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Sports Medicine

Osteochondral Allograft Transplantation Using the Chondrofix Implant

Andreas H. Gomoll, MD

Osteochondral allograft transplantation has become an accepted, and increasingly popular, choice for cartilage repair. Its widespread application, however, remains limited by the availability of fresh grafts. Even minimal tissue contamination precludes graft processing, and limited chondrocyte viability necessitates a small window for implantation, generally within the first month after retrieval. A potential solution to these issues comes from a new processing technique to manufacture a preserved osteochondral allograft that is sterile and has an extended shelf life. This article reviews the background and surgical technique of this newly available implant.

KEYWORDS osteochondral allograft transplantation, cartilage repair, chondrofix

Cartilage defects continue to present a treatment challenge to orthopaedic surgeons. Recent years have seen the introduction of new technologies to improve upon limitations of currently available techniques.

Fresh osteochondral allograft transplantation has become an increasingly popular technique for cartilage repair. This popularity has led to bottlenecks with increased patient wait times because the supplies of fresh grafts remain limited. Only grafts from younger patients with intact knee joints are considered, and many potential grafts fail biological safety testing for viral and bacterial contamination. To preserve the viability of articular chondrocytes, grafts cannot be "rescued" by radiation or chemical decontamination of even minimal amounts of bacterial contamination. Finally, the window of implantation prior to decreased chondrocyte viability is quite short, further complicating scheduling, shipping, and thus graft availability.

A new implant has recently become clinically available that has the potential to address the supply shortage limiting the use of osteochondral allograft transplantation. The manufacturer treats preshaped osteochondral allograft plugs with a proprietary process to remove lipids and decontaminate the tissue, while preserving the hyaline cartilage matrix.

This article discusses the background and surgical technique of this allograft, the chondrofix implant.

Regulatory Perspective

Given the vast expense and time involved in the development of biological implants that fall under the direct jurisdiction of the Food and Drug Administration (FDA), manufacturers have recently focused on implants that are regulated in the "minimally manipulated tissue" category.

Human tissue and tissue-based products are not considered, and therefore regulated, by the FDA as medical devices, drugs, or biologics under certain specific conditions. The tissue has to be only minimally processed and cannot be combined with another active compound; it has to be intended for homologous use only and can act only locally rather than systemically.

If these criteria are fulfilled, the FDA only regulates safety aspects of the process but does not require efficacy data from clinical trials prior to clinical use. [Title 21 of the Code of Federal Regulations Part 1271 (21 CFR 1271)]. The safety aspects are mainly related to the potential for transmission of infectious disease, and require extensive serologic, bacterial, and viral testing, donor screening, procurement, storage requirements, and graft quarantine until negative testing is assured.[1,2] The risk of HIV transmission is estimated to be approximately 1 in 1.6 million, and there have been no reported cases of this route of disease transmission since the

Cartilage Repair Center, Dept. of Orthopaedic Surgery, Brigham and Women's Hospital, Boston, MA.

Conflict of Interest: AHG participates in a prospective clinical trial of Chondrofix. No research grant or consulting payments by Zimmer to declare.

Address reprint requests to Andreas H. Gomoll, MD, Cartilage Repair Center, Dept. of Orthopaedic Surgery, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115. E-mail: agomoll@yahoo.com

1060-1872/13/$-see front matter © 2013 Elsevier Inc. All rights reserved.
doi:http://dx.doi.org/10.1053/j.otsm.2013.03.002

late 1980s.[1] In addition to the FDA Good Tissue Practice guidelines, most tissue banks adhere to the even stricter standards of the American Association of Tissue Banks.

Processing

Chondrofix is a preserved (nonfresh) osteochondral allograft consisting of decellularized hyaline cartilage matrix and subchondral bone. The tissue is obtained from weightbearing areas of cadaveric human joints procured by an FDA and American Association of Tissue Banks accredited Tissue Bank; currently by LifeNet Health. Although grafts could potentially be retrieved from any diarthrodial joint, currently only knee joints are used as donors.

Grafts are prepared in 4 different diameters (7, 9, 11, and 15 mm) and a constant length of 10 mm. The tissue then undergoes a proprietary process to remove lipids and bone marrow elements. Finally, the grafts are soaked in methylene blue under light illumination as a viral inactivation process, resulting in the typical blue staining. This method has been utilized for more than 10 years for viral inactivation of fresh frozen plasma.[3,4] Low-dose gamma irradiation completes the process, resulting in a Sterility Assurance Level of 10^{-6} [Chondrofix Packaging Insert].

Biological and Mechanical Properties

The implant underwent biocompatibility testing according to ISO 10993 in various in vitro and in vivo models to determine the potential for allergic sensitization, tissue irritation, genotoxicity, carcinogenicity, and reproductive toxicity, and was found to be biocompatible.[5]

When compared with nonprocessed osteochondral allograft tissue obtained from corresponding anatomical locations, the implant has equivalent thickness and compressive modulus of the hyaline cartilage component. Similarly, the subchondral bone shows equivalent compressive failure strength and compressive modulus. The processing decreases lipid content by more than 90% from 35% to 2% of dry weight.[6]

Indications

Indications for osteochondral allograft transplantation traditionally included traumatic or degenerative osteochondral lesions of the femoral condyles greater than 2 cm^2, particularly when the accompanying bone loss is greater than 6 mm. Recently, these indications have been broadened by many to include defects limited to the articular surface, even with normal subchondral bone.[7]

Osteochondral allografts are an ideal technique to revise prior failed cartilage repair procedures, especially when changes in the subchondral bone are present, such as subchondral cysts and persistent bone marrow edema.

Contraindications are infection, inflammatory arthritis, and diffuse advanced degenerative changes.[2,8-11]

Surgical Technique

Generally, defects in the femoral condyles are best suited for this technique, which is closely related to that of osteochondral autograft transfer. The trochlea, owing to its complex geometry, is a more difficult location; defects in the relatively flat medial and lateral trochlear facet are amendable to osteochondral allograft transplantation with this implant, whereas the both concave or convex central trochlear shape cannot be matched by the biconvex plugs.

Both arthroscopic and open techniques are available depending on the plug size. The instrumentation for 7-, 9-, and 11-mm diameter implants is designed to allow (but not require) an all-arthroscopic approach, whereas the larger 15-mm diameter plug is implanted through a miniarthrotomy.

Unless this information is available from prior arthroscopy or high-resolution MRI, starting the procedure with a diagnostic arthroscopy can be helpful to determine the precise location, shape, and size of the defect. This allows selection of the appropriate size and number of plugs required to fill the defect, and to decide whether an open approach is required. Sizing guides are provided to assist with this determination (Fig. 1).

Technique for 7-, 9-, and 11-mm Plugs

The sizing guide is removed and replaced with a punch of the corresponding size. The obturator is removed after the punch has been introduced into the joint, and the punch is impacted perpendicularly to the articular surface to a depth corresponding to the length of the intended plug, generally 10 mm (Fig. 2). Using the punch as a drill guide, the bone is then removed using a drill bit. Both drill bit and punch are removed (Fig. 3) and the depth of the recipient site confirmed with the sizing guide.

The implant is provided in sterile packaging that includes a small amount of transport medium (sterile phosphate buffered

Figure 1 Chondrofix instrumentation (top); Implant (bottom left); and Sizing guides (bottom right). (Color version of the figure is available online.)

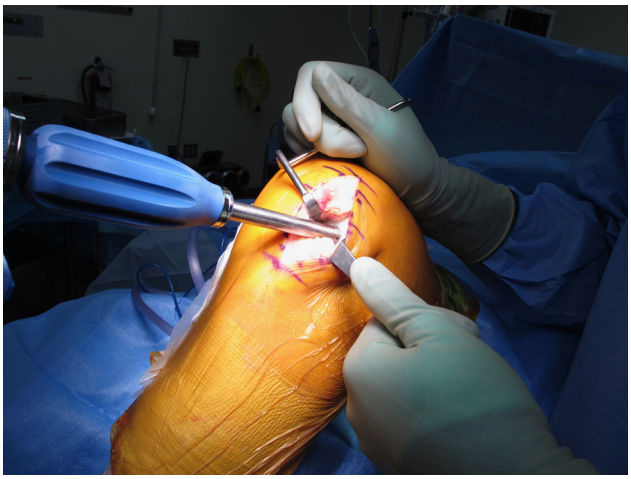

Figure 2 The punch has been impacted to a depth of 10 mm (this defect required multiple plugs and was therefore approached open, rather than arthroscopic).

saline) to avoid desiccation of the tissue during storage (Fig. 4). Once removed from the packing, the plug is implanted with a holding device (Fig. 5) and seated fully flush with the surrounding cartilage using an oversized tamp (Fig. 6).

Technique for 15-mm Plug

Once the defect has been exposed through the appropriate surgical approach (Fig. 7), the 15-mm sizing guide is placed perpendicularly on the defect. A guide pin is drilled through the central cannulation and seated securely in the subchondral bone. The sizing guide is removed and a cannulated

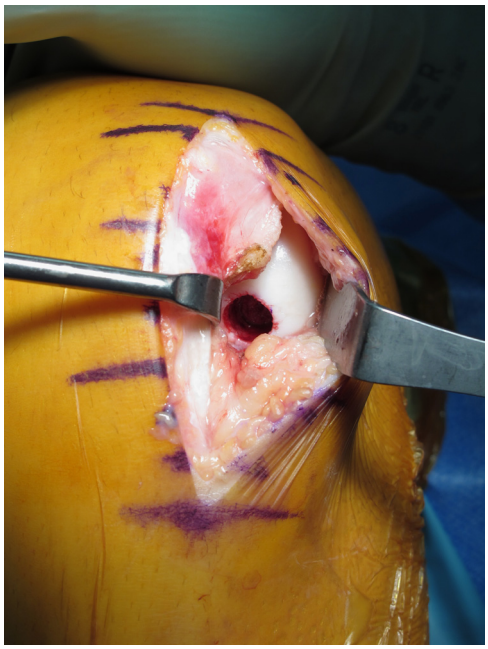

Figure 3 The defect in the lateral femoral condyle after reaming.

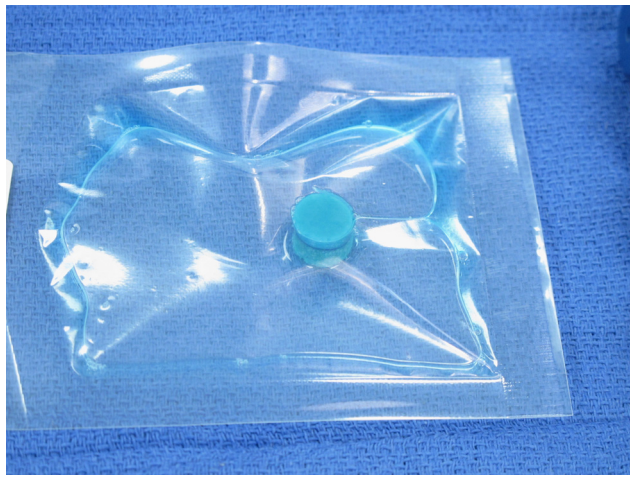

Figure 4 The implant in the sterile pouch.

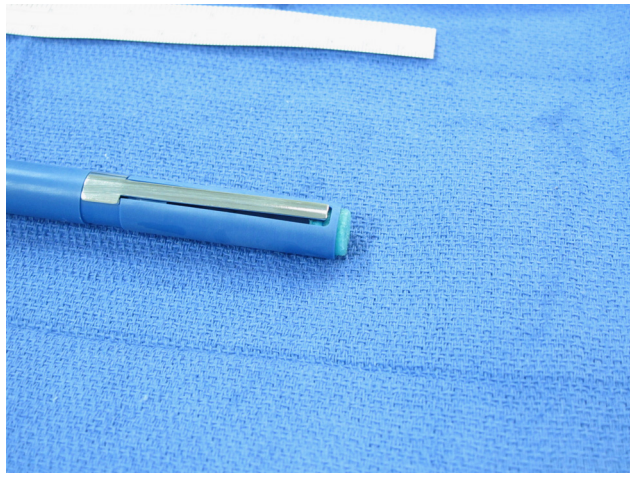

Figure 5 The implant loaded into the holding device.

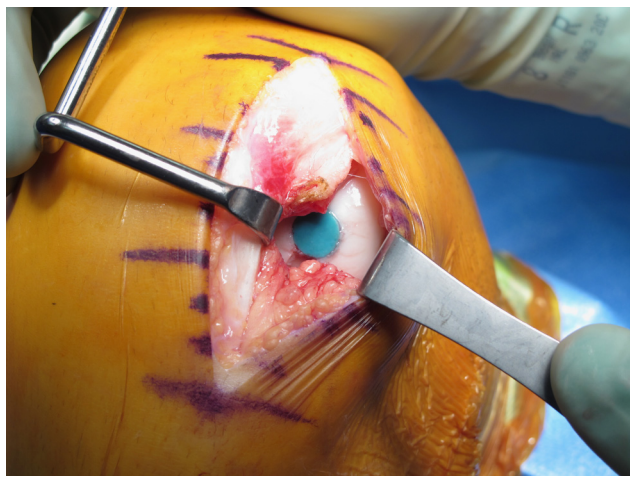

Figure 6 The implant after placement (subsequently, a 2nd plug was placed distal to the 1st).

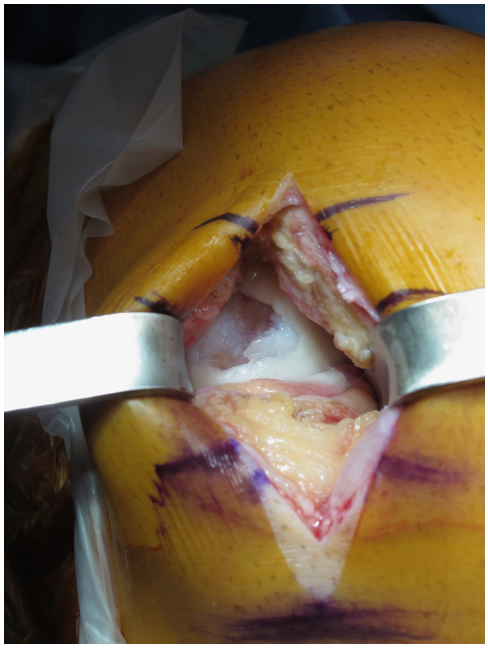

Figure 7 A large defect in the lateral femoral condyle after patellar dislocation.

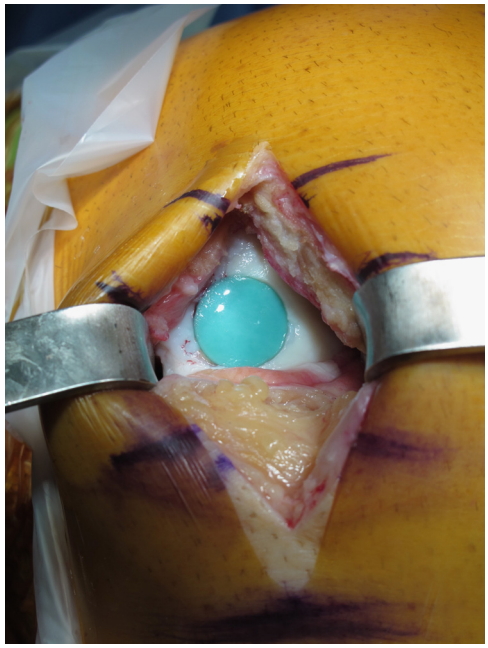

Figure 9 The implant after placement (15-mm plug).

reamer is used to prepare the recipient site (Fig. 8). The implants are provided with a standard length of 10 mm; however, slight variations exist, and the site should be reamed to a depth corresponding to the length of the intended plug. The final depth is confirmed using the sizing guide. The plug is then implanted with the holding device and seated fully flush with the surrounding cartilage using an oversized tamp (Fig. 9).

If multiple plugs are utilized, the steps are repeated until the defect is completely covered, with individual plugs either adjacent to each other or overlapping.

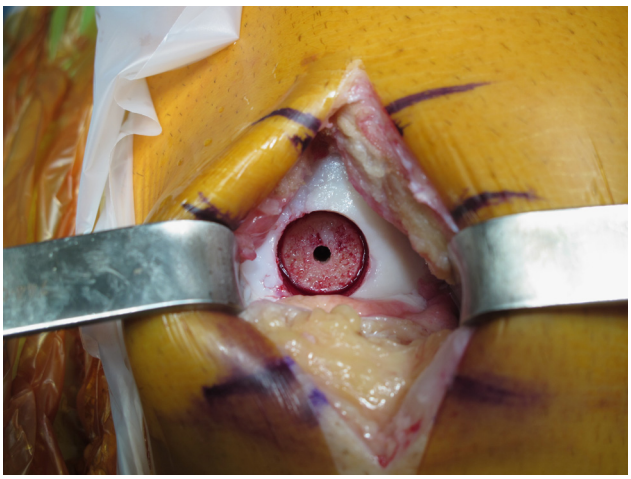

Figure 8 The defect after reaming to a depth of 10 mm. With the open technique, reaming is performed with a cannulated reamer using a guide pin.

Rehabilitation

With single plugs, patients can progress to weightbearing as tolerated and discontinue crutches once full weightbearing has been achieved, usually at or even before 6 weeks. Multiple plugs should be protected for at least 6 weeks with touch-down or partial weightbearing precautions. Range of motion is not restricted and the use of a brace is optional. Stationary biking with minimal resistance can be started as soon as pain and swelling allows, whereas weightbearing exercises such as minisquats or lunges should be delayed until 6 weeks postoperation.

Clinical Outcomes

No reports have been published regarding the clinical results of the chondrofix implant. A prospective registry study is currently enrolling patients to describe the clinical and radiologic outcomes [www.clinicaltrials.gov; Identifier: NCT01410136].

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