

CASE REPORT

Alveolar ridge augmentation with 3D-printed synthetic bone blocks: A clinical case series

Alexandre Perez¹  | Benjamin Lazzarotto² | Laurine Marger² | Stéphane Durual² 

¹Unit of Oral Surgery and Implantology, Division of Oral and Maxillofacial Surgery, Department of Surgery, Faculty of Medicine, University of Geneva & University Hospitals of Geneva, Geneva, Switzerland

²Division of Fixed Prosthodontics and Biomaterials, Biomaterials Laboratory, University of Geneva, University Clinics of Dental Medicine, Geneva, Switzerland

Correspondence

Stéphane Durual, Division of Fixed Prosthodontics and Biomaterials, Biomaterials Laboratory, University of Geneva, University Clinics of Dental Medicine, 1 Rue Michel Servet, 1204 Geneva, Switzerland.
Email: stephane.durual@unige.ch

Abstract

This report documents the clinical and histological outcome of 3D-printed calcium phosphate blocks placed in two-stage procedures to successfully rehabilitate atrophic alveolar ridges. This approach yielded a functionally favorable result. Histological evaluations were performed after healing periods of 6 months and showed ongoing bone regeneration and sprouting capillaries.

KEYWORDS

3D-printing, alveolar bone regeneration, bone block grafting, calcium phosphate

1 | INTRODUCTION

Loss of alveolar bone is an inevitable issue after tooth lost. When the deficient ridge does not allow a correct three-dimensional positioning of the implants and primary stability cannot be ensured, a bone augmentation must be conducted. Furthermore, the extent of atrophy of the alveolar crest dictates whether the ridge augmentation can be performed simultaneously with implant placement or as a staged procedure.^{1,2}

Different surgical techniques are currently being used to restore appropriate bone volumes quantitatively and qualitatively, including guided bone regeneration, bone block grafts, osteotomies of the ridge, distraction osteogenesis, or a combination of the above.³⁻⁵ To do so, a variety of grafting materials have been developed and classified

according to their origin: autogenic, allogenic, xenogenic, and alloplastic (i.e., synthetically produced).^{6,7}

Numerous combinations of techniques and materials have been studied, with different levels of evidence.

Regarding severely compromised ridges, where the planned implant position is outside the bony envelope, a staged surgical protocol is indicated. The current routine technique for extensive augmentation is the use of autologous corticocancellous bone blocks harvested from intra-oral sites.⁸⁻¹⁰ This method is considered the gold standard as the graft is osteogenic (i.e., containing bone cells precursors), osteoinductive (i.e., containing bone growth factors), and osteoconductive (i.e., acting as support for bone growth). Clinical results are excellent with high survival rates.¹¹ However, low bone volumes available, limited donor sites combined to surgical morbidity represent

Alexandre Perez and Benjamin Lazzarotto contributed equally to this work.

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severe limitations^{12,13} that led to the development of new materials as substitutes for alveolar bones. Among the variety of non-autologous materials, alloplastic biomaterials are a large group in which calcium and other elements are combined, for example, hydroxyapatite (HA), tricalcium phosphate (TCP), and calcium sulfate. Alloplastic graft materials stand as an ambitious alternative to autogenic bone grafts, as they are highly biocompatible and support bone formation, although entirely synthetic.¹⁴ They act as a scaffold supporting bone growth thanks to their porosity and three-dimensional architecture. Thus, they only display osteoconductive properties but may be combined to growth factors, for example, BMPs to gain additional osteoinduction.^{15–17}

Bone grafts' architectural control is an essential parameter to optimize both bone and vascular tissue growth. With that respect, 200–500 μm interconnected porosity is believed the ideal ranging.^{18–20} As for the issue of a random versus a regular and controlled porosity, it remains an opened question even if regular pores seem to improve early bone and vascular growth.²¹ However, random porosity is still largely used with successful result.²² These bone grafts are presented in the form of blocks or particulates, either from natural (auto-, allo-, or xeno-genic) or synthetic origin. The random porosity is conserved from native bone in natural grafts when several techniques are described to obtain it in synthetic ones.²¹

In another hand, if one want to obtain a regular and controlled porosity, 3D printing is a method of choice. In a series of studies, we have characterized a calcium phosphate 3D-printed scaffold and demonstrated its powerful ability to promote early bone regeneration.^{23,24} 3D printing should eventually allow for designing and producing defect-adapted grafts in terms of morphology, all with complete control of the internal architecture. Another possibility consists in milling of synthetic bone blocks into the digitally planned shape based on patient's defects.^{25–27} By using this method, the surgical procedure appears to be simplified compared to conventional procedures, which are based on manual intraoperative modeling of the block.

Considering the synthetic 3D printed grafts, it is in fact the latter conventional solution that is clinically available at this time. Once these 3D-printed blocks will have clinically proven satisfactory, which should not be a problem given the preclinical results, adapting the printing process within a 100% digital process of taking an impression of the defect will probably be solved very quickly.

Therefore, the objective of this case series was to achieve a first milestone in this context and to document the clinical and histological outcomes of 3D-printed alloplastic block grafts made of calcium phosphate and used in the indication of augmentation of the atrophic alveolar ridge.

2 | CASE SERIES SETUP

This case series documents the treatment of two patients that consented to undergo routine dental implant therapy following bone augmentation at the University Hospital Geneva (Switzerland) in 2020. Written informed consent was obtained from all patients to treat, document and publish the treatment-related data. Treatments and reporting adhered to the Helsinki Declaration of ethical principles by the World Medical Association. The study did not require approval of the Ethics Commission on Human Research of Geneva (CCER-Geneva) according to the Federal Human Research Act (Art.3a1.a) since the study involved less than five patients.

3 | CASE 1

A 39-year-old woman consulted the Unit of Oral Surgery and Implantology of the Geneva University Hospitals with a request to restore a missing mandibular left canine, which was removed years ago due to deep impaction. The patient was healthy, she took no medication and was a non-smoker. A complete clinical and radiographic examination was carried out. Cross-sectional images were acquired, showing severe horizontal bone atrophy at site 33 (Figure 2A,B). The treatment plan comprised a staged horizontal block graft augmentation.

A mucoperiosteal flap was raised on the facial and lingual aspects to obtain a clear view of the underlying absorbed alveolar ridge. Small perforations were drilled in the remaining alveolar bone, in order to favor revascularization of the graft. A synthetic bone block (Innotere 3D Scaffold, Innotere GmbH) was manually shaped to the recipient site anatomy, then fixated and stabilized by means of a titanium screw (Medartis) (Figures 1A,B; 2C,D). In addition, xenogenic bone particles (OsteoBiol GenOs, Tecness) and a collagen membrane (OsteoBiol Evolution, Tecness) were used to cover the augmented site entirely. After a periosteal-releasing incision, soft tissues were carefully reapproximated and sutured for primary wound closure (Figure 1C). The patient received oral antibiotics (amoxicillin with clavulanic acid 2 g/d for 5 days), and was instructed to rinse daily with chlorhexidine 0.12%.

After an uneventful healing period of 6 months, a re-entry surgery was performed. The fixation screw was removed. A bone core biopsy was obtained with a trephine drill in the grafted implant bed at site 33, drilling being prosthetically guided with a surgical template (Figures 1D,E). Bone core retrieved from the implant site was processed and stained according to standard protocols. Histological evaluation of the augmented bone is detailed further.

FIGURE 1 (A) Preoperative situation. (B) Fixation of the scaffold is obtained by means of a small titanium screw. (C) 10 days after surgery sutures are removed. (D) Augmented site after a healing period of 6 months, when reentry surgery is performed. (E) The site of the core biopsy is marked on the augmented ridge. (F) Implant depth gauge positioned subsequently of the core-biopsy. (G) Local status after a healing period of 5 months. (H) The definitive restoration is delivered. (I) 22-months follow-up examination.

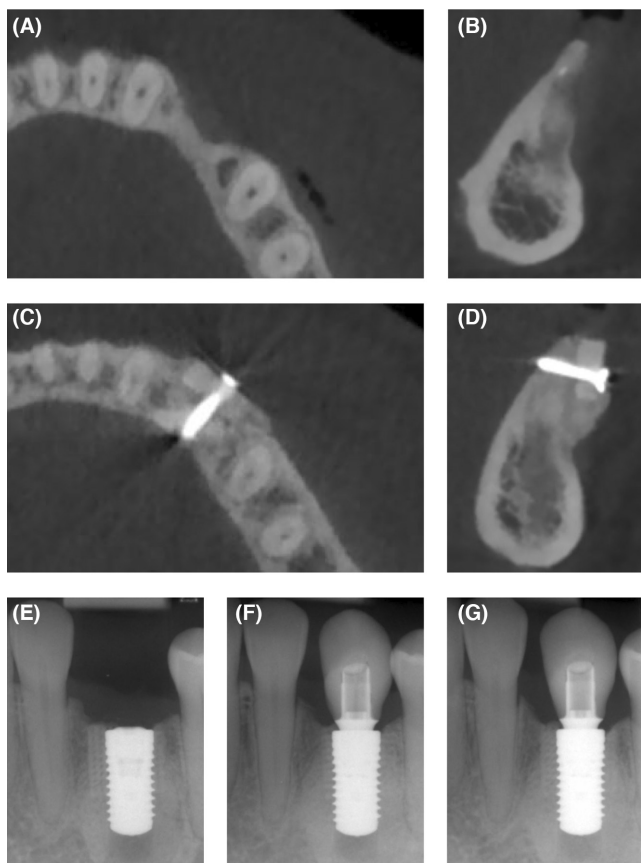
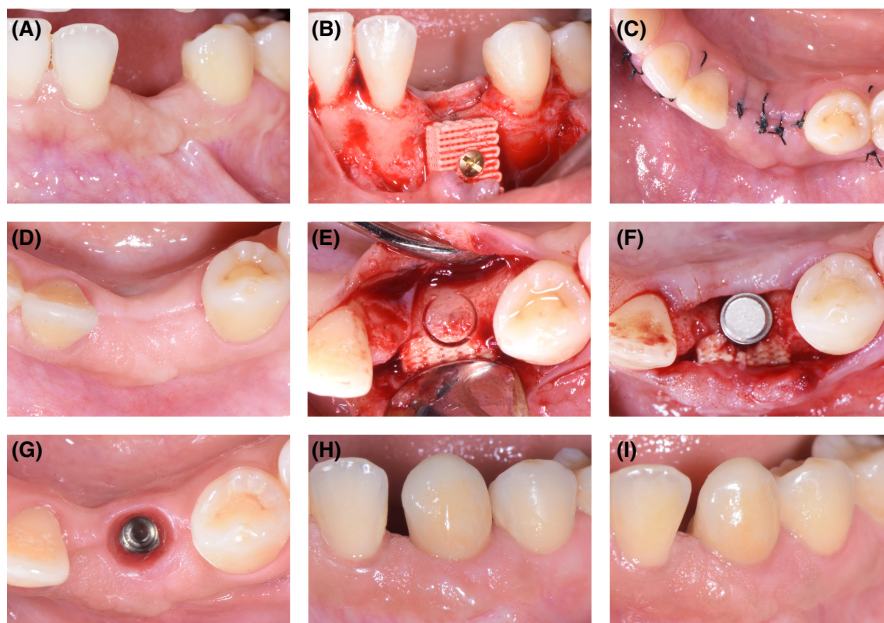


FIGURE 2 (A, B) Pre-operative CBCT, axial and sagittal views, respectively. (C, D) Post-operative 3D examination, axial and sagittal views, respectively, shown at the level of the titanium screw. (E) Periapical 2D radiographs taken immediately after implant placement and (F) after the screw-retained restoration is delivered. (G) Radiographic examination after a 22-months follow-up period.

Then, upon completion of site preparation ([Figure 1F](#); [2E](#)), one implant was inserted at site 33 in accordance with the restorative plan, and achieved adequate primary stability.

After a healing period of 5 months, implant was restored with a screw-retained single-unit crown ([Figures 1G,H](#); [2F](#)). The implant-supported restoration showed good esthetic and functional results after a follow-up period of 22 months after loading ([Figure 1I](#); [2G](#)).

4 | CASE 2

A 61-year-old woman presented with a request to restore her multiple posterior edentulous sites with fixed implant-supported restorations. The patient was systematically healthy and a nonsmoker. A cone-beam computed tomography was taken, demonstrating severe horizontal bone atrophy at site 24–26 and 45. A staged ridge augmentation was necessary for each site.

For each site preparation, surgical procedure was basically performed as discussed in case 1. After site preparation, synthetic bone blocks (Innotere 3D Scaffold, Innotere GmbH) were shaped to surgical sites and stabilized using fixation screws. Blocks were covered with a collagen membrane (OsteoBiol Evolution, Tecness). Flaps were closed by primary intention without tension after interrupting the periosteal layer and releasing the flap.

The post-bone grafting protocol also followed similar guidelines. After 6 months of healing, the sites were reentered. A bone core biopsy was performed to obtain bone sample in each grafted site, and detailed analysis is

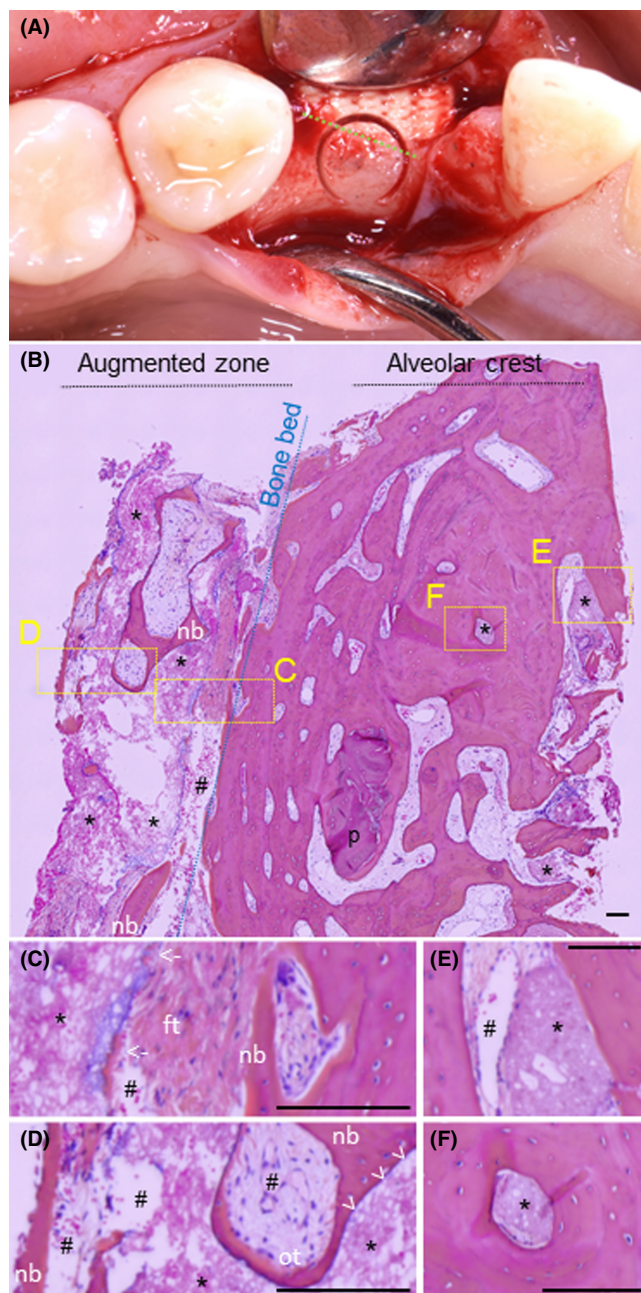


FIGURE 3 Representative picture and histological slides (hematoxylin staining) showing a reconstructed alveolar crest by using a 3D-printed alloplastic block after 6 months healing. (A) Picture of the surgical site on which the biopsy was harvested before implant placement. Green dotted line: histology cut axis. (B) The bone substitute block was integrated to the crest profile and largely colonized by new bone and active osteoid or fibrous granulation tissue largely vascularized. The block was nicely osseointegrated in bone growing zone (C, D) as well as in mature bone zones in which the bone substitute supported lamellar bone formation (E, F). Bone and new bone appear as purple. (nb: new bone, P: tecnoss particle, *: alloplastic 3D-printed block, #: capillaries). (C) Higher magnification of the interface between the block and bone bed in which a vascularized fibrous granulation tissue (ft) ongoing ossification (\rightarrow) is observed. New bone from the bone bed is not fully mature and presents signs of remodeling. (D) Higher magnification of the bone block at ca. 500–1000 μm from the bone bed. Canals from the block are filled with growing new bone and highly vascularized osteoid tissue (ot). Note the tight contact between the block and the new bone that reflects a great osseointegration ($>$). (E) Another example of the block osseointegration, higher magnification from the posterior view of the bone bed. (F) Higher magnification of a bone block strut osseointegrated and supporting mature lamellar bone. Posterior view from the bone bed. Black bars: 100 μm .

reported further. Implants were subsequently placed at site 24, 26, and 45 in accordance with the restorative plan, with good primary stability.

Five months later, following successful osseointegration, screw-retained restorations were provided. The seventeen-months follow-up examination demonstrated satisfactory esthetic and functional outcomes.

5 | HISTOLOGY

Bone core biopsies were fixed in formalin 10% and then decalcified in EDTA for 3 weeks before dehydration and embedding in paraffin. Samples were sectioned transversally along an axis showing the maximum of bone tissue,

bone bed, and bone substitute (Figure 3A) (thickness of 5 μm). Hematoxylin–Eosin staining was then performed and slices were observed with a stereo video microscope (VHX-5000, Keyence).

Macroscopically, the bone substitute was integrated to the alveolar crest to depict a natural profile. Bone from the crest was mature, active and largely vascularized. New bone tissue was observed within the scaffold canals (Figure 3B–D). The bone substitute was largely osseointegrated even at the bone bed level and at distance from the latter. At the interface between the bone bed and the scaffold, new bone was seen as well as fibrous granulation tissue highly vascularized underway of ossification (Figure 3C). At distance from the bone bed (about 1 mm), new bone tissue was observed as well as a largely vascularized and active osteoid tissue with rows of osteoblast (Figure 3D). The bone substitute also supported the growth of mature lamellar bone (Figure 3E,F). We could not observe any sign of scaffold resorption, as well as any sign of inflammation.

6 | DISCUSSION

We present onlay techniques using 3D printed alloplastic bone blocks, for extensive horizontal augmentation of deficient alveolar ridges. This work falls within an extensive preclinical research project dealing with synthetic bone substitutes.

Patients presented severe atrophy of the alveolar ridge, with marked reduction of the horizontal width. To overcome mandibular atrophy, an onlay approach was selected. The graft procedures we present resulted in an uneventful healing process, without dehiscence or membrane exposure. No signs of inflammation or adverse material reactions were detected. Six months after alveolar augmentation, the radiographic evaluation showed well integrated blocks. Primary stability of the implants was achieved in all cases. All implants were osseointegrated, and no failures or dropouts occurred. All patients were enrolled in a maintenance program for the entire follow-up period in order to obviate a common risk factor of implant failure.²⁸ Other factors such as systemic conditions, which have also been linked with an increased risk of implant failure,^{29,30} are not discussed in the present research but may be relevant when considering treating patients with the present surgical protocol.

Although oral and maxillo-facial practitioners are more used to granular form of synthetic bone substitutes, current manufacturing technology allows optimizing osteoconductive properties, and permit to consider the use of synthetic bone blocks. The blocks herein used are printed with a clinical grade phosphocalcic cement and gamma sterilized once hardened. Their chemical composition that is a combination of α TCP and calcium-deficient hydroxyapatite, combined to an optimal porosity of ca. 60% and an architecture designed for osteo- and vasculo-conduction make it the ideal bone scaffold in terms of biocompatibility.

Osteoconductive properties of the implanted material have already been tested in different preclinical settings. When these blocks were grafted on sheep calvaria, they over performed traditional granular bone substitutes, either xenogenic or synthetic, by two-fold.²³ The blocks also proved satisfaction when used for mandibular bone augmentation in dogs.²¹

Samples from the present study, taken during the implant bed preparation, allowed a remarkable histological insight of the block integration. Core-biopsies demonstrated new bone surrounding the biomaterial particles, many large vessels and in some fields osteoblasts apposing bone directly on the particle surface, which is perfectly in line with the preclinical results.

Stabilization and fixation of the block is of crucial importance in the treatment outcome. In the reported cases, standardized bone blocks were trimmed chair-side. The requirement for manual, intraoperative shaping of the blocks has often been a key concern. Indeed, surgeons are forced to spend a variable amount of operating time adapting the block to the defect's geometry. The procedure is demanding with regard to surgical skills, and may result in an unsatisfactory donor-recipient fit. A poor adaptation may result

in intraoperative block fracture, and have already been demonstrated to compromise the bony integration in orthopedics applications of BCPs.³¹ In order to further simplify the surgery, reduce the surgical time and maximize the fitting to the recipient site, 3D-impression of custom-made scaffolds appears to be the logical evolution of the product, and is feasible with the present phosphocalcic cement. There is currently no commercial service for this application but a series of clinical studies using this technology demonstrated highly encouraging results.^{32,33} This augmentation technology is promising and may fulfill the technical needs of reconstruction of complex bone defects, opening new horizons for alveolar ridge augmentation.

It is important to note that the block has a resistance similar to trabecular bone, that is, 12MPa. However, its highly porous architecture combined to a brittle phosphocalcic major compound makes it a relatively fragile material. In addition, the block has to be fixed and customized, two prerequisites needing a drilling to let the fixing screw passing and to adapt the block morphologically to the bone bed. These treatments may fragilize the block by creating microcracks within the structure. Considering these mechanical statements, it is highly recommended to keep in mind that implants need to be placed in a junctional and mix of native – augmented bone, so that the primary stability is not only ensured by the scaffolded bone but partially with native bone. Once the scaffolds will be printed with fixation holes and a design intimately adapted to the defect, scaffold resistance should be largely improved and may permit further latencies in implant placement.

Regarding alloplastic grafts, degree of graft incorporation has been a matter of controversy. As the new tissue develops, it is expected for an optimal biomaterial to undergo gradual substitution until complete disappearance. Concerning biphasic calcium phosphate, variable degradation processes were described, with indeed little change observed in the macrostructures over a long period of time,³¹ a trend confirmed preclinically with our 3D-printed blocks.²⁴ This statement is also verified with some of the most used particulate xenogenic scaffolds.^{4,34,35} The cases that were described in this study also confirm this delay in material resorption. In this context, it will be interesting to focus on indications where long-term maintenance of soft tissue and anatomical structure is required. That being said, no stability problems were observed after a follow-up period of almost 2 years, and patients did not experience any discomfort or feeling of instability of their implant in the cases herein described. Finally, if it is well known that these types of ceramics may spend several years to be resorbed,¹⁴ they will be resorbed in any case in the end to give way to the endogenous tissue. We were able to show in preclinical studies that by accelerating bone metabolism, the material could be largely resorbed.²⁴

7 | CONCLUSION

The use of 3D-printed alloplastic block seems to represent a valuable and predictable surgical alternative technique for reconstruction of extensive alveolar ridge defects. This case series may provide more clinical and histological data on the use of synthetic materials. Further investigations, especially in terms of long-term stability of both augmented bone and implants, are undeniably needed to conclude regarding the performance of alloplastic blocks.

AUTHOR CONTRIBUTIONS

Alexandre Perez: Conceptualization; investigation; methodology; writing – review and editing. **Benjamin Lazzarotto:** Investigation; methodology; writing – original draft; writing – review and editing. **Laurine Marger:** Investigation; methodology; writing – review and editing. **Stéphane Durual:** Conceptualization; formal analysis; investigation; resources; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest. No benefit of any kind has been or will be received either directly or indirectly by the authors.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

ORCID

Alexandre Perez  <https://orcid.org/0000-0002-7804-2388>

Stéphane Durual  <https://orcid.org/0000-0002-9772-8406>

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