

Musculoskeletal Tissue Banking: in Orthopaedic Perspective

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Abstract: Tissue bank is an establishment that collects, harvests, stores and delivers human tissue for the purposes of future use in transplant and medical research. For many years, such banks are dispensing tissue to the orthopaedic area, which has been using reconstructive techniques with allografts. The harvesting, preparation, and delivery of musculoskeletal tissue used for transplantation is an intricate process coupled with varying practices among different musculoskeletal tissue banks. Musculoskeletal allografts are used in a wide variety of orthopaedic surgeries ranging from primary bone defects, trauma, and carcinoma to congenital defects. Tissue banking guidelines and policies need to be specific and effective in minimizing potential harms to donors, donor families, as well as to future tissue research and product development. All tissue bank policies and procedures for donor screening, serologic and microbiologic testing should meet current standards and regulations established by the American Association of Tissue Banks (AATB) and the United States Food and Drug Administration (FDA). The musculoskeletal banks should follow the improvement of the patient care, trauma elimination, morbidity associated with secondary surgical procedures, reduction of the prolonged hospital stays etc. This article provides the reader with information on current standards and practices in musculoskeletal banking.

Key words: Tissue bank, Musculoskeletal tissue banks, Musculoskeletal allografts, Orthopaedic surgeries

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I. Introduction

Tissue bank is defined as an organization that provides donor screening, recovery, processing, storage and distribution of allograft tissue. Beside bone banking tissue banks can be dedicated eye banks, sperm banks, cardiovascular banks, embryo banks, or skin banks. There are dedicated general or multi tissue banks that supply musculoskeletal tissues.

The term 'graft' is commonly used to refer to either an allograft or an autograft. Tissue allografts are commonly used in orthopaedic surgical procedures. Musculoskeletal allografts are used in a wide variety of orthopaedic surgeries, ranging from anterior cruciate ligament reconstructions to spinal fusions.¹ First human bone transplant using aseptic conditions was occurred in 1881.² In 2001, U.S. tissue banks distributed approximately 875,000 musculoskeletal allografts, as compared with 350,000 in 1990.³ The otherwise healthy people often become donors as the result of an unexpected death. Musculoskeletal allografts are safe and the use of these allografts provides the opportunity for improved function and enhancement concerning quality of life. The orthopaedic surgeon also has the responsibility to inform the patient about the risks, benefits, and alternatives of using allograft tissue.

During the last decade, musculoskeletal tissue transplantation has become well established internationally,⁴ and tissue banking has gained increasing importance even also in the Asia Pacific region. The awareness of tissue banking and the demand for bone and soft-tissue allografts in this region have increased substantially.⁵

II. Allografts Used In Orthopaedic Procedures

The Musculoskeletal Transplant Foundation reports that more than 900,000 allografts are used each year in the United States. Connective tissues commonly distributed by the tissue banks are bone-patellar tendon-bone (95%), Achilles tendon (90%), fascia lata (86%), and meniscus (33%).⁶ The bone-patellar tendon-bone, Achilles tendon, fascia lata, and hamstring tendon allografts are used for ACL reconstruction. Meniscal allografts have become more common in recent years for meniscal transplantation. More recently, osteochondral allografts have been made available by bone banks for transplantation into large focal articular surface defects in the knee.⁷

Bone

- Demineralized bone products (osteoinductive)
- Osteochondral long bone (cryoprotected cartilage)
- Structural – cortical segments, shafts, long bones, pelvis, acetabulum

- Cortical/cancellous – powder, chips, wedges, dowels, crests, pegs, and screws
- Ribs, mandible, calvarium, ear ossicles

Soft Tissue

- Patellar ligament and Achilles tendon (bone block), other assorted tendons
- Fascia lata, rotator cuff

Cartilage

- Meniscus, osteoarticular segments (fresh and cryoprotected), costal cartilage.

III. Donor Screening and Awareness

All tissue bank policies and procedures for donor screening, serologic and microbiologic testing should meet current standards and regulations established by the American Association of Tissue Banks (AATB) and the United States Food and Drug Administration (FDA).

The AAOS believes that musculoskeletal allografts represent a therapeutic alternative for appropriate patients. These tissues should be acquired from facilities that demonstrate compliance, use well-accepted banking methodology and follow Food and Drug Administration (FDA) Good Tissue Practices.

After a potential donor is being notified necessary information is obtained to determine donor suitability. A detailed medical/social history is obtained from the donor's next of kin or from someone who can provide reliable donor historical information. This evaluation consists of more than 50 questions on medical history, high-risk social behaviour, unusual environmental exposure, and medical conditions such as cancer. The decision to accept or reject the donor tissue is based on the responses to these questions.

A tissue procurement team is sent to the operating room, morgue, or tissue bank facility; acquire the tissue from a suitable donor. The tissue needs to be obtained aseptically within 24 hours of the donor's death, using techniques similar to those used by orthopaedic surgeons in the operating room and under strict guidelines imposed by AATB accreditation.

Using standard surgical principles the donor's limbs are prepped and draped, and the tissue is recovered by an experienced surgical staff. Many types of tissues can be recovered, including stem cells, bone, soft tissues (tendon, ligament) and skin. All grafts are cultured prior to processing to determine the level of bacterial contamination. Fresh articular cartilage is initially refrigerated and then placed in a culture medium to maintain its viability for up to 28 days.

If tissue culture results indicate the presence of "virulent organisms" such as *Clostridia* species, enterococci, or fungi, the tissues are discarded. Typically, the recovery/procurement and pre-processing cultures are taken using a swab-culturing technique but it is sometime unreliable.⁸ Thus, as part of the final sterility tests, newer techniques, such as bacterial extraction, are used to detect any low levels of bacterial growth.

Testing of donor blood and tissue samples began at the site of recovery and continued throughout processing. Donor blood samples taken prior to or at the time of recovery were tested by laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and 42 CFR Part 493 and were found negative using FDA licensed tests⁶ for:

HBsAg Hepatitis B Surface Antigen
HBc (Total) Hepatitis B Core Total
HCV Hepatitis C Antibody
HIV 1/2-Ab Antibody to Human Immunodeficiency Virus Types 1 and 2
HTLV I/II Human T-Lymphotropic Virus Types I and II
RPR/STS/FTA confirm Syphilis Detection
HIV NATHIV Nucleic Acid Test
HCV NAT HCV Nucleic Acid Test

Additional tests that may have been performed

HBV NAT HBV Nucleic Acid Test
CMV IgM or IgG Avidity Cytomegalovirus Antibody Test

Furthermore, important stage of the capture process is donor reconstruction. The body should be delivered to the family free from any deformation and as close as possible to its appearance before the tissue removal. This is because the fear of deformation has been one of the main causes of refusals of bone donation by the family.⁹

Strides have been made to have allografts become even safer through further FDA Regulations and Guidelines and AATB Standards and Joint Commission Standards for Tissues. While the incidence of disease transference with allografts is very low, careful donor screening and tissue processing are crucial in order to minimize potential risk to the recipient. Collaboration by the orthopaedic community with a broad range of scientific, tissue bank, regulatory organizations, and clinical interest groups can help ensure that the musculoskeletal allografts available for human transplantation can be used safely.¹⁰

Informed consent is taken, for both the donor family and the recipient of human tissue, in accordance with local, state and federal regulations and laws. The AAOS encourages the establishment of a national network to maximize the availability, equitable distribution and utilization of these scarce transplantable musculoskeletal tissues. Such a network should also serve as a means to acquire data and information reflecting the on-

going clinical experience with musculoskeletal allografts, while providing a vehicle for public and professional education.

IV. Musculoskeletal Tissue Processing

4.1 Principle

Tissue processing is a complex multistage procedure.¹¹ The following principle should be practiced.

- Using accredited facility following current Good Tissue Practice
- Following a Quality Control/Quality Assurance Program
- Evaluation of bacteriologic bioburden (pre-processing and in-processing cultures to evaluate contamination)
- Potential discards of donor tissue based on certain types of early bacteriologic contamination (*Streptococcus Group A, Clostridium*)
- Final review by tissue bank medical director of screening/testing prior to release of tissue for transplantation

4.2 Aseptic Tissue Processing

Tissues may be contaminated before they reach the tissue-processing facility. This contamination may be the result of an occult infection in the donor, post-mortem invasion of the tissue by bacteria from the gastrointestinal tract, or potential contamination introduced during the recovery process. The term “aseptic processing” refers to methods used by a manufacturer to avoid adding contamination to a product.¹² Aseptic processing neither removes contamination nor does it remove all blood, lipids, and other cellular elements from the tissue.

The graft is prepared from tissue procured from a cadaver donor using aseptic surgical techniques. Processing cleaning, cutting, sizing, shaping, container sterilization, and filling are performed using aseptic techniques in a controlled, clean environment.¹³ The aseptic handling of the tissue that continues throughout processing and final release is based on a validated sterilization process.

4.3 Tissue Sterilization

Sterilization has been defined as the process or act of inactivating or killing all forms of life, especially microorganisms.¹⁴ However, sterilization of musculoskeletal tissue has associated challenges. The biomechanical properties of tissue can be adversely affected by heat and irradiation.¹⁵ All sterilizing agents (especially gases and liquids) have not quality of adequate tissue penetration. Without good tissue penetration, sterility cannot be assured. In contrast to synthetic materials such as metals or plastics, musculoskeletal tissues may be contaminated with large numbers of organisms (that is, have a high bioburden).¹⁶ The higher the number of microorganisms, the longer or more concentrated the treatment must be to achieve sterilization. Tissue is an organic material that can serve to protect microorganisms and may cause sterilization-process failure. To be considered sterile, allografts should have fewer than 10^{-6} microorganisms; for medical devices, the requirement is fewer than 10^{-3} microorganisms.¹³

As noted by the CDC, “When possible, a method that can kill bacterial spores should be used to process tissue. Existing sterilization technologies used for tissue allografts, such as gamma irradiation or E beam radiation 10-18 kilogray (10 kilogray ~ 1 Mrad) are effective against bacterial spores, should be considered. Unless a sporicidal method is used, aseptically processed tissue should not be considered sterile, and health-care providers should be informed of the possible risk for bacterial infection.”¹⁷

4.4 Allograft Storage

Allograft storage is a complex process. Knee allograft tissue preservation before storage are cooling and fresh transplantation within 24 days, freeze-drying, and deep freezing at -80°C or -196°C . Preservation and storage methods for the meniscal and ligament tissue can differ significantly from those for articular cartilage and bone.

Cryopreservation, a process of controlled-rate freezing with extraction of cellular water by means of dimethylsulfoxide and glycerol, is one method used for preserving menisci and ligaments at some tissue banks. Because of damage to the cartilage matrix during freezing, cryopreservation of articular cartilage has not proved as satisfactory as the use of fresh grafts.

A typical cryopreservation process may include the following steps: Grafts are initially cooled to 0°C and processed within 48 hours of donor death. After decontamination with antimicrobial solutions, allografts are subjected to controlled-rate freezing to -135°C and packed in a cryoprotectant solution. Cryopreserved grafts can be stored at -196°C for as long as 10 years.¹⁸ Deep-freezing is the simplest and most widely used method of ligament and meniscal allograft storage. After recovery, the graft may be frozen, pending the results of donor screening and testing, after which it is thawed and processed. Freezing to -80°C is typical for frozen storage. It can then be stored for 3 to 5 years.

Freeze-drying (lyophilisation) can be used for ligament, bone and meniscal allografts. Standard graft processing is followed by freezing and lyophilisation to a predetermined residual moisture level. The graft can

then be vacuum packaged and stored at room temperature for up to 3 to 5 years. Rehydration of freeze-dried ligament grafts with attached bone plugs requires a minimum of 30 minutes before implantation.¹⁷

Currently, most osteochondral allografts are transplanted fresh, which better preserves both cartilage cells and matrix. These grafts contain marrow elements within the bone, which increases both the antigen exposures to the recipient and the possibility of disease transmission.¹¹ Viable chondrocytes can be maintained in lactated Ringer's solution cooled to 2° to 4°C for 7 to 14 days.¹⁹ Generally, fresh articular cartilage allograft is transplanted within days of harvesting, with the understanding that the longer the wait, the greater the death of cartilage cells.

V. Common Uses in Orthopaedic Procedures

Indications of allograft transplantation - revision total hip arthroplasty, nonunion of the humerus diaphysis, revision total knee arthroplasty, patellar fracture, humeral fracture, tibia plateau fracture, nonunion of the clavicle, opening wedge osteotomy, osteotomy of the tibia, osteotomy of the femur, humeral head fracture, nonunion of an osteotomy, protrusion of the acetabulum, comminuted elbow fracture, tibia fracture, calcaneal fracture, delayed union of the radius, fracture of an enchondroma, giant cell tumour. This spectrum is expanding day by day.

VI. Evolution of Musculoskeletal Tissue Bank In Bangladesh

Utilization of human tissues has been practicing in many countries and it has a long history. Today it can be seen that tissue transplantations in general are on the rise. Events such as officialization in the legislation and the creation of public promotion policies corroborate this evolution. Considering bone transplants alone, 30 x growths has been observed in the last 5 years (Brazilian Transplantation Register, 2010). The University Hospital Hradec Králové, Czech Republic, established tissue bank in 1952.²⁰ The gradual demands of allografts have encouraged the development of institutional bone banks, first in the United States and subsequently in other countries.^{21, 22, 23} National University of Singapore (NUS) Bone Bank was established in October 1988.²⁴ International Atomic Energy Agency (IAEA) in 1995 was the first into distance learning in tissue banking. Sri Lanka also started fully operated tissue banking based upon the financial support of IAEA since 1998.²⁵

However, Bangladesh is new in the field of tissue banking activities to treat degenerative bone diseases, congenital deformities, bone tumour, bone fractures, gap non-union from traumatic accidents, dental defects, traumatic open wound etc. Bangladesh Atomic Energy Commission has initiated the processing of human tissue for utilization in reconstructive surgery as allograft in cooperation with the IAEA.

For ethical and legal concern, the healthcare personnel have been working under the law of "Human Organ / Tissue Donation and Transplantation Act", as the National Parliament of the People's Republic of Bangladesh has approved the declaration on 13th April-1999 requiring consent from the donor or next of kins.

At present in Bangladesh, 109 hospitals and clinics and more than 300 surgeons and physicians are involved with this unit through utilization of radiation sterilized tissue allografts. In 2008 Tissue banking and Biomaterial Research Unit of Bangladesh Atomic Energy Commission, collected, processed and supplied encouraging amount of bone allografts. They collected Human femoral head 423 pieces, graft processed 3810 (chips/segment), graft supplied 3172 (chips/segments) and patient served with Giant cell tumour (GCT) 76, Aneurysmal bone cyst 18, Simple bone cyst (SBC) 13, Fibrous dysplasia (FD) 19, Gap non-union 27, Bone fracture 66, Spinal fusion/scoliosis 02, Osteomyelitis and other 03 total 224.²⁶

VII. Conclusion

With the advancement of technology, use of musculoskeletal allograft tissue transplantation will continue to improve and expand which would enhance the patient's quality of life. It is essential that orthopaedic surgeons who use allograft tissue understand the tissue banking process and the origins of the allograft tissue they use. The ethics, moral principles, and legal aspects regarding bone banking should be disseminated enormously to the general public of the country as they could be more aware and interested to tissue donation thereby more people will contribute to alleviate sufferings and more lives will save.

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