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Review Article

Bone Grafts – A Valuable Substitute for Replacing Bony Defects- A Review

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Abstract

Numerous graft materials are in use of which autografts are considered as a gold standard. Autografts have the uniqueness of having osteogenic, osteoinductive and osteoconductive potential. At the same time, they have well identified disadvantages too which include donor site morbidity, graft availability and the risk of disease transmission. Synthetic graft substitutes do not have osteoinductive or osteogenic properties. Composite grafts are also being used effectively for osteogenesis. The limited availability of suitable bone grafts has ushered in the era of tissue engineering for bone repair. Additive manufacturing, also known as 3D printing, is considered as an ideal method for orthopedic applications such as bone grafting. Here in this review the scope of bone grafts and graft substitutes used for different clinical applications is discussed.

Keywords: Bone Graft; Bone Graft Substitute; Autografts; Allografts; Xenografts; Alloplast; Mesenchymal Cells

Introduction

Bones provide the framework for the body which makes up 14.84% of the body weight. In a healthy adult eighty percent of bone is made up of the outer cortical bone, and the remaining 20% is inner trabecular bone. Cortical bone consists of 70% inorganic mineral (hydroxyapatite), 22%organic protein (collagen, cells, hyaluronic acid) and 8% water [1]. Bone is a dynamic organ which can regenerate and repair by itself [2]. In certain situations, if the defect is large or if it occurs as a sequel to treatment of pathological situations, the self-healing ability will be lost and bone grafting becomes necessary to promote healing and to restore its anatomy. Hence it is stated that bone grafts are used to repair and reconstruct the defects of bone that are unable to heal by itself. Bone is one of the most popularly transplanted tissue in the hu-

man body [3]. At present the demand for bone grafts is high, and that is mainly due to the advancements in maxillofacial reconstruction and increased use of dental implants. The main goal of bone grafting is to restore the original contour, to get a dense bony architecture substituting the dead space, and to enhance healing of soft tissue and bone. The common techniques used for eliminating the bony defects are bone grafting procedures, guided bone regeneration, distraction osteogenesis and use of growth factors and stem cells. Bone grafting is a surgical procedure in which the missing bone is replaced by the patient's own bone, bone obtained from genetically identical twins, bone from cadavers, bone from bovine source and an artificial synthetic or natural substitute (Figure 1).

Figure 1: Bone grafting.

History

The treatment option of replacing missing bone tissue has been in active consideration for centuries. Susruta Samhitha and Charaka Samhitha compiled during first millennium BCE to 500 CE, which are the foundational works of Ayurveda have mentioned the use of herbal preparations in the healing of bony defects and fractures. In 17th century a Dutch surgeon Job Van Meekeren repaired the cranial defect in a soldier using a piece of bone harvested from a dog's skull [1]. Probably this was the first reported clinical incident in bone grafting. In 1821 in Germany, the very first auto graft was used. MacEwen used an allograft harvested from tibia to restore a humeral defect in 1881. Later in 1892 Calcium sulfate was used as a bone substitute for restoring tubular cavities present in long bones [2]. An entire knee joint was transplanted in 1907. In 1942 the use of preserved bone was first reported in orthopedic surgery. In 1991, the first commercial demineralized bone matrix was made available.

Properties of an ideal bone grafting material

Muschler and Lane (BGM) have defined a bone graft material as any implantable material which alone or in combination with other materials can promote bone healing by providing osteogenic, osteoinductive, and osteoconductive activity to the local site [4]. The graft material should have certain qualities to meet its goal. It should have adequate porosity which is inter connected and the pore size should be a minimum of 100 µm to allow diffusion of bone cells, nutrients and exchange of waste products. To allow vascularization and thereby new bone formation, a pore size of more than 300µm is recommended [5]. The surface of bone grafting material should allow vascular ingrowths, migration, proliferation and attachment of bone cells. The material should have adequate compressive strength and elasticity to absorb the load from the surrounding tissues. The material should be biodegradable so that the resorption occurs without much inflammation during remodeling. Slow resorption helps to maintain the volume of new bone formation. An ideal graft material is replaced by new bone and this remodeling occurs by tailored resorption of the graft. The material should have adequate handling properties and dimensional stability so that it can be adapted during chair side procedures and dimensional stability helps in maintaining the graft volume. For bone regeneration the graft material should contain osteoprogenitor mesenchymal cells or living osteoblasts, growth factor that promotes regenerative process and a framework that mechanically supports the adhesion, growth and proliferation of cells. Extensive research has been conducted but a material that fulfils all the required properties are yet to be developed.

As mentioned earlier, the bone graft material should be capable of providing osteogenic, osteoinductive, and osteoconductive activities. Of the three, a graft material should have at least two properties [6]. A material can be called as osteogenic when it contains living cells which can differentiate into new bone. Osteogenesis can be defined as the process of new bone formation, caused by the transplantation of osteoprogenitor cells and growth factors from bone graft to host bed. An osteoinductive material provides biological stimulus that induces the transplanted cells or host cells to differentiate into mature osteoblasts; in other words, the mesenchymal stem cells are gathered from host tissue to differentiate into osteoblasts. Osteoconductive materials act as a scaffold or frame work which permit the ingrowth of host micro vasculature, perivascular tissue and mesenchymal stem cells. The structure of scaffold microscopically resembles the cancellous bone [7] (Figure 2).

Figure 2: Osteo conduction, osteo induction, osteo genesis.

Classification of bone graft materials

Titsinidesetal, classified bone graft materials by different criteria viz. histological architecture, embryologic origin, blood supply and form of the graft (Table 1). With regards to the source of origin, grafts can be identified as Autografts, Allografts, Xenografts and Synthetic bone substitutes [8] (Table 2). The materials of different origins vary in their bone regeneration potential. Bone grafts can also be natural or synthetic or a composite material (Figure 3).

Table 1: Classification of bone grafting materials by selection of different criteria.

Source	Histologic architecture	Embryologic origin	Blood supply	Form of the graft
Autologous	Cortical	Endochondral	Free Graft	Bone block
Allografts	Cancellous	Membranous	Regional Flap	Particulate bone
Xenografts	Corticocancellous			Bone slurry
Alloplasts				Bone paste

Table 2: Bone grafts classified according to their source of origin.

Graft category	Graft type	Advantages	Disadvantages
Autografts +Isografts	Extra-oral: Cranium, Fibula, Iliac crest, Radius, Rib, Tibia Intra-oral: Anterior maxillary sinus wall, Anterior nasal spine, Ascending ramus, Coronoid process, Incisive fossa, Mandibular symphysis, Maxillary tuberosity, Palate, Torus, Zygomatic body	Osteogenic Osteoinductive Osteoconductive No disease transmission or immunogenicity	Donor site morbidity Limited quantity Possibility of general anaesthesia and hospitalization (for extra-oral sites)
Allografts. Possibility of	Fresh and/or frozen bone, freeze dried bone, Demineralized freeze-dried bone	Osteoinductive Osteoconductive Relative availability	disease transmission and immunogenicity Variability of properties depending on productive method
Xenografts Bovine	Porcine, Equine, Coralline, Algae	Osteoconductive High availability Low cost	Possibility of disease transmission and immunogenicity Variability of properties depending on productive method
Synthetic bone substitutes	Calcium phosphate Hydroxyapatite Calcium carbonate Calcium sulphate HTR polymer Bioactive glasses	Osteoconductive Availability Low cost	Variability of properties depending on productive method

Figure 3: Classification of bone graft.

Autografts

Currently the only osteogenic graft material available is the autogenous bone and it is considered as the gold standard for bone augmentation procedures [9]. The presence of viable cells and growth factors from the donor site initiates the differentiation of mesenchymal stem cells to osteoblasts. The graft shares the same biological origin and hence eliminates the immune reaction and possible rejection. The success rate is more than 95% [10]. The need for second surgical intervention, limited volume of bone, bleeding and infection at the donor site are considered as drawbacks. The graft can be obtained from intraoral and extraoral sites. The advantages of intraoral site are, the proximity of donor and recipient sites, easy surgical access, lack of scarring and minimal postoperative morbidity. Membranous ossification of maxilla and mandible, presence of high concentration of growth factors and angiogenetic potential result in better integration of the graft material. The extra oral sites provide large volume grafts [11]. The need for general anesthesia, hospitalization, increased morbidity, and additional training for the clinician are necessary for harvesting the graft.

The common intra oral sites include mandibular symphysis, maxillary tuberosity ascending ramus and exostoses. Less resorption is associated with mandibular bone compared to extraoral sites like iliac crest. There is less morbidity of the donor sites but the bone volume obtained will be less. More volume of graft can be obtained from extraoral sites; the common sites are anterior and posterior iliac crest, tibia, cranium etc. (Table 2). Greatest volume of autogenous cancellous graft is obtained from the posterior iliac crest region 140ml, followed by anterior iliac crust 70ml, tibia 20 – 40ml, ascending ramus 5 -10 ml and the symphysis 5ml. Due to the presence of abundant viable cells and growth factors along with the availability of huge areas of trabecular architecture, iliac crest has become the most popular source of auto graft.

Cancellous autograft gives trabecular bone with high osteogenic potential due to the abundance of growth factors and cytokines [12]. Revascularization and incorporation of the host stem cells readily occur because the pH of the recipient site and low oxygen tension attracts host pluripotent undifferentiated stem cells to the host site. Osteogenic process and bone healing mechanism have many similarities. Initially there is hematoma formation at the grafted site followed by inflammation, neovascularization and osteoinduction. This process is continuous and bone formation/resorption occurs throughout the period of four weeks after surgery. In the second phase of graft - host bone osteo-integration, osteoclasts resorb the graft and new bone remodeling occurs on the graft surfaces. Osteoblasts which get differentiated from mesenchymal stem cells lay down osteoid in close proximity to the dead trabeculae of the graft. Afterwards, osteoclasts remove the necrotic bone tissue of the graft and which gets replaced by new host cells (Figure 4).

Allografts

Allografts are obtained from cadavers or from living relatives of the patient. Non-relatives can also serve as donors. The mate-

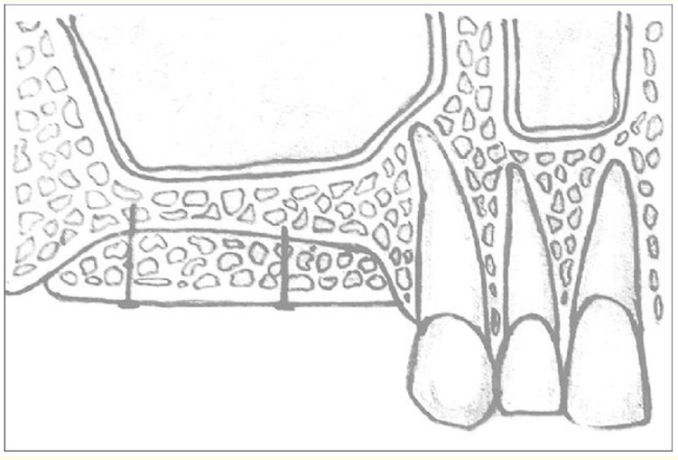

Figure 4: Block-auto graft.

rial obtained from living donors or cadavers, is subjected to further processing in order to neutralize the transmission of infectious diseases and the immune response [13]. The graft is available as cortical, cancellous or corticocancellous forms and in various sizes and shapes [14]. The commonly used types include

- Fresh frozen bone (FFB) - frozen at -800^{0}Cto avoid degradation by enzymes. The graft is not irradiated, lyophilized, or demineralized. It is acellular, the presence of bone morphogenic proteins makes it more osteoinductive and osteoconductive. Presently this type of graft is not used because of the high immune response and risk of disease transmission.
- Freeze dried bone allograft (FDBA) - to decrease the antigenicity, these grafts are dehydrated and frozen without demineralization. Freeze drying eliminates the osteo progenitor cells and thus the osteoinduction is lost and the graft has only osteoconductive potential.
- Demineralized Freeze - dried bone allograft (DFDBA)- these materials have both osteoinductive and osteoconductive potential. It is dehydrated and the inorganic part is removed. The remaining organic part contains the bone morphogenic proteins (BMP).

FDBA is available in both mineralized and demineralized form. It is more effective in repair and restoration of fenestrations, ridge augmentation, filling fresh extraction sites, sinus lift procedures, repair of dehiscence and failing implants. The use of DFDBA is limited to the treatment of periodontal defects.

Cancellous allografts are available in the form of small cuboid chips which can be packed into the osseous defect. They lack mechanical strength and the preparation process eliminates the growth factor that promotes osteoinduction. Cortical allografts provide structural support and it is used to fill larger defects[6]. When properly stabilized it allows for early weight bearing. Use of allografts eliminates the need for another surgery thus it reduces the surgical time and eliminates the donor site morbidity. It is available in adequate quantity, size, shape and the results are predictable (Figure 5).

Xenografts

Xenografts are derived from different species and are transplanted to the recipient. Xenografts are osteoconductive, with limited resorptive potential and is usually combined with either growth factors or bone grafts obtained from other sources. Different types of bone substitutes are available in this category. It can be processed in large quantities with a relatively affordable cost [8]. The disadvantages are that the bone characteristics differ from that of the human bone. The processing procedures affect the physical and chemical properties and thereby the possibility of disease transmission and stimulation of immunogenicity.

Bovine bone substitutes were the first and foremost xenografts used in patients. In this category, a wide range of products are commercially available. They are identified as osteoconductive. They are deproteinized and lyophilized, and hence do not cause any im-

Figure 5: Allograft

mune response. Granules of these materials are absorbed slowly. High temperature processing of these grafts avoids transmission of infectious diseases and do not cause immune reactions, and allergies. Bovine xenografts are widely used in maxillofacial applications [5].

Coral substitutes: Madreporic corals including species Lobophyllia, Porites, Acropora, Pocillopora Goniopora and Polyphillia are very similar to the cancellous bone. Jaw defects are restored with coral bone grafts. They have osteoconductive properties and act as carriers for growth factors. It is observed that initially the graft material exhibits poor strength. Effectiveness in born formation depends on the blood supply of the grafted site. Many investigators have reported the use of coral material in dentoalveolar reconstruction and showed encouraging results.

Equine substitutes: Bone grafts from equine source are produced by treating equine tissues to an antigen-elimination process with enzymes and partial bone collagen denaturation. Complete de-antigenation of the equine bone is done by specific enzymes kept at low temperature and which allows to preserve the natural mineral structure and at the same time retaining fragmented type I collagen of the equine bone [14,15]. Enzyme-treated equine bone serves as an optimal scaffold for the differentiation of mesenchymal stem cells *in vitro*. Enzyme-treated equine xenograft has an advantage that it can retain its volume with the patient's newly formed bone. In due course of time, newly formed bone progressively replaces the equine xenograft. They are used for various oral and maxillofacial procedures, including the treatment of periapical lesions, and in maxillary sinus augmentation. For more than two decades, this material is available in the market [15]. Equine-derived bone substitutes were introduced as a scaffold for bone regeneration. They can induce osteoblastic differentiation and angiogenesis even during the absorption by the osteoclasts. In addition to new bone formation, bone remodeling was observed around the graft material six months postoperatively.

Porcine substitutes - Recently developed porcine-derived substitutes, are considered to exhibit similarities to human bone in structure and formation. They exhibit osteoconductive characteristics and have low risk of disease transmission. However, it has been reported that these materials exhibit reduced absorption capacity over a period of time and poor development of neovascularization. Some investigators consider porcine bone and bovine-derived bone implants are equally effective. Sinus lift procedures have also been performed with porcine bone implants (Figure 6).

Alloplastic materials

Risk of infectious disease, morbidity of the donor site, cost and advances in the field of biomaterials led to the development different types of natural and synthetic materials as an alternative to other grafts. Pore size, physicochemical structure and immunological response can be controlled [5,16]. They have osteoconductive properties. The most common synthetic bone substitutes are calcium phosphate, calcium sulfate, bioactive glass and combinations.

Calcium phosphate -Calcium phosphate-based bone graft material i.e., hydroxyapatite (HA) and tricalcium phosphate (TCP) has greatest similarity to minerals in bone. So, they have excellent biocompatibility, biodegradability and osteoconduction. It is available in different forms and products, including ceramics, powders, and cements [17]. Calcium phosphate-based bone grafts materials

Figure 6: Porcine bone graft.

degrade relatively slow compared to calcium sulfate. Biphasic Calcium phosphate is made by mixing HA and TCP in various proportions to get desired mechanical properties and absorption rate.

HA has low mechanical properties with fracture toughness <1 MPa $m^{1/2}$so its application has been limited to non-load bearing sites [18-20]. Heidari F, reported compressive strength value of about 0.15 MPa for the hydroxyapatite prepared from bones which was sintered at 1100 °C. Hariani PL, reported a hardness value of 17 HV for hydroxyapatite prepared from fish bone which was sintered at 1000 °C for 2 h, Thangamani*., et al.* Reported a flexural strength value of 15 MPa for the hydroxyapatite sintered at 1100 °C for 3 h. Hardness value of 14.8 HV was reported for hydroxyapatite, sintered at 1000 °C by Irza Sukmana (HV – Hardness according to Vickers) [18].

Calcium sulfate - is used as a grafting material since centuries [2]. It is biocompatible, bioactive, osteoconductive and has low cost. It resorbs rapidly and much faster than the new bone formation. The resorption can be delayed by combining it with other materials. It is extensively used in treating periodontal and dentoalveolar defects.

Hard tissue replacement (HTR) polymeric substitute - poly methyl methacrylate is the most commonly used polymer for bone augmentation. It is a porous, osteoconductive material with elasticity and compressive strength similar to cortical bone [8].

Bioactive glass - composed of active silicate-based glass. It is stronger than calcium phosphate and forms a strong bond between glass and host bone through HA crystals [8]. Resorption rate varies with the quantity of sodium oxide, calcium oxide, silicon dioxide and phosphorus (Figure 7).

Tissue engineering

Tissue engineering is a new field of biomedical science that applies the principles of biology and engineering in order to develop functional substitutes for tissues and organs [21]. It demands multidisciplinary expertise in biological sciences and it recreates functional tissues and organs lost in different situations [22]. Based on the principles of cellular biology, different tissues like bone, oral mucosa, dentine and pulp, skin, and salivary glands, can be grown *in vitro*. Organic tissues can be made *in vivo* or *ex vivo*, through cellular proliferation and which may effectively be combined with a scaffolding material and appropriate growth factors. A live tissue, containing the cells appropriate to the receptor site is the primary requirement. Cell cultures are then developed in the laboratory, where the cells of interest are expanded and seeded onto selected polymer matrices, so that later they can be reinserted into the organism [23]. The triads that act as the basis of tissue engineering with reparative objectives are:

- The matrices or scaffolds, with various presentations or forms (gels, permeable membranes, fibrous matrices,),
- The progenitor cells (undifferentiated stem cells, or cells with preliminary differentiations) and
- The growth factors (Figure 8).

Figure 7: Alloplast.

Figure 8: Tissue engineering.

Mesenchymal stem cells (MSC)

The two large groups of stem cells in tissue engineering are totipotent or pluripotent embryonic stem cells and the lineages of unipotent or multipotent adult stem cells are found in differentiated tissues. Embryonic stem cells are capable of generating variety of cell lines which can offer great clinical potential in the field of tissue engineering; but they have limitations too in the usage, due to intricate legal and regulatory policies and ethical considerations. The adult stem cells have gained popularity because of their ability to regenerate bone, pulp and periodontal tissues. Availability of adult stem cells is not scarce and they do not raise significant ethical or immunoreactive issues [21].

Autogenous MSCs are collected from bone marrow or adipose tissue and have high differentiation potential necessary for tissue engineering. In addition to this, these cells possess a high proliferative capability [24]. MSCs can be stored without difficulty in freezing conditions and without altering their osteogenic potential and they can adhere to plastic surfaces. Osteoblastic characteristics of MSCs are directly linked to the presence of bone morphogenic proteins (transforming growth factor beta (TGF-b) family) and also to the number of viable cells that can initiate bone growth. When cultivated *in vitro*, they are placed in a culture to induce pre-differentiation and generate cells with an osteoblast phenotype. There are

documentations that indicate the use of ascorbic acid, dexamethasone and b-glycerol phosphate for the same purpose. Isolation, characterization and analysis of the differentiation of MSCs derived from the adipose tissue of rabbits, rats, and pigs was done by Arrigoni., *et al*. [21-23]. After exposure to an osteogenic stimulus, these cells exhibit a significant increase in the expression of bone markers, such as alkaline phosphatase, osteocalcin, osteonectin and extracellular calcium deposits.

The dental tissues which are excellent sources for collecting MSCs are: dental pulp of exfoliated deciduous teeth, the dental pulp of impacted third molars, periodontal ligament, and dental follicles. Cells obtained from these sites may differentiate into different types of tissues viz. bones or nerves. In an invitro experiment Honda., *et al*. isolated stem cells from the human dental follicle and cultured them to cause subsequent osteogenic induction. They were placed into the bone defects present in rats [23,24]. After 4 weeks, the bone defects were partially or completely healed. The histological appearance was similar to that usually seen in intramembranous ossifications. Cells of the dental follicle are promising sources for multipotent precursor cells capable of generating organic tissues.

Cellular matrix: When used in tissue engineering the extracellular matrix provides the framework for oxygen, nutrients and metabolic waste transportation required for the cells in the medium. This framework should be biocompatible, biodegradable and also should have a firm consistency to facilitate easy handling of the formed tissue during its insertion into the body. A matrix should also promote adherence, migration, proliferation, and differentiation of the cells within its own structure [22,23]. Cell matrices are made from different allogenous materials like bone matrix, intestinal submucosa and skin; biological polymers such as collagen, hyaluronic acid, and fibrin; ceramic bases or minerals such as tricalcium phosphate, hydroxyl apatite, and calcium sulfate; metals and alloys, such as titanium and synthetic copolymer poly coglycotyde acid (Figure 9).

Figure 9: Mesenchymal stem cells.

Growth factors in tissue engineering

Platelet-rich plasma (PRP) is mainly used in alveolar bone grafting for dental implants and periodontal and maxillofacial surgeries. Presence of various growth factors provides the regenerative capacity of PRP. Biologically PRP is composed of plasma, leucocytes, and platelets. The platelets accumulate and release growth factors locally. These growth factors act as mediators and regulate the actions over cellular events that usually take place during tissue repair and regeneration [23,24]. PRP has three principal proteins namely platelet derived growth factor (PDGF), TGF-b and insulin like growth factor (IGF-I). PDGF stimulates cellular mitogenesis, angiogenesis, increases the number of cells responsible for the healing process and regulates the influence of other growth factors. Thus, improving the fibroblastic and osteoblastic cellular differentiation and function. TGF-b1 and TGF-b2 initiates bone regeneration and remain at the healing site; it is responsible for the remodeling and maturation of the bone grafts during mid- and long-term healing processes. IGF-I, produced by osteoblasts during the collagen type I and II synthesis plays an important role in tissue regeneration. IGF-I has an effect to increase the quantity of reparative osteogenesis and regulates the osteoblasts and the deposition of the bony matrix (Figure 10).

Discussion

Autologous bone grafts are considered as the gold standard for treating osseous defects. They have osteogenic, osteoinductive and osteoconductive properties. Autografts contain living cells. They are biomechanically stable and serve as scaffolds and allow cells and blood vessels to adhere and build up new tissues. They secrete growth factors that are necessary to induce the maturation

Figure 10: Platelet rich plasma.

of undifferentiated stem cells and pre-osteoblasts into mature osteoblasts. Disadvantages include limited availability of the graft, donor site morbidity and need for additional surgical procedures for harvesting, accompanied by the risk of infections, hematoma and chronic pain. These disadvantages can be avoided by the use of allografts, which are osteoconductive. Since allografts are obtained from same species but different genus, they carry the risk of disease transmission from donor to recipient and can cause immunogenic reactions. A promising alternative to autografts and allografts is xenografts which are derived from donors of a different species. Possibility of disease transmission and stimulation of immunogenicity cannot be ruled out. Alloplastic materials were developed in order to reduce the risk of infectious disease transmission and immunoreactive issues. A promising alternative to all these graft materials are tissue engineered bone substitutes [21]. The term tissue engineering describes the production of organic tissues through cellular proliferation *in vivo* or *ex vivo*, and which may be combined with a scaffolding material or growth factors [22].

It is challenging to design a graft material with mechanical properties similar to the host bone and to design a graft substitute which resembles the shape of the defect. Development in the field of bio materials and advanced manufacturing systems such as 3D printing (3DP) can be effectively utilized for this purpose [25]. Thus, additive manufacturing (AM) technique along with computer - aided design can be used to print bone grafts or scaffolds with complex shapes. 3DP enables fabrication of heterogeneous tissue structures consisting of deposited cells, growth factors, extracellular matrix and the required biomaterials. These grafts or scaffolds can be used in biomedical applications ranging from customized medical implant design to tissue engineering. O' Brien., *et al*. provided a concise overview of the application of these different AM techniques for fabrication of tissue - engineered scaffolds in the fields of bone, osteochondral, neural and vascular tissue regeneration [25]. Klammert., *et al*. fabricated brushite (di CaP dihydrate) and monetite (di CaP anhydrous) 3D scaffolds for reconstruction of cranial defects and concluded that 3DP implants provided an adequate fit [25]. Anatomically shaped scaffolds were fabricated using CAD files generated by scanning a human cadaver skull having specific cranial defects. Tada., *et al*. used implants fabricated from HA - TCP for reconstruction of facial defects [26]. Three - dimensional patient CT data was used to fabricate a life - sized CAD model consisting of the defect and this CAD model was used for shaping the artificial HA - TCP implantable bone. They concluded that anatomically shaped templates and implants helped in optimizing the implant design and resulted in better contouring in patients with complex defects [26].

Conclusions

Success in bone augmentation can be ensured by the careful combination of an appropriate surgical technique and graft material. Either adequate number of osteoblasts or primitive mesenchymal cells that can transform into osteoblasts must be present in the bone matrix. Other factors that contribute to the success are adequate blood supply, stabilization of graft during healing and suturing without tension on the incision. Clinical evaluation of the quality of bone present at the defect should precede the careful selection of the type of graft material to be used. A wide variety of grafting materials are available and the possibility of combining different materials should be explored.

Active research is being carried out on bone augmentation materials all over the world to create an ideal graft which has adequate strength, molecular composition, biodegradability, biocompatibility, osteoinductive, osteoconductive and osteogenic potential. Natural bone and synthetic materials are used alone or in combinations. In future, a combination of biomaterials coupled with 3D printing will enable us to fabricate anatomically shaped implants that results in better contouring of the defect sites. Various growth factors that will improve the osteogenic, osteoinductive, and osteoconductive properties can be incorporated to such anatomically designed implants bringing in greater satisfaction both to the patient and to the professional who is engaged in the noble task of treating the suffering human being.

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