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Osteochondral Allograft Reconstruction: Improvements in Surgical Techniques and Allograft Processing

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Fresh osteochondral allograft (OCA) transplantation has more than a 100-year clinical history. Many clinical and basic scientific studies have been performed with the result that allografting is now part of the cartilage repair paradigm for the treatment of chondral or osteochondral lesions. In the knee joint, allografting has also been successfully used in complex joint reconstruction for the treatment of osteonecrosis, fracture malunion, and selected cases of osteoarthritis. Unlike many other cartilage repair techniques, OCAs have the ability to restore mature, hyaline articular cartilage to the affected area. By virtue of their composite structure (cartilage and bone), allografts also can restore diseased or damaged bone often present in large or complex lesions. The surgical techniques of allografting are relatively straightforward, and many clinical studies have shown excellent results. OCAs do present the surgeon with unique and important differences from other cartilage repair techniques, such as limited allograft tissue availability and the potential for transmission of infectious disease from the graft or immunologic response by the recipient. Ongoing investigations continue to clarify the indications, surgical techniques, and clinical outcomes of fresh OCAs.
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Introduction

The concept of treating articular cartilage diseases with bone and cartilage substitutions in the knee has now a history of more than a century, since the first joint transplantation described by Lexer[1,2] in 1908. Animal and clinical studies concerning transplantation and immunology were carried out in the 1960s, demonstrating that transplanted fresh cadaver cartilage is viable.[3-5] In the 1970s, Gross et al began reporting on their experience with small fragment and partial joint OCAs for posttraumatic and periarticular tumor reconstruction.[6,7] In the 1980s, Meyers et al[8] first applied this technique to specific chondral and osteochondral diseases such as chondromalacia, osteoarthritis, and osteonecrosis, developing the shell-shaped graft. Later in the 1990s, Garrett[9] first reported on the use of allograft plugs for the treatment of osteochondritis dissecans of the knee. In the past 20 years, a large number of basic scientific and clinical studies have been performed. These studies and the increasing availability of fresh allografts have led to an increasing popularity of fresh allografts and the inclusion of this procedure as part of the cartilage repair paradigm for the treatment of chondral or osteochondral lesions (OCDs) in the knee.

Allograft Recovery, Processing, and Storage

Before 1998, the use of fresh OCA in North America was restricted to 2 institutions, which maintained their own systems for retrieving, processing, and storing tissues for their own clinical use.[10] These allografts were stored in lactated Ringer's solution, which could maintain the biochemical and

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biomechanical properties of the graft for 7 days, with transplantation within 1 week of donor's death.[11] Around 1999, OCAs became commercially available from tissue banks, whose guidelines for procurement and processing were established by the American Association of Tissue Banks under oversight from the Food and Drug Administration.[12] Allograft tissue is harvested within 24 hours of donor's death, ideally from donors between the ages of 13 and 35 years with grossly healthy articular cartilage.

Chondrocyte viability is critically important for maintenance of the material properties of the graft, which correlates directly with the clinical success of OCA transplantation.[13,14] Chondrocytes maintain the extracellular matrix, thereby maintaining the material properties of the graft if they are kept viable in storage. Gross et al[15] demonstrated that long-term survival of OCAs in vivo depended on the presence of viable chondrocytes, intact extracellular matrix, and incorporation of host bone. Furthermore, chondrocyte viability at the articular surface (superficial zone) is important for long-term graft survival.[16] Following transplantation, several studies have demonstrated preservation of chondrocyte viability over time. Haudenschild et al[17] demonstrated that OCA chondrocytes are viable, retain gene expression, and have chondrogenic potential 3 years after transplantation. Retrieval studies of OCAs after revision have shown high donor chondrocyte viability many years after transplantation.[18] Jamali et al[19] demonstrated that donor chondrocytes could survive up to 29 years after transplantation.

The processing and storage of OCAs (frozen, cryopreserved, or fresh) has different effects on chondrocyte viability. Biomechanical and biochemical composition of cartilage deteriorates over storage time, correlating with decreasing chondrocyte viability.[20] Freezing grafts at −80°C maintains less than 5% chondrocyte viability, and the extracellular matrix deteriorates owing to a lack of viable chondrocytes to maintain the matrix.[21,22]

Currently, fresh OCAs maintain the highest chondrocyte viability among the available storage options.[23] Chondrocyte viability begins to decrease, and biomechanical properties deteriorate in fresh OCAs stored hypothermically at 4°C for greater than 7 days.[24] A 2009 study by Pallante et al demonstrated increased chondrocyte viability throughout all zones when fresh grafts were stored at 37°C as compared with 4°C, with acceptable percentage of viable chondrocytes after 28 days of storage. This study increased the effective length of time a graft could be stored before transplantation.[23] This increased timeframe is critically important, as tissue banks currently hold OCA tissue until the completion of microbiologic and serologic testing, generally a minimum of 14 days.[12,25] Other recent studies have also indicated that a transition of storage to physiological (37°C) or room temperature (25°C) improves the viability of OCAs during storage.[23,26] In general, our current recommended maximum time from harvest to transplantation is 28 days, correlating to at least 70% chondrocyte viability at implantation when stored at 4°C.[20,27] Improved allograft processing that may safely allow for earlier graft implantation (as was practiced before commercialization) and storage technology that may increase chondrocyte viability and preserve extracellular matrix properties to allow longer storage continue to be active areas of research.[28-30]

There is tremendous interest outside the United States in fresh allograft technology. However, numerous regulatory, logistic, and cultural issues have historically been difficult to overcome. Setting up an allograft program outside the United States is facilitated by an association with an existing university-affiliated tissue bank. In addition, every country has unique regulations that need to be considered, depending on whether the health care system is public or private. Rizzoli institute in Bologna, Italy, has an established program as does the University of Toronto in Canada.

In most developing countries, the main health care system is public, and typically, tissue banks are within the domain of a public university. Recently, one of the authors set up a fresh OCA program in Brazil in collaboration with the Institute of Orthopedics and Traumatology tissue bank located at the University of São Paulo. As organ donation was already routine in São Paulo, and tendons and bone were routinely recovered for other orthopaedic uses, some minor changes had to be put in place to make fresh allografts feasible. The main change was to approve a regulatory amendment on the existing tissue-banking legislation, making it legal to store fresh grafts in tissue culture media for 30 days after the recovery date. Before 2009, tissue-banking regulations only allowed fresh grafts to be stored until 14 days after recovery, which was not enough to have all required testing completed. In 2012, the first fresh allograft was performed in Brazil.

Indications for OCAs

Fresh OCAs possess the ability to restore a wide spectrum of chondral and osteochondral pathologies. As a result, the clinical indications cover a broad range of pathology (Table 1). In our experience, allografts can be considered as a primary treatment option for OCDs >2 cm in diameter, as is typically seen in osteochondritis dissecans and osteonecrosis (Fig. 1). Allografts are useful as a revision cartilage restoration procedure when other cartilage treatments, such as microfracture, osteochondral autologous transfer, or autologous chondrocyte implantation, have been unsuccessful. Allografts

Table 1 Indications for Osteochondral Allografts in the Knee

Complex Reconstruction	Cartilage Repair
Posttraumatic periarticular fracture malunion	Chondral or osteochondral defects larger than 2 cm^2
Single-compartment arthritis or multifocal degenerative lesions	Osteochondritis dissecans
Massive type III or IV osteochondritis dissecans	Revision of previous failed cartilage repair surgery
Osteonecrosis of the femoral condyle	Subchondral bone lesions without full-thickness cartilage defect