Autografts and Allografts in the Treatment of Focal Articular Cartilage Lesions

Policy # 00091
Original Effective Date: 08/26/2002
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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Autologous Chondrocyte Implantation for Focal Articular Cartilage Lesions is considered in medical policy number 00006.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider osteochondral autografts/mosaicplasty and osteochondral allografts in the treatment of focal articular cartilage lesions to be eligible for coverage when patient selection criteria are met.

Patient Selection Criteria

Autograft
Coverage eligibility will be considered when ALL of the criteria listed below are met and no exclusion criteria are present (see exclusion criteria below):

- Size of cartilage defect is between 1.0 to 2.5 cm² total area; and
- Focal, full thickness, (grade III or IV) isolated defect of the knee involving the weight bearing surface of the medial or lateral femoral condyles, trochlear or patellar region caused by acute or repetitive trauma; and
- Age 15-55 years, or when > 55 years of age must not have arthritis present on x-ray; and
- Persistent symptoms of disabling localized knee pain for at least six months, which has failed to respond to conservative treatment; and
- Discrete lesion, single and unipolar (involving only one side of the joint – “kissing lesions” are not eligible for coverage), largely contained with near normal surrounding articular cartilage and articulating cartilage, (grades 0, 1, 2); and
- Normal joint space present; and
- Patient is willing and able to comply with post-operative weight-bearing restrictions and rehabilitation.

Allograft
Coverage eligibility will be considered when ALL of the criteria listed below are met and no exclusion criteria are present (see exclusion criteria below):

- Size of cartilage defect is greater than or equal to 2 cm² total area; and
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- Focal, full thickness, (grade III or IV) isolated defect of the knee involving the weight bearing surface of the medial or lateral femoral condyles or trochlear region caused by acute or repetitive trauma; and
- Age 15-55 years; and
- Persistent symptoms of disabling localized knee pain for at least six months, which has failed to respond to conservative treatment; and
- Inadequate response to a prior arthroscopic or other surgical repair procedure; and
- Intact meniscus; and
- Discrete lesion, single and unipolar (involving only one side of the joint - "kissing lesions" are not eligible for coverage), largely contained with near normal surrounding articular cartilage and articulating cartilage, (grades 0, 1, 2); and
- Normal joint space present. The lesion is largely contained with near normal surrounding articular cartilage and articulating cartilage, (grades 0, 1, 2); and
- Patient is willing and able to comply with post-operative weight-bearing restrictions and rehabilitation.

Exclusion Criteria
Coverage is not available for patients when ANY of the criteria listed below are present:
- Active infection, inflammation or osteoarthritis present in the joint; or
- Uncorrected maltracking/malalignment of the knee; or
- Unstable knee; or
- History of malignancy in bones, cartilage, fat or muscle in the treated leg; or
- Body Mass Index (BMI) of greater than 30.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

The use of osteochondral autografts/mosaicplasty and osteochondral allografts in the treatment of focal articular cartilage lesions when patient selection criteria are not met is considered investigative.*

Based on review of available data, the Company considers the use of osteochondral autograft/mosaicplasty and osteochondral allograft transplantation for joints other than the knee, including but not limited to, the ankle (talus) to be investigative.*

Based on review of available data, the Company considers the treatment of focal articular cartilage lesions with autologous minced cartilage to be investigative.*

Based on review of available data, the Company considers treatment of focal articular cartilage lesions with allogeneic minced cartilage to be investigative.*

Based on review of available data, the Company considers treatment of focal articular cartilage lesions with decellularized osteochondral allograft plugs (eg, Chondrofix) to be investigative.*
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Based on review of available data, the Company considers treatment of focal articular cartilage lesions with reduced osteochondral allograft discs (eg, ProChondrix, Cartiform) to be investigational.*

**Background/Overview**

Damaged articular cartilage can be associated with pain, loss of function, and disability, and can lead to debilitating osteoarthritis over time. These manifestations can severely impair an individual's activities of daily living and quality of life. Autologous or allogeneic grafts of osteochondral or chondral tissue have been proposed as treatment alternatives for patients who have clinically significant, symptomatic, focal defects of the articular cartilage. It is hypothesized that the implanted grafts chondrocytes retain features of hyaline cartilage that is similar in composition and property to the original articulating surface of the joint. If true, the restoration of a hyaline cartilage surface might restore the integrity of the joint surface and promote long-term tissue repair, thereby improving function and delaying or preventing further deterioration.

There are 2 main categories of conventional therapy for patients who have significant focal defects of the articular cartilage: symptom relief and articular surface restoration.

First, there are procedures intended to primarily achieve symptomatic relief: débridement (removal of debris and diseased cartilage); lavage (saline washout); and rehabilitation.

Second, there are procedures intended to restore the articular surface. Treatments may be targeted to the focal cartilage lesion and most such treatments induce local bleeding, fibrin clot formation, and resultant fibrocartilage growth. These include: abrasion arthroplasty, microfracture, and drilling, all of which are considered standard therapies. Fibrocartilage is generally considered to be less durable and mechanically inferior to the original articular cartilage. Thus various strategies for chondral resurfacing with hyaline cartilage have been investigated. Alternatively, treatments of very extensive and severe cartilage defects may resort to complete replacement of the articular surface either by osteochondral allotransplant or artificial knee replacement.

Efficacy of the microfracture technique was examined in a 2009 systematic review. Twenty-eight studies (total N=3122 patients) were selected; 6 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. A prospective longitudinal study of 110 patients by Solheim et al (2016) found that, at a mean of 12 years (range, 10-14 years) after microfracture, 45.5% of patients had poor outcomes, including 43 patients who required additional surgery.

Both fresh and cryopreserved allogeneic osteochondral grafts have been used with some success, although cryopreservation decreases the viability of cartilage cells, and fresh allografts may be difficult to obtain and create concerns regarding infectious diseases. As a result, autologous osteochondral grafts have been investigated as an option to increase the survival rate of the grafted cartilage and to eliminate the risk of disease transmission. Autologous grafts are limited by the small number of donor sites; thus allografts are typically used for larger lesions. In an effort to extend the amount of the available donor tissue, investigators have used multiple, small osteochondral cores harvested from non-weight-bearing sites in the knee for treatment of full-thickness chondral defects. Several systems are available for performing this procedure:
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the Mosaicplasty System (Smith and Nephew), the Osteochondral Autograft Transfer System (OATS; Arthrex), and the COR and COR2 systems (DePuy Mitek). Although mosaicplasty and OATS may use different instrumentation, the underlying mode of repair is similar (ie, use of multiple osteochondral cores harvested from a non-weight-bearing region of the femoral condyle and autografted into the chondral defect). These terms have been used interchangeably to describe the procedure.

Preparation of the chondral lesion involves débridement and preparation of recipient tunnels. Multiple individual osteochondral cores are harvested from the donor site, typically from a peripheral non-weight-bearing area of the femoral condyle. Donor plugs range from 6 to 10 mm in diameter. The grafts are press fit into the lesion in a mosaic-like fashion into the same-sized tunnels. The resultant surface consists of transplanted hyaline articular cartilage and fibrocartilage, which is thought to provide “grouting” between the individual autografts. Mosaicplasty or OATS may be performed with either an open approach or arthroscopically. Osteochondral autografting has also been investigated as a treatment of unstable osteochondritis dissecans lesions using multiple dowel grafts to secure the fragment. While osteochondral autografting is primarily performed on the femoral condyles of the knee, osteochondral grafts have been used to repair chondral defects of the patella, tibia, and ankle. With osteochondral autografting, the harvesting and transplantation can be performed during the same surgical procedure. Technical limitations of osteochondral autografting are difficulty in restoring concave or convex articular surfaces, incongruity of articular surfaces that can alter joint contact pressures, short-term fixation strength and load-bearing capacity, donor-site morbidity, and lack of peripheral integration with peripheral chondrocyte death.

Filling defects with minced articular cartilage (autologous or allogeneic), is a single-stage procedure that is being investigated for cartilage repair. The Cartilage Autograft Implantation System (CAIS, Johnson and Johnson, Phase III trial) harvests cartilage and disperses chondrocytes on a scaffold in a single-stage treatment. BioCartilage™ (Arthrex) consists of a micronized allogeneic cartilage matrix that is intended to provide a scaffold for microfracture. DeNovo NT Graft (Natural Tissue Graft) is produced by ISTO Technologies with exclusive distribution rights by Zimmer. DeNovo NT consists of manually minced cartilage tissue pieces obtained from juvenile allograft donor joints. The tissue fragments are mixed intraoperatively with fibrin glue before implantation in the prepared lesion. It is thought that mincing the tissue helps both with cell migration from the extracellular matrix and with fixation.

A minimally processed osteochondral allograft (Chondrofix™; Zimmer) is now available for use. Chondrofix is composed of decellularized hyaline cartilage and cancellous bone; it can be used “off the shelf” with precut cylinders (7-15 mm). Multiple cylinders may be used to fill a larger defect in a manner similar to OATS or mosaicplasty.

ProChondrix™ (AlloSource) and Cartiform™ (Arthrex) are wafer-thin allografts where the bony portion of the allograft is reduced. The discs are laser etched or porated and contain hyaline cartilage with chondrocytes, growth factors, and extracellular matrix proteins. ProChondrix is available in dimensions from 7 to 20 mm and is stored fresh for a maximum of 28 days. Cartiform is cut to the desired size and shape and is stored frozen for a maximum of 2 years. The osteochondral discs are typically inserted after microfracture and secured in place with fibrin glue and/or sutures.
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DeNovo ET graft (ISTO Technologies) uses juvenile allogeneic cartilage cells.

Autologous chondrocyte implantation (ACI) is another method of cartilage repair involving the harvesting of normal chondrocytes from normal non-weight-bearing articular surfaces, which are then cultured and expanded in vitro and implanted back into the chondral defect. ACI techniques are discussed in policy 00006.

**FDA or Other Governmental Regulatory Approval**

**U.S. Food and Drug Administration (FDA)**
The FDA considers orthopedic manual surgical instruments as class I devices. If a manufacturer's device falls into a generic category of exempted class I devices as defined in 21 CFR Parts 862-892, a premarket notification application and FDA clearance were not required before marketing the device in the United States. Harvesting and implantation are surgical procedures and therefore not subject to regulation by FDA.

Because there is no use of chemicals and minimal manipulation, allograft tissue does not require approval for marketing. FDA regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation (CFR) title 21, parts 1270 and 1271.

DeNovo® ET Live Chondral Engineered Tissue Graft (Neocartilage) is marketed by ISTO Technologies outside of the United States. FDA approved ISTO's investigational new drug application for Neocartilage in 2006, which allowed ISTO to pursue phase 3 clinical trials of the product in human subjects.

**Centers for Medicare and Medicaid Services (CMS)**
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

**Rationale/Source**
The most recent literature update for this policy was performed through October 10, 2016.

Assessment of the efficacy for a therapeutic intervention involves a determination whether the intervention improves health outcomes compared to available alternatives. The optimal study design for this purpose is a RCT that compares the therapeutic intervention with existing alternative treatments and includes clinically relevant measures of health outcomes. It is recognized that RCTs are extremely important to assess treatments of cartilage repair procedures, due to the expected placebo effect and the subjective nature of pain. The present review focuses on cartilage repair procedures of the knee, ankle, foot, and shoulder using autografts and autografts compared to débridement, marrow-stimulating procedures, and ACI. Following is a summary of key references to date.

**OSTEOCHONDRAL AUTOGRRAFT FOR ARTICULAR CARTILAGE LESIONS OF THE KNEE**
The evidence on osteochondral autograft transplantation surgery (OATS; mosaicplasty) for articular cartilage lesions of the knee includes systematic reviews and a number of RCTs that compare outcomes from OATS with marrow stimulation or ACI.
Systematic Reviews
A 2016 Cochrane review by Gracitelli et al evaluated surgical interventions (microfracture, drilling, osteochondral autografts, allograft transplantation) for the treatment of isolated cartilage defects of the knee in adults. Three RCTs selected compared OATS to microfracture for isolated cartilage defects. The evidence was assessed as of very low quality with high or unclear risk of bias.

In a 2008 systematic review, at short-term follow-up, neither of the “advanced” cartilage repair techniques (osteochondral transplantation or autologous chondrocyte transplantation) showed superior outcomes compared with traditional abrasive techniques. Finding 5 RCTs and 1 prospective comparative trial, Magnussen et al concluded that no single technique produced superior clinical results for treatment of articular cartilage defects, however, “any differences in outcome based on the formation of articular rather than fibrocartilage in the defect may be quite subtle and only reveal themselves after many years of follow-up. Similarly, complications such as donor-site morbidity in OATS may be late in their presentation and thus not be detected at short follow-up.” However, in a mid-term meta-analysis that included 5 RCTs (described below), Pareek et al (2016) found that Tegner Activity Scale (TAS) scores were higher and failure rates lower with OATS compared to microfracture. In subgroup analysis, activity scores were higher in the subset of patients treated with OATS who had lesions greater than 3 cm² at midterm follow-up.

In a 2011 systematic review, Harris et al evaluated whether outcomes from cartilage repair/restoration techniques remained successful if combined with meniscal allograft. Six level IV studies (case series) with 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 improved clinical outcomes at final follow-up compared with the preoperative condition. Outcomes were also compared with historical outcomes of each procedure performed in isolation. Four of the 6 studies found outcomes equivalent to procedures performed in isolation, suggesting that the combined procedures did not result in poorer outcomes.

Subsection Summary: Systematic Reviews
Several systematic reviews have evaluated osteochondral autografting for cartilage repair. Evidence is of low quality, and not all reviews found a benefit compared to abrasion techniques. However, there is evidence that, in patients with larger lesions and longer follow-up, treatment with osteochondral autografts decreases failure rates compared with abrasion techniques (eg, microfracture, drilling).

Randomized Controlled Trials
Osteochondral Autografts vs Microfracture
Studies included in the systematic reviews described above included 3 RCTs from the same group of investigators, 1 RCT with mid-term follow-up, and 1 RCT with long-term follow-up; they compared OATS to microfracture. These RCTs are detailed below.

Gudas et al (2005) reported on a blinded comparison of arthroscopic OATS versus microfracture for lesions of the femoral condyle (1-4 cm²) in 60 athletes between 15 and 40 years of age (mean, 24.3 years). Follow-up with 95% of the athletes for up to 3 years after surgery showed that more athletes returned to sports activities (mean, 6.5 months) following OATS (93% vs 52%) and fewer required revision (1 of 28 vs 9 of 29),
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both respectively. Overall, 96% of patients treated by OATS had an excellent or good result compared with 52% treated by microfracture. At 1-year follow-up, scores on the International Cartilage Repair Society (ICRS) cartilage grading system were higher in the OATS group and at 3-year follow-up, results from the Harris Hip Score (HSS) improved more in the OATS group. Blinded arthroscopic and histologic assessment in a subset of patients showed hyaline cartilage of normal appearance following transplantation, whereas microfracture frequently resulted in surface fibrillation and soft fibroelastic tissue. At 10-year follow-up, there were 4 (14%) failures in the OATS group and 11 (38%) failures in the microfracture group. TAS scores decreased in both groups over time, but remained significantly better following OATS than microfracture. In the subgroup of patients younger than 25 years of age at the time of surgery, 15 (75%) of 20 in the OATS group and 8 (37%) of 22 in the microfracture group maintained the same level of activity (competitive athletes or frequently sporting) as before the injury. The level of sporting activity was reported to decrease in older patients because of age or reasons unrelated to their knee injuries.

Another report by Gudas et al (2013) compared mosaicplasty to microfracture or débridement. One hundred two patients with lesions associated with anterior cruciate ligament (ACL) injury were randomized to 1 of the 3 procedures to repair their ACLs. A matched control group of 34 patients with ACL injury but no articular cartilage lesion was included as a comparator. The postoperative rehabilitation protocol was the same for the 3 treatment groups. At a mean 36.1-month follow-up, patients were evaluated with the International Knee Documentation Committee (IKDC) score, TAS score, and clinical assessment. All groups showed a significant improvement in the IKDC score compared with before surgery. Patients without cartilage lesions had significantly better IKDC subjective scores than patients with cartilage lesions. For the 3 groups with cartilage lesions, the mosaicplasty group's IKDC subjective knee evaluation was significantly better than those for the microfracture or débridement groups, although the differences between the groups were modest. TAS scores were similar for the mosaicplasty (7.1) and microfracture (6.9) groups, and slightly lower for the débridement group (6.2).

Gudas et al (2009) also published a randomized trial of OATS (n=25) versus microfracture (n=25) in children 12 to 18 years of age (mean, 14.3 years). Only children with grade 3 or 4 osteochondritis dissecans (OCD) defects of the femoral condyles were selected. The OCD defects were between 2 and 4 cm² in area, and the mean duration of symptoms was 24 months. Follow-up was obtained in 94% of patients. After 1 year, the proportion of excellent-to-good outcomes was similar for the 2 groups (92% for OATS vs 86% for microfracture). However, after a mean 4.2 years of follow-up (range, 3-6 years), the microfracture group showed 9 (41%) of 22 failures. By comparison, there were no failures in the OATS group, and good-to-excellent outcomes were obtained in 83% of the children. Magnetic resonance imaging (MRI) at a mean of 18 months after surgery showed no evidence of graft loosening or migration, with excellent or good repair in 19 (91%) of 21 children. By comparison, blinded evaluation showed excellent or good repair in 10 (56%) of 18 children after microfracture.

In 2012, Lim et al reported on an RCT comparing OATS (n=22), ACI (n=18), and microfracture (n=30). Outcomes were measured using the Lysholm Knee Scale (LKS), TAS, and HSS. All 3 procedures showed improvement in functional scores, with no significant differences between the groups. Arthroscopy at 1 year showed excellent or good results in about 80% of patients.
In 2014, Ulstein et al reported on a long-term randomized trial (median, 9.8 years; range, 4.9-11.4 years) comparing OATS to microfracture. This smaller study enrolled 25 patients with a lesion of the femoral condyle or trochlea, with an area between 2 and 6 cm\(^2\). There were no significant differences between the OATS and microfracture groups in patient-reported outcomes (LKS, Knee Injury and Osteoarthritis Outcome Score [KOOS]), muscle strength, or radiologic outcome. However, 4 of 11 patients in the microfracture group underwent a second cartilage procedure compared with none in the OATS group.

### Subsection Summary: Osteochondral Autografts vs Microfracture

We identified 5 RCTs that compared osteochondral autografting with microfracture. They are summarized in the systematic reviews. Although the quality of the studies is not high, there is evidence of lower rates of reoperation and higher activity levels, particularly in patients with larger lesions and at longer follow-up, when treated with osteochondral autografting. A limitation of this body of evidence is that most data came from a single research group.

### Osteochondral Autografts vs ACI

Several RCTs have compared OATS to ACI for the treatment of articular cartilage lesions. Bentley et al (2003) randomized 100 consecutive patients with larger symptomatic lesions of the knee (average, 4.7 cm\(^2\); range, 1-12 cm\(^2\)) to ACI or mosaicplasty. Seventy-four percent of lesions were on the femoral condyle and 25% were on the patella. Ninety-four patients had had 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 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. The lack of healing may be related to both the relatively large lesion size and the unusual prominent placement of the plugs in this study, which was intended to allow contact with the opposite articular surface. 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.

Dozin et al (2005) reported results from a multicenter RCT compared ACI with mosaicplasty. Forty-four subjects, who had a focal, symptomatic chondral injury of Outerbridge grade III or IV with no previous surgical treatment, were randomized to ACI or mosaicplasty 6 months after undergoing arthroscopic débridement. Average lesion size was 1.9 cm. There was a high dropout rate, with only about 50% of patients undergoing the procedure; 10 patients were cured by debridement. With intention-to-treat analysis, the percentages of patients who achieved complete success were 89% (16/18 evaluable cases) in the mosaicplasty arm versus 68% (13/19 evaluable cases) in the ACI arm (p=NS). The high rate of spontaneous improvement after simple débridement raises questions about the appropriateness of additional surgical intervention in patients with small lesions similar to those included in this trial.

Horas et al (2003) reported 2-year follow-up on a study of 40 patients (age range, 18-42 years) with an articular lesion of the femoral condyle (size range, 3.2-5.6 cm\(^2\)) who were randomized to undergo ACI or OATS. Eleven (28%) had had prior surgical treatment. Authors reported that both treatments improved symptoms (85% of each group), although those in the OATS group responded more quickly. Histomorphologic evaluation of 5 biopsy specimens at 2 years or less after transplantation indicated that the
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Osteochondral cylinders had retained their hyaline character, although investigators noted a persistent interface between the transplant and the surrounding original cartilage.

Subsection Summary: Osteochondral Autografts vs ACI
Of 3 RCTs identified that compared OATS with ACI, interpretation of 2 is limited. The study by Bentley et al may have been affected by the use of prominent plugs, while the study by Dozin et al included patients with smaller lesions, many of whom did not proceed to surgery. The third RCT included 40 patients with larger lesions (3.2-5.6 cm²) and reported similar improvements in symptoms for the 2 treatments.

Observational Studies
While observational studies do not provide evidence of efficacy or comparative efficacy, they may provide information about the durability of any observed improvements and potential impacts of patient selection factors. Observational studies have reported longer term outcomes and an impact of sex, age, and size and location of the lesion.

Hangody, who first reported use of the mosaicplasty technique in humans in 1992, has coauthored several different summaries and case series. A 2008 summary paper included descriptions of a prospective multicenter comparison of 413 resurfacing procedures and follow-up from 1097 mosaicplasties at the authors’ institution. Although authors reported that the comparative study found hyaline-like resurfacing to result in a better clinical outcome than other techniques, the cited study is not as a publicly available in a peer-reviewed publication. For the retrospective analysis, Hangody et al reported 789 implantations on the femoral condyles, 147 in the patellofemoral joint, 31 on the tibia condyles, 98 on talar domes, 8 on the capitulum humerici, 3 on humeral heads, and 11 on femoral heads. Clinical scores at long-term follow-up suggested good-to-excellent results in 92% of patients with femoral condylar implantations, 87% of tibial resurfacings, and 74% of patellar and/or trochlear mosaicplasty. Based on their experience with this procedure, Hangody et al considered the optimal indications to be lesions 1 to 4 cm² in diameter, patients 50 years of age or younger (due to decreased repair capacity with aging), and correction of instability, malalignment, and meniscal or ligamental tears.

Ollat et al (2011) reported a retrospective multicenter study from the French Society of Arthroscopy that included 142 patients at a mean follow-up of 8 years. (This technique has been used extensively in France due to restrictive legislation on restoration techniques, including chondrocyte transfer.) Mean lesion size was 2.29 cm², and mean number of plugs was 4 (range, 1-14). Most patients (81.8%) were satisfied or very satisfied with their functional outcomes and there was significant improvement in the ICRS, IKDC function, and Hughston scores at follow-up. Factors for a good prognosis were: male sex, location of the defect in the medial femoral condyle, OCD, deep, small defects, and a short interval before surgery.

Solheim et al (2010, 2013) reported 5- to 9-year (N=69) and 10- to 14-year (N=73) follow-up from patients treated for 1 to 5 cm² articular cartilage defects. The LKS score improved from 49 at baseline to 72 at mid-term and long-term follow-up. Visual analog scale (VAS) score for pain improved from 58 at baseline to 27 at mid-term follow-up and 33 at long-term follow-up. However, a poor outcome, defined as a Lysholm score of 64 or less or subsequent knee replacement, was observed in 40% of the patients by 10 to 14 years. Factors associated with a poor outcome were patient age (≥40 years at the time of surgery), female sex,
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and articular cartilage defects of 3 cm$^2$ or more. The failure rate was 83% for females 40 years or older with a defect area of 3 cm$^2$ or more compared to 12.5% for males younger than 40 years old with an articular cartilage defect less than 3 cm$^2$.

Other reports have focused on OATS for treating patellar lesions. In 2014, Astur et al prospectively analyzed 33 patients with symptomatic patellar lesions (diameter, 1-2.5 cm) treated with OATS. At a minimum 2-year follow-up (range, 24-54 months), all patients were reported to have significant improvement in functional scores, as measured by the LKS, Kujala, and Fulkerson scores and the 36-Item Short-Form Health Survey quality of life score. Nho et al (2008) reported average 29-month follow-up following patellar resurfacing with osteochondral autografts in 22 patients. Mean lesion size was 1.6 cm$^2$, filled with an average of 1.8 plugs per defect. The IKDC score improved from 47 preoperatively to 74 at follow-up. The activity of daily living score increased from 60 preoperatively to 85 at follow-up.

The importance of concomitant realignment procedures is addressed by other studies. Laprell and Petersen (2001) reported 6- to 12-year follow-up from 29 (83%) of 35 patients with severe osteochondral defects (77% with OCD) who were treated by autologous OATS. Average age of the patients at the time of surgery was 26 years. Clinical evaluation at an average of 8 years after the procedure found 12 (41%) patients to be normal, 14 (48%) as nearly normal, and 3 (10%, all of whom refused correction of malalignment) as abnormal. Another report (2007) described 7-year follow-up of 30 patients treated with autologous OATS for symptomatic grade III to IV chondral lesions (average, 1.9 cm; range, 1.0-2.5 cm). Nineteen patients received other procedures (ACL reconstruction, meniscectomy, medial collateral ligament repair) at the same time. MRI at 7 years showed complete bone integration in 96% of patients, complete integration of the grafted cartilage in 75% of cases, complete filling of the cartilage defect in 63%, and congruency of the articular surface in “some” patients.

Subsection Summary: Observational Studies

A number of observational studies have provided additional information with longer follow-up and factors (ie, patient age at the time of surgery, lesion size, location of lesion) associated with outcomes after treatment with osteochondral autografts. Overall, these studies have indicated that outcomes of osteochondral autografting are superior in younger male patients who have lesions smaller than 3 cm$^2$. Outcomes are reported to be superior in lesions of the femoral condyles, although treatment of patellar lesions has also been reported to improve pain and function.

Section Summary: Osteochondral Autograft for Articular Cartilage Lesions of the Knee

Several systematic reviews of RCTs have evaluated OATS for cartilage repair of the knee at short and mid term. The RCTs are not high quality, and not all reviews found a benefit compared to abrasion techniques. However, compared to abrasion techniques (eg microfracture, drilling), there is evidence that OATS decreases failure rates and improves outcomes in patients with medium size lesions (eg, 2-6 cm$^2$) when measured at longer follow-up. This is believed to be due to better durability of the natural hyaline cartilage compared to the fibrocartilage that is obtained with abrasion techniques. The least problematic RCT, which compared OATS to ACI in patients with lesions measuring 3.2 to 5.6 cm$^2$, found similar improvements in symptoms for both treatments. Factors shown to affect success in observational studies are younger male patients with lesions smaller than 3 cm$^2$. Thus, there is a relatively narrow range of lesion size for which
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OATS is most effective. In addition, the best results have been observed with lesions on the femoral condyles, although treatment of trochlea and patella lesions also improves outcomes. Correction of malalignment is important for success of the procedure.

OSTEOCHONDRAL ALLOGRAFT FOR ARTICULAR CARTILAGE LESIONS OF THE KNEE

Systematic Reviews
The 2016 Cochrane review by Gracitelli et al did not identify any RCTs on allograft transplantation.

A 2015 systematic review by De Caro et al included 11 articles that had at least 10 patients and were published in the previous 5 years. Articles included a combined total of 374 knees in 358 patients treated with osteochondral allografting. The size of the lesions ranged from 1 to 27 cm². Different outcome measures were used, but overall results showed improvement in objective and subjective clinical scores, a high rate of return to some level of sport or active duty, and graft survival rates of 82% at 10 years and 66% at 20 years. Although bony integration was usually achieved, cartilage integration was limited. In a 2015 review of indications, techniques, and outcomes, Chui et al stated that osteochondral allografting is indicated for lesions greater than 2 cm² for which other techniques such as microfracture, OATS, and ACI are inadequate due to the size, location, or depth of the lesion. Reviewers also considered osteochondral allografting to be a salvage procedure for previously failed restoration treatments of the knee.

Observational Studies
Long-term outcomes with osteochondral allografting have been reported in other case series. Emmerson et al (2007) reported mean 7.7 year follow-up (range, 2-22 years) for 66 knees of 64 patients who underwent fresh osteochondral allografting for OCD of the femoral condyle. All patients had undergone previous surgery, with an average of 1.7 prior surgeries on each knee. Mean allograft size was 7.5 cm². One knee was lost to follow-up. Of the remaining 65 knees, 10 (15%) knees had additional surgery, 47 (72%) were rated good to excellent, and 8 (13%) were rated fair to poor. Kaplan-Meier analysis demonstrated a 91% graft survival rate at 5 years and 76% graft survival rates at 10 and 15 years. The mean D’Aubigne and Postel score improved from 13.0 (fair) preoperatively to 16.4 (good) at the most recent follow-up. Subjective knee function improved from a mean of 3.4 to 8.4 on a 10-point scale.

Gross et al (2005) reported minimum 5-year follow-up on a series of 60 patients who received femoral condylar grafts and 65 patients who received tibial plateau grafts for knee defects. Eligible recipients of allografts were younger than 60 years and had traumatic unipolar osteochondral defects of at least 3 cm in diameter and 1 cm deep. If the meniscus was also significantly damaged, it was resected and replaced with allograft meniscus. Realignment of the involved leg was also performed to unload the graft. Patients were assessed preoperatively and postoperatively using the modified HSS. If there were no outcome data in the database within the last 12 months, the patients were contacted and a follow-up visit was arranged or a questionnaire was administered by telephone. Referring physicians were also contacted to obtain recent radiographs of the knee. Follow-up was obtained for 86% of patients who received a femoral graft (average, 10 years) and 97% of patients with a tibial graft (average, 11.8 years). For the femoral grafts, 12 failed and required graft removal or conversion to total knee replacement. At the end of the study period, 48 (80%) of the 60 femoral grafts were in situ with an average HSS of 83 out of 100. Kaplan-Meier analysis showed a 95% graft survival rate at 5 years, 85% at 10 years, and 74% at 15 years. For the tibial grafts, 21 failed at a
mean interval of 9.7 years. At the end of the study, 44 (68%) of 65 tibial grafts were in situ and functioning with an HSS greater than 70 points. Survival analysis revealed a 95% graft survival rate at 5 years, 80% at 10 years, and 65% at 15 years.

Osteochondral allografting for patellar cartilage injury was reported by Gracitelli et al (2015). Of 28 knees (27 patients) that had osteochondral transplantation, 8 (28.6%) were considered failures and 9 (45%) required further surgery. Allograft survival was estimated to be 78.1% at 10 years and 55.8% at 15 years. The mean follow-up duration was 9.7 years (range, 1.8-30.1 years) for the 20 knees (71.4%) with intact grafts.

Section Summary: Osteochondral Allograft for Articular Cartilage Lesions of the Knee
The evidence on osteochondral allografts for articular cartilage lesions includes case series and systematic reviews of case series. Due to the lack of alternatives, this allograft procedure may be considered a salvage operation in younger patients for full-thickness chondral defects of the knee caused by acute or repetitive trauma when other cartilage repair techniques (eg, microfracture, osteochondral autografting, ACI) would be inadequate due to the size, location, or depth of the lesion.

OSTEOCHONDRAL AUTOGRAPH FOR ARTICULAR CARTILAGE LESIONS OF THE ANKLE
One small RCT and several case series have been identified on osteochondral autografting for lesions of the talus.

Systematic Reviews
Zengerink et al published a systematic review on treatment of osteochondral lesions of the talus in 2010. Fifty-one nonrandomized and 1 randomized trial were included. Success rates averaged 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, reviewers concluded that bone marrow stimulation is the treatment of choice for primary osteochondral talar lesions.

Randomized Controlled Trials
The sole RCT identified assigned 32 patients with osteochondral lesions of the talus to chondroplasty, microfracture, or OATS. This 2006 study found similar improvements (≥40 points) for the 3 treatment groups, as measured by the American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Score (baseline score, 31-37) and the Subjective Assessment Numeric Evaluation (baseline score, 35-36). Complication rates were also similar. Postoperative pain, measured by numeric pain intensity scores, was greater following OATS (5.25) than after chondroplasty (3.3) or microfracture (3.4).

Observational Studies
The largest prospective series included 32 patients who underwent open osteochondral autografting of the talus for OCD. Osteochondral grafts were harvested from the ipsilateral knee and placed in the talus after medial malleolar osteotomy. At baseline, average AOFAS Ankle-Hindfoot Score was 59.1. At a mean of 16.8 months of follow-up (range, 12-24 months), the AOFAS score had improved to 87.9. All patients showed an improvement of at least 20 points. The LKS score, used to assess donor-site morbidity, was 88
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points at 6 weeks postoperatively and 98 points at 6 months. Two patients had persistent knee pain at the last follow-up.

A number of retrospective series have assessed OATS for various types of lesions. Many of these patients had already failed a prior surgical intervention such as microfracture. For example, Scranton et al (2006) reported on 50 consecutive patients with a type-V cystic talar defect who were treated with a single osteochondral graft (15 mm) taken from the ipsilateral knee. Thirty-two (64%) patients had undergone a previous surgical procedure on the ankle; further surgery was required in 17 (34%) patients. In 2006, Kreuz et al reported outcomes from a series of 35 patients who underwent osteochondral grafting from the ipsilateral talar articular facet (with or without osteotomy) following failed bone marrow stimulation. Six of the patients had previously undergone osteochondral or cancellous bone grafting of the defect area. Mean lesion size was 6.3 mm. At a mean follow-up of 49 months (range, 33-77 months), the AOFAS Ankle-Hindfoot Score had improved from 54.5 (range, 47-60) to 89.9 points (range, 80-100).

Longer term outcomes following osteochondral autografts of the talus were reported in 2011 in 28 consecutive patients. The osteochondral grafts were harvested from the femoral condyles and malleolar osteotomies were performed whenever the osteochondral defect could not be reached from the anterior incision. One patient was lost to follow-up and 2 had a surgical revision of the ankle. For 16 (64%) of the remaining 25 patients, the autograft was the first line of treatment, and in 9 (36%) patients, it was a second surgical intervention. Between baseline and an average 7 years of follow-up (range, 53-124 months), the AOFAS Ankle-Hindfoot Score increased from 50 to 78 points, the TAS score increased from 3.1 to 3.7, and VAS score for pain decreased from 7.8 to 1.5. Patients who had transplant as a second procedure had significantly worse AOFAS (62 vs 87) and TAS scores (2.0 vs 4.6) and higher VAS scores (3 vs 0.6), all respectively.

Osteochondral autografting for OCD was reported by Hangody et al (2001) for 36 consecutive patients. Most patients had previous surgical interventions and presented with stage III or IV lesions (completely detached or displaced fragment). The average size of the defect was 1 cm, and the average number of grafts per patients was 3 (range, 1-6). At mean follow-up of 4.2 years, ankle function measured by the Hannover scoring system showed good-to-excellent results in 34 (94%) cases. Examination by radiograph, computed tomography (CT), and MRI showed incorporation into the recipient bed and congruency of the articular surface.

Donor-Site Morbidity

One study (2007) evaluated donor-site morbidity in 11 of 15 patients who had undergone graft harvest from the knee (mean, 2.9 plugs) for treatment of osteochondral lesions of the talus. At an average 47-month follow-up (range, 7-77 months), 5 patients were rated as having an excellent LKS score (95-100 points), 2 as good (84-94 points), and 4 as poor (≤64 points). Reported knee problems were instability in daily activities, pain after walking 1 mile or more, having a slight limp, and difficulty squatting. Hangody et al (2001) reported that some patients had slight or moderate complaints with physical activity during the first postoperative year, but there was no long-term donor-site pain in a series of 36 patients evaluated 2 to 7 years after OATS. A 2009 report from Europe described OATS for lesions of the talus in 200 patients, 112 of whom had been followed for a minimum of 2 years. The focus of this study was to determine factors...
contributing to donor-site morbidity in the knee, rather than outcomes for the talus. The number of grafts, size of the transplanted plugs, and patient age were not related to donor-site morbidity. Body mass index (BMI) was significantly associated with knee scores, with a decrease in Lysholm score by 1 point (1%) for each point increase in BMI. Interpretation of these results was limited by the lack of preoperative assessment of knee pain and function.

**Section Summary: Osteochondral Autograft for Articular Cartilage Lesions of the Ankle**
A systematic review and an RCT (included in the systematic review) found similar improvements in outcomes following either microfracture or OATS. Given the lack of benefit compared to microfracture and the increase in donor-site morbidity with graft harvest from the knee, the current evidence does not support the use of OATS as a primary treatment for articular cartilage lesions of the ankle. There are observational studies on patients whose ankles failed a prior surgical procedure (not presented here). Donor-site morbidity has also been reported. Further study in prospective trials is needed to evaluate outcomes for this procedure.

**OSTEOCHONDRAL ALLOGRAFT FOR ARTICULAR CARTILAGE LESIONS OF THE ANKLE**
Use of allografts for large defects of the talus has been reported in case series. Due to the relatively rare occurrence of this condition, most series have fewer than 20 patients.

The largest series, from Bugbee et al (2013), reviewed outcomes of 86 ankles (82 patients) treated with bipolar fresh osteochondral allografts for arthritis of the tibiotalar joint. All patients had declined arthrodesis. Patients who did not present for follow-up were contacted via telephone and/or mail to obtain subjective outcomes. At a mean follow-up of 5.3 years (range, 2-11 years), 36 (42%) ankles had undergone additional surgery. Twenty-five (29%) ankles were considered clinical failures (ie, revision allograft, conversion to total ankle arthroplasty, arthrodesis, amputation) and 11 (13%) ankles had undergone surgeries that did not involve graft removal. Radiographic evaluation categorized 29 (46%) of 63 ankles as failures, with graft collapse observed in 11 (38%) of the 29. Survival of the osteochondral allografts estimated by Kaplan-Meier analysis was 76% at 5 years and 44% at 10 years. For patients who did not undergo additional surgery, 62% were classified as having excellent-to-good results, 26% as fair, and 12% as poor.

Two prospective studies also reported high failure rates. In 2012, Haene et al prospectively studied fresh talar osteochondral allografts in 16 patients (17 ankles) with large osteochondral lesions of the talus. CT at an average follow-up of 4.1 years (range, 2-6 years) identified failure of graft incorporation in 2 ankles, osteolysis in 5, subchondral cysts in 8, and degenerative changes in 7 ankles. Clinically, 5 (29%) ankles were considered failures, and 2 (12%) required additional surgery. Berlet et al reported a 2011 prospective study in 12 patients who had received an osteochondral allograft for talar defects. All patients had failed at least 1 prior surgical treatment and had a mean lesion size of 1.5 cm². At follow-up (mean, 3.3 years), AOFAS Ankle-Hindfoot Scores improved from 61 at baseline to 79. Radiographs and MRI performed yearly showed radiolucencies in 3 (25%) grafts, edema in 4 (33%), and failure to incorporate for 1 graft.

El-Rashidy et al (2011) retrospectively reviewed 38 of 42 patients treated with osteochondral allografts. All patients had failed conservative management; mean lesion size of 1.5 cm². At an average follow-up of 38 months. Including scores from 4 (10.5%) patients in whom graft failure occurred, the AOFAS Ankle-Hindfoot
Section Summary: Osteochondral Allograft for Articular Cartilage Lesions of the Ankle

The evidence on osteochondral allografts for articular cartilage lesions of the ankle includes case series. The largest series included 86 ankles. It reported a failure rate of nearly 30% with revision to a second allograft, ankle arthroplasty, fusion, or amputation.

OSTEOCHONDRAL AUTOGRAPH FOR ARTICULAR CARTILAGE LESIONS OF THE ELBOW

Systematic Reviews

A 2016 systematic review by Westermann et al included 24 case series (total N=492 patients) that assessed return to sports after operative treatment for OCD of the capitulum. The most common primary sport was baseball (371/464) followed by gymnastics (35/464). The overall return to sports was 86% at a mean 5.6 months. Average lesion size was similar for the different treatments among 8 studies with information available. Among all 24 studies, patients were more likely to return to their preoperative sport after OATS (0.95; 95% CI, 0.89 to 0.99) compared with débridement or microfracture (0.62; 95% CI, 0.46 to 0.77; p<0.001) or fixation with pins, wires, or screws (0.72; 95% CI, 0.51 to 0.89; p=0.01). Grafts were taken from the lateral femoral condyle or ribs.

Donor-Site Morbidity

Nishimura et al (2011) evaluated recovery of the donor knee after osteochondral autograft harvesting for capitellar OCD in 12 young athletes (age range, 12-17 years). Pain and function were assessed at 1, 2, 3, 6, 12, and 24 months after the surgery. Knee joint effusion persisted in 7 of the 12 patients at 1 month, but none had effusion at 3 months. At 3 months, muscle power of the knee extensor was reduced in 8 patients compared with the preoperative level. At 12 months, 11 patients had reached preoperative knee extensor muscle strength. All patients were pain-free at the donor site by 6 months (mean Lysholm score, 100) and returned to the previous competitive level of their sport.

Section Summary: Osteochondral Autograft for Articular Cartilage Lesions of the Elbow

OCD of the elbow typically occurs in patients who play baseball or do gymnastics. The literature on OATS for advanced OCD of the elbow consists of small case series, primarily from Europe and Asia, and a systematic review of case series. Although the meta-analysis suggested a benefit of OATS compared to débridement or fixation, RCTs are needed to determine the effects of the procedure with greater certainty.

OSTEOCHONDRAL AUTOGRAPH FOR ARTICULAR CARTILAGE LESIONS OF THE SHOULDER

A 2009 European study reported 9-year follow-up after OATS for cartilage defects of the shoulder in 7 patients. One additional patient was reported to have had donor-site morbidity at the knee and chose not to return for follow-up. All plugs showed full integration with the surrounding bone, and 6 of 7 patients showed a congruent joint surface. The Constant score improved from 76 points preoperatively to 90 points at 33 months and remained at 91 points at the 9-year follow-up. Subscores for pain and activities of daily living showed significant improvement at 33-month follow-up, with a very slight nonsignificant decline at 9-year follow-up. None of the patients required additional shoulder surgery.
MINCED CARTILAGE FOR ARTICULAR CARTilage LESIONS

Autologous Minced Cartilage

In 2011, Cole et al. reported a multicenter trial with 29 patients (out of 582 screened) randomized in a 1:2 ratio to microfracture or CAIS. In the single-stage CAIS procedure, autologous hyaline cartilage was harvested, minced, affixed on a synthetic absorbable scaffold, and then fixed on the lesion site with absorbable staples. At baseline, there were no significant differences between groups in the duration of symptoms, ICRS grade, and area and depth of the chondral defect. There was a difference in the gender and work status of the 2 groups. At 3 weeks and 6 months’ follow-up, there were no significant differences in outcomes between the 2 groups, but at later time points, there were differences reported. The IKDC score was significantly higher in the CAIS group compared to the microfracture group at both 12 (73.9 vs. 57.8) and 24 (83.0 vs. 59.5) months. All subdomains of the KOOS (Symptoms and Stiffness, Pain, Activities of Daily Living, Sports and Recreation, Knee-related Quality of Life) were significantly increased at 24 months in the CAIS group compared with microfracture patients. Qualitative analysis of MRI at 3 weeks and 6, 12, and 24 months showed no differences in fill of the graft bed, tissue integration, or presence of subchondral cysts. Adverse events were similar for the 2 groups.

Allogeneic Juvenile Minced Cartilage

Knee

Evidence on the efficacy of DeNovo NT is limited to case reports and small case series. The largest series identified was an industry-sponsored prospective study by Farr et al (2014), which included 25 patients with cartilage lesions of the femoral condyle or trochlea.49 Patients had symptomatic, focal, contained chondral lesions of the femoral condyles or trochlea with defect areas ranging between 1 cm² and 5 cm² (mean, 2.7 cm²; range 1.2-4.6 cm²). Mean number of prior surgeries was 1.1, with 18 patients reporting prior débridement and/or microfracture. Patients returned for follow-up at 3, 6, 12, 18, and 24 months for radiographs, IKDC examination, and completion of questionnaires. Outcomes included the KOOS, IKDC, Marx Activity Scale, and 100-mm VAS score for pain. IKDC score improved over the 24 months of follow-up. At 24 months, IKDC score had improved from 45.7 preoperatively to 73.6 of 100. There were also significant improvements in KOOS subscores (p<0.001) and VAS pain score (from 43.7/100 at baseline to 11.1 at 24 months, p<0.001). MRI showed a mean lesion fill of 109.7% with mild graft hypertrophy identified in 20.7% of patients. Of 11 elective second look arthroscopies at 24 months, 2 grafts (18%) showed either partial or complete delamination. Histology from 8 patients with biopsy showed a mixture of hyaline and fibrocartilage; areas with hyaline cartilage varied across sections. There was good integration with the surrounding native cartilage.

A 2013 study included 13 patients (15 knees) who received particulated juvenile allograft to the patella. Ten of the 15 knees underwent concomitant procedures, limiting interpretation of functional outcomes. Cartilage repair assessed at a mean of 28.8 months was reported to be nearly normal in 73% of knees while 27% of knees had evidence of graft hypertrophy. Currently available evidence is insufficient to evaluate the effect of this technology on health outcomes.

Ankle

Use of DeNovo NT for the talus has been reported in small case series. The largest series is from a preliminary report of a larger study. In this 2013 preliminary report, 24 ankles (23 patients) with
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Osteochondral lesions of the talus were treated with DeNovo NT. Fourteen of the ankles (58%) had failed at least 1 prior bone marrow stimulation procedure. At an average follow-up of 16.2 months, 78% of ankles had good-to-excellent scores on the AOFAS Ankle-Hindfoot Score, with a final mean VAS score of 24/100. However, 18 (76%) ankles had at least 1 concomitant procedure (hardware removal and treatment for impingement, synovitis, instability, osteophytes, malalignment), limiting interpretation of the functional results. One treatment failure was caused by partial graft delamination. Bleazey and Brigado (2012) retrospectively reviewed 7 patients treated with juvenile minced cartilage (DeNovo NT) together with sponge allograft. All had failed conservative therapy (walking boot, physical therapy), and 4 patients had failed microfracture. Patients were evaluated with VAS for pain and activity at 6-month follow-up. All showed clinically significant improvement. Pain during walking decreased from an average of 7.7 at baseline to 1.9 at 6 months. Ability to walk 4 blocks improved from a score of 4.8 to 9.2.

Section Summary: Minced Cartilage for Articular Cartilage Lesions

The evidence on autologous minced cartilage includes 1 small RCT from 2011. The evidence on allogeneic minced cartilage includes case reports and case series. The case series have suggested an improvement in outcomes compared with baseline, but there is also evidence of graft hypertrophy and delamination. For articular cartilage lesions of the knee, further evidence, preferably from RCTs, is needed to evaluate the effect on health outcomes compared with other available procedures. For articular cartilage lesions of the ankle, there are few treatment options and, in the largest case series, over half of the patients had failed prior marrow stimulation. However, the concomitant procedures performed in that study limited interpretation of its results. A randomized comparison with microfracture in patients who have not received prior treatment would permit greater certainty about conclusions on the effectiveness of this procedure.

Decellularized Osteochondral Allograft

The first report of use of decellularized osteochondral allograft plugs (Chondrofix) was published by Farr et al in 2016. Review of records for 32 patients identified high failure rates. With failure defined as structural damage of the graft identified by MRI or arthroscopy, or any reoperation resulting in removal of the allograft, 23 (72%) of 32 knees were considered failures.

Summary of Evidence

For individuals who have full-thickness articular cartilage lesions of the knee who receive osteochondral autografts, the evidence includes RCTs, systematic reviews of RCTs, and longer term observational studies. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Several systematic reviews have evaluated osteochondral autografting for cartilage repair at short and midterm. Compared to abrasion techniques (eg, microfracture, drilling), there is evidence that osteochondral autografting decreases failure rates and improves outcomes in patients with medium-size lesions (eg, 2-6 cm²) when measured at longer follow-up. This is believed to be due to the higher durability of hyaline cartilage compared to the fibrocartilage that is formed from abrasion techniques. There appears to be a relatively narrow range of lesion size for which osteochondral autografting is most effective. The best results have also been observed with lesions on the femoral condyles, although treatment of lesions on the trochlea and patella may also improve outcomes. Correction of malalignment is important for success of the procedure. The evidence suggests that osteochondral autografts may be considered an option for moderate-sized symptomatic full-thickness chondral lesions of the femoral condyle, trochlea, or patella. The
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evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have full-thickness articular cartilage lesions of the knee who receive osteochondral allografts, the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Due to the lack of alternatives, this procedure may be considered a salvage operation in younger patients for full-thickness chondral defects of the knee caused by acute or repetitive trauma when other cartilage repair techniques (eg, microfracture, osteochondral autografting, autologous chondrocyte implantation) would be inadequate due to the size, location, or depth of the lesion. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have full-thickness articular cartilage lesions of the ankle who receive osteochondral autografts, the evidence includes 1 small RCT, observational studies, and a systematic review of these studies. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The systematic review and an RCT found similar improvements in outcomes after microfracture or osteochondral autografting. Given the lack of established benefit compared to microfracture and the increase in donor-site morbidity with graft harvest from the knee, evidence does not support the use of osteochondral autografts as a primary treatment for articular cartilage lesions of the ankle. There are some observational studies in patients who have a failed a prior surgical procedure. Further study in prospective trials is needed to evaluate outcomes for osteochondral autografting as a secondary procedure. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have full-thickness articular cartilage lesions of the ankle who receive osteochondral allografts, the evidence includes 1 case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. These series have indicated high failure rates. The largest had a failure rate of nearly 30% with revision to a second allograft, ankle arthroplasty, fusion, or amputation. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have full-thickness articular cartilage lesions of the elbow who receive osteochondral autografts, the evidence includes a meta-analysis of case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Osteochondritis dissecans of the elbow typically occurs in patients who play baseball or do gymnastics. The literature on osteochondral autografts for advanced OCD of the elbow consists of small case series, primarily from Europe and Asia, and a systematic review of case series. Although the meta-analysis suggested a benefit of osteochondral autographs compared to débridement or fixation, RCTs are needed to determine the effects of the procedure with greater certainty. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have full-thickness articular cartilage lesions of the shoulder who receive osteochondral autografts, the evidence includes a case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Evidence on osteochondral autografting for the shoulder is very limited. The evidence is insufficient to determine the effects of the technology on health outcomes.
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For individuals who have full-thickness articular cartilage lesions of the knee, ankle, elbow, or shoulder who receive autologous or allogeneic minced articular cartilage, the evidence includes a small RCT and small case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The evidence on autologous minced cartilage includes 1 small RCT from 2011. The evidence on allogeneic juvenile minced cartilage includes a few small case series. The case series have suggested an improvement in outcomes compared with preoperative measures, but there is also evidence of graft hypertrophy and delamination. For articular cartilage lesions of the knee, further evidence, preferably from RCTs, is needed to evaluate the effect on health outcomes compared with other procedures. There are fewer options for articular cartilage lesions of the ankle. However, further study in a larger number of patients is needed to assess the short- and long-term effectiveness of this technology. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have full-thickness articular cartilage lesions of the knee, ankle, elbow, or shoulder who receive decellularized osteochondral allograft plugs or reduced osteochondral allograft discs, the evidence includes 1 small case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The single case series on decellularized osteochondral allograft plugs reported delamination of the implants, and high failure rates. No studies have been identified on reduced osteochondral allograft discs. The evidence is insufficient to determine the effects of the technology on health outcomes.

CLINICAL INPUT FROM 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.

2011 Input
In response to requests, input was received from 3 academic medical centers while this policy was under review in 2011. Clinical input generally agreed with the stated criteria for osteochondral grafting, with the exception of the following: input was mixed on the requirement for an inadequate response to a prior surgical procedure, the size of the lesion, and the requirement for an absence of meniscal pathology. Input was also mixed on the investigational status of osteochondral grafts in other joints, including the patellar and talar joints, and for the use of autologous minced cartilage.

2008 Input
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. All reviewers agreed that osteochondral autografts and allografts are considered reasonable for patients with full-thickness chondral defects who meet specific criteria.

ONGOING AND UNPUBLISHED CLINICAL TRIALS
Some currently unpublished trials that might influence this review are listed in Table 1.
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Table 1. Summary of Key Trials

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<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<td>Ongoing</td>
<td>NCT01347892* Post Market, Longitudinal Data Collection Study of Articular Cartilage Lesions in the Ankle Treated With DeNovo(R) NT</td>
<td>205</td>
<td>Sep 2019</td>
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<td>NCT01329445* Post Market, Longitudinal Data Collection Study of DeNovo NT for Articular Cartilage Defects of the Knee</td>
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<td>NCT01670617* A Stratified, Post-Market Study of DeNovo NT for the Treatment of Femoral and Patellar Articular Cartilage Lesions of the Knee</td>
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<td>Dec 2021</td>
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<td>Unpublished</td>
<td>NCT01410136* A Post Market Study to Evaluate the Chondrofix Osteochondral Allograft Utilized for Treatment of Subjects With Cartilage Lesions in the Knee</td>
<td>29</td>
<td>Terminated (enrollment)</td>
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NCT: national clinical trial.
* Denotes industry-sponsored or cosponsored trial.

References

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12/14/2004 Medical Policy Committee review. Coverage eligibility criteria revisions. Policy expanded to address osteochondral allografts as well as Osteochondral autografts.
01/31/2005 Managed Care Advisory Council approval
02/01/2006 Medical Director review
02/15/2006 Medical Policy Committee review
02/23/2006 Quality Care Advisory Council approval
07/07/2006 Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
04/04/2007 Medical Director review
04/18/2007 Medical Policy Committee approval. No change to coverage eligibility.
04/02/2008 Medical Director review
04/16/2008 Medical Policy Committee approval. No change to coverage eligibility.
04/02/2009 Medical Director review
04/15/2009 Medical Policy Committee approval. No change to coverage eligibility.
04/08/2010 Medical Director review
04/21/2010 Medical Policy Committee approval. No change to coverage eligibility.
04/07/2011 Medical Policy Committee approval
04/13/2011 Medical Policy Implementation Committee approval. No change to coverage eligibility.
04/12/2012 Medical Policy Committee review
04/25/2012 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/04/2013 Medical Policy Committee review
04/24/2013 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/03/2014 Medical Policy Committee review
04/23/2014 Medical Policy Implementation Committee approval. Investigational statements added on autologous and allogeneic minced cartilage.
09/03/2015 Medical Policy Committee review
09/23/2015 Medical Policy Implementation Committee approval. Added defect of patella area to eligibility criteria for osteochondral autografting. Title change.
11/03/2016 Medical Policy Committee review
01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
02/02/2017 Medical Policy Committee review
02/15/2017 Medical Policy Implementation Committee approval. Patient age limit in criteria changed from 50 to 55. Investigational statements added for decellularized osteochondral allograft plugs (eg, Chondrofix) and reduced osteochondral allograft discs (eg, ProChondrix, Cartiform).

Next Scheduled Review Date: 02/2018

Coding
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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
   1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
   2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
   3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and

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C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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