Autologous Chondrocyte Implantation

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Section: Surgery

Place(s) of Service: Inpatient

I. Description

A variety of procedures are being developed to resurface articular cartilage defects. Autologous chondrocyte implantation (ACI) involves harvesting chondrocytes from healthy tissue, expanding the cells in vitro, and implanting the expanded cells into the chondral defect under a periosteal or fibrin patch. Second and third generation techniques include combinations of autologous or allogeneic chondrocytes, minced cartilage, scaffolds, and growth factors.

Background

Damaged articular cartilage typically fails to heal on its own and can be associated with pain, loss of function, and disability, and may lead to debilitating osteoarthritis over time. These manifestations can severely impair an individual’s activities of daily living and adversely affect quality of life. Conventional treatment options include debridement, subchondral drilling, microfracture, and abrasion arthroplasty. Debridement involves the removal of synovial membrane, osteophytes, loose articular debris, and diseased cartilage, and is capable of producing symptomatic relief. Subchondral drilling, microfracture, and abrasion arthroplasty attempt to restore the articular surface by inducing the growth of fibrocartilage into the chondral defect. Compared to the original hyaline cartilage, fibrocartilage has less capability to withstand shock or shearing force and can degenerate over time, often resulting in the return of clinical symptoms. Osteochondral grafts and ACI attempt to regenerate hyaline-like cartilage and thereby restore durable function.

With autologous chondrocyte implantation, a region of healthy articular cartilage is identified and biopsied through arthroscopy. The tissue is sent to a facility licensed by the U.S. Food and Drug Administration (FDA) where it is minced and enzymatically digested, and the chondrocytes are separated by filtration. The isolated chondrocytes are cultured for 11–21 days to expand the cell population, tested, and then shipped back for implantation. With the patient under general anesthesia,
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an arthrotomy is performed, and the chondral lesion is excised up to the normal surrounding cartilage. A periosteal flap is removed from the proximal medial tibia and sutured to the surrounding rim of normal cartilage. The cultured chondrocytes are then injected beneath the periosteal flap. ACI may be considered more effective for larger lesions than microfracture or osteochondral grafts, but it is technically difficult, requiring two procedures and harvesting of periosteum. In addition, use of the FDA-indicated periosteal cover may result in hypertrophy, as well as donor-site morbidity.

Methods to improve the ACI procedure are being investigated, including the use of a scaffold or matrix-induced ACI (MACI) composed of biocompatible carbohydrates, protein polymers, or synthetics. Desired features of articular cartilage repair procedures are the ability to 1) be implanted easily, 2) reduce surgical morbidity, 3) not require harvesting of other tissues, 4) enhance cell proliferation and maturation, 5) maintain the phenotype, and 6) integrate with the surrounding articular tissue. In addition to the potential to improve the formation and distribution of hyaline cartilage, use of a scaffold with MACI eliminates the need for harvesting and suture of a periosteal patch. A scaffold without cells may also support chondrocyte growth.

Regulatory Status

The culturing of chondrocytes is considered by the FDA to fall into the category of manipulated autologous structural cells (MAS), which are subject to a biologic licensing requirement. At the present time, only Cartice (Genzyme) has received FDA approval for the culturing of chondrocytes through a biologics license. In 1997, Carticel received FDA approval for the repair of clinically significant, “...symptomatic cartilaginous defects of the femoral condyle (medial lateral or trochlear) caused by acute or repetitive trauma....” The labeled indication was revised in October 1999 to read as follows:

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

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

A number of second generation methods for implanting autologous chondrocytes in a biodegradable matrix are currently in development/testing. These include ChondroCelect (characterized chondrocyte implantation, TiGenex, Phase III trial), BioCart II (ProChon Biotech, Phase II trial), Cartilix (polymer hydrogel, Cartilix), MACI (matrix-induced ACI, Verigen, available outside of the U.S.), Cartipatch (solid scaffold with an agarose-alginate matrix, TBF Tissue Engineering, Phase III trial), NeoCart (ACI with a 3-dimensional chondromatrix, Histogenics, Phase II trial), Hyalograft C (ACI with a hyaluronic acid-based scaffold, Fidia Advanced Polymers), and CAIS (Cartilage Autograft Implantation System, which harvests
cartilage and disperses chondrocytes on a scaffold in a single stage treatment, Johnson and Johnson). Although clinical use of these second-generation ACI products has been reported in Europe, none are approved for use in the U.S. at this time.

DeNovo NT Graft (Natural Tissue Graft) and DeNovo ET Live Chondral Engineered Tissue Graft (Neocartilage) are 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 intra-operatively 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. As there is no use of chemicals and minimal manipulation, the allograft tissue does not require FDA approval for marketing. DeNovo NT is currently available in the U.S. and 4 U.S. sites are participating in a company-sponsored observational study with 25 subjects; the expected completion is 2013. DeNovo ET graft (Neocartilage) uses juvenile allogeneic cartilage cells engineered by ISTO Technologies. The FDA approved ISTO’s Investigational New Drug (IND) application for Neocartilage in 2006, which allowed them to pursue clinical trials of the product in humans.

The entire autologous chondrocyte implantation (ACI) procedure consists of four steps: 1) the initial arthroscopy and biopsy of normal cartilage, 2) culturing of chondrocytes, 3) a separate arthrotomy to create a periosteal flap and implant the chondrocytes, and 4) post-surgical rehabilitation. The initial arthroscopy may be scheduled as a diagnostic procedure; as part of this procedure, a cartilage defect may be identified, prompting biopsy of normal cartilage in anticipation of a possible chondrocyte transplant. The biopsied material is then sent for culturing and returned to the hospital when the implantation procedure (i.e., arthrotomy) is scheduled.

II. Criteria/Limitations

A. ACI is covered (subject to Limitations/Exclusions and Administrative Guidelines) for the treatment of disabling full-thickness articular cartilage defects of the knee caused by acute or repetitive trauma, in patients who have had an inadequate response to a prior surgical procedure, when all of the following criteria are met:

1. Adolescent patients are skeletally mature with documented closure of growth plates
2. Adult patients that are too young to be considered an appropriate candidate for total knee arthroplasty or other reconstructive knee surgery (e.g., younger than 55 years)
3. Focal, full-thickness (grade III or IV) unipolar lesions on the weight bearing surface of the femoral condyles or trochlea at least 1.5 cm$^2$ in size
4. Minimal to absent degenerative changes in the surrounding articular cartilage (Outerbridge Grade II or less), and normal-appearing hyaline cartilage surrounding the border of the defect
5. Normal knee biomechanics, or alignment and stability that can be achieved concurrently with ACI
6. Absence of meniscal pathology
III. Limitations/Exclusions

A. If debridement is the only prior surgical treatment, consideration should be given to marrow-stimulating techniques before ACI is performed.

B. Misalignment and instability of the joint are contraindications. Therefore, additional procedures such as repair of ligaments or tendons or creation of an osteotomy for the realignment of the joint may be performed at the same time. If normal knee biomechanics or alignment and stability cannot be achieved concurrently with ACI, the patient is not a good candidate for this surgery.

C. The charges for the culturing component of the procedure are submitted as part of the hospital bill.

D. ACI for all other joints, including patellar and talar, and any indications other than those listed above do not meet payment determination criteria.

E. Matrix-induced autologous chondrocyte implantation does not meet payment determination criteria.

F. Treatment of focal articular cartilage lesions with autologous minced cartilage does not meet payment determination criteria.

G. Treatment of focal articular cartilage lesions with allograft, either allogeneic minced cartilage (DeNovo Natural Tissue Graft) or allogeneic cartilage cells (e.g., DeNovo Engineered Tissue Graft) does not meet payment determination criteria.

IV. Administrative Guidelines

A. Precertification is not required. HMSA reserves the right to perform retrospective review using the above criteria to validate if services rendered met payment determination criteria.

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V. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.
This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VI. References