2 CE CREDITS

Developments in Bone Grafting

CONTINUING EDUCATION
Selection of Bone Grafting Materials, Techniques

PRODUCT UPDATE
New Syringe-Delivered Alloplastic Bone Graft Substitute

CASE REPORT
Extraction Site Preservation

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FROM THE EDITOR-IN-CHIEF

Dear Reader

Bone replacement in the human body has a long history that involves a variety of graft materials, growth enhancers, barriers, and more. The origin of such materials, their rationale for use, and how they are removed or eliminated from the surgical site are all key issues facing surgeons when considering bone graft procedures.

In this supplement to *Compendium of Continuing Education in Dentistry*, supported by Sunstar, we examine developments—both old and new—in the area of bone grafting. A continuing education article reviews the issues surrounding tooth extraction, ridge augmentation, and sinus grafting and underscores the value of understanding the various materials used when performing these procedures. Also, this supplement highlights an in-situ hardening alloplastic bone grafting material composed of $\beta$-TCP granules coated with PLGA. Its use is aimed at preserving the dimensions and architecture of the alveolar ridge after atraumatic extraction.

I would like to thank our sponsor for bringing you this educational opportunity and hope that you find the information helpful for your own clinical practice. I welcome your feedback. Please contact me at lrose@aegiscomm.com.

Louis F. Rose, DDS, MD
Editor-In-Chief

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BONE GRAFTING: HISTORY, RATIONALE, AND SELECTION OF MATERIALS AND TECHNIQUES

Robert A. Horowitz, DDS; Minas D. Leventis, DDS, MS, PhD; Michael D. Rohrer, DDS, MS; and Hari S. Prasad, BS, MDT

ABSTRACT

In the 100-year history of bone replacement in the human body for different purposes, a wide variety of surgical approaches and materials have been used. The techniques and materials selected significantly affect the outcome of bone replacement procedures in terms of bone formation volume and the quality and amount of vital bone. The choices facing the dental surgeon at the time of extraction, ridge augmentation, or sinus graft are wide-ranging. When choosing a bone graft material the surgeon should consider its ultimate effect on healing patterns in and around the alveolar bone at the endpoint of the procedure. As this article concludes, a better understanding of the materials and the results that can be predictably achieved with them can be valuable to the appropriately trained surgeon when preparing for these procedures.

LEARNING OBJECTIVES

+ Discuss the choices and related issues faced by surgeons at the time of tooth extraction, ridge augmentation, or sinus graft
+ Describe the different materials used for bone replacement
+ Explain how the surgeon’s ultimate goal impacts decisions regarding material choices and methods used

The history of bone replacement in the human body using different materials that can be purchased, processed, or harvested dates back more than a century. Significant issues related to graft materials and growth enhancers concern their origin, rationale for use, how they are removed or eliminated from the surgical site, and their associated biologic “costs.” Another key issue when considering bone graft materials is the goal of the surgeon regarding “repair” or “regeneration” in the specific area treated.

Repair is the replacement of a part with something that is physically similar but is neither biologically nor physiologically identical to the original structure. In contrast, regeneration involves a complex series of material usage and events that enable the missing body part to be replaced by a biological structure or group of structures in all ways identical to what was lost. Surgeons contemplating replacement via either repair or regeneration should consider the options in bone replacement graft materials, growth enhancers, and barriers in terms of their expected ultimate biologic impact at the endpoint of the surgical procedure. Depending on the procedure, there may be tradeoffs between percentage of vital bone, volume augmentation, and speed of healing, versus the simplicity of the procedure.

Guided tissue regeneration involves a number of steps to achieve the goal of bone formation in an area. It requires a scaffold on which the bone is laid down. Blood vessels must enter the area to bring nutrients and the necessary cells. Calcium is important for mineralization of the organic matrix formed. Osteoblasts will deposit the collagen that will become bone. Signaling molecules assist in the attraction of the precursor cells (osteoblasts, endothelial cells) to enter the area where their specific tissues will be built. It can be daunting to complete these tasks in an area of the mouth where there is trauma from food and masticatory muscles, bacteria, and saliva—challenges that can be further complicated in a non- or poorly compliant patient. Having a better understanding of the materials and the results that can be predictably achieved with them can help the appropriately trained surgeon prepare for these surgical endeavors.

Considerations for Bone Replacement

The choices facing the surgeon at
the time of extraction, ridge augmentation, or sinus graft are numerous, and are concerned mainly with the following:

MODE OF ENTRY TO THE SITE—Modes of entry may be flapless, minimally invasive, or a “conventional” large flap may be used for access.

SOURCE OF BONE REPLACEMENT GRAFT MATERIALS—Autogenous bone, allogeneic bone, alloplast, xenografts, or an autogenous blood harvested/concentrated product comprise the options for bone replacement graft materials.

TYPE OF GRAFT USED IN THE PROCEDURE—Grafts may be particulate, putty, or block. They are available with large or small particles, a combination of porosities, and from specific locations of origin (eg, cortical, cancellous).

SPECIFIC CHARACTERISTIC OF EACH GRAFT—There may be varying degrees of mineralization, material composition and formation, and resorbability. Also to be considered is whether the material is osteoconductive or osteoinductive and how quickly—or slowly, or if at all—the graft will resorb.

BARRIER TYPE—The barrier may be synthetic or it could be collagen—in which case its source should be considered; it may be cross-linked or processed in a “natural” way; it also may be resorbable or removable, bioactive, or inert.

Early studies on extraction therapy demonstrated that placement of neither a graft nor a barrier resulted in vital bone formation in the socket. While in principle, this is an outstanding result, there are concerns related to using this as the only mode of preservation of the alveolus at the time of tooth removal. Fickl et al in 2008 investigated the differences between flap elevation and flapless extraction, with and without bone replacement grafting, in dogs. They found that raising the mucoperiosteal tissues resulted in more loss of alveolar width and height than leaving the soft tissues intact at the time of surgery. They also noted more, though not full, preservation of the dimensions by placement of a combination bone graft with anorganic bovine bone mineral in collagen than no grafting. Iasella et al demonstrated that more vital bone was formed when no graft material was placed at the time of tooth extraction, but there was a more than 30% loss of ridge width than when a mineralized allograft was inserted into the defect and covered with a resorbable collagen barrier. A 2004 study showed excellent volume preservation and that close to 60% vital bone formed when a hemihydrate form of calcium sulfate was used with no barrier. A novel bone replacement graft material described in a 2012 report is biphasic in nature, containing both hemi- and di-hydrate calcium sulfate. This material is self-setting in the presence of blood or saliva, is reinforced, and can be used with or without a barrier membrane. The report presented findings on its use in multiple types of defects, all demonstrating significant amounts of bone histologically. In addition, there was significant preservation or augmentation of the alveolar ridge width.

Fickl et al in 2008 investigated the differences between flap elevation and flapless extraction, with and without bone replacement grafting,≥

Grafting and Barrier Materials
Calcium Sulfate
Other graft materials that have been used at the time of tooth extraction include synthetic materials. Calcium sulfate has been used in many configurations as a graft and/or enhancer (Figure 1). A 2004 study showed excellent volume preservation and that close to 60% vital bone formed when a hemihydrate form of calcium sulfate was used with no barrier. A novel bone replacement graft material described in a 2012 report is biphasic in nature, containing both hemi- and di-hydrate calcium sulfate. This material is self-setting in the presence of blood or saliva, is reinforced, and can be used with or without a barrier membrane. The report presented findings on its use in multiple types of defects, all demonstrating significant amounts of bone histologically. In addition, there was significant preservation or augmentation of the alveolar ridge width.

The patient shown in Figure 1 had presented after significant endodontic-related abscesses reduced the height of both buccal and lingual plates of bone. Covering
the biphasic calcium sulfate (BCS) graft with a dense polytetrafluoroethylene (PTFE) barrier for 3 weeks enhanced healing in the site. Clinically, it is apparent that the ridge volume was maintained over 5 years and supported keratinized tissue (Figure 2). Most importantly, there was, on histologic evaluation, 58% vital bone, with no remnants of the bone replacement graft material (Figure 3).

**Beta-Tricalcium Phosphate**

There are concerns that graft materials that fully resorb in a short timeframe may contribute to site collapse. Pure-phase beta-tricalcium phosphate (β-TCP) (Figure 4) was one of the materials developed to address this concern. In a clinical and histologic study, extraction sockets were shown to have 91% of ridge width preserved when grafted with β-TCP (Cerasorb®, Curasan, Inc., www.curasaninc.com) and covered with either a collagen or dense PTFE barrier. Dental implants were placed in these patients at 4 to 6 months postoperatively, a later time period than in the calcium sulfate studies. The patient shown in Figure 4 had only three maxillary teeth remaining, supporting an ill-fitting removable prosthesis. Due to the significant occlusal forces that were to be demanded on this single-tooth, implant-supported restoration, it was deemed advantageous to maximize the amount of vital bone in the recipient site. The area was left to heal for 7 months before flap exposure (Figure 5), implant placement in an ideal location, and graft analysis in the largest part of the defect. Analysis of the retrieved specimen showed 85% vital bone in the apical 90% of the core and a thin layer of nonresorbed β-TCP at the crestal portion (Figure 6).

**TCP Coated with PLGA**

A new form of tricalcium phosphate has been developed for ease of use in a syringe system, which sets the material in the grafted site. The system is made up of one syringe containing 99% β-TCP granules coated with poly(lactide-co-glycolide) (PLGA). This is mixed with an ampule containing BioLinker® (N-methyl-2-pyrrolidone and water) (GUIDOR® easy-graft®, Sunstar, www.GUIDOR.com) (Figure 7). A study demonstrated the biocompatibility and resorption of this material in extraction sockets. With its ability to resorb slowly and fully and to maintain its shape during healing, GUIDOR easy-graft is potentially an ideal bone replacement graft for defects of varying sizes, either with or without a barrier.
Figure 7 demonstrates the handling of the material as it is inserted into a large, mandibular molar extraction socket. The graft was covered with a collagen barrier, but no primary closure was either planned or obtained. The area healed uneventfully and was reentered with a flap procedure at 8 months for implant placement (Figure 8). Based on Figure 8 it is evident that much of the graft material had resorbed and was replaced with vital bone while the width of the alveolar ridge was preserved to facilitate ideal placement of an endosseous dental implant.

**Barriers**

In response to challenges with exposure and infection using expanded PTFE barriers, dense, nonporous barriers have been studied and shown to be successful for about 20 years. Using a dense PTFE barrier (Cytoplast™ TXT, Osteogenics, www.osteogenics.com) alone for protecting a blood clot has been shown in numerous papers to preserve alveolar ridge width to a great extent. In these cases, it was demonstrated radiographically and histologically that the former sockets were filled with vital bone suitable for osseointegration as early as 3 months post extraction in humans. In some instances, whether for the comfort of the surgeon or to support the membrane to maintain a larger alveolar bone volume, the site was filled with a graft material (as was shown in Figure 1 through Figure 3).

To obtain a different type of barrier required engineering with a number of components. A resorbable barrier was designed to be space-maintaining due to its rigid nature and space between the inner and outer layers (GUIDOR® Matrix Barrier, Sunstar). The porous nature of the surfaces, made of a combination of a citric acid ester and polylactic acid, enables tissue ingrowth to stabilize the barrier. Additionally, there is nutrient perfusion from the periosteum to the treated defect. The material has been shown to have a low incidence of inflammation and infection and complete resorbability in the time required for guided tissue regeneration in humans. These barrier characteristics may be quite useful to the dental surgeon in cases where osseous defects are present, either around implants or where bone regeneration is required prior to their placement.

In a case presented in Figure 9 through Figure 11, the synthetic barrier was inserted at the time of removal of a tooth with significant bone loss on the palatal aspect (Figure 9). The rigidity of the material not only enabled containment of the bone replacement graft material, but also the initial formation of the site in the desired alveolar ridge shape (Figure 10). Six weeks later, there was no evidence of inflammation and the area was healing quite well (Figure 11). Not only was the alveolar ridge back to its ideal shape at the crest, but there was also a widened zone of keratinized tissue where primary closure was not attempted over the barrier.

**Putties**

To overcome some of the issues associated with conventional particulate bone graft materials, some putties have been developed for multiple uses, including sockets, lateral-approach sinus grafts, and alveolar ridge augmentations. The previously mentioned BPCS and PLGA/TCP are two such materials. Another is a combination demineralized/mineralized allograft in a collagen gelatin carrier (Optecure®, Exactech, www.exac.com), a semi-rigid material for ridge augmentation. Because the material has, according to the manufacturer, tested positive for osseoinductivity, the amount of vital bone formed in
these cases is significant.

The patient shown in Figure 12 presented with an alveolar ridge in the anterior mandible that was 1 mm wide starting 2 mm below the alveolar crest. The allograft putty was hydrated in sterile saline, covered with calcium sulfate (3D Bond™, Augma Biomaterials, www.augmabio.com) and an Ossix® Plus (Datum Dental Ltd, www.ossixdental.com) barrier, and primary closure was obtained. Narrow-diameter implants (ANEW®, Dentatus, www.dentatus.com) were used to assist in retention of a fixed transitional prosthesis. Four months later, dental implants were inserted, then restored another 4 months later. The clinical result is shown in Figure 13, which provides a 3-year post-loading view of the anterior mandible demonstrating the thickness and health of both the alveolar ridge and keratinized tissue.

Anorganic Bovine Bone Mineral

Early studies on lateral-approach sinus augmentation used anorganic bovine bone mineral as a graft. In a series of publications over many years, this xenograft was used alone, mixed with autogenous bone harvested from the patient, or mixed with growth factors from various sources. When the materials were used alone but covered with a barrier membrane covering the lateral window, there was a vital bone percentage ranging from 12% to 17% between 6 and 10 months postoperatively. Although this material has been shown to yield a high success rate when utilized in this manner, other materials and techniques have been investigated. One study demonstrated implant placement at the same time as sinus augmentation with only platelet-rich fibrin harvested from the patient as the material used to elevate the Schneiderian membrane. In this multi-center study, 25 patients had implants placed in 1.5 mm to 6 mm of residual maxillary bone at the same time as sinus augmentation. The resulting 50% vital bone at 6 months postoperatively enabled significantly faster restoration to function of the treated patients.

Conclusion

In their discussion of the histologic analysis of socket grafting with medical-grade calcium sulfate hemihydrate, Guarneri et al stated, “The goal of any grafting procedure is to achieve formation of 100% living bone tissue surrounding implants.” Depending on the size and location of the defect treated relative to adjacent sources of both progenitor cells and vasculature, this may or may not be possible. According to long-term studies on implant success rates in grafted bone, the incorporation of non-vital, non- or slowly resorbing particles may not make a difference. However, in studies that were done with fully resorbable materials, there appears to be a trend supporting earlier placement of dental implants than in other papers.

The bone replacement graft, barrier, and growth-enhancing materials presented in this discussion should give the surgeon some guidelines. Varying surgical approaches and types of materials affect both the volume of bone formed and the quality and amount of vital bone it contains. By determining the endpoint of the procedure 3, 6, 9, or more months down the line, an appropriate choice of technique and materials can be made. In this way, patients can receive optimal therapy backed by science, literature, and predictability.

DISCLOSURE

Dr. Leventis is a consultant to Sunstar Suisse SA, Etoy, Switzerland.


GUIDOR® easy-graft®

A NEW SYRINGE-DELIVERED, MOLDABLE, ALLOPLASTIC BONE GRAFT SUBSTITUTE

Kurt Ruffieux, PhD

Bone defects are treated using various sources. Autogenous bone is harvested from the patient at a donor site, eg, in the oral cavity or the iliac crest. This is the preferred solution for large defects. Autogenous bone contains living cells and factors that support bone regeneration. The grafted tissue is resorbed during the healing process and is gradually replaced by newly formed bone in a process called creeping substitution.1

When autogenous bone is placed on the alveolar ridge, volume losses of 30% to 60% have been observed over 1 year.2 Depending on the donor site and the technique, continuing problems such as loss of sensitivity and pain have been reported at the donor site in up to 55% of cases.3,4 Intraorally harvested bone chips are often contaminated with bacteria.5

Bone Graft Substitutes (BGS)
The limited availability of autogenous bone grafts and the risk of complications at the donor site have driven the development of bone graft substitutes (BGS) from an early stage. Bone graft substitutes act as an osteoconductive scaffold. They support bone formation, which starts from the wall of the defect and spreads through the bone graft substitute to the center of the defect. Bone graft substitutes also support and stabilize the surrounding structures and prevent volume loss at the site of the defect. They are classified by their origin.

Allogenic bone graft substitutes consist of processed human bone, generally from cadavers. The human material has the advantage of being available from accredited tissue banks. Allogenic bone is often available in a demineralized, freeze-dried form. Although allogenic materials yield good clinical results, they also have disadvantages that must be considered, such as the risk of disease transmission, particularly if the origin of the bone is obscure, and possible rejection reactions.6

Xenogenic bone graft substitutes are manufactured from non-human bone, such as bovine, porcine, or equine sources, and are therefore readily available. Xenogenic bone particles are known to resorb slowly and have been shown to remain embedded in newly formed bone after 11 years.7

Synthetic (alloplastic) bone graft substitutes are manufactured from mineral raw materials; their composition is precisely defined and availability is unlimited. There is no possibility of transmission of disease pathogens or rejection reactions. In general, patients do not have any ethical concerns when synthetic bone graft substitutes are used.

The most commonly used alloplastic bone graft substitutes consist of calcium phosphates, such as β-tricalcium phosphate (β-TCP) and hydroxyapatite (HA). Calcium phosphates have been in use in oral surgery for more than 20 years with very good results and are thoroughly scientifically documented.8 Their resorption characteristics can be controlled by the composition, ranging from fully resorbable to practically insoluble.

Use of the different bone graft substitutes varies worldwide from country to country (Figure 1). In the United States, allografts are preferred; in Europe, xenografts are used the most. Millenium Research9,10 attributes the highest...
growth rate to synthetics (Europe 9.9%, US 8.4%) due to the appearance of newly engineered products, such as GUID® easy-graft® (Sunstar, www.GUIDor.com), as well as increasing patient concerns regarding human- or animal-derived products.

**Improvement Potential for BGS**

Bone graft substitutes are mainly offered in the form of granules, which need to be placed in a bowl, mixed with blood or saline, transferred in several steps to the defect site, and be completely covered by a membrane to keep the granules stable in the site. This suboptimal handling procedure was the motivation to engineer a better, more user-friendly, less cumbersome product. The objective was to create a product that could be placed from the syringe directly into the defect, be moldable to the contours of the defect, and then harden to a stable scaffold. This goal was achieved by creating a novel composite biomaterial supplied in a syringe (as described below). Because of its unique easy handling properties it was named easy-graft.

GUIDOR easy-graft products are fully synthetic and do not contain any substances of human or animal origin. The granules in the syringe consist primarily of porous calcium phosphate (β-TCP). The unique handling of GUIDOR easy-graft is based on an extremely thin (10-μm) coating of polylactide around the granule (Figure 2). In medicine, polylactide is used to manufacture devices such as dental membranes, suture materials, resorbable screws, plates, and suture anchors for orthopedics. Before application, the granules are mixed with BioLinker® (Sunstar). This consists of water and N-methyl-2-pyrrolidone (NmP). NmP is a non-volatile solvent that has been in use in various medical products for more than 10 years. The

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Biolinker turns the coated granules into a sticky mass and allows moldability of the biomaterial (Figure 3), which starts to harden when in contact with blood (Figure 4).

**Resorption of Graft Material and Bone Formation**

The resorption process of GUIDOR easy-graft products has three stages:

1. N-methyl-2-pyrrolidone (NMP) is extracted within hours.
2. The polylactide coating (PLGA) is resorbed over a period of a few weeks.
3. The β-TCP resorbs and new bone is formed over the course of several months.

In the defect, NMP is extracted by incoming blood, which leads to hardening of the material. More than 90% of the NMP is removed from the bone graft substitute within 3 hours (unpublished in-vitro data, Sunstar Degradable Solutions AG). NMP itself and its resorption products are primarily excreted through the patient’s urine within 1 to 3 days. Once in the body the polylactide coating is resorbed over 3 to 6 weeks. Throughout this period the connection between the granules becomes gradually weaker until the adhesion is completely lost. During this time, the porous biomaterial is invaded by tissue, so the material becomes stabilized with the body’s own tissue.

The resorption of the polylactide releases small amounts of lactic acid and glycolic acid. Lactic acid is found naturally in the body. It is degraded in the body by metabolic processes. Glycolic acid is a fruit acid and can be degraded in the body or excreted with the urine.

When the β-TCP granule is exposed, it is accessible for the tissue. The larger pores between the granules provide space for the formation of new bone and for the development of blood vessels, which are required for supplying the new tissue and to remove metabolic products. Fully microporous calcium phosphates (pore size 1 μm to 10 μm) have increased osteoconductivity and increased bone formation in comparison with materials without micropores. Full resorption in a few months has been confirmed.

The GUIDOR easy-graft granules are openly microporous. Micropores exist in the spaces between the round, pressure-resistant granules and the interior of the particles.
To simplify clinical handling, new materials should comprise a matrix with optimal cell ingrowth capacities and good mechanical properties, providing space for tissue regeneration. No membrane and no specific procedures for mechanical fixation should be necessary.

(Figure 5 through Figure 7). The total porosity is approximately 70%. In this development of bone graft substitutes, attention was paid to ensuring that the material would not fragment or crumble during application to make sure that a comprehensive, intact pore system is retained. Figure 8 shows bone formation around the granules in a rabbit cranial model after 16 weeks.¹⁵

**Unique Properties**

As formulated by Hammerle and Jung in 2003: “Developments in bone augmentation procedures can be related either to simplification of the clinical handling or to influencing of biological process.

**About the Author**

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**References**

CASE REPORT

EXTRACTION SITE PRESERVATION USING AN IN-SITU HARDENING ALLOPLASTIC BONE GRAFT SUBSTITUTE

Minas D. Leventis, DDS, MS, PhD; Peter Fairbairn, BDS; and Robert A. Horowitz, DDS

ABSTRACT

This case report highlights the use of an in-situ hardening alloplastic bone grafting material composed of beta-tricalcium phosphate (β-TCP) granules coated with poly(lactic-co-glycolic acid) (PLGA) to preserve the dimensions and architecture of the alveolar ridge after atraumatic extraction. This material provided a stable scaffold that, although left uncovered, deterred the ingrowth of unwanted soft tissue, allowing newly formed keratinized soft tissue to proliferate over the healing grafted socket and gradually cover the site. At re-entry after 4 months adequate newly formed bone was observed, allowing for the correct positional placement of an implant. The results of this case suggest that an in-situ hardening alloplastic grafting material can be successfully utilized with minimally invasive procedures to preserve the bone and the soft-tissue profile of the alveolar ridge for future implant rehabilitation.

Clinical and experimental studies have shown that tooth extraction leads to bone resorption and atrophy of the alveolar ridge, especially when associated with disease, which may complicate proper future implant placement. Atraumatic extraction followed by immediate socket grafting seems to be a predictable way to preserve the dimensions, contour, and architecture of the alveolar frame and the residual ridge.1-3 Surgical methods that do not require primary soft-tissue closure by flap mobilization have the added benefit of further minimizing patient discomfort and morbidity, while allowing for the preservation of the soft-tissue profile for optimum esthetics and greater predictability.4

In clinical practice several bone graft substitutes of biologic or synthetic origin are being used for socket preservation and bone regeneration prior to implant placement. These materials may

FIG 1. Initial clinical situation. Mandibular right lateral incisor was fractured.

FIG 2. Atraumatic extraction without flap raising. The socket was grafted with the in-situ hardening alloplastic material. No primary closure was necessary. Vertical cross-mattress sutures were placed to stabilize the adjacent papillae.
vary in composition, mechanical characteristics, and biological mechanism of function regarding resorption and new bone formation, each having its own advantages and disadvantages.¹²

Alloplasts represent a group of synthetic osteoconductive, biocompatible bone substitutes that are free of any risk of transmitting infections or diseases by themselves, and their availability is unlimited. One of the most promising groups of alloplastic bone substitutes are calcium phosphate ceramics, and among them β-TCP is very commonly used.⁵ Coating the alloplastic graft granules with pLGA can enhance the handling properties and biomechanical characteristics of the material, and produce an in-situ hardening, stable, and at the same time porous and osteoconductive bone graft substitute.⁶

**Case Report**

A 65-year-old male patient, non-smoker, without medical contraindication for implant therapy presented with a fractured mandibular right lateral incisor (Figure 1). After thorough examination a delayed implant placement protocol was decided. After administration of local anesthesia the fractured tooth was atraumatically extracted using periomes without raising a flap. Care was given not to damage the surrounding soft and hard tissues and especially the thin buccal bone plate that was identified intact after removal of the tooth fragments. After thorough debridement and rinsing with sterile saline, an alloplastic in-situ hardening bone substitute (GUIDOR® easy-graft® CLASSIC, Sunstar, www.GUIDOR.com) was used to graft the site (Figure 2). It consists of β-TCP granules, which are coated with PLGA. The granules are mixed in a syringe with the provided BioLinker® (N-methyl-2-pyrrolidone solution) (Sunstar). Upon contact with blood or saliva the graft granules adhere to each other forming a sticky, easy-to-handle, moldable mass that begins to harden. Wet gauze can be used to compact the material and accelerate this process so as to form a hard, osteoconductive, porous scaffold for the host osseous regeneration.

The grafted socket was left uncovered in order to heal by secondary intention. A prefabricated provisional removable one-tooth bridge was placed after the surgery without applying pressure to the grafted site. The postoperative healing was uneventful. The biomechanical characteristics of the grafting material permitted the gradual proliferation of the epithelium over the grafted site (Figure 3 and Figure 4), and after 4 months the area was covered with newly formed keratinized epithelium. At that time point clinical examination showed that the volume and architecture of the ridge were adequately preserved (Figure 5).

At re-entry after 4 months, the post-extraction site was filled with newly formed bone. Residual granules were visible, embedded, and in continuity with the regenerated hard tissue (Figure 6). An implant (Paltop Advanced Dental Solutions Ltd., www.paltopdental.com) 3.25 mm in diameter and 11.5 mm in length was inserted at the optimal position (Figure 7), achieving good initial stability (final seating torque: 50 Ncm). The final titanium abutment was placed and a provisional acrylic restoration with a non-functional occlusion was temporarily cemented (Figure 8).

After allowing the soft tissue to mature for 3 months the abutment-level impression was taken and a final metal-ceramic restoration was fabricated (Figure 9). The final clinical outcome was esthetically successful. The radiological examination from the initial situation to the final outcome demonstrated that the socket grafting and the subsequent bone regeneration of the site had been successful regarding biological and functional parameters (Figure 10).

**Discussion**

In this case a minimally invasive, flapless protocol was followed. No membrane was used to cover the grafted post-extraction site. The mechanical stability of the site, provided by the unique biomechanical
properties of the in-situ hardening bone graft substitute, allowed the site to heal by secondary intention. This resulted in the preservation of the attached keratinized gingiva buccally and permitted the development of newly formed keratinized soft tissue over the grafted site. Primary flap closure patients generally experience more discomfort and the mucogingival junction is significantly more coronally displaced, which may result in esthetic problems and could negatively influence peri-implant soft-tissue health and long-term stability.

The use of β-TCP as a resorbable socket grafting material can preserve space for bone formation until new bone is formed, obtaining high-quality regenerated vital bone, without any nonresorbable grafting material embedded in the bone matrix after several months. Thus, the peri-implant bone will be able to adapt according to Wolff’s law after the occlusal loading of the implant through functional remodeling. It is suggested that the long-term presence of residual nonresorbable or slowly resorbable graft particles might interfere with normal bone healing and remodeling, may reduce the bone-to-implant contacts, and have a negative effect on the overall quality and architecture of the bone that surrounds the implant.

Conclusion
In the presented case, an in-situ hardening alloplastic bone grafting substitute was used in a minimally invasive, successful, and predictable way for socket preservation, resulting in pronounced regeneration of bone capable of supporting implant placement after a 4-month healing period, and capable of remodeling and maturing after loading. The in-situ hardening property of this material may enable clinicians to utilize a flapless procedure without primary wound closure that reduces patient morbidity, preserving the attached keratinized gingiva and allowing for further production of newly formed keratinized soft tissue. Thus, both hard- and soft-tissue preservation and regeneration have been utilized in achieving an optimal soft-tissue profile both esthetically and functionally allowing for improved long-term implant stability.

DISCLOSURE
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