# Progress in Alveolar Ridge Preservation after Tooth Extraction Using Tooth grafts

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**Abstract:** Autologous tooth grafts are a new, highly biocompatible option for alveolar ridge preservation. The inorganic component of the tooth acts as a scaffold to maintain volume and allows donor cells to attach and proliferate, while the organic component contains a variety of proteins and growth factors that promotes bone reconstruction and repair. The composition of dentin is similar to that of alveolar bone, which is the rationale for tooth grafts to be a ideal option of bone graft material. In recent years, some progress has been made in the field of autologous tooth grafts materials, and studies have confirmed their safety and feasibility after successful clinical application. Compared with other bone repair materials such as autologous bone, allogeneic, xenograft and allogeneic bone substitutes, autologous dental-derived materials have unique properties. Here we introduce the basic components and characteristics of autologous tooth grafts, and summarize the clinical randomized controlled trials to provide reference for scholars and clinicians.

**Keywords:** tooth graft, alveolar ridge preservation, randomized controlled trials

## 1. Introdution

The absence of a tooth in its alveolus triggers a cascade of biological events that typically result in significant local anatomic changes[1]. Preclinical and clinical studies have demonstrated that alveolar ridge volume loss post extraction is a common sequelae that involves both horizontal and vertical reduction[2-4]. Following extraction of premolar and molar teeth, Schropp et al. found an average loss in ridge width of 6.1 mm, approximately 50% of the total baseline ridge width, within a year after tooth extraction. Furthermore, they found that two-thirds of this loss occurred in the first 3 months following extraction[3].

The atrophy of the alveolar bone may compromise functional and structural aspects of treatment for the prosthetic replacement of teeth and orthodontics. A strategy that has been proven effective in mitigating the loss in residual alveolar ridge width and height post-extraction is alveolar ridge preservation (ARP). ARP procedures have been introduced to maintain an acceptable ridge contour in areas of aesthetic concern, as well as to prevent alveolar ridge atrophy and maintain adequate dimensions of bone in order to facilitate implant placement in prosthetically driven positions. This approach gained popularity over the years because of its conceptual attractiveness and technical simplicity.

Biomaterials used for alveolar ridge preservation are crucial, whose biocompatibility and osteogenic efficacy determine the effect of bone preservation. Tooth grafts using extracted tooth is a new biological material with excellent performance, which has received more and more attention in recent years. This article is a review of the latest research progress in the application of tooth grafts in alveolar ridge preservation.

## 2. Therapies for Alveolar RidgePreservation

The first therapeutic attempt to prevent alveolar ridge resorption was reported in 1974. They were performed with root retention and the main goal is to maximize the stability of the removable prosthesis[5]. However, root retention is not always feasible due to fractures, caries and/or strategic reasons

Root retention were abandoned due to its undesirable effects and various uncertainties. " Socket grafting" appeared in the mid-1980s. Filling the spaces left by extractions with biomaterials was plausible, which would mimic the 'root retention effect' that favors bone preservation[6].

 

Up to date, several methods have already been investigated for ARP in preclinical or clinical studies, such as socket grafting with autogenous bone[7], autogenous tooth[8-10], allograft[11], xenografts, like deproteinized bovine-bone mineral (DBBM)[12], alloplasts, like bone cement, hydroxyapatite (HA)[13], tricalcium phosphate (TCP)[14], gelatin[15], polylactide and polyglycolide sponge[16], hyaluronic acid gel[17], et al. However, these alloplasts have insufficient formation ability of bone due to their manufacturing process, poor porosity, and an unfavorable host response[18].

A meta-analysis[19] included a total of 2805 patients and 3073 sockets showed that alveolar ridge preservation was effective in reducing both horizontal and vertical shrinkage compared with untreated sockets. More importantly, the bioactive agents combined with the allograft outperformed other materials in maintaining ridge size and platelet concentrates in new bone formation. And alloplasts, xenografts, and allografts combined with alloplasts performed well consistently in majority of the clinical comparisons. Regrettably, the meta-analysis didn't include the randomized controlled trial (RCT) for autografts.

Bioactive agents such as bone morphogenic proteins 2 (BMP-2)[20], concentrated growth factors (CGFs)[21] have been proved to be very effective in promoting new bone formation.Guided bone regeneration (GBR) with or without bone grafts has also been evaluated. The rapid development of barrier membrane materials makes GBR technique more flexible and diverse, with more possibilities. Polylactic acid membrane[22, 23], crosslinked collagen membranes[24], polycaprolactone membranes[25] are several common membranes applied in combination with grafts. More complex and effective membranes can be made by adding active ingredients or blend several materials. Engineered bone grafts utilizing mesenchymal stem cells, scaffolds, and bioactive factors or molecules to regenerate bone could be very effective and promising in the future; however, this technology is still in its infancy and its chairside or commercial readiness is still not widespread[26, 27].

## 3. Characteristic of Tooth Grafts

All the literature and evidence so far suggest that the autogenous bone source is the best， and it has been considered as the gold standard for any hard tissue regeneration procedure[28-31]. However, disadvantages such as inevitable additional surgery, donor site morbidity, transmission of living viruses, unpredictable resorption and limited available quantities have resulted in the use of alternative bone-substitute materials[32]. Autogenous tooth bone graft utilizes the extracted teeth of the same person to prepare the graft material, providing such a valuable source without any harm. Since the teeth have already been extracted, there is no need for donor site surgery[33]. Due to the structural similarity between dentin and alveolar bone (both exhibit low crystalline HA, comparable calcium to phosphorus ratios, and type I collagen as the major extracellular matrix component)[34], tooth graft has been introduced into an increasing number of clinical applications and have shown acceptable clinical results[32, 35].

### Physical Properties

Some scholars used a scanning electron microscope to compare the surface characteristics of tooth grafts and the results showed that the pattern associated withtooth grafts bear a lot of resemblance to autogenous cortical bone. Under high magnification, the root portion of tooth grafts showed a rough pattern while the crown portion was relatively smooth. Then they used an X-ray diffraction analysis (XRD) to study the crystalline nature of tooth grafts. It showed a crystalline structure similar to autogenous cortical bones. In the CaP dissolution test, the amount of calcium and phosphorus dissolution in tooth grafts was significant from the beginning, while displaying a pattern similar to that of autogenous cortical bones[14].

### Demineralization

Since growth factors can be easily released after the demineralization process[36], demineralized dentin matrix (DDM) has a greater osteogenic effect than non-demineralized dentin matrix and the bone inductivity of autogenous teeth comes from the dentin[36]. Demineralization has been proposed to expose dentin's collagen matrix, in order to release growth factors that were trapped in the mineralization[37, 38]. It has been reported that DDM induces bone formation in 4 weeks, whereas partial DDM which contains around 30% mineral content takes around 8–12 weeks to show bone formation[39]. DDM is an absorbable acid-resistant collagen that contains microtubule structures with coagulation properties. The presence of collagen I and III, dentin sialophospoprotein (DSPP), BMP and TGF-β on DDM exerts osteogenic and osteoinductive effects[39]. The inorganic components include five different types of calcium phosphates and trace elements such as zinc, chloride and iron. Calcium phosphates include HA, tricalcium phosphate, amorphous calcium phosphate, dicalcium phosphate dehydrate, and octacalcium phosphate[40]. These calcium phosphates enables the material to act as a scaffold which has osteoconductive properties[41]. Nevertheless, demineralization has its insufficiency. It prolongs preparation time[36] and reduces usable graft volume[42], and prolonged acid exposure may also lead to growth factor depletion[43] and collapse of dentin three-dimensional structure[44].

**Biocompatibility and Bioactivity**

Tooth grafts are available in powder and block forms, both with excellent biocompatibility and regeneration potential. Tooth grafts absorbs slowly and is gradually replaced by new bone [45]. A histological study showed that recipient bone and tooth grafts material form a direct combination upon graft healing[46]. Clinical evaluation showed that grafted bone displayed similar bleeding characteristics to normal surrounding bone[47]. The osteoinductive potential of these odontogenic graft materials has been found to be similar to that of Bio-Oss[39].

Dentin contains 70-75% inorganic, 20% organic, and 10% water; and alveolar bone contains 65%, 25%, and 10% inorganic, organic, and water, respectively [36]. Type I collagen accounts for 90% of the organic contents in dentin and plays a supporting and connecting role during bone formation[48]. The remaining 10% of the organic fraction of dentin consists of non-collagenous proteins (NCPs), which may be critical for the tissue healing process andinduce bone formation, such as insulin-like growth factor-II (IGF-II) and transforming growth factor-beta (TGF-β)[48], vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), epidermal growth factor (EGF). These growth factors can induce mesenchymal stem cells to exert their effects [49, 50]. In the relationship between non-collagen organic material and bone repair, BMP is akey factor[51].BMPs extracted from the dentin-derived matrix of human teeth exhibit osteoconductive and osteoinductive potential in human and xenogeneic models via the BMP receptor and its downstream molecules Smad 1/5/8[52].VEGF promotes angiogenesis, EGF stimulates prostaglandins E2, which influence bone formation, and IGF has a direct effect on collagen production by osteoblasts[39].

More importantly, other proteins in dentin, such as osteopontin, osteonectin, osteocalcin, dentin-sialoprotein, alkaline phosphatase, etc, play a role in bone formation and promote/maintain the calcification of bone[53]. In addition, LIM-1 was found in human dentin, which has osteogenic potential[54]. Non-collagenous proteins present in the tooth grafts work as a signal transmitter in new bone formation and bone remodeling. For example, DSPP potentiates crystal formation in the apatite, bone connexin binds minerals and collagen, osteocalcin regulates bone mineralization through activating osteoblasts, osteopontine remodels bone via the induction of osteoblasts and osteoclasts, and alkaline phosphatase has a developmental role in the biomineralization of teeth and bones.

**4. Method of Preparation of Tooth Grafts**

Until now, there have been many methods of preparing tooth grafts. There are differences in these methods due to different types of tooth grafts we need to prepare, the method is slightly different, but the main steps are roughly the same.

It is better to use the sound teeth. If there are caries or restorations, using a high-speed fine finishing stone and saline irrigation. Use a minimally harmful approach to extract the teeth which require removal, in order to protect the buccal and lingual cortical plates. For producing the powder-type tooth grafts, the extracted teeth should be thoroughly cleaned to make sure it without debris, periodontal ligaments or any soft tissue attachment. Some methods will separate the crown portions from the root, while some will use the whole tooth. Then the root portion or the whole tooth is placed in a grinder and is ground for approximately 30s in order to produce a 300–1200 micron dentine powder. Then put the powder in the cleanser for about 10 minutes. This cleaner is a high pH solution of alkaline sodium hydroxide that removes bacteria and all residual organic material. Once the cleaning process is complete, use sterile absorbent gauzes to remove the excess cleanser[55]. Next, soak the dentin particulate material in phosphate buffered saline for 3 minutes. After soaking, pour off excess liquid and blot dry with gauze. The tooth grafts are ready for immediate use and can be easily transferred to the recipient site. [35, 45].

To prepare the block type tooth grafts, the teeth do not need to be ground, and the rest of the process is basically the same. Small holes can be drilled into the block graft to improve the ingrowth of blood vessels into the graft material at the recipient site. After that, it can be put into the extraction socket for socket protection[48, 56].

**5. RCTs of AUTO-BG for ARP**

In order to verify the clinical effects of various tooth grafts, we searched all the literatures of PubMed, Web of Science, Embase and Cochrane in the past 10 years, and selected 8 randomized controlled trials. RCTs randomly divide the research subjects into different groups and implement different interventions to control the difference in effect. It has many advantages, such as avoiding various biases that may occur in the design and implementation of clinical trials, balancing confounding factors, and improving the effectiveness of statistical tests. It is recognized as the gold standard for evaluating interventions.

From these RCT we can conclude that tooth grafts has an excellent effect on ARP. Tooth grafts can significantly promote the effect of ARP in many different aspects, for example, the loss of buccal bone heights, lingual bone heights and horizontal ridge width reduced, the formation of new bone increased, and the pocket depth decreased. Through different indicators, these RCTs demonstrate the feasibility of tooth graft as an excellent material for ARP.

The specific measurement indicators are shown in the table below.

**Table1 RCTs of tooth grafts for ARP**

| STUDY ID | PATIENT | | | | ARMS | | | | PERIOD (MONTHS) | OUTCOMES | STUDY TYPE (STUDY Desing) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | NUMBER | age(year) | gender(M/F) | site | experienment | | control | | | | |
| | | | | | grafts | number | grafts | Number | | | |
| Gyu-Un Jung,2018[57] | 30 | 27-79 | 16/14 | extraction sockets | DDM graft | 10 | Bio-Oss® Collagen (Geistlich, Wolhusen, Switzerland) graft | 10 | 4 | Epithelialization degree，soft tissue volume, bone volume, buccal bone heights, lingual bone heights, horizontal ridge width, grafted area, new bone area, soft tissue area | RCT, three arms |
| | | | | | | | DDM graft combined with | 10 | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | rhBMP-2 (rhBMP-2/DDM) | | | | |
| Chaitanya Pradeep Joshi, 2016[58] | 15 | 28–45, 35.6 ± 5.7 | 9/6 | extraction sockets | autogenous tooth graft (ATG) | 15 | β-TCP alloplast | 15 | 4 | Vertical ridge height lost, Horizontal ridge width lost | RCT, split-mouth |
| | | | | | | | Ungrafted | 15 | | | |
| Mohammed Nadershah,2019[59] | 7 | 24 | | Mandibular Third Molar Extraction Sockets | Autogenous Dentin Graft | 7 | Ungrafted | 7 | 7 days (T1), 42 days (T2), and 92 days | pocket depth (PD), gum recession(GR), Clinical Attachment level (CAL), Measurement of pain, swelling and healing, | RCT,split-mouth |
| Ezgi Yu¨ceer-Cetiner,2021[60] | 9 | 31-62 | 4/5 | extraction sockets | autogenous dentin graft | 20 | empty | 16 | 3 | The average percentages of new bone, connective tissue, graft and blood vessel volumes, BMP-2 expression, RUNX-2 expression, trabecular bone structure, dentin particle, Dens fibrous structures | RCT,three arms |
| | | | | | | | mixture of undemineralized autogenous dentin graft and platelet-rich fibrin(PRF) | 21 | | | |
| Ahmed Elfana, 2021[34] | 20 | test group: 33.5 ± 7.37; control group: 31.2 ± 6.44 | 4/16 | extraction sockets | autogenous demineralized dentin graft (ADDG) | 10 | autogenous whole tooth (AWTG) | 10 | 6 | ridge width reduction, buccal ridge height reduction, lingual ridge height reduction, inflammatory reactions, new bone area, graft remnants | RCT, parallel arms |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | area and soft tissue area | |
| Luis Sánchez-Labrador ， 2020[61] | 15 | 18-25 | 4/11 | alveoli | autogenous dentin | 15 | heal spontaneously (blood coagulate). | 15 | 3 | probing depth (PD） on disto-vestibular (DV), disto-medial (DM)and disto-lingual (DL) surfaces | RCT, two arms |
| | | | | | | | | | 6 | probing depth (PD） on disto-vestibular (DV), disto-medial (DM)and disto-lingual (DL) surfaces, Bone density, Degree of Corticalization , inferior alveolar nerv（IAN）-Crestal Bone Distance | |
| | | | | | | | | | 7 days | Pain, rescue analgesics taken, , inflammation, mouth opening capacity | |
| | | | | | | | | | | Intra- and Post-Operative Complications | |
| Kang-Mi Pang,2017[62] | 24 | ≥20 | 11/13 | graft sites | autogenous tooth graft material (AutoBT) c | 21 | anorganic bovine bone (Bio-Oss, Geistlich, Switzerland) | 12 | 6 | vertical bone gain, implant stability quotient (ISQ), the percentages of newly formed bone w, the average percentages of residual graft material, the | RCT, two arms |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | average percentages of soft tissue components | |
| Peng Li, 2018[63] | 40 | 20-60 | 24/16 | periodontal postextraction sites | Autogenous DDM granules | 22 | Bio-Oss cancellous granules | 21 | 6，18 | The implant stability quotient (ISQ), The marginal bone resorption | RCT，two arms |

**6. Conclusion**

Teeth are unique organs of the human body with similar properties to bones. After continuous attempts by researchers, autologous tooth grafts have been improved in various ways to become better bone graft materials for ARP. Clearly, autologous tooth grafts have many advantages. They are osteoconductive and osteoinductive, have high biocompatibility and are easy to obtain. In addition, they do not require high temperature or other treatment procedures to alter their internal structure. Therefore, they retain a large amount of organic matter to enhance bone regeneration. And inorganic matter can serve as a scaffold for bone repair, and raw materials of calcium and phosphorus for bone surface redeposition. Therefore, autologous dental materials should be classified as a new type of bone substitutes that can be used as bone grafts and are expected to have broad development prospects.

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