Case Report

Tooth Transformer®: A New Method to Prepare Autologous Tooth Grafts – Histologic and Histomorphometric Analyses of 11 Consecutive Clinical Cases

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Abstract

Introduction: Human dentin matrix could be successfully used for bone grafting procedures. It was well accepted that dentin grafts can induce osteoblast proliferation. An innovative preparation method, using the dedicated automated device Tooth Transformer®, which can transform autologous teeth in suitable grafting material, has been recently introduced. The aim of the present article is to analyze the histologic outcomes in 11 consecutive human cases, in which autologous tooth graft materials, starting from the whole tooth of the patient, were used for bone regeneration. **Results:** The bone defects were completely filled by newly formed tissue after 4 months of healing. Histologic analysis revealed no inflammatory or infective reactions against the tooth graft. Tooth granules were surrounded by newly formed bone. Some tooth granules were incorporated in the bony trabeculae, and they appeared partially resorbed. This fact testified that tooth grafts underwent remodeling processes just like the native bone. **Discussion:** Results from the present histologic case series analysis revealed that tooth graft appeared well integrated in the regenerative tissue without any inflammatory or infective reaction. The tooth of the patient may be used as an autologous regenerative material, avoiding any foreign graft material.

Keywords: Bone regeneration, dentin graft, osteoinduction, tooth

Introduction

The tooth grafting procedure has been introduced by Yeomans and Urist more than 50 years ago, when they discovered the osteoinduction potential of demineralized dentin matrix.[1,2] More recently, Bessho *et al*. demonstrated the presence of bone morphogenetic proteins (BMPs) in human dentin matrix. In particular, bone formation and osteoblasts' presence were observed in rat muscle after demineralized human dentin matrix graft.[3]

It was clear that both bone and dentin matrices contained fundamental growth factors (GFs) for bone regeneration. It represents an efficient reserve of BMPs, bioactive GFs, such as transforming growth factor-B (TGF-B), which are well known to be involved in the bone-repairing processes.[4] Some authors have theorized that the demineralization process allows better bone augmentation than nondemineralized dentin.[5]

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Moreover, the chemical composition of bone and dentin was almost the same with the presence of an inorganic portion made of hydroxyapatite and an organic one, mainly composed by collagen Type 1 and other secondary proteins.

Heterologous or alloplastic grafting materials, on the other hand, have been used for bone augmentation procedures for more than 35 years, but they work as mechanical scaffold for host cells and do not offer any osteoinduction stimulus.[6-9] The efficacy and safety of autogenous partially demineralized dentin matrix prepared onsite, for clinical application in bone regeneration procedures related to implant dentistry, including

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socket preservation, alveolar ridge augmentation, and maxillary sinus floor augmentation, were recently demonstrated in some human studies.[10,11]

Recently, an innovative medical device (Tooth Transformer® SRL, Via Washington, 59 – Milan, Italy) to obtain suitable tooth graft materials starting from the whole tooth of the patient was introduced to the market [Figures 1 and 2]. This machine ensures completely automated disinfection, grinding, and demineralizing processes without any possible mistake induced by human manipulation of the process.

This new device represents an advanced system in the area of tissue engineering because it can process and transform an extracted tooth into clinically useful bone graft material in a short period of time. The graft material, produced starting from the whole tooth, showed high wettability that allowed for easy handling and positioning at the host site. A previous case series described the successful clinical outcomes of bone regeneration after autologous tooth grafting using this new device and demonstrated the complete filling of bony defects by hard tissue without any complications.[12]

The present article aims to describe the histologic and histomorphometric analyses of regenerated tissue after innovative autologous tooth grafting procedures in 11 consecutive cases of socket preservation.

Materials and Methods

The whole extracted tooth was first cleaned of any residual calculus using piezoelectric instruments. The root surface was polished using diamond burs with abundant irrigation to remove any residual periodontal ligament present. Any filling materials (gutta-percha, composite, etc.) were carefully removed from the tooth. The tooth was then cut into small pieces, and they were inserted in the mill area of the device.

A small box containing liquids was inserted into the device in its correct position (indicated by arrows). According to the manufacturer, these solutions guarantee maximum release of BMP-2 and collagen as well as a decontamination of the root.[13] When all the components were inserted, the cover of the machine was closed, and the device was started using the general button. The demineralized dentin graft was ready in 25 min to be placed into the patient's mouth.

The present case series included 11 patients (6 males and 5 females), ranged in age between 22 and 64 years. All patients were in good health condition and were nonsmokers. In all cases, the patient required guided bone regeneration procedures.

In all cases, the graft was covered by a resorbable porcine pericardium membrane (BEGO Implant Systems GmbH and Co. KG, Wilhelm-Herbst-Straße, Bremen, Germany). An immediate postoperative radiological check was performed. Each patient underwent clinical examination after 10 and 30 days in order to evaluate the healing process.

After 4 months of healing, all patients underwent a surgical re-entry session for dental implant placement. The osteotomy

Figure 1: The Tooth Transformer®

Figure 2: The Tooth Transformer open

site was prepared using a trephine drill of 3-mm inner diameter that allowed retrieval of a bone sample for each osteotomy. Specimen retrieval would allow histological analysis of the grafted site to determine the conversion of the tooth graft to the host bone.

The specimens were immediately fixed in 10% neutral buffered formalin and processed for histologic analysis. After dehydration, the specimens were infiltrated with a methyl-methacrylate resin from a starting solution of 50% ethanol/resin and subsequently 100% resin, with each step lasting 24 h. After polymerization, the blocks were sectioned and then ground down to about 40 μ. Toluidine -blue staining was used to analyze the different ages and remodeling pattern of the bone. The histomorphometric analysis was performed by digitizing the images from the microscope via a JVC TK-C1380 Color Video Camera (JVC Victor Company, Yokohama, Japan) and a frame grabber. The images were acquired with a 10x objective over the entire specimen section surface. Subsequently, the digitized images were analyzed by image analysis software IAS 2000 (Delta Sistemi, Roma, Italy). For each section, the two most central sections were analyzed.

Results

The bone defects were completely filled by newly formed tissue after 4 months of healing. In all cases, a complete filling by hard tissue was evident by clinical and radiographic observation. The healing of soft tissues after grafting procedures was free of complications. No active or chronic infective processes were observed. Histomorphometric data of bone defects after bone regeneration are summarized in Table 1. The clinical outcomes were presented in a previous case series study.[12]

The histomorphometric analysis showed a mean bone volume percentage (BV%) of 43.97 ± 7.38 and a residual graft percentage (RG%) of 24.51 ± 15.95.

The newly formed tissue, observed during the surgical re-entry (after 4 months of healing), showed a compactness similar to that of the medium-density bone. No graft particles in submucous connective tissues were observed during flap elevation. The regenerated tissue aspect was homogeneous, and tooth particles or grains were not distinguishable. A D2–D3 tactile bone density during harvesting drilling procedures was noted at osteotomy preparation.

Table 1: Radiological and histomorphometric data of each case

Patient no.	Description	Tooth Used	Initial Radiological Defect (CBCT data)	Defect Radiological Filling (CBCT after 4 months)	%Bone Volume	% Residual Graft
1	Socket preservation	1.6	Mesio - Distal: 9.69 mm Bucco - Lingual: 7.04 mm Height: 5.40 mm	Mesio - Distal: 9.08 mm Bucco - Lingual: 9.80 Height: 4.20 mm	33.69	26.04
2	Socket preservation.	3.5	Mesio -Distal: 8.94 mm Height: 7.23 mm	Mesio - Distal: 8.94 mm Height: 7.20 mm	42.48	40.37
3	Vertical guided bone regeneration	1.8	Mesio - Distal: 11.55 mm Height: 10.05 mm	Mesio - Distal: 11.55 mm Height: 10 mm	34.41	33.15
4	Socket preservation.	2.1	Mesio - Distal: 11.30 mm Bucco - Lingual: 10.37 mm Height: 10.53 mm	Mesio - Distal: 11.30 mm Bucco - Lingual: 12.22 mm Height: 10.56 mm	58.24	56.01
5	Socket preservation	1.1	Mesio -Distal: 13.18 mm Bucco - Lingual: 14.47 mm Height: 7.79 mm	Mesio -Distal: 13.18 mm Bucco -Lingual: 14.50 Height: 7.80 mm	39.49	16.65
6	Socket preservation	2.6	Mesio -Distal: 11.30 mm Bucco - Lingual: 9.27 mm Height: 8.23 mm	Mesio -Distal: 11.30 mm Bucco - Lingual: 8.89 mm Height: 8 mm	39.66	1.24
7	Socket preservation	3.4 and 3.5	Bucco - Lingual: 7 mm Height: 8 mm	Bucco - Lingual: 10.03 mm Height: 8.2 mm	46.11	25.28
8	Socket preservation.	2.7	Mesio -Distal: 8.52 mm Bucco - Lingual: 10.72 mm Height: 11.7 mm	Mesio -Distal: 9 mm Bucco - Lingual: 10.66 mm Height: 10.95 mm	48.86	24.43
9	Socket preservation.	3.1	Mesio -Distal: 12.04 mm Bucco - Lingual: 7 mm Height: 10.91 mm	Mesio -Distal: 12 mm Bucco - Lingual: 6 mm Height: 10.34 mm	51.24	6.46
10	Socket preservation.	Deciduous teeth	Mesio -Distal: 8.57 mm Bucco - Lingual: 4.72 mm Height: 10.10 mm	Mesio -Distal: 8.58 mm Bucco - Lingual: 4.80 mm Height: 10.50 mm	48.04	31.35
11	Socket preservation.	2.6	Mesio -Distal: 13.18 mm Bucco - Lingual: 14.47 mm Height: 8 mm	Mesio -Distal: 13 mm Bucco - Lingual: 14.50 mm Height: 8 mm	41.52	8.73
	Mean Value				43.97±7.38	24.51±15.95

CBCT: Cone-beam computed tomography

The histologic analysis revealed no inflammatory or infective reactions against the tooth graft. The tooth granules were surrounded by newly formed bone [Figures 2-4]. It is possible to note the presence of some enamel granules completely surrounded by new bone [Figure 5]. Woven bone and numerous round-shaped osteocytes were also visible. In the medullary bone area, large vascular canals were present [Figure 6]. Some tooth granules were incorporated in the bone trabeculae, which appeared partially resorbed [Figure 7]. This fact testified that tooth graft underwent remodeling processes just like the native bone. In some cases, dentin granules appeared completely incorporated in the woven bone and surrounded by osteoid tissue layer in development. Some more coronal granules were surrounded by fibrous tissue [Figure 8].

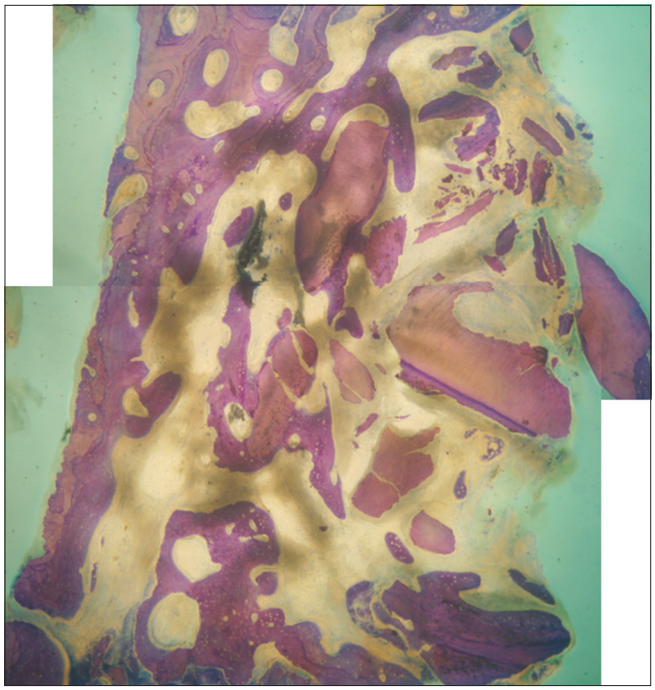

Figure 3: Overview of the biopsy at low magnification: Tooth granules and newly formed bone were visible (toluidine blue, ×8)

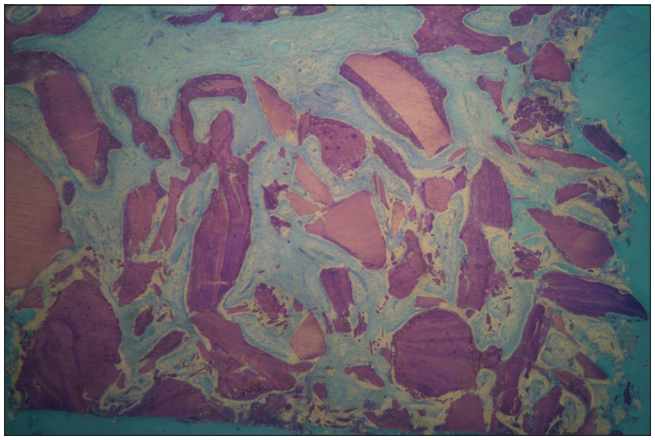

Figure 5: Newly formed bone trabeculae and graft particles were observed (toluidine blue, ×25)

Discussion

The use of autogenous bone has been considered the gold standard in bone regeneration procedures for many years. However, several studies have highlighted some problems related to the use of autologous bone such as donor-site morbidity, severe pain, or patient hospitalization.[14] In addition, the long-term stability of autologous bone graft has been investigated for many years, and some authors report a high reabsorption rate.[15] To overcome the bone resorption, other authors suggested a mix of autogenous bone with Xenograft particles.[16]

An ideal grafting material should be stable and, at the same time, should promote bone-forming cell proliferation and bone apposition.[17] Xenograft and alloplastic bone substitutes have been used for many years with success in oral implantology, and many authors described that these materials represent an efficient mechanical support for cell migration, but they are not able to induce the osteogenesis process.[18-21]

In addition, the chemical or physical processes to eliminate any organic residuals, in which all xenograft materials are subjected,

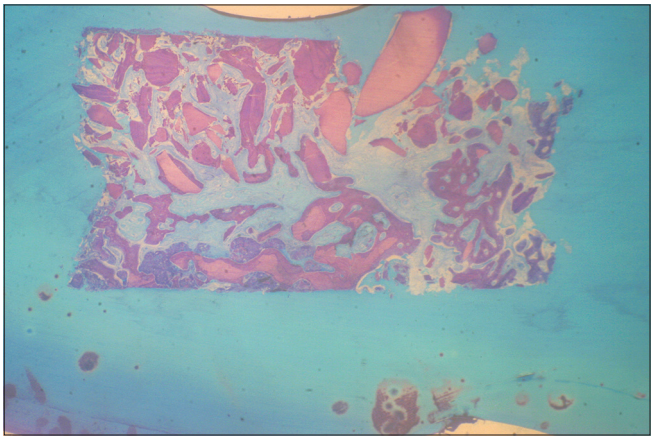

Figure 4: Overview of the biopsy at low magnification: Tooth granules were surrounded by newly formed bone (toluidine blue, ×8)

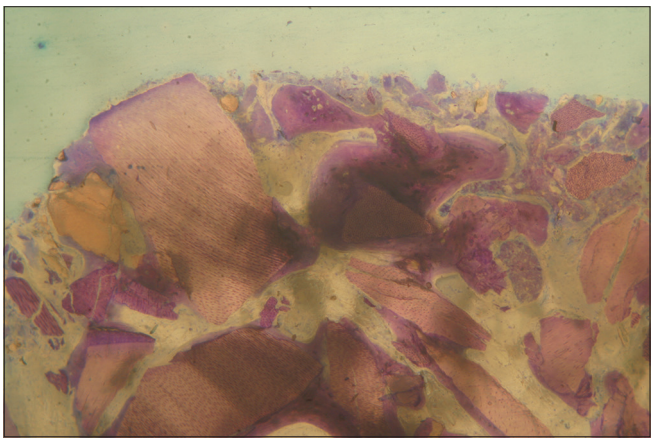

Figure 6: Tooth graft grains appeared well integrated in the new bone. The dentin grain showed numerous characteristic dots that corresponded to dentinal tubules. An enamel granule (in light yellow) is also visible surrounded by the new bone (toluidine blue, ×50)

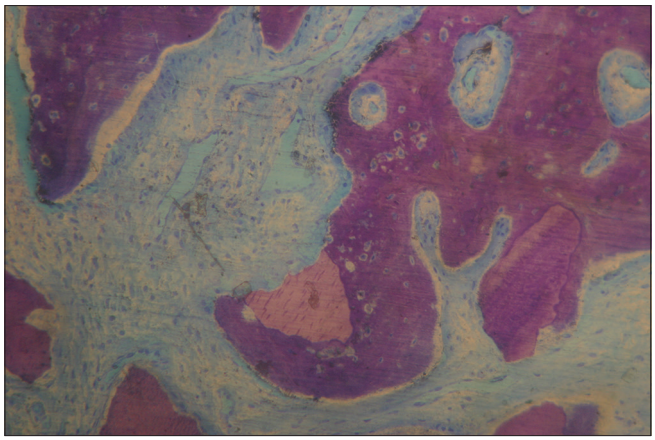

Figure 7: Woven bone and numerous round-shaped osteocytes were present. Osteoid bands were also visible. Large vascular channels were observed in the medullary portion. Some dentin granules were incorporated in the bone trabeculae, which appeared partially resorbed. The presence of this process demonstrated that the dentin graft underwent remodeling processes just like the native bone. (toluidine blue, ×100)

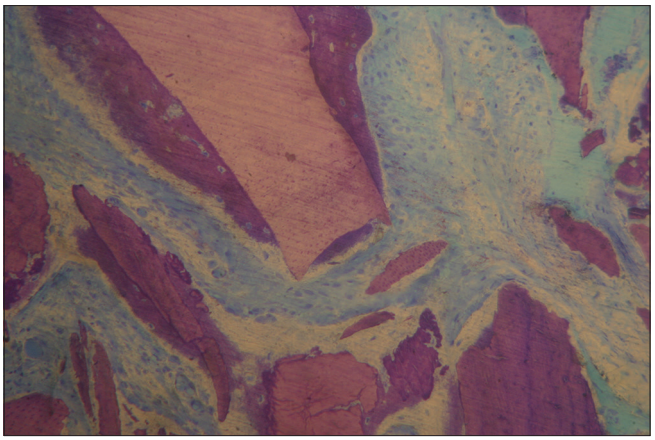

Figure 8: Dentin granule (200 × 500 μm) completely incorporated in the woven bone and surrounded by osteoid tissue layer (toluidine blue, ×100)

destroyed all proteins that are fundamental in bone regeneration promotion. Furthermore, we cannot completely exclude the possibility of human–animal cross infection by prions.

The results of the present study demonstrated that the values of BV% after bone regeneration procedures are superimposable to those that the literature attributes to other grafting materials in humans.[22,23] In addition, the RG% of 24.51 ± 15.95 was lower than that reported for commonly used xenograft materials;[24] this datum testified that the tooth graft underwent physiologic bone remodeling phenomena and, at the same time, supported bone regeneration.

A previously published literature review, analyzing 108 studies about autogenous teeth used as graft material, reported an implant survival rate of 97.7% but found that dehiscence of the wound was a frequent complication.[25] Another animal study showed an accelerated bone healing in defects treated by autogenous demineralized dentin matrix and polytetrafluoroethylene (PTFE) membrane with respect to PTFE membrane alone.[26]

Many authors demonstrated that demineralized dentin can maintain the intactness of the autogenous GFs (such as osteopontin, dentin sialoprotein, and BMP) and, for this reason, could induce bone formation (osteoinduction).[27-29] It was also demonstrated that these GFs, such as insulin-like GF, bone morphogenetic protein-2 (BMP-2), and TGF-β, are preserved over time allowing to use for bone regeneration autologous tooth preserved for years (i.e., previously extracted wisdom tooth or deciduous teeth).[30]

The phenomenon of dentoalveolar ankylosis, often seen after tooth replantation, is an excellent explanation of the osteoinductive properties of demineralized dentin matrix which acts as a slow-releasing carrier of bone morphogenic proteins (BMP).

While osteoconduction means that bone grows on a surface, osteoinduction could be explained as the process by which osteogenesis is induced, and it is a phenomenon regularly seen in any type of bone-healing process. It implies the recruitment of immature cells and the stimulation of these cells to develop into preosteoblasts.[31]

The autologous tooth graft, described by the present article, may induce osteoblast proliferation and bone induction and at the same time eliminating any risk of cross infection (such as prion infections).

An innovative preparation technique, to transform autologous teeth into suitable grafting material, allows for preserving the organic autologous components, removing any contaminants (to avoid inflammatory or infective reactions), and preparing the inorganic part to be easily colonized by osteoblasts. The demineralization process is required for freeing the various GFs and proteins because the release of GFs is sometimes blocked by the presence of hydroxyapatite crystals.[32] Through the reduction of the mineral phase, demineralization supports the release of such GFs from the tooth matrix.[33]

An *in-vitro* study, testing the graft material obtained by this new device starting from whole tooth, demonstrated that the demineralization process leads to an increase of BMP-2 bioavailability.[34] The same authors, in a subsequent study, showed that the demineralization treatment made by Tooth Transformer in deciduous teeth led to a dramatic decrease in relative Ca and P content while preserving native protein conformation and activity.[13] Furthermore, the demineralization process led to a great rise in the bioavailability of BMP-2 that was also proved to be very effective in enhancing alkaline phosphatase activity, thus in the osteodifferentiation of SAOS-2 cells *in vitro*.

These studies demonstrated the complete absence of bacteria in the tooth graft treated by Tooth Transformer method and that the BMP-2 content, found in all demineralized teeth even in deciduous teeth extracted many years before, is very effective in inducing cell osteodifferentiation.

Conclusions

The histological analysis of the present case series demonstrated bone regeneration and no inflammatory reactions around dentin granules. The graft, in all cases analyzed, was subjected to the physiological bone remodeling phenomena, demonstrating an excellent integration with the host tissues.

Future controlled and randomized studies with long-term follow-up period are needed in order to better evaluate the potential of demineralized dentin autografts in bone regeneration field.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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