

## AUTOLOGOUS CHONDROCYTE IMPLANTATION

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Epidemiological research has advanced our understanding of the magnitude and impact of the burden of obesity, cigarette smoking, alcohol abuse and illicit drug use. Plan members who lead a healthy lifestyle are optimizing the potential for a good treatment outcome. Plan members who do not lead a healthy lifestyle should be encouraged and supported to alter their habits and counseled about the associated risks to which they will be exposed.

### Overview

Articular cartilage defects of the knee are common, and are encountered in approximately 60% of knee arthroscopies. (Heir S, et al. 2010) The extent of pathology ranges from small focal defects to widespread damage to the articular surface, with corresponding changes in the underlying subchondral bone. Widespread cartilage damage with changes in the subchondral bone represents osteoarthritis, which is the most common presentation of symptomatic cartilage problems. Focal cartilage defects can either have a traumatic or insidious onset, with an approximately even distribution between both causes. Although it may seem intuitive that small chondral defects will progress to more widespread cartilage damage and osteoarthritis, the natural history of focal chondral defects has not been clearly established. (Gomoll et al., 2010)

Diagnostic imaging is required to diagnose articular cartilage defects and should begin with a standard weight-bearing, anteroposterior (AP) radiograph of both knees in full extension, a non-weight-bearing 45-degree flexion lateral view and an axial view of the patellofemoral joint. Additionally, a 45-degree flexion weight-bearing posteroanterior (PA) radiograph can help identify subtle joint-space narrowing that traditional extension views may fail to uncover. Special studies such as a long-cassette mechanical axis view or a magnetic resonance imaging (MRI) evaluation should be done as needed. If joint-space narrowing is present on the 45-degree flexion weight-bearing PA radiograph, an MRI is rarely necessary. Generally, MRI examination should be reserved for difficult cases in which the diagnosis remains unknown, especially in the setting of completely normal radiographs. The greatest strength of the MRI is its ability to evaluate the subchondral bone (ie, osteochondral fractures, osteonecrosis, and osteochondritis dissecans).

X-rays with arthroscopic assessment are the gold standard for determining whether a symptomatic patient is a candidate for ACI. Arthroscopic assessment of the joint for possible ACI should include a careful and systematic evaluation of the articular surfaces with an arthroscopic probe to determine the size of the defect and the quality of the cartilage surrounding the defect. The opposing articular surface must be probed throughout to ensure that the meniscus is intact, the articular surface is healthy, and any chondromalacia is not greater than superficial fissuring.

The severity of symptoms attributable to focal chondral defects does not correlate with the size of the defect. Small defects can be as disabling as endstage osteoarthritis. (Heir et al., 2010) Much like osteoarthritis, focal cartilage defects can have a wide variety of symptoms, ranging from asymptomatic to severe. The bone underlying articular cartilage is richly supplied with nerve endings and can become painful when exposed after articular loss. Pain, as a result of cartilage loss, may limit activities of daily living (ADLs) and recreational activities, thus impacting quality of life. The goal of treatment is to relieve pain and restore normal knee function.

Nonoperative therapy is the first line of treatment for symptomatic chondral defects, except in the presence of osteoarticular fragments which is an indication for operative treatment, particularly in the setting of mechanical symptoms. Nonoperative treatment options for focal cartilage defects consist of observation, weight loss, unloading braces, medications, corticosteroid injections, and viscosupplementation. These treatments are rarely definitive, and do not usually lead to healing of the defect. Rather, they provide symptomatic relief for a period, usually measured in months. In older patients, nonoperative temporizing measures are a reasonable long-term treatment plan. If there is progression of the articular cartilage damage over time, knee arthroplasty is a reliable surgical option. The younger the patient, the less attractive knee arthroplasty is as a surgical option because of concerns over prosthesis function, wear, and longevity. Current data indicates that 85% of knee prostheses will function well for approximately 20 years. Age younger than 55 at the time of knee arthroplasty, male gender, diagnosis of osteoarthritis, obesity, and presence of comorbid conditions are risk factors for revision. The results of revision knee arthroplasty are not as good as those for primary knee arthroplasty.

There are several operative treatments available to treat focal cartilage defects. There are relative advantages and disadvantages to each technique. Procedures are classified by their relative ability to promote and restore the damaged articular surface. Considering size of the defect alone is insufficient to guide treatment due to overlapping indications for many of the available treatment options. In addition to lesion size, assessing the patient's current and desired activity level, symptom intensity, and response to previous treatment is helpful to compartmentalize treatment options. Operative treatment options for cartilage defects can be broadly categorized as follows:

1. Arthroscopic lavage and/or debridement
2. Marrow stimulating techniques (microfracture, subchondral drilling, and abrasion arthroplasty)
3. Osteochondral autograft (Mosaicplasty, OATS)<sup>1</sup> or allograft
4. Cell-based replacement (e.g., autologous chondrocyte implantation)
5. Knee replacement

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<sup>1</sup> Several systems are available for performing this procedure, including but not limited to the Mosaicplasty System (Smith and Nephew), and the Osteochondral Autograft Transfer System (OATS, Arthrex, Inc.). These terms have been used interchangeably to describe the procedure. Although Mosaicplasty and OATS may use different instrumentation, the underlying principle is similar; i.e., the use of multiple osteochondral cores harvested from a non-weight-bearing region of the femoral condyle and autografted into the chondral defect. This procedure is best for small defects, <15-20mm in size, this is due to a limit in the number of harvest sites available. One of the problems with this technique is what is known as donor site morbidity.

For many patients, arthroscopic lavage and/or debridement is a palliative procedure which temporarily alleviates symptoms and allows for arthroscopic chondral evaluation. Lavage is basically washing out the knee joint and debridement is removing any unstable or degenerative articular cartilage flaps. Patients who receive long-term benefit from this procedure are those with small defects ( $< 1 \text{ cm}^2$ ), lower demand and localized mechanical symptoms. In relatively young or active individuals with moderate symptoms and larger lesions ( $>2 \text{ cm}^2$ ), results have been less promising, demonstrating only temporary, symptomatic relief.

Marrow stimulation procedures involve surgical penetration of the subchondral bone, allowing for stimulation and migration of marrow elements (mesenchymal cells) and the formation of a surgically induced fibrin clot that subsequently results in the production of fibrocartilage at the defect site. The technique of marrow stimulation is applied to several procedures, including microfracture, subchondral drilling, and abrasion arthroplasty. Microfracture is the most widely used cartilage repair procedure worldwide. (Mithoefer et al., 2009) Overall, most clinical studies evaluating the outcome of microfracture have reported improvement in knee function in 70% to 90% of patients. Long-term results vary, with 60% to 75% of patients reporting reductions in symptoms and improvement in function. (William et al. 2007) Proper patient selection and meticulous attention to technical detail are critical to achieving a successful outcome following microfracture. Microfracture is recommended for smaller lesions ( $<2 \text{ cm}^2$ ) in active patients with no more than moderate symptoms, or for larger lesions ( $>2 \text{ cm}^2$ ) in lower-demand patients with mild symptoms.

Kreuz et al. (2006) compared the results of microfracture in 85 consecutive patients and found that patients less than 40 years of age had significantly better results than those over 40. Even with meticulous attention to operative technique and proper patient selection, the results of microfracture appear to deteriorate over time. Mithoefer et al. (2006) found that the results of microfracture deteriorated over time in 47% of elite athletes. Similar results have been found in other studies as well. One of the concerns with microfracture is that it does not stimulate the growth of normal joint cartilage (hyaline cartilage) but stimulates the growth of fibrocartilage. A comparative study with ACI reported that of 35 patients treated with microfracture, 11.4% were predominantly hyaline cartilage, 17.1% were a fibrocartilage-hyaline mix, and 51.4% were fibrocartilage at 2 years. (Knutsen et al. (2004) Fibrocartilage lacks the structure and mechanical properties, and in most instances the durability of articular cartilage. Even though this tissue covers the subchondral bone, it may fail to distribute loads across the articular surface in a way that avoids pain with loading. Moreover, the repair tissue integrates poorly with native cartilage, and its collagenous fibrillar network has been found neither to project into native tissue nor to intermingle with its fibrils. As the cartilage stimulated by a microfracture procedure may not persist over time, the technique may not be the best therapy for durable repair of cartilage defects of the knee.

Despite advances in the repair of cartilage defects, no current therapy can mimic the biomechanical properties of cartilage. This observation has driven research in cell-based technologies, such as autologous chondrocyte implantation (ACI). ACI has generated a high level of interest in the orthopedic community since its introduction in Sweden more than 20 years ago. (Brittberg et al. 1994) This high level of interest is

largely due to the troublesome nature of articular cartilage defects, particularly in young patients. An extensive and growing evidence base indicates that ACI facilitates healing with formation of hyaline or hyaline-like cartilage and produces successful clinical outcomes in patients with large, disabling articular cartilage defects in the knee. In the United States, there is currently only one FDA-approved autologous chondrocyte product and that is Carticel® (manufactured by Genzyme, Cambridge, Massachusetts).<sup>2</sup> Carticel® is FDA-approved to be injected under a periosteal flap. Although long-term studies are lacking, short-term and mid-term evidence indicates that ACI can improve pain and function in some patients with focal cartilage defects of the knee. These patients, who are too young for knee arthroscopy, have limited options.

ACI for repair of focal cartilage defects of the knee involving injection of cultured chondrocytes under a periosteal flap is often referred to as first generation ACI. ACI requires two separate procedures. During the initial procedure, the patient's own chondrocytes are removed arthroscopically from a non load-bearing area, either the intercondylar notch or the superior ridge of the medial or lateral femoral condyles. The cells that are harvested are grown in vitro for approximately six weeks or until the population reaches 10-12 million cells. After this cell proliferation period, the patient undergoes a second procedure (typically, an arthrotomy under general anesthesia) in which the damaged cartilage is removed and the cultured chondrocytes are surgically injected under a periosteal flap, which has been sutured over the affected area. The implanted chondrocytes then integrate with surrounding tissue under the flap with the goal of generating hyaline-like cartilage. The primary advantage of ACI is the development of hyaline-like cartilage rather than fibrocartilage in the defect, presumably leading to better long-term outcomes.

As with any cartilage repair procedure, good results cannot be expected if coexisting knee pathology is not thoroughly addressed. Biomechanical malalignment and ligamentous insufficiency can lead to excessive forces and abnormal compressive loads that can destroy repair tissue. Therefore, it is critical that any associated knee pathology responsible for or contributing to the chondral defect be identified and corrected before or in conjunction with the cells being implanted. Concomitant procedures facilitate the healing process of the hyaline-like repair tissue by unloading overloaded compartments, ensuring proper tracking, and balancing soft tissues.

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<sup>2</sup> Carticel® (autologous cultured chondrocytes)

#### INDICATIONS AND USAGE

Carticel is an autologous cellular product indicated for the repair of symptomatic cartilage defects of the femoral condyle (medial, lateral or trochlea), caused by acute or repetitive trauma, in patients who have had an inadequate response to a prior arthroscopic or other surgical repair procedure (e.g., debridement, microfracture, drilling/abrasion arthroplasty, or osteochondral allograft/autograft).

Carticel should only be used in conjunction with debridement, placement of a periosteal flap and rehabilitation.

Carticel is not indicated for:

- Treatment of cartilage damage associated with generalized osteoarthritis.
- Patients with total meniscectomy unless surgically reconstructed prior to or concurrent with Carticel implantation.

It is important to recognize that patients enrolled in randomized controlled clinical trials represent a select group not representative of the total population of patients with focal cartilage defects of the knee. To identify appropriate candidates for ACI, all factors that could compromise a successful outcome should be considered. In an observational study of the natural history of cartilage defects, the knees of 325 subjects (mean age, 45 years) were examined by MRI at baseline and two years later. Ding et al (2006) observed that the rate of cartilage defects was higher in subjects with a BMI of 25 or higher (38%) compared to subjects with a BMI less than 25 (25%), and furthermore, weight loss was associated with decreases in knee cartilage defect scores. A normal BMI correlates with higher scores for activities of daily living as well as better Short-Form 36 Physical Component Summary scores following knee cartilage repair procedures. (Mithoefer et al. 2005) Knutsen and colleagues excluded patients with a BMI > 30 in their randomized controlled study comparing ACI to microfracture. The mean BMI in the Carticel® Repair Registry (Zaslav et al.2008) was 27.9 (+/- 4.6). In a case-controlled study of 80 patients, Jaiswal et al. (2008) found that the wound infection was rate significantly higher in patients with a BMI greater than 25. Results from these studies and other studies suggest that BMI is an important predictor of outcome after ACI.

The concept of a slow, gradual time course of healing is critical to understand for rehabilitation following ACI. If the intraarticular environment is protective, remodeling and maturation will continue. However, if the graft is overloaded, failure can occur. There is a degree of individual variation with the rehabilitation process, and the program should be designed according to the patient's status and needs, as well as factors such as the size and location of the defect and any concomitant procedures performed. The foundation principles of a successful ACI rehabilitation program are centered on graft protection, mobility and motion exercises, muscle strengthening, protected weight bearing, and patient education. It is critical that there is a regular dialogue between the physician, patient and physical therapist, especially during the first 3 to 12 months following ACI. Most patients start to experience good symptom relief during this period, however the process of tissue maturation continues long after this point and excessive activity may cause repair tissue degeneration.

Randomized, controlled outcome studies for ACI (Carticel®) of the knee are available. Harris et al. (2010) conducted a systematic review of Level I and II studies<sup>3</sup> comparing ACI with another cartilage repair or restoration technique. Thirteen studies (917 subjects) were included. Patients underwent ACI (n = 604), microfracture (n = 271), or

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<sup>3</sup> I. Strong evidence from at least one systematic review of multiple well-designed randomised controlled trials.

II. Strong evidence from at least one properly designed randomised controlled trial of appropriate size.

III. Evidence from well-designed trials such as pseudo-randomised or non-randomised trials, cohort studies, time series or matched case-controlled studies.

IV. Evidence from well-designed non-experimental studies from more than one centre or research group or from case reports.

V. Opinions of respected authorities, based on clinical evidence, descriptive studies or reports of expert committees.

osteochondral autograft (n = 42). All surgical techniques demonstrated improvement in comparison with the preoperative status. Three of seven studies showed better clinical outcomes after ACI in comparison with microfracture after one to three years of follow-up, whereas one study showed better outcomes two years after microfracture and three other studies showed no difference in these treatments after one to five years. Clinical outcomes after microfracture deteriorated after eighteen to twenty-four months (in three of seven studies). ACI and osteochondral autograft demonstrated equivalent short-term clinical outcomes, although there was more rapid improvement after osteochondral autograft (two studies). Although outcomes were equivalent between first and second-generation ACI and between open and arthroscopic ACI, complication rates were higher with open, periosteal-cover, first-generation ACI (four studies). Younger patients with a shorter preoperative duration of symptoms and fewer prior surgical procedures had the best outcomes after both ACI and microfracture. A defect size of  $>4 \text{ cm}^2$  was the only factor predictive of better outcomes when ACI was compared with a non-ACI surgical technique. Harris et al. concluded that cartilage repair or restoration in the knee provides short-term success with microfracture, ACI, or osteochondral autograft. There are patient-specific and defect-specific factors that influence clinical outcomes. ACI is indicated in higher-demand patients with large (between  $2 \text{ cm}^2$  and  $10 \text{ cm}^2$ ) symptomatic deep grade III or IV lesions of the medial or lateral femoral condyle or trochlea that have failed other operative treatment options. (For defects  $> 10 \text{ cm}^2$  osteochondral allograft is recommended.)

First generation ACI for repair of cartilage defects is not without limitations and several second generation variations are being investigated in Europe, including techniques that do not use a periosteum cover, thus avoiding periosteal hypertrophy. (Graft hypertrophy is a major complication seen in ACI with a periosteal flap.<sup>4</sup>) Variations of the original periosteum-cover technique include the use of porcine-derived type I/type III collagen as a cover (ACI-C) and matrix-associated autologous chondrocyte implantation (MACI®, Genzyme Europe) using a collagen membrane seeded with chondrocytes. Bartlett et al. (2005) conducted a prospective, randomized comparison of ACI-C and MACI for the treatment of symptomatic chondral defects of the knee in 91 patients, of whom 44 received ACI-C and 47 MACI grafts. Both treatments resulted in improvement of the clinical score after one year. Hyaline-like cartilage or hyaline-like cartilage with fibrocartilage was found in the biopsies of 43.9% of the ACI-C and 36.4% of the MACI grafts after one year. The rate of hypertrophy of the graft was 9% (4 of 44) in the ACI-C group and 6% (3 of 47) in the MACI group. While ACI-C and MACI are technically attractive, long-term studies are needed. These procedures represent off-label use Carticel® in the United States.

Promising clinical data are beginning to emerge in support of the use of bone marrow-derived mesenchymal stem cells (BMSC) for regenerative applications. Nedjadjnik et al. (2010) conducted a comparative study to compare the clinical outcomes of patients (N = 72) treated with first generation ACI to patients treated with BMSCs. There was

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<sup>4</sup> Periosteal hypertrophy overlapping the surrounding normal cartilage may cause symptoms of clicking, catching, or crepitus. This complication may appear between 3 and 9 months postoperatively and, in most patients, disappears spontaneously during continued rehabilitation. When this problem interferes with the rehabilitation, it is first handled with change and modification of the rehabilitation program and then with gentle arthroscopic resection. The frequency of periosteal complications has been reported between 5% and 65%.

significant improvement in the patients' quality of life (physical and mental components of the Short Form 36 after cartilage repair in both groups. There was no difference between the BMSC and the ACI group in terms of clinical outcomes except for Physical Role Functioning, with a greater improvement over time in the BMSC group. The subjective knee evaluation scores (Lysholm and Tegner) did not show any significant difference between groups over time, however, in general, men showed significantly better improvements than women. Patients younger than 45 years of age scored significantly better than patients older than 45 years in the ACI group, but age did not make a difference in the BMSC group. Nedjadjnik et al. concluded that using BMSCs in cartilage repair is as effective as chondrocytes for articular cartilage repair, and in addition, required one less operative procedure, reduced donor site morbidity and cost less. Phase I trials are underway.

At this time Carticel® is FDA-approved as a second-line treatment following failure of another cartilage repair procedure (e.g., arthroscopic debridement, microfracture, drilling/abrasion arthroplasty, or osteochondral allograft/autograft). This is because of a concession made by the FDA at the request of Genzyme Corp. who was unable to fulfill the post-approval contingencies. (As a condition of approval, the FDA requested that Genzyme conduct two randomized controlled studies, one to establish the contribution of cultured chondrocytes to the treatment of femoral cartilage defects, and another to compare outcomes in patients treated with Carticel® to outcomes achieved through marrow stimulation procedures.) Some authors have suggested that prior cartilage repair procedures may compromise the results of ACI. Minas et al. (2009) reported on a cohort study of 321 consecutive patients treated at one institution with ACI for full-thickness cartilage defects. Patients were grouped based on whether they had undergone a prior cartilage repair procedure. Within the groups that had previously undergone marrow stimulation (drilling, abrasion arthroplasty and microfracture) there was a 28%, 27% and 20% failure rate respectively compared to an 8% failure rate in the control group (no prior cartilage repair procedure). Minas concluded that prior marrow stimulation techniques have a strong negative effect on subsequent cartilage repair with ACI and therefore should be used judiciously in larger cartilage defects that could require future treatment with ACI. The results of this and other studies show that ACI is a valuable surgical procedure for failed articular cartilage repair procedures. The results of ACI used as the primary procedure appear to be better than when used secondary after another procedure fails. Randomized, controlled clinical trials are needed to determine whether marrow stimulation techniques reduce the success rates of subsequent ACI or whether patients who fail marrow stimulation techniques would fail ACI regardless of whether they had a prior marrow stimulation.

### **Definitions**

**Arthroplasty** – knee arthroplasty, or knee replacement, or is a surgical procedure to replace diseased or damaged articular surfaces with metal and plastic components which are designed to glide smoothly against one another.

**Arthroscopy** – Arthroscopy is a minimally invasive surgical procedure by which the internal structure of a joint is examined for diagnosis and/or treatment using an instrument called an arthroscope. The technique of arthroscopy involves inserting an arthroscope, a small tube that contains optical fibers and lenses, through a small incision in the skin into the joint to be examined. The arthroscope is connected to a

video camera and the interior of the joint is seen on a television monitor. If procedures are performed in addition to examining the joint with the arthroscope, this is called arthroscopic surgery. There are a number of procedures that are done in this fashion. If a procedure can be done arthroscopically instead of by traditional surgical techniques, it usually causes less tissue trauma, results in less pain, and may promote a quicker recovery. Arthroscopy is commonly used in the evaluation of knees and shoulders but can also be used to examine and treat conditions of the wrist, ankles, and elbows. Common knee joint injuries for which arthroscopy is considered include cartilage tears (meniscus tears), ligament strains and tears, and cartilage deterioration. Finally, loose tissues, such as chips of bone or cartilage, or foreign objects, that become lodged within the joint can be removed with arthroscopy.

**Articular** – of or relating to a joint or joints.

**Articular cartilage** – The cartilage covering the articular surfaces (the surfaces of a joint at which the ends of the bones meet) of the bones forming a synovial joint. Articular cartilage provides for a smooth low friction articulation, joint lubrication, and proper stress distribution in order to minimize peak force on subchondral bone.

**Cartilage** -- is a flexible connective tissue found in many areas in the bodies of humans and other animals, including the joints between bones, the rib cage, the ear, the nose, the elbow, the knee, the ankle, the bronchial tubes and the intervertebral discs.

Cartilage is not as hard and rigid as bone but is stiffer and less flexible than muscle.

There are three major types of cartilage in the body: 1) hyaline cartilage, 2) fibrocartilage, and 3) elastic cartilage. Elastic cartilage exists in the epiglottis and the eustachian tube. Fibrocartilage is present in three major locations in the body: 1) the intervertebral disks of the spine, 2) as a covering of the mandibular condyle in the temporomandibular joint, and 3) in the meniscus of the knee. Fibrocartilage often exists temporarily at fracture sites. The third type of cartilage, hyaline cartilage, is most prominently found in diarthroidal joints covering long bones. In addition, hyaline cartilage forms the growth plate by which long bones grow during childhood.

**Chondral** – pertaining to cartilage.

**Classification of articular cartilage defects** – there are several different classification systems for the description of articular cartilage defects, each has certain limitations and deficiencies which can lead to confusion. One frequently used classification system is the Modified Outerbridge Classification System:

- Grade 0: normal cartilage
- Grade I: cartilage with softening and swelling
- Grade II: a partial-thickness defect with fissures on the surface that do not reach subchondral bone or exceed 1.5 cm in diameter (<50% loss of cartilage thickness)
- Grade III: fissuring to the level of subchondral bone in an area with a diameter more than 1.5 cm (>50% loss of cartilage thickness)
- Grade IV, exposed subchondral bone

**Focal cartilage defect** – injury or trauma causing partial or full-thickness cartilage defect in a well-defined isolated (focal) area.

**Osteochondral** – pertaining to bone and cartilage.

**Synovial joint** – also known as a diarthroidal joint, a joint in which the opposing bony surfaces are covered with a layer of hyaline cartilage or fibrocartilage, there is a joint cavity containing synovial fluid, lined with synovial membrane and reinforced by a fibrous capsule and ligaments, and there is some degree of free movement possible.

## Policy

**Autologous cultured chondrocytes (HCPCS code J7330) and autologous chondrocyte implantation (CPT code 27412) require prior authorization by an FCHP Medical Director.**

FCHP covers autologous chondrocyte implantation when documentation (i.e., reports of standing X-rays, arthroscopy results, operative notes, and medical records) addressing all of the following medical necessity criteria are submitted:

1. The plan member is skeletally mature and between 18 and 55 years of age. Carticel® is not FDA-approved for use in pediatric patients; there is insufficient evidence on the safety or efficacy of ACI in children and skeletally immature adolescents. (Mithofer et al. 2005)<sup>5</sup> Knee arthroplasty is the primary operative treatment for adults 55 years of age and older. Cartrichel® is not FDA-approved for use in adults over the age of 65.
2. The plan member has no known history of hypersensitivity to gentamicin, other aminoglycosides or materials of bovine origin.
3. The plan members' body mass index (BMI) is less than or equal to 30.
4. The plan member is nicotine free prior to ACI.<sup>6</sup>
5. The plan member has persistent symptoms (pain, catching, locking and/or swelling) with reduction in ADLs, which have failed to respond to at least six months of documented non-operative treatment. (Nonoperative treatment options for focal cartilage defects may include observation, weight loss, unloading braces, medications, corticosteroid injections, and viscosupplementation.)
6. The plan member has a single, focal cartilage defect located on the medial or lateral femoral condyle or trochlea.<sup>7</sup> ACI is not covered for multiple defects or any defect that involves patellar cartilage.
7. The defect is caused by acute or repetitive trauma. Acute trauma includes falls, contact sports, and other sources of impact. Repetitive trauma includes overuse. ACI is not covered when the defect is due to osteochondritis dissecans.<sup>8</sup>

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<sup>5</sup> Wall et al. (2008) conducted a study of 42 skeletally immature patients with stable osteochondritis dissecans lesions. Six months of nonoperative treatment that included activity modification and immobilization resulted in progressive healing in two-thirds of patients. Skeletally immature patients with stable lesions that have not healed with nonoperative treatment should have consideration given to arthroscopic drilling to promote healing before the lesion progresses and requires more involved treatment with a less optimistic prognosis. (Kocher et al., 2006)

<sup>6</sup> Numerous studies have shown that nicotine impairs wound healing. Patients who smoke have worse preoperative function and obtain less benefit from ACI than non-smokers (Minas T, 2001; Riebel et al., 1995; Raikin et al., 1998; Jaiswal et al., 2009)

<sup>7</sup> The location of the injury plays a role in the success of the procedure, with clinical improvement seen in >90% for isolated femoral condylar lesions, with follow-up as long as 9 years, and as low as 60% for lesions of the patella. (Peterson et al., 2000)

<sup>8</sup> Although studies of ACI have included subjects with osteochondritis dissecans(OCD), use of Carticel® for the treatment of this condition is off-label. OCD is an acquired, potentially reversible lesion of the subchondral bone that may result in separation and instability of the overlying articular cartilage. The exact cause of OCD remains unknown. Multiple causes of OCD have been postulated, including endocrine imbalance, familial predisposition, vascular insufficiencies, epiphyseal abnormalities, and trauma. OCD is becoming increasingly more common as a cause of knee pain in teenagers and young adults. This may be due to earlier and

8. The cartilage defect is full-thickness (modified Outerbridge grade III or IV), and measures between 2 and 10 cm<sup>2</sup> in area after debridement to healthy cartilage.
  - a. Arthroscopic debridement is recommended for defects < 1 cm<sup>2</sup>
  - b. A marrow stimulation technique (abrasion, drilling or microfracture) or osteochondral autograft is recommended and for defects 1 – 2 cm<sup>2</sup>
  - c. Osteochondral allograft is recommended for defects greater than 10 cm<sup>2</sup>
9. In cases where the depth of the defect exceeds 8 – 10 mm, bone grafting is planned either at the time of the biopsy, as a separate procedure, or at the time of implantation of the cultured chondrocytes.
10. The plan member has failed a prior surgical repair procedure (e.g., arthroscopic debridement, microfracture, drilling/abrasion arthroplasty, or osteochondral allograft/autograft).
11. The plan member has intact, fully functional menisci and ligaments, normal alignment and normal joint space. The following conditions should be assessed and treated prior to or concurrent with implantation with Carticel®:
  - a. Unstable meniscus tears should be repaired or resected.
  - b. If the patient has had a total meniscectomy, absent meniscus should be reconstructed.
  - c. Instability of the knee may adversely affect the success of the procedure and should be corrected. The anterior and posterior cruciate ligaments should be free of laxity as well as stable and intact. It is recommended that cruciate deficiencies be corrected.
  - d. Abnormal weight-distribution within the joint may adversely affect the success of the procedure and should be corrected. The tibial/femoral joint should be properly aligned. When treating trochlear defects, abnormal patellar mechanics should be assessed and corrected.
12. The plan member does not have an arthritic condition that appears on standing X-rays as joint space narrowing, osteophytes, or changes in the underlying bone. The plan member does not have an inflammatory (rheumatoid or other) or degenerative (osteoarthritis) arthritis.
13. The plan member has no known malignancies in the area of the cartilage biopsy or implant. The potential exists for in vitro expansion and subsequent implantation of malignant or dysplastic cells present in biopsy tissue. In addition, implantation of normal autologous chondrocytes could theoretically stimulate growth of malignant cells in the area of the implant.
14. The plan member has been thoroughly educated about the procedure and rehabilitation. The plan member has realistic expectations and agrees to comply with the rehabilitation protocol which may include a period of non-weight-bearing followed by limited weight-bearing for many weeks.

### Exclusions

1. ACL in pediatric patients (the safety and efficacy of Carticel® in pediatric patients has not been established). Carticel® is not FDA-approved for use in pediatric patients.

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increasingly competitive athletic endeavors. In addition, the widespread use of MRI as a diagnostic tool for evaluating knee injuries has undoubtedly led to earlier recognition of OCD lesions. In patients with open growth plates, healing is reported in 50% of lesions within 10 to 18 months when treated with immobilization and non-weight bearing. (Owens and Latterman, 2009)

2. ACI in adults over age 65 (the safety and efficacy of Carticel® in adults over the age of 65 has not been established). Carticel® is not FDA-approved for use in adults over the age of 65.
3. ACI for the treatment of articular cartilage defects on the patella (the safety and efficacy of Carticel® for the treatment of patellar cartilage defects has not been established). Carticel® is only FDA-approved to treat articular cartilage defects on the medial or lateral femoral condyle or trochlea.
4. ACI for the treatment of articular cartilage defects on the talus (the safety and efficacy of Carticel® for the treatment of talar cartilage defects has not been established). Carticel® is only FDA-approved to treat articular cartilage defects on the medial or lateral femoral condyle or trochlea.

### Coding

Codes	Number	Description
CPT	29870	Arthroscopy, knee, diagnostic, with or without synovial biopsy
	27412	Autologous chondrocyte implantation, knee
HCPCS	J7330	Autologous cultured chondrocytes, implant

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### Reference

1. Hayes Directory. Autologous Chondrocyte Implantation of the Knee. October 28, 2008. © Winifred S. Hayes, Inc.
2. Hayes Update Search. Autologous Chondrocyte Implantation of the Knee. October 12, 2010. © Winifred S. Hayes, Inc.
3. Harris JD, Siston RA, Pan X, Flanigan DC. Autologous Chondrocyte Implantation: A Systematic Review. *J Bone Joint Surg Am.* 2010 Sept;92(12):2220-33.
4. Nejadnik H, Hui JH, Feng Choong EP et al. Autologous Bone Marrow-Derived Mesenchymal Stem Cells Versus Autologous Chondrocyte Implantation: An Observational Cohort Study. *Am J Sports Med.* 2010 Jun;38(6):1110-6.
5. Heir S, Nerhus TK, Rotterud JH, et al. Focal Cartilage Defects in the Knee Impair Quality of Life as Much as Severe Osteoarthritis: A Comparison of Knee Injury and Osteoarthritis Outcome Score in 4 Patient Categories Scheduled for Knee Surgery. *Am J Sports Med.* 2010;38(2):231-7.
6. Ding C, Cicuttini F, Scott F, et al. Natural History of Knee Cartilage Defects and Factors Affecting Change. *Arch Intern Med.* 2006;166:651-8.
7. Gomoll AH, Farr J, Gillogly SD, Kercher J, Minas T. Surgical Management of Articular Cartilage Defects of the Knee. *J Bone Joint Surg Am.* 2010;92(14):2470-90.
8. Dozin B, Malpeli M, Cancedda R et al. Comparative Evaluation of Autologous Chondrocyte Implantation and Mosaicplasty: A Multicentered Randomized Clinical Trial. *Clin J Sport Med.* 2005 Jul;15(4):220-6.
9. Felson DT, Ahang Y, Anthony JM, Naimark A, Anderson JJ. Weight Loss Reduces the Risk for Symptomatic Knee Osteoarthritis in Women. The Framingham Study. *Ann Intern Med.* 1992;116(7):535-9.
10. Mithoefer K, McAdams T, Williams RJ, Kreuz PC, Mandelbaum BR. Clinical Efficacy of the Microfracture Technique for Articular Cartilage Repair in the Knee: An Evidence-Based Systematic Analysis. *Am J Sports Med.* 2009;37(10):2053-63.

11. William R, Harnly H. (2007) Microfracture: Indications, Technique and Results. *Instr Course Lect.* 56:419-28.
12. Mithoefer K, Williams RJ 3rd, Warren RF, et al. Chondral Resurfacing of Articular Cartilage Defects in the Knee with the Microfracture Technique. *Surgical Technique. J Bone Joint Surg Am.* 2006;88 Suppl 1:294-304.
13. Mithoefer K, Williams RJ 3<sup>rd</sup>, Warren RF, et al. High Impact Athletics After Knee Articular Cartilage Repair: A Prospective Evaluation of the Microfracture Technique. *Am J Sports Med.* 2006;34:1413-8.
14. Kreuz PC, Erggelet C, Steinwachs MR et al. Is Microfracture of Chondral Defects in the Knee Associated with Different Results in patients Aged 40 Years or Younger? *Arthroscopy.* 2006;22:1180-6.
15. Bedi A, Feeley BT, Williams RJ 3rd. Current Concepts Review. Management of Articular Cartilage Defects of the Knee. *J Bone Joint Surg Am.* 2010;92:994-1009.
16. Henn RF 3rd, Comoll AH. A Review of the Evaluation and Management of Cartilage Defects in the Knee. *The Physician and Sportsmedicine.* 2011 Feb;1(39):101-7.
17. Brittberg M, Lindahl A, Nilsson A, et al. Treatment of Deep Cartilage Defects in the Knee with Autologous Chondrocyte Transplantation. *N Engl J Med.* 1994;331(14):889-95.
18. Mithoefer K, Williams RJ 3rd, Warren RF, et al. The Microfracture Technique For The Treatment Of Articular Cartilage Lesions In The Knee: A Prospective Cohort Study. *J Bone Joint Surg Am.* 2005;87: 1911–1920.
19. Choi YS, Potter HG, Chun TJ. MR Imaging of Cartilage Repair in the Knee and Ankle. *RadioGraphics.* 2008 Jul-Aug;28(4) 1043-59.
20. Jaiswal PK, Macmull S, Bentley G, et al. Does Smoking Influence Outcome After Autologous Chondrocyte Implantation? *J Bone and Joint Surg Br.*2009;91-B(12):1575-8.
21. Jaiswal PK, Park DH, Jagiello J, et al. Is Autologous Chondrocyte Implantation Effective in Overweight Patients? *J Bone and Joint Surg Br* 2008;90-B(Supp III):578.
22. Wall EJ, Vourazeris J, Myer GD, et al. The Healing Potential of Sable Juvenile Osteochondritis Dissecans Knee Lesions. *J bone Join Surg Am.* 2008;90:2644-64.
23. Kocher MS, Tucker R, Ganley TJ and Flynn JM. Management of Osteochondritis Dissecans of the Knee: Current Concepts Review. *Am J Sports Med.* 2006 Jul;34(7):1181-91.
24. U.S. Food and Drug Administration (FDA). Center for Biologics Evaluation and Research. Product Approval Information, Autologous Cultured Chondrocytes (Carticel®). (Package Insert Revision). FDA; June 21, 2007. <http://www.fda.gov/downloads/BiologicsBloodVaccines/CellularGeneTherapyProducts/ApprovedProducts/UCM109339.pdf>.
25. Gudas R, Kalesinskas RJ, Kimtys V, et al. A Prospective Randomized Clinical Study of Mosaic Osteochondral Autologous Transplantation Versus Microfracture For The Treatment Of Osteochondral Defects in yhe Knee Joint In Young Athletes. *Arthroscopy.* 2005;21:1066-1075.
26. Peterson L, Minas T, Brittberg M, Nilsson A, Sjogren-Jansson E, Lindahl A. Two to Nine Year Outcome After Autologous Chondrocyte Transplantation of the Knee. *Clin Orthop Relat Res.* 2000;374:212-234.
27. Minas T. Autologous Chondrocyte Implantation For Focal Chondral Defects of the Knee. *Clin Orthop Relat Res.* 2001;391S:S349-S361.
28. Riebel GD, Boden SD, Whiteside TE, Hutton WC. The Effect of Nicotine on Incorporation of Cancellous Bone Graft in an Animal Model. *Spine.* 1995;20:2198-2202.

29. Raikin SM, Landsman JC, Alexander VA, Froimson MJ, Plaxton NA. Effect of Nicotine on the Rate and Strength of Long Bone Fracture Healing. *Clin Orthop Relat Res.* 1998;353:231-237.
30. Bartlett W, Skinner JA, Gooding CR et al. Autologous Chondrocyte Implantation Versus Matrix-Induced Autologous Chondrocyte Implantation for Osteochondral Defects of the Knee: A Prospective, Randomised Study. *J Bone Joint Surg Br.* 2005 May;87(5):640-5.
31. Owens JB and Latterman C. Management of Osteochondritis Dissecans of the Knee. In: Cole BJ II and Gomoll A, eds. *Biologic Joint Reconstruction: Alternatives to Arthroplasty.* 2009 SLACK Incorporated.

### Products to Which This Policy Applies

- ⊕ FCHP Direct & Select Care
- ⊕ Fallon Preferred Care (PPO)
- ⊕ Major Medical
- ⊕ Commonwealth Care
- ⊕ Companion Care
- ⊕ MassHealth
- ⊕ Fallon Senior Plan™
- ⊕ NaviCare
- ∅ Summit Elder Care® PACE (With the exception of emergency care, all services for Summit ElderCare® PACE participants must be authorized and arranged by the Summit ElderCare (SE) Interdisciplinary Team (IDT) overseeing the care for that participant. The applicable IDT can be determined by the HCO code on the participant ID card. A Summit ElderCare clinician is always on call and can be reached by dialing any of the site telephone numbers.)

### Committee review dates:

Technology Assessment Committee: 10/01/03, 01/25/11, 06/28/11

#### IMPORTANT NOTE

**Not all services are covered for all products or employer groups.** This medical policy expresses FCHP's determination of whether certain services or supplies are medically necessary, experimental or investigational or cosmetic. FCHP has reached these conclusions based upon the regulatory status of the technology and a review of clinical studies published in peer-reviewed medical literature. Even though this policy may indicate that a particular service or supply is considered covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. Members and their providers need to consult the Evidence of Coverage to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and the plan of benefits, the provisions of the benefits plan will govern. However, applicable state mandates will 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. With respect to Medicare and Medicaid members, this policy will apply unless Medicare and Medicaid policies extend coverage beyond this medical policy.