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Review

Bone Grafting, Its Principle and Application: A Review

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ABSTRACT

Bone grafting is a surgical procedure that replaces missing bone through transferring bone cells from a donor to the recipient site and the graft could be from a patient's own body, an artificial, synthetic, or natural substitute. Bone grafts and bone graft substitutes are indicated for a variety of orthopedic abnormalities such as comminuted fractures (due to car accidents, falling from a height or gunshot injury), delayed unions, non-unions, arthrodesis, osteomyelitis and congenital diseases (rickets, abnormal bone development) and are used to provide structural support and enhance bone healing. Autogenous, allogeneic, and artificial bone grafts are common types and sources of grafts and the advancement of allografts, synthetic bone grafts, and new operative techniques may have influenced the use of bone grafts in recent years. Osteogenesis, osteoinduction, osteoconduction, mechanical supports are the four basic mechanisms of bone grafting and help bone tissue to regenerate completely. A bone graft can be harvested from the iliac crest, proximal tibia, proximal humerus, proximal femur, ribs, and sternum. An ideal bone graft substitites should be biologically inert, readily available, must possess osteogenic, osteoinductive and osteoconductive properties, provide mechanical support, easily adaptable in terms of size, shape, length and substituted by the host bone. Bone banks are the source of bone grafts and implants and necessary for providing biological material for a series of orthopedic procedures. Bone grafts and implants can be selected as per clinical problems, the equipment available and the preference of the surgeon. A search for an ideal bone graft is on and may continue from time to time.

Keywords
Application; Bone; Bone graft; Bone replacement; Bone bank; Principle.

INTRODUCTION

Bone grafting is a surgical procedure that uses transplanted bone tissues and implants to repair and rebuild diseased or damaged bones. It is a common procedure that have several advantages in veterinary medicine and indicated for the treatment of various anomalies such as malunions, delayed unions and refractory non-unions, mandibular and calvarial reconstruction, as well as for aggressive tumor resection. Moreover, it is also indicated to repair the composite defect (bone, skin, and muscle), to replace comminuted fragments, to lengthen bones, to help ensure union in the treatment of fresh fractures, to hasten early production of bone and osteomyelitis[1-3]

Bone is the second most commonly implanted material in the human body, after blood transfusion, with an estimated 600,000 grafts performed annually. Healing of contaminated fractured bone is still one of the most challenging features in trauma surgery in all species especially in larger animals such as horses. Thus, bone grafts and synthetic bone graft substitutes (replacements) are used to fill and support bone healing and formation. These grafts should have no antigen-antibody reaction and good bioresorbable quality. Also, bone grafts act as a mineral reservoir which induces new bone formation.[3] In general, bone graft used is a framework to provide stability, treatment of pseudoarthrosis and to stabilize spinal segments and the addition of bone stock in total joint replacement.[4] The first recorded attempt to use bone graft was by the Dutch surgeon Job Van Meek'ren in 1668. Church literature mentions the first transplantation of a bone graft in a Russian soldier with a dog's cranial bone in 1682.[5]

As history reported, the transplantation of animal tissues

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into humans has been attempted since the time of Hippocrates. Different evidences suggest that the ancient Hindus and Egyptians also undertook transplantation experiments; however, the first documented xenograft is attributed to Dutch surgeon Job van Meek'ren, who in the 1600s attempted to fill a defect in a soldier's cranium with a piece of dog's skull.[6] In 1821, the first experimental autogenous bone grafting procedure was performed successfully in Germany in experimental defects created in animal skulls. Sir William MacEwan introduced allografting in 1879 by successfully replacing the proximal two-thirds of a humerus in a 4-year-old boy with bone procured from other patients.[7] Nowadays, bone transplantation is frequently used and most surgeons transplant bone at least 10 times more often than any other transplantable organ.[8-10]

Nowadays, a bone graft is a dynamic tool that supports normal forces and incorporates itself into the bed, revascularize as new bone forms. Additionally, bone graft and its substitutes provide structural support for several healing defects. The recent advancement in recombinant deoxyribonucleic acid (DNA) technology has contributed to the development of bone graft since it allows surgeons to apply growth factors to defects in therapeutic quantities to facilitate regeneration.[10,11]

Currently, there are different types of bone transplantation or grafting techniques. The development of allografts, synthetic bone grafts, and new operative techniques may have improved the use of bone grafts in recent years. Besides, an autograft is a graft of tissue from one portion of the body to another of the same animal or person whereas isograft is material that is taken from one individual and transplanted into another genetically identical individual, such as an identical twin. A graft of tissue from between individuals of the same species is called allograft (earlier called a homograft) whereas transplantation of tissue between individuals of different species is called xenograft (formerly known as a heterograft).[7,9]

Bone grafts may be either cortical or cancellous and can be grafted either from dead or alive persons or animals. A great deal of controversy exists regarding the transplantation of live bone and its ability to survive. The greatest chance for the successful transplantation of live bone is with a cancellous autograft or with the vascularized pedical cortical autograft.[5,10]

The ideal bone graft or bone graft substitute should offer three vital elements including an osteoconductive matrix, osteoinductive properties or factors; and osteogenic cells.[9,12] Among the different types of grafts, the autogenous cancellous bone graft is considered as the "gold standard" of bone transplantation since it satisfies all three attributes of ideal bone graft. However, there are several potential complications involved with autogenous grafting such as donor-site morbidity, limited availability for harvest, and increased operative blood loss. It has, therefore, become necessary to find suitable alternatives, particularly when a large graft is required.[13,14]

All grafts are eventually replaced with host tissue by a process called creeping substitution and it is the process of bone remodeling by osteoclastic resorption and the creation of new vascular channels with osteoblastic bone formation resulting in new Haversian systems.[15] Besides, it is the method by which strong cortical bone is formed from grafted material. Accordingly, bone graft facilitates the faster bone healing process by filling the voids/injured parts because it provides an osteoconductive scaffold for host bone to grow on and native, osteoinductive bone morphogenetic proteins (BMPs) that attract osteoblasts to the site. Moreover, this technique helps for faster recovery and healing of the patients and also increases the chances of a successful healing outcome.[16,17] Thus, this review was prepared to highlight the techniques and development of bone grafting over the past years.

PRINCIPLES OF BONE GRAFTING

The science of bone grafting has advanced significantly, particularly in the past two decades, with the fundamental understanding of osseous healing now incorporating principles of cellular and molecular biology. Nowadays, bone grafts are used in reconstructive orthopedics, from the treatment simple type of fractures to extensive limb salvage procedures and complex spinal reconstructions. Thus, several factors affects the successful incorporation of grafted bone, including the type of bone graft used, the site of implantation, preservation techniques, local and systemic factors, the vascularity of the graft and the host-graft interface that include the immunogenetics between the donor and the host, and the mechanical properties of bone that depend on the size, shape, and type of graft used.[7,18]

The ideal bone graft or bone replacements should provide three essential elements including an osteoconductive matrix; osteoinductive properties or factors; and osteogenic cells. Osteoconduction is the process of infiltration of capillaries, perivascular tissue that involves stimulation of osteoprogenitor cells to differentiate into osteoblasts and then begins the formation of new bone. It uses osteoinductive cell mediators called BMPs. Osteoinduction is the stimulation of a tissue to produce osteogenic elements and it is also controlled primarily by growth factors such as BMPs that are capable of inducing differentiation of mesenchymal cells into cartilage and bone producing cells. Osteogenic cells are mesenchymal-type cells that can be summoned from the host or graft bone marrow.[7,19]

Autologous cancellous bone grafts fulfill all the attributes of ideal bone grafts and are mostly utilized in the techniques of bone grafting. Hydroxyapatite and collagen provide an osteoconductive framework and induce both the regenerative and augmentation processes. For these reasons, the autogenous cancellous bone graft is considered the "gold standard" of bone transplantation.[8] Thus, during grafting, the graft should have the following attributes including (i) Osteogenic activity or potentiality of the transplant material, (ii) The ability of the graft to survive and proliferate, (iii) The immune response of the host, (iv) The degree of induction that the newly transplanted material will experience and (v) Affinity, which the host tissue exhibit towards the interstices of the implanted bone.[9,20]

CLASSIFICATION AND TYPE OF GRAFTS

The classification of bone graft is based on the source of the graft and the knowledge is necessary to understand the indications, functions, biology, and contraindications of various types of bone grafts.[9,19]

Autograft is transplantation into the same individual; allograft is the transplant of an organ or tissue from one individual to another of the same species with a different genotype while xenograft is the transplantation of living cells, tissues or organs from one species into different species and isografts (syngeneic grafts) is a graft of tissue between two genetically identical individuals or the same family. Alloimplants are nonviable grafts. Cancellous graft (30-90% porosity) has a greater osteogenic ability. Cortical grafts (5-30% porosity) most commonly used to provide stability.[9,21,22] Autogenous/aspirated bone marrow used to provide live undifferentiated mesenchymal. Corticocancellous grafts are a combination of cortical and cancellous bone. An osteochondral graft is a method of treating cartilage injuries that expose the underlying bone and used to replace both the articular cartilage on the surface and the underlying bone. Small chips of bone are particulate graft.[23]

Fresh grafts are removed and used immediately. Free grafts are not vascularized and depend upon the local environment and ingrowth of new vessels to function. Vascularized grafts are segments of whole bone removed with blood vessels and placed with the anastomosis.[13,24] Onlay grafts are bone grafts applied to the outside of the recipient bone and simple or massive slats of bone. Inlay grafts are cortical parts of bone used for the direct inlay or sliding inlay in long bones. The receiver is carefully prepared and held in place by wedge effect, cortical bone screw, cerclage steel bands, and Smillie nails. The grafts with muscle insertion are muscle pedicle transplanted into a surgically created slot in the posterior femoral neck in young patients.[8,23]

The fibula and the rib are commonly used for the spine as strut grafts. Clothespin grafts are pieces of bones shaped like a clothespin and used as a bone graft in spine fusion operations to bridge several vertebrae. Orthotopic grafts are grafts transferred to the same or normal anatomic site of another individual whereas Heterotopic grafts are placed at an inappropriate site or into a position that it normally does not occupy. Demineralized bone grafts are specialized allograft product and bone graft extender prepared by leaching minerals from the bone and contains type I collagen, non-collagenous proteins, and a variable number of osteoinductive growth factors such as BMP, insulin-like growth factor (IGF), Transforming growth factor-beta (TGF-β). Synthetic grafts are grafts developed in the interest of creating an alternative osteoconductive porous material that can be implanted into bone. It includes calcium sulfate and calcium phosphate and helps to avoid morbidity in the recipient but is not vascularized, thus may be infectious, toxic or carcinogenic.[9,25,26]

Also, bone grafts can be classified based on material groups into five main groups (Table 1).

ROLES AND BIOLOGY OF BONE GRAFTS

A bone graft helps to fill an area where the bone is absent or help provide structural stability. Bone grafts serve a combined mechanical and biologic function; depending on the desired clinical outcome, one function may be more important than the other. For instance, massive osteochondral grafts in limb salvage procedures for tumors serve a predominantly mechanical support function. Besides, autogenous bone graft derived from the iliac crest for posterolateral spine fusions provides a biologic stimulus for new bone formation, with little or no mechanical function. A complex relationship exists at the host-graft interface, and to ensure the desired clinical result, the surgeon must be aware of the properties of both the graft and the recipient site.[23,28]

Moreover, bone grafts are either utilized in the block (which includes from the chin or ascending ramus location of the decrease jaw) or particulated, so that it will be capable of adapt it better to a disorder. The grafted, vascularized fibulas have been used to restore skeletal integrity to lengthy bones of limbs in which congenital bone defects exist and to replace segments of bone after trauma or malignant tumor invasion. The periosteum and nutrient artery are commonly removed with a bit of bone so that the graft will stay alive and develop when transplanted into a new host web site. Once the transplanted bone is secured into its new vicinity, it normally restores blood deliver to the bone on

Table 1. *Definition of Terms and Common Examples*

Term	Definition	Example
Allograft-based bone graft	It uses allograft bone alone or in combination with other materials	Grafton, OrthoBlast.
Factor-based bone graft	They are natural and recombinant growth factors that are used alone or in combination with other materials	Transforming Growth Factor-Beta (TGF-Beta), Platelet-Derived Growth Factor (PDGF), Fibroblast Growth Factors (FGF), and Bone Morphogenic Protein (BMP).
Cell-based bone grafts	It uses cells to generate new tissue alone or is added onto a support matrix.	Mesenchymal stem cells
Ceramic-based bone graft	These substitutes include calcium phosphate, calcium sulphate, and bioglass used alone or in combination	OsteoGraf, ProOsteon, OsteoSet
Polymer-based bone graft	It uses degradable and nondegradable polymers alone or in combination with other materials.	Open porosity polylactic acid polymer.

Source: [3, 27]

which it's been attached.

The most common use of bone grafting is its application of dental implants to restore the edentulous area of a missing tooth. Moreover, bone grafts are either utilized in the block (which includes from the chin or ascending ramus area of the lower jaw) or particulated, to be able to adapt it better to a defect. The grafted, vascularized fibulas have been used to restore skeletal integrity to long bones of limbs in which congenital bone defects exist and to replace segments of bone after trauma or malignant tumor invasion. The periosteum and nutrient artery are usually removed with a piece of bone so that the graft will remain alive and grow when grafted into a new host site. Once the grafted bone is secured into its new location, it generally reestablishes blood supply to the bone on which it has been attached. Besides, bone grafting is mainly used in dental implants to fuse joints and prevent movement, repair broken bones that have bone loss and have not yet healed.[3,29,30]

Depending on the type of graft, bone performs different functions when it is incorporated into host tissue. Thus, the biologic mechanisms that provide a rationale for bone grafting are osteogenesis, osteoinduction, osteoconduction and mechanical support.[3,19]

Osteogenesis

Osteogenesis is the development and formation of bone from cells derived from either the graft or the host. The handling and survival of the graft cells (cortical and cancellous grafts) is the most important and initial phase in bone repairing and remodeling. In contrast to other grafts, cancellous grafts have a large surface area consist of an intimate trabecular structure lined with osteoblasts that makes them more attractive at sites where new bone formed. Besides, the concept of osteogenesis provides the biologic justification of decortication for spinal fusion. Exposing the intramedullary space of the transverse processes, lamina, and pedicles with a burr opens local bone marrow to the fusion site. Marrow elements then provide the fusion bed with osteoinductive proteins, potential osteogenic cells, and local blood supply.[18]

Osteoinduction

Osteoinduction is the process by which mesenchymal stem cells (MSCs) at and around the host site are recruited to differentiate into chondroblasts and osteoblasts. Recruitment and differentiation are modulated by grafting matrix-derived growth factors whose activity is triggered when a bone mineral is removed. These growth factors include bone morphogenetic proteins -2, -4, and -7, which are members of the transforming growth factor-β superfamily. Other factors involved with bone formation include mitogens, such as platelet-derived growth factors, interleukins, fibroblast growth factors, insulin-like growth factors, granulocyte colony-stimulating factors, and granulocyte-macrophage colony-stimulating factors. Angiogenic factors, such as vascular endothelial-derived growth factors, also are released.[31,32]

Osteoconduction

Osteoconduction is the process of bone growth on the surface of an implanted graft and provides the capability to allow new cell colonization, bone in-growth, and blood vessel formation (vascularization). This scaffold permits the formation of new bone along a predictable pattern determined by the biology of the graft and the mechanical environment of the host-graft interface.[27] For bone grafting to be successful, osteogenic activity and bone formation alone are insufficient. The new bone must be distributed evenly in the grafted volume and must unite with the local host bone. Failure results in discontinuous bone formation without adequate mechanical strength to support function.[7,18,32]

Mechanical Support

Bone grafts, besides filling large bony defects, provide mechanical and weight-bearing supports for the affected bone. Besides, the graft must be stabilized with compression developed at the host-graft interface by using rigid internal fixation to ensure the stability of the graft within the recipient site. There are several potential complications of bone grafting that depends on the type of graft used and includes (i) Surgical invasion at the donor site and limited bone source in autografts, (ii) Immune-mediated rejection of allografts and alloimplants, (iii) Transmission of infectious agents with allografts and alloimplants, (iv) Technical difficulty with vascularized grafts, (v) Fracture, pain, seroma, hemorrhage, and infection at harvesting sites, (vi) Infection and instability at the graft site causes failure.[7,18,19]

Accordingly, graft site preparation is important to the success of the grafting procedure, and meticulous adherence to surgical principles is essential. Care must be taken to ensure adequate surface area contact between the graft and recipient site without the interposition of soft tissue. Overzealous use of a reamer or burr may cause excessive heat generation, leading to necrosis at the graft site. Efforts must be made to preserve the osteogenicity of corticocancellous autografts, including decreased harvest-to-implant time, storage in covered containers, and attention to hydration.[7,18]

TYPES AND SOURCES OF BONE GRAFT SUBSTITUTES

Autograft

Autologous or autogenous graft is a graft of tissue from one point to another of the same individual's body. Such types of grafts can be collected from the iliac crest, mandibular symphysis (chin area), and anterior mandibular ramus (coronoid process). Besides, autogenous bone is the most preferred when applying a block graft since there is less risk of graft rejection as the graft is originated from the patient's body.[27] Furthermore, autograft has osteoinductive, osteogenic and osteoconductive properties. However, autologous grafts need additional surgical site and these cause a lot of post-operative pain and complications in patient.[9]

All bones require blood supply in the transplanted site.

Depending on the transplant site and the size of the graft, an additional blood supply may be required. For these types of grafts, a free flap graft that is obtained by extraction of the part of the periosteum and accompanying blood vessels along with the donor bone is required.[3]

Allografts

Allografts can be harvested from humans and cadavers. Unlike autografts, allografts are harvested from an individual other than the one receiving the graft. There are three types of bone allograft available including (i) Fresh or fresh-frozen bone, (ii) forms-freeze dried bone allograft (FDBA), (iii) demineralized freeze dried bone allograft (DFDBA).[33,34]

Allografts should be collected from healthy bone and the use of allografts for bone repair often requires sterilization and deactivation of proteins. The extracellular matrix of bone tissue contains various types of bone growth factors, proteins, and other bioactive materials necessary for osteoinduction and successful bone healing. Besides, the desired factors and proteins are removed from the mineralized tissue by using a demineralizing agent such as hydrochloric acid. The mineral content of the bone is degraded, and the osteoinductive agents remain in a demineralized bone matrix (DBM).[12]

Synthetic Variants

Hydroxyapatite (HA) composite has a mineral to organic matrix ratio, approximating that of human bone. Depending on solubility in the physiological environment, artificial bone can be formed from ceramics like calcium phosphates HA and tricalcium phosphate), calcium sulphate and bioglass that are biologically active.[35] These materials combine with growth factors, ions such as strontium or mixed with bone marrow aspirate to increase biological activity. The presence of elements such as strontium can result in higher bone mineral density (BMD) and enhanced osteoblast proliferation.[3]

Xenograft

Xenografts are bone grafts from a species other than humans, such as bovine and are used as a calcified matrix.[13,29]

Alloplastic Grafts

Alloplastic grafts can be made from hydroxyapatite made from bioactive glass. Hydroxyapatite is a synthetic bone graft that is the most preferred choice recently due to its hardness, compatibility with bone and osteoconduction. Some synthetic bone grafts are made of calcium carbonate, which starts to decrease in usage because it is completely resorbable in a short time and makes the breaking of the bone easier. Finally used is the tricalcium phosphate in combination with hydroxyapatite and thus giving the effect of both, osteoconduction and resorbability.[26,36]

Growth Factors

Growth factors enhanced grafts are produced using recombinant DNA technology. They consist of either human growth BMPs in conjunction with a carrier medium, such as collagen. These factors and proteins that exist in bone are responsible for regulating cellular activity. The growth factors bind to receptors on cell surfaces and stimulate intracellular environment to act. In general, this activity translates to a protein kinase that induces transcription of messenger ribonucleic acid (mRNA) and results in the formation of a protein to be used intracellularly or extracellularly. The combination and simultaneous activity of many factors results in controlled production and resorption of bone. These factors, residing in the extracellular matrix of bone, include TGF-beta, insulin-like growth factors I and II, platelet-derived growth factor (PDGF), fibroblast growth factors (FGF), and BMPs.[37,38]

Cell-based Bone Graft Substitutes

Stem cells are cultured in the presence of various additives such as dexamethasone, ascorbic acid, and b-glycerophosphate to direct the undifferentiated cell towards osteoblast lineage. The addition of TGF-beta and BMP-2, BMP-4, and BMP-7 to the culture media can also influence the stem cells towards osteogenic lineage. Mesenchymal stem cells have also been seeded onto bioactive ceramics conditioned to induce differentiation to osteoblasts.[8,10,38]

Ceramic-based Bone Graft Substitutes

The majority of bone grafts available involve ceramics, either alone or in combination with another material such as calcium sulfate, bioactive glass, and calcium phosphate. Calcium phosphates are ceramic calcium hydroxyapatite that has osteoconductive and osteointegration, in some case osteoinductive properties. They require high temperatures for scaffold formation and have brittle properties.[10,27]

Calcium sulfate is also known as plaster of Paris and it is biocompatible, bioactive, and resorbable after 30-60-days. However, the applications are questionable since they significantly lose their mechanical strength upon its degradation; thus, it is not a choice for load-bearing. Osteoset is another type of graft substitute that is found in calcium sulfate tablets and used for bone defect packing. It is degraded in approximately 60-days. Moreover, allomatrix is an osteoset combined with DBM that forms a putty or injectable paste.[3]

Bioactive glass (bioglass) is a biologically active silicate-based glass, having high modulus and brittle nature. It is consists of sodium-calcium salts, phosphates, and silicon dioxide and has been used in combination with polymethylmethacrylate to form bioactive bone cement and facilitates the chemical bonding of implants to the surrounding bone. There are different types of calcium phosphates such as tricalcium phosphate, synthetic hydroxyapatite, and coralline hydroxyapatite; available in pastes, putties, solid matrices, and granules. Besides, when this material comes into contact with tissue fluids, the surface of the particles gets coated with hydroxyl-carbonate apatite, incorporates glycosaminoglycans attracts osteoblasts that rapidly form bone.[8,39,40]

Polymer-based Bone Graft Substitutes

Polymer-based bone graft substitutes can be divided into natural polymers and synthetic polymers. Besides, it is subclassified into degradable and nondegradable types. Among polymer-based bone graft substitutes, Healos and Cortoss are some common types of graft substitutes. Healos is a natural polymer-based product and a polymer-ceramic composite consisting of collagen fibers coated with hydroxyapatite and indicated for spinal fusions whereas Cortoss is an injectable resin-based product with applications for load-bearing sites.[13,21] Degradable synthetic polymers have been widely used and have greatly promoted the development of biomedical fields because of their biocompatibility and biodegradability. The benefit of having the implant resorbed by the body is that the body can heal itself completely without remaining foreign bodies.[3,8]

BANKING BONE

Bone banks have been used in veterinary orthopedics for many years and were strongly advocated by Brinker. Bone bank concept was laid by the American Association of Tissue Bank (AATB) and it has been used in veterinary orthopedics for many years.[1,27] Bone grafts can be harvested from the wing of ileum, proximal humerus, proximal tibia, distal radius, sternum, and ribs.[14] The specimens are collected in sterile containers and deep-frozen. The retardation of autolysis by cooling would suggest that the lower the temperature the longer the graft would remain useful.[5]

According to previous studies, bones have been stored for up to one year with colder temperatures. Freeze-dried grafts may be stored at room temperature under vacuum or be frozen up to five years. Grafts that have been frozen to -70 °C can be successfully used up to 2-years after collection. Careful attention to sterility in the collection process is mandatory.[9] Bone should be collected using aseptic techniques, with special attention paid to the skin preparation since most common bacterial contaminant of the grafts are organisms on the skin. It is better to culture and reculture all specimens at the time of collection and implantation respectively, to help ensure quality control. The preserved grafts are removed before use, prepared and stored. There are different techniques of preserving and sterilizing grafts including boiling, autoclaving, deproteinizing, aqueous methylating, freeze-drying (-15 °C to -30 °C), ethylene oxide sterilization and radiation.[41]

Frozen graft should be thawed in warm physiological solutions just before use. Cell death results from all these techniques and the grafts functions mainly as a space filler and as a scaffold. Careful donor selection is necessary to ensure that the donor is not going to transfer its disease condition to the recipient. Careful donor screening and strict adherence to aseptic harvesting techniques are not necessary when using ethylene oxide to sterilize bones grafts and graft can be stored up to 3-years. The lower the temperature the longer would remain useful.[9] The grafted cells should be properly labeled with the donor's identification, the date, and the bone location. The graft is recultured and radiograph at the time of placement.[39,41]

Donor Sites

In the dog and cat, various locations can be used as sites to obtain autograft tissue. Cancellous grafts are the most common type of graft and can be harvested from the wing of the ilium, the proximal tibia, and the proximal humerus. Sometimes the amount of graft that is needed may demand that more than one site be used. The approach to the wing of the ilium is easy and straight-forward. A 2 cm long incision is made over and parallel to the wing of the ilium. The skin and subcutaneous tissue are retracted and the fascia of the middle gluteal muscle is incised along the rim of the ilium. A periosteal elevator is used to separate the muscle from the bone and the periosteum from the bone. A rongeur is used to open the medullary cavity of the bone and a curette is inserted to scoop the cancerous bone out of the cavity; it is placed within a blood-soaked sponge or in a basin. During harvesting, the patient's blood is the best tool to keep the bone moist. The viability of the graft cells are best ensured by disturbing them as little as possible. The use of saline-soaked sponges would be detrimental in this regard.[29]

The graft is obtained from the tibia *via* the proximal medial surface just caudal to the tibial tuberosity and distal to the physeal line. The incision is made through the skin down to the bone. A hole is drilled through the cortex with a large Steinmann pin inserted into a Jacob's chuck. The graft material is then removed with a curette. Grafts can be collected from the proximal humerus in a very similar manner to the tibial procedure. The skin incision is made over the proximal cranial aspect of the humerus just distal to the greater tubercle.[13,21,42]

Recipient Sites

The recipient site is usually easily well-defined especially incase of fresh fractures. The cancerous graft is placed into and around the defect being grafted. The application of the graft may be thought of as the placement of the callus. The bone graft helps to form the scaffold for bone production and to fill the defect and ensure bone union. When dealing with delayed unions or nonunion, the application site of the graft may be more difficult to determine. In the case of the old fracture site, the placement of the graft is difficult due to the fibrous connective tissue surrounds the fracture site. In these cases, the fibrous connective tissue must be removed so that the graft can come into contact with the bone fragments and the surrounding vascularized tissues.[5,9,42]

MANIPULATING AND ENHANCING THE HEALING RESPONSE OF BONE

Recently, research has been focused on understanding the healing mechanism of bone, the effect of the immune response, and the role of endogenous growth factors to manipulate and enhance the healing process of bone. The strength of bone is determined by the balance of two opposing processes: osteoblastic bone formation and osteoclastic resorption. Increased mechanical stress shifts this balance toward the formation, and states of disuse and chronic disease shift it toward resorption. Two mechanisms have been postulated for the regulation of bone formation and resorp-

tion: systemic regulation by calcium and phosphate-regulating hormones (e.g., parathyroid hormone, vitamin D, calcitonin) and local regulation.[5,9,42]

Several growth-promoting substances involved in local regulation have been identified at the site of fractures. These substances can be divided into two groups: peptide-signaling molecules (generally referred to as growth factors) and immunomodulatory cytokines such as interleukin-1 and interleukin-6.[43,44] The polypeptide factors are recognized to exert multiple effects on cells. These polypeptide factors include BMPs, TGF-I, platelet-derived growth factor, fibroblast growth factors, IGF-I and IGF-II, microglobulin, osteogenic growth peptide, and a variety of hematopoietic factors, including lymphokines and monokines.[29,45] Recombinant technology has allowed the isolation and production of individual factors for use in osteoinduction and osteoconduction to promote the healing of bony defects.[5,12,42]

CONCLUSION

In conclusion, a bone graft is a surgical procedure used to fix problems with bones or joints due to trauma. It's also useful for growing bone around an implanted device where there is bone loss or a fracture. Bone grafting used to fill an area where the bone is absent and provides structural stability and also enhances the bone healing process in veterinary orthopedic patients. There are different types of graft cells used to treat different orthopedic problems. Among these, autogenous cancellous bone graft provides the cellular components and matrix proteins that can accelerate bone healing dramatically. Allografts provide immediate mechanical support for fracture repair and patient function, but unlike autogenous cancellous bone graft, these grafts do not create the osteogenic environment. Xenograft bone implants may also hold a place for use in fracture management. Accordingly, the knowledge of osteoconduction, osteoinduction, osteogenesis is the most important point for orthopedists and these help in a careful selection of the appropriate type of bone graft, bone substitutes, and bioactive factors that have a great role for remarkable regeneration of the bone. Thus, bone grafting still holds a strong place in orthopedic surgery when dealing with bone defects in animals.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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