



Autologous Chondrocyte Implantation Clinical Coverage Criteria

Description

Autologous chondrocyte implantation (ACI) is an advanced surgical procedure used for the repair of cartilage defects in the knee. The technique involves the transplantation of a patient's own healthy cartilage cells (chondrocytes) into the damaged area to stimulate cartilage regeneration and repair. The goal of ACI is to promote the formation of new cartilage tissue and repair the damaged area, thereby improving joint function and reducing pain. In December 2016, MACI (Vericel Corporation, Cambridge, MA) received FDA approval. MACI (autologous cultured chondrocytes on porcine collagen membrane) is an autologous cellularized scaffold product that is indicated for the repair of single or multiple symptomatic, full-thickness cartilage defects of the adult knee, with or without bone involvement. MACI is the third and current generation ACI technique with advantages over the second-generation technique. In MACI, the cells are seeded or loaded into a collagen membrane, which is implanted into the defect.

Policy

This Policy applies to the following Fallon Health products:

- Medicare Advantage (Fallon Medicare Plus, Fallon Medicare Plus Central)
- MassHealth ACO
- NaviCare HMO SNP
- NaviCare SCO
- PACE (Summit Eldercare PACE, Fallon Health Weinberg PACE)
- Community Care

Autologous chondrocyte implantation requires prior authorization from a Fallon Health Medical Director.

Medicare Advantage (Fallon Medicare Plus, Fallon Medicare Plus Central)

Fallon Health complies with CMS's national coverage determinations (NCDs), local coverage determinations (LCDs) of Medicare Contractors with jurisdiction for claims in the Plan's service area, and applicable Medicare statutes and regulations when making medical necessity determinations for Medicare Advantage members. When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, Fallon Health may create internal coverage criteria under specific circumstances described at § 422.101(b)(6)(i) and (ii).

Medicare statutes and regulations do not have coverage criteria for autologous chondrocyte implantation. Medicare does not have a National Coverage Determination (NCD) for autologous chondrocyte implantation. National Government Services, Inc., the Part A/B Medicare Administrative Contractor with jurisdiction in the Plan's service area does not have a Local Coverage Determination (LCD) for autologous chondrocyte implantation (Medicare Coverage Database search 04/19/2024).

Coverage criteria for autologous chondrocyte implantation are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, therefore, Fallon Health Clinical Coverage Criteria are applicable.

MassHealth ACO

Fallon Health follows Medical Necessity Guidelines published by MassHealth when making medical necessity determinations for MassHealth members. In the absence of Medical Necessity Guidelines published by MassHealth, Fallon Health may create clinical coverage criteria in accordance with the definition of Medical Necessity in 130 CMR 450.204.

MassHealth does not have Medical Necessity Guidelines for autologous chondrocyte implantation (MassHealth website search 04/19/2024), therefore the Plan's Clinical Coverage Criteria are applicable.

NaviCare HMO SNP, NaviCare SCO

For plan members enrolled in NaviCare, Fallon Health first follow's CMS's national coverage determinations (NCDs), local coverage determinations (LCDs) of Medicare Contractors with jurisdiction for claims in the Plan's service area, and applicable Medicare statutes and regulations when making medical necessity determinations.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, or if the NaviCare member does not meet coverage criteria in applicable Medicare statutes, regulations, NCDs or LCDs, Fallon Health then follows Medical Necessity Guidelines published by MassHealth when making necessity determinations for NaviCare members.

PACE (Summit Eldercare PACE, Fallon Health Weinberg PACE)

Each PACE plan member is assigned to an Interdisciplinary Team. PACE provides participants with all the care and services covered by Medicare and Medicaid, as authorized by the interdisciplinary team, as well as additional medically necessary care and services not covered by Medicare and Medicaid. With the exception of emergency care and out-of-area urgently needed care, all care and services provided to PACE plan members must be authorized by the interdisciplinary team.

Fallon Health Clinical Coverage Criteria

Effective for dates of service on or after May 1, 2024, Fallon Health will use InterQual® criteria when making medical necessity determinations for autologous chondrocyte implantation.

For coverage criteria, refer to the InterQual® Criteria in effect on the date of service:

- InterQual® CP:Procedures, Arthroscopy or Arthroscopically Assisted Surgery, Knee
- InterQual® CP:Procedures, Arthroscopy or Arthroscopically Assisted Surgery, Knee (Pediatric)

Fallon Health makes InterQual criteria available to the public through the transparency tool on our website, effective January 1, 2024.

Notes:

The safety and effectiveness of MACI in patients over the age of 55 years have not been established. Adolescent patients should be skeletally mature with documented closure of growth plates.

A physician-prescribed rehabilitation program that includes early mobilization, joint range of motion, and weight bearing is recommended to promote graft maturation and reduce the risk of graft delamination, postoperative thromboembolic events, and joint stiffness. Stage this program to promote a progressive return to full joint range of motion and weight-bearing as well as muscle

strengthening and conditioning. Return to recreational and sporting activity should be in consultation with healthcare professionals.

Anigwe et al., 2023 evaluated reoperation rates and associated risk factors following MACI® in a large retrospective cohort study using the PearlDiver Mariner Database. In the entire cohort, older age (OR = 1.07; 95% CI, 1.05-1.09; P < 0.001) and tobacco use (OR = 2.13; 95% CI, 1.06-3.94; P = 0.022) were associated with increased risk of conversion to total knee arthroplasty. Between 2017-2019, the mean age of patients (n = 584) undergoing MACI® was 32.9 ± 11.2 years. Because of its association with an increased risk of conversion to arthroplasty, it is recommended that patients quit smoking before surgery.

Exclusions

- Absolute contraindications for MACI include known history of hypersensitivity to gentamicin, other aminoglycosides, or products of porcine or bovine origin; severe osteoarthritis, inflammatory arthritis, inflammatory joint disease and uncorrected congenital blood coagulation disorders.
- Plan members who unable to comply with the postoperative rehabilitation and weight-bearing protocol should not be treated with MACI.
- MACI after failed microfracture appears to be associated with a significantly higher failure rate and inferior clinical outcome when compared with MACI as a first-line treatment (Pestka et al., 2018).
- The effectiveness of MACI for the treatment of articular cartilage defects in joints other than the knee has not been established.

Summary of Evidence

Background

Autologous chondrocyte implantation (ACI) is a well-established two-stage cartilage restoration procedure. The techniques of ACI have evolved over the years, but the principle has remained the same. In the first generation of ACI placed in the defect, in liquid form, and then covered with a cap made from periosteum (ACI-P). This required a procedure to harvest the periosteum, which caused discomfort to the patient afterwards. In second-generation ACI, the periosteal cover was replaced by a collagen cover (ACI-C), but the cells were still in liquid suspension, and the cover still had to be stitched in place. Gomoll et al. 2009, compared two cohorts, one that had a periosteal patch (ACI-P) and one that had a collagen cap (ACI-C). The reoperation rates were 26% and 5%, respectively. One development in ACI has been 'characterization', a process in which the cells thought to have the best ability to form hyaline cartilage are selected during culture. In the third generation of ACI, the cells are seeded or loaded into a collagen membrane, which is implanted into the defect. This is referred to as matrix-applied chondrocyte implantation (MACI).

In December 2016, MACI (Vericel Corporation, Cambridge, MA) received FDA approval. MACI (autologous cultured chondrocytes on porcine collagen membrane) is an autologous cellularized scaffold product that is indicated for the repair of single or multiple symptomatic, full-thickness cartilage defects of the adult knee, with or without bone involvement. The effectiveness of MACI in joints other than the knee has not been established. Safety and effectiveness of MACI in patients over the age of 55 years have not been established. See Full Prescribing Information for more information. Postoperative rehabilitation of the ACI patient plays a critical role in the outcome of the procedure. MACI consists of autologous chondrocytes that are cultured onto a bioresorbable porcine-derived collagen membrane. In 2017, production of Carticel was phased out, and currently MACI is the only autologous chondrocyte implantation product available in the United States.

MACI is the third and current generation ACI technique with advantages over the second-generation technique. During the first stage the patient's own chondrocytes are harvested from a non-weight bearing area of the knee. The chondrocytes from the cartilage specimen are cultured

for approximately 6-8 weeks before being seeded onto a collagen membrane. During the second stage implantation procedure the chondral defect is prepared via arthrotomy with debridement of all damaged cartilage down to but not penetrating the subchondral bone. After measuring the defect, the collagen membrane is trimmed to a similar shape and secured to the underlying bone using a layer of fibrin glue. Collagen membrane is characterized by good biocompatibility and complete integration with the adjacent native cartilage. The use of fibrin glue avoids second injury caused by suturing.

Randomized Controlled Trials

Two RCTs (Saris et al., 2014, Basad et al., 2010) compared MACI to microfracture in patients with a symptomatic cartilage defect in the knee.

U.S. FDA approval of MACI was based on results from the SUMMIT Study and the SUMMIT Study Extension. The Summit Study was a two-year prospective, multicenter, randomized, open-label study comparing MACI (n=72) to microfracture (n=72). The results of the SUMMIT Study were published by Saris et al., 2014. The SUMMIT Study (NCT00719576) was conducted at 16 sites across seven countries in Europe from July 2008 to March 2012. SUMMIT enrolled subjects ages 18 to 55 years (mean age 33.8 years and a mean BMI of 26 kg/m²), with ≥1 symptomatic Outerbridge grade III or IV focal cartilage defect on the medial femoral condyle, lateral femoral condyle, and/or the trochlea at least 3 cm² in size and a baseline Knee Injury and Osteoarthritis Outcome Score (KOOS) pain score <55. Exclusion criteria included any knee joint surgery within 6 months prior to screening (not including diagnostic arthroscopy); modified Outerbridge Grade III or IV defect(s) on the patella or tibia; symptomatic musculoskeletal condition in the lower limbs that could impede efficacy measures in the target knee joint; total meniscectomy, meniscal allograft, or bucket handle tear or displaced tear requiring >50% removal of the meniscus in the target knee; malalignment requiring an osteotomy to correct tibial-femoral or patella-femoral alignment; Kellgren-Lawrence grade 3 or 4 osteoarthritis; inflammatory disease or other condition affecting the joints; or septic arthritis within 1 year prior to screening.

At 104 weeks, the improvement with the MACI implant over microfracture in the co-primary endpoint subscores (pain and function) was clinically and statistically significant ($p=0.001$). The percentage of patients who responded to treatment at 104 weeks, with at least a 10-point improvement from baseline in both KOOS pain and function scores, was significantly greater ($P=0.016$) for the MACI group (87.5%) than the microfracture group (68.1%). The number of treatment failures (nonresponders) was 12.5% for MACI vs 31.9% for microfracture ($p=0.016$). MRI evaluation of structural repair was performed in 134 patients at 52 weeks and in 139 patients at 104 weeks. MRI evaluation of structural repair at both time points showed improvement in defect filling for both treatment groups but with no statistically significant differences. Two years after treatment, 83% of patients in the MACI® group and 77% of patients in the microfracture group showed a degree of defect fill that was more than 50% of the defect depth. One hundred sixteen patients (MACI® implant n=60; microfracture n=56) had a second-look arthroscopy and biopsy. Overall, structural repair tissue was very good; however, the mean microscopic ICRS II overall assessment score between the 2 groups (63.8 versus 62.3) was not significantly different ($P=0.717$).

Results of the SUMMIT Extension Study were published by Brittberg et al., 2018. The SUMMIT Extension Study (NCT01251588) examined the clinical efficacy and safety results at 5 years. Of the 144 patients randomized in the SUMMIT trial, 65 MACI patients (90.3%) and 63 microfracture patients (87.5%) consented to participate in the SUMMIT Extension study. Sixty-five subjects (65/65) in the MACI® group and 59 subjects (59/63) in the microfracture group were available at the 5 year follow-up (total retention = 97%). The mean scores in KOOS pain and KOOS function remained fairly stable for an additional three years in both treatment groups. Five years after treatment, the improvement in MACI over microfracture in the co-primary endpoint of KOOS pain and function was maintained and was clinically and statistically significant ($p = 0.022$). As in the 2-year SUMMIT results, the MRI evaluation showed improvement in defect filling for both

treatments; however, no statistically significant differences were noted between treatment groups. Two factors will have reduced the chance of improvement: the long duration of symptoms before ACI (5.8 years) and the high proportion (37%) that had had previous surgery (not counting arthroscopy).

Basad et al., 2010 was a single center RCT conducted in Germany between 2000 and 2005. This study enrolled patients aged ≥ 18 and ≤ 50 with post-traumatic, single, isolated, symptomatic chondral defects (4–10 cm²) of the femoral condyle or patella. Patients were randomized 2:1 to MACI (n=40) or microfracture (n=20). Exclusion criteria included the presence of chronic inflammatory arthritis, instability of the knee joint, prior or planned meniscectomy (>30% of the meniscus), BMI>30, varus or valgus abnormality, osteonecrosis, osteoarthritis and chondrocalcinosis. At baseline all patients underwent symptomatic evaluation were assessed for their eligibility for inclusion and gave their written informed consent. Patients were allocated consecutive numbers in the order of their study entry and then randomized to receive either MACI or microfracture via a computer-generated randomization. Treatment of concomitant cartilage or meniscus lesions during treatment was permitted. Preoperative MRI scanning alone is not adequate in determining the extent and severity of cartilage lesions, thus an initial arthroscopy was conducted to assess the fulfilment of arthroscopic inclusion criteria (isolated defect >4 cm²). Patients in both treatment groups were followed for 2 years. Outcome measures were the Tegner (activity levels), Lysholm (pain, stability, gait, clinical symptoms) and ICRS scores. MRIs were taken 1 week post-operatively to check for delamination and graft hypertrophy. The efficacy population was defined as those patients who provided data from at least one follow-up visit ≤ 6 months post-operatively. Completers were defined as those patients providing 2 years follow-up data. Patients were required to follow a post-operative rehabilitation program appropriate to either MACI or microfracture.

Patients diagnosed with osteochondral defects were withdrawn from the study as they were unable to receive MACI or microfracture. These patients were treated with MACI combined with bone grafting. The efficacy population was 56 patients (39 MACI, 17 microfracture). By August 2006, 48 patients (33 (84.6%) MACI, 15 (88.2%) microfracture) had completed 2 years follow-up.

Concomitant lesions treated during the study were ACL lesions (one patient, microfracture group) and smaller meniscal lesions (two patients in the MACI group, three patients in the microfracture group).

The mean Lysholm score in the MACI group improved from 52 at baseline to 95 at 12 months. This improvement was maintained at 24 months (mean score 92). In the microfracture group, these scores improved from 55 at baseline to 81 at 12 months but then declined to 69 at 24 months. The difference between baseline and 24 months post-operatively for both treatment groups was significant ($p < 0.0001$), but MACI was significantly more effective over time than microfracture ($p = 0.005$).

The median Tegner score improved from level 2 at baseline to level 4 at 12 months in the MACI group, and this improvement was maintained at 24 months. The median Tegner scores improved from level 2 at baseline to level 3 at 12 months in the microfracture group, and this improvement was maintained at 24 months. The difference between baseline and 24 months post-operatively for both treatment groups was significant ($p < 0.0001$), but MACI was significantly more effective over time than microfracture ($p = 0.04$).

The difference between ICRS patient scores at baseline and 24 months post-operatively was significant for both treatment groups ($P < 0.0001$), but MACI was significantly more effective over time than microfracture ($p = 0.03$).

There were no treatment-related safety issues during the study. The primary finding of this study is that MACI is superior to microfracture in the treatment of larger (>4 cm²), symptomatic articular

defects over 2 years. Microfracture, despite its minimally invasive nature, did not produce better clinical results than MACI probably due to the limited durability of the regenerative tissue. MACI and microfracture are complementary procedures for the treatment of articular cartilage defects, depending on the size of the defect and symptom recurrence.

Ongoing Randomized Clinical Trials

PEAK (A Study of MACI in Patients Aged 10 to 17 Years With Symptomatic Chondral or Osteochondral Defects of the Knee) is an ongoing clinical trial to compare the efficacy and safety of MACI® vs arthroscopic microfracture in the treatment of patients aged 10 to 17 years with symptomatic articular chondral or osteochondral defects of the knee (NCT03588975). The estimated study completion date is June 2027. The primary outcome measure is the proportion of patients with at least a 10-point change (improvement) in both the KOOS-Child Pain and Function (Sports and Recreational activities) scores from Baseline scores at 24 months.

The large (n=390) Autologous Chondrocyte Transplantation/Implantation Versus Existing Treatments (ACTIVE) trial (<https://www.isrctn.com:ISRCTN48911177>) compares ACI against surgeon selected standard of care, the majority being microfracture. The ACTIVE trial is comparing ACI (including ACI-P, ACI-C and MACI) against standard treatments (microfracture, abrasion, drilling, mosaicplasty). The ACTIVE trial will eventually have 10 years of follow-up for all patients. Data from this ongoing trial contributed to the positive Health Technology Assessment (HTA) of ACI in 2017 (Mistry et al., 2017) but the results from the study cannot be published until trial completion.

Patellofemoral MACI

Until recently, most studies have investigated the use of ACI in the tibiofemoral joint. Early studies reported poor performance in the patellofemoral joint. This may have been due in part to the first and second-generation ACI techniques and because patellofemoral malalignment was often not addressed. In recent years, several small, non-comparative prospective studies have shown encouraging clinical and radiological outcomes in patients undergoing patellofemoral MACI (Gigante et al., 2008, Ebert et al., 2011, Marlovits et al., 2012, Meyerkort et al., 2014, Zhang et al., 2014, Ebert et al., 2015).

In 2017, Ebert and colleagues published two year clinical and radiological outcomes for patients undergoing tibiofemoral or patellofemoral MACI. Between September 2002 and December 2012, 204 patients were prospectively enrolled in an institutional research program and underwent MACI. Even though the indication for MACI was not dictated by the duration of symptoms or requirement to initially trial nonoperative management and/or other treatments, all patients had symptomatic, full-thickness grade 3 or 4 chondral lesions per the International Cartilage Regeneration & Joint Preservation Society classification system. The two year analysis reported by Ebert et al. 2017, included 194 patients (95.1%). Of these, 127 patients underwent tibiofemoral MACI to the medial femoral condyle or lateral femoral condyle (n=94 and n=33, respectively) with 67 patients underwent patellofemoral MACI to the patella (n=35) or trochlea (n=32). No significant differences (p >0.05) were seen in demographics, defect size, prior injury or surgical history, between the two groups. Patients were eligible for MACI if they were 15-65 years of age and deemed able to follow a structured rehabilitation program. Preoperative MRI was undertaken in all patients to assess the location and size of the chondral defect, as well as concomitant pathology. Patients were excluded if they had ligamentous instability, had undergone a prior extensive meniscectomy (greater than one third of the meniscus), had ongoing progressive inflammatory arthritis or had varus/valgus lower limb mal-alignment (as indicated by > 3° TF anatomic angle). Mean age was 37.7 (15-62) years and 37.9 (20-65) years for the tibiofemoral and patellofemoral groups, respectively. Thirteen patients were 51-60 years of age, and 3 patients were 61-65 years of age. Mean defect size was 3.1 cm² and 3.0 cm² for the tibiofemoral and patellofemoral groups, respectively. Mean BMI was 26.4 and 26.3 for the tibiofemoral and patellofemoral groups, respectively. In the tibiofemoral MACI group, 78 (61%) had been treated previously with one or more surgical procedures to address knee pain and/or symptoms,

including: arthroscopy (n=70), microfracture (n=5), partial meniscectomy (n=68), anterior cruciate ligament (ACL) reconstruction (n=9), extensor realignment (n=2) and lateral release (n=4). In the patellofemoral MACI group, 42 (63%) patients had been treated with one or more surgical procedures prior to their MACI procedure to address knee pain, including: arthroscopy (n=45), ACL reconstruction (n=2), extensor realignment (n=3) and lateral release (n=11). While the majority of patient-reported outcomes were similar between the two groups pre-surgery, the patellofemoral group did report significantly worse scores for the KOOS ADLs and QOL subscales, which may be partly explained by specific KOOS ADL items more relevant to symptomatic patellofemoral patients, such as descending and ascending stairs, and rising from sitting.

Of the 127 tibiofemoral MACI patients included in this analysis, 24 underwent concomitant surgeries at the time of MACI, including ACL reconstruction (n=7), posterior cruciate ligament (PCL) reconstruction (n=3), lateral release (n=1), partial meniscectomy (n=11) and high tibial osteotomy (n=4). Of the 67 patellofemoral MACI patients, 26 underwent concomitant patellofemoral realignment via a combined lateral PF retinacular release and anteromedial TTT, at the time of their MACI surgery.

At 24 months, a significant time effect ($p < 0.05$) existed for all patient reported outcome measure (PROM) scores throughout the pre- and post-operative timeline. A significant group effect existed between the tibiofemoral and patellofemoral groups for the KOOS ADL ($p = 0.008$), QOL ($p = 0.008$) and Sport ($p = 0.017$) in favor of the tibiofemoral group. However, patients in the patellofemoral group had significantly lower values at baseline for the KOOS sub-scales overall, and actually displayed a similar net improvement over time compared to the tibiofemoral group. Furthermore, despite the significantly worse scores for the KOOS QOL sub-scale in the patellofemoral group, compared with the tibiofemoral group, the largest net improvement over the pre- and post-operative timeline was still noted in the patellofemoral group.

In the 67 patellofemoral patients, there were no significant ($p > 0.05$) differences observed in any of the clinical scores, between those who did (n=26), or did not (n=41), undergo concomitant realignment surgery.

At 24 months, overall, 90.5% (n=115) of the tibiofemoral group and 83.6% (n=56) of the patellofemoral group were satisfied with the results of their MACI surgery.

MRI findings revealed a significant time effect ($p < 0.05$) for the MRI composite score, as well as graft infill, signal intensity, subchondral lamina, subchondral bone and joint effusion over the 24 month period. While subchondral lamina scored significantly better in the tibiofemoral group ($p = 0.002$), subchondral bone scored significantly better in the patellofemoral group ($p < 0.0001$). At 24 months, the overall MRI composite score was classified as Good-Excellent in 98 patients (77%) in the tibiofemoral group and 54 patients (81%) in the patellofemoral group. The degree of graft infill was Good-Excellent in 111 tibiofemoral patients (87%) and 55 patellofemoral patients (82%). At 24 months, 11 tibiofemoral grafts (8.6%) had failed, including 7 on the MFC and 4 on the LFC, as indicated by no discernible tissue on MRI. Only 3 patellofemoral grafts (4.5%) failed, including 2 on the patella and 1 in the trochlea.

A number of early post-operative complications were reported, including wound site opening with or without an associated local infection (tibiofemoral n=3; patellofemoral n=2), deep vein thrombosis (tibiofemoral n=2; patellofemoral n=1) and the development of a post-operative hematoma (tibiofemoral n=1; patellofemoral n=1). These early complications were treated accordingly without further issue. At 24 months post-surgery, a significantly greater ($p < 0.001$) percentage of tibiofemoral patients (n=42, 32.1%) displayed hypertrophic grafts on MRI, compared with patellofemoral patients (n=7, 10.4%). At 24 month follow-up, all hypertrophic cases remained asymptomatic clinically, without patient-reported mechanical symptoms or associated pain. At 24 months, 11 tibiofemoral grafts (8.6%) had failed, including 7 on the medial

femoral condyle and 4 on the lateral femoral condyle, as indicated by no discernible tissue on MRI. Only 3 patellofemoral grafts (4.5%) had failed, including 2 on the patella and 1 in the trochlea. The authors concluded that MACI in the patellofemoral joint with simultaneous correction of patellofemoral maltracking if required, leads to similarly good clinical and radiological outcomes compared to MACI of the tibiofemoral joint through 24 months post-surgery.

In 2024, Ebert et al. reported ten-year results for this group of patients. Of the 204 patients initially recruited, 168 patients (182 grafts) were assessed at the final review, with 151 grafts undergoing MRI at the final follow-up. Patients with joint malalignment were included if malalignment was addressed at the time of MACI. Therefore, of the 168 patients with 10-year review, those with tibiofemoral malalignment (n = 4) underwent an offloading osteotomy if evaluated with significant varus or valgus lower limb deformity (as indicated by a $>3^\circ$ tibiofemoral anatomic angle), whereas those with patellofemoral malalignment (assessed via computed tomography imaging and >0.9 -cm lateralization of tibial tuberosity) underwent Fulkerson osteotomy (n = 26). Furthermore, other concomitant surgeries performed specifically at the time of MACI included anterior cruciate ligament reconstruction (n = 6), posterior cruciate ligament reconstruction (n = 2), isolated lateral release (n = 8), and partial meniscectomy (n = 8).

Of the 151 grafts reviewed via MRI scans at the final 10- year review, 55 grafts (36.4%) demonstrated excellent graft infill, 49 (32.5%) demonstrated good infill, 15 (9.9%) demonstrated fair infill, 14 (9.3%) demonstrated poor infill, and 18 grafts (11.9%) demonstrated an element of graft hypertrophy, per the MOCART scoring tool. Of the 151 grafts reviewed via MRI scans at the final 10-year review, 14 (9.3%) had failed (defined by graft delamination or no discernible graft tissue on MRI scans). Of the 36 patients (of the prospectively recruited 204) who were not available for longer-term review, 7 had already proceeded to total knee arthroplasty (TKA), and 1 patient had undergone secondary MACI at the same medial femoral condyle site because of earlier graft failure. Therefore, 22 patients (10.8%) essentially had graft failure at or before the final review time.

No group differences were observed between patients who underwent tibiofemoral and patellofemoral MACI in preoperative descriptive and injury or surgery variables or between preoperative patient-reported outcome measures (PROMs). At the final 10-year follow-up, 92% of patients were satisfied with the knee pain relief provided by MACI, 76% were satisfied with their ability to participate in sports, and 89% were satisfied overall. Patients who underwent MACI in the tibiofemoral (versus patellofemoral) joint demonstrated a significantly better MOCART tissue infill score ($p=0.027$; tibiofemoral mean, 3.2; patellofemoral mean, 2.9), although there were no other differences in MRI-based scores, including the overall MRI composite score ($p=0.481$; tibiofemoral mean, 3.0; patellofemoral mean, 3.1). Patients undergoing tibiofemoral (vs patellofemoral) MACI reported significantly better 10- year KOOS subscale scores for QOL ($p=0.010$; tibiofemoral mean, 65.8; patellofemoral mean, 57.8) and Sport ($p<0.001$; tibiofemoral mean, 71.4; patellofemoral mean, 57.0), as well as a greater knee extensor strength LSI ($p=0.002$; tibiofemoral mean, 96.0%; patellofemoral mean, 85.8%).

Findings from this 10-year study demonstrate significantly improved clinical scores, with the maximal improvement at 2 years and no significant change in any PROM from 2 years to the final review at 10 years after surgery. High levels of patient satisfaction, clinical and MRI-based outcomes were largely sustained during the 2 to 10 years after surgery, with an acceptable graft failure rate over the assessment period. Patients undergoing tibiofemoral (vs patellofemoral) MACI reported significantly better 10-year clinical outcomes for the KOOS subscales of QOL and Sport, as well as knee extensor strength symmetry), as well as degree of tissue infill, despite a similar overall MRI composite score. Currently, there is a lack longer-term MRI-based outcomes after third-generation MACI, it was encouraging in this larger cohort that no significant change (deterioration) was observed in MRI-based parameters of graft repair. Although a significant difference in quadriceps strength LSIs was observed postoperatively between patients who underwent tibiofemoral and patellofemoral MACI, strength was not assessed preoperatively (and

realistically would have been affected regardless by underlying pain and symptoms that drove patients toward cartilage repair surgery intervention). The authors are therefore unable to ascertain how much limb strength asymmetry was also present preoperatively (especially given the mean preoperative duration of symptoms reported by patients) or whether the primary contribution came specifically as a result of the surgery and the subsequent inability to restore deficits as a result of the rehabilitation intervention.

There are limitations to this study. First, no comparative cohort was investigated. Other cartilage repair surgical procedures are available and may be deemed suitable, particularly for smaller chondral lesions (≤ 4 cm²). Second, only 82% of the recruited cohort was available for 10-year review; it is unknown how this cohort would have potentially changed 10 year results.

Analysis of Evidence (Rationale for Determination)

For individuals who have focal articular cartilage lesion(s) of the weight-bearing surface of the femoral condyles, trochlea, or patella who receive autologous chondrocyte implantation, the evidence for MACI, includes observational studies and randomized controlled trials (RCTs).

Overall, outcomes for MACI tended to be better for younger patients (< 30 or < 35 years), more active patients, patients with shorter symptom duration, and patients who had not had a previous failed surgical intervention. Results also tended to be better for smaller lesions overall, whereas MACI produced better results than microfracture in larger lesions.

The main limitation for MACI is the lack of long-term follow-up data. Data on long-term results come mainly from first generation ACI. Unpublished data from the ongoing ACTIVE trial, contributed to the positive assessment of ACI in the Health Technology Assessment (HTA) conducted by Mistry et al., 2017. Based principally on functional outcome over time and survival analysis, the concluding message from the HTA was that ACI offered long-term superiority compared with microfracture and was cost-effective across a range of scenarios.

Little is known about the longer-term clinical and radiological outcomes of MACI performed in the patellofemoral knee joint.

Coding

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

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

References

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2. U.S. Food & Drug Administration (FDA). Package Insert. MACI® (autologous cultured chondrocytes on porcine collagen membrane). Revised: 6/2021. Available at: <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/maci-autologous-cultured-chondrocytes-porcine-collagen-membrane>. Accessed 04/20/2024.
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Policy history

Origination date:	05/01/2014
Review/Approval(s):	Technology Assessment Committee 12/18/2013 (Adopted InterQual Criteria). 01/28/2015 (annual review), 01/27/2016 (annual review), 01/25/2017 (annual review), 01/24/2018 (annual review) 1/23/2019 (annual review); 05/27/2020 (Adopted proprietary criteria); 2/23/2021, 6/22/2021 (annual review; added coverage for patella defects; removed requirement for prior surgical repair procedure; added clarifying language related to Medicare Advantage, NaviCare and PACE under policy section), 04/23/2024 (annual review; adopted InterQual Criteria; added Summary of Evidence and Analysis of Evidence (Rationale for Determination)); updated References).

Not all services mentioned in this policy are covered for all products or employer groups. Coverage is based upon the terms of a member's particular benefit plan which may contain its own specific provisions for coverage and exclusions regardless of medical necessity. Please consult the product's Evidence of Coverage for exclusions or other benefit limitations applicable to this service or supply. If there is any discrepancy between this policy and a member's benefit plan, the provisions of the benefit plan will govern. However, applicable state mandates take precedence with respect to fully-insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, federal mandates will apply to all plans.