

Risk of Infection and Disease Transmission With Allogenic Bone Graft Use in Foot and Ankle Surgery

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INTRODUCTION

The use of bone grafting is considered an essential complement for the repair of some osseous defects and other reconstructive procedures within the field of foot and ankle surgery. Examples of these include arthrodesis and particularly revisional arthrodesis procedures, traumatic reconstructions involving bone loss, and opening wedge osteotomies such as the Evans and Cotton procedures. Bone graft is the most commonly transplanted tissue other than blood, and it is estimated that approximately 1 million bone grafts are implanted annually in the US (1,2).

As the concerns for donor site morbidity associated with autograft harvest have increased, the use of allograft material has become more commonplace. However, it has been our clinical experience that this increased utilization may not necessarily be associated with both physician and patient education on the specific risks of allogenic tissue transplantation. The objectives of this review are to discuss the procurement and processing of allogenic bone, and to review the risk of communicable disease transmission with allogenic bone graft utilization in lower extremity foot and ankle reconstructive surgery.

ALLOGRAFT PROCUREMENT

Allogenic material is made available through tissue donation from either living or deceased individuals (3-7). Bone allografts may specifically be harvested from numerous sites including the humerus, rib, acetabulum, iliac crest, femur, patella, tibia, and fibula. This is a wide range of anatomy involving both the axial and appendicular skeleton, differing ratios of cortical and cancellous bone, and various originating osseous mechanical constructs. Through the various screening processes herein detailed, approximately 90% of donors are rejected (2).

Regulation and Oversight

With the use of any donated human tissue, there is naturally the risk for disease transmission and contamination. The American Association of Tissue Banks (AATB), the Clinical Laboratory Improvement Amendments (CLIA), and the Food and Drug Administration (FDA) regulate tissue donation, including bone allografts, and monitor these risks in the US (5-7).

The AATB was founded in 1976 by a group of physicians who recognized the need to develop standards for and increase human tissue donation, as there was an increasing demand for tissue transplantation. The AATB is a private accreditation program and comprises more than 100 accredited tissue banks and 1,000 individual members (7). The CLIA, a division of the Centers for Medicare and Medicaid Services (CMS), regulates all laboratory testing performed on humans to ensure the quality of laboratory testing. The CLIA regulates approximately 244,000 laboratories (5,6).

In 1997, the FDA in their “Reinventing Government” report in conjunction with the Vice-President’s National Performance Review focused on a new approach to their regulation of human cellular and tissue-based products. This was multifactorial and focused on preventing the use of contaminated tissues and transmitting infectious diseases, preventing improper handling or processing that could contaminate or damage the donor tissues, and ensuring the clinical safety and effectiveness for those tissues that are highly processed, used for non-natural purposes, combined with non-tissue components, or are used for metabolic purposes (5,6). The FDA also formed the Tissue Reference Group (TRG), which provides a point of contact for any questions received by the FDA concerning the jurisdiction and regulation of human cells, tissues, and cellular- and tissue-based products (URL: TissueReference-Group@fda.hhs.gov). This group provides a list of licensed donor

screening tests for hepatitis B virus, hepatitis C virus, human immunodeficiency virus (HIV) 1 and 2, human T-lymphotrophic virus (HTLV) types I and II, *Trypanosoma cruzi* (Chagas Disease), West Nile virus (WNV), as well as cleared nucleic acid tests for *Chlamydia trachomatis* and *Neisseria gonorrhoea*, cleared donor screening tests for Cytomegalovirus (CMV), and cleared tests for *Treponema pallidum* (5,6).

Procurement and processing

The process of obtaining specific tissue from a donor is called *recovery*. This can be performed in a tissue bank facility or in the hospital if the donor cannot be transferred. It is completed under surgical principles and clean room protocols. After tissue is recovered, it is initially placed in quarantine until the donor can be fully evaluated (3,4). To determine if the donor is suitable for donation, autopsy and medical records are reviewed, and the donor's family is interviewed. All musculoskeletal allograft donors undergo a detailed medical, behavioral, and sexual history to assess for disease risk factors, and further undergo serological testing for HIV 1 and 2, hepatitis B and C, syphilis, HTLV, and prion disease (3,4). The tissue bank medical director makes the final decision regarding the use of the donor tissue after reviewing the details of the case.

Once the donor is approved, the tissue is moved out of quarantine and into final processing. Tissue must be void of any aerobic, anaerobic, or fungal organisms whose presence would preclude tissue from transplantation. Each piece of donor tissue is sampled for final microbial testing using swab cultures, destructive tests, or fluid extraction, evaluated to specifications to ensure graft acceptability, packaged in a sealed sterile pouch, and labeled with the donor, type of tissue, product ID, size, description, expiration date, and storage instructions (3,4).

ALLOGRAFT PREPARATION

There is not a uniform protocol for the preparation of bone allograft, and several of the processes utilized have the potential to alter the mechanical and structural properties of the tissue. Although important, these specific effects are not the focus of this review and have been detailed elsewhere (8). There are a variety of potential preparation processes and most allografts are at least physically cleaned and chemically treated. These chemical methods involve the use of detergents, surfactants, hydrogen peroxide, organic solvents, acids, and alcohols. They are used to physically remove organic materials such as blood, lipids, cells, and bone marrow (9).

Gamma radiation

Gamma radiation is the most common method for the terminal preparation of bone (10-16). It eradicates bacteria, spores, fungi, and to a lesser extent, viruses. It also, however, has the potential to weaken the mechanical structure of a graft in a dose-dependent manner as the effects of radiation on bone are directly proportional to the amount of radiation exposure (10).

Dosing at 25 kilogray (kGy) or less has been found to generally maintain graft integrity and strength, and has no deleterious effects on either bone incorporation or its mechanical properties (10,11,13,16). The standard dose for preparation is between 25-35kGy. This dose achieves sterility-assurance levels of 10^6 for most bacteria assuming modest initial bioburdens, but is not high enough to kill all viruses and prions (11). For eradication of prions, the specimens need to be additionally cleansed with sodium hydroxide or sodium hypochlorite. Damage via gamma radiation occurs through two different mechanisms: splitting of polypeptides and radiolysis of water molecules (12,13). This process, especially at higher levels, leads to weakening of the collagen network that is both less thermally stable and less connected than normal, non-irradiated bone (14). Cancellous bone is more resistant to gamma irradiation when compared to cortical bone at high levels of radiation.

Ethylene oxide

Exposure of tissue to ethylene oxide gas is another potential preparation method (17-23). This is relatively cost-effective, but may negatively affect the mechanical strength or biologic activity of the graft. Although it does not appear to have any impact on the osteoconductive properties of the bone, it appears to have a negative impact on its osteoinductive potential. The process involves exposure of the specimen to the gas for approximately 60 hours.

Heat

Heat can cause changes in the mechanical properties of the bone, reduce incorporation, and can also decrease the osteoinductive factors that are present (24,25). The heating process also causes dehydration and this has a statistically significant effect on the strength and stiffness of bone. Drying at any temperature causes significantly lower bone toughness compared to the toughness of fully hydrated bone. Plasticity has been found to be virtually removed by dehydration with any increase in temperature.

Freeze drying

Freeze drying changes the strength of grafts in terms of torsional strength, but not compressive resistant strength. These grafts need to be rehydrated before implantation. If not adequately rehydrated appropriately, then the bone is often brittle and has decreased biomechanical properties (8).

RISK OF DISEASE TRANSMISSION

Bacterial

The risk of bacterial infection from bone allograft is likely low, but it is difficult to determine the exact rates of transmission as postoperative bacterial infection is a risk of any surgical intervention regardless of whether bone allograft is used. The risk of postoperative bacterial infection following the insertion of large bone allograft has been reported to be as high as 12% (26-28), but the risk of postoperative infection following smaller bone grafts (i.e. morsalized bone) is as low as 0.7% (29,30). The Centers for Disease Control and Prevention reported 26 possible cases of bacterial musculoskeletal allograft infections from 1996 to 2002, including 13 *Clostridium* species and 11 gram-negative bacilli. All cases could be traced to a single tissue bank processor, and only 3 of these grafts were gamma irradiated (31,32).

Viral

Because viral transmission is rare and allograft preparation protocols have changed over time, the contemporary risks are based on estimations rather than incidence statistics (32). Bone allografts containing marrow pose a relatively higher risk than cancellous chips that have been processed to remove the marrow, for example. There have been no published reports of disease transmission with demineralized bone matrix (2).

The prevalence of hepatitis C in the general population is 1.8%, and 50% are unaware of their condition, while the prevalence of HIV in the general population is less than 0.4% and 20% are unaware of their condition (2). Among prospective tissue donors, however, the incidence rates are 0.03% for HIV and 0.012% for hepatitis C. The probability of false-negative serological donor testing is approximately 18 in 1 million (1 in 55,000) for HIV and 24 in 1 million (1 in 42,000) for hepatitis C (33,34). With the addition of nucleic acid testing, the probability is reduced to 6 in 1 million (1 in 173,000) for HIV and 2 in 1 million (1 in 421,000) for hepatitis. The risk is theoretically reduced even further with virucidal tissue processing methods (33,34). In comparison, the estimated risk of HIV and hepatitis C transmission with nucleic acid testing for blood transfusion is 1 in 1.8 million and 1 in 1.6 million, respectively (35).

Prion

Prions are protein-based infectious agents similar to viruses. Transmission of prion disease has been reported with dural allograft, pericardial xenograft, corneal graft, and neurosurgical instruments and implants. Although no cases have been documented of prion disease from bone allografts, the concern may be valid because the infectious particle has

been isolated in blood products of affected individuals and since some other graft material is bovine derived (2).

In conclusion, the preceding was intended as a basic science review of allogenic bone graft use in foot and ankle reconstructive surgery. It is our hope that detailing the procurement and processing procedures used for allogenic harvest, as well as the risks of specific disease transmission will assist foot and ankle surgeons in improving their overall knowledge in addition to improving their communication with and consent of surgical patients.

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