Bone graft material derived from extracted tooth: A review literature

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Bone graft material derived from extracted tooth: A review literature

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ABSTRACT

Dental extraction is common procedure as a treatment for severely damaged, non-restorable, malaligned, crowded or disease affected tooth such as periodontitis, adjacent to pathologic lesion requiring excision, pulp necrosis and periapical lesions. Endodontic treatment is applicable but somehow patient's as well as other factors might necessitate the its removal. Many previous studies observed that following tooth extraction alveolar process undergoes structural and dimensional change even often atrophy, repairing the deficiency remains a major challenge.

Several bone grafts are present, used to preserve or augment the defects of alveolar process supporting the tooth, autogenous bone graft is considered gold standard, since they have the property to induce osteogenesis, osteoinduction, osteoconducton and also have rapid healing and least immune rejection.

However, limited availability, rapid resorption of autogenous bone, defects of donor site and morbidity or discomfort from distant extraoral grafts to the patients, in cases of large bone, hinder the use of this kind of bone. Many short comings of several types of available bones lead to demand of novel grafting material over the years.

Tooth and bone exhibit similar biochemical composition hence could be utilized as bone grafting material. Osteogenic capacity of tooth derived (mainly dentin) bone graft material has been shown in many studies with significant possibility of future use. Therefore, this article discusses the similarity between bone and tooth, the use of tooth derived bone graft.

1. Introduction

Tooth extraction is one of the most common procedures in dentistry, with almost all the extracted teeth is regarded as clinical wastes and hence discarded. It is well known that alveolar process is a structure dependent on tooth, its volume and shape is controlled by the form, axis and inclination of the teeth [1]. The evidence provided by many previous studies by Atwood in 1957, Hedegård in 1962 and Tallgren in 1972, following tooth extraction alveolar process undergoes structural and dimensional change thereby causing ridge atrophy [2]. Hence, restoring the normal functions and suitable esthetic of the patient, ridge augmentation with bone grafting materials is required.

In dentistry several bone grafting materials are available that helps in ridge preservation and augmentation of the defects in the alveolar process supporting teeth [3]. These materials used in dentistry [3–5] ranges from 1) autogenous, 2) allogeneic, 3) xenogeneic, and 4) synthetic or alloplastic.

However autogenous bone graft is considered gold standard, since they have the property to induce osteogenesis, osteoinduction, osteoconducton [6]. However, limited availability and rapid resorption of autogenous bone, defects of donor site and morbidity or discomfort from distant extraoral grafts to the patients, in case of large bone needed, hinder the use of this kind of bone [7–9]. Many clinicians would rather prefer the use of allograft, xenograft, or synthetic bone graft materials, due to above mentioned drawbacks and since satisfactory results have been achieved with these types of bone graft materials.
2. Graft characteristics

Nevertheless, non-autogenous source of bone grafting materials also is present with some shortcomings. Allografts are deemed expensive; may pose risks of infection since the donor’s information provided is restricted or sometimes inadequate [5,10]. In addition to similar drawbacks to allografts, xenografts could also be a source of zoonotic disease transmission [5]. The use of xenograft has raised some ethical and religious concerns, since the use of animal derived products should be considered before use with patients consent for various religions and individuals [11,12]. While synthetic or alloplastic materials lacks in property of osteogenesis and osteoinduction [5,10]. The limitations of non-autogenous source of bone, lead to finding a novel source of autogenous bone graft that is processed from human tooth.

The aim of this article is to review some previous published article and summarize the resemblance between bone and tooth with the discussion of the recent use of tooth derived bone graft. The keys of tooth usage as bone graft material is its similarity to the human bone and the utilization of this autogenous source have been attempted by many researchers across the world. Keywords used to search for all related articles were tooth derived bone grafts in dentistry and tooth derived bone grafts used in humans or animals, preparation technique and viable particle sizes for bone grafting.

3. Resemblance between bone and tooth

Tooth and bone exhibit similar biochemical composition, comprising mainly of organic and inorganic constituents. Alveolar bone comprised of 65% inorganic and 35% organic with the percentage comparable to dentine (inorganic 65-70% and organic 30-35%) and cementum (inorganic 45-50% and organic 50-55%) [13,14]. Another remarkable property of dentin and cementum is the presence type I, type III collagen and number of growth factors including bone morphogenetic protein (BMP), insulin-like growth factor-II (IGF-II), and transforming growth factor-β (TGF-β), which play a major role in promoting bone remodeling [15,16]. Majority of proteins found in bone like osteopontin (OPN), osteocalcin (OC), bone sialoprotein (BSP), osteonectin and Cbfal (Runx2) have also been identified in dentin, which could make it an effective substitute for another bone grafting materials available [17–20].

The bone is made up of numerous Harversian’s system, while dentin is complex structure comprising of dentinal tubules [21,22]. When dentin is demineralized, the tubules become broader exposing collagen fibers making it more permeable causing an outward flow of dentinal fluid with it several enzymes and growth factors [23]. X-ray diffraction analysis (XRD) have confirmed the presence of hydroxylapatite (HA), and also small amounts of tricalcium phosphate (TCP), amorphous calcium phosphate (ACP), and octacalcium phosphate (OCP) in different area of the tooth [24–26]. The previous study by Kim et al. conducted to compare the traditional grafting materials and autogenous tooth, they also showed using XRD that the crystalline structures autogenous tooth had similar pattern to autogenous bones [25,26].

The use of scanning electron microscope (SEM) to examine the surface structure of autogenous tooth had also been performed in the previous studies [24,26]. SEM reveals that after preparation of autogenous tooth; it is mostly homogenous with dentinal tubules and dense collagen matrix clearly visible [24]. Energy Dispersive Spectroscopy (EDS) used to study the phase of calcium phosphate apatites in tooth or Ca/P ratio, showing extensive calcium dissolution during the early phase, which is similar to autogenous bones [26]. Owing to this property the study by Priya et al. reported that extensive dissolution of calcium phosphate releasing its ions induces the reprecipitation of the apatite onto the surfaces [27]. Priya et al also observed that the calcium phosphate composite dissolution had rough surface and macroporous regions formation, which allowed the proliferation of both biological cells and bone growth [27]. This desired property of biocompatible materials is the ability tocompletely absorbed in living organisms via biodegradation, since poor biodegradation prohibits natural bone growth for prolonged periods [26,27].

4. Evidence of osteoinductivity from autogenous tooth

The prospect of inducing new bone formation of dentin has been described in many previous studies. The presence of 90% of organic matrix in the form of Collagen type I and other non-collagenous proteins as growth factors like endogenous BMP, phosphoproteins, osteocalcin, proteoglycans, osteonectin and sialoprotein in dentin is well documented [20,28–30]. The first documented evidence of regenerative potential of autogenous demineralized dentin matrix (DDM) was provided by the study of Yeomans and Urist and according to the study of Urist, BMP in DDM and bone possesses the osteoinductive property [31]. The study of Bessho et al, purified BMP was homogenous and could induce bone formation when implanted in muscle pouch of wistar rats within 3 weeks. Even though the BMP derived from dentin was different to BMP from bone, the mode of action of both is identical [28]. In other words, two types of BMP exhibit the same action in the body [28,32,33]. Since BMP belongs to the family of TGF-β and are the only signaling molecules that can solely induce de novo bone formation at orthotopic and heterotopic sites, making them clinically valuable as substitutes to bone graft [28,34].

LIM mineralization protein 1 (LMP-1) was first defined by the study of Boden et al, which regulates differentiation and maturation of osteoblasts and hence bone formation [35]. Later the previous study of Wang et al. identified the expression of LMP-1 mainly in preodontin, odontoblasts and the endothelial cells of blood vessels of teeth with suggestion that LMP-1 plays an important role in differentiation of odontoblast and also mineralization of dentin matrix of human teeth [36]. The osteoinductive property of autogenous demineralized dentin matrix (ADDM) on experimental surgical bone defects in the parietal bone of rabbits using the guided bone regeneration (GBR) technique incorporating human amniotic membrane (HAM) was evaluated in the study of Gomes et al. The experimental bone defect repaired faster, and new bone formation was stimulated in groups that used ADDM slices. The ADDM slices were entirely integrated into the newly formed bone tissue, having been resorbed during the bone remodeling process [37].

DDM granules derived from human impacted tooth by the study of Murata et al., independently induced bone and cartilage formation in subcutaneous tissues of nude mice, showing property of bone induction [38]. The previous study by Kim Kyung-Wook in 2014 showed when DDM was grafted into the muscle of nude mouse (subcutaneously) and evaluated for hard tissue induction histo-morphologically, that induced cartilage and bone independently in soft tissues Hence human DDM could be good alternative to autogenous bone graft materials [39].

5. Previous study reporting osteoconductivity of autogenous tooth

Besides the property of osteoinduction, BMP present in the ADDM also could act as matrix or framework for new and native bone to perpetuate and regenerate, thereby showing osteoconductivity property [40]. Previous studies published by Carvalho et al, Catanzaro Guimaraes, Gomes et al., have investigated the osteopromotive property of ADDM. The protein substrate that exists in ADDM was found to be free from degradation and helped in socket repair [37,41,42]. Furthermore, Gomes et al. also observed an increase in the osteogenic cells after implantation of ADDM in wounds [37]. Similarly, the study of Carvalho et al 5 mm defect at buccal bone of mandibular molar area in 36 rabbits and dividing them into four groups as control group (untreated defect), polytetrafluoroethylene (PTFE) barrier group, PTFE + ADDM group and experimental group (ADDM). The experimental group had normal bone formation with less inflammation postoperatively and ADDM was
completely incorporated in the newly formed bone tissue and was re-
sorbed during bone remodeling [42]. The previous study of Nampo et al suggested that material prepared from extracted teeth may have the potential as bone grafting material for jawbone formation since it is more predictable and show less resorption [17].

Several proteins are common to bone, dentin and cementum such as OPN and DSP, BSP, osteocalcin, DMP-1, osteonectin and Runx2, and these are reportedly involved in bone formation and resorption [20,28,33]. It is commonly acknowledged that these NCPs play key biological roles in the formation of bone and dentin [43]. Apart from these, the previous article of de Oliveira et al. immunostaining of BMP-2 and BMP-4 in osteoblasts during the upper second molar sockets wound healing of Holtzmann rats when filled with human DDM showed DDM acting as a scaffold for osteoblast differentiation and actively producing new bone. The effects of human DDM in the healing process of tooth sockets were, in some part, owed to matrix degradation, resulting from controlled delivery of BMP-2 and BMP-4 since the immuno-reactivity of both proteins were increased in extraction sockets at 10 days when almost entire DDM was degraded [44].

The animal model from cranium of mini pig and sinus of porcine showed excellent osteo-conductive healing capacity of human DDM when placed in bony defects, which could be attributed to minerals present in DDM, such as low-crystallinity HA and TCP [45,46]. A study conducted in New Zealand rabbit calvarium with 3 circular defects, the CT-scan after one and six weeks of defects filled the dentin had a higher mineral (density) content showing a higher density than the autologous bone and was incorporated in the bone without inflammation and gradually resorbed and replaced by new bone [47]. Similar result was seen in bony defect (5 mm) in femur of New Zealand White rabbits, when autogenous dentin treated with liquid nitrogen at −196 °C for 20 min was used [48].

6. Suitable particle size of autogenous tooth preparation as grafting

Previously mentioned article showed for extracted tooth to be turned into efficient bone grafting materials was a tedious process and required special center or time consuming demineralization technique [18,49,50]. However, since more and more dentists and researchers around the world have seen the tooth, once considered as clinical wastes, as inexpensive autogenous alternative to several commercially available grafting materials the cumbersome preparation technique is being replaced by much quicker, more chairside and less inexpensive ways. A remarkable study of Koga et al. showed that partially demineralized dentin matrix (PDDM) induced prominent bone regeneration [51]. Since previous studied showed that demineralization of tooth exposed the tubule and as they become wider it serves as a channel for releasing essential proteins, which may promote growth and differ-
entiation of osteoblasts. However process of demineralization is time consuming and could destroy some of the growth factors [15]. Thereby, PDDM prepared by the previous study of Koga et al. took just 40 min to prepare and also superior bone inductivity compared to completely demineralized dentin matrix or non-demineralized dentin [51].

Both animal model and clinical studies of Koga et al. and Minamizato et al., showed that PDDM grafting could successfully in-
duced alveolar bone regeneration in implant dentistry without any complications. Histological examination also showed APDDM was surrounded by newly formed bone and osteoelastic activity (Howship’s lacunae) was prominent suggesting remodeling and biocompatibility of grafting material [51,52]. The additional previous study of Bindermann et al. suggested that autogenous mineralized dentin particulate, which takes 20 min to prepared, was firmly integrated with newly formed bone, creating a solid site for anchorage of dental implants [49,53]. The APDDM or mineralized dentin particulates prepared instantly after tooth extraction for bone augmentation, taking benefit of the relatively little preparation time with partial or no demineralization, has possibility of becoming one of the options for bone substitute in implant dentistry [51,52].

The particles sizes of most commercially available bone grafting ranges from 300 μm to 1500 μm. Several previous studies have focused on the influence of particle size of graft materials on bone regeneration [49,53]. However, there is no consensus on optimal particle size of graft materials for bone regeneration. Some graft material such as xenografts and FDBA resulted in superior bone formation, and more absorbability with smaller particles in certain sites in oral cavity. On the other hand larger sized particles could be successfully used at other areas in the oral cavity [54–56]. Nevertheless, this article is more concern about the suitable particle size for tooth derived bone grafts and hence a notable previous study of Minamizato et al. has shown that particle size ranging between 400 μm to 800 μm showed superior new bone formation in 16 patients that underwent bone augmentation prior to implant placement [52]. The previous article of Koga et al. showed particle size of 200 μm to 1000 μm of the PDDM in rat calvarial bone defect all had deflected spaces filled with newly formed bone especially at 8 weeks after surgery using images of μCT [51]. From this time, the authors suggested mixture of particles with variable sizes may have better results [51,52]. The study of Bindermann et al. using Smart Dentin Grinder by KometaBio, USA found that mineralized dentin particulates ranging between 300–1200 μm successfully used for socket preservation, bone augmentation in sinuses or filling bone defects. Similarly many authors also suggested fine particulate < 300 μm is considered as a non-efficient particulate size for bone grafting [49,53].

7. Autogenous tooth in clinical applications

Several published previous clinical studies have shown the potential applications of autogenous tooth as a bone grafting material. The process of preparation of this autogenous tooth varies from center to center, depending on its clinical use which could be either in block or particulate forms [50]. Since it is autogenous the risk of immune re-
jection and nonpathogenic. As discuss earlier the use of tooth derived bone graft in animal model have been shown to be effective with excellent biocompatibility, hence the clinical applications of tooth derived bone graft are illustrated in Table 1.

8. Discussion

The use of extracted tooth, which is considered as biomedical waste and hence disposed, unlocks the simple and readily available bone substitution material. The different and various preparation methods of extracted tooth provide their potential use as bone substitutes. Various previous published studies had shown the possibility of tooth derived bone graft materials. The demineralized dentin matrix is exceedingly biocompatible with the property of both osteoinductive and osteoconductive which have been highlighted in previous studies conducted in vitro as well as in animal models [31,37,38,41,71]. The resemblances between tooth and bone makes it safe and ef-
fective grafting materials. Another remarkable property of dentin and cementum is the presence type I, type III collagen and of number of growth factors including BMP, IGF-II, and TGF-β, which play a major role in promoting bone remodeling [13–16]. Majority of proteins found in bone like OPN, osteocalcin, BSP, osteonectin, type I collagen and Cbfalpha (Runx2) have also been identified in dentin, which could make it an effective substitute for another bone grafting materials available, since these reportedly involved in bone formation and resorption [17–20].

The first documented evidence of regenerative potential of auto-
genous demineralized dentin matrix (DDM) was provided the previous study of Yeomans and Urist in animal model and according to Urist, BMP in DDM and bone possesses the osteoinductive property which led to more and more advancement and development that would define its use in human [31]. The first clinical case in human was sinus lifting procedure using autogenous DDM in the 2003 reported at IADR.

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<table>
<thead>
<tr>
<th>Author &amp; Year of Publication</th>
<th>Graft</th>
<th>Number of Patients</th>
<th>Anatomical Site</th>
<th>Result</th>
<th>Reported Follow Up Period</th>
<th>Complication</th>
<th>Level of Evidence</th>
</tr>
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<tbody>
<tr>
<td>Murata M., 2003 [57]</td>
<td>Crushed autogenous DDM</td>
<td>1</td>
<td>Sinus lifting (24-26 area)</td>
<td>- 5 months after sinus lifting, 3 implants could be placed at the DDM grafted site</td>
<td>&gt; 5 months</td>
<td>Not Reported</td>
<td>First clinical case report</td>
</tr>
<tr>
<td>Gomes MF. et al., 2006 [58]</td>
<td>Autogenous demineralized dentin matrix (ADDM)</td>
<td>14 patients (27 dental sockets)</td>
<td>Mandibular third molar dental sockets</td>
<td>The radiographic analysis of ADDM + PTFE group showed greater homogenous bone radiopacity than the Control group and PTFE group, during all the observation times.</td>
<td>90 days</td>
<td>Not Reported</td>
<td>Clinical study</td>
</tr>
<tr>
<td>Kim YK. et al., 2010 [23]</td>
<td>Autogenous tooth (AutoBT) particle size (0.5-1 or 1-2 mm) in diameterb</td>
<td>6</td>
<td>Maxilla: 5 Mandible: 1</td>
<td>Histologic exam of AutoBT grafted area revealed gradual resorption &amp; replacement with new bone.</td>
<td>3-6 months</td>
<td>Not Reported</td>
<td>Case Study</td>
</tr>
<tr>
<td>Kim YK. et al., 2011 [59]</td>
<td>Autogenous tooth bone graft in powder or block forms</td>
<td>2</td>
<td>Socket preservation in mandible &amp; maxilla with simultaneous sinus lifting</td>
<td>Good healing</td>
<td>3-3.5 months</td>
<td>Not Reported</td>
<td>Case Report</td>
</tr>
</tbody>
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Table 1 (continued)

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<tbody>
<tr>
<td><strong>Result</strong></td>
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<tr>
<td>Anterior maxilla</td>
<td>Bone grafting at defect of pyogenic granuloma with DDM, post-operative radiography indicated excellent bone healing by remodeling with dentin matrix after 1 year</td>
<td>48 extraction sites filled with particulate dentin after 4 months the particulate and newly formed bone restored distal root of tooth 47</td>
<td>Normal postop healing with prosthetic restoration</td>
<td>All cases showed increased and complete cortico-cancellous bone formation at the final follow-up compared with follow-up after the second surgery.</td>
</tr>
<tr>
<td>Mandibular third molar</td>
<td>Post-operative radiographs showed the extracted socket healed fully with new bone</td>
<td>No sign of bone loss around dental implants placed after bone grafting with autogenous dentin particulate</td>
<td>The average peri-implant probing pocket depth after 5 years ranged between 1.86 mm (ML) and 2.07 mm (DB)</td>
<td>Decrease in buccal height and alveolar ridge width ranged from -0.4 to -3.3 mm and from -0.4 to -4.2 mm, respectively</td>
</tr>
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<td>Sinus opening filled with particulate dentin healed in 2 months with 3 implants inserted after 3 months and immediate solid anchorage was achieved</td>
<td>The average peri-implant bone resorption during the 1st year was 0.63 mm, with lowest = 0 mm and maximum = 2.9 mm</td>
<td>The change in bone area ranged from -8.1 to -36.2%</td>
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<td>Immuno-histochemical showed new vessel formation in the augmented area.</td>
<td>Histological evaluation showed osteoconductive and osteogenesis with encapsulation of tooth enamel and dentin and partial resorption of the tooth graft</td>
<td></td>
</tr>
<tr>
<td><strong>Complication</strong></td>
<td>Not Reported</td>
<td>Not Reported</td>
<td>Not Reported</td>
<td>Imm of buccal marginal bone loss in 1 case after 6 years 7 months</td>
</tr>
<tr>
<td><strong>Level of evidence</strong></td>
<td>Case Report</td>
<td>Case Series</td>
<td>Case Report</td>
<td>Prospective longitudinal case series</td>
</tr>
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</table>

| **Number of patients**       | 15 patients per 3 extraction sites | 15 patients per 4 extraction sites | 18 patients            | 24 patients with 33 graft sites |
| Out of 3 sites,             | 1: ATG                         | Out of 4 sites,                   |                        |                          |
| 2: β-TCP                        | 2: dentin allograft (DA)       | 1: whole tooth allograft (WTA)    | AutoBT: 21 sites of 15 patients | ApoB: 12 sites of 9 patients |
| 3: freeze-dried bone allograft (FDBA) | 3: freeze-dried bone allograft (FDBA) | AutoBT: 21 sites of 15 patients | Bio-Oss®: 12 sites of 9 patients |                          |

| **Anatomical site**          | Total 45 sites (15 of each grafting material) | Total 60 sites (15 of each grafting material) | Maxilla: 26 (WTA: 9, DA: 7, and FDBA: 10) | Maxilla: 21 |
| Maxilla: 10                  | Mandible: 10                    | Maxilla: 10                          |                                    |            |
| Mandible: 12                 | Mandible: 10                    | Mandible: 12                         |                                    |            |

| **Result**                   |                                                                 |                                                                 |                                                                  |                                                                 |
| Statistic difference in width and height of alveolar crest compared within all the 3 groups | ARTB is well incorporated and remodeled into cortico-cancellous bone with dental implant | Compared to other sites, WTA and DA consistently showed superior results showing least reduction in alveolar crest height and width which was statistically significant (P < 0.05) | Like autogenous DDM, no remarkable early and late complications were observed with the use of alloplastic DDM | Both groups showed favorable wound healing, similar implant stability and histologically confirmed new bone formation |
| Among 3 sites, ATG-grafted sites showed superior results (minimal reduction in alveolar crest height and width) | The shape and volume were maintained with little marginal bone loss | Histological analysis also confirmed more new bone formation at WTA and DA sites | The VD of alveolar bone increased by 5.38 ± 2.65 mm in AutoBT group and 6.56 ± 3.54 mm in Bio-Oss® group at 6 months | The VD of alveolar bone increased by 5.38 ± 2.65 mm in AutoBT group and 6.56 ± 3.54 mm in Bio-Oss® group at 6 months |
| Histological analysis also showed the same trend with more new bone formation at ATG-grafted sites | ARTB is well incorporated and remodeled into cortico-cancellous bone with dental implant | Compared to other sites, WTA and DA consistently showed superior results showing least reduction in alveolar crest height and width which was statistically significant (P < 0.05) | Like autogenous DDM, no remarkable early and late complications were observed with the use of alloplastic DDM | Both groups showed favorable wound healing, similar implant stability and histologically confirmed new bone formation |

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Table 1 continued

<table>
<thead>
<tr>
<th>Author &amp; year</th>
<th>Study type</th>
<th>Evidence</th>
<th>Description of study</th>
<th>Implant stability quotient (ISQ)</th>
<th>Follow-up period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joshi et al. 2016</td>
<td>Clinical Pilot study</td>
<td>Prospective, randomized</td>
<td>Bone biopsy samples in 4 patients showed new bone surrounding APDDM.</td>
<td>72.80 ± 10.81</td>
<td>12 months</td>
</tr>
<tr>
<td>Kim et al. 2017</td>
<td>Case Series</td>
<td>Prospective, randomized controlled pilot clinical trial</td>
<td>Bone samples placed in AutoBT-grafted sites measured 70.0 ± 2.86.</td>
<td>Not Reported</td>
<td>6 months</td>
</tr>
<tr>
<td>Pang et al. 2017</td>
<td>Clinical Pilot study</td>
<td>Prospective, randomized</td>
<td>Bone samples placed in Bio-Oss grafted sites measured 70.0 ± 12.86.</td>
<td>Not Reported</td>
<td>4 months</td>
</tr>
<tr>
<td>Minamizato et al. 2018</td>
<td>Clinical Pilot study</td>
<td>Prospective, randomized controlled pilot clinical trial</td>
<td>Bone samples placed in Autogenous bone grafted sites measured 70.0 ± 12.86.</td>
<td>Not Reported</td>
<td>24 months</td>
</tr>
</tbody>
</table>

In conclusion with consequently, several previous studies are initiated to find and alternative source such as allogeneic teeth however the risks of transmission disease could not be fully disregarded. Currently off-the-shelf, like other commercially available bone grafting materials are still far-fetched. On the other hand, with future technology and advancement the use of extracted tooth as an effective bone grafting material could become more readily accessible and successful.

References

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