Viable Osteochondral Allograft for the Treatment of a Full-Thickness Cartilage Defect of the Patella

Jarret M. Woodmass, M.D., F.R.C.S.C., Heath P. Melugin, M.D., Isabella T. Wu, B.A., Daniel B. F. Saris, M.D., Ph.D., Michael J. Stuart, M.D., and Aaron J. Krych, M.D.

Abstract: Isolated cartilage defects can lead to significant pain and disability, prompting the development of a number of options for restorative treatment. Each method has advantages and limitations, and no single technique has gained widespread use. We present a technique for implantation of a cryopreserved osteochondral allograft (Cartiform) for the treatment of full-thickness cartilage defects. Cartiform is a cryopreserved osteochondral allograft composed of chondrocytes, chondrogenic growth factors, and extracellular matrix proteins. This implant allows for regenerative treatment of full-thickness cartilage lesions in a single surgical procedure.

Isolated cartilage defects show an increased incidence that may be related to a rise in sports participation among young athletes.[1,2] These injuries can lead to significant pain and disability.[3]

Restorative treatment options for isolated full-thickness cartilage lesions include osteochondral autograft transfer, osteochondral allograft transplantation (OCA), and autologous chondrocyte implantation (ACI). Each of these techniques has advantages and limitations. For instance, donor morbidity associated with osteochondral autograft transfer limits the defect size that can be treated. Alternatively, OCAs and ACI can be used to treat large lesions. However, OCA requires size-matched donor grafts,[4] and ACI requires 2 operations and significant expense.[5,6]

We present a technique for implantation of a cryopreserved osteochondral allograft (Cartiform; Arthrex, Naples, FL) for the treatment of full-thickness cartilage defects. Cartiform is a cryopreserved osteochondral allograft composed of chondrocytes, chondrogenic growth factors, and extracellular matrix proteins. This implant allows for regenerative treatment of full-thickness cartilage lesions in a single surgical procedure.

Surgical Technique

Indications and Contraindications for Cartiform

The indications for Cartiform with its thin osseous layer are similar to those previously described for ACI (Table 1).[7] Cartiform is a viable option for treatment of full-thickness cartilage defects with minimal subchondral bone loss. Cartiform can be a beneficial choice for patients preferring only 1 procedure and is typically used for smaller defects (1-2 cm^2)[8] on either the femur or patella.[9] Contraindications include more than 5 mm of subchondral bone loss due to its minimal osseous portion. In addition, concomitant pathology including mechanical malalignment, patellofemoral instability, ligamentous laxity, and meniscal incompetence should be addressed prior to or preferably simultaneously to

From the Departments of Orthopedic Surgery and Sports Medicine, Mayo Clinic (J.M.W., H.P.M., I.T.W., D.B.F.S., M.J.S., A.J.K.), Rochester, Minnesota, U.S.A.; Department of Orthopaedics, University Medical Center Utrecht (D.B.F.S.), Utrecht; and Department of Reconstructive Medicine, University of Twente (D.B.F.S.), Enschede, The Netherlands.

The authors report the following potential conflicts of interest or sources of funding: M.J.S. is a board member of the American Journal of Sports Medicine *(money paid to institution); consultant for Arthrex (money paid to institution); and receives grants from Stryker (money paid to institution). D.B.F.S. is an editorial or governing board member of* Cartilage *(money paid to institution); is a paid consultant for Cartiheal, Smith & Nephew, and Vericel; and receives research support from Arthrex, Ivy Sports, and Smith & Nephew (money paid to institution). A.J.K. is a consultant for Arthrex (money paid to institution); grants from Arthritis Foundation, Ceterix, and Histogenics (money paid to institution); and payment for lectures including service on speakers bureaus, from Arthrex (money paid to institution). Full ICMJE author disclosure forms are available for this article online, as supplementary material.*

Received March 28, 2017; accepted June 26, 2017.

Address correspondence to Aaron J. Krych, M.D., Mayo Clinic, 200 First Street SW, Rochester, MN 55905, U.S.A. E-mail: krych.aaron@mayo.edu

2212-6287/17420

http://dx.doi.org/10.1016/j.eats.2017.06.034

Table 1. Indications and Contraindications for the Described Technique

Indications	Contraindications
Isolated, full-thickness cartilage defect of the knee	Significant subchondral bone loss >5 mm
Defects size 1-2 cm^2	Femoral defect with uncorrected malalignment, meniscal deficiency or ligament instability
Primary or revision cases	Patellar defect with uncorrected maltracking
Contained lesions	Uncontained lesions

any cartilage restoration procedure. This technique requires specialized equipment (Table 2).

Graft Preparation

Cartiform is an allograft osteochondral implant harvested from human cadaveric specimens. The allograft consists of full-thickness articular cartilage and a thin layer of subchondral bone (Fig 1) that is thoroughly tested for sterility and cellular composition. Perforations in the articular cartilage allow for flexible conformity and improved integration to the underlying subchondral bone. The chondrocytes in a type II collagen matrix along with extracellular matrix proteins, chondrogenic factors, and a thin osseous portion are cryopreserved at −80°C and can remain viable for up to 2 years.[10-12]

Patient Positioning and Visualization

The patient is positioned supine on the operating table (Video 1). The lower extremity is prepped and draped in the usual sterile fashion. The extremity is exsanguinated with an elastic wrap and tourniquet inflated to 250 mm Hg. The arthroscope is used to assess and document the size, location, and grade of cartilage defects within the knee and ensure that the patient is a candidate for Cartiform prior to opening the implant (Table 3). The joint is carefully assessed to ensure that there are no areas with more than 5-mm subchondral bone loss prior to opening the implant.

Arthrotomy and Visualization

A 6- to 8-cm longitudinal incision is made over the medial or lateral third of the patella depending on the defect location. A parapatellar arthrotomy is performed with identification and preservation of the meniscus at the distal extent. Traction sutures (No. 0 Vicryl) sutures are placed in the fascial cuff on the patella to assist with eversion, allow easy instrument passage, and prevent surrounding iatrogenic cartilage damage.

Table 2. Equipment Required to Perform a Cryopreserved Osteochondral Allograft Transplantation

Special Equipment/Instrumentation
Donor site preparation
- Ring curette
- PowerPick microdrilling system
- Cartiform viable osteochondral allograft implant
- 2.5-mm PushLock anchors (×3-4)
- 4-0 Monocryl suture (×3-4)
- 6-0 absorbable suture
- Fibrin glue

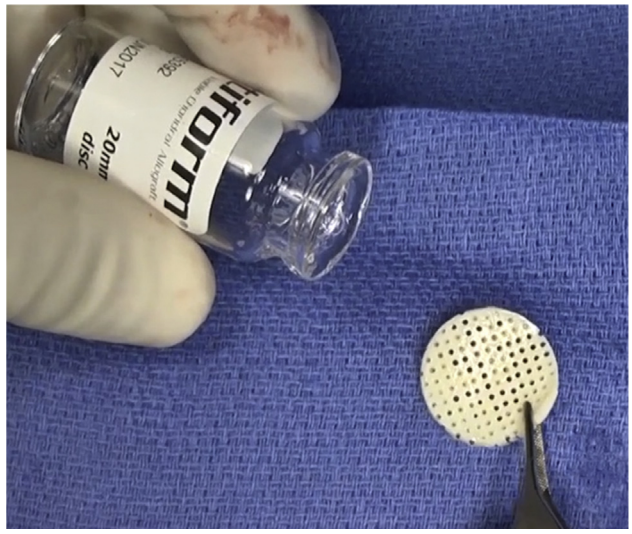

Fig 1. Cartiform implant (Arthrex).

Graft Site Preparation

A no. 15 scalpel blade sharply defines the desired peripheral wall of normal cartilage to create a stable border. A curette removes the pathologic cartilage and the calcified cartilage layer throughout the base of the defect (Fig 2A). Microdrilling to a depth of 4 mm using a PowerPick (Arthrex) accesses the bone marrow. Holes are initially drilled along the periphery of the defect, followed by sequentially more central positions. An osseous bridge of 2 to 3 mm is maintained between each drill hole (Fig 2B).

Table 3. Pearls and Pitfalls

Pearls	Pitfalls
Perform a diagnostic arthroscopy to ensure patient is a candidate prior to arthrotomy and opening of the implant	Performing an unnecessary arthrotomy to find a contraindication (e.g., subchondral defect)
Debride cartilage back to stable vertical borders and remove diseased surrounding cartilage	Failure to debride cartilage to create a contained lesion
Maintain 2-3 mm osseous bridges between drill holes	Creating a subchondral defect as a result of tunnel coalition between microfracture sites
Regularly assess the orientation of the allograft during preparation and implantation	Incongruent graft placement or loss of graft suitability as a result of error in orientation/preparation

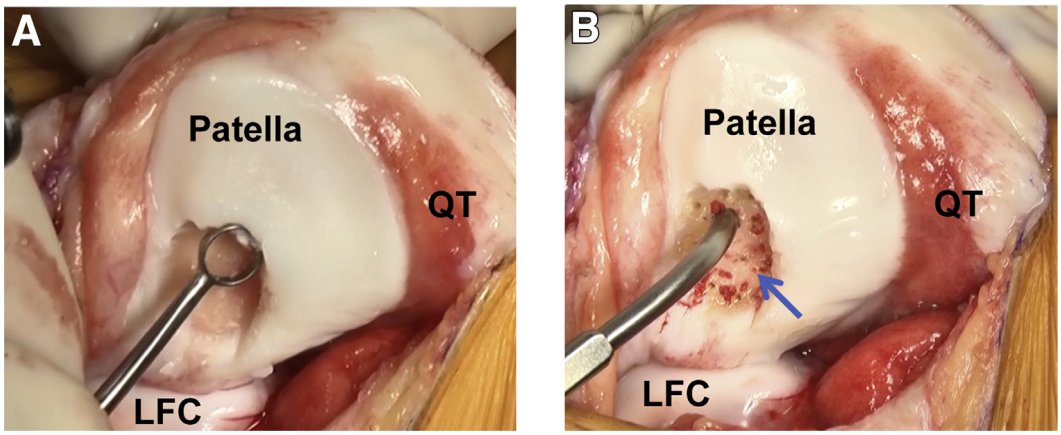

Fig 2. Intraoperative images of a left knee (supine positioning) with a lateral parapatellar arthrotomy. A 2 × 2-cm full-thickness cartilage defect on the undersurface of the patella is being prepared for Cartiform implantation. (A) A curette is being used to debride the pathologic cartilage to a stable border peripherally with removal of the calcified cartilage layer. (B) Microdrilling of the defect leaving 3- to 4-mm osseous bridges between drill holes (blue arrow). (LFC, lateral femoral condyle; QT, quadriceps tendon.)

Graft Implantation

The cryopreserved osteochondral allograft implant is then placed over the defect and marked for peripheral resection to fit the lesion. It is critical to carefully examine the allograft and ensure that the osseous surface is oriented toward the subchondral bone before the graft is trimmed to perfectly fit the lesion. We prefer to pass no. 4-0 Vicryl suture in mattress fashion in the location of the anticipated suture anchors. A drill is passed through the subchondral bone at the most superolateral margin of the defect in preparation for 2.5-mm mini-PushLock anchor insertion (Fig 3A). This is repeated at the superomedial and inferior margins to allow for 3-anchor fixation of the graft. The 3 knotless anchors are sequentially placed into the drill holes, taking great care not to overtension and rip through the graft, reducing the graft into the defect (Fig 3B). If an unstable edge of the Cartiform implant is identified, it is secured to the normal cartilage rim with no. 6-0 absorbable suture. The tourniquet is deflated and the graft is covered with a thin layer of fibrin glue (Fig 4).

Closure

The wound is closed in layers using no. 0 Vicryl for the deep fascia, no. 2-0 Monocryl for the subcutaneous tissue, and a running no. 3-0 Monocryl for the skin. Steri-Strips are applied to the incision followed by

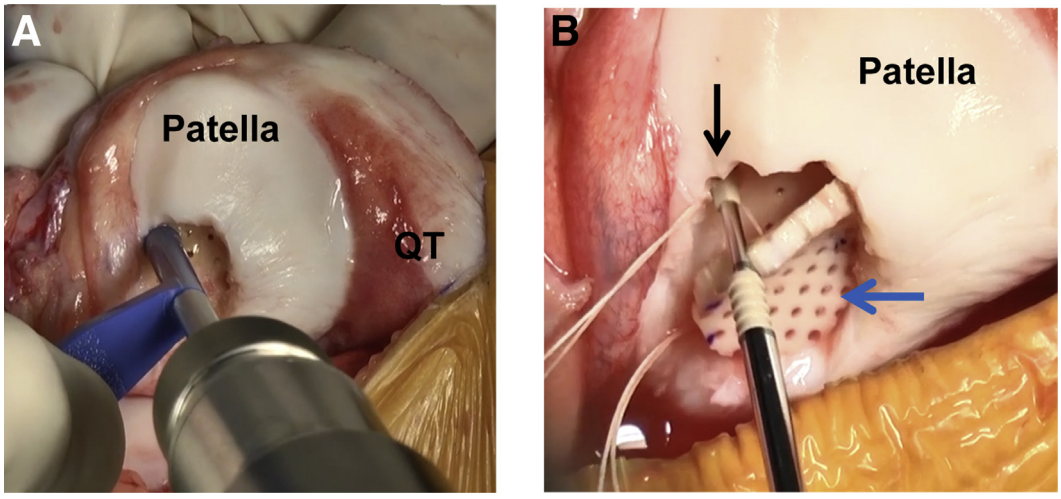

Fig 3. Intraoperative images of the left knee (supine positioning) with a lateral parapatellar arthrotomy showing Cartiform implantation into a full-thickness cartilage defect on the undersurface of the patella. (A) A 2-mm hole is drilled for suture anchor placement (1 of 3 suture anchors). (B) A PushLock (Arthrex) anchor is being advanced into place after the suture has been passed through the implant. (black vertical arrow, PushLock anchor; blue horizontal arrow, Cartiform implant; QT, quadriceps tendon.)

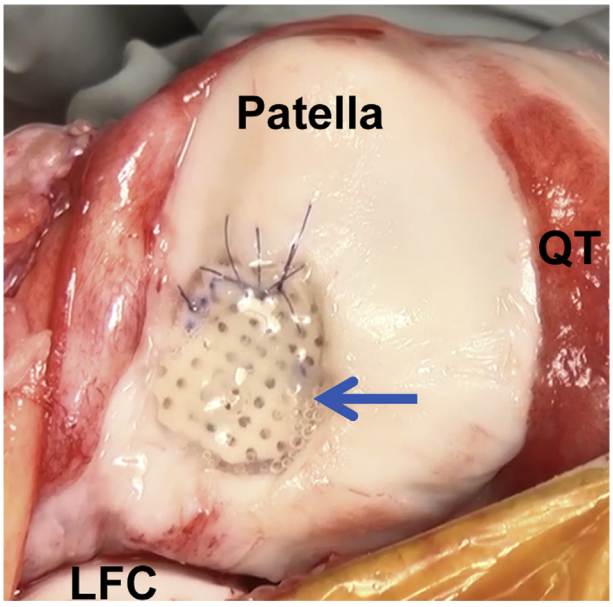

Fig 4. Intra-operative images of a left knee (supine positioning) with a lateral parapatellar arthrotomy. A Cartiform implant has been secured into a 2 × 2-cm full-thickness cartilage defect on the undersurface of the patella. (blue horizontal arrow, Cartiform implant; LFC, lateral femoral condyle; QT, quadriceps tendon.)

sterile dressing. A hinged knee brace is fit and locked in full extension.

Rehabilitation

0 to 6 weeks: Partial weight bearing in full extension while wearing a knee brace; immediate active and passive range of motion as tolerated.

6 weeks to 4 months: Gradual weight bearing as tolerated; the brace is discontinued; full knee range of motion; no knee loading beyond 90° of flexion.

>4 months: Able to return to activity as tolerated.

Table 4. Advantages and Disadvantages of Cryopreserved Osteochondral Allograft Implantation

Advantages	Disadvantages
Single operation	Single implant limits to a 2-cm-diameter defect
No donor site morbidity	Unable to fill/restore a large osseous defect
Allograft is flexible and can contour to match lesion size/shape.	Theoretical risks with allograft tissue of disease transmission
Off the shelf use with long shelf-life	Unknown if subchondral bone should be microfractured or not to optimize ingrowth conditions

Discussion

Isolated full-thickness cartilage lesions can result in significant pain and disability.[3] Multiple treatment options currently exist but no single technique has gained widespread use. Osteochondral autograft transfer is commonly used for smaller lesions but donor site morbidity limits its use for larger defects.[13] OCA and ACI are viable alternatives for larger defects.[4,8] ACI is an expensive technique, requires a minimum of 2 operations, and has been associated with adverse events such as delamination and tissue hypertrophy.[5,14]

Cartiform provides several advantages for the treatment of full-thickness cartilage defects (Table 4). First, the osseous surface allows for bone-to-bone integration that may reduce the risk of delamination.[15] Second, the cryopreserved implant has greater shelf-life and the chondrocytes remain functional after thawing.[16] Third, the perforated implant can be trimmed and conformed to anatomically match the defect, which eliminates the need for preoperative templating and patient specific sizing.[15]

In vivo and in vitro results have shown promising results. Geraghty et al.[16] used a goat model to show the ability of cryopreserved, viable osteochondral allografts to heal osteochondral defects. Histologic assessment at 12 months revealed defect fill with highly cellular, hyaline-like repair tissue. Hoffman et al.[15] reported similar results in an in vitro case study. The patient showed full range of motion, reported no pain, and had returned to sports at 9 months after implantation of a 10 × 10-mm Cartiform implant into the femoral trochlea. MRI showed an isointense graft as compared to the surrounding cartilage. Repeat arthroscopy revealed a well-integrated and congruent graft. Biopsy of the graft site showed 85% hyaline cartilage.

Potential disadvantages of Cartiform include implant cost, size restrictions, and inability to fill osseous defects. Expense is an important consideration; however, this technique in contrast to ACI can be performed in a single procedure. The largest circular implant has a 2 cm diameter, but newer shapes and sizes may become available. The thin osseous layer on the Cartiform implant is designed to promote bone-to-bone healing but is not sufficient to fill deeper bone defects that are typically treated with osteochondral allograft transplantation.[17]

References

1. Curl WW, Krome J, Gordon ES, Rushing J, Smith BP, Poehling GG. Cartilage injuries: A review of 31,516 knee arthroscopies. *Arthroscopy* 1997;13:456-460.
2. Krych AJ, Pareek A, King AH, Johnson NR, Stuart MJ, Williams RJ 3rd. Return to sport after the surgical management of articular cartilage lesions in the knee: A meta-

analysis. *Knee Surg Sports Traumatol Arthrosc* August 18, 2016. [Epub ahead of print.]
3. Bedi A, Feeley BT, Williams RJ 3rd. Management of articular cartilage defects of the knee. *J Bone Joint Surg Am* 2010;92:994-1009.
4. Camp CL, Stuart MJ, Krych AJ. Current concepts of articular cartilage restoration techniques in the knee. *Sports Health* 2014;6:265-273.
5. Samuelson EM, Brown DE. Cost-effectiveness analysis of autologous chondrocyte implantation: A comparison of periosteal patch versus type I/III collagen membrane. *Am J Sports Med* 2012;40:1252-1258.
6. Minas T, Gomoll AH, Rosenberger R, Royce RO, Bryant T. Increased failure rate of autologous chondrocyte implantation after previous treatment with marrow stimulation techniques. *Am J Sports Med* 2009;37:902-908.
7. Minas T. Autologous chondrocyte implantation for focal chondral defects of the knee. *Clin Orthop Relat Res* 2001;391:S349-S361 (suppl).
8. Knutsen G, Drogset JO, Engebretsen L, et al. A randomized trial comparing autologous chondrocyte implantation with microfracture. Findings at five years. *J Bone Joint Surg Am* 2007;89:2105-2112.
9. Brittberg M, Lindahl A, Nilsson A, Ohlsson C, Isaksson O, Peterson L. Treatment of deep cartilage defects in the knee with autologous chondrocyte transplantation. *N Engl J Med* 1994;331:889-895.
10. Osiris Therapeutics I. Characterization of Cartiform® viable osteochondral allograft. Cartiform White Paper 2015.
11. Osiris Therapeutics I. Cartiform® retains endogenous viable cells after two years storage at −80°C. Cartiform White Paper 2015.
12. Osiris Therapeutics I. Cartiform promotes mesenchymal stem cell migration and chondrogenesis. Cartiform White Paper 2015.
13. Jakob RP, Franz T, Gautier E, Mainil-Varlet P. Autologous osteochondral grafting in the knee: Indication, results, and reflections. *Clin Orthop Relat Res* 2002:170-184.
14. Wood JJ, Malek MA, Frassica FJ, et al. Autologous cultured chondrocytes: Adverse events reported to the United States Food and Drug Administration. *J Bone Joint Surg Am* 2006;88:503-507.
15. Hoffman JK, Geraghty S, Protzman NM. Articular cartilage repair using marrow stimulation augmented with a viable chondral allograft: 9-month postoperative histological evaluation. *Case Rep Orthop* 2015;2015:617365.
16. Geraghty S, Kuang JQ, Yoo D, LeRoux-Williams M, Vangsness CT Jr, Danilkovitch A. A novel, cryopreserved, viable osteochondral allograft designed to augment marrow stimulation for articular cartilage repair. *J Orthop Surg Res* 2015;10:66.
17. Demange M, Gomoll AH. The use of osteochondral allografts in the management of cartilage defects. *Curr Rev Musculoskelet Med* 2012;5:229-235.