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The use of osteochondral allografts in the management of cartilage defects

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Abstract Large symptomatic osteochondral defects in a young active population represent a therapeutic challenge for orthopedic surgeons, since standard interventions such as debridement, microfracture and autologous osteochondral transfer are not suitable for the treatment of these larger lesions. Fresh osteochondral allograft transplantation provides a surgical option for these challenging defects, both as a primary procedure and for salvage of prior failed treatment attempts. This article reviews the basic science, indications, technique, and evidence for osteochondral allograft transplantation in the knee.

Keywords Cartilage repair · Osteochondral allograft transplantation · Biologic joint reconstruction

Introduction

Articular cartilage has a very limited capacity for healing. Symptomatic cartilage lesions, especially in young active individuals, can be debilitating and these patients are poor candidates for arthroplasty [1, 2]. The goals of surgical intervention are to provide pain relief and improve function in hopes of delaying or obviating the need for arthroplasty. The results of debridement, microfracture and osteochondral autograft transfer (OAT) in large lesions are not encouraging, and are therefore generally not recommended. Fresh osteochondral allograft transplantation is a suitable treatment option for these larger chondral defects, especially when associated with abnormalities of the underlying bone. Its major benefit is the replacement of the entire osteochondral unit with mature, hyaline cartilage and bone.

Fresh osteochondral allograft transplantation was introduced decades ago [3–7]. While initially reserved for the treatment of large osteochondral defects after trauma or resection of malignant tumors, it has become an increasingly popular choice for acute or degenerative chondral and osteochondral defects in an otherwise healthy joint. In the past two decades, multiple clinical studies have demonstrated the efficacy of fresh osteochondral allograft transplantation [6, 8–13]. Initially, grafts were implanted within 24 hours of procurement. Due to safety concerns related to transmission of viral and bacterial infections, meticulous screening is currently required before implantation [14]. Therefore, fresh osteochondral allografts are seldom implanted before a 7–10 day screening period. Studies have investigated the implantation of prolonged fresh osteochondral allografts up to 42 days after harvest, and have demonstrated good clinical results, even though chondrocyte viability decreases with time [15, 16].

Allograft preservation

Prolonged storage decreases chondrocyte viability, cell density, and tissue metabolism, but has only minimal effects on the extracellular matrix (ECM) and bone [17]. During fresh refrigerated storage, the chondrocyte viability and density will decrease over time: nearly all chondrocytes remain viable for up to four days when stored at 4°C, and up to 98 % are viable for seven days [18]. Due to the need for viral and bacteriologic screening tests, fresh allografts may be stored longer, typically for seven to ten days. By three weeks, chondrocyte viability falls to approximately 70 % and by seven weeks, to 67 %[18–21]. The precise association of cell viability and

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clinical outcomes, however, remains unknown [22, 23]. Current recommendations therefore advise 42 days as the maximum storage period for a fresh allograft [24]. The ideal preservation medium and storage temperature for fresh osteochondral allograft tissue remains controversial [25]. Ringer lactate solution preserves biochemical and biomechanical properties of the graft for only seven days [22]; more advanced proprietary solutions are in use to improve storage times. Currently, osteochondral allografts are stored at 4°C; however, Pallanteet al. found higher chondrocyte viability at 37°C compared to 4°C at 28 days [19]. Pennocket al. showed that the cartilage to bone ratio does not affect the chondrocyte degradation rate, supporting the current practice of storing the entire hemicondyle [26].

Frozen allografts are also available, but cartilage may fissure and delaminate, with breakdown of the articular surface, since freezing of mature articular cartilage (opposed to cell suspensions) causes chondrocyte death and damage to the ECM [27, 28••]. Ranawatet al. showed superior histological and biomechanical properties of cold stored allografts compared to deep freeze specimens in porcine models [24]. Possible causes for the inability to successfully freeze whole tissue specimens are the poor penetration of cryopreservative, unequal rate of freezing, and high water content within the extracellular matrix.

Recently, de-cellularized osteochondral allografts that are manufactured in specific sizes and have a long shelf-life at room temperature have become available. Clinical studies are currently pending to evaluate short-term and mid-term outcomes.

Immunogenicity

The surrounding dense avascular ECM makes the chondrocytes relatively "immunologically privileged." Phipatanakulet al. showed immunologic response to cartilage-specific protein antigens in patients treated with fresh osteochondral allograft [29]. The main immunogenic component is the subchondral bone, more specifically, the remaining bone marrow elements contained within [30]. The immunologic response of the host usually shows maximum activity between the second and third weeks. The initial inflammatory reaction to the graft typically diminishes over time, but can persist for up to 18 months. Even so, there appears to be no need for immunosuppression or tissue matching, although marrow elements should be removed with pulsatile lavage.

Graft healing

Bone healing of the graft occurs via creeping substitution. This is a slow process of bone remodeling by osteoblastic bone formation and osteoclastic resorption [17]. Williams et al. reported that at six months postoperative, trabecular incorporation of the allograft bone was complete in three, partial in eleven, and poor in four of 19 grafts based on MRI evaluation [15]. Minimizing the amount of transplanted bone may reduce the healing time; conversely, the cartilage component is mature and does not undergo any further healing. Donor chondrocytes survive for years; Jamaliet al. detected surviving female donor chondrocytes in a male host after 29 years [31]. Long-term analyses of retrieval specimens after revision of prior osteochondral allograft demonstrated high donor chondrocyte viability [12, 32].

Clinical evidence

There are numerous clinical studies supporting the use of fresh or prolonged fresh osteochondral allograft transplantation (Table 1). McCullochet al. (2007) reported a 96 % graft survival rate at a minimum of two years [16]. LaPradeet al. reported complete graft survival and good clinical results with refrigerated allografts stored between 15 and 28 days after an average follow-up of three years [28••]. Davidsonet al.

Table 1 Knee fresh osteochondral allograft case series studies

Study	Mean follow up (y)	Number of knees	Cause of chondral or osteochondral lesion	Failure rate	Graft survival rate
McCulloch et al. [16]	2.9	25	Various	4 %	96 %
LaPradeet al. [28••]	3	23	Various	0 %	100 %
Williamset al. [15]	4	19	Various	21 %	79 %
Gortzet al. [34••]	5.6	28	Steroid associated osteonecrosis	18 %	89 %
Emmersonet al. [9]	7.7	66	Osteochondritis dissecans	15 %	91 % at 5 year follow-up (y f/u), 76 % at 10 y f/u,76 % at 15 y f/u
Grosset al. [35]	10	60	Post traumatic; Osteochondritis dissecans	20 %	95 % at 5 y f/u, 85 % at 10 y f/u, 74 % at 15 y f/u

described second-look arthroscopic evaluation and biopsy at a mean of 40 months after implantation in eight patients (ten knees). Biopsy specimens of the graft and native articular cartilage were not statistically different for cell density and viability [33].

Treatment of steroid-associated osteonecrosis has demonstrated acceptable results [34••], but inferior to posttraumatic osteochondral lesions [35]. The treatment of osteocondritis dissecans lesions has shown good to excellent results in up to three quarters of the patients [9].

Return to athletic or high demand activity has been reported after osteochondral allograft surgery. Krychet al. evaluated the return to athletic activity after osteochondral allograft transplantation in 43 athletes treated with fresh osteochondral allografts. The authors found a high rate of return to sports, but age over 25 years and duration of symptoms over 12 months predicted a lowered probability of returning to sports [36••].

The use of fresh osteochondral allografts to the patellofemoral joint has been reported with poorer results compared to the femoral condyle or tibial plateau. Torga Spak et al. retrospectively reviewed 14 fresh allografts (11 patients) with average follow-up of ten years (range, 2.5 to 17.5 years). In this series, at the last follow-up, eight grafts were in place, four for more than 10 years and two for more than 5 years. Of the non-surviving allografts, three survived more than 10 years [37]. Jamali et al. reported five failures in 20 knees (18 patients) treated for patellofemoral lesions [38].

Use of osteochondral allografts in other joints

Shoulder

Osteochondral allografts have been described in the treatment of glenoid lesions and glenhohumeral arthritis. Skendel and Sekiya described a technique of arthroscopic anteroinferior glenoid reconstruction using glenoid osteochondral allograft without subscapularis takedown [39]. Provencher et al. reported the use of a distal tibia allograft for the treatment of glenoid bone deficiency [40]. Giannini et al. described a case report of bipolar fresh osteochondral allograft for the treatment of glenohumeral posttraumatic arthritis with good short term clinical results [41].

Talus

The use of osteochondral allografts for lesions in the talus is common practice. Gortz et al. reported results in 12 ankles (11 patients) with partial, unipolar grafts of the talar dome, implanted through an anterior approach without osteotomy, under temporary distraction. In this series, the failure rate was 17 % (two ankles), one treated with graft revision and one conversion to arthrodesis [42]. El-Rashidy et al. reported the clinical outcomes of 42 patients. Graft failure occurred in four patients; patient satisfaction was rated as good or excellent by 28 of 38 patients [43]. Berlet et al. reported on 12 patients with a minimum follow-up of two years, showing radiolucencies in three, edema in four, and failure to incorporate in one, but none had subsidence [44]. Janis et al. reported short-term results of 15 patients: nine lesions had no evidence of lucency and six demonstrated mild lucency. Most patients exhibited no step-off deformity or arthrosis [45].

Indications, patient selection and preoperative planning

Large focal full-thickness chondral and osteochondral defects (>2 cm^2) on the femoral condyles are typical indications for fresh osteochondral allograft transplantation. Patients with chondral lesions without bone disease should also be considered for autologous chondrocyte implantation, while osteochondral defects such as osteonecrosis, or traumatic osteochondral defects, may be approached with fresh osteochondral allograft transplantation. Also, allografts can be utilized to revise prior failed cartilage repair. A detailed history of surgeries helps in predicting the condition of the cartilage and subchondral bone in patients with previous attempts to treat their osteochondral lesions.

Patellofemoral joint defects, especially when bipolar, show poorer results with allograft transplantation and we usually perform ACI, with or without bone grafting. We also avoid operating on smokers, obese patients, those with inflammatory arthritis, and those with advanced osteoarthrosis.

Radiographs and magnetic resonance imaging (MRI) should be performed as part of the pre-operative evaluation. The former includes lower extremity alignment views, as well as weight-bearing anteroposterior and flexion posteroanterior radiographs, lateral and patellar views. For sizing of the allograft, radiographs can be obtained with sizing markers to accommodate for magnification; or sizing can be determined directly from MRI/CT scans. Altered load distribution due to mal-alignment results in abnormal stress increases on the articular cartilage [46]. In the normally aligned knee, the center of pressure of the tibiofemoral force passes slightly to the medial side of the knee during stance [47]. We consider 3^o of varus or valgus malalignment as a threshold for corrective osteotomy [48].

MRI allows evaluation of lesion size, condition of the subchondral bone, and associated meniscal or ligament deficiency. Cartilage lesions are typically underestimated during preoperative MRI measurements. Usually, the final defect area at surgery is over 60 % larger than predicted by the preoperative imaging [49]. Surgeons should consider

this fact whenever interpreting an MRI to choose the correct treatment modality.

Surgical technique

There are two main surgical techniques: cylindrical press-fit plugs or free-hand shell grafts. Size-matched and compartment-matched allograft are preferred for either technique, and graft matching may take many months. Sending the sizing information to multiple tissue banks may increase the chance of expedient matching.

Before the procedure, the surgeon should carefully plan all concurrent procedures, if needed. Limited lateral or medial arthrotomy without dislocation of the patella is usually sufficient for smaller defects. When dealing with larger defects, patella subluxation may be necessary. In this situation, we perform quadriceps-sparing approaches such as a subvastus approach whenever possible. Care should be taken to avoid damaging the articular cartilage and the anterior meniscal horn during arthrotomy. In very posterior lesions, the anterior horn of the meniscus may need to be detached and reattached during closure.

For the press-fit plug technique, a sizing cylinder is positioned over the lesion. A guide wire is placed in the center of the sizing cylinder, perpendicular to the articular surface. A reamer then removes tissue down to healthy cancellous bone; generally, a shallow bed of approximately 5 to 8 mm total thickness (cartilage and bone) is sufficient to avoid the transplantation of large quantities of allograft bone. Deeper reaming may be necessary in the presence of necrotic bone from osteochondritis dissecans or osteonecrosis. Bone grafting may be necessary in deep lesions and may be collected from the reaming. The depth of the recipient site in all four quadrants is then measured to harvest a matching plug from the donor condyle.

Ideally the plug should be harvested from the corresponding topography on the allograft hemicondyle. Anatomical parameters such as the *sulcus terminalis* and distance to the posterior condyle usually help to select the appropriate donor site. The graft hemicondyle is fixed in a workstation and a matching coring reamer is used to harvest the cylindrical plug. The recipient site depth should be marked with a surgical pen on the plug, which is then cut to the appropriate thickness.

Before graft insertion, the bony edges of the allograft are beveled to facilitate insertion, which should occur without the use of excessive forces that could injure the chondrocytes. To access graft stability the knee is taken through a full range of motion. Typically there is no need for supplemental fixation; however, if there are any concerns over graft stability, metal or resorbable pins and screws can be used and should be recessed well below the articular surface.

Larger defects may require the use of multiple plugs in the so-called snowman technique, which consists of placing and fixing the first plug, then drilling a second recipient site next to, or partially over the first one (Fig. 1).

Occasionally, defects are not amenable to the plug technique; for example, very posterior defects that cannot be accessed perpendicularly, or defects of the tibial plateau. Here, the shell technique is utilized, which essentially creates a geometric recipient site through the use of bur and osteotomes. A matching shape is formed from the donor tissue, which is then fixed with screws and pins. A foil or paper template helps to mold the graft in the same geometric shape as that of the recipient site.

Postoperative care

The goal of postoperative rehabilitation after osteochondral allograft transplantation includes preventing graft overload until bone healing occurs, while avoiding arthrofibrosis and minimizing muscle atrophy. In the tibiofemoral joint, we typically recommend touch-down weight bearing for six weeks, but massive or less stable grafts can occasionally require longer. The smaller and inherently more stable the graft, the earlier weight bearing may be progressed. Early passive range of motion is encouraged and continuous passive motion devices may be helpful in the early postoperative period, but are less essential than for cell-based therapy such as microfracture or ACI.

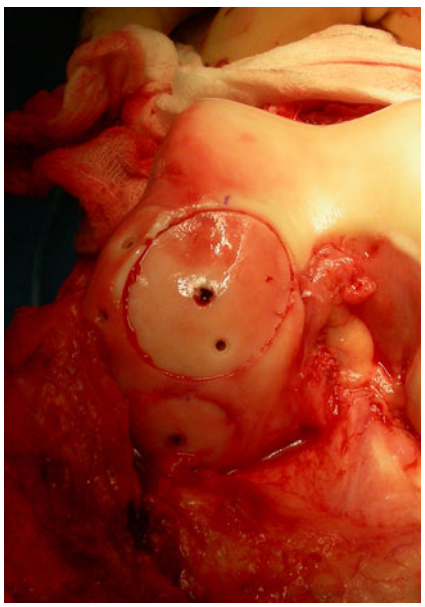

Fig. 1 Intra-operative image of two osteochondral plugs directly adjacent to each other. The patient is a 21-year-old male with osteonecrosis of the medial femoral condyle after high-dose steroid therapy for leukemia. The plugs are fixed with resorbable screws and pins

Braces may be used to protect the graft. Unloading braces can be considered, especially for bipolar defects, or when performed concurrently with meniscal transplantation.

Risks and complications

Allograft-associated infection is exceedingly rare but may potentially be fatal. Clostridium contamination risk increases with the length of time between donor death and procurement [50, 51]. Safety guidelines established by the American Association of Tissue Banks (AATB) advocate donor screening, extensive serologic, bacterial, and viral testing; procurement and storage requirements; and graft quarantine until negative testing results are ensured [52]. Deep infection following allograft transplantation should be considered for surgical debridement and graft removal. To improve the safety of allograft use, tissue banks and surgeons must keep tracking information and report any allograft-related infection [53].

Failure in the osseous portion of the allograft is most common, where subchondral collapse, delayed union or nonunion may occur. Larger and bulkier grafts are associated with higher risks of these complications. Graft fragmentation and collapse are among the main failure mechanisms usually presenting as new onset of pain, joint effusion, and mechanical symptoms. As a milder complication, allograft subsidence may occur in up to 30 % of the patients [54]. Whenever patients remain asymptomatic despite radiological graft subsidence, observation may be indicated. Ideally, postoperative imaging reveals a well-incorporated flush graft with marrow signal consistent with fat, and an articular cartilage signal that is isointense to normal cartilage [15].

Some patients have persistent pain after fresh osteochondral allografts, potentially due to a low-grade chronic inflammatory reaction to the graft.

Authors' preferred algorithm

Initially, we evaluate the size of the cartilage lesion and the condition of the subchondral bone on radiographs and MRI. Although osteochondral allograft transplantation does not require an initial arthroscopy such as needed for ACI, given the complexity of these cases, a staging arthroscopy is often helpful to thoroughly assess the joint and create a comprehensive plan for reconstruction. Small cartilage defects up to 2 cm^2 are treated with osteochondral autograft transfer or microfracture. Larger cartilage defects without subchondral bone disease are considered for autologous chondrocyte implantation. Larger cartilage defects with subchondral bone edema, cysts, or intralesional osteophytes may be treated with osteochondral allograft transplantation or sandwich ACI. Most lesions can be treated successfully with the plug technique, while a shell technique rarely becomes necessary. Limb alignment and ligament reconstruction is generally performed concurrent to allograft transplantation.

Conclusion

Fresh osteochondral allograft transplantation is an appropriate option for the treatment of large osteochondral defects with good long-term survivorship of over 70 % in most patients and indications. Better outcomes are seen in younger patients, unipolar defects, and with treatment less than 12 months from the onset of symptoms. Bipolar disease, osteoarthritis, and steroid-induced osteonecrosis show less favorable outcomes. Fresh grafts should be implanted within one month due to decreasing chondrocyte viability. As with any cartilage repair procedure, articular co-morbidities need to be carefully assessed and treated in a concurrent or staged fashion.

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