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HISTOLOGICAL EVALUATIONS OF A SERIES OF SOCKET PRESERVATION PROCEDURES USING TOOTH AS GRAFT MATERIAL

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ABSTRACT – *Objective:* In this multicenter study, we assessed the effectiveness of a novel autologous bone substitute obtained directly from the processing of extracted teeth. A total of 34 consecutive tooth grafting procedures were performed.

Materials and Methods: Immediately following atraumatic extraction for restorative or endodontic purposes, the bone defect was filled and covered with an Osseoguard© membrane, using autologous material derived from the extracted tooth. Zimvie T3 PRO© implants with platform switching were placed in 34 patients.

Results: After a 5-month healing period, the defects were significantly filled with newly formed hard tissue. Bone biopsies were subsequently taken during dental implant placement to assess histological outcomes. The tissue demonstrated a density comparable to medium-density bone, with a homogeneous and uniform appearance, showing no visible signs of inflammation. The post-operative healing phase was uneventful, with no infectious complications or evidence of graft particles within the regenerated bone structure. Histomorphometric analyses revealed the following results: average bone volume (BV) of 52.35% (±17.25). The average residual graft (RG) rate was 10.79% (±12.26), while new bone (NB) accounted for 41.56% (±22.02) of the samples.

Conclusions: Bone grafts resorb very quickly, while xenograft materials maintain space over time, facilitating bone regeneration. Unfortunately, xenograft materials are not osteoinductive, meaning they do not stimulate bone growth; rather, they provide a supportive structure for new bone formation. The findings of the current study revealed a significant increase in three-dimensional bone volume and a substantial percentage of vital bone formation across all socket preservation sites. The possibility of transforming the extracted tooth of the patient chairside into suitable osteoinductive grafting material offers interesting perspectives in the field of bone regeneration for dental implant purposes. The study demonstrated successful bone healing in guided regenerative surgery procedures utilizing autologous tooth grafts. However, further studies with an extended follow-up period are necessary to fully evaluate the potential of demineralized dentin autografts.

KEYWORDS: Autogenous dentin graft, Bone regeneration, Dental biomaterials, Granules, Socket preservation, Tooth graft.

Note

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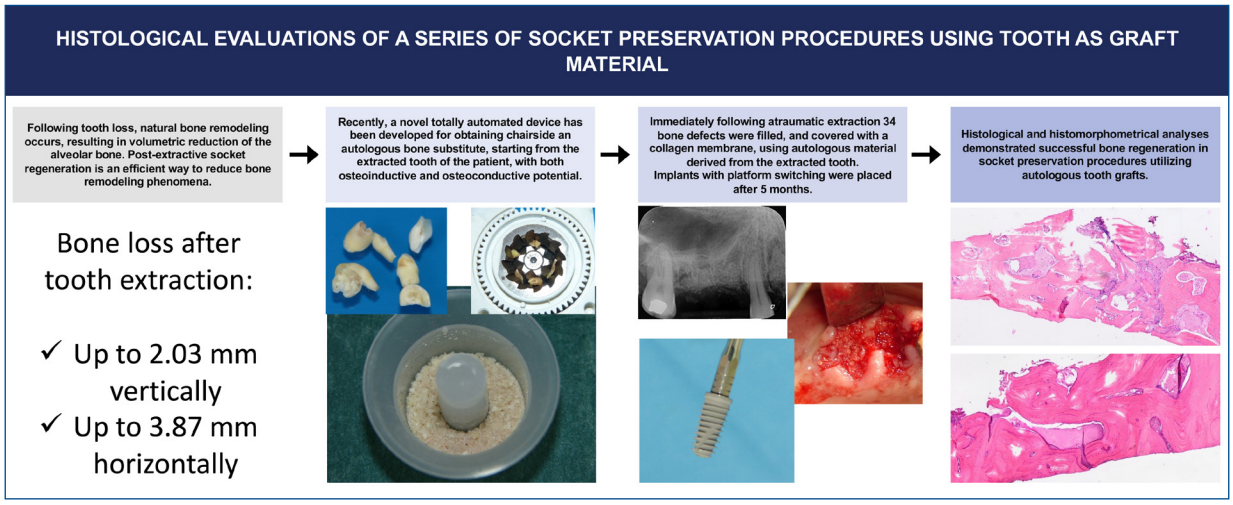

Graphical Abstract. Innovative protocol to use autologous tooth graft in GBR procedures.

INTRODUCTION

Following tooth loss, natural bone remodeling occurs, resulting in volumetric reduction of the alveolar bone – approximately 1.67-2.03 mm vertically and 3.87 mm horizontally[1]. Hard and soft tissue remodeling is most pronounced during the first year[2,3]. To prevent volumetric bone reduction, various surgical techniques have been proposed, both with and without the use of graft materials, incorporating either resorbable or non-resorbable membranes[4].

Graft materials have been widely used for pre- and peri-implant bone augmentation procedures for over 35 years, proving to be reliable techniques[5,6].

The most used graft materials are of animal, synthetic, or human origin. In these cases, bone regeneration is stimulated solely by the host organism, rather than by the donor material, which can slow down or reduce the regenerative potential[1,7].

Autologous bone grafting is considered the gold standard for repairing alveolar bone defects; however, it is associated with potential complications, donor site morbidity, and limited availability[8].

The human dentin matrix offers a promising alternative to both autologous and heterologous bone grafts. The use of teeth as a graft material has demonstrated favorable qualities similar to those of autologous bone, as initially proven by Yeomans and Urist[9]. In their animal study, various tissues – such as tendons, muscles, decalcified and sterilized cortical bone, and dentin – were used as graft materials and analyzed over up to 12 weeks. While tendons and muscles were replaced by fibrous tissue, the cortical bone matrix was resorbed within 4 weeks. Dentin exhibited slower resorption and a significant induction of osteogenesis. The literature presents several protocols for demineralizing grafting materials, including the use of hydrochloric acid (HCl) solutions for 48 hours, 70% ethyl alcohol, ethylenediaminetetraacetic acid (EDTA) at various pH levels, acetic acid, and nitric acid. A key factor in the process is the preparation technique used to transform autologous teeth into a suitable graft material. Developing an effective regenerative protocol is essential for restoring and maintaining the long-term dimensions of both hard and soft tissues. Additionally, the choice of graft material and its inherent properties play a critical role in determining clinical outcomes[10,11].

The use of teeth as graft material was first proposed in 1967 when Bang and Urist[12] demonstrated the osteoinductive properties of demineralized autologous dental matrix. The concept of utilizing autologous teeth instead of bone for grafting procedures originated from the observation of the similar chemical composition between dentin and bone. Both consist of 70% inorganic material (hydroxyapatite), 18% collagen, 2% proteins, and 10% fluids. Additionally, both tooth and alveolar bone derive from neural crest cells and share the same type I collagen composition.

In 1989, Kawai and Urist[13] were the first to identify partially purified bone morphogenetic proteins (BMPs) in bovine dental matrix. In 1991, Bessho et al[14] demonstrated the presence of bone morphogenetic proteins (BMPs) in the dentin matrix of human teeth by utilizing extracted human teeth. This finding suggests that both dentin and bone matrices serve

as reservoirs for growth factors such as BMPs and fundamental fibroblast growth factors. Reports indicate that demineralized human dental matrix, when combined with osteoblastic cells, can promote the formation of bone and cartilage in mouse models[15]. Studies have also suggested that demineralized human dental matrix, when combined with osteoblastic cells, has the capability to promote the formation of bone and cartilage in mouse models[16]. Recently, a novel technique has been introduced in the dental market for obtaining an autologous bone substitute with both osteoinductive and osteoconductive potential. This material is derived from processing extracted teeth and can be reintroduced into the patient as microgranules following a specific procedure that utilizes a specialized device[17]. Literature reviews have highlighted various studies that demonstrate its positive regenerative potential and confirm its safety from a microbiological standpoint[18,19].

A critical aspect of the overall procedure is the technique used to prepare autologous teeth as graft material. Preserving the organic autologous components is essential for stimulating bone progenitor cells, while removing contaminants is necessary to prevent inflammatory or infectious reactions. Proper preparation of the inorganic portion ensures that osteoblasts can effectively colonize the graft. The demineralization process is crucial for releasing growth factors and proteins, as the presence of non-resorbable hydroxyapatite crystals can sometimes obstruct their release[20,21].

Demineralization exposes collagen, allowing for faster resorption of the dentin granule. The resorption releases the proteins contained within the tooth[22].

To produce a dental-origin graft, an Italian company, TT Tooth Transformer® Srl (Milan, Italy), has developed a device that automatically grinds, demineralizes, and detoxifies, thereby eliminating potential human errors. The use of 0.1M HCl and 10% H_2O_2, washing with demineralized water, temperature variations, and UVA exposure ensures standards suitable for regenerative techniques, producing an autologous biomaterial that contains autologous proteins, thereby guaranteeing osteoinduction[23].

This treatment increases the size of dentinal tubules, enhancing wettability and thus improving cell adhesion[24].

Studies[25,26] have demonstrated the presence of BMP-2 in the tooth after the reduction of mineralization and the elimination of bacteria by the Tooth Transformer©.

This article aims to present the histological results of 34 socket preservation cases using teeth treated with the TT Tooth Transformer as graft material and covered with Osseoguard© membrane (Zimvie, FL, USA).

MATERIALS AND METHODS

The study was conducted in accordance with the guidelines established by the University of Chieti Ethics Committee. The clinical study protocol was approved on March 21, 2019, and is registered under number 638-21/3/19. All clinical centers adhered to the same protocol under that single IRB number.

This study was conducted on a series of patients treated at private offices in Italy between February 2023 and May 2024.

Inclusion criteria

The study included patients over 18 years of age who required tooth extraction, were in good health (classified as ASA-1 and ASA-2), and were able to undergo dental surgical and restorative procedures. Tooth extractions were necessitated by trauma, caries, or periodontal disease. Alveolar socket preservation procedures were performed to maintain bone volume for future dental implant rehabilitation following tooth extraction.

Exclusion criteria

Pregnant individuals, patients with a history of allergies, recent tobacco use (within the last six months), diabetes, cancer, HIV, bone or metabolic diseases, those on immunosuppressive agents, systemic corticosteroids, or intramuscular/intravenous bisphosphonates, and patients undergoing radiotherapy or chemotherapy were excluded from the study.

Surgical procedure

One hour before surgery, patients were administered 2 g of amoxicillin and clavulanic acid (Augmentin; Roche, Milan, Italy) as antibiotic prophylaxis[27].

The surgical procedure began with a careful tooth extraction aimed at minimizing mechanical trauma to the surrounding bone. Following extraction, the socket was thoroughly debrided.

After the tooth extraction, the patient underwent the following treatment: removal of tartar residue using a piezoelectric instrument, cleaning of the root surface with diamond burs, and removal of any remaining filling materials (such as gutta-percha or composite). The tooth was then divided into smaller sections to facilitate grinding. These sections were placed into the Tooth Transformer grinder, which included a dis-

posable single-use vial, correctly positioned according to the provided arrows.

Before conducting tooth extraction and/or regeneration procedures, each patient underwent 3D radiological analysis. After thorough drying, the tooth was placed into the device. In all cases, a resorbable Osseoguard© membrane (Zimvie, Palm Beach Gardens, FL, USA) was applied to cover the graft.

Histological sampling was conducted during the implant placement procedure, 5 months after the procedure. CBCT scans were taken before implant placement. Bone samples were obtained concurrently with implant placement. Following patient consent, a 3 mm trephine bur (Meisinger USA, L.L.C., Centennial, CO, USA) was used to prepare the implant site. Specialized implant drills, with ample saline irrigation, were then employed. The bone extracted during the creation of the surgical implant socket was collected. The sample was thoroughly rinsed with physiological solution to remove any blood or tissue fragments, then promptly placed into a freshly prepared fixative solution (10% neutral-buffered formalin) in a light-protected, hermetically sealed container, ensuring a volume of at least 10 cc without air bubbles. During the surgical reentry, 34 titanium dental implants (T3 pro Zimvie, FL, USA) were placed. These implants are in platform-switched T3 PRO©, the outer edge of the implant-abutment interface is repositioned inwardly and away from the outer edge of the implant platform[28].

Histological analysis

All samples were washed and dehydrated using increasing concentrations of alcohol solutions (Sigma-Aldrich, St. Louis, MO, USA) and then infiltrated with methacrylic resin (Sigma-Aldrich, St. Louis, MO, USA) for histological analysis. The samples were then processed to obtain non-decalcified sections using the LS2 disk abrasion system (Remet, Bologna, Italy) and the Micromet diamond disk cutting system (Remet, Bologna, Italy), resulting in slides approximately 200 microns thick. Subsequently, all samples were treated with low-abrasive paper on a lapping machine (Buehler, Lake Bluff, IL, USA) with thickness control, gradually reducing the sample thickness to around 40-50 microns. The specimens were polished, stained with basic fuchsin and toluidine blue, and examined using light and polarized light microscopy (Olympus, Shinjuku, Tokyo, Japan). Histological images obtained from the transmitted light microscope (Olympus, Shinjuku, Tokyo, Japan) were digitized using a digital camera and analyzed with image analysis software, IAS 2000 (QEA, Billerica, MA, USA). For each sample, the percentage of residual bone volume excluding medullary tissues (BV%), the percentage of remaining graft excluding bone and marrow (Graft%), and the percentage of vital bone excluding the medulla and residual graft (BV%) were measured and recorded.

Patient selection overview

This clinical study was conducted across multiple dental centers over a period of approximately one year, during which patient recruitment and observation took place. However, the study does not include a power calculation or provide a clear rationale for selecting the sample size of 34 patients.

RESULTS

A total of 34 subjects (19 men and 15 women), with an average age of 58.17 years (±10.26), were enrolled in the study. Fourteen cases were in the maxillae and twenty in the mandible (Table I, Figure 1). In total, 34 teeth were extracted and used for alveolar socket preservation therapy. After 5 months of healing, no complications were reported, and the defects were fully filled with newly formed bone. All cases showed complete bone filling, as determined by clinical and radiographic observations. The newly formed tissue observed during surgical reentry exhibited a density comparable to medium-density bone, with no graft particles or granules present in the submucosal connective tissues. The regenerated bone appeared homogeneous and uniform, free from visible graft particles or granules. The bone density encountered during implant drilling ranged from D2 to D3, ensuring high primary stability for all implants. Following healing, complete osseointegration of the implants was achieved.

Histological analysis revealed an average bone volume excluding medulla and residual graft (BV)

Table I. Type of subjects, graft position and healing time.

34 subjects	
Male	19
Female	15
Position	
Mandible	20
Maxillae	14
Average time to collect the samples	
5.35 months	

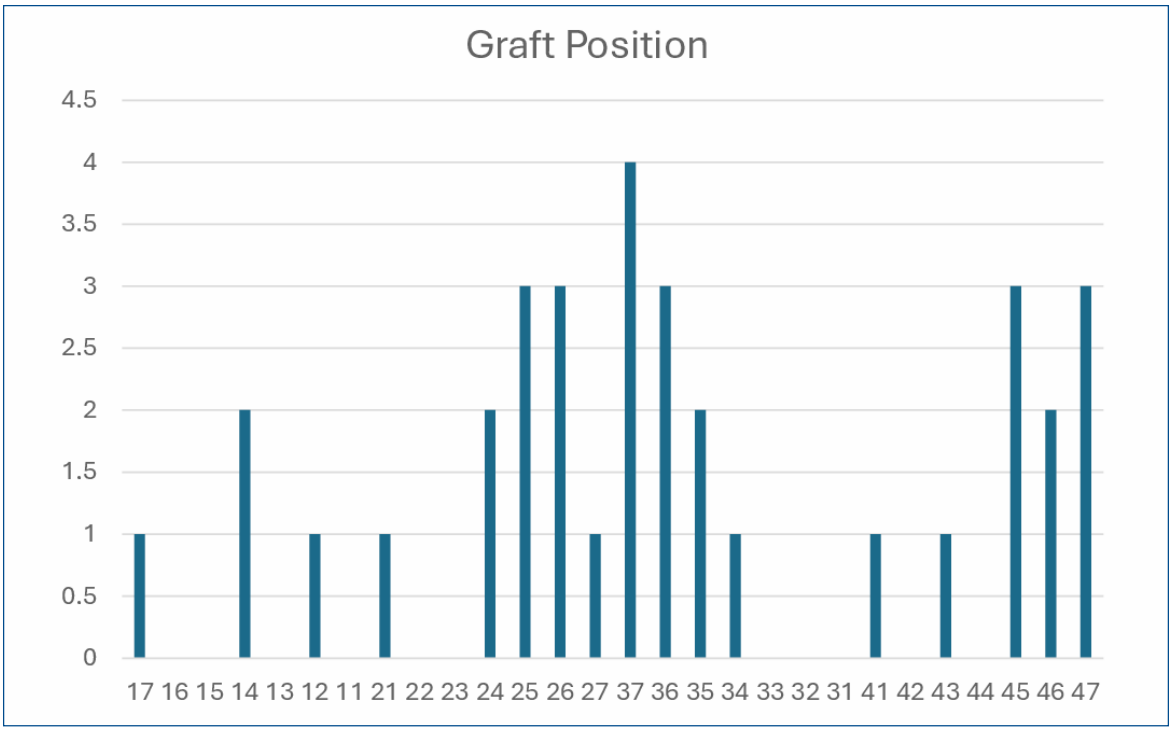

Figure 1. Graft tooth position and numerosity. The table indicates where the graft was made. The vertical axis indicates the number of grafts performed on each position.

of 52.35% (±17.25). The average residual graft (RG) rate was 10.79% (±12.26), while new bone (NB) accounted for 41.56% (±22.02) of the samples (Table II). None of the specimens showed signs of inflammation, necrosis, or the presence of endodontic materials. Dentin and residual enamel matrices were observed in all samples (Figures 2-5, Table III).

Table II. The table indicates the average histomorphometric value of all 34 histologies performed.

Bone volume %	52.35% (±17.25)
Residual graft %	10.79% (±12.26)
New bone %	41.56% (±22.02)

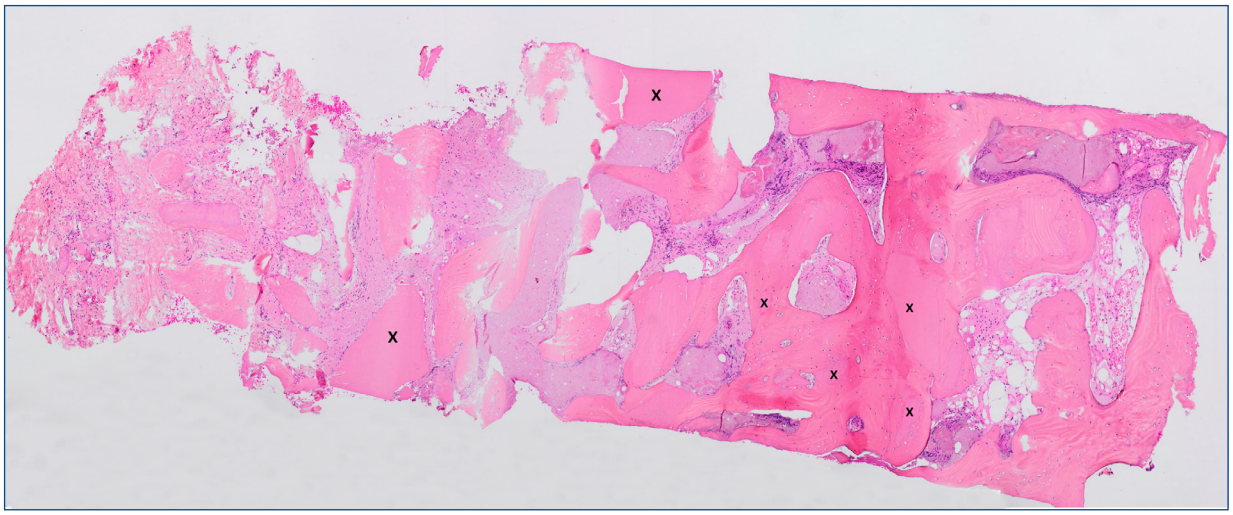

Figure 2. Histological analysis. The residual graft particles are signed with the X sign. An interesting aspect is the coloration of the granules characterized by the maintenance of the same chromaticity of the tissues, indicating a very similar tissue composition. Coloration Hematoxylin and Eosin (Histology performed by P. Savadori, Department of Biomedical, Surgical, and Dental Science, University of Milan, 20100 Milan, Italy) – magnification 70x.

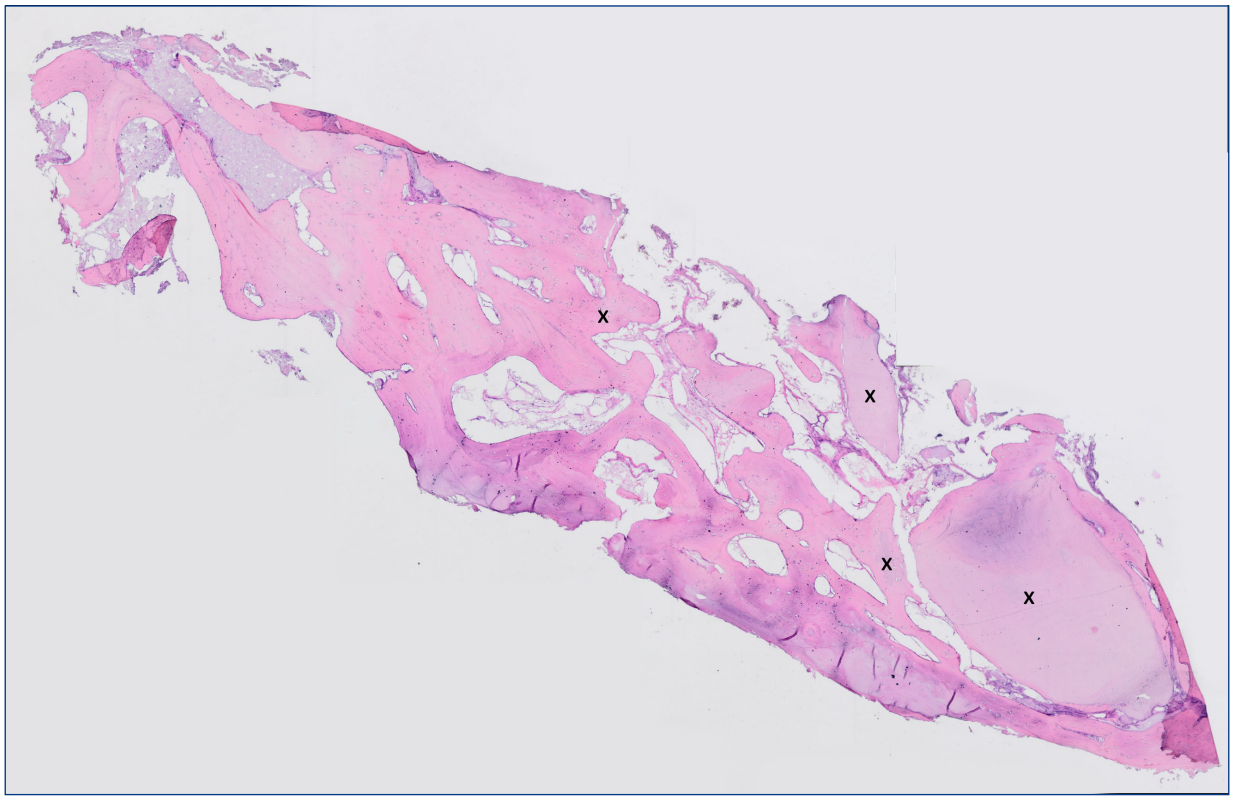

Figure 3. Histological analysis. The residual graft particles are signed with the X sign. The granules appear almost identical to the bone tissue in terms of coloration but are distinguishable by the presence of dentinal tubules. Coloration Hematoxylin and Eosin (Histology performed by P. Savadori, Department of Biomedical, Surgical, and Dental Science, University of Milan, 20100 Milan, Italy) – magnification 70x.

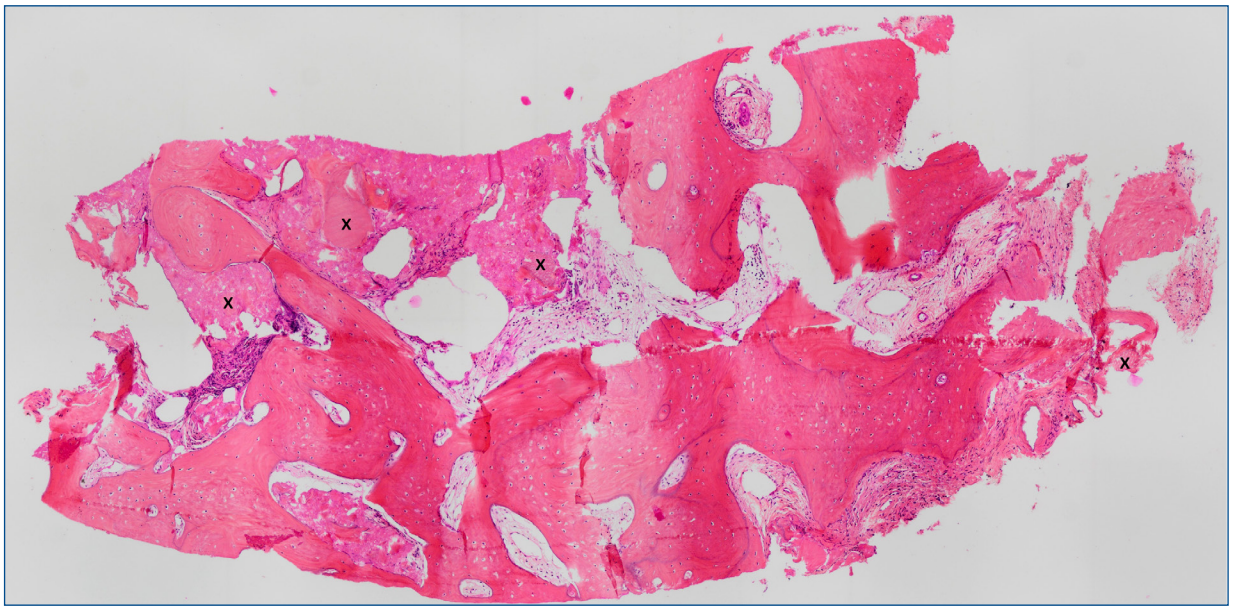

Figure 4. Histological analysis. The residual graft particles are signed with the X sign. Some residual particles graft appeared partially resorbed testifying that partial demineralized tooth underwent to natural remodeling phenomena like native bone. Coloration Hematoxylin and Eosin (Histology performed by P. Savadori, Department of Biomedical, Surgical, and Dental Science, University of Milan, 20100 Milan, Italy) – magnification 70x.

DISCUSSION

Numerous graft materials have been studied during the healing phases of regeneration[29].

Numerous literature reviews have indicated that alloplastic materials leave a residue of 12.4-21.11%, while xenograft and allograft materials leave a residue of 37.14% and 37.23%,

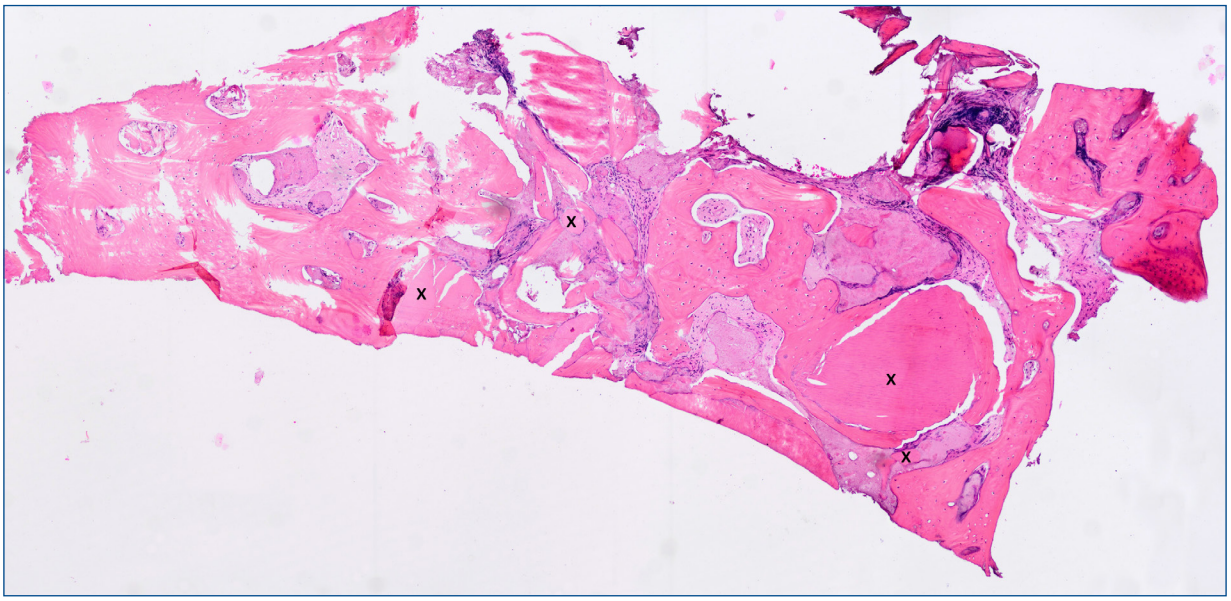

Figure 5. Histological analysis. The residual graft particles are signed with the X sign. It Is interesting to note the residual granules are distributed along the entire length of the histological sample. This clearly indicates that the sample is an integral part of a regeneration where most of the tooth granules have been resorbed. Coloration Hematoxylin and Eosin (Histology performed by P. Savadori, Department of Biomedical, Surgical, and Dental Science, University of Milan, 20100 Milan, Italy) – magnification 70x.

respectively[30]. From a clinical perspective, xenograft materials reduce the three-dimensional resorption of the crest but show incomplete resorption over time. The ideal material should be replaced by bone tissue through stimulation (osteoinduction) and space maintenance (osteoconduction)[31].

The present clinical study is not a controlled study, and the absence of a direct comparator (e.g., xenograft or allograft) certainly represents a limitation of the study itself. On the other hand, the multicenter design offers clinical results obtained by different clinicians, which testify that the protocol utilized is well-standardized and can be easily replicated.

The xenograft biomaterial family, however, has been extensively described by international literature over the years, and it is well known that in most bone regenerations it allows a bone volume of approximately 40%, but this percentage often includes particles of biomaterial that are not reabsorbed and incorporated into the bone tissue.

Xenograft biomaterial offers host cells a 3D scaffold (osteoconduction) but does not contain proteins or growth factors that could induce bone proliferation.

Autologous bone grafting has always been considered the gold standard, although the harvesting process can cause additional pain for the patient. Donor bone substitutes have high costs. For these reasons, alternative bone substitutes are being explored[32,33].

Bone grafts resorb very quickly, while xenograft materials maintain space over time, facil-

Table III. Histomorphometrical data.

Figure 1		Figure 3	
Bone volume %	46.196	Bone volume %	57.791
Residual graft %	7.805	Residual graft %	0.813%
New bone %	38.392	New bone %	56.978%
Figure 2		**Figure 4**	
Bone volume %	65.899	Bone volume %	58.940
Residual graft %	15.112	Residual graft %	8.252
New bone %	50.787	New bone %	50.688

itating bone regeneration. Xenograft materials lack osteoinductive proteins and act primarily as osteoconductive scaffolds[34,35]. The proteins contained in bone tissue are eliminated by the processes used to remove organic structures (heat or chemical treatments). These proteins are responsible for bone stimulation and cells recruitment. A few years ago, the autologous tooth was recognized as a potential source of osteoinductive material since the tooth can be considered mineralized bone and contains the same proteins[36].

A study on 33 cases, evaluating the outcomes of using dentin versus xenograft material, showed that dentin should be considered an effective biomaterial for promoting bone regeneration[37].

The presence of BMP-2 proteins after treatment with the Tooth Transformer device has been demonstrated in a recent study, indicating that the tooth-derived biomaterial has osteoinductive properties. In addition, another clinical study including sixteen post-extractive sockets without buccal and/or palatal bone walls, grafted with the autologous tooth material treated by the same device, reported good volume maintenance and no infective or inflammatory complications[38].

A multicenter study involving 504 patients and 483 implants placed in sites regenerated using teeth treated with the Tooth Transformer©, after 4 months, analyzed histologies and, after 12 months, the implant survival rate. The histological analysis showed a bone volume excluding medulla and residual graft (BV) of 43.58% (±12.09), with new vital bone (NB) accounting for 32.38% (±17.15). No signs of inflammation or necrosis were found. The implant survival rate was 98.2%[39].

The medical device used, being totally automatic, guarantees total detoxification in every single case through the combined chemical action of 10% hydrogen peroxide and 0.1 M HCl, as well as the physical action of UVA irradiation at 40. The clinician should only remove from the extracted tooth any foreign material (such as gutta-percha, resin, cement) and divide the tooth into small fragments. These small fragments must be inserted into the Tooth Trasformer© device that automatically manages all the phases of grinding, demineralization, and decontamination/detoxification without any possibility of human error. This automatic and standardized procedure ensures the same results.

The extracted autologous tooth is ground and fully decontaminated by the Tooth Transformer© device, converting it into grafting material. The processing time is approximately 25 minutes and can produce up to 3 grams of material per cycle. This material is highly effective due to its similarity to bone tissue[40].

CONCLUSIONS

The findings of the current study revealed that this socket preservation procedure was able to reduce bone remodeling phenomena, maintaining the three-dimensional bone volume. Furthermore, it was observed that a substantial percentage of vital bone formation occurred across all socket preservation sites. The use of the innovative grinding device facilitates the rapid processing and application of the patient's tooth as a bone graft. The device manages all decontamination, disinfection, and demineralization processes electronically, minimizing the risk of error or human injury.

The re-use of extracted teeth of the patient represents an opportunity that could reduce morbidity by avoiding a second surgical donor site for harvesting autologous bone.

Further studies with extended follow-up periods and larger sample size, are required to fully assess the potential of demineralized dentin autografts. These histological results are consistent with previous studies, reinforcing the efficacy of this approach in bone regeneration[41].

Ethics Approval

On March 21st, 2019, the University of Chieti Ethics Committee (Italy) authorized the clinical study protocol on a human model registered under the number: 638-21/3/19.

Informed Consent

The present study was carried out following the principles embodied in the Helsinki Declaration, in its latter form. Patient data were anonymized. Each patient gives a written consent for the publication of personal surgical and histological data.

Availability of Data and Materials

All data and material are available from Prof. Elio Minetti in Milan, Italy.

Conflict of Interest

The authors have no conflict of interest to declare.

Authors' Contributions

Cavellini P. clinical procedures, data collection; Andreatta L. data curation, data collection; Alì F. data analysis; Bavetta G. data collection; Veruggio P. data analysis, Cesca A. manuscript preparation, Righi D. data collection, Farina V. data curation; Berardini M. manuscript preparation, manuscript revision, data analysis; Iorio Mauro data collection; Zambelli C. data collection; Iorio Marco data analysis; Gianfreda F.

study design; Palermo A. conceptualization; Minetti E. study design, data analysis, manuscript preparation, conceptualization.

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REFERENCES

1) Weijden FVD, Dell'Acqua F, Slot DE. Alveolar bone dimensional changes of post-extraction sockets in humans: A systematic review. J Clin Periodontol 2009; 36: 1048-1058.
2) Schropp L. Bone healing and soft tissue contour changes following single-tooth extraction: A clinical and radiographic 12-month prospective study. J Prosthet Dent 2004; 91: 313-323.
3) Araújo MG, Silva CO, Misawa M, Sukekava F. Alveolar socket healing: What can we learn? Periodontol 2000 2015; 68: 122-134.
4) Orgeas GV, Clementini M, Risi VD, Sanctis MD. Surgical Techniques for Alveolar Socket Preservation: A Systematic Review. Int J Oral Maxillofac Implants 2013; 28: 1049-1061.
5) Boyne PJ. Experimental Evaluation of the Osteogenic Potential of Bone Graft Materials. Am Inst Oral Biol 1969; 13-21.
6) Mummolo S, Mancini L, Quinzi V, D'Aquino R, Marzo G, Marchetti E. Rigenera® Autologous Micrografts in Oral Regeneration: Clinical, Histological, and Radiographical Evaluations. Appl Sci 2020; 10: 5084.
7) Inchingolo AM, Inchingolo AD, Nardelli P, Latini G, Trilli I, Ferrante L, Malcangi G, Palermo A, Inchingolo F, Dipalma G. Stem Cells: Present Understanding and Prospects for Regenerative Dentistry. J Funct Biomater 2024; 15: 308.
8) Mellonig JT, Bowers GM, Cotton WR. Comparison of bone graft materials. Part II. New bone formation with autografts and allografts: a histological evaluation. J Periodontol 1981; 52: 297-302.
9) Yeomans JD, Urist MR. Bone induction by decalcified dentine implanted into oral, osseous and muscle tissues. Arch Oral Biol 1967; 12: 999-1008.
10) Inchingolo F, Ballini A, Cagiano R, Inchingolo AD, Serafini M, De Benedittis M, Cortelazzi R, Tatullo M, Marrelli M, Inchingolo AM, Vermesan D, Del Corso M, Malcangi G, Diteodoro S, Mura SA, Cantore S, Cortelazzi A, Paduanelli G, Resta G, Muollo F, Cirulli N, Pettini F, Farronato D, De Vito D, Caprio M, Haragus H, Dipalma G. Immediately loaded dental implants bioactivated with platelet-rich plasma (PRP) placed in maxillary and mandibular region. Clin Ter 2015; 166: e146-e152.
11) Dang QT, Huynh TD, Inchingolo F, Dipalma G, Inchingolo AD, Cantore S, Paduanelli G, Nguyen KCD, Ballini A, Isacco CG, Tran CT. Human Chondrocytes from Human Adipose Tissue-Derived Mesenchymal Stem Cells Seeded on a Dermal-Derived Collagen Matrix Sheet: Our Preliminary Results for a Ready to Go Biotechnological Cartilage Graft in Clinical Practice. Stem Cells Int 2021; 23; 2021: 6664697.
12) Bang G, Urist, MR. Bone Induction in Excavation Chambers in Matrix of Decalcified Dentin. Arch Surg 1967; 94: 781-789.
13) Kawai T, Urist MR. Bovine tooth-derived bone morphogenetic protein. J Dent Res 1989; 68: 1069-1074.
14) Bessho K, Tanaka N, Matsumoto J, Tagawa T, Murata M. Human dentin-matrix-derived bone morphogenetic protein. J Dent Res 1991; 70: 171-175.
15) Um IW, Lee JK, Kim JY, Kim YM, Bakhshalian N, Jeong YK, Ku JK. Allogeneic Dentin Graft: A Review on Its Osteoinductivity and Antigenicity. Materials (Basel) 2021; 14: 1713.
16) Kim KW. Bone Induction by Demineralized Dentin Matrix in Nude Mouse Muscles. Maxillofac Plast Reconstr Surg 2014; 36: 50-56.
17) Minetti E, Berardini M, Trisi P. A New Tooth Processing Apparatus Allowing to Obtain Dentin Grafts for Bone Augmentation: The Tooth Transformer. The Open Dent J 2019; 13: 6-14.
18) Minetti E, Giacometti E, Gambardella U, Contessi M, Ballini A, Marenzi G, Celko M, Mastrangelo F. Alveolar Socket Preservation with Different Autologous Graft Materials: Preliminary Results of a Multicenter Pilot Study in Human. Materials (Basel) 2020; 13: 1153.
19) Minetti E, Taschieri S, Corbella S. Autologous Deciduous Tooth-Derived Material for Alveolar Ridge Preservation: A Clinical and Histological Case Report. Case Rep Dent 2020; 18; 2020: 2936878.
20) Kim YK, Lee J, Um IW, Kim KW, Murata M, Akazawa T, Mitsugi M. Tooth-derived bone graft material. J Korean Assoc Oral Maxillofac Surg 2013; 39: 103-111.
21) Scarano A, Inchingolo F, Murmura G, Traini T, Piattelli A, Lorusso F. Three-Dimensional Architecture and Mechanical Properties of Bovine Bone Mixed with Autologous Platelet Liquid, Blood, or Physiological Water: An In Vitro Study. Int J Mol Sci 2018; 19: 1230.
22) Pietrzak WS, Woodell-May J, McDonald N Assay of bone morphogenetic protein-2, -4, and -7 in human demineralized bone matrix. J Craniofac Surg 2006; 17: 84-90.
23) Franceschelli S, Lagioia R, De Cecco F, Minetti E, Ballini A, Panella V, Speranza L, Grilli A, Mastrangelo F. Biological Evaluation of the Osteoinductive Potential of Dry Teeth after Chemical Demineralization Treatment Using the Tooth Transformer Device. Biomolecules 2023; 13: 1727.
24) Koga T, Minamizato T, Kawai Y, Miura K, I T, Nakatani Y, Sumita Y, Asahina I. Bone Regeneration Using Dentin Matrix Depends on the Degree of Demineralization and Particle Size. PLoS One 2016; 11: e0147235.
25) Bono N, Tarsini P, Candiani G. Demineralized dentin and enamel matrices as suitable substrates for bone regeneration. J Appl Biomater Funct Mater 2017; 15: e236-e243.
26) Kawashima N. Characterisation of dental pulp stem cells: a new horizon for tissue regeneration? Arch Oral Biol 2012; 57: 1439-1458.
27) Esposito M, Grusovin MG, Loli V, Coulthard P, Worthington HV. Does antibiotic prophylaxis at implant placement decrease early implant failures? A Cochrane systematic review. Eur J Oral Implantol 2010; 3: 101-110.
28) Traini T, Berardini M, Congedi F, Sinjari B, Trisi P, Caputi S. Impact of Second Stage Surgery on Bone Remodel-

ing Around New Hybrid Titanium Implants: A Prospective Clinical Study in Humans. Implant Dent 2017; 26: 121-128.
29) Esposito M, Felice P, Worthington HV. Interventions for replacing missing teeth: augmentation procedures of the maxillary sinus. Cochrane Database Syst Rev 2014; 2014: CD008397.
30) Corbella S, Taschieri S, Francetti L, Weinstein R, Del Fabbro M. Histomorphometric Results After Postextraction Socket Healing with Different Biomaterials: A Systematic Review of the Literature and Meta-Analysis. Int J Oral Maxillofac Implants 2017; 32: 1001-1017.
31) Nampo T, Watahiki J, Enomoto A, Taguchi T, Ono M, Nakano H, Yamamoto G, Irie T, Tachikawa T, Maki K. A new method for alveolar bone repair using extracted teeth for the graft material. J Periodontol 2010; 81: 1264-1272.
32) Jambhekar S, Kernen F, Bidra AS. Clinical and histologic outcomes of socket grafting after flapless tooth extraction: a systematic review of randomized controlled clinical trials. J Prosthet Dent 2015; 113: 371-382.
33) Crespi R, Capparè P, Gherlone E. Comparison of magnesium-enriched hydroxyapatite and porcine bone in human extraction socket healing: a histologic and histomorphometric evaluation. Int J Oral Maxillofac Implants 2011; 26: 1057-1062.
34) Romasco T, Tumedei M, Inchingolo F, Pignatelli P, Montesani L, Iezzi G, Petrini M, Piattelli A, Di Pietro N. A Narrative Review on the Effectiveness of Bone Regeneration Procedures with OsteoBiol® Collagenated Porcine Grafts: The Translational Research Experience over 20 Years. J Funct Biomater 2022; 13: 121.
35) Ortiz-Vigón A, Suarez I, Martínez-Villa S, Sanz-Martín I, Bollain J, Sanz, M. Safety and Performance of a Novel Collagenated Xenogeneic Bone Block for Lateral Alveolar Crest Augmentation for Staged Implant Placement. Clin Oral Implant Res 2018; 29: 36-45.
36) Kim YK, Kim SG, Yun PY, Yeo IS, Jin SC, Oh JS, Kim HJ, Yu SK, Lee SY, Kim JS, Um IW, Jeong MA, Kim GW. Autogenous teeth used for bone grafting: a comparison with traditional grafting materials. Oral Surg Oral Med Oral Pathol Oral Radiol 2014; 117: e39-e45.
37) Pang KM, Um IW, Kim YK, Woo JM, Kim SM, Lee JH. Autogenous demineralized dentin matrix from extracted tooth for the augmentation of alveolar bone defect: a prospective randomized clinical trial in comparison with anorganic bovine bone. Clin Oral Implants Res 2017; 28: 809-815.
38) Minetti E, Palermo A, Berardini M. Comparison of Different Techniques in Post-Extractive Socket Regeneration Using Autologous Tooth Graft: Histological and Clinical Outcomes. Eur J Dent 2024; 18: 477-484.
39) Minetti E, Celko M, Contessi M, Carini F, Gambardella U, Giacometti E, Santillana J, Beca Campoy T, Schmitz JH, Libertucci M, Ho H, Haan S, Mastrangelo F. Implants Survival Rate in Regenerated Sites with Innovative Graft Biomaterials: 1 Year Follow-Up. Materials (Basel) 2021; 14: 5292.
40) Kumar GS. Orban's Oral Histology & Embryology-E-Book; Elsevier Health Sciences: Amsterdam, The Netherlands, 2015; ISBN 978-81-312-4505-7.
41) Minetti E, Corbella S, Taschieri S, Canullo L. Tooth as graft material: Histologic study. Clin Implant Dent Relat Res 2022; 24: 488-496.