Clinical Policy Bulletin: Autologous Chondrocyte Implantation

Number: 0247

Policy

I. Aetna considers autologous chondrocyte implants medically necessary for repairing cartilage defects of the knee in members who meet the following selection criteria:

Member has symptoms of disabling knee pain related to a full thickness, focal chondral defect with all of the following:

A. Age of 15 to 60 years; and
B. Body mass index (BMI) less than or equal to 35 (see Appendix); and
C. Cooperative person for post-operative weight bearing restrictions and activity restrictions together with a potential for completion of post-operative rehabilitation; and
D. Failure of conservative therapy (minimum of 2 months of physical therapy) as well as established surgical interventions (i.e., microfracture, drilling, abrasion, or osteochondral autograft) (diagnostic arthroscopy, lavage, or debridement is not considered adequate to meet this criterion); and
E. Focal articular cartilage defect down to but not through the subchondral bone on a load bearing surface of the femoral condyle (medial, lateral, trochlear) (not in the patella); and
F. Informed consent with realistic expectations; and
G. No active inflammatory or other arthritis, clinically and by X-ray; and
H. Presence of disabling pain and/or knee locking; and
I. Procedure is not being done for treatment of degenerative arthritis (osteoarthritis); and
J. Size of defect measures less than 7 mm in depth, less than 6.0 cm in length, and area ranging from 1.6 to 10 square cm; and
K. Stable knee with intact meniscus and normal joint space on X-ray.
II. Aetna considers autologous chondrocyte implants experimental and investigational for patellar or talar lesions, or lesions of other joints (e.g., hip and shoulder) and all other indications because the effectiveness of autologous chondrocyte implants for these lesions has not been established.

III. Aetna considers matrix-induced chondrocyte implantation including the use of Bio-Gide (resorbable bilayer membrane made of porcine collagen) experimental and investigational for the treatment of osteochondral defects/lesions and all other indications because its effectiveness has not been established.

IV. Aetna considers combined meniscal allograft and autologous chondrocyte implantation of the knee experimental and investigational because of insufficient evidence of its effectiveness.

See also CPB 0637 - Osteochondral Autografts (Mosaicplasty, OATS).

**Background**

Articular cartilage damaged through acute or chronic trauma or osteochondritis dessecans, has limited ability to regenerate, leading to the symptoms of pain, restricted mobility and locking. Current treatment methods to stimulate repair of the cartilage include shaving the margins of the damaged cartilage to remove mechanical obstructions or irritants (abrasion or debridement) or drilling through the cartilage through the underlying bone into the vascular marrow in order to permit the ingrowth of fibrocartilage from the marrow. Long-standing severe damage to the articular cartilage can lead to debilitating osteoarthritis, which ultimately may require a total knee arthroplasty.

Autologous chondrocyte implants (autologous chondrocyte transplant) (Carticel, Genzyme Inc., Cambridge, MA) has been investigated as a means of a 3-step treatment for repairing cartilage defects in the knee. First, normal cartilage is harvested from a joint margin during an arthroscopic biopsy procedure. This biopsy of an articular surface serves as the source of cultured chondrocytes. This specimen of live articular cartilage is placed into a culture medium. Under a strictly controlled environment the cells are separated from the cartilage. These cells are then multiplied using a cell-culture technique. They are stored in the frozen state and are thawed and have a final culturing process before they are shipped to the operating room on the day of the implantation. It takes about 6
weeks to culture chondrocytes for implantation. Approximately 12 million cartilage
cells are present in the 0.4ml medium that is ultimately implanted into the defect.
The cultured chondrocytes are implanted into the cartilage defect in a second
open arthrotomy procedure.

Patients are referred for autologous chondrocyte implantation after already having
had surgery for an articular cartilage problem. If the patient remains symptomatic,
and the patient and the surgeon decide that autologous chondrocyte implant is the
best option, then an arthroscopic biopsy is planned.
Ideally, candidates for autologous chondrocyte implant should be between 15 and 60 years of age, have full thickness localized defects of the femoral condyles, have intact menisci, have no generalized chondromalacia, have no limb misalignment and are willing and able to undergo vigorous rehabilitation. This procedure is not recommended for patients who have an unstable knee and for patients sensitive to materials of bovine origins. It is also not recommended for use in children, and not yet in any joint other than the knee.

There is a paucity of evidence on the comparative efficacy of autologous chondrocyte implants to established surgical procedures for articular cartilage defects. An assessment by the BlueCross BlueShield Association Technology Evaluation Center (TEC, 2003) stated that there was insufficient evidence that the unique components of autologous chondrocyte implantation -- the implantation of cultured chondrocytes -- improves clinical outcomes. The TEC assessment noted that autologous chondrocyte implantation has 4 components -- (i) debridement of the injured area, (ii) coverage of the injured area with a periosteal tissue flap, (iii) implantation of cultured chondrocytes, and (iv) physical rehabilitation. The TEC assessment noted that 3 of the 4 components of autologous chondrocyte implantation -- use of a periosteal flap, debridement and rehabilitation -- are not unique to autologous chondrocyte implantation, and these components of the procedure may account for some or all of the clinical improvements noted in uncontrolled studies of this procedure. The TEC assessment stated: "[t]he available evidence is not sufficient to permit conclusions about the independent effect of the novel components of [autologous chondrocyte transplantation] ACT on health outcomes. The available evidence reports that ACT for the treatment of clinically significant, focal defects of the femoral condyle is associated with improved health outcomes such as diminished pain and improved joint function over the short term. However, the available evidence is not sufficient to determine if the improvements are caused by the use of autologous chondrocytes (the defining feature of ACT) or how the outcomes achieved with ACT compare with the outcomes achievable simply by use of debridement with rehabilitation."

The main deficiency of the existing evidence is that there are no published controlled studies that actually compare the outcomes of ACT with any other treatments or even with the natural progression of the disease. The available studies do report the proportions of patients treated with ACT who achieved various levels of outcomes, but there is no way to determine if those outcomes are better than, the same as, or worse than, the outcomes that would have occurred with other treatments.

Other published structured evidence reviews have reached similar conclusions about the paucity of comparative studies of autologous chondrocyte implantation (ACI). The National Institute for Clinical Excellence (2005) reviewed the evidence supporting the use of autologous chondrocyte implantation for full-thickness cartilage defects in knee joints. The assessment noted the paucity of prospective controlled clinical studies comparing the outcomes of autologous chondrocyte implantation to alternative treatment modalities. The assessment noted that most of the available evidence for autologous chondrocyte implant is from uncontrolled case series, and that this literature is subject to bias because of the inherent weakness of case series. The assessment also noted that the long-term impact of
Autologous chondrocyte implantation is poorly documented. The assessment concluded that it is not possible to draw definitive conclusions about the clinical effectiveness of this technology based on available literature. Quality Improvement Scotland (NHS QIS, 2005) concurred with the conclusions of the NICE assessment.

A evidence review prepared for the Cochrane Collaboration by Wasiak et al (2006) concluded that "[t]he use of ACI and other chondral resurfacing techniques is becoming increasingly widespread. However, there is at present no evidence of significant difference between ACI and other interventions." Four randomized controlled trials including 266 participants met inclusion criteria. One trial of ACI versus mosaicplasty (Bentley et al, 2003) reported statistically significant results for ACI at 1 year, but only in a post-hoc subgroup analysis of participants with medial condylar defects; when taking into account all participants, no significant differences were noted. A second trial of ACI versus mosaicplasty found no statistically significant difference in clinical outcomes at 2 years (Horas et al, 2003). There was no statistically significant difference in outcomes at 2 years in a trial comparing ACI with microfracture (Knutsen et al, 2004). In addition, 1 trial of matrix-guided ACI (MACI) versus microfracture did not contain enough long-term results to reach definitive conclusions (Basad et al, 2004). The review concluded that "[a]dditional good quality randomised controlled trials with long-term functional outcomes are required." An updated Cochrane review () reached similar conclusions, stating that "[t]here is insufficient evidence to draw conclusions on the use of ACI for treating full thickness articular cartilage defects in the knee. Further good quality randomised controlled trials with long-term functional outcomes are required."

An assessment by the National Coordinating Centre for Health Technology Assessment (NCCHTA) (Jobanputra et al, 2001) concluded that "autologous chondrocyte transplantation should be regarded as an experimental therapy." More recently, a cost-effectiveness analysis from NCCHTA (Clar et al, 2005) concluded that "[t]here is insufficient evidence at present to say that ACI is cost-effective compared with microfracture or mosaicplasty."

An assessment of autologous chondrocyte transplantation by the French National Authority for Health (HAS, 2005) concluded: "It is difficult to determine either the benefit/risk ratio or the role of the technique in managing isolated chondral tissue defects in young subjects, as there are insufficient comparative trials of a good level of evidence or long-term follow-up. Autologous chondrocyte transplantation is an emerging technique which is still very much in the development stage."

A systematic evidence review of autologous chondrocyte transplantation by the Galician Agency for Health Technology Assessment (AVALIA-T, 2005) found that "[t]here is no evidence showing that ACI is better than other procedures on the treatment of chondral lesions of the knee." A reassessment of ACI by the Galician Agency for Health Technology Assessment (AVALIA-T, 2006) reached similar conclusions: "Most of the articles are poor-quality case series; and cohort studies do not improve existing evidence. Clinical trials do not suggest better outcomes when comparing ACI against other procedures (mosaicplasty); but they point MACI [matrix-guided ACI] to be safer than ACI, mainly due to a decrease on the risk of periosteal hypertrophy." The assessment concluded that ACI has yet to
be proven superior to other procedures for osteochondral lesions of the knee, and
that randomized controlled clinical trials of ACI and MACI of the knee and ankle
are needed.

A systematic evidence review of ACI and MACI by the Ludwig Boltzmann Institute
for Health Technology Assessment (LBIHTA) concluded that MACI and ACI
should be considered as experimental techniques (Kunzl et al, 2009). The
systematic evidence review identified controlled clinical studies of at least 20
patients and follow-up of at least 1 year. The systematic evidence review
identified 9 comparative clinical trials that met inclusion criteria and 6 systematic
reviews. Among these studies, a total of 566 patients were treated with
mosaicplasty versus ACI, microfracture versus ACI, and ACI versus ACI. The
authors said that the results of their systematic evidence review shows
consistency and confirms the conclusions of earlier systematic evidence reviews.
The authors found that there is no evidence that ACI or MACI leads to better
outcomes in the treatment of osteochondral lesions than any of the alternative
treatments, and that ACI is not superior, and is at best equal, at is much higher
cost. The authors stated that the short term (1 to 2 years) and mid-term (5 years)
non-inferiority in highly selected active patients is proven; however, long-term data
are lacking. The authors concluded that "(M)ACI methods must be considered --
though often applied -- as experimental techniques. The risks of cultivated
chondrocycts cannot be ignored, and have to be seen as a risk."

An assessment of autologous chondrocyte implantation and matrix-induced
autologous chondrocyte implantation by the Australian Medical Services Advisory
Committee (2010) found that, overall, the safety, and, in the short to medium term,
the effectiveness of MACI/ACI appears to be comparable to those comparator
procedures evaluated in the MSAC assessment. The assessment stated that the
available studies were heterogeneous in terms of the patients recruited, the
MACI/ACI technique used and the measures used to assess patient outcomes,
which made it difficult to draw direct comparisons between the different
procedures across studies. The assessment stated that a further limitation of the
included studies was the length of follow-up reported. The assessment noted that
it has been suggested that any differences in outcome based on formation of
articular rather than fibrocartilage in the defect may be subtle and may only reveal
themselves after many years of follow-up (five to 10 years). However the majority
of studies in this assessment reported short to medium-term (one to three years)
follow-up of patients.

Published controlled clinical trials have compared autologous chondrocyte implant
to established procedures. Although results of available clinical studies have not
been consistent, the strongest available evidence suggests that outcomes of
microfracture may be superior to autologous chondrocyte implant. Knutsen et al
(2004) compared short-term clinical outcomes of autologous chondrocyte
implantation and microfracture in a randomized controlled clinical trial involving 80
persons with a single large symptomatic cartilage defect on the femoral condyle.
At 2-year follow-up, these investigators reported significantly better improvement
in functional status (according to the SF-36 physical component score) in the
microfracture group than in the autologous chondrocyte implantation group.
Knutsen et al (2007) reported on the results of 5-year follow-up. The investigators
found no significant difference in the clinical and radiographic results between the
Autologous Chondrocyte Implantation

A study reported in abstract form by Anderson et al (2003) compared autologous chondrocyte implantation with microfracture in 46 patients with full-thickness cartilage lesions greater than 2-cm in size. The investigators reported a mean improvement in the Cincinnati score was 3.1 for autologous chondrocyte implantation and 1.3 for microfracture. The investigators reported that the reduction in pain was also better with autologous chondrocyte implantation compared with microfracture. Although this study was prospective, there was no random assignment to treatment groups; thus this study is of weaker design than the previously reported studies by Knutsen et al (2004, 2007). In addition, this study has been criticized for having a high percentage of worker's compensation patients, and 5 of the 23 patients treated with microfracture were lost to follow-up.

There is inadequate evidence that the prior performance of marrow stimulation techniques affect the outcome of subsequent autologous chondrocyte implantation. Evidence from the Study of Treatment of Articular Repair (STAR) clinical trial found no significant difference in outcome of ACI between subjects whose prior surgery had been a marrow stimulation technique and subjects whose prior surgery had been a debridement. In this multi-center clinical study, 154 patients with failed treatment for articular cartilage defects of the knee received autologous chondrocyte implantation and were followed for 4 years. Outcomes included change from baseline in knee function, knee pain, quality of life, and overall health. The investigators reported that 126 patients (82 %) completed the protocol; 76 % of patients were treatment successes at study end, while 24 % were deemed treatment failures. Mean improvements were observed from baseline to all time points for all outcome measures. The investigators reported that results did not differ between patients whose primary surgery had been a marrow-stimulating procedure and those whose primary procedure had been a debridement alone.

Minas et al (2009) reported on a single institution study of 321 consecutive patients treated with autologous chondrocyte implantation for full-thickness cartilage defects that reached more than 2 years of follow-up. Patients were grouped based on whether they had undergone prior treatment with a marrow stimulation technique. Outcomes were classified as complete failure if more than 25 % of a grafted defect area had to be removed in later procedures because of persistent symptoms. The investigators reported that there were 522 defects in 321 patients (325 joints) treated with autologous chondrocyte implantation. On average, there were 1.7 lesions per patient. Of these joints, 111 had previously undergone surgery that penetrated the subchondral bone; 214 joints had no prior treatment that affected the subchondral bone and served as controls. Within the marrow stimulation group, there were 29 (26 %) failures, compared with 17 (8 %) failures in the control group.

Both of these studies are limited by their cohort nature. In addition, the study by Minas et al (2009) is subject to bias as all of the ACIs were treated by a single investigator, and the investigator's assessments and subsequent treatment decisions may have been influenced by the investigator's knowledge of the patients' prior procedures. Randomized controlled clinical trials are needed to
better assess whether marrow-stimulation techniques reduce the likelihood of success of subsequent ACI, or whether patients who fail marrow stimulation techniques would be more likely to fail ACI regardless of whether they had a prior marrow stimulation.

Two controlled clinical trials comparing autologous chondrocyte implantation with osteochondral transplant procedures have been published in recent years, with inconsistent results. Bentley et al (2003) reported on the results of a randomized controlled clinical trial comparing autologous chondrocyte implantation to mosaicplasty in 100 patients with symptomatic defects of the articular cartilage of the knee. After a mean follow-up of 19 months, functional assessment using the modified Cincinnati and Stanmore scores and objective clinical assessment showed that 88% had excellent or good results after autologous chondrocyte implantation compared with 69% after mosaicplasty. Horas et al (2003) reported on the results of a randomized clinical study comparing transplantation of an osteochondral cylinder to autologous chondrocyte implantation in 40 patients with an articular cartilage lesion of the femoral condyle. The investigators reported that the improvements in function in subjects receiving autologous chondrocyte implantation lagged behind subjects receiving osteochondral cylinder transplantation. In addition, the investigators reported that the defects treated with autologous chondrocyte implantation were primarily filled with fibrocartilage rather than hyaline cartilage. These studies have been criticized for the short duration of follow-up. LaPrade (2003) commented that "[f]urther study with a minimum follow-up of 5 years as well as a complete and thorough histologic analysis is needed to determine which technique, [autologous chondrocyte implantation] or autogenous osteocartilaginous transfer, is best."

There are no adequate prospective clinical studies of the effectiveness of autologous chondrocyte implantation on defects of the patella or talus. Prospective, randomized clinical studies are needed to assess the impact on functional status, disability, and pain. In addition, studies need to compare the effectiveness of autologous chondrocyte implantation to established methods of treatment of patellar or talus defects.

Mont et al (1999) reported on the use of autologous chondrocyte implantation for indications not supported by adequate clinical data, including the use of autologous chondrocyte implantation for patellar lesions. The investigators concluded: "The results of this study underscore the importance of controlled, application-limited experience before the release of new procedures for widespread clinical applications. The uncontrolled use of this procedure may negatively skew the overall results for this technique, prejudicing a procedure that may be successful for the correct indications."

Mandelbaum et al (2007) stated that the treatment of trochlear cartilage lesions is challenging given the likely presence of other patellofemoral joint pathologies, the topography of the area, and the limited available treatment options. Only 1 other study has examined the effectiveness of ACI for lesions of the patellofemoral joint. These researchers hypothesized that patients treated with ACI for moderate-to-large isolated lesions located on the trochlea will report improvement in the modified overall condition scale score of the Cincinnati Knee Rating System at a minimum 2-year follow-up. Using modified scales of the Cincinnati Knee Rating
System, a total of 40 Cartilage Repair Registry patients rated their overall condition and symptoms at baseline and at a mean follow-up of 59 +/- 18 months were studied. Factors likely to affect outcomes also were analyzed. At baseline, patients were between the age of 16 to 48 years, had a mean total defect size of 4.5 cm(2), and reported an overall condition score of 3.1 points (poor). Many failed a prior marrow-stimulation procedure (48 %). Other procedures performed before baseline included tibio-femoral osteotomy in 23 % and lateral release or Fulkerson for patella mal-tracking in 13 %. A total of 43 % of the patients were receiving workers’ compensation at baseline. Patients reported statistically significant improvement in their mean overall condition (3.1 points pre-operatively to 6.4 points post-operatively), pain (2.6 to 6.2 points), and swelling (3.9 to 6.3 points) scores. Eleven patients experienced 17 subsequent procedures, and no patients had a failed implantation. The authors concluded that ACI appears to improve function and reduce symptoms in young-to-middle aged patients with symptomatic, full-thickness articular cartilage lesions of the trochlea.

Farr (2007) noted that many patients with patellofemoral pain have multiple knee disorders, such as chondral defects, mal-alignment, and ligament insufficiency. This investigator reviewed a treatment approach that included ACI and biomechanical altering procedures to reduce impairment and symptoms in patients with patello-femoral lesions and biomechanical disorders. Thirty-eight patients (39 knees; mean age of 31.2 years) had large isolated (trochlear, 4.3 cm2; patellar, 5.4 cm2) or bipolar (mean total surface area of 8.8 cm2) patello-femoral lesions. The minimum follow-up was 0.5 years (median of 3.1 years; range of 0.5 to 5.1 years). The author observed a median improvement for the following patient and physician scores: modified Cincinnati Knee Rating System scores (3 points each), Lysholm score (31 points), and visual analog scale scores for resting (2 points) and maximum pain (3 points). At a mean follow-up of 1.2 years in the 22 patients (23 knees) undergoing second-look arthroscopy, ACI-repaired tissue scored a median of 11 of 12 points using the International Cartilage Repair Society cartilage repair assessment. Twenty-five patients had 32 subsequent surgeries, including 14 to remove hardware from a prior osteotomy; ACI failed in 3 patients. The authors stated that despite the high rate of re-operation, the data suggested that combined treatment of ACI and biomechanical altering procedures may be a reasonable option for selected patients with co-existing patello-femoral lesions and mechanical disorders.

In a case-series study, McNickle and colleagues (2009) examined the clinical results of a patient cohort undergoing ACI and elucidated factors associated with subjective improvement after implantation. The cohort included 137 subjects (140 knees) who underwent ACI of the knee. Mean defect size per patient was 5.2 +/- 3.5 cm(2) (range of 0.8 to 26.6 cm(2)). Patients averaged 30.3 +/- 9.1 years of age (range of 13.9 to 49.9 years) and were followed for 4.3 +/- 1.8 years (range of 2.0 to 9.7 years). Outcomes were assessed via clinical assessment and established outcome scales, including the Lysholm scale, International Knee Documentation Committee scale, and Short Form-12. A significant improvement after surgery was observed in all outcome assessments including the Lysholm (41 to 69; p < 0.001) and International Knee Documentation Committee (34 to 64; p < 0.001) scales. Subjectively, 75 % of patients indicated they were completely or mostly satisfied with the outcome and 83 % would have the procedure again. Pre-operatively, 32 % of patients had a Tegner score of 6 or greater, compared with 82
% before injury and 65% at most recent follow-up. Multi-variate analysis identified age (p < 0.021) and receiving workers' compensation (p < 0.018) as independent predictors of follow-up Lysholm score. Twenty-one patients (16%) required debridement of the ACI site secondary to persistent symptoms, whereas 9 knees (6.4%) clinically failed and underwent a revision procedure. The authors stated that ACI is a viable treatment option for chondral defects of the knee, resulting in durable functional and symptomatic improvement. Age and workers' compensation status are independent predictors of outcome.

Moreover, the authors noted that "although this study was able to assess the outcomes of a large cohort of patients treated with ACI, its retrospective design has several limitations. No control or comparison group was followed, and these patients were not randomized into treatment groups. Additionally, there were no set protocols for consistent reimagining or second-look arthroscopy. For the majority of patients, these options were only pursued with ongoing symptoms. Although the overall cohort size was large, several of the subsets (e.g., lesion location and concurrent procedures) were sufficiently small so as to underpower the multivariate analysis of their effects".

Nam et al (2009) reported the first U.S. prospective study of ACI of the talus. A total of 11 patients (6 women and 5 men; mean age of 33 years) underwent ACI of the talus after previous failed surgical management. There were 9 medial and 2 lateral lesions, with a mean size of 21 x 13 mm (273 mm2). Five patients underwent ACI of the talus alone; 6 had it with a "sandwich procedure." Ten patients underwent a second-look arthroscopy with screw removal. Mean follow-up was 38 months. Pre-operatively, 10 patients rated their ankles as poor and 1 as fair, using the simplified symptomatology evaluation. At latest follow-up, 3 patients were classified as excellent, 6 as good, and 2 as fair. Tegner activity level improved from 1.3 +/- 1.0 (mean +/- SE) pre-operatively to 4.0 +/- 1.6 (p < 0.002) post-operatively. The Finsen score (modified Weber score) showed significant improvement in the total score (p < 0.001). There was also overall agreement between the Finsen score and the American Orthopaedic Foot and Ankle Society ankle hindfoot score, with significant improvement from 47.4 +/- 17.4 preoperatively to 84.3 +/- 8.1 post-operatively (p < 0.001). At repeat arthroscopy, complete coverage of the defect was seen in all patients. The authors concluded that ACI of the talus yields significant functional improvement; however, further investigation is necessary to determine the long-term structural and biomechanical properties of the repair tissue.

The Bio-Gide, a resorbable bilayer membrane, consists of highly purified collagen types I and III (porcine origin). The membrane is highly biocompatible and supports wound healing. The 3-dimensional, natural fiber structure promotes cell adhesion, serves as a matrix for soft tissue support and provides a barrier to the ingrowth of overlying soft tissue into underlying bony defects. According to the product labeling, the Bio-Gide is used in dental surgery. There is a lack of evidence in the peer-reviewed literature on the use of Bio-Gide for ACT procedures.

The traditional ACT technique entails injection of a suspension of cells into the cartilage defect, which is covered with a periosteal flap or collagen membrane. This procedure requires extensive suturing to create an effective seal; however,
cell leakage remains a potential problem. Matrix-induced autologous chondrocyte implantation (MACI) circumvents this potential problem by using a membrane on which chondrocytes are seeded and cultured for several days, before the membrane is cut to the correct size and shape of the defect. As a consequence, time-consuming extensive suturing is unnecessary.

Bartlett et al (2005) performed 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 1 year. The mean modified Cincinnati knee score increased by 17.6 in the ACI-C group and 19.6 in the MACI group (p = 0.32). Arthroscopic assessments performed after 1 year showed a good to excellent International Cartilage Repair Society score in 79.2 % of ACI-C and 66.6 % of MACI grafts. Hyaline-like cartilage or hyalin-like cartilage with fibrocartilage was found in the biopsies of 43.9 % of the ACI-C and 36.4 % of the MACI grafts after 1 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. The frequency of re-operation was 9 % in each group. The authors concluded that the clinical, arthroscopic and histological outcomes are comparable for both ACI-C and MACI. While MACI is technically attractive, further long-term studies are required before the technique is widely adopted.

Zheng et al (2007) noted that MACI has been a treatment of cartilage injury since 2000, but little is known of the histological paradigm of tissue regeneration after implantation. MACI is a stable cell-based delivery system that enables the regeneration of hyaline-like cartilage. From a cohort of 56 MACI patients, these researchers examined the phenotype of chondrocytes seeded on type I/III collagen scaffold, and conducted progressive histological assessment over a period of 6 months. Chondrocyte-seeded collagen scaffolds from patient implants were analyzed by electron microscopy, immunohistochemistry (type II collagen and S-100), and reverse transcription polymerase chain reaction (RT-PCR) (aggrecan and type II collagen). Co- incidental cartilage biopsies were obtained at 48 hours, 21 days, 6 months, 8 months, 12 months, 18 months, and 24 months. These findings showed that chondrocytes on the collagen scaffold appeared spherical, well-integrated into the matrix, and maintained the chondrocyte phenotype as evidenced by aggrecan, type II collagen, and S-100 expression. Progressive histological evaluation of the biopsies showed the formation of cartilage-like tissue as early as 21 days, and 75 % hyaline-like cartilage regeneration after 6 months. The authors stated that this preliminary study has suggested that MACI may offer an improved alternative to traditional treatments for cartilage injury by regenerating hyaline-like cartilage as early as 6 months after surgery.

Ebert et al (2008) determined the effectiveness of "accelerated" compared to "traditional" post-operative load bearing rehabilitation protocols following MACI. A randomized controlled study design was used to investigate clinical, biomechanical and radiographic assessment at 3 months post-surgery in 62 patients following MACI to the medial or lateral femoral condyle. Both rehabilitation interventions sought to protect the implant for an initial period, then incrementally increase load bearing. Under the "accelerated" protocol, patients reached full weight bearing at 8 weeks post-surgery, compared to 11 weeks for the
"traditional" group. Patients in the "accelerated" group achieved greater 6 min-walk distances and daily activity levels as measured by accelerometry (p < 0.05) compared to the "traditional" group. Furthermore, the "accelerated" group reported significantly better improvement in knee pain at 12 weeks as indicated by the Knee Injury and Osteoarthritis Outcome Score (p < 0.05), and regardless of the rehabilitation protocol employed, no patient suffered any adverse effect to the implant as assessed by magnetic resonance imaging at 3 months. Comparison of each rehabilitation group with an unaffected control group revealed a significant difference in peak knee adduction and flexion moments for the traditional group (p < 0.05). However, there was no difference for accelerated patients (p > 0.05), which may demonstrate a faster return to knee loading patterns typically observed in unaffected subjects. The authors concluded that the "accelerated" load bearing approach that reduced the length of time spent ambulating on crutches resulted in reduced knee pain, improved function, no graft complications and may speed up the recovery of normal gait function. They stated that patient follow-up to at least 24 months would be required to observe longer-term graft outcomes.

Safran et al (2008) stated that managing articular cartilage injury continues to be a difficult challenge for the clinician. Although the short- and intermediate-term results of autologous chondrocyte implantation appear to be favorable, resources are being directed toward research to improve the technology. One promising area of investigation is the combination of cultured chondrocytes with scaffolds. Clinicians desire techniques that may be implanted easily, reduce surgical morbidity, do not require harvesting of other tissues, exhibit enhanced cell proliferation and maturation, have easier phenotype maintenance, and allow for efficient and complete integration with surrounding articular cartilage. The characteristics that make scaffolds optimal for clinical use are that they be biocompatible, biodegradable, permeable, reproducible, mechanically stable, non-cytotoxic, and capable of serving as a temporary support for the cells while allowing for eventual replacement by matrix components synthesized by the implanted cells. Clinical experience is growing with 3 scaffold-based cartilage repair techniques, each using a different type of scaffold material: (i) MACI, (ii) a hyaluronic acid-based scaffold, and (iii) a composite polylactic/polyglycolic acid polymer fleece. The authors stated that clinical results are encouraging; future directions in scaffold-based cartilage repair include bioactive and spatially oriented scaffolds.

Brittberg (2010) reviewed the current evidence of the MACI procedure; and discussed the characteristics of type I/III collagen membranes, behavior of cells associated with the membrane, surgical technique, rehabilitation, clinical outcomes, and quality of repair tissue. Relevant publications were identified by searching Medline from its inception (1949) to December 2007; peer-reviewed publications of preclinical and clinical cell behavior, manufacturing process, surgical technique, and rehabilitation protocols were identified. Pre-clinical and clinical studies were included if they contained primary data and used a type I/III collagen membrane. Data from these studies demonstrated that patients treated with MACI have an overall improvement in clinical outcomes. Reduced visual analog scale pain levels (range of 1.7 to 5.32 points) and improvements in the modified Cincinnati (range of 3.8 to 34.2 points), Lysholm-Gillquist (range of 23.09 to 47.6 points), Tegner-Lysholm (range of 1.39 to 3.9 points), and International Knee Documentation Classification scale (p < 0.05) were observed. Patients had
good-quality (hyaline-like) repair tissue as assessed by arthroscopic evaluation (including International Cartilage Repair Society score), magnetic resonance imaging, and histology, as well as a low incidence of post-operative complications. The author concluded that the findings suggested that MACI is a promising third-generation cell therapy for the repair of symptomatic, full-thickness articular cartilage defects.

Giza et al (2010) evaluated the results of MACI for the treatment of osteochondral defects of the talar dome using a technique that does not require an osteotomy of the tibia or fibula. A prospective investigation of MACI was performed on 10 patients with full-thickness lesions of the talus. Participants had a documented talus lesion on MRI, failure of conservative treatment and arthroscopic debridement/curettage, persistent ankle pain and swelling, the absence of tibiotalar arthritis and a stable ankle. A total of 5 males and 5 females, with an average of 1.7 previous procedures prior to MACI, were included in this study. All patients were available for follow-up at 1 and 2 years. Lesions were graded during the harvesting procedure using the Cheng-Ferkel grading system, the Outerbridge classification, and the International Cartilage Repair Society system. Clinical and functional evaluation was done pre-operatively, and at 1 and 2 years post-operatively using the American Orthopaedic Foot and Ankle Society (AOFAS) hind-foot evaluation and the SF-36 Health Survey. Pre-operative AOFAS hind-foot scores were 61.2 (range of 42 to 76) that improved 1 year post-operatively to 74.7 (range of 46 to 87) (p < 0.05) and 2 years post-operatively to 73.3 (range of 42 to 90) (p = 0.151). At both 1 and 2 years post-operatively, the results of the SF36 evaluation demonstrated a significant improvement in the Physical Functioning (p = 0.002) and Bodily Pain (p < 0.001) components. Subjectively, all 10 patients believed this procedure helped them. The authors concluded that these findings suggest that MACI may be an effective way to treat full-thickness lesions of the talus using harvested chondrocytes from the talus without malleolar osteotomy. The results of this small study need to be validated by well-designed studies.

In a meta-analysis, Niemeyer et al (2012) evaluated the effectiveness of ACI for talar lesions. An OVID-based literature search was performed to identify any published clinical studies on autologous chondrocyte implantation (ACI) for the treatment of pathologies of the ankle including the following databases: MEDLINE, MEDLINE preprints, EMBASE, CINAHL, Life Science Citations, British National Library of Health, and Cochrane Central Register of Controlled Trials (CENTRAL). Literature search period was from the beginning of 1994 to February 2011. Of 54 studies that were identified, a total of 16 studies met the inclusion criteria of the present meta-analysis. Those studies were systematically evaluated. All studies identified represented case series (EBM Leven IV). A total of 213 cases with various treatment for osteochondral and chondral defects with a mean size of 2.3 cm(2) (+/- 0.6) have been reported. A total of 9 different scores have been used as outcome parameters. Mean study size was 13 patients (SD 10; range of 2 to 46) with a mean follow-up of 32 +/- 27 months (range of 6 to 120). Mean Coleman Methodology Score was 65 (SD 11) points. Overall clinical success rate was 89.9%. The authors concluded that evidence concerning the use of ACI for osteochondral and chondral defects of the talus is still elusive.

Ebert et al (2010) examined knee biomechanics during gait in 61 patients following MACI, in conjunction with either "accelerated" or "traditional" approaches to post-
operative weight-bearing rehabilitation. Gait analysis was performed at 3, 6 and 12 months post-surgery in both patient groups, and 2 matched, unaffected control groups for comparison. The spatio-temporal and ground reaction force parameters were similar between patient groups and their respective control groups at all-time points. When compared with controls, both patient groups demonstrated significantly reduced knee extension moments up until, and including, 12 months. The traditional group demonstrated a significantly reduced knee adduction moment at 3, 6 and 12 months, and a significantly reduced knee flexion moment at 3 months. There were no differences in these knee moments between the accelerated patient group and controls. The authors concluded that overall, a higher level of gait dysfunction was observed in patients who underwent traditional rehabilitation. They stated that future research is needed to investigate the recovery of normal gait following MACI, and its effect on repair tissue development.

Genovese et al (2011) defined magnetic resonance (MR) arthrography imaging findings of MACI grafts of the knee in order to describe implant behavior and compared findings with validated clinical scores 30 and 60 months after MACI implant. A total of 13 patients were recruited (3 females and 10 males) with a total number of 15 chondral lesions. Each patient underwent an MACI procedure and MR arthrography 30 and 60 months after surgery. Magnetic resonance arthrography was performed using a dedicated coil with a 1.5-Tesla unit. The status of the chondral implant was evaluated with the modified MOCART scoring scale. The lining of the implant, the integration to the border zone, the surface and structure of the repaired tissue were assessed, and the presence of bone marrow edema and effusion was evaluated. For clinical assessment, the Cincinnati score was used. At 60 months, the abnormality showed worsening in 1 out of 15 cases. Integration showed improvement in 3 out of 15 cases, and worsening in 3 out of 15 cases. Two surfaces of the implant showed further deterioration at 60 months, and 1 afflicted implant fully recovered after the same time interval. Implant contrast enhancement at 30 months was seen in 2 out of 15 cases, 1 of which recovered at 60 months. According to the MOCART score, 4 cases were rated 68.4 out of 75 at 30 months and 65 out of 75 at 60 months. The mean clinical score decreased from 8.6 out of 10 at 30 months to 8.1 out of 10 at 60 months. The authors concluded that MR arthrography improved the evaluation of implants and facilitated the characterisation of MACI integration with contiguous tissues. The follow-up showed significant changes in MACI, even at 60 months, allowing for useful long-term MR evaluations.

Benthien et al (2011) performed a systematic review of studies concerning current treatment of chondral defects of the knee. The relevance for evidence based data and for successful surgical treatment of cartilage defects was evaluated. From 56,098 evaluated studies, 133 studies could be further pursued. These supplied data concerning microfracturing, OATS, ACI and MACI. The modified Coleman Methodical Score (CMS) and the level of evidence (LOE) were applied to evaluate the quality. In these studies, a total of 6,920 patients were reviewed with a median of 32 patients per study and a mean follow-up of 24 months. The mean CMS was 58 of 100 points. No study reached 100 points in the CMS. Three studies reached a level above 90; 10 studies were Level I; 5 studies reached Level II; 7 studies reached Level III; and 111 studies Level IV. Magnetic resonance imaging scans to verify the clinical data were used by only 72 studies. The means
in the modified CMS for the different procedures were as follows: ACI 58 points, MACI 57 points, microfracturing 68 points and OATS 50 points. A total of 24 studies applied the Lysholm Score (LS) for clinical evaluation of cartilage surgery. All operative procedures yielded comparable improvements of the LS (non-significant) meaning that no operative procedure proved superior. The authors concluded that as the majority of studies evaluated by this review is insufficient for evidence-based method purposes, more coherent studies with LOE of I or II are needed.

Ebert et al (2011) noted that the availability remains limited of mid-term clinical and radiological results into MACI. Outcomes are required to validate the efficacy of MACI as a suitable surgical treatment option for articular cartilage defects in the knee. A prospective evaluation was undertaken to assess clinical and MRI-based outcomes to 5 years in 41 patients (53 grafts) after MACI to the knee. After MACI surgery and a 12-week structured rehabilitation program, patients underwent clinical assessments (Knee injury and Osteoarthritis Outcome Score, SF-36, 6-minute walk test, knee range of motion) and MRI assessments at 3, 12, and 24 months, as well as 5 years after surgery. The MRI evaluation assessed 8 previously defined pertinent parameters of graft repair, as well as a combined MRI composite score. A significant improvement (p < 0.05) was demonstrated for all Knee injury and Osteoarthritis Outcome Score and SF-36 subscales over the post-operative timeline, as well as the 6-minute walk test and active knee extension. A significant improvement (p < 0.0001) was observed for the MRI composite score, as well as several individual graft scoring parameters. At 5 years after surgery, 67 % of MACI grafts demonstrated complete infill, whereas 89 % demonstrated good to excellent filling of the chondral defect. Patient demographics, cartilage defect parameters, and injury/surgery history demonstrated no significant pertinent correlations with clinical or MRI-based outcomes at 5 years, and no significant correlations existed between clinical and MRI-based outcome measures. At 5 years after surgery, 98 % of patients were satisfied with the ability of MACI surgery to relieve knee pain; 86 %, with improvement in their ability to perform normal daily tasks; and 73 %, with their ability to participate in sport 5 years after MACI. The authors concluded that these results suggest that MACI provides a suitable mid-term treatment option for articular cartilage defects in the knee. Moreover, they stated that long-term follow-up is essential to confirm whether the repair tissue has the durability required to maintain long-term patient quality of life.

Dixon et al (2011) presented the functional outcomes of MACI for a single surgeon series in a general hospital setting. A total of 27 patients, mean age of 41, were reviewed at 3.7 (range of 1 to 5) years. Patients were assessed using the AOFAS hindfoot scale, Tegener activity score and University of California lower extremity activity scale. Magnetic resonance imaging findings were also reviewed. While most patients report a significant improvement in symptoms with full return to activities of daily living, 36 % of those under 40 and 78 % of those over 40 reported restricted recreational activity. Of the patients under 40 years of age, 86 % were able to run compared with 23 % of those over 40. Of patients over 40, 64 % continued to have moderate or severe pain. The authors concluded that careful pre-operative counseling is required for patients of all ages regarding likely outcomes. In patients over 40, the procedure is unlikely to give good pain relief and alternative options should be considered.
Schneider et al (2011) reported a prospective multi-center study of MACI of the knee using a new type I collagen hydrogel (CaReS). From 2003 to 2008, 116 patients (49 women and 67 men; mean age of 32.5 +/- 8.9 years) had CaReS implantation of the knee in 9 different centers. On the basis of the International Cartilage Repair Society (ICRS) Cartilage Injury Evaluation Package 2000, the International Knee Documentation Committee (IKDC) score, pain score (visual analog scale [VAS]), SF-36 score, overall treatment satisfaction and the IKDC functional status were evaluated. Patient follow-up was performed at 3, 6, and 12 months after surgery and annually thereafter. Mean follow-up was 30.2 +/- 17.4 months (range of 12 to 60 months). There were 67 defects of the medial condyle, 14 of the lateral, 22 of the patella/trochlea, and 3 of the tibial plateau, and 10 patients had 2 lesions. The mean defect size was 5.4 +/- 2.4 cm(2); 30 % of the defects were less than 4 cm(2) and 70 % were greater than 4 cm(2). The IKDC score improved significantly from 42.4 +/- 13.8 pre-operatively to 70.5 +/- 18.7 (p < 0.001) at latest follow-up. Global pain level significantly decreased (p < 0.001) from 6.7 +/- 2.2 pre-operatively to 3.2 +/- 3.1 at latest follow-up. There also was a significant increase of both components of the SF-36 score. The overall treatment satisfaction was judged as very good or good in 88 % by the surgeon and 80 % by the patient. The IKDC functional knee status was grade I in 23.4 %, II in 56.3 %, III in 17.2 %, and IV in 3.1 % of the patients. The authors concluded that MACI employing the CaReS technology for the treatment of chondral or osteochondral defects of the knee is a safe and clinically effective treatment that yields significant functional improvement and improvement in pain level. However, they stated that further investigation is necessary to determine the long-term viability and clinical outcome of this procedure.

In a prospective, multi-center study, Enea et al (2012) evaluated (i) the quality of the repair tissue obtained from biopsies taken during second-look arthroscopy and (ii) the relationship between the histological outcome, the macroscopic appearance of the repair and functional status in patients who have undergone MACI for chondral defect repair. A total of 33 second-look core biopsies from 30 patients treated with MACI were analyzed. At the time of biopsy, the surgeon reported the reason for the second-look arthroscopy, the quality of the repair tissue and the patient's functional status on a standardized form. Biopsies together with patient data were sent to the authors' center to undergo blind histological evaluation and data analysis. The median overall ICRS II histological score of the examined population was 57 (1st to 3rd quartile 41 to 75). According to the ICRS cartilage repair assessment (CRA) arthroscopic evaluation, 10 biopsies (30 %) were classified as normal, 17 (51 %) as nearly normal, 4 (12 %) as abnormal and 2 (6 %) as severely abnormal. The histological outcome was not significantly related either to the macroscopic appearance of the lesion or to the patient's functional status at the time of biopsy. The authors concluded that in the examined population, the macroscopic appearance of the repair tissue gave an overly favorable impression in comparison with the real histological composition of the tissue, which was possibly still maturing in many cases. The healing process after MACI needs to be better understood through a larger histological study, and a longer follow-up is needed to better clarify the relationship between histology and long-term functional status.
Filardo et al (2012) analyzed the clinical outcome obtained with arthroscopic second generation ACI associated with bone grafting for the treatment of knee osteochondritis dissecans (OCD) at medium-term follow-up. A total of 34 knees affected by symptomatic OCD grade III or IV on the International Cartilage Repair Society (ICRS) scale were treated and prospectively evaluated at 12, 24 months of follow-up, and at a final mean 6 +/- 1 years of follow-up. The mean age at treatment was 21 +/- 6 years. The average size of the defects was 3 +/- 1cm(2). Patients were evaluated with IKDC, EQ-VAS, and Tegner scores. A statistically significant improvement in all scores was observed after the treatment. The IKDC subjective score improved from 38 +/- 13 to 81 +/- 20, and 91 % of the knees were rated as normal or nearly normal in the objective IKDC at the final evaluation. EQ-VAS and Tegner scores showed a statistically significant linear trend of improvement over time passing from 52 +/- 18 to 83 +/- 14 and from 2 +/- 1 to 5 +/- 3, respectively, at 6 years’ follow-up. A better outcome was obtained in men, sport active patients, and smaller lesions. The authors concluded that 2nd generation ACI associated with bone grafting is a valid treatment option for knee OCD and may offer a good and stable clinical outcome at mean 6 years of follow-up. They stated that further studies are needed to confirm the results over time, and determine if there is only a symptomatic improvement, or if this procedure may also prevent or delay further knee degeneration.

Pestka et al (2012) examined if ACI used as a second-line treatment after failed arthroscopic microfracturing is associated with a higher failure rate and inferior clinical results compared with ACI as a first-line treatment. A total of 28 patients with isolated cartilage defects at the knee joint were treated with ACI after microfracture as a first-line treatment had failed (failure defined as the necessity of re-intervention). These patients were assigned to group A and compared with a matched-pair cohort of patients of identical age, defect size, and defect location (group B) in which ACI was used as a first-line treatment. Failure rates in both groups were assessed. Post-operative knee status was evaluated with the IKDC score and Knee injury and Osteoarthritis Outcome Score (KOOS), and sporting activity was assessed by use of the Activity Rating Scale. Mean follow-up times were 48.0 months (range of 15.1 to 75.1 months) in group A and 41.4 months (range of 15.4 to 83.6 months) in group B. Differences between groups A and B were analyzed by Student’s t-test. Group A had significantly greater failure rates (7 of 28 patients) in comparison with group B (1 of 28 patients; p = 0.0241). Mean (SD) post-operative IKDC scores revealed 58.4 (22.4) points in group A with a trend toward higher score results (69.0 [19.1] points) for patients in group B (p = 0.0583). Significantly different results were obtained for KOOS pain and activity of daily living subscales, whereas the remaining KOOS subscales did not show significant differences. Despite the significantly higher failure rate observed in group A, those patients did not participate in fewer activities or perform physical activity less frequently or at a lower intensity. The authors conclude that autologous chondrocyte implantation after failed microfracturing appears to be associated with a significantly higher failure rate and inferior clinical outcome when compared with ACI as a first-line treatment.

Jordan et al (2012) performed a systematic review of clinical outcomes following various treatments for chondral lesions of the hip and defined the techniques for the treatment of these cartilage defects. The full manuscripts of 15 studies were
reviewed for this systematic review including case studies, case series, and clinical studies. A variety of techniques have been reported for the treatment of symptomatic chondral lesions in the hip. Microfracture, cartilage repair, ACI, mosaicplasty, and osteochondral allografting have all been used in very limited case series. Although good results have been reported, most studies lacked both a control group and a large number of patients. The authors concluded that the findings in this article do provide a good foundation for treatments and stimulant for further study in an inherently difficult to treat young patient population with articular cartilage defects in the hip.

Gross et al (2012) conducted a systematic review of clinical outcomes after cartilage restorative and reparative procedures in the glenohumeral joint, identified prognostic factors that predict clinical outcomes, provided treatment recommendations based on the best available evidence, and highlighted literature gaps that require future research. These investigators searched Medline (1948 to week 1 of February 2012) and Embase (1980 to week 5 of 2012) for studies evaluating the results of arthroscopic debridement, microfracture, osteochondral autograft or allograft transplants, and ACI for glenohumeral chondral lesions. Other inclusion criteria included minimum 8 months' follow-up. The Oxford Level of Evidence Guidelines and Grading of Recommendations Assessment, Development and Evaluation (GRADE) recommendations were used to rate the quality of evidence and to make treatment recommendations. A total of 12 articles met inclusion criteria, which resulted in a total of 315 patients; 6 articles pertained to arthroscopic debridement (n = 249), 3 to microfracture (n = 47), 2 to osteochondral autograft transplantation (n = 15), and 1 to ACI (n = 5). Whereas most studies reported favorable results, sample heterogeneity and differences in the use of functional and radiographic outcomes precluded a meta-analysis.

Several positive and negative prognostic factors were identified. All of the eligible studies were observational, retrospective case series without control groups; the quality of evidence available for the use of the afore-mentioned procedures was considered "very low" and "any estimate of effect is very uncertain". The authors concluded that more research is needed to determine which treatment for chondral pathology in the shoulder provides the best long-term outcomes. They encouraged centers to establish the necessary alliances to conduct blinded, randomized clinical trials and prospective, comparative cohort studies necessary to rigorously determine which treatments result in the most optimal outcomes. At this time, high-quality evidence is lacking to make strong recommendations, and decision making in this patient population is performed on a case-by-case basis.

Petri et al (2013) compared the CaReS(®) technique, which is a MACI technique, to microfracture for treating patello-femoral articular cartilage lesions. Between May 2003 and December 2005, a total 17 patients with an isolated patella-femoral cartilage defect (International Cartilage Repair Society III/IV) were treated with the CaReS(®) technique. After adjusting for inclusion and exclusion criteria, 10 of these patients could be included in this study; 10 patients treated with microfracture were chosen as a matched-pair group. Clinical outcome was evaluated 3 years after surgery by the 36-item Short Form Health Survey Questionnaire (SF-36), International Knee Documentation Committee (IKDC) subjective evaluation of the knee, Lysholm Score, and Cincinnati Modified Rating Scale scores. Patients treated with CaReS(®) had statistically significantly improved IKDC, Lysholm, and Cincinnati scores 36 months after surgery.
compared with pre-operatively. When comparing outcome between groups 36 months after surgery, there was no statistically difference in IKDC, Lysholm, and Cincinnati scores. The authors concluded that this the first trial comparing the CaReS® technique and microfracture for treating patella-femoral articular cartilage lesions, and results show that CaReS® yielded comparable results to microfracture. The authors noted that the small number of patients is a limiting factor of the study, leading to results without statistical significance. They stated that a multi-centric prospective randomized study comparing the 2 procedures is desirable.

Appendix

*BMI is calculated by dividing the person's weight (in kilograms) by height (in meters) squared:

\[
BMI = \text{weight (kg)} \times [\text{height (m)}]^2
\]

Note: To convert pounds to kilograms, multiply pounds by 0.45. To convert inches to meters, multiply inches by 0.0254

or

For a simple and rapid calculation of BMI, please click below and it will take you to the Obesity Education Initiative.

*http://www.nhlbisupport.com/bmi/bmicalc.htm

CPT Codes / HCPCS Codes / ICD-9 Codes

CPT codes covered if selection criteria are met:

27412
29870

Other CPT codes related to the CPB:

27447
29871
29874
29877
29879

HCPCS codes covered if selection criteria are met:

J7330 Autologous cultured chondrocytes, implant
S2112 Arthroscopy, knee, surgical, for harvesting of cartilage (chondrocyte cells)
ICD-9 codes covered if selection criteria are met (not all-inclusive):

- 715.16  Osteoarthrosis, localized, primary, lower leg
- 715.26  Osteoarthrosis, localized, secondary, lower leg
- 715.36  Osteoarthrosis, localized, not specified whether primary or secondary, lower leg
- 715.96  Osteoarthrosis, unspecified whether generalized or localized, lower leg
- 717.0 - 717.9  Internal derangement of knee
- 718.86  Other joint derangement, lower leg
- 719.46  Pain in joint, lower leg
- 719.86  Other specified disorders of joint
- 732.7  Osteochondritis dissecans
- 959.7  Injury, knee, leg, ankle, and foot
- V85.0 - V85.35  Body Mass Index less than 19, adult - 35.9 [BMI less than or equal to 35]

ICD-9 codes not covered for indications listed in the CPB (not all-inclusive):

- 711.00 - 712.99  Arthropathy associated with infections or crystal arthropathies
- 714.0 - 714.9  Rheumatoid arthritis and other inflammatory polyarthropathies
- 718.00 - Articular cartilage disorders (except lower leg)
  - 718.05,
  - 718.07 -
  - 718.09
- 718.80 - Other joint derangement, not elsewhere classified (except lower leg)
  - 718.85,
  - 718.87 -
  - 718.89
- 719.80 - Other specified disorders of joint (except lower leg)
  - 719.85,
  - 719.87 -
  - 719.89
- V85.36 – Body Mass Index 36.0 and over
- V85.45
Combination Meniscal Allograft and Autologous Chondrocyte Implantation:

CPT codes not covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tr>
<td>27412</td>
<td>Autologous chondrocyte implantation, knee</td>
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<tr>
<td>29868</td>
<td>Arthroscopy, knee, surgical; meniscal transplantation (includes arthrotomy for meniscal insertion), medial or lateral</td>
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</table>

The above policy is based on the following references:


