Bone Substitute Materials in Modern Dentistry

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ABSTRACT

People lose their teeth because of various causes. After the tooth loss, alveolar ridge resorption occurs, and then implantation becomes a challenge for the oral surgeon. On purpose to create sufficient properties for implantation, various procedures are being performed with teeth extraction in order to protect the bone, if the tooth was lost earlier – bone augmentation procedures may be performed to recreate the bone volume. Materials that are used for bone augmentation according to the origin may be classified as follows: autogenous, xenogenous, allogenous and alloplastic or synthetic. This article purpose is to review the bone substitute materials that are the most used nowadays.

Keywords: bone substitute materials, alveolar ridge, augmentation

1. INTRODUCTION

Healthy alveolar ridge keeps soft tissue relief around natural teeth or implants, gives the contour to the gingiva. There are several different alveolar ridges:

1. Visually seen areas, in which bone structure is critical for aesthetics and function
2. Visually unseen areas, in which alveolar ridge is needed as teeth or implant support, maintaining the longevity of the tooth or implant.

People lose their teeth because of various causes: periodontal disease, trauma, periapical lesions and other pathologic causes. After the tooth loss, alveolar ridge resorption occurs, causing functional and aesthetic problems and it becomes a problem for implantologist or prosthodontist\(^1\). Poulias et al.\(^2\) stated that during the first four months after tooth removal in total ~3.7mm or 45% of alveolar ridge width is being lost in teeth area. Alveolar ridge height is being affected less – vertical resorption is about ~1.6mm in the mean. Buccal bone is usually more affected than lingual. Because of structural and textural properties, the maxilla is usually more sensitive to resorption than mandible\(^3\).

Implantation – one of the most used methods for dental defects rehabilitation. Even though implantation methods are modern, however in order to reach ideal aesthetic and functional results, sufficient amount of bone and favorable alveolar ridge architecture is needed\(^4\). On purpose to create sufficient properties for implantation, various procedures are being performed with teeth extraction in order to protect the bone. If the tooth was lost earlier – bone augmentation procedures might be performed to recreate the bone volume\(^1\).

In order to better undertint the benefits of augmentations, knowledge about the remodelation after tooth extraction is needed. Ohta et al.\(^5\) examined the changes after tooth loss and classified them to five phases:

1. Granulation phase, lasting for five days. Early granulation tissue appears at the bottom of the alveolus and spreads to the sides.
2. Angiogenesis phase, lasting for the first week simultaneously with granulation phase. It involves vascularization, spreading to the blood clot.

3. Bone formation phase, which starts at two weeks post-extraction.

4. Bone increase phase, starting at 4-5 weeks. During this phase, 2/3 alveolus is being filled with trabeculae, lightly mineralized bone.

5. Reorganization phase, which starts at six-week post-extraction. During this phase, primary spongy bone transforms to mineralized, organized, structural tissue.

After the tooth loss, different changes appear in molecular, cellular and tissue levels. Tooth extraction starts the inflammatory reactions cascade\(^9\). Blood from injured blood vessels fill the alveolus, creating the mixture of proteins and affected cells, during the first 24 hours wound is being filled with fibrin clot\(^7\). 2/3 alveolus is being filled with partly mature bone in 28 days\(^8\). Alveolar dig examinations showed that after tooth extraction, alveolar ridge is prone to lingual migration from the occlusal point of view\(^9\). Misch et al.\(^{10}\) determined that after the tooth loss vertical and horizontal dimensional changes of alveolar ridge appear because of the shrinkage of alveolus clot and dense plate remodeling, starting when insufficient vascularization is present. Atwood et al.\(^{11}\) classified the factors that cause alveolar ridge changes in four groups: anatomical, functional, metabolic and prosthesis caused. Changes after the tooth extraction impede implantation procedure and decrease the success probability.

This article purpose is to review the bone substitute materials that are the most used nowadays.

2. BONE REGENERATION MECHANISMS

Bone regeneration can onset according to three different mechanisms; osteogenesis, osteoinduction, and osteoconduction\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\). Osteogenesis is the bone formation and development even with the absence of local stem cells. Osteogenic transplant may ease different phases of bone regeneration, with the result of faster osteogenesis. Osteogenic transplant is an organic material, which may be produced or composed from live human bone tissue and may be used individually by same patient bone augmentation\(^\)\(^\)\(^\)\(^\)\(^\). Osteoinduction is the undifferentiated mesenchymal cells transformation to osteoblasts or chondroblasts, because of the various growth factors found in live bone. Osteoinductive transplants improve and ease bone regeneration and sometimes even expand the process\(^\)\(^\)\(^\)\(^\)\(^\). Osteoconduction is a process, which gives bioinertic frame or physical matrix, which is suitable for new bone formation. Osteoconductive transplant (which is usually inorganic) result in bone opposition from surrounding areas or lets the differentiated mesenchymal cells to grow on the transplant surface. Not all the transplants can affect the bone growth if they are implanted in soft tissues. All the materials that are used in bone augmentation procedures have one or all of these three action mechanisms\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\).\

3. BONE SUBSTITUTES

Materials that are used for bone augmentation according to the origin may be classified as follows: autogenous, xenogenous, allogenous and alloplastic or synthetic. According to the size of defects, localization, patient’s state, the best material is selected, best for the clinical situation. The gold standard is autogenous transplant because of genetically identity\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\).

Autogenous transplants

Transplants are charged from recipient’s bone tissue. This is the only osteogenic transplant. Three stages are seen during the healing: osteogenesis, osteoinduction, and osteoconduction\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\). Transplants can be taken from\(^\)\(^\)\(^\)\(^\): 

1. Extra oral areas (iliac crest, cranial bones, ribs)
2. Intraoral areas (mandible symphysis, maxillary torus, mandible ramus, osseous exostosis)

Transplant’s organic matrix – collagen, determine the elasticity, strength, stability, and inorganic – hydroxyapatite – determines the hardness. Autogenous transplant’s bone may be trabecular, cortical or cortico-trabecular. Many osteogenic cells are found in trabecular bone and less in cortical bone. However, high amount of BMP proteins is found in cortical bone, which is important for bone formation and mesenchymal cells differentiation to osteoblasts\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\)\(^\). After bone augmentation, the healing process may continue in three ways:

1. Transplant becomes vital and gets the local bone properties
2. Transplant is partially or fully resorbed

Autogenous bone transplants are very osteogenic and are the best according to all theoretical bone regeneration requirements. However, there are some disadvantages:

1. Transplant’s collection require additional surgical intervention, which results in postoperative discomfort for the patient
2. Defect is made in bone collection are, which may increase the risk of infection or morbidity
3. More intense resorption is seen in iliac bone transplants. Transplants from mandible cause less resorption (because of the same embryonic origin between donor and recipient sites)
4. Limited amounts of transplant material can be taken from intraoral donor sites
5. When the transplant is harvested from chin area, the risk of teeth roots or sensory nerves damage appear.
6. This material is uncomfortable to work with\(^1\)\(^1\),\(^2\),\(^3\),\(^4\),\(^5\)

Autogenous transplants cause various difficulties for the doctor and require additional surgical intervention; usually, alternative materials are used in dentary for bone regeneration: allogenous, xenogenous, alloplastic.

**Allotransplants**

Allotransplants are the transplants that are harvested from the same species individ (genotypes of donor and recipient are different)\(^6\),\(^7\),\(^8\),\(^9\),\(^10\),\(^11\). Donors can be relatives, non-relatives, and even corpses. Transplants are processed under sterile conditions and kept in bone banks. Schwartz et al.\(^12\) published an article about six different bone banks materials and evaluated that augmentation results are related to donor’s age, sex, health state, material preparation (the time of demineralization, sterilization methods, the size of particles). In order to minimize the immunologic reactions to transplant, transplants are processed: they are dried at a very low temperature (FDBA-freeze – dried allografts), demineralized and dried in low temperature (DFDBA-de-mineralized freeze-dried allografts), affected by ionic radiation (ICBA-irradiated cancellous bone allografts). Different bone types are used for transplants. However cortical bone is better for allogeneic transplant production, due to the low antigenic activity and high collagen volume\(^13\). It should be noted, that sterilization with ionic radiation demolish the high levels of BMP protein. DFDBA transplant is osteoinductive, affecting patient’s undifferentiated mesenchymal cells, until the onset of vascularization. Also, osteoconductive properties are present. Allotransplant plays a role in a bridge formation for new bone. Scientists did not find any statistically significant differences between bone regeneration with a use of FDBA or DFDBA transplants\(^19\),\(^26\),\(^27\). The particle size of allogenic material can vary. Shapoff et al.\(^28\) examined FDBA transplant’s particle size influence on the augmentation success and found that 100-300 um is a perfect size, which results in best augmentation outcomes. Particles were kept in place for long period and changed by new bone afterward. Particles that were smaller (<125um) initiated macrophage’s reaction, which leads to fast transplant’s resorption, therefore less or no new bone formation was seen. With the use of bigger than 300um particles sequestration occurs.

Benefits of allogenous transplants:

1. Easy accessibility
2. Easy usage
3. Elimination of surgical procedures in donor sites
4. Shorter anesthesia and operation time
5. Less blood loss

Limitations of allogenous transplants:

1. Quality is influenced by donor health conditions (it is important, whether infectious diseases, oncologic diseases, degenerative bone processes, sexually transmitted diseases, autoimmune disorders are present. Therefore, careful donor selection is needed\(^24\),\(^28\),\(^29\),\(^30\),\(^31\))
2. The risk of rejection
3. The risk of infection
4. The risk of coalescing with recipient site
5. The risk of fast resorption

**Xenogenous transplants**

Xenogenous transplants are taken from other species individuals than the recipient. Typically transplanted materials are natural hydroxyapatite and deorganated bovine bone.

Natural hydroxyapatite is synthesized from calcium carbonate (CaCO\(_3\))\(^12\),\(^13\). It has a 3D microstructure, which is typical for bovine bone, in which internal...
porosity reaches 200 µm. This material has good biocompatibility, and it easily incorporates with surrounding structures of hard and soft tissues. Because of permeable porous structure and three-dimensional reciprocal connections, transplant and ingrowth bone tissue are remodelled and are affected same chemical and biomechanical forces as natural recipient’s bone. Transplant’s resistance to a pressure significantly increases after ingrowth of bone tissues, and it becomes sufficient to withstand mastication forces\(^{(20,32)}\). There are several limitations of hydroxyapatites:

1. Porosity is inversely proportional to strength
2. Fragile
3. Difficult to work with
4. During the healing process, migration due to pressure is possible
5. Can be used in areas without inflammation\(^{(20)}\)

Treated bovine’s origin transplant is inorganic bone substitute. It is chemically and thermally processed in order to eliminate all organic components. This procedure can vary. Some xenogenous transplants are processed in extremely high temperature (1100°C), others are deorganated in relatively low temperature (300°C) with the result of unchanged porosity and trabecular alignment of the bone. When a xenogenous transplant is processed at low temperature, it keeps its natural structure. It is important for later transplant’s remodellation and stability. Xenogenous transplant, which is processed in this way, after remodellation is fully integrated into human’s bone tissue, therefore it is known as one of the most physiological transplants\(^{(12,16,33)}\). Some limitations of deorganated bovine origin transplants:

1. Higher risk of recipient’s immunological reaction
2. Fragility
3. Possible migration
4. It is recommended to use it with autogenous bone graft and GTR (guided tissue regeneration) membranes
5. Slow resorption may have negative influence to newly formed bone
6. Risk of infection\(^{(13,14)}\)

There isn’t united opinion about the success of xenogenous transplants usage. Some studies show that xenogenous transplants speed up the healing time and improve new bone formation. However other authors report opposite results – xenogenous transplants slow down the healing time and disturb new bone formation\(^{(34,35,36,37,38)}\).

4. ALLOPLASTIC MATERIALS

Alloplastic materials help in avoiding complications seen in bone augmentation with xenogenous or allogenous materials. These days synthetic materials show good biocompatibility and are wide used in bone augmentation procedure and shows good clinical results. There are various types of alloplastic materials: absorbable and non-absorbable, with microporosity (<350µm), macroporosity (>350µm), without porosity; crystal and non-crystal structure; granulated and in different shapes. These materials show many positive features\(^{(39,40)}\):

1. Easy to use (transplant is present before the procedure)
2. Sterile
3. Easy to supervise
4. Safe
5. Well tolerated
6. No risk of infection

All alloplastic materials are osteoconductive. However, they differ according to chemical-physical features. Therefore the best material should be selected by a doctor, according to the clinical situation. There are three main groups of alloplasts:

1. Ceramic (synthetic hydroxyapatite, tricalcium phosphate, and glass)
2. Calcium carbonate
3. Composite polymers (absorbable and non-absorbable)\(^{(16,20)}\)

A. Ceramic

**Synthetic calcium hydroxyapatite**

Synthetic calcium hydroxyapatite (HA) \(\text{Ca}_{10} (\text{PO}_4)_6 (\text{OH})_2\) is a primary inorganic natural bone component, which composes 60-70 % of human’s skeleton and 98 % of tooth enamel. The ratio of calcium and phosphorus in this material is 10:6. This material is biocompatible, and it easily connects surrounding hard and soft tissues\(^{(13,41)}\). Clinical usage of this material depends on physical and chemical features of material used. Possible physical forms; porous (micro and macro porosity) or non-porous, block or small particles, absorbable (small particles are easily resorbed) or non-absorbable (big particles are not resorbed). Chemical features depend on calcium and phosphorus ratio, recipient area pH,
impurities of other elements\textsuperscript{[20]. The solubility of materials depends on crystal structures, and the porosity affects the blood permeability and vessels ingrowth into transplant. 250-350 µm porosity is ideal for bone ingrowth. HA limitations:

1. Strength is inversely proportional to porosity
2. Fragile
3. Possible migration during the healing process\textsuperscript{[13,14,42]}

It is possible to produce firm and porous HA in the laboratory, however clinically this material is hard to process and contour. Sometimes calcium sulfate (CaSO\textsubscript{4}) is used in combination with HA, which protects HA from the ingrowth of soft tissues, premature resorption and it helps to stabilize the transplant. These days the use of HA is limited, and is more used for bone defects fillings (e.g.: after tooth extraction\textsuperscript{[43,44,45].}

Tricalcium phosphate

Tricalcium phosphate (TCP) is chemically similar to HA. However, it doesn’t have the same chemical structure as natural bone. The ratio of calcium and phosphorus in this compound is 3:2 and some of it is transformed to HA in the organism. The speed of resorption depends on material chemical structure. TCP have 2 phases: alpha (α) and beta (β). When the material is heated to 900 oC temperature, β-TCP is produced, which is fully absorbable and is transformed to the natural bone after 8-12 months. Therefore it is appropriate to clinical usage. α-TCP can be produced, when materials heated in higher than 1180 oC temperature. α-TCP is characterized with slow resorption and can be found in bone after many years. Therefore it is not recommended to use this material in clinical practice. It is recommended to use tricalcium phosphate only in places without any inflammation and in composition with autogenous or allogeneous transplants. By this composition, the features and osteoinduction of TCP are improved\textsuperscript{[13,46].}

Bioactive glass

Bioactive glass is a composition of calcium salts, phosphate, sodium salts and silicon, which is necessary for bone mineralization. The size of pellets varies from 90 to 710 µm with the mean of 300-355 µm. This material connects with a bone with the formation of hydroxyapatite layer on the glass particles surface. The incorporation of recipient’s tissues is seen. At the junction of bone and transplant, the collagen layer with the mean thickness of 0.3 µm appears, which is similar to natural periodontal ligament according to the dimensions. Therefore it is believed, that this feature of bioactive glass can help in the reconstruction of the periodontal ligament. Bone transformation and regeneration onset inside the calcium phosphate chambers and the defect is quickly filled with new bone, which is simultaneously remodeled.

In the studies, performed with animals and humans, it was found, that bioactive glass pallets are easy to work with compared to HA granules. The reason is that bioactive glass pallets are not prone to migrate from recipient area and to spread into surrounding tissues\textsuperscript{[47]. This material, together with blood, forms firm mass, which supports the position during the hemorrhage. Stem cells formation to osteoblasts positively influence the transplant, however in clinical practice, it was found that bioactive glass material is sensitive to oral fluids, that can cause decomposition of material and increase the risk of infection when the direct contact is reached\textsuperscript{[48,49,50,51].}

B. Calcium carbonate

Calcium carbonate transplant is an inorganic material, which is composed of aragonite (more than 98% CaCO\textsubscript{3}), which is porous more than 45%. The mean porosity size is about 150 µm, the diameter of granules is 300 – 450µm and 630–1000µm. This material is slow absorbable. Calcium carbonate does not need the changing of the surface in order to start the new bone formation and growth cascade (in other material the surface is transformed to HA from carbonate), however, with the use of CaCO\textsubscript{3}, this step is eliminated, which results in faster new bone formation in augmented areas. Calcium carbonate transplants show better hemostatic features; they are prone to keeping the position and don’t migrate from recipient zone. The main limitation of this material – fragility\textsuperscript{[12].}

C. Composite polymers

There are two types of composite polymers; non-absorbable and absorbable.

Absorbable

Synthetic absorbable polymers are well known in medical practice. Many years before suture materials, fixation screws and other products were manufactured from polilactate and polyglycolic acids. Most polymers are high molecular mass compounds with slow resorption (\textasciitilde 3y). The final decomposition
products of these materials are carbon dioxide and water. Polymer’s biologic decomposition depends on many factors: patient’s age, immune system, tissue tolerance, localization of the defects and surface configuration. Slow density poliolactate and polyglycolic acidic copolymers are decompositions in 3-8 months. They can be found in three different forms; powder, gel, and sponge, which can be combined with each other to allow the reconstruction of different defects. Powders are used in three walls defects, sponges – in two and three walls bone defects. These materials are mixed with saline water or patient’s blood and are formed with a sharp instrument before the insertion into the bone defects. The gel is used in deep bone defects reconstruction. Small transplant’s mass and wide surface allow easy fibroblasts penetration and absorption initiation as well as cells colonization. It is easy to work with this material, however usually GTR membranes should be used with these materials.

Non-absorbable

Non-absorbable composite polymers are the compounds of polymethylmethacrylate (PMMA), polyhydroxethylmethacrylate (PHEMA), small amounts of barium sulfate (rentgenocontrastical) and calcium hydroxide, which directly interact with recipient’s bone, creating CaCO3 appetites. PMMA is a synthetic polymer, which is used in medical practice for long time. Intraocular lenses, artificial heart valves, etc. are produced from this material. A primary internal layer of this transplant is covered with hydrophilic PHEMA polymer. PHEMA has unique hollow spherical structure. Porosity reaches 350 µm and the size of particles ~ 750. It lets the bone tissue to ingrow into the material and around the material. After the healing, only 10-12% of the reconstructed defect is composed of this material, and 88-90% is newly formed bone. Synergic action of compounds’ materials determines unique features. The main feature – negative electric charge of the surface (-10mV0. It was found that negative electric charge of surface ease and improve the healing and formation of the bone. Even though this material does not have bacteriostatic or bactericidal features, bacteria hardly colonize the surface, because of the transplant, same as the bacteria, have negative electric charge of the surface, which results in the inflammation prevention effect. The negative charge also provide material adhesion to recipient’s bone surface, which has positive electric charge, it attracts the pluripotentive stem cells, which transform into osteoblasts, it gives better adhesion to metals, which improves osteointegration. This transplant does not migrate to surrounding structures after the augmentation and does not have to be covered with GTR membranes.

5. CONCLUSION

Every bone transplant has positive and negative features. According to each material’s characteristics, bone defect localization and size, patient’s general health and requests, the doctor has to decide, which material should be used in specific clinical situation.

CONFLICT OF INTEREST AND SOURCE OF FUNDING

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