nearly normal/good (IRCS score = 8 to 11), abnormal/fair (ICRS score = 7–4), or severely abnormal/poor (ICRS score = 1 to 3). Thirty-three small case series and RCTs (N=1511 patients) were included. Thirty evaluated ACI or one of its subtypes, six evaluated microfracture (MF), and seven evaluated osteochondral autografting (OATS). No significant difference was found cartilage quality using ICRS grading criteria among OATS, ACI-C, MACI, and ACI-P (ranging from 8.8 to 9.59 – nearly normal/good), however, ICRS scores for microfracture were significantly poorer compared to other treatments. Interestingly, the reviewers were unable to correlate histological outcomes with clinical outcomes, regardless of the method used.

In 2016, Adrade published a SR of surgical outcomes from articular cartilage and/or osteochondral lesions in the knees of soccer players.[21] Five studies were included in the review that met inclusion criteria, one of which was a small case series that used ACI as treatment[22] and one small nonrandomized study that compared matrix-induced ACI (MACI) to microfracture.[23] The other included studies were small case series using mosaicplasty, microfracture and chondral debridement as surgical treatments. The reviewers reported that ACI treatment provided the slowest return to competition and slower clinical and functional results compared to all other treatments reviewed. However, ACI and MACI procedures appeared to enhance longstanding clinical and functional results. Overall, chondral debridement was concluded to be the surgical technique that yielded the most positive results for all outcomes measured.

A 2011 SR by Harris included 13 randomized and nonrandomized controlled trials of 917 subjects who underwent ACI (n=604), microfracture (n=271), or osteochondral autograft (OA) (n=42).[24] The mean study quality was rated as 54 of 100, with no studies considered of good or excellent quality, seven were considered fair, and six were considered poor. Four studies compared different generations of ACI, finding no difference in outcomes but higher complication rates with open, periosteal cover, first-generation ACI. At 1- to 5-year follow-up, three of the seven studies showed better clinical outcomes after ACI in comparison with microfracture, one study showed better outcomes after microfracture, and three studies showed no difference in these treatments. Clinical outcomes after microfracture were found to deteriorate after 18 to 24 months in three of the seven studies. Studies comparing ACI and OA showed similar short-term clinical outcomes, with more rapid improvement but an increase in arthrofibrosis and donor site morbidity following OA. Younger patients with a shorter

preoperative duration of symptoms and fewer prior surgical procedures had the best outcomes after surgical intervention. A defect size greater than 4 cm^2 was the only factor predictive of better outcomes when ACI was compared with other surgical techniques.

A 2010 publication by Vasiliadis reviewed combined meniscal allograft transplantation and cartilage repair/restoration.[25] Six level IV studies (case series) with a total of 110 patients were included in the review. Patients underwent meniscal allograft transplantation with either ACI (n=73), osteochondral allograft (n=20), OA (n=17), or microfracture (n=3). All studies showed improvement in clinical outcomes at final follow-up compared with the preoperative condition. Outcomes were also compared with historical outcomes of each individual procedure performed in isolation. Four of the six studies found outcomes equivalent to procedures performed in isolation, while two studies found that outcomes with combined surgery were not as good as the historical controls. Across the six studies, 13 failures (12%) were reported; these included 11 isolated meniscal allograft transplantation failures, one combined meniscal allograft and ACI failure, and one isolated ACI failure. Three knees with failed meniscal allograft transplantation were converted to total knee arthroplasty. Nearly 50% of the patients underwent one or more subsequent surgeries after combined meniscal allograft transplantation and cartilage repair/restoration procedures.

A 2008 SR by Magnussen assessed whether “advanced” cartilage repair techniques (osteochondral transplantation or autologous chondrocyte transplantation) showed superior outcomes in comparison with traditional abrasive techniques for the treatment of isolated articular cartilage defects. Finding a total of five randomized controlled trials and one prospective comparative trial that met their selection criteria, Magnussen and colleagues concluded that no one technique had been shown to produce superior clinical results for treatment of articular cartilage defects with the available follow-up. They stated that, “any differences in outcome based on the formation of articular rather than fibrocartilage in the defect may be quite subtle and only reveal themselves after many years of follow-up.“

Randomized Controlled Trials

Many of the trials evaluating ACI have been summarized in at least one of the SRs or TEC Assessment above.[26-37] Studies not included in at least one SR above are discussed below.

Snow (2026) published a randomized controlled trial comparing autologous chondrocyte implantation (ACI) to alternative surgical cartilage management in 390 patients (mean age 35.4 years, 64% male) with symptomatic knee cartilage defects who had failed previous treatment.[38] At 10-year follow-up, the ACI group demonstrated significantly higher mean Lysholm knee scores compared to the alternative treatment group (mean difference 7.3 points, 95% CI 2.5-12.1, $p < 0.05$), with 70% completing all patient scores and 94% contributing to analysis. Treatment failure rates were comparable between groups (29% ACI vs 25% alternative, HR 1.04, 95% CI 0.69-1.6), and ACI outcomes were not negatively impacted by prior marrow stimulation, whereas alternative treatment outcomes were significantly worse in patients with prior marrow stimulation.

Yoon (2024) published a mean 5-year follow-up of a prospective randomized trial evaluating the outcomes of costal chondrocyte-derived pellet-type autologous chondrocyte implantation (CCP-ACI) compared to microfracture.[39] A total of 25 (out of 30 at one year) patients were included in this study. The Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) score in the CCP-ACI group was significantly higher than that in the microfracture group at 5 years (62.3 vs 26.7, respectively; $p < 0.0001$). The Lysholm score and KOOS score

in the CCP-ACI group were significantly higher than those in the microfracture group at 5 years (84.5 vs 64.9, respectively, and 390.9 vs 303.0, respectively; p = 0.023 and p = 0.017, respectively). There was one case of treatment failure that occurred in the microfracture group. The authors concluded that the results of both procedures clinically and statistically significantly improved at 1 and 5 years' follow-up in treating cartilage defects, but the results of CCP-ACI were superior to those of microfracture. Magnetic resonance imaging conducted at 1 year and 5 years after CCP-ACI revealed statistically significant superior structural integration with native cartilage tissue compared with microfracture.

Snow (2023) published a SR comparing long term (5 year) outcomes of ACI to alternative forms of cartilage management in patients (N = 390) after a failed previous treatment for chondral or osteochondral defects in the knee.[40] Patients (18 – 55 years old) with failed surgical procedure at least six months prior were randomized to ACI or alternative management. Lysholm scores were improved by 1 year in both groups (15.4 points [95% CI, 11.9 to 18.8] and 15.2 points [95% CI, 11.6 to 18.9]) for ACI and alternative, with this improvement sustained over the duration of the trial. However, no evidence of a difference was found between the groups at 5 years (2.9 points; 95% CI, -1.8 to 7.5; P = .46). Approximately half of the participants (55%; 95% CI, 47% to 64% with ACI) were still experiencing benefit at 5 years, with time to cessation of treatment benefit similar in both groups (hazard ratio, 0.97; 95% CI, 0.72 to 1.32; P > .99). There was a differential effect on Lysholm scores in patients without previous marrow stimulation compared with those with marrow stimulation (P = .03; 6.4 points in favor of ACI; 95% CI, -0.4 to 13.1). More participants experienced a serious adverse event with ACI (P = .02). Previous marrow stimulation had a detrimental effect on the outcome of ACI.

The Superiority of Matrix-induced autologous chondrocyte implant versus Microfracture for Treatment of symptomatic articular cartilage defects (SUMMIT) trial was the pivotal, industry-sponsored, multicenter randomized open-label trial; it was reported by Saris (2014) and compared MACI with microfracture for larger cartilage defects (≥3 cm2), which typically fare worse than smaller lesions when treated with microfracture.[26] This study was included in the Migliorini SR above. Brittberg (2018) reported on a five-year follow-up of the SUMMIT trial.[41] Five years post-procedure, the pain and function scores were still significantly better, both clinically and statistically, for MACI than for microfracture (p=.022). Changes from baseline to year five were also higher for MACI than microfracture for activities of daily living (p=.007), quality of life (p=.070), and other symptoms (p=.078). Over five years, four patients (one MACI, three microfractures) had treatment failures. The proportion of patients who required subsequent surgical procedures was similar in the two groups (10.8% in MACI and 9.5% in microfracture). Limitations were potential bias from allowing subjects to choose whether to continue with the extended study. In addition, the SUMMIT study was not blinded. However, the use of standardized surgical and rehabilitation procedures, validated clinical outcome instruments, and consistent outcomes among the multiple investigators strengthened the study.

In 2012, Bentley published long-term follow-up data from a 2003 trial of ACI or mosaicplasty in 100 patients[34]. With six patients lost to follow-up at a minimum 10-years after the index surgery, repair was found to have failed in 17% of patients treated with ACI and 55% of patients treated with mosaicplasty.[42]

Nonrandomized Studies

A variety of issues have been addressed with observational studies, including durability of the procedure, influence of age, comparison of femoral versus patellar defects, combination treatment with meniscal allograft, influence of prior marrow stimulation, and treatment of early OA. These are discussed below.

Marrow Stimulation Procedures

Montgomery reported a study of articular cartilage procedures of the knee from a national database of insurance billing records.[43] There were 216 million orthopedic procedures identified over a 6-year period. For the 163,448 articular cartilage procedure codes reported over this period, 98% were microfracture (n=36,095) or chondroplasty (n=125,245). Efficacy of the microfracture technique was examined in a 2009 SR.[44] Twenty-eight studies describing 3122 patients were included in the review; six of the studies were RCTs. Microfracture was found to improve knee function in all studies during the first 24 months after the procedure, but the reports on durability were conflicting. A prospective longitudinal study of 110 patients by Solheim et al found that at a mean of 12 years (range, 10-14) after microfracture, 45.5% of patients had poor outcomes, including 43 patients who required additional surgery.[45]

Other Nonrandomized Studies

Triana (2024) published a retrospective cohort study examining clinical outcomes and return-to-sport rates between osteochondral allograft (OCA) transplantation and autologous chondrocyte implantation/matrix-induced autologous chondrocyte implantation (ACI/MACI) for patellofemoral articular cartilage defects.[46] The study included 95 patients (78% follow-up rate) with 55 cases receiving ACI/MACI (57.9%) and 40 receiving OCA (42.1%) at a mean five-year follow-up. Results showed that OCA patients had significantly worse Knee Injury and Osteoarthritis Outcome Score (KOOS) pain scores compared to ACI/MACI patients (74.7 vs 83.6, p=0.012), while other KOOS subscores were similar between groups; return-to-sport (RTS) rates were comparable (52% vs 58%, p=0.738), with an overall 54% return rate, 27% reoperation rate, and 5% graft failure rate. Study limitations include its retrospective design (Level III evidence), potential selection bias with OCA patients having more degenerative lesions, and the relatively high loss to follow-up rate of 22%.

Manjunath (2024) published a retrospective comparison cohort study to compare the short-term clinical outcomes of matrix-induced autologous chondrocyte implantation (MACI) to those seen following traditional autologous chondrocyte implantation (ACI) in the management of symptomatic cartilage lesions of the knee.[47] A total of 56 patients (39 ACI and 17 MACI) with a minimum of 18 months follow-up were included in the study. Visual analog scale (VAS) for pain scores improved significantly in both groups, with MACI patients demonstrating significantly lower postoperative pain scores compared to those treated with ACI. In the ACI group, there was a decrease in the Tegner Activity score compared to the preoperative baseline, while no significant difference was seen between pre- and postoperative activity levels in the MACI group. Patients were generally satisfied with the outcome of their procedures, and there was no significant difference in satisfaction between groups. No patients re-quired additional surgery during the follow-up period. Both ACI and MACI demonstrated good short-term postoperative clinical results with improved pain and activity levels compared to the preoperative baseline. Patients treated with the MACI technique demonstrated greater reductions in pain scores compared to ACI, and while ACI resulted in a decrease in levels of postoperative activity, activity levels for MACI remained stable.

Seiferth (2022) published a propensity-score matched analysis of 730 patients who underwent autologous chondrocyte implantation for cartilage repair of the knee following previous unspecified knee surgery (matched to 690 similar patients who did not have a knee surgery history prior to autologous chondrocyte implantation).[48] Propensity scoring incorporated age, sex, body mass index, duration of symptoms, smoking status, size, International Cartilage Regeneration & Joint Preservation Society grade, localization, and cause of the defect, and integrity of the corresponding joint service. The authors found that patients undergoing autologous chondrocyte implantation with history of prior knee surgery had significantly lower KOOS scores than those without prior knee surgery at 6 months, but no difference was identified between groups at subsequent follow-up ranging from 1 to 3 years. The authors performed a similar analysis in patients with (n=317) and without (n=254) history of prior treatment of the chondral site; in this analysis, mean KOOS scores were significantly lower in patients undergoing autologous chondrocyte implantation with history of failed chondral treatment compared to those without history of failed chondral treatment at all timepoints ranging from 6 to 36 months.

In 2016, Niethammer published results from a small prospective study assessing third-generation ACI (NOVOCART 3D) to treat cartilage defects in the knee joint.[49] The investigators analyzed graft integration into the surrounding cartilage and graft thickness. The average graft thickness significantly increased between three and six months after ACI, and continued to increase over two years post-operatively. However, 44 cases (55.7%) had mild to moderate incomplete filling of the defect, which occurred significantly more often in women ($p = 0.021$).

ACI for patellar cartilage defects is typically reported as less effective than ACI for lesions of the femoral condyles, and some studies have reported biomechanical alignment procedures and unloading to improve outcomes for retropatellar ACI.[50, 51] In 2014, Gomoll reported a multicenter registry study of the treatment of mono or bipolar patellar defects with ACI in 110 patients with a minimum of 4-year follow-up (mean, 90 months; range, 48-192 months). Concurrent surgical procedures included tibial tubercle osteotomy in 69% of patients, lateral release in 41%, vastus medialis advancement in 20%, and trochleoplasty in 5%. At the latest follow-up, statistically and clinically significant improvements in pain and function were obtained on the IKDC, Cincinnati Rating Scale, WOMAC and KSS, although it was noted that results were inferior to ACI for cartilage lesions of the femoral condyles. Excluding repeat arthroscopy for graft hypertrophy or lysis of adhesions, nine patients were considered treatment failures. Results were not divided according to the type of implant (ACI or matrix-induced ACI), although it was reported that two patients with hypertrophy of the implant were from the group treated with periosteal patch covered ACI. In addition, these results are limited by the retrospective design and loss to follow-up and would be applicable only to those patients without varus or valgus deformity.

In 2014. Biant published results from a prospective study of long-term follow-up study of patients who were treated between 1998 and 2001 after ACI for large cartilage defects of the knee, including lesions on the patella.[52] Out of 104 total procedures, 36 were performed for the patella. Seventy percent of patients had undergone a prior surgical procedure. Clinicians who were independent of the original surgery conducted the assessment at 10 to 12 years follow-up and were able to contact all but four patients. Twenty six percent of patients overall experienced graft failure at a mean of 5.7 years after ACI. The percentage of failures in the subgroup with ACI of the patella was similar; 25% experienced graft failure at a mean of 5.8 years after ACI. Out of the 32 patients who had not undergone a prior surgery, six (19%) had

failed, compared with 21 of 72 (29%) who had a prior cartilage repair procedure, supporting other recent studies showing poorer outcomes for lesions that had failed after a prior surgical procedure.

In 2012, Pestka reported a matched-pair comparison of ACI after failed microfracture versus ACI as a first-line treatment.[53] A total of 56 patients were retrospectively matched for sex, age, defect size, and defect location. The average defect size was 4.65 cm^2. Follow-up was conducted by mail, with a mean follow-up time of 48.0 months for ACI as a second-line treatment and 41.4 months for ACI as a first-line treatment. The failure rate was significantly greater when ACI was used as a second-line treatment (25% vs 3.6%), and there was a trend (p=0.058) for lower IKDC scores (58.4 vs 69.0). Two Knee Injury and Osteoarthritis Outcome Score (KOOS) subscales (Pain and Activities of Daily Living) were significantly lower for second-line treatment; there was a trend for lower scores in the remaining subscales. There are several limitations to this study; one is a potential for selection bias if patients who respond poorly to microfracture also respond poorly to ACI. Time since symptom onset might also be a factor.[54] However, the results add to a growing body of literature suggesting inferior outcomes when ACI is performed following a failed microfracture.[37]

In 2010, Minas assessed the influence of ACI on the need for joint replacement surgery in 153 patients (155 knees) with a mean age of 38 years (range, 17-60 years), evidence of early OA at the time of surgery (peripheral intra-articular osteophyte formation and/or 0%-50% joint space narrowing), and 2 years or more of follow-up.[55] (Patients with >50% loss of joint space were not eligible for treatment with ACI.) Patients were also included in the study if they had normal radiographs but evidence of bipolar lesions or generalized chondromalacia noted at the time of surgery. An average of 2.1 defects per knee were treated, with a mean defect size of 4.9 cm^2 and a total mean defect area of 10.4 cm^2. Defects were located on the femoral condyle (n=150), trochlea (n=85), patella (n=60), and tibial plateau (n=14). There were 42 (27%) bipolar lesions, most of which were patellofemoral. Concurrent procedures included correction of tibiofemoral malalignment (31% of knees) and patellar maltracking (28% of knees). At 5 years postoperatively (range, 24-132 months), 12 knees (8%) were considered treatment failures and underwent arthroplasty due to graft failure (n=3), inadequate pain relief (n=1), and progression of osteoarthritic disease beyond the originally transplanted defect area (n=8). The remaining 92% of patients showed improvements in all scores from baseline to final follow-up. For example, there was 52% improvement in WOMAC subscales, and the proportion of patients who experienced severe or extreme pain while walking on a flat surface decreased by 73%. Subsequent surgical procedures after the index implantation were performed in 95 knees (61%), including 52 cases of periosteal hypertrophy, 32 cases of arthrofibrosis, 23 graft complications, and 11 for periosteal delamination.

In 2009, Pascual-Garrido reported outcomes from 52 patients (83% follow-up) who underwent ACI of the patellofemoral joint (patella or trochlea).[56] In addition to ACI of the patella, 67% of patients had concomitant procedures performed, including anteromedialization (n=28), lateral release (n=4), lateral meniscal transplant (n=2), and OA (n=1). Questionnaires were administered preoperatively, 6-months and 1-year postoperatively, and then annually. At an average follow-up of 4-years (range, 2-7 years), there was significant improvement in the Lysholm, IKDC, KOOS Pain, KOOS Symptoms, KOOS Activities of Daily Living, KOOS Sport, Cincinnati, Tegner, and SF-12 Physical. Patients reported the overall condition of their knee as excellent, very good, or good in 71% of the cases. There were four failures (8%), defined as poor clinical outcome accompanied by evidence of graft failure or need for conversion to knee arthroplasty or OA. In 2008, a study from Europe described clinical results from 70 of 95

patients (74%) treated with ACI or matrix-induced ACI (MACI) for full-thickness defects of the patella.[57] Objective evaluation performed by an independent examiner who was blinded to data obtained at the time of surgery showed normal or nearly normal results in 47 patients (67%) at an average follow-up of 38 months.

In 2008, Rosenberger reported an average 4.7-year follow-up (range, 2-11 years) on a cohort of 56 patients (45-60 years old) with lesions of the femoral condyle (49%), trochlea (29%), or patella (22%).[58] Results were generally similar to those observed in younger patients, with 72% rating themselves as good or excellent, but 43% requiring additional arthroscopic procedures for periosteal-related problems and adhesion.

In 2007, Farr described outcomes from a prospective series of 36 patients who underwent ACI together with meniscal transplantation in the same compartment.[59] Lesions ranged from 1.5 to 12.1 cm². Patients identified with advanced chondrosis during staging arthroscopy were excluded from the study. Four patients received treatment for bipolar lesions, while 16 of the procedures were done concomitant with another procedure such as osteotomy, patellar realignment, or ACL reconstruction. Four patients (11%) were considered failures before 2-years, and three were lost to follow-up (8%), resulting in 29 evaluable patients at an average of 4.5-years after surgery. The Lysholm score improved from an average score of 58 to 78; maximum pain decreased an average 33% (from 7.6 to 5.1). Excluding the four failures, 68% of the patients required additional surgeries; 52% had one additional surgery, and 16% required two or more additional surgeries. The most common procedures were trimming of periosteal overgrowth or degenerative rims of the transplanted meniscus. Another report described average 3.1- years of follow-up from a prospective series of 30 patients (31 procedures) who had undergone combined meniscal allograft transplantation with ACI (52%) or OA transplantation (48%).[60] The Lysholm score improved in both the ACI (from 55 to 79) and OA (from 42 to 68) groups; 48% of patients (60% ACI, 36% OA) were considered to be normal or nearly normal at the latest follow-up. Patients treated with OA were on average older (average, 37 vs 23 years) and with larger lesions (5.5 cm^2 vs 3.9 cm^2). Two patients were considered failures (7%) and five (17%) underwent subsequent surgery. Although results seemed promising, evidence is insufficient to permit conclusions regarding the effect of combined transplantation-implantation procedures on health outcomes.

In 2005, Browne published five-year outcomes from 87 of the first 100 patients (40 centers, 87% follow-up) treated with ACI for lesions on the distal femur from the FDA-regulated Carticel safety registry maintained by Genzyme Biosurgery.[61] The registry is a multicenter program initiated in 1995, and was designed to longitudinally track changes in function and symptoms in patients treated with ACI or other cartilage repair procedures. Patients were an average of 37-years old, with a mean lesion size of 4.9 cm^2 (range, 0.8-23.5 cm^2). Seventy percent of the patients had failed at least one previous cartilage procedure. At 5-years following the index procedure, the average self-rated overall condition had improved from 3.2 (poor to fair) to 5.8 (fair to good), a 2.6-point improvement on the 10-point scale. Sixty-two patients (71%) reported improvement, 25 (29%) reported no change or worsening. Thirty-seven patients (42%) had 51 operations after ACI. The most common findings were adhesions (n=6), hypertrophic changes of the graft (n=5), loose bodies (n=4), loose or delaminated periosteal patch (n=4), and meniscal tears (n=4). In 2010, this group of investigators published a 6- to 10-year follow-up (mean, 9.2 years) on 72 patients in the cartilage repair registry.[62] Fifty-four patients (75%) met the eligibility criteria of the study, which included ACI treatment of lesions on the distal femur and improvement at the one- to five-year follow-up period. Of these 54 patients, 47 (87%) sustained a mean improvement of 3.8 points from baseline at the later follow-up period. For

the cohort of 72 patients, 69% reported improvement, 17% failed, and 12.5% reported no change from baseline to follow-up.

Other studies from Europe reported patellofemoral cartilage defects treated with second generation matrix-induced ACI implants;[63-66] however, these products are not approved in the United States and are, therefore, considered investigational.

AUTOLOGOUS CHONDROCYTE IMPLANTATION FOR JOINTS OTHER THAN THE KNEE

There has been interest in applying ACI to cartilage defects in other joints, particularly in the treatment of osteochondral lesions of the talus.

Systematic Reviews

Wen (2025) reported a systematic review of 11 studies (N=166) in patients with osteochondral lesions of the talus who underwent MACI.[67] Defect sizes ranged from 1.21 to 3.4 cm2. Preoperative AOFAS scores ranged from 36.9 to 70.1. All studies indicated AOFAS improvement postoperatively. Complications ranged from 0% to 59% in the 9 studies that reported complication outcomes. MACI for OLTs is associated with improved AOFAS scores and RTA/RTS rates at short-term follow-up. Reported complication and revision rates ranged from 0% to 59% and 0% to 45%, respectively. No included studies reported minimal clinically important difference, patient acceptable symptom state, or substantial clinical benefit metrics, limiting the interpretation of patient-level clinical improvements.

Migliorini (2022) published a systematic review (SR) of outcomes following surgical procedures augmented with cell therapies for chondral defects of the talus.[68] Primary outcomes of interest were improvement in patients reported outcomes measures (PROMs) and complication rate. Data from 477 procedures with a mean follow-up of 34.8 ± 9.7 months were included in the review. Overall, improvements in Visual Analogic Scale (VAS) of 4.4/10 (p=0.002) and American Orthopaedic Foot and Ankle Score (AOFAS) of 31.1/100 (p=0.0001) points were observed. No improvement in Tegner score was found. Rate of reoperation and failure at last follow-up were 0.06% and 0.03%, respectively. The authors conclude that although the current evidence is suggestive of safety and effectiveness for cell therapies for chondral defects of the talus, there continues to be a need for randomized controlled trials with larger sample sizes and longer follow-up.

A SR with meta-analysis published by Hu (2021) was conducted to assess the effectiveness of ACI for osteochondral defects of the talus.[69] The analysis included 23 case series (N= 458) of patients with osteochondral defects of the talus who underwent treatment with ACI. A random-effects model was used to calculate the incidence of success rate and American Orthopaedic Foot and Ankle Society (AOFAS) score for patients after ACI treatment. Across the case series, the success rate was 89% (95% confidence interval [CI] 85%-92%; $p < 0.001$) and the AOFAS score was 86.33 (95% CI 83.33-89.33; $p < 0.001$). Subanalysis found that the AOFAS score after ACI is significantly impacted by age of the patients. This analysis is limited by the inclusion only of case series and lack of comparison to standard of care.

Shimozono (2017) published a SR of scaffold-based therapies for osteochondral lesions of the talus.[70] Seven studies were found on use of MACI and five studies were found on Hyalograft C. All studies were case series; the quality of evidence was rated as fair in two studies and poor in the remaining 11 studies. Sample sizes ranged from 10 to 46 patients (mean, 22 patients) and follow-up ranged from 21 to 87 months (mean, 46 months). Twelve of 13 studies

reported preoperative and postoperative American Orthopaedic Foot and Ankle Society (AOFAS) scores; mean AOFAS score improved from 59 to 87.

In 2016, Marquez-Lara published results from a SR of arthroscopic treatments of chondral defects of the hip, comparing debridement, microfracture and ACI treatments from 12 studies.[71] Included studies were case series, comparative studies, but no RCTs. There were 579 (64.7%) debridements, 279 (31.2%) microfracture, and 37 (4.1%) ACIs performed. Patients were followed for an average of 27.1 months (range: 5 to 72 months). All lesions treated with either a microfracture or ACI were high grade (Outerbridge 3 to 4). However, lesion size was significantly larger in ACI-treated patients compared with those who underwent microfracture (357.3 ± 96.0 mm(2) compared to 149.5 ± 20.7 mm(2); p = 0.020). The reviewers reported no difference in improvement of clinical outcomes between the three treatments in patients with high-grade chondral defects in the hip in the short- and midterm follow-up. In addition, although there were no differences in patient characteristics and demographics based on the surgical technique, lesion size varied significantly between arthroscopic techniques, patients undergoing ACI having the largest lesion size.

In 2011 Niemeyer published results from a SR that included 16 studies (213 patients) on ACI or MACI for lesions of the talus.[72] All were case series with a mean of 13 patients (range, 2-46 patients) and mean follow-up of 32 months (range, 6-120 months). Most of the studies were prospective. In six studies periosteum-covered ACI was applied while 10 studies used second-generation MACI. MACI uses a matrix seeded with cultured autologous chondrocytes, and unlike first-generation ACI, does not require tibial or fibular osteotomy to gain adequate surgical access. For the studies using periosteum-covered ACI, the number of subjects ranged from 4 to 12. Nine different methods were used to evaluate pre- and postoperative clinical function, with the most common being the AOFAS Ankle-Hindfoot Score. Overall clinical success rate, defined as the percentage of good and excellent results, was 89.9% (range, 50-100%). Interpretation of these results is limited by the inclusion of poor-quality studies, lack of a comparator, and lack of blinding.

Zengerink published a SR of treatment of osteochondral lesions of the talus in 2010.[73] Fifty-one nonrandomized and one randomized trial were included in the review. Success rates were 85% for bone marrow stimulation, 87% for osteochondral autografting, and 76% for ACI. Because of the high cost of ACI and the morbidity seen with osteochondral autografting in the knee, the authors concluded that bone marrow stimulation is the treatment of choice for primary osteochondral talar lesions.

Randomized Controlled Trials

One RCT from Italy randomized 32 patients with osteochondral lesions of the talus to chondroplasty, microfracture, or osteochondral autograft transfer (OAT).[63] This small study found similar improvements (approximately 40 points) for the three treatment groups as measured by the American Orthopedic Foot and Ankle Society Ankle-Hindfoot Score (baseline score of 31 to 37) and the Subjective Assessment Numeric Evaluation (baseline score of 35 to 36). Complication rates were also similar, with persistent pain reported by one patient following chondroplasty, by two patients following microfracture, and by two patients following OAT. Postoperative pain, measured by Numeric Pain Intensity Scores, was greater following OAT (5.25) than chondroplasty (3.3) or microfracture (3.4).

PRACTICE GUIDELINE SUMMARY

AMERICAN ACADEMY OF ORTHOPEDIC SURGEONS

In the 2023 updated guidelines on the diagnosis and treatment of osteochondritis dissecans, the American Academy of Orthopedic Surgeons did not recommend for or against a specific cartilage repair technique in symptomatic skeletally immature or mature patients with an unsalvageable osteochondritis dissecans lesion, or symptomatic skeletally immature patients with unsalvageable fragment.[74] This finding of insufficient evidence for symptomatic skeletally mature patients with an unsalvageable osteochondritis dissecans lesion was based on a systematic review that found four level IV studies addressing cartilage repair techniques for an unsalvageable osteochondritis dissecans lesion. Because each level IV article used different techniques, different outcome measures, and differing lengths of follow-up, the Academy deemed the evidence for any specific technique inconclusive. The finding of insufficient evidence for symptomatic skeletally immature patients with unsalvageable fragments was based on a Level II study; this study did not address many outcomes and techniques and had inconclusive results.

SUMMARY

Medically Necessary

Current evidence indicates that autologous chondrocyte implantation (ACI) can improve symptoms in some patients with lesions of the articular cartilage of the knee. These patients, who are too young for total knee replacement, have limited options. Therefore, ACI may be considered medical necessary when criteria are met..

Investigational

Autologous chondrocyte implantation for treatment of lesions of the articular cartilage of the knee in patients that do not meet criteria is considered investigational due to lack of evidence showing improvement in health outcomes.

The evidence is currently insufficient to evaluate the efficacy of autologous chondrocyte implantation (ACI) for joints other than the knee. Additionally, the current evidence is insufficient to determine the impact of these procedures on health outcomes. Lastly, there are no clinical practice guidelines that recommend the use of ACI for the treatment of cartilage lesions of any type. Therefore, ACI for all other joints, including the patella and talar, are considered investigational.

REFERENCES

1. Wang AS, Nagelli CV, Lamba A, et al. Minimum 10-Year Outcomes of Matrix-Induced Autologous Chondrocyte Implantation in the Knee: A Systematic Review. *Am J Sports Med.* 2024:3635465231205309. PMID: 38312085
2. Colombini A, Libonati F, Lopa S, et al. Autologous chondrocyte implantation provides good long-term clinical results in the treatment of knee osteoarthritis: a systematic

review. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA.* 2023;31(6):2338-48. PMID: 35716187
3. Ginesin E, Chari NS, Barnhart J, et al. Cartilage Restoration for Isolated Patellar Chondral Defects: An Updated Systematic Review. *Orthop J Sports Med.* 2023;11(5):23259671231153422. PMID: 37152547
4. Migliorini F, Eschweiler J, Prinz J, et al. Autologous chondrocyte implantation in the knee is effective in skeletally immature patients: a systematic review. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA.* 2023;31(6):2518-25. PMID: 36329188
5. Migliorini F, Eschweiler J, Götze C, et al. Matrix-induced autologous chondrocyte implantation (mACI) versus autologous matrix-induced chondrogenesis (AMIC) for chondral defects of the knee: a systematic review. *Br Med Bull.* 2022;141(1):47-59. PMID: 35175354
6. Angele P, Zellner J, Schröter S, et al. Biological Reconstruction of Localized Full-Thickness Cartilage Defects of the Knee: A Systematic Review of Level 1 Studies with a Minimum Follow-Up of 5 Years. *Cartilage.* 2022;13(4):5-18. PMID: 36250517
7. Dhillon J, Decilveo AP, Kraeutler MJ, et al. Third-Generation Autologous Chondrocyte Implantation (Cells Cultured Within Collagen Membrane) Versus Microfracture for Focal Chondral Defects of the Knee Joint: A Systematic Review of Randomized Controlled Trials at Minimum Two-Year Follow-Up. *Arthroscopy.* 2022. PMID: 35283221
8. Colombini A, Libonati F, Lopa S, et al. Autologous chondrocyte implantation provides good long-term clinical results in the treatment of knee osteoarthritis: a systematic review. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA.* 2022. PMID: 35716187
9. Abraamyan T, Johnson AJ, Wiedrick J, et al. Marrow Stimulation Has Relatively Inferior Patient-Reported Outcomes in Cartilage Restoration Surgery of the Knee: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Am J Sports Med.* 2022;50(3):858-66. PMID: 33890799
10. Su CA, Trivedi NN, Le HT, et al. Clinical and Radiographic Outcomes After Treatment of Patellar Chondral Defects: A Systematic Review. *Sports health.* 2021;13(5):490-501. PMID: 33885342
11. Zamborsky R, Danisovic L. Surgical Techniques for Knee Cartilage Repair: An Updated Large-Scale Systematic Review and Network Meta-analysis of Randomized Controlled Trials. *Arthroscopy.* 2020;36(3):845-58. PMID: 32139062
12. Gou GH, Tseng FJ, Wang SH, et al. Autologous Chondrocyte Implantation Versus Microfracture in the Knee: A Meta-analysis and Systematic Review. *Arthroscopy.* 2020;36(1):289-303. PMID: 31708355
13. Migliorini F, Berton A, Salvatore G, et al. Autologous Chondrocyte Implantation and Mesenchymal Stem Cells for the Treatments of Chondral Defects Of The Knee- A Systematic Review. *Curr Stem Cell Res Ther.* 2020. PMID: 32081109
14. Andrade R, Nunes J, Hinckel BB, et al. Cartilage Restoration of Patellofemoral Lesions: A Systematic Review. *Cartilage.* 2019:1947603519893076. PMID: 31845590
15. Jones KJ, Kelley BV, Arshi A, et al. Comparative Effectiveness of Cartilage Repair With Respect to the Minimal Clinically Important Difference. *Am J Sports Med.* 2019;47(13):3284-93. PMID: 31082325
16. Coughlin RP, Gupta A, Sogbein OA, et al. Cartilage Restoration in the Adolescent Knee: a Systematic Review. *Curr Rev Musculoskelet Med.* 2019;12:486-96. PMID: 31773480

17. Sacolick DA, Kirven JC, Abouljoud MM, et al. The Treatment of Adult Osteochondritis Dissecans with Autologous Cartilage Implantation: A Systematic Review. *The journal of knee surgery.* 2019;32(11):1102-10. PMID: 30396204
18. Mistry H, Connock M, Pink J, et al. Autologous chondrocyte implantation in the knee: systematic review and economic evaluation. *Health technology assessment (Winchester, England).* 2017;21(6):1-294. PMID: 28244303
19. DiBartola AC, Wright BM, Magnussen RA, et al. Clinical Outcomes After Autologous Chondrocyte Implantation in Adolescents' Knees: A Systematic Review. *Arthroscopy.* 2016. PMID: 27161508
20. DiBartola AC, Everhart JS, Magnussen RA, et al. Correlation between histological outcome and surgical cartilage repair technique in the knee: A meta-analysis. *Knee.* 2016;23(3):344-9. PMID: 26898766
21. Andrade R, Vasta S, Papalia R, et al. Prevalence of Articular Cartilage Lesions and Surgical Clinical Outcomes in Football (Soccer) Players' Knees: A Systematic Review. *Arthroscopy.* 2016;32(7):1466-77. PMID: 27090724
22. Mithofer K, Peterson L, Mandelbaum BR, et al. Articular cartilage repair in soccer players with autologous chondrocyte transplantation: functional outcome and return to competition. *Am J Sports Med.* 2005;33:1639-46. PMID: 16093535
23. Kon E, Filardo G, Berruto M, et al. Articular cartilage treatment in high-level male soccer players: a prospective comparative study of arthroscopic second-generation autologous chondrocyte implantation versus microfracture. *Am J Sports Med.* 2011;39:2549-57. PMID: 21900624
24. Harris JD, Cavo M, Brophy R, et al. Biological Knee Reconstruction: A Systematic Review of Combined Meniscal Allograft Transplantation and Cartilage Repair or Restoration. *Arthroscopy.* 2011;27(3):409-18. PMID: 21030203
25. Vasiliadis HS, Wasiak J. Autologous chondrocyte implantation for full thickness articular cartilage defects of the knee. *The Cochrane database of systematic reviews.* 2010(10):CD003323. PMID: 20927732
26. Saris D, Price A, Widuchowski W, et al. Matrix-Applied Characterized Autologous Cultured Chondrocytes Versus Microfracture: Two-Year Follow-up of a Prospective Randomized Trial. *Am J Sports Med.* 2014;42:1384-94. PMID: 24714783
27. Knutsen G, Engebretsen L, Ludvigsen TC, et al. Autologous chondrocyte implantation compared with microfracture in the knee. A randomized trial. *J Bone Joint Surg Am.* 2004;86-A(3):455-64. PMID: 14996869
28. Knutsen G, Drogset JO, Engebretsen L, et al. A randomized trial comparing autologous chondrocyte implantation with microfracture. Findings at five years. *J Bone Joint Surg Am.* 2007;89(10):2105-12. PMID: 17908884
29. Zaslav K, Cole B, Brewster R, et al. A prospective study of autologous chondrocyte implantation in patients with failed prior treatment for articular cartilage defect of the knee: results of the Study of the Treatment of Articular Repair (STAR) clinical trial. *Am J Sports Med.* 2009;37(1):42-55. PMID: 18927254
30. Minas T, Von Keudell A, Bryant T, et al. The John Insall Award: A minimum 10-year outcome study of autologous chondrocyte implantation. *Clin Orthop Relat Res.* 2014;472(1):41-51. PMID: 23979923
31. Peterson L, Vasiliadis HS, Brittberg M, et al. Autologous chondrocyte implantation: a long-term follow-up. *Am J Sports Med.* 2010;38(6):1117-24. PMID: 20181804
32. Gomoll AH, Gillogly SD, Cole BJ, et al. Autologous chondrocyte implantation in the patella: a multicenter experience. *Am J Sports Med.* 2014;42(5):1074-81. PMID: 24595400

33. Gooding CR, Bartlett W, Bentley G, et al. A prospective, randomised study comparing two techniques of autologous chondrocyte implantation for osteochondral defects in the knee: Periosteum covered versus type I/III collagen covered. *Knee.* 2006;13(3):203-10. PMID: 16644224
34. Bentley G, Biant LC, Carrington RW, et al. A prospective, randomised comparison of autologous chondrocyte implantation versus mosaicplasty for osteochondral defects in the knee. *J Bone Joint Surg Br.* 2003;85(2):223-30. PMID: 12678357
35. Dozin B, Malpeli M, Cancedda R, et al. Comparative evaluation of autologous chondrocyte implantation and mosaicplasty: a multicentered randomized clinical trial. *Clin J Sport Med.* 2005;15(4):220-6. PMID: 16003035
36. Horas U, Pelinkovic D, Herr G, et al. Autologous chondrocyte implantation and osteochondral cylinder transplantation in cartilage repair of the knee joint. A prospective, comparative trial. *J Bone Joint Surg Am.* 2003;85-A(2):185-92. PMID: 12571292
37. Minas T, Gomoll AH, Rosenberger R, et al. Increased failure rate of autologous chondrocyte implantation after previous treatment with marrow stimulation techniques. *Am J Sports Med.* 2009;37(5):902-8. PMID: 19261905
38. Snow M, Middleton L, Mehta S, et al. Ten year follow-up of a randomized trial of autologous chondrocyte implantation versus alternative forms of surgical cartilage management in the knee. *Osteoarthritis Cartilage.* 2026;34(8):1243-51. PMID: 41833791
39. Yoon KH, Lee J, Park JY. Costal Chondrocyte-Derived Pellet-Type Autologous Chondrocyte Implantation Versus Microfracture for the Treatment of Articular Cartilage Defects: A 5-Year Follow-up of a Prospective Randomized Trial. *Am J Sports Med.* 2024;52(2):362-67. PMID: 38230875
40. Snow M, Middleton L, Mehta S, et al. A Randomized Trial of Autologous Chondrocyte Implantation Versus Alternative Forms of Surgical Cartilage Management in Patients With a Failed Primary Treatment for Chondral or Osteochondral Defects in the Knee. *Am J Sports Med.* 2023;51(2):367-78. PMID: 36661257
41. Brittberg M, Recker D, Ilgenfritz J, et al. Matrix-Applied Characterized Autologous Cultured Chondrocytes Versus Microfracture: Five-Year Follow-up of a Prospective Randomized Trial. *Am J Sports Med.* 2018;46(6):1343-51. PMID: 29565642
42. Bentley G, Biant LC, Vijayan S, et al. Minimum ten-year results of a prospective randomised study of autologous chondrocyte implantation versus mosaicplasty for symptomatic articular cartilage lesions of the knee. *J Bone Joint Surg Br.* 2012;94(4):504-9. PMID: 22434467
43. Montgomery SR, Foster BD, Ngo SS, et al. Trends in the surgical treatment of articular cartilage defects of the knee in the United States. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA.* 2014;22(9):2070-5. PMID: 23896943
44. Mithoefer K, McAdams T, Williams RJ, et al. Clinical efficacy of the microfracture technique for articular cartilage repair in the knee: an evidence-based systematic analysis. *Am J Sports Med.* 2009;37(10):2053-63. PMID: 19251676
45. Solheim E, Hegna J, Inderhaug E, et al. Results at 10-14 years after microfracture treatment of articular cartilage defects in the knee. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA.* 2014. PMID: 25416965
46. Triana J, Hughes AJ, Rao N, et al. Comparable Clinical and Functional Outcomes Between Osteochondral Allograft Transplantation and Autologous Chondrocyte Implantation for Articular Cartilage Lesions in the Patellofemoral Joint at a Mean Follow-Up of 5 Years. *Arthroscopy.* 2025;41(3):745-58. PMID: 38844011

47. Manjunath AK, Fried JW, Alaia EF, et al. Matrix-Induced Autologous Chondrocyte Implantation Versus Autologous Chondrocyte Implantation of the Knee A Retrospective Comparison. *Bull Hosp Jt Dis (2013).* 2024;82(2):118-23. PMID: 38739659
48. Seiferth NL, Faber SO, Angele P, et al. Effect of Previous Knee Surgery on Clinical Outcome After ACI for Knee Cartilage Defects: A Propensity Score-Matched Study Based on the German Cartilage Registry (KnorpelRegister DGOU). *Am J Sports Med.* 2022;50(4):994-1005. PMID: 35373607
49. Niethammer TR, Pietschmann MF, Ficklscherer A, et al. Incomplete defect filling after third generation autologous chondrocyte implantation. *Arch Med Sci.* 2016;12:785-92. PMID: 27478460
50. Henderson IJ, Lavigne P. Periosteal autologous chondrocyte implantation for patellar chondral defect in patients with normal and abnormal patellar tracking. *Knee.* 2006;13(4):274-9. PMID: 16750370
51. Farr J. Autologous chondrocyte implantation improves patellofemoral cartilage treatment outcomes. *Clin Orthop Relat Res.* 2007;463:187-94. PMID: 17960681
52. Biant LC, Bentley G, Vijayan S, et al. Long-term results of autologous chondrocyte implantation in the knee for chronic chondral and osteochondral defects. *Am J Sports Med.* 2014;42:2178-83. PMID: 25002462
53. Pestka JM, Bode G, Salzmann G, et al. Clinical outcome of autologous chondrocyte implantation for failed microfracture treatment of full-thickness cartilage defects of the knee joint. *Am J Sports Med.* 2012;40(2):325-31. PMID: 22056348
54. Vanlauwe J, Saris DB, Victor J, et al. Five-year outcome of characterized chondrocyte implantation versus microfracture for symptomatic cartilage defects of the knee: early treatment matters. *Am J Sports Med.* 2011;39(12):2566-74. PMID: 21908720
55. Minas T, Gomoll AH, Solhpour S, et al. Autologous chondrocyte implantation for joint preservation in patients with early osteoarthritis. *Clin Orthop Relat Res.* 2010;468(1):147-57. PMID: 19653049
56. Pascual-Garrido C, Slabaugh MA, L'Heureux DR, et al. Recommendations and treatment outcomes for patellofemoral articular cartilage defects with autologous chondrocyte implantation: prospective evaluation at average 4-year follow-up. *Am J Sports Med.* 2009;37 Suppl 1:33S-41S. PMID: 19861699
57. Niemeyer P, Steinwachs M, Erggelet C, et al. Autologous chondrocyte implantation for the treatment of retropatellar cartilage defects: clinical results referred to defect localisation. *Arch Orthop Trauma Surg.* 2008;128(11):1223-31. PMID: 17710423
58. Rosenberger RE, Gomoll AH, Bryant T, et al. Repair of large chondral defects of the knee with autologous chondrocyte implantation in patients 45 years or older. *Am J Sports Med.* 2008;36(12):2336-44. PMID: 18725654
59. Farr J, Rawal A, Marberry KM. Concomitant meniscal allograft transplantation and autologous chondrocyte implantation: minimum 2-year follow-up. *Am J Sports Med.* 2007;35(9):1459-66. PMID: 17435058
60. Rue JP, Yanke AB, Busam ML, et al. Prospective evaluation of concurrent meniscus transplantation and articular cartilage repair: minimum 2-year follow-up. *Am J Sports Med.* 2008;36(9):1770-8. PMID: 18483199
61. Browne JE, Anderson AF, Arciero R, et al. Clinical outcome of autologous chondrocyte implantation at 5 years in US subjects. *Clin Orthop Relat Res.* 2005(436):237-45. PMID: 15995447
62. Moseley JB, Jr., Anderson AF, Browne JE, et al. Long-term durability of autologous chondrocyte implantation: a multicenter, observational study in US patients. *Am J Sports Med.* 2010;38(2):238-46. PMID: 20448191

63. Gobbi A, Kon E, Berruto M, et al. Patellofemoral full-thickness chondral defects treated with second-generation autologous chondrocyte implantation: results at 5 years' follow-up. *Am J Sports Med.* 2009;37(6):1083-92. PMID: 19465733
64. Gigante A, Enea D, Greco F, et al. Distal realignment and patellar autologous chondrocyte implantation: mid-term results in a selected population. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA.* 2009;17(1):2-10. PMID: 18941738
65. Filardo G, Kon E, Andriolo L, et al. Treatment of "patellofemoral" cartilage lesions with matrix-assisted autologous chondrocyte transplantation: a comparison of patellar and trochlear lesions. *Am J Sports Med.* 2014;42(3):626-34. PMID: 24302700
66. Niemeyer P, Pestka JM, Kreuz PC, et al. Characteristic complications after autologous chondrocyte implantation for cartilage defects of the knee joint. *Am J Sports Med.* 2008;36(11):2091-9. PMID: 18801942
67. Wen J, Syed B, Ansari U, et al. Favorable Short-Term Outcomes of Matrix-Associated Autologous Chondrocyte Implantation for Osteochondral Lesions of the Talus: A Systematic Review. *Arthroscopy.* 2025;41(12):5492-502.e1. PMID: 40972779
68. Migliorini F, Eschweiler J, Goetze C, et al. Cell therapies for chondral defects of the talus: a systematic review. *J Orthop Surg Res.* 2022;17(1):308. PMID: 35690865
69. Hu M, Li X, Xu X. Efficacy and safety of autologous chondrocyte implantation for osteochondral defects of the talus: a systematic review and meta-analysis. *Arch Orthop Trauma Surg.* 2021. PMID: 34128117
70. Shimozono Y, Yasui Y, Ross AW, et al. Scaffolds based therapy for osteochondral lesions of the talus: A systematic review. *World journal of orthopedics.* 2017;8(10):798-808. PMID: 29094011
71. Marquez-Lara A, Mannava S, Howse EA, et al. Arthroscopic Management of Hip Chondral Defects: A Systematic Review of the Literature. *Arthroscopy.* 2016;32(7):1435-43. PMID: 27117866
72. Niemeyer P, Salzmann G, Schmal H, et al. Autologous chondrocyte implantation for the treatment of chondral and osteochondral defects of the talus: a meta-analysis of available evidence. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA.* 2011. PMID: 22037894
73. Zengerink M, Struijs PA, Tol JL, et al. Treatment of osteochondral lesions of the talus: a systematic review. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA.* 2010;18(2):238-46. PMID: 19859695
74. Surgeons AAoO. Diagnosis and Treatment of Osteochondritis Dissecans (2023). [cited 09/01/2026]. 'Available from:' https://www.aaos.org/quality/quality-programs/osteochondritis-dissecans/.

CODES

Codes	Number	Description
CPT	27412	Autologous chondrocyte implantation, knee
HCPCS	J7330	Autologous cultured chondrocytes, implant
	S2112	Arthroscopy, knee, surgical for harvesting of cartilage (chondrocyte cells)

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