



Kansas City

An Independent Licensee of the Blue Cross and Blue Shield Association

Autologous Chondrocyte Implantation for Focal Articular Cartilage Lesions

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Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for autologous chondrocyte implantation when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered

Autologous chondrocyte implantation may be considered **medically necessary** for the treatment of disabling full-thickness articular cartilage defects of the knee caused by acute or repetitive trauma, in patients who have had an inadequate response to a prior surgical procedure, when all of the following criteria are met:

- 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)
- Focal, full-thickness (grade III or IV) unipolar lesions on the weight bearing surface of the femoral condyles or trochlea at least 1.5 cm² in size
- Documented minimal to absent degenerative changes in the surrounding articular cartilage (Outerbridge Grade II or less), and normal-appearing hyaline cartilage surrounding the border of the defect
- Normal knee biomechanics, or alignment and stability achieved concurrently with autologous chondrocyte implantation

When Policy Topic is not covered

Autologous chondrocyte implantation for all other joints, including patellar and talar, and any indications other than those listed above is considered **investigational**.

Matrix-induced autologous chondrocyte implantation is considered **investigational**.

Considerations

This policy should not be confused with the policies for Meniscal Allograft Transplantation, Bone Allograft Transplantation (the mosaic or OATS procedures) or bone marrow transplant.

If in smaller lesions (e.g., smaller than 4 cm²) debridement is the only prior surgical treatment, consideration should be given to marrow-stimulating techniques before autologous chondrocyte implantation is performed.

The average defect size reported in the literature is about 5 cm²; many studies treated lesions as large as 15 cm².

Severe obesity, e.g., body mass index (BMI) greater than 35 kg/m², 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. The charges for the culturing component of the procedure are submitted as part of the hospital bill.

The entire autologous chondrocyte implantation (ACI) procedure consists of four steps: 1) the 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) post-surgical rehabilitation. The initial arthroscopy may be scheduled as a diagnostic procedure; 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.

There is a specific CPT category I code for ACI of the knee:

- 27412: Autologous chondrocyte implantation, knee

Arthroscopic harvesting of chondrocytes from the knee is reported using CPT code 29870. There is a HCPCS code for the autologous cultured chondrocyte implant - J7330.

Description of Procedure or Service

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 or allogeneic chondrocytes, minced cartilage, scaffolds, and growth factors.

Background

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 an individual's activities of daily living and adversely affect quality of life. Conventional treatment options include debridement, 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 to 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. Osteochondral grafts for the treatment of articular cartilage defects are discussed in a separate policy.

With autologous chondrocyte implantation, a region of healthy articular cartilage is identified and biopsied through arthroscopy. The tissue is sent to a facility licensed by the U.S. 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 11–21 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 2 procedures and harvesting of periosteum. In addition, use of the FDA-indicated periosteal cover may result in hypertrophy, as well as donor-site morbidity.

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) be implanted easily, 2)

reduce surgical morbidity, 3) not 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

The culturing of chondrocytes is considered by the 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™ (Genzyme) 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..." The labeled indication was revised in October 1999 to read as follows:

"Carticel is indicated for the repair of symptomatic cartilaginous defects of the femoral condyle (medial, lateral, or trochlear), caused by acute or repetitive trauma, in patients who have had an inadequate response to a prior arthroscopic or other surgical repair procedure." Thus, the revised labeling suggests a more restricted use of autologous chondrocytes, i.e., as a second-line therapy after failure of initial arthroscopic or surgical repair.

"Carticel is not indicated for the treatment of cartilage damage associated with osteoarthritis. Carticel should only be used in conjunction with debridement, placement of a periosteal flap and rehabilitation. The independent contributions of the autologous cultured chondrocytes and other components of the therapy to outcome are unknown. Data regarding functional outcomes beyond 3 years of autologous cultured chondrocyte treatment are limited."

A number of second-generation methods for implanting autologous chondrocytes in a biodegradable matrix are currently in development/testing. These include BioCart II (ProChon Biotech, Phase II trial), Cartilix (polymer hydrogel, Cartilix), MACI® (matrix-induced ACI, Verigen, available outside of the U.S.), Cartipatch (solid scaffold with an agarose-alginate matrix, TBF Tissue Engineering, Phase III trial), NeoCart (ACI with a 3-dimensional chondromatrix, Histogenics, Phase II trial), Hyalograft C (ACI with a hyaluronic acid-based scaffold, Fidia Advanced Polymers), and CAIS (Cartilage Autograft Implantation System, which harvests cartilage and disperses chondrocytes on a scaffold in a single stage treatment, Johnson and Johnson). ChondroCelect (characterized chondrocyte implantation, TiGenex, Phase III trial) uses a gene marker profile to determine in vivo cartilage-forming potential and thereby optimizes the phenotype (e.g., hyaline cartilage vs. fibrocartilage) of the tissue produced with each ACI implantation cell batch. Each batch of chondrocytes is graded based on the quantitative gene expression of a selection of positive and negative markers for hyaline cartilage formation. Although clinical use of these second-generation ACI products has been reported in Europe, none are approved for use in the U.S. at this time.

Rationale

This policy was based on a 2003 TEC Assessment of autologous chondrocyte implantation (ACI), which updates earlier 1996, 1997, and 2000 TEC Assessments on the same subject. (1-4) The 2003 TEC Assessment separately evaluated the data regarding ACI when performed as either a first-line or second-line therapy in various subgroups of patients. (4) At the time of this TEC Assessment, only one ACI product (Carticel™) had been evaluated in the published literature.

Subsequent literature searches, conducted between 2003 and May 1, 2013, identified the following published studies. Some of these subsequent studies used Carticel™, while others have evaluated newer, second-generation ACI products. The evidence for the second generation products is discussed separately from the evidence on Carticel™.

First Generation ACI (Carticel™) for Treatment of the Knee

First Generation ACI (CarticeTM) for Treatment of the Knee: Systematic Reviews. A 2010 systematic review by Harris and colleagues included 13 randomized and non-randomized controlled trials of 917 subjects who underwent ACI (n=604), microfracture (n=271), or osteochondral autograft (n=42). The mean study quality was rated as 54 out of 100, with no studies considered of good or excellent quality, 7 considered fair, and 6 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, 3 of 7 studies showed better clinical outcomes after ACI in comparison with microfracture, 1 study showed better outcomes after microfracture, and 3 studies showed no difference in these treatments. Clinical outcomes after microfracture were found to deteriorate after 18 to 24 months in 3 of 7 studies. Studies comparing ACI and osteochondral autograft showed similar short-term clinical outcomes, with more rapid improvement but an increase in arthrofibrosis and donor site morbidity following osteochondral autograft. 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 cm² was the only factor predictive of better outcomes when ACI was compared with other surgical techniques.

Another publication by Harris et al. in 2010 was a systematic review of combined meniscal allograft transplantation and cartilage repair/restoration. (5) 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), osteochondral autograft (n=17), or microfracture (n=3). All studies showed improvement in clinical outcomes at final follow-up compared to the preoperative condition. Outcomes were also compared with historical outcomes of each individual procedure performed in isolation. Four of the 6 studies found outcomes equivalent to procedures performed in isolation, while 2 studies found that outcomes with combined surgery were not as good as the historical controls. Across the 6 studies, 13 failures (12%) were reported; these included 11 isolated meniscal allograft transplantation failures, 1 combined meniscal allograft and ACI failure, and 1 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.

Efficacy of the microfracture technique alone was examined in a 2009 systematic review. (6) Twenty-eight studies describing 3,122 patients were included in the review; 6 of the studies were randomized controlled trials (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.

First Generation ACI (CarticeTM) for Treatment of the Knee: Comparative Studies: ACI (CarticeTM) versus Marrow-Stimulating Techniques. In an RCT of 80 patients randomized to either ACI or microfracture of the knee (an arthroscopic marrow-stimulation procedure), Knutsen and colleagues reported no significant differences in the treatment groups at 2-year follow-up in macroscopic and histologic findings. (7) The Lysholm and pain scores were also not significantly different at 1 and 2 years. The physical component score of the Short Form (SF)-36 was worse in the ACI group, which the authors suggest may be related to the greater surgical involvement. Five-year follow-up on all 80 patients revealed 9 failures (23%) for both groups. (8) There was a trend (p=0.10) for earlier failure in the ACI group (26 vs. 38 months, respectively) with no difference in subjective measures of pain or function between the ACI and microfracture groups. Thus, the more invasive ACI open surgical procedure was not associated with any added clinical benefit.

In Visna et al., 50 patients with full-thickness, moderate to large chondral defects of 2.0–10.0 cm² of the femoral condyle, trochlea, or patella (43 cases due to injury) were randomized to either Johnson abrasion techniques or ACI of the knee using a preparation of autologous chondrocytes using a fibrin tissue glue rather than a periosteal patch to seal the implanted chondrocytes. (9) The study reported improvements after 12 months in the Lysholm, International Knee Documentation Committee, and Tegner activity scores, which were significantly better among the 25 ACI patients compared with the 25 patients in the abrasion group. Additional procedures (28 in the ACI group and 20 in the abrasion group) included anterior cruciate ligament (ACL) replacement, meniscectomy, and lateral release.

First Generation ACI (CarticeTM) for Treatment of the Knee: Comparative Studies: ACI (CarticeTM) versus Osteochondral Autografts. Horas and colleagues reported 2-year follow-up on a study of 40 patients (between 18 and 42 years of age) with an articular lesion of the femoral condyle (range: 3.2 to 5.6 cm²) who were randomly assigned to undergo either autologous chondrocyte transplant or osteochondral autografting. (10) Eleven (28%) had received prior surgical treatment. The authors reported that both treatments resulted in an improvement in symptoms (85% of each group), although those in the osteochondral autografting group responded more quickly. Histomorphologic evaluation of 5 biopsy specimens at 2 years or less after transplantation indicated that the osteochondral cylinders had retained their hyaline character, although the investigators noted a persistent interface between the transplant and the surrounding original cartilage. Evaluation of autologous chondrocyte implants indicated a rigid, elastic tissue, with partial roughening and the presence of fibrocartilage.

Bentley and colleagues randomized 100 consecutive patients with symptomatic lesions of the knee (average 4.7 cm²; range: 1 to 12 cm²) to ACI or mosaicplasty. (11) Seventy-four percent of lesions were on the femoral condyle, and 25% of lesions were on the patella. Ninety-four patients had undergone previous surgical interventions, and the average duration of symptoms before surgery was 7 years. Clinical assessment at 1 year showed excellent or good results in 98% of the ACI patients and in 69% of the mosaicplasty patients. The mosaicplasty plugs showed incomplete healing of the spaces between the grafts, fibrillation of the repair tissue, and disintegration of the grafts in some patients. This finding may be related to the unusual prominent placement of the plugs in this study, which was intended to allow contact with the opposite articular surface. Arthroscopy at 1 year showed filling of the defects following ACI, but soft tissue was observed in 50% of patients. Biopsy specimens taken from 19 ACI patients revealed a mixture of hyaline and fibrocartilage. With 6 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. (12)

Dozin et al. reported results from a multicenter randomized, clinical trial in which ACI was compared to osteochondral autografting. (13) Forty-four individuals (61% male, 39% female) aged 16-40 years (mean 28.7 +/- 7.8), who had a focal, symptomatic chondral injury of Outerbridge grade III or IV with no previous surgical treatment, were randomly assigned to ACI or mosaicplasty 6 months after undergoing arthroscopic debridement. The average lesion size was 1.9 cm. Only 12 of 22 (54%) in the ACI group and 11 of 22 (50%) of the mosaicplasty group actually underwent the assigned procedure. Dropouts comprised 14 patients (32%) who reported spontaneous improvement following arthroscopy and did not undergo subsequent surgery, 5 who did not show up at the presurgery examination and could not be further traced, and 2 who refused surgery for personal reasons. Because of the substantial dropout rate, the original primary outcome measure, the mean Lysholm Knee Scoring Scale (LKSS) assessed 12 months post-surgery was converted into a scale in which improvement was categorized by proportions of responders (LKSS <60, LKSS 60–90, LKSS 90–100). With this scale, and including 10 patients who were cured by debridement (intention-to-treat analysis) the percentages of patients who achieved complete success were 89% (16 of 18 evaluable cases) in the mosaicplasty arm versus 68% (13 of 19 evaluable cases) in the ACI arm (test for trend p=0.093). The high rate of spontaneous improvement after simple debridement raises questions about the appropriateness of additional surgical intervention in patients similar to those included in this trial. These results are not sufficient to permit conclusions regarding the effect of ACI on health outcomes in comparison with mosaicplasty or to demonstrate an independent effect of the use of ACI versus debridement and exercise rehabilitation.

First Generation ACI (CarticeTM) for Treatment of the Knee: Other Controlled Trials. Gooding and colleagues randomized 68 patients with osteochondral defects (mean: 4.5 cm²; range: 1–12 cm²) of the femoral condyle (54%), trochlea (6%), or patella (40%) to ACI with either a periosteal or collagen cover. (14) At 2 years, 74% of the patients with the collagen cover had good to excellent results compared with 67% of the patients with the periosteal cover. Hypertrophy required shaving in 36% of patients treated with the periosteal cover. None of the collagen covers required shaving.

In 2012, Pestka et al. reported a matched-pair comparison of ACI after failed microfracture versus ACI as a first-line treatment. (15) A total of 56 patients were retrospectively matched for gender, age, defect

size, and defect location. The average defect size was 4.65 cm². 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 ($p=0.0583$) for lower International Knee Documentation Committee (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. (16) However, the results add to a growing body of literature suggesting inferior outcomes when ACI is performed following a failed microfracture. (17)

First Generation ACI (Carticel™) for Treatment of the Knee: Observational Studies. Results from the Study of the Treatment of Articular Repair (STAR) trial have been published; these were previously available in the Carticel package insert and from a meeting presentation in July 2007. (18-20) STAR was a prospective, open-label 4-year study in 154 patients (mean age: 35 years; 69% male) from 29 clinical centers. Each patient served as his or her own control, undergoing ACI after having failed or experienced an inadequate response to a prior cartilage repair procedure (for example, 78% underwent debridement, 29% microfracture, 12% subchondral drilling) on a distal femur index lesion (109 medial femoral condyle, 32 lateral femoral condyle, 46 trochlea). The median lesion size was 4.6 cm² (range of 1-30 cm²), with 26% involving osteochondritis dissecans. Fifty patients (32%) had multiple lesions in the reference knee, and 29 (19%) received multiple cellular implants. Prior treatment inadequacy was defined as both patient and surgeon agreement that the patient's symptoms or function required surgical retreatment of the defect and a patient's rating of overall condition of the knee was a score of 5 or less, using the Modified Cincinnati Knee Rating System (MCKRS). In this group, the median time to meet the failure criteria was 3.4 months for the prior index procedure, with more than 90% of patients having failed within 10.3 months. Patients who met these criteria were treated with ACI and assessed every 6 months for up to 4 years.

The primary outcome, treatment failure for ACI, was defined as any of the following: 1) a patient underwent surgical retreatment that violated the subchondral bone or repeated ACI for the same index defect; 2) complete delamination or removal of the graft; or 3) a patient's rating of the overall condition of the knee using the MCKRS failed to improve from the baseline knee score over 3 consecutive 6-month time intervals. Withdrawals from the study were considered as failures at the last follow-up. The mean overall MCKRS for the entire patient population at baseline was 3.3 ($n=154$), and 126 (82%) completed 4-year follow-up. Thirty-seven patients (24%) were considered failures; 11 failed based on the surgical failure criterion, and 26 failed based on the MCKRS criterion. Most of the 37 failures (92%) occurred within 30 months. At 48 months, three-fourths of all patients in the study (76%) showed good to excellent results with a mean MCKRS score of 6.3 ($n=115$). Secondary outcome measures also showed improvement, including pain, symptoms, sports and recreation, knee-related quality of life, and activities of daily living. There was no relationship between the size of the lesion at baseline and treatment outcomes with ACI.

Over half of the population (54%) experienced at least one serious adverse event secondary to ACI, and 40% of patients underwent subsequent surgical procedures on the index knee related to ACI. Adverse events included arthrofibrosis (16%), graft overgrowth (15%), chondromalacia or chondrosis (12%), graft complications (i.e., fraying or fibrillation, 10%), graft delamination (6%), and joint adhesion (5%). Subsequent surgical procedures (regardless of relationship to ACI) included debridement of cartilage lesion (31%), lysis of adhesions (14%), other debridement (10%), meniscectomy (6%), loose body removal (5%), microfracture of the index lesion (5%), and scar tissue removal (5%). The most common cause for a subsequent surgical procedure was periosteal patch hypertrophy. A majority (61%) of patients who had a subsequent surgical procedure went on to have successful results, while 39% were eventually considered treatment failures. The results of the STAR trial suggest that ACI may improve knee symptoms and function in some patients with severe, debilitating, previously treated

cartilage lesions of the distal femur for at least 4 years after the procedure. Additional surgical procedures may be expected.

Browne et al. published 5-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. (21) The registry is a multicenter program initiated in 1995 and 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 cm² (range: 0.8 to 23.5 cm²). Seventy percent of the patients had failed at least one previous cartilage procedure, and the average self-rated overall condition was 3.2 (poor to fair). At 5 years following the index procedure, the average follow-up score was 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). Factors associated with failure in 6 patients were nonadherence with the postoperative protocol, additional injury, and uncorrected malalignment. Defect size was not found to be significantly associated with outcome; self-reported outcomes were associated with workers' compensation claims. In 2010, this group of investigators published 6- to 10-year follow-up (mean 9.2 years) on 72 patients in the cartilage repair registry. (22) Information on adverse events, treatment failures, and operations after ACI were reported on follow-up questionnaires or came from patient and surgeon reports. 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 1- to 5-year follow-up period. Of these 54 patients, 47 (87%) sustained a mean improvement of 3.8 points from baseline to the later follow-up period. During the 6- to 10-year follow-up period, ACI failed in 3 patients at a mean of 8 years after implantation. For the cohort of 72 patients, 69% reported improvement, 17% failed, and 12.5% reported no change from baseline to follow-up. During the study period, 30 patients (42%) had 42 operations after ACI, the majority of which met the study definition of treatment failure.

In 2010, Peterson and colleagues reported on 224 patients who replied to questionnaires at 10- to 20-year follow-up. (23) This represents 38% of a total of 590 patients who underwent ACI at their institution between 1987 and 1998. The average age of the patients was 33 years (range, 14 to 61) at the time of the ACI, and the indication for treatment was any symptomatic full-thickness cartilage lesion up to 16 cm², including patients with meniscal (34% of patients) or ACL lesions (19%). Fifty-five patients (25%) had multiple lesions, 73 patients (33%) had unipolar or bipolar patellar lesions, and 26 patients (12%) had osteochondritis dissecans. Three hundred and forty-one surveys were mailed to the treated patients; the response rate was 65%. Information about baseline measurements was collected from the patients' charts or from prior studies and when available, compared with the questionnaire responses at follow-up. At a mean of 12.8 years' follow-up, 74% of the patients reported their status as better or the same as the previous years, and 92% were satisfied with the operation. The average Lysholm score improved from 60.3 preoperatively to 69.5 postoperatively, the Tegner from 7.2 to 8.2, and the Brittberg-Peterson from 59.4 to 40.9. At the final measurement, the KOOS score averaged 74.8 for pain, 63 for symptoms, 81 for activities of daily living, 41.5 for sports, and 49.3 for quality of life. The average Noyes score was 5.4. Patients with bipolar lesions had a worse final outcome than patients with multiple unipolar lesions. The presence of meniscal injuries before ACI or history of bone marrow procedures before the implantation did not seem to affect the final outcomes.

Rosenberger et al. reported average 4.7 years' follow-up (range: 2–11 years) on a cohort of 56 patients (45 to 60 years of age) with lesions of the femoral condyle (49%), trochlea (29%), or patella (22%). (24) 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. A European group reported complications in 309 consecutive patients, 52 of whom (17%) had undergone revision surgery for persistent clinical problems. (25) Three different ACI techniques had been used, periosteum-covered, membrane-covered (Chondrogide Geistlich Biomaterials, Switzerland), and 3-dimensional matrix (BioSeed-C, Biotissue Technologies, Germany). Follow-up at a mean of 4.5 years showed that the highest rate of revision surgery was in patients with

periosteum-covered ACI (27%) in comparison with membrane-covered or matrix-induced ACI (12% and 15%, respectively). There was a trend ($p=0.09$) for a higher incidence of hypertrophy with patellar defects in comparison with the femoral condyles or trochlea.

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. (26, 27) A 2008 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. (28) The average defect was 4.4 cm². Depending on surgeon preference, patients received ACI with a periosteal patch, Chondrogide membrane, or MACI. Fourteen patients (15%) were lost to follow-up, and 11 patients (12%) were excluded from the follow-up study due to dysplasia of the femoropatellar joint and significant (more than 5 degrees) varus or valgus deformity. In addition to patient responses for the Cincinnati Sports Activity scale, Lysholm score, and International Knee Documentation Committee (IKDC) score, a physical examination was performed by an independent examiner who was blinded to data obtained at the time of surgery, including defect size and location. Objective evaluation at an average follow-up of 38 months showed normal or nearly normal results in 47 patients (67%). Results were classified as abnormal in 14 patients (20%), and 9 patients (13%) were considered failures. Results were not divided according to the type of implant (ACI or MACI), although it was reported that 2 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. Other studies from Europe report patellofemoral cartilage defects treated with second-generation MACI implants. (29, 30) These products are not approved in the U.S. and are, therefore, considered investigational.

In 2009, Pascual-Garrido et al. reported outcomes from 52 patients (83% follow-up) who underwent ACI of the patellofemoral joint (patella or trochlea). (31) The mean defect size was 4.2 cm². 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 osteochondral autograft ($n=1$). Questionnaires were administered preoperatively, 6 months and 1 year postoperatively, and then annually. At an average follow-up of 4 years (range, 2 to 7), there was significant improvement in the Lysholm (37 to 63), IKDC (31 to 57), KOOS Pain (48 to 71), KOOS Symptoms (51 to 70), KOOS Activities of Daily Living (60 to 80), KOOS Sport (25 to 42), Cincinnati (43 to 63), Tegner (4 to 6), and Short Form (SF)-12 Physical (38 to 41). Patients reported the overall condition of their knee as excellent, very good, or good in 71% of the cases; 81% of the patients were satisfied with the procedure. There were 4 failures (8%), defined as poor clinical outcome accompanied by evidence of graft failure or need for conversion to knee arthroplasty or osteochondral allograft.

Farr et al. described outcomes from a prospective series of 36 patients who underwent ACI together with meniscal transplantation in the same compartment. (32) 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 3 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 4 failures, 68% of their patients required additional surgeries; 52% had one additional surgery, and 16% required 2 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 osteochondral allograft transplantation (OA; 48%). (33) The Lysholm score improved in both the ACI (from 55 to 79) and OA (from 42 to 68) groups; 48% of patients (60% ACI and 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 cm² vs. 3.9 cm²). Two patients were considered failures (7%) and 5 (17%) and underwent subsequent surgery. Although results seemed promising, evidence is insufficient to permit

conclusions regarding the effect of combined transplantation-implantation procedures on health outcomes.

A 3-fold increased failure of ACI after previous treatment with marrow stimulation techniques was found in a cohort of 321 patients with more than 2 years of follow-up (of 332 treated). (17) The average lesion was 8 cm², and the indications for treatment of cartilage defects with ACI included 1 or more full-thickness chondral defects of the knee, with consistent history, physical examination, imaging, and arthroscopy; no or correctable ligamentous instability, malalignment, or meniscal deficiency; and not more than 50% loss of joint space on weight-bearing radiographs. Independent analysis showed a failure rate of 8% of joints (17 of 214) that did not have prior marrow stimulation of the lesion, compared with 26% (29 of 111 joints) that had previously been treated with marrow stimulation.

Minas and colleagues 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 to 60), evidence of early osteoarthritis at the time of surgery (peripheral intra-articular osteophyte formation and/or 0% to 50% joint space narrowing), and equal to or greater than 2 years of follow-up. (34) (Patients with more than 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 cm² and a total mean defect area of 10.4 cm². 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, the majority 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 to 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 Western Ontario and McMaster Universities Arthritis Index (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.

First Generation ACI (Carticel™) for Joints Other Than the Knee

There has been interest in applying ACI to cartilage defects in other joints. The most commonly reported is use of ACI for the talus.

In 2010, Zengerink et al. published a systematic review of treatment of osteochondral lesions of the talus. (35) Fifty-one nonrandomized and 1 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 knee morbidity seen with osteochondral autografting, the authors concluded that bone marrow stimulation is the treatment of choice for primary osteochondral talar lesions. A 2009 report examined the association between defect size and outcomes following marrow stimulation techniques in 120 ankles. (36) Eight ankles subsequently underwent osteochondral transplantation, and 22 ankles were considered clinical failures (American Orthopaedic Foot and Ankle Society [AOFAS] Ankle-Hindfoot score <80). Linear regression suggested a cutoff defect size of 1.5 cm² for marrow stimulation techniques, with an 80% failure rate compared to a 10.5% failure rate for ankles with a defect size of less than 1.5 cm². Three of 58 ankles (5.2%) with a defect area of less than 1 cm² showed clinical failure, while 7 of 37 ankles (18.9%) with a defect area between 1.0 and 1.5 cm² failed.

A systematic review by Niemeyer et al. included 16 studies (213 patients) on ACI or MACI for lesions of the talus. (37) All were case series with a mean of 13 patients (range, 2-46) and mean follow-up of 32 months (range, 6-120). A majority of the studies were prospective. In 6 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 American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Score. Overall clinical success rate, defined as the percentage of good and excellent results, was 89.9% (range, 50% to 100%). Interpretation of these results is limited by the inclusion of poor quality studies, lack of a comparator, lack of blinding, and the use of techniques that are not approved for use by the FDA.

A 2006 study from Italy randomized 32 patients with osteochondral lesions of the talus to chondroplasty, microfracture, or osteochondral autograft transfer (OAT). (38) This small study found similar improvements (approximately 40 points) for the 3 treatment groups as measured by the AOFAS 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 1 patient following chondroplasty, by 2 patients following microfracture, and by 2 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).

Second Generation ACI Products

Second Generation ACI Products: Systematic Reviews. Kon et al. published a systematic review of matrix-assisted ACI in 2013. (39) The review identified 51 articles, including 3 randomized controlled trials, 10 comparative studies, 33 case series, and 5 case reports that reported on functional or clinical outcomes. The review found an expanding evidence base that reports good results at short to medium follow-up, although long-term follow-up and randomized controlled trials are needed to compare MACI with other available treatments.

Second Generation ACI Products: Randomized, Controlled Trials. There are 3 RCTs of ACI using matrix assistance. Two of these compared matrix-assisted ACI with marrow-stimulating techniques, and the third RCT compared matrix-assisted ACI with ACI done without matrix assistance.

Second Generation ACI Products: MACI®. Basad et al. reported a small randomized trial that compared MACI® (n=40) to microfracture (n=20) in patients with a single post-traumatic chondral defect between 4-10 cm². (40) Both groups improved at the 2-year follow-up, with a significant advantage of MACI over microfracture on the Lysholm (92 vs. 69), Tegner (4 vs. 3), and International Cartilage Repair Society (ICRS) patient (a higher percentage of patients with an ICRS score of I) and ICRS surgeon scores.

Second Generation ACI Products: NeoCart. In 2012, Crawford et al. reported results of an industry-sponsored, FDA-regulated, multi-center randomized Phase II trial. (41) Thirty patients with lesions less than 8 cm² were randomized to NeoCart (n=21) or to microfracture (n=9). The SF-36, KOOS, IKDC and VAS pain scores were assessed at up to 24 months by intent-to-treat analysis, and patients were classified as responders if they had at least a 12-point improvement in the pain score of the KOOS and a 20-point improvement in the IKDC subjective score. At 24 months, there was no significant difference in the mean KOOS pain scores or IKDC scores. The NeoCart group showed significantly greater improvement in the KOOS pain score, KOOS sports, KOOS QOL, IKDC, and visual analog scale (VAS) pain scores compared to microfracture. There was a trend for a greater number of responders in the NeoCart group (p=0.097); 79% of NeoCart patients were considered to be responders, compared to 44% of the microfracture group.

Second Generation ACI Products: Bioseed. Zeifang et al. conducted a small (n=21) randomized trial comparing MACI and ACI. (42) The average size of the cartilage defects was 4.3 cm², and patients had undergone an average of 2 prior surgeries on the affected knee. Postoperatively, there was no significant difference between the 2 groups on the IKDC score at either 12 months (72.0 for MACI and

76.7 for ACI), or 24 months (70.1 for MACI and 77.1 for ACI). Exploratory analysis found a significant inverse correlation with age ($r = -0.52$ at 12 months and $r = -0.49$ at 24 months) indicating that better results were observed in younger patients. There was no significant difference between the groups in the SF-36. The Lysholm score showed a significant improvement only in the ACI group (from 61.3 at baseline to 86.3 at 12 months and 84.0 at 24 months). The Tegner activity score did not change significantly in either group.

Second Generation ACI Products: ChondroCelect. Saris et al. published a multicenter, randomized trial of characterized chondrocyte implantation ($n=57$) versus microfracture ($n=61$) in 2008; the average lesion size was 2.8 cm². (43) Chondrocytes were isolated from a cartilage biopsy specimen and expanded ex vivo (ChondroCelect, TiGenix, Belgium). ChondroCelect is not approved for use in the U.S. Chondrocytes that were predicted to form stable hyaline cartilage in vivo were implanted by arthrotomy approximately 27 days after chondrocyte harvest. Surgical and rehabilitation procedures were standardized, and evaluation of a biopsy specimen at 12 months was conducted by an independent evaluator. Histologic analysis showed better results with ACI for some measures of structural repair such as cartilage surface area, safranin O and collagen II ratio, and cell morphology. However, measures of integration (e.g., subchondral bone abnormalities, basal integration, vascularization) and surface architecture were not improved relative to the microfracture group. Self-assessed pain and function with the Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire were similar following ACI or microfracture at 12 or 18 months' follow-up. Joint swelling and joint crepitation were greater in the ACI group, particularly following the arthrotomy. Thus, although histologic results were somewhat improved, in this study characterized chondrocyte implantation did not improve health outcomes in comparison with microfracture at short-term follow-up.

In 2009, Saris et al. published 36-month outcomes (100% follow-up) from this randomized trial. (43, 44) The mean improvement in the overall KOOS was greater in the ACI group than the microfracture group (21 vs. 16 points, respectively). More ACI than microfracture-treated patients were considered to be treatment responders (83% vs. 62%, respectively), defined as an increase from baseline of at least 10 percentage points in at least 3 of the 4 KOOS subdomains or a decrease of at least 20 percentage points in visual analog scale (VAS) scores for pain. At 36 months after surgery, 2 ACI (3.9%) and 7 microfracture patients (11.5%) had failed treatment and subsequently underwent reintervention. Magnetic resonance imaging (MRI) showed greater worsening of the subchondral bone reaction with microfracture compared with ACI. At 5 years after treatment, the number of treatment failures was comparable for the ACI ($n=7$) and microfracture ($n=10$) groups. (16) There was a trend for the overall KOOS score to be more improved following ACI than microfracture (21 vs. 14, $p=0.068$). Planned exploratory subgroup analysis indicated that ACI resulted in a better outcome (both statistically and clinically significant) in patients who had a time since symptom onset of less than 3 years, with a change in KOOS of 26 compared to 15 for the microfracture group. For patients with symptom onset of 3 years or more, the change in KOOS was similar for the 2 groups (13 ACI vs. 17 microfracture). Subgroup analyses for age did not show a difference for patients who were younger than 35 years of age compared to patients who were 35 years or older.

Second Generation ACI Products: Hyalograft C. In 2011, Kon et al. reported a prospective comparative study of second generation ACI (Hyalograft C) versus microfracture in 41 professional or semiprofessional male soccer players. (45) This was a pragmatic clinical trial, with treatment allocation based on the center that patients went to; 1 center performed ACI and 2 centers performed microfracture. The 2 patient groups were comparable for age, defect size, location, previous and combined surgery, and follow-up. Patients were evaluated prospectively at 2 years and at a final mean 7.5-year follow-up (minimum, 4 years). The percentage of patients who returned to competition was similar, with 80% in the microfracture group and 86% in the ACI group. Patients treated with microfracture needed a median of 8 months before playing their first official soccer game, whereas the ACI group required a median time of 12.5 months. The International Knee Documentation Committee (IKDC) subjective score showed similar results at 2 years' follow-up but significantly better results in the ACI group at the final evaluation. In the microfracture group, results decreased over time (from 86.8 at 2 years to 79.0 at final follow-up), whereas the ACI group had stable results between 2 years and final

follow-up (90.5 and 91.0, respectively). The IKDC objective score was similar in the 2 groups, with 90-95% of knees considered to be normal or nearly normal. Subjective evaluation of functional level was significantly better in the ACI group at final follow-up (91 vs. 84).

Ongoing Clinical Trials

A search of the online clinical trials database www.clinicaltrials.gov in May 2013 identified a number of trials with second and third generation ACI/MACI. In addition, Zimmer Orthobiologics is conducting 2 large post-marketing studies with DeNovo NT, Natural Tissue Graft, for the knee (NCT01329445) and ankle (NCT01347892). Both studies will have 5-year follow-up with estimated completion in 2018.

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2008

In response to requests, input was received from 1 physician specialty society and 3 academic medical centers while this policy was under review in 2008. The reviewers generally agreed that ACI should be considered when all other treatments have been unsuccessfully tried in individuals who have a localized chondral defect in an otherwise normal joint articular surface. Reviewers noted the lack of alternative options for larger lesions (e.g., >4 cm²). Additional literature was provided, which was subsequently reviewed.

2011

In response to requests, input was received from 2 physician specialty societies and 3 academic medical centers while this policy was under review in 2011. The clinical input was generally in agreement with the stated criteria for ACI with the exception of the following: input was mixed regarding the requirement for an inadequate response to a prior surgical procedure and the requirement for an absence of meniscal pathology. Input was also mixed regarding the investigational status of ACI in patellar and talar joints..

Summary

Although evidence from long-term studies is limited, evidence indicates that autologous chondrocyte implantation (ACI) can improve symptoms in some patients with lesions of the articular cartilage of the knee who have failed prior surgical treatment. These patients, who are too young for total knee replacement, have limited options. Therefore, based on the clinical input, highly suggestive evidence from randomized controlled trials and prospective observational studies, it is concluded that ACI may be considered an option for the FDA-approved indication of disabling full-thickness chondral lesions of the femoral condyles or trochlea caused by acute or repetitive trauma, in patients who have had an inadequate response to a prior procedure. Additional studies are needed to evaluate whether marrow stimulation at the time of biopsy affects implant success. Recent evidence indicates that ACI combined with meniscal allograft results in outcomes similar to either procedure performed alone; therefore, combined procedures may be considered medically necessary. Evidence is currently insufficient to evaluate the efficacy of ACI in comparison with other surgical repair procedures as a primary treatment of large lesions or to evaluate the efficacy of ACI for the patella or for joints other than the knee.

Results from second generation ACI procedures (MACI) from Europe appear promising. These products use a variety of biodegradable scaffolds and have the potential to improve consistent hyaline cartilage formation and reduce complications associated with injection under a periosteal patch. To date, there are a smaller number of RCTs with short-term follow-up comparing MACI to ACI, and no MACI products are approved in the U.S.; therefore, these are considered investigational.

Practice Guidelines and Position Statements

In a 2010 clinical practice guideline on the diagnosis and treatment of osteochondritis dissecans (OCD), the American Academy of Orthopaedic Surgeons (AAOS) was unable to recommend for or against a specific cartilage repair technique in symptomatic skeletally immature or mature patients with an unsalvageable osteochondritis dissecans lesion. (46) This recommendation of insufficient evidence was based on a systematic review that found 4 level IV studies that addressed cartilage repair techniques for an unsalvageable OCD lesion. Since each of the level IV articles utilized different techniques, different outcome measures, and differing lengths of follow-up, the work group deemed that the evidence for any specific technique was inconclusive.

In 2005, the National Institute for Health and Clinical Excellence (NICE) issued an updated Technology Appraisal Guidance on the use of autologous chondrocyte implantation. (47) The NICE guidance cited insufficient evidence to determine the benefits of autologous chondrocyte implantation and indicated this technology “should not be used for the treatment of articular cartilage defects except where the treatment is part of a clinical study.” The guidance noted many limitations in available trial data including length of follow-up, comparison to conservative treatment, assessment of the quality of cartilage produced, and the impact of cartilage produced on functional outcomes and health-related quality of life.

Medicare National Coverage

There is no national coverage determination.

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Billing Coding/Physician Documentation Information

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

Other non-specific codes that might be used are:

- 27330** Arthrotomy, knee; with synovial biopsy only
- 27331** Arthrotomy, knee; including joint exploration, biopsy, or removal of loose or foreign bodies
- 27332** Arthrotomy, with excision of semilunar cartilage (meniscectomy) knee; medial OR lateral
- 27333** Arthrotomy, with excision of semilunar cartilage (meniscectomy) knee; medial AND lateral
- 27334** Arthrotomy, with synovectomy, knee; anterior OR posterior
- 27335** Arthrotomy, with synovectomy, knee; anterior AND posterior including popliteal area
- 27403** Arthrotomy with meniscus repair, knee

- 29870** Arthroscopy, knee, diagnostic, with or without synovial biopsy (separate procedure)
- 29871** Arthroscopy, knee, surgical; for infection, lavage and drainage
- 29873** Arthroscopy, knee, surgical; with lateral release
- 29874** Arthroscopy, knee, surgical; for removal of loose body or foreign body (eg, osteochondritis dissecans fragmentation, chondral fragmentation)
- 29875** Arthroscopy, knee, surgical; synovectomy, limited (eg, plica or shelf resection) (separate procedure)
- 29876** Arthroscopy, knee, surgical; synovectomy, major, 2 or more compartments (eg, medial or lateral)
- 29877** Arthroscopy, knee, surgical; debridement/shaving of articular cartilage (chondroplasty)
- 29879** Arthroscopy, knee, surgical; abrasion arthroplasty (includes chondroplasty where necessary) or multiple drilling or microfracture
- 29880** Arthroscopy, knee, surgical; with meniscectomy (medial AND lateral, including any meniscal shaving) including debridement/shaving of articular cartilage (chondroplasty), same or separate compartment(s), when performed
- 29881** Arthroscopy, knee, surgical; with meniscectomy (medial OR lateral, including any meniscal shaving) including debridement/shaving of articular cartilage (chondroplasty), same or separate compartment(s), when performed
- 29882** Arthroscopy, knee, surgical; with meniscus repair (medial OR lateral)
- 29883** Arthroscopy, knee, surgical; with meniscus repair (medial AND lateral)
- 29884** Arthroscopy, knee, surgical; with lysis of adhesions, with or without manipulation (separate procedure)
- 29885** Arthroscopy, knee, surgical; drilling for osteochondritis dissecans with bone grafting, with or without internal fixation (including debridement of base of lesion)
- 29886** Arthroscopy, knee, surgical; drilling for intact osteochondritis dissecans lesion
- 29887** Arthroscopy, knee, surgical; drilling for intact osteochondritis dissecans lesion with internal fixation

The entire ACT procedure consists of 4 steps: (1) the 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) post-surgical rehabilitation. The initial arthroscopy may be scheduled as a diagnostic procedure; 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. At the time of arthrotomy, additional procedures may be done, such as repair of ligaments or tendons or creation of an osteotomy for realignment of the joint. Therefore, it may be difficult to attribute the initial arthroscopy or subsequent arthrotomy entirely to the chondrocyte transplant procedure. The charges for the culturing component of the procedure are submitted as part of the hospital bill.

Additional Policy Key Words

DeNovo NT

Policy Implementation/Update Information

- 8/1/00 New policy, considered medically necessary. Requires prior authorization.
- 8/1/01 Policy statement revised to include transplantation for the treatment of meniscal defects as investigational. Temporary codes added to the policy.
- 8/1/02 No policy statement changes.
- 9/1/03 Policy statement revised to indicate this procedure is considered investigational. New temporary s-codes added. Prior Authorization no longer required.
- 8/1/04 No policy statement changes.
- 2/1/05 No policy statement changes. New specific CPT code added to policy.
- 8/1/05 Policy statement revised to indicate this procedure is investigational for the treatment of cartilage defects.

2/1/06	No policy statement changes.
8/1/06	No policy statement changes.
2/1/07	No policy statement changes.
8/1/07	No policy statement changes. Policy titled changed from Autologous Chondrocyte Transplantation or Implantation to Autologous Chondrocyte Transplantation.
8/1/08	No policy statement changes.
11/13/08	Policy statement changed, ACI of the knee medically necessary if previous surgical treatments have failed; all other indications considered investigational.
3/1/10	Policy statement added; Matrix-induced autologous chondrocyte implantation (MACI) is considered investigational.
11/1/10	Policy statements added on minced cartilage and allogeneic cartilage cells; considered investigational. Title changed to include "Other Cell-based Treatments of Focal Articular Cartilage Lesions."
3/1/11	No policy statement changes.
3/1/12	Meniscal pathology removed from policy statement per policy 7.01. 15
3/1/13	No policy statement changes.
3/1/14	Sections and policy statements on minced cartilage moved to policy No. 7.01. 78 (Autografts and Allografts in the Treatment of Focal Articular Cartilage Lesions) and "Other Cell-based Treatments" removed from title.

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