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The Use of Allografts in Orthopaedic Surgery

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Introduction

Tissue grafts can be divided into autografts, allografts, and xenografts. An autograft is tissue from the same individual, such as an autogenous iliac cancellous bone graft. An allograft is tissue from the same species but is not genetically identical. A frozen distal femoral allograft for tumor reconstruction is an example. A xenograft is tissue from a different species, such as the use of bovine xenograft bone graft that was popular during the 1970s.

Autogenous tissue is still considered the gold standard for reconstructive orthopaedic surgery. These grafts are nonimmunogenic and represent a good alternative to replace missing bone, ligaments, and cartilage. Autogenous cancellous graft, for example, is osteogenic, osteoconductive, and rapidly revascularized. Cancellous autograft also possesses living cells that participate in the bone repair process. This type of graft, however, does not provide structural support. Cancellous graft undergoes stages of healing.[1-5] Initially there is hemorrhage and inflammation. The grafted cancellous bone cells subsequently die except for the surface osteoblasts, which remain viable. The cancellous graft is next invaded by blood vessels that deliver osteoclasts from the peripheral circulation. These osteoclasts remove the cancellous bone while it is replaced by living bone. Osteoblasts line the necrotic bone graft, and eventually osteoid is produced. This process continues until the osseous defect is replaced with living bone. The final phase of graft incorporation is remodeling. This occurs as the bone responds to stress. Graft remodeling can occur for many months after the grafting procedure.

One or more of the authors or the departments with which they are affiliated have received something of value from a commercial or other party related directly or indirectly to the subject of this chapter.

Autogenous bone grafts can come from many different sites, most commonly from the ilium in the form of cancellous or combination cortical and cancellous grafts when needed. Other donor sites include the upper tibia, distal radius, olecranon, and distal tibia. Cancellous grafts are useful to fill contained osseous defects and for bone fusions in an onlay or inlay technique. When the bone defect is larger, such as an intercalary defect of a long bone, vascularized autogenous grafts can be used, such as a vascularized fibular autograft.[6-13] Vascularized fibular autografts provide structural support, maintain bone viability, and undergo stress remodeling, often leading to hypertrophy. Graft resorption occurs to a lesser extent than with nonvascularized grafts. This maintains the strength of the cortical bone that aids in its mechanical properties.

Soft-tissue autografts are commonly used in reconstructive surgery, primarily in sports medicine. Bone-patellar tendon-bone autografts are commonly used to reconstruct the anterior cruciate ligament (ACL), as are hamstring tendon and quadriceps tendon-bone autografts.

The problem with all autogenous graft tissue is the potential for donor site morbidity. For example, donor site complications reported with autogenous iliac bone graft include infection, hematoma, fracture of the ilium, nerve injury, and prolonged pain.[14-18] The use of autogenous iliac bone graft sometimes is the only reason for hospitalization and adds to the cost of patient care. Additionally, there is a limited amount of autogenous graft available. This is especially true in children.[19] Soft-tissue autografts also are associated with donor site patellofemoral pain after bone-patellar tendon-bone harvest and prolonged hamstring weakness after hamstring harvest.

Allografts

Although allografts solve the problem of donor site morbidity, they have inherent disadvantages because of limited graft availability, cost, the potential for disease transmission, and, in many clinical applications, slower and less complete graft incorporation compared to autograft tissue. Despite these limitations, however, enthusiasm has increased in recent years for the use of allografts in reconstructive orthopaedic surgery.

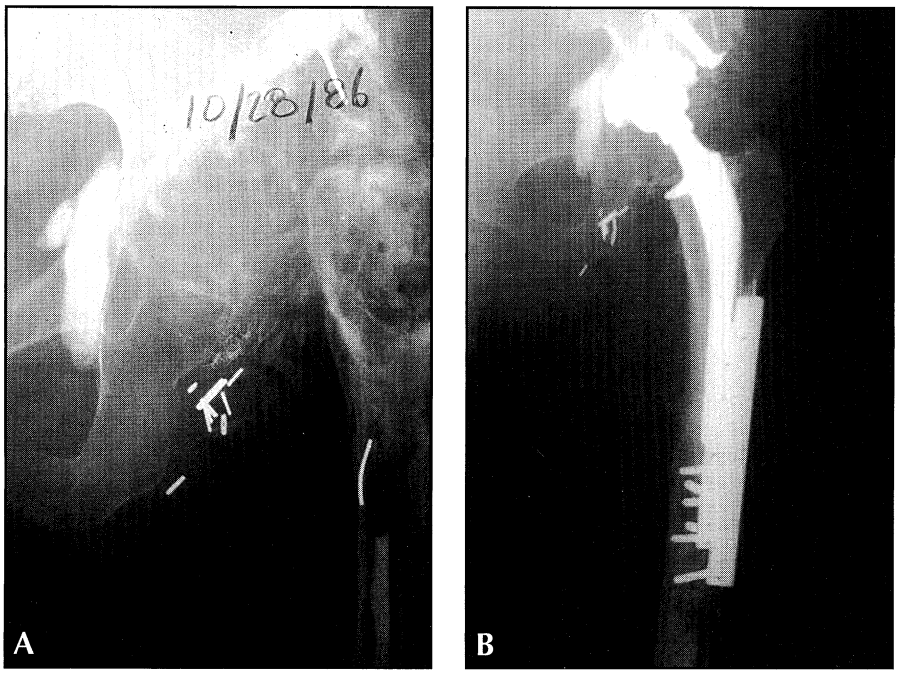

Fig. 1 A, AP radiograph of left hip in a patient after multiple hip arthroplasties now with marked bone loss. **B,** AP radiograph of the left hip. The proximal femur has been replaced with an allograft-prosthetic composite. Note the healing at the allograft-host junction.

Allografts generally are either fresh or processed. Fresh allografts are transplanted immediately after procurement and include fresh articular cartilage, fresh menisci, and fresh composite grafts. A limb transplant is a fresh vascularized composite allograft. Fresh allografts are true transplants because the tissue is alive. All other allografts are actually biologic implants rather than transplants because of limited cell viability. The types of processed allografts include frozen long bone, frozen tendon/ligament, cryopreserved menisci, frozen osteoarticular, frozen machined bone, freeze-dried cancellous bone, freeze-dried long bone, freeze-dried tendon/ligament, and demineralized bone matrix. In addition, allografts can be combined with implants. An example of an allograft-prosthesis composite is a combination of a proximal femoral allograft with a femoral prosthesis to restore missing bone of the upper femur (Fig. 1). Demineralized bone matrix can be combined with a carrier to improve handling characteristics. These allografts differ in important ways. Each has different biologic and mechanical properties that need to be considered during selection.

The use of allografts is not new.[20-30] Bone allografts were first used during the late 1800s, mostly in reconstructive tumor surgery. Carrel,[31] at the turn of the century, is credited with introducing the cold storage of human allografts to prevent degradation. The US Navy Tissue Bank was established in 1949. It was the first dedicated tissue bank in the United States, distributing grafts across the country. During the middle of the 20th century, three separate orthopaedic centers popularized the use of bone allografts. Ottolenghi[32] in Argentina, Parrish[33] in the United States, and Volkov and Imamaliyev[34] in the Soviet Union implanted bone allografts for various indications. Approximately one third of their patients had excellent results and one third had fair results; one third of the grafts failed. Mankin and associates[35-38] in the United States later developed great experience with frozen bone allografts and established some of the guiding principles for success. It has been found that deep-freezing the allograft diminishes its immunogenicity and improves success.[39-42]

Immune Response

The immune response to an allograft is the result of a cell-mediated process to cell surface antigens.[43-62] Class I and class II antigens are recognized by key lymphocytes and are responsible for the immune response. Allograft rejection can occur via cell-mediated cytotoxicity as well as antibody formation. Class I antigens are present on organs and tissue and generally are the first antigens to initiate the immune response. The most active immune response, however, is mediated by CD4 and CD8 cytotoxic T cells. These cells secrete cytokines that can result in allograft resorption. Patients who are responders demonstrate an immune response to class II antigens after allograft implantation and generally have a less successful clinical outcome than do nonresponders.

The intensity of the immune response depends on the antigen mismatch between graft and host.[56,63-65] Residual bone marrow cells within long bone allografts represent one of the major antigens in transplantations.[66] These cells are actively involved in the immune response. Cartilage allografts, on the other hand, are immunologically different from bone allografts. Although allogeneic chondrocytes do invoke both a cellular and humeral immune response, this response is clinically negligible after composite bone-cartilage allograft implantation.[67-74] This is explained by the class I and class II cell surface antigens on chondrocytes, which are relatively isolated from the immune system because of the proteoglycan matrix surrounding these cells. The most

immunogenic of allografts is a fresh vascularized composite graft. From least to most immunogenic, rank order is freeze-dried allograft, fresh-frozen allograft, fresh nonvascularized allograft, and fresh vascularized composite graft. Allograft processing, discussed in the following paragraphs, is important to reduce graft immunogenicity.

There are several ways to alter the immune response to human allografts. Immunosuppression of the recipient is one technique.[75] Immunosuppression is not commonly used, however, except in whole limb transplants. The only way to keep these vascularized composite allografts alive is to suppress the immunity of the host. Histocompatibility matching is another technique that can diminish the immune response. This is especially true for class II histocompatibility antigens. This technique, however, is impractical in clinical practice because of limited graft availability. The most common method for diminishing immunogenicity of allografts is freezing. It has long been known that either freeze-drying or fresh-freezing the allograft will diminish the immune response. These techniques kill the cells responsible for the most active route of rejection. A frozen bone allograft can thus be considered relatively nonimmunogenic for all practical purposes. The freezing, though, while desirable for immunity, is undesirable for bone repair. The graft completely loses its ability to make bone because of the absence of viable osteogenic cells.

Articular cartilage is particularly vulnerable to the deep-freezing process. Cartilage is 80% water, and deep-freezing osteoarticular allografts leads to the formation of ice crystals, which cause the death of the chondrocytes. Tomford and Mankin[76] and others[77-80] investigated cryopreservation techniques and found that cryoprotective agents, such as glycerol and dimethyl sulfoxide, diminish chondrocyte death during the freezing process. Cartilage therefore is immersed in these cryoprotective agents, which prevent crystal formation during the freezing process, and a variable number of chondrocytes may remain viable. Cryopreservation, however, does not have a significant effect on the mechanical properties of cartilage. Cryopreservation is technique sensitive[81-85] and is therefore not generally used clinically for articular cartilage transplantation (Fig. 2). Cryopreservation is, however, commonly used for meniscal tissue, as discussed in subsequent paragraphs.

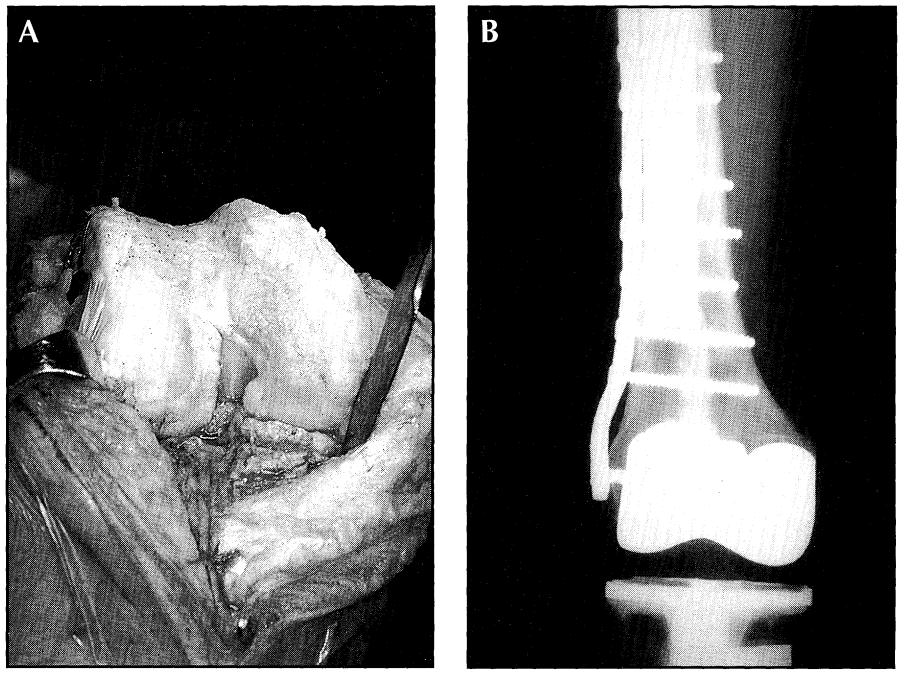

Fig. 2 A, Intraoperative photograph of frozen osteoarticular allograft 5 years after implantation. This graft was cryopreserved with glycerol. Note the loss of articular cartilage. This was salvaged with a standard total knee arthroplasty. **B,** Postoperative radiograph of the total knee arthroplasty using the allograft for bone stock.

Table 1
Substitute Graft Strength at Time of Implantation

Graft Type	Strength	Maximum Force (Newton)
Bone-patellar tendon-bone		
Central 1/3 13.8 mm	158%	2734
Medial 1/3 14.9 mm	168%	2900
ACL	100%	1725
Semitendinosus	70%	1216
Gracilis	49%	838
Iliotibial band		
15.6 mm	36%	628
45 mm	44%	1800
Fascia lata	36%	628
Retinaculum	21%	266

(Reproduced with permission from Jackson DW, Rosen M., Simon TM: Soft-tissue allograft reconstruction: The knee, in Czitrom AA, Gross AE (eds): Allografts in Orthopaedic Practice. *Baltimore, MD, Williams & Wilkins, 1992, pp 197-216.)*

Table 2
Hip Scores for Allograft Reconstruction

Allograft Designation	Mean Preoperative Score	Mean Postoperative Score	Mean Increment Score
Calcar	37	77	40
Proximal femur	30	66	36
Cortical femoral strut	37	79	42
Minor column	31	72	41
Major column	29	75	46
Protrusio cemented	32	74	42
Protrusio uncemented	42	80	38
Protrusio bicentric	33	59	26

(Reproduced from Allan DG, Lavoie GJ, Rudan JF, Gross AE: The use of allograft bone in revision total hip arthroplasty, in Friedlaender GE, Goldberg VM (eds): Bone and Cartilage Allografts: Biology and Clinical Applications. *Park Ridge, IL, American Academy of Orthopaedic Surgeons, 1991, p 271.)*

Table 3
Microorganisms Cultured at Tissue Recovery

Site	% of Allografts Contaminated	Microorganism type	% of Contaminated Grafts
Distal femur-proximal tibia	18.5	Gram-positive cocci	94.7
		Gram-negative rods	1.8
		Gram-positive rods	3.5
		Other	0.0
Femoral head	31.8	Gram-positive cocci	94.7
		Gram-negative rods	1.8
		Gram-positive rods	6.1
		Other	2.0
Iliac crest	46.6	Gram-positive cocci	69.3
		Gram-negative rods	26.4
		Gram-positive rods	3.7
		Other	0.6
Achilles tendon	70.3	Gram-positive cocci	91.7
		Gram-negative rods	2.5
		Gram-positive rods	5.0
		Other	0.8
Overall contamination rate	37.9		

(Reproduced wtih permission from Forsell JH: Irradiation of musculoskeletal tissues, in Tomford WW (ed): Musculoskeletal Tissue Banking. *Philadelphia, PA, Raven Press, 1993, pp 149-180.)*

Mechanical Integrity

As experience with the use of human bone allografts increased, issues of mechanical integrity became apparent.[86-88] Because the frozen bone allograft does not participate in osteogenesis, success depends on the host, especially at the allograft-host bone junction. The host needs to provide the repair process for the union of the allograft. Rigid internal fixation of long-bone allografts is an important principle. Rigid internal fixation can be achieved either by an intramedullary implant or a plate and screws. Some surgeons use step-cuts to increase the surface area at the allograft-host bone junction to improve union. Even if union occurs, fracture of long-bone allografts is a significant problem. Holes drilled into the allograft represent a significant risk for fracture because of the resultant stress riser and a potential site for revascularization. Revascularization weakens the allograft because of the resorption of cortical bone. It is important that the entire allograft be instrumented. Noninstrumented gaps or intervals in a long-bone allograft are common sites of fractures. Some surgeons even inject methylmethacrylate into the medullary space of the allograft to improve its mechanical properties.

Soft-Tissue Allografts

Following the introduction and success of large-bone allografts, soft-tissue allografts were introduced,[89-100] including bone-patellar tendon-bone, other tendons, fascia, and menisci. Frozen bone-patellar tendon-bone allografts are used extensively to restore the ACL. These tendon allografts actually exceed the strength of the normal ACL (Table 1). Other allograft options for the ACL include the Achilles, quadriceps, and hamstring tendons. These same grafts also can be used for posterior cruciate ligament and posterolateral corner reconstruction. After implantation, these grafts are thought to undergo a process of ligamentization that essentially uses the tissue as a biologic scaffold. Jackson and associates[101] described this as a series of sequential events that includes graft necrosis, cell repopulation, graft revascularization, and collagen remodeling, a process that occurs over a variable period, leading to adequate graft strength within 9 months to 3 years. The most common applications include multiple ligament reconstruction, revision surgery, structurally inferior autogenous sources (eg, in older patients), posterior cruciate reconstruction because of surgeon preference, and patient preferences related to cosmesis and decreased postoperative pain. The clinical results

of allograft ligament reconstruction in general are quite similar to autograft reconstruction, although long-term data are lacking.

Of particular interest (and discussed in greater detail in subsequent paragraphs) is the renewed interest in fresh osteochondral and meniscal allograft transplantation. Locht and associates[102] and McDermott and associates[103] popularized the use of fresh osteochondral allografts, especially those used for joint restoration. They found that fresh cartilage allografts maintained nearly 100% cartilage cell viability. Osteochondral allograft processing is typically carried out within 24 hours of the death of the donor. Graft processing includes excising the knee with the intact capsule in the operating room and maintaining it in Ringer's lactate with added cefazolin and bacitracin at 4°C. The limitations of fresh osteochondral allograft transplantation are logistic and partially related to the need for implantation before the final determination of bacterial contamination. Recipients need to be available at all times for immediate transplantation. Currently, extensive research in the area of prolonged fresh cartilage preservation is underway. These techniques use tissue-culture methods to maintain allograft cell viability. Once perfected, fresh transplantation will be less of a logistic concern.

Allograft meniscal tissue is now available, having been transplanted with great success.[104-108] There are four methods for preparing meniscal allografts, including fresh preservation (maintaining the tissue at 4°C), lyophilization, fresh-freezing, and cryopreservation. Fresh grafts rarely are used because of logistic concerns. Lyophilized (ie, freeze-dried) and fresh-frozen grafts have a negligible number of cells that survive processing. Cell viability maintained with cryopreservation ranges between 10% and 40%.[107,108] Unlike fresh osteochondral grafts, cell viability in meniscal allografts does not seem to improve the morphologic or biochemical characteristics of the graft and, thus, the most commonly implanted grafts are either fresh-frozen or cryopreserved.

The reported outcomes with all allografts in orthopaedic reconstructive surgery are generally good.[35-37,41,82,109-113] Mankin and associates[41] in 1991 reported 76% excellent or good results at an average 5-year follow-up of 401 patients who received long-bone allografts. The types of grafts included osteoarticular (232 patients), intercalary (77 patients), allograft composite (50 patients), and allograft arthrodesis (42 patients). Allan and associates[114] in 1991 reported a nearly 30-point mean improvement in hip scores (Table 2) in 73 patients in whom allografts were used for hip revision surgery. Czitrom and Gross[40] in 1992 reported on 55 patients with fresh osteochondral allografts, which were undertaken mostly for traumatic knee defects. Forty-two of 55 patients had successful outcomes, with an improvement in knee rating scores of 10 points. These reports represent a small sampling of the clinical experience with allografts.

Demineralized Bone Matrix

One of the most commonly used bone allograft materials at the present time is demineralized bone matrix.[115-128] Demineralized bone matrix has been used as a bone-graft substitute for many years. Urist and associates[129-132] found that demineralized cortical bone could be an effective osteoinductive material. Demineralization releases cytokines from the cortical bone. These cytokines participate in the complex cascade of events leading to bone repair. Currently, demineralized bone matrix is produced from human donors. Not all demineralized bone matrix, however, is active in bone repair. The variability is probably related to the donor and to the method of processing. Various bioassays are now being used to quantify the activity of demineralized bone matrix. One such assay uses an osteosarcoma cell line.[133] This assay measures mitogenic activity in this cell line, and it has been highly correlated with in vivo bone formation (a correlation coefficient of 0.85).

A multistep process produces demineralized bone matrix. Human cortical bone is first cleansed and ground into small particles. It is then demineralized by acid washes to reduce its calcium content. At the end of the process, a proteinaceous material containing osteoinductive cytokines is produced. The problem with demineralized bone matrix is its handling properties. Initially, demineralized bone matrix is a powdery material. Although it can be placed in a cavitary defect in bone, it is subject to being washed out by blood and other fluids. For this reason, some demineralized bone matrix products place these proteins in a carrier. One product (Allomatrix, Wright Medical Technology, Arlington, TN) combines demineralized bone matrix with a calcium sulfate carrier in the form of putty. Another product (Grafton, Osteotech, Eatontown, NJ) uses a glycerol carrier to improve handling characteristics. It is important to select a product that suits the clinical application, and the user should be familiar with the source of the product in terms of its biologic activity, cost, safety, and efficacy.

Procurement of Human Allografts for Orthopaedic Surgery

The regulation of tissue banks in the United States is principally by the Food and Drug Administration and the American Association of Tissue Banks.[134,135] These two regulatory bodies have generated guidelines for the procurement and processing of human tissue. Various standards have been established that most tissue banks follow to promote safety and consistency. Potential donors are first evaluated by

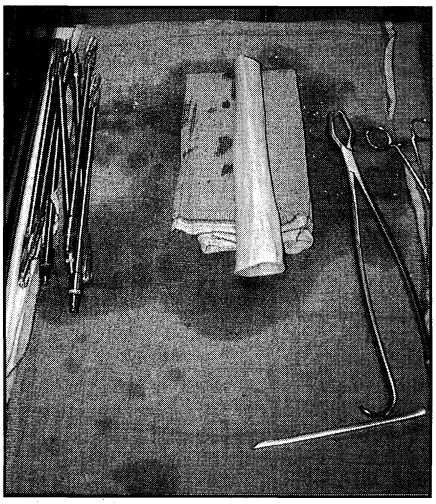

Fig. 3 Intraoperative photograph of a long-bone allograft. This graft has been cleared of all soft tissue and bone marrow elements.

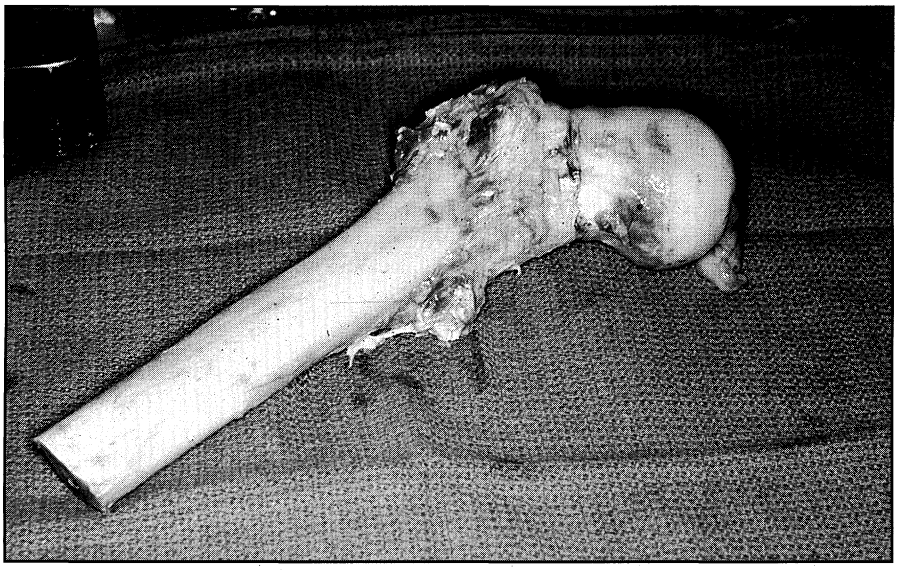

Fig. 4 Proximal femoral allograft. This graft has cryopreserved articular cartilage and tendons for abductor repair.

history and physical examination. The donors are screened for systemic illnesses such as cancer, infection, and other underlying problems that can affect the safety of donated tissue. Some donors are autopsied to rule out occult disease. Potential historical risk factors for acquired immuno deficiency syndrome and hepatitis infection are determined.

Two donor settings are used to acquire tissue: the operating room and a clean room. The operating room donor also is typically an organ donor. After the declaration of brain death, this donor requires the maintenance of life support. The consents are then obtained from the donor family after lengthy discussion regarding procurement and transplantation. The donor is transported to the operating room, and first the organs are procured. The life support is then discontinued, and the tissue is next procured. The donor sites are prepared and draped in a fashion similar to any orthopaedic surgical procedure, and the tissue is procured using standard extensile longitudinal surgical approaches under sterile conditions. After procurement, the tissue is cultured and then sterilely wrapped. A series of serologic examinations are obtained to screen for hepatitis and human immunodeficiency virus (HIV).[136-144]

The Food and Drug Administration as well as the American Association of Tissue Banks has guidelines for the donor evaluation. Tissue cultures are obtained from all donated tissue. The donor is screened for syphilis using the serologic test for syphilis, rapid plasma reagin test, and fluorescent treponemal antibody test. Hepatitis is screened using hepatitis B core antibody, hepatitis B surface antigen, and hepatitis C antibody. HIV is screened using HIV-1 and HIV-2 antibodies and human T-cell lymphotropic virus type I (HTLV-I) antibody. In addition, most tissue banks require HIV-1/2 polymerase chain reaction testing, which improves the ability to detect the virus and significantly reduces the seroconversion window (from as much as 6 months to about 19 days). Using these extensive screens, the risk of acquired immunodeficiency transmission is approximately 1 in 1.6 million and actually may be substantially lower than this. The last reported case of HIV transmission through transplantation was in 1992. This transplantation was from bone procured in 1985, before mandatory testing. With today's testing, this graft would likely have been detected as HIV positive.

Ultimately, depending on the clinical need, these grafts are processed. The tissue cultures are evaluated and classified into four types[145-148] (Table 3). Tissues that are culture negative or culture positive for low virulent organisms are sent for processing. Both of these graft categories are then processed and recultured and, if they are bacteria free, are released for clinical use. A third group includes grafts that culture virulent organisms such as *Staphylococcus aureus*. These grafts are sent for processing but are ultimately secondarily sterilized with gamma irradiation. Finally, grafts that are culture positive with highly virulent microorganisms, such as *Clostridium* species and yeast, are discarded and not sent to the processing facility.

Some grafts are procured in a clean room rather than in an operating room. These are from non-organ donors. These grafts must be refrigerated within 12 hours of asystole, and tissue recovery must take place within 24 hours of asys-

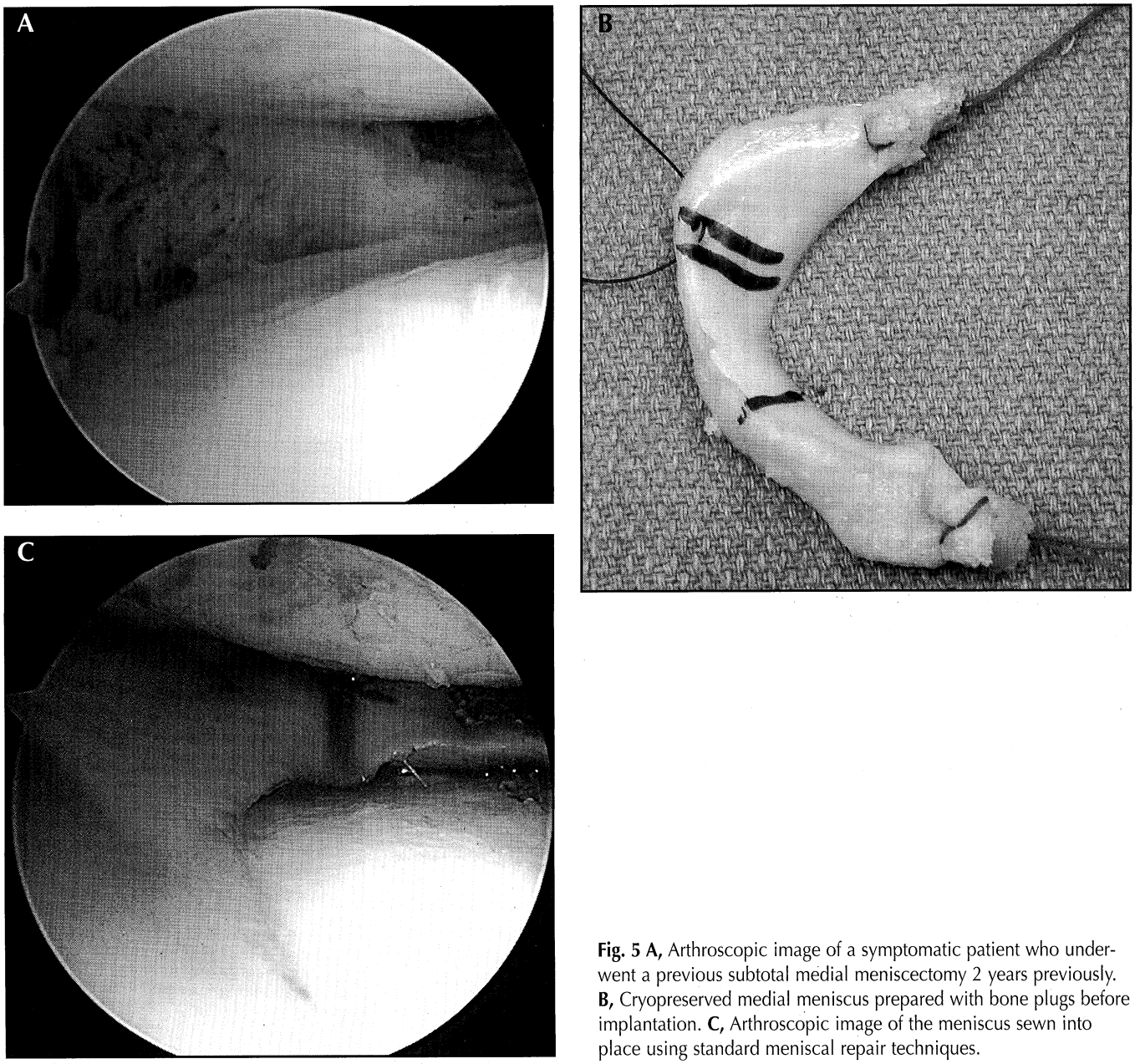

Fig. 5 A, Arthroscopic image of a symptomatic patient who underwent a previous subtotal medial meniscectomy 2 years previously. **B,** Cryopreserved medial meniscus prepared with bone plugs before implantation. **C,** Arthroscopic image of the meniscus sewn into place using standard meniscal repair techniques.

tole. If the graft is not refrigerated within 12 hours, recovery must take place within 15 hours of asystole. The tissues are procured in a clean room in the same manner as in the operating room. Sterile techniques are rigidly adhered to, and all grafts are cultured and screened in a similar manner. Many donors are further examined by autopsy. This additional level of screening increases graft safety. Occult processes such as malignancies or infection can be detected at autopsy and they thus rule out a donor. In addition, medical examiners will frequently screen the donor for drugs of various types that may also preclude tissue donation.

Once all appropriate donor information is available, the medical director or physician designee reviews the medical record. This is an individual familiar with the donor process and donor screening. This review adds another level of security before releasing human tissue. The next step in the production of human allograft tissue is allograft processing.

Processing Human Allografts

Once the grafts have been procured and screened, some of the tissue is processed, which will have a significant impact on tissue performance. Some of the processing techniques used include

demineralization, freeze-drying, fresh-freezing, cryopreservation, machining, and sterilization.[149-158] These processing techniques are selected based on biologic and biomechanical requirements. All of these processing techniques have variable effects on the mechanical and immunoreactive properties of the tissue.

The first step in allograft processing is tissue débridement. This occurs under sterile conditions using high-flow ventilation. Long-bone allografts are typically cleaned of muscle attachments, but the tendinous attachments are left in place. When tendinous attachments are required for a surgical reconstructive procedure, it is particularly important that the surgeon specify this at the time of the tissue request. In addition, long-bone allografts are lavaged of blood elements and fatty marrow (Fig. 3). This cleaning process is done with high-pressure lavage and antibiotic solutions. The removal of marrow elements removes a significant antigenic cell population that is responsible for rejection.

After the completion of graft cleaning, the tissue is cultured, and, if sterile, the grafts are frozen and later released for implantation (Fig. 4). Frozen grafts are the simplest to handle and the most widely used. The grafts are generally packaged without solution and maintained at –80°C. Stored frozen, the shelf life ranges from 3 to 5 years.

Grafts that after processing have positive cultures with type II organisms (eg, S aureus) are secondarily sterilized. The two most common methods of sterilization are gamma irradiation and ethylene oxide. Ethylene oxide sterilization, however, is of limited use because of limited tissue penetration as well as an associated inflammatory reaction to residual gas deposited at the time of sterilization. The dose of gamma radiation used for allografts ranges from 1.7 to 2.5 mrad. The mean dose is 2.0 mrad. The dose required to kill viruses is not well determined and may well exceed 2.5 mrad. Radiation has a significant impact on the biomechanical properties of human bone, however. If the dose applied exceeds 2.5 mrad, there is a percent reduction in compression, torsion, and bending strength of a long-bone allograft. For example, a dose of 6 mrad diminishes these properties in human femurs by 20% to 35%. Irradiation can also diminish the osteoinductive performance of demineralized bone matrix. For example, Urist and Hernandez[159] demonstrated a 60% reduction in osteoinduction when the demineralized bone was irradiated with 2.0 to 3.5 mrad. The effects of radiation need to be considered when selecting the appropriate graft material. After irradiation, cultures are checked to be certain the grafts are no longer colonized with bacteria. Optimally, the preferred method of graft procurement includes sterile harvest, antibiotic soaks, and low-dose or no irradiation (ie, less than 2.5 mrad).

Freeze-drying is another technique used to process grafts. This removes the water content of the tissue and allows prolonged storage. Because the residual moisture within these grafts is less than 5%, the grafts can be stored at room temperature for 3 to 5 years. These grafts typically require about a 30-minute period of rehydration before implantation. Freeze-drying also weakens the graft mechanically. For example, freeze-drying can reduce compression loading strength by as much as 10% to 20% at temperatures of –20°C to –196°C. The effect of freeze-drying on the mechanical strength of the graft also is dependent on the method and rate of rehydration. Freeze-drying may not completely destroy the HIV virus. On the other hand, freeze-drying has a beneficial effect in reducing immunogenicity.

As mentioned previously, cryopreservation is most commonly used for meniscal allograft preservation in an effort to maintain cell viability. Typically, the grafts are procured and transported at 4°C. The grafts are soaked in antibiotic solution for 24 hours at room temperature and undergo a slow, controlled-rate freezing down to –135°C, leading to reduced crystal formation. The process involves the extraction of cellular water with dimethyl sulfoxide or glycerol and storage in liquid nitrogen. The shelf life can potentially exceed 10 years.

Clinical Application of Meniscal and Cartilage Allografts

In a symptomatic patient who has a deficient meniscus or discrete areas of chondral or osteochondral loss, allograft meniscal transplantation and fresh osteochondral grafting are promising treatment options and may be the ideal means to prevent the progression of arthritis. The relationship between the loss of the load-bearing function of the meniscus after meniscectomy and the development of arthritis is well documented, with loads increasing up to threefold in the involved compartment.[160-164] Allograft meniscal transplantation has been demonstated to provide excellent and predictable relief of the pain associated with secondary arthrosis that may occur after meniscectomy.[165-171] Meniscal transplantation is indicated for patients with prior meniscectomy, persistent pain in the involved compartment, intact articular cartilage or low-grade arthrosis (less than grade III), normal alignment, and a stable joint. Simultaneous or staged ligament reconstruction or realignment procedures are done as indicated. Significant articular disease (late grade III or IV) changes generally are associated with inferior results and are considered the most common contraindicaton. Additional contraindications include inflammatory arthritis, obesity, previous infection, femoral condylar flattening, and uncorrected comorbidities (eg, malalignment, ligament insufficiency).

Good and excellent results af-

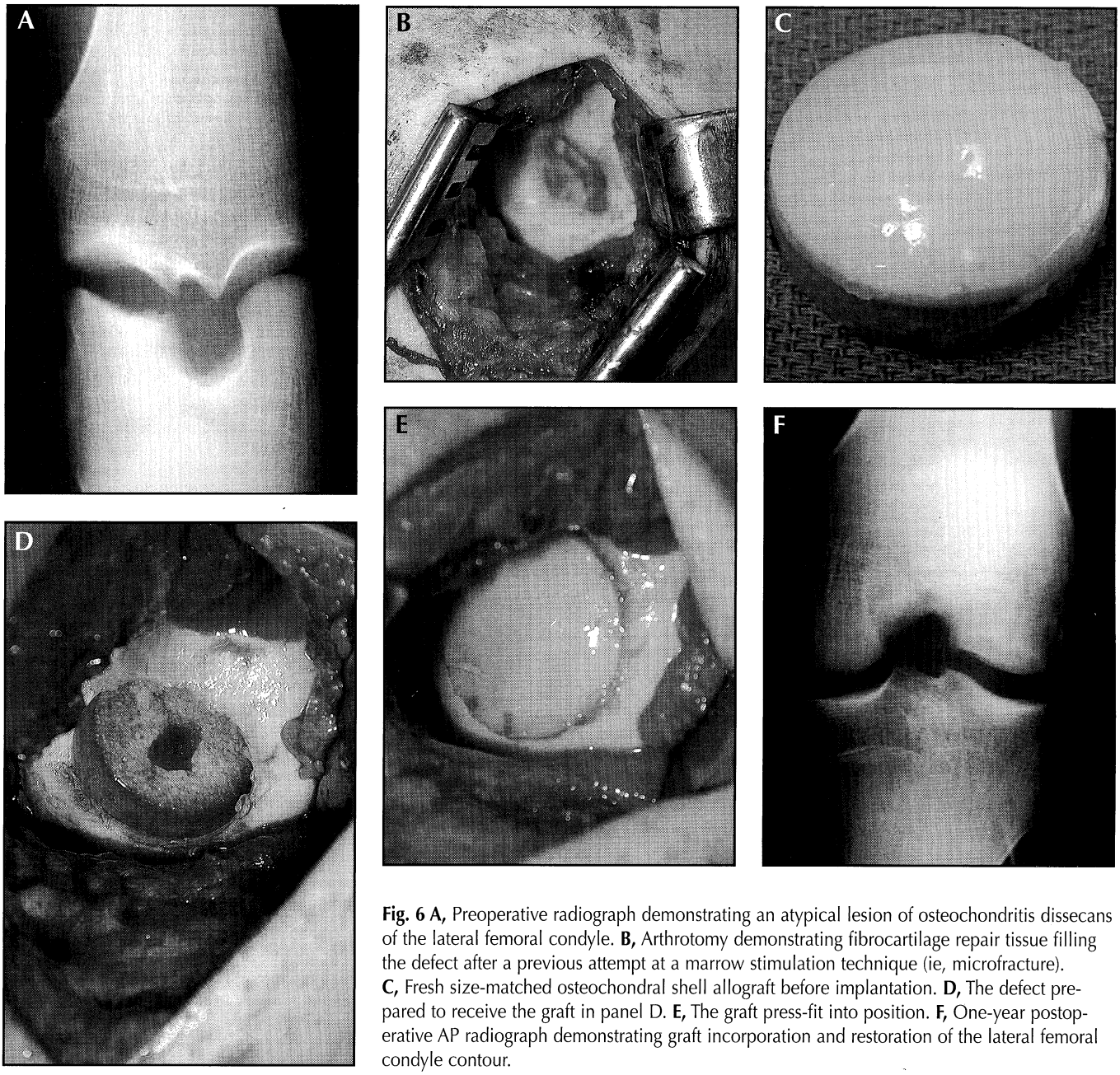

Fig. 6 A, Preoperative radiograph demonstrating an atypical lesion of osteochondritis dissecans of the lateral femoral condyle. **B,** Arthrotomy demonstrating fibrocartilage repair tissue filling the defect after a previous attempt at a marrow stimulation technique (ie, microfracture). **C,** Fresh size-matched osteochondral shell allograft before implantation. **D,** The defect prepared to receive the graft in panel D. **E,** The graft press-fit into position. **F,** One-year postoperative AP radiograph demonstrating graft incorporation and restoration of the lateral femoral condyle contour.

ter allograft meniscal reconstruction approach 75% to 85% at a minimum 3-year follow-up when the indications are respected.[169-171] Second-look arthroscopies demonstrate early peripheral healing. Failures typically are caused by graft shrinkage and posterior horn rupture. No studies are available with more than 5 years of follow-up.

A cryopreserved or fresh-frozen meniscus is size-matched on the basis of measurements on plain radiographs, taking magnification into account.[172] The procedure typically is performed with an arthroscopically assisted approach with the use of a small anterior arthrotomy to place the meniscus into the joint. The meniscus in anchored by either a bone block or interference fit (laterally) or bone plugs (medially), and repair is performed using standard meniscal repair techniques (Fig. 5). Partial weight bearing is permitted immediately postoperatively, and range of motion starts from 0° to 90°. After 4 weeks, full range of motion is obtained and by 12 weeks, running is permitted. Full activities generally are allowed at 4 months. Regardless of the preservation method, meniscal allografts

are revascularized and rapidly repopulated (within 6 weeks) by the host cells.[173-176] Thus, the need for viable cells present in fresh or cryopreserved menisci remains questionable.

Reconstruction of chondral and osteochondral defects of the knee in young active patients poses a major challenge to orthopaedic surgeons and is the subject of several review articles.[177-180] Currently, there are two main techniques with which to restore articular cartilage using osteochondral grafts: the local transfer of osteochondral autograft plugs and osteochondral allograft transplantation. Small localized lesions (less than 2 to 3 cm^2) may be appropriate for osteochondral autografting, also known as mosaic chondroplasty.[181-186] Autografts are taken from relatively non–weight-bearing sites, such as the lateral trochlea or intercondylar notch, and are placed in the defects. These composite bone and cartilage grafts maintain their viability by the nutrients supplied by synovial fluid and the surrounding subchondral bone bed. Because of the limitations of donor site availability and the associated morbidity, osteochondral allograft is primarily indicated for relatively small symptomatic defects in the weight-bearing surface of the femoral condyle.

Because of widely available instrumentation and an improved understanding of the biology of fresh osteoarticular allograft transplantation, acceptance of this procedure has increased for some of the more challenging chondral lesions of the knee. The rationale for this procedure includes the presence of viable and functioning chondrocytes. Additionally, evidence suggests that the bony portion of these grafts is replaced by host bone in a uniform fashion within 2 to 3 years, with chondrocyte viability confirmed at 17 years.[40,69,81,82,85,102,103] Most patients who have osteochondral allografting have failed alternative measures used to treat symptoms resulting from documented osteoarticular disease. Potential sites for resurfacing include the weight-bearing portion of the femoral condyle, trochlea, patella, and tibial plateau.

Indications include large (greater than 2 to 3 cm^2) unipolar lesions resulting from localized degenerative disease, posttraumatic arthritis, osteonecrosis, and osteochondritis dissecans (Fig. 6). Similar to allograft meniscal transplantation, ligament instability and malalignment must be corrected either concomitantly or in a staged fashion. In the setting of meniscal deficiency, combined allograft meniscal transplant-ation may be considered. Contraindi-cations include inflammatory arthritis, steroid dependency, uncorrected comorbidities (eg, malalignment, ligament insufficiency, subtotal meniscectomy), and any other general medical condition that may affect graft incorporation. Relative contraindications include bipolar lesions ("kissing" lesions).

Gross and associates[187,188] demonstrated a clinical success rate at 5 years of 95%, at 10 years of 77%, and at 20 years of 66%. The results of fresh osteochondral grafting for bipolar lesions are considerably less favorable. The grafts are size-matched based on plain radiographs corrected for magnification. Typically, the width of the proximal tibia 1 cm below the joint line on the AP radiograph is sufficient to determine the appropriate size match. Unlike allograft meniscal transplantation, exact size-matching is less critical because of the instrumentation available to harvest and place the graft. It is important that the graft not be used to correct malalignment; rather, osteotomy is used to correct mechanical axis abnormalities, either simultaneously or in a staged fashion. Postoperatively, patients are kept non–weight bearing for 6 to 8 weeks, with liberal use of continuous passive motion. Return to high-level activities generally is delayed until graft incorporation, which can take up to 12 months.

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