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Type of the Paper (Case report)

Design techniques to optimize the scaffold performance: freeze-dried bone custom-made allografts for maxillary alveolar horizontal ridge augmentation

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Abstract: Background: The aim of the present investigation was to evaluate the clinical success of horizontal ridge augmentation in the severely atrophic maxilla (Cawood and Howell class IV) using freeze-dried custom made bone harvested from cadaver donors tibial hemiplateau and to analyze the marginal bone level gain prior dental implants placement at 9 months after bone grafting and before prosthetic rehabilitation.

Methods: A 52-year-old woman received custom made bone grafts. Patient underwent CT scans 2 weeks prior and 9 months after surgery for graft volume and density analysis.

Results: The clinical and radiographic bone observations showed a very low rate of resorption after bone graft and implant placement.

Conclusions: The custom-made allograft material was a highly effective modality for restoring the alveolar horizontal ridge, resulting in this way to reduce the need to obtain autogenous bone from a secondary site with predictable procedure. Further studies are needed to investigate its behavior at longer time points.

Keywords: Geometry optimization of scaffolds; allograft; block bone grafts; custom made bone; design techniques for scaffold; precision and translational medicine.

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1. Introduction

Implant-supported rehabilitation of the edentulous ridge require adequate volume and integrity of the alveolar bone [1].

Bone resorption in the maxillary ridge, due to trauma, pathology or tooth loss, frequently results in a knife-edged deformity, which complicates implant placement and stabilization, particularly in the posterior jaw [2-4]. Grafting with allograft bone has been documented to be a useful tool in reconstructing jaw anatomy, [5] restoring esthetics [6] and providing biomechanical support for the placement of dental implants [7].

Clinically, the most useful banked allografts are fresh-frozen, freeze-dried, and demineralized bone [8]. Frozen bone is harvested aseptically from live or cadaveric donors and then frozen. It is available for human recipients after at least 6 months of quarantine at −80°C [9] and no additional preparation is required, and the osteoinductive proteins are preserved [10]. Strict guidelines for tissue harvesting and storing at -80°C make the risk of primary infections and antigenicity acceptably low [11].

Frozen bone is available as cancellous granules/blocks, corticocancellous granules/blocks, and cortical granules or chips. Once thawed, it has the same handling qualities as does fresh bone [8].

Bone density can be measured with high reproducibility by means of Cone-Beam-Computed-Tomography (CBCT) scans, which provide standardized values on the Hounsfield scale (HU) [12]. Other methods, which have been used, as intraoral radiographies, do not guarantee appropriate accuracy in density determination [13].

The aim of this study was to evaluate the clinical success of horizontal ridge augmentation in the severely atrophic maxilla (Cawood and Howell class IV) using custom made bone harvested from tibial hemiplateau of cadaver donors and to analyze the marginal bone level of dental implants placed at 9 months after bone grafting and before prosthetic rehabilitation. Moreover a subjective and objective evaluations were performed.

2. Materials and Methods

A 52-year-old woman presented compromised anterior maxillary ridges, who presented for the placement of dental implants, were included in this pilot study. Written and verbal information were given to the patients before enrollment, and written informed consent was obtained. The study was conducted in full accordance with the World Medical Association Declaration of Helsinki on experimentation involving human subjects, as revised in 2008.

Inclusion criteria was a horizontal severely atrophic maxilla (Cawood and Howell class IV), needing a bone grafting procedure prior to implant placement. Exclusion criteria were history of recent infection, pregnancy, metabolic disorders, immunocompromised status, drug or alcohol abuse, history of radiation therapy in the head and neck, psychiatric disorders and inability to understand the described procedure and to sign the informed consent form. Plaque index score was maintained ≤25% throughout the study [14].

Graft Samples Blocks

The processing was performed on corticocancellous bone blocks obtained from a proximal tibial epiphysis, in the anatomical region between the articular surface of the tibial plateau and tuberosity.

Human allogeneic bone blocks were collected from cadaveric donors, stored at -80° C and processed in the accredited public non-profit Musculoskeletal Tissue Bank of IRCCS Istituto Ortopedico Rizzoli (Bologna, IT), authorized by Italian National Transplant Center for the collection, processing and distribution of human musculoskeletal tissue [http://www.trapianti.salute.gov.it/trapianti/dettaglioContenutiCnt.jsp?lingua=italiano&area=cnt&menu=chiSiamo&sottomenu=rete&id=237] and registered in the European Tissue Establishment list (code IT000096). The

choice of the block to be machined occurred considering dimensions slightly greater than the machining area defined accordingly with the graft design.

After thawing, each block was fixed with clamps on a special stainless-steel table in a GMP-Class A Clean Room environment. Then, the table was fixed inside the CNC milling machine (model Bright, Delta Macchine, Rieti, Italy). After tool fixing, a 3 mm diameter ball mill, the execution of the machining trajectory was started and accurately monitored by operator.

At the end of the processing, the block was removed and finished: the supports were broken by hand and sharp edges and rough corners were hand-refined using sterile rasps. Then, grafts were cleaned with organic solvents, washed with sterile water, and freeze-dried (VirTis Genesis 25, SP Scientific, Warminster, PA, USA). Finally, grafts were individually wrapped in triple pack. Microbiological sampling was performed during the processing of grafts and after the lyophilization protocol in order to exclude microbial contamination and declare tissues suitable for implantation.

According to the Guidelines of the Italian National Transplant Center lyophilized bone grafts are preserved at room temperature for a maximum of 5 years.

Graft design

Digital Imaging and COmmunications in Medicine (DICOM) data of the maxilla [Figure 1] were acquired by Cone Beam Computerized Tomography (CBCT) scanner (GinoX) and imported into the 3DSlicer software (www.slicer.org) [16-18].

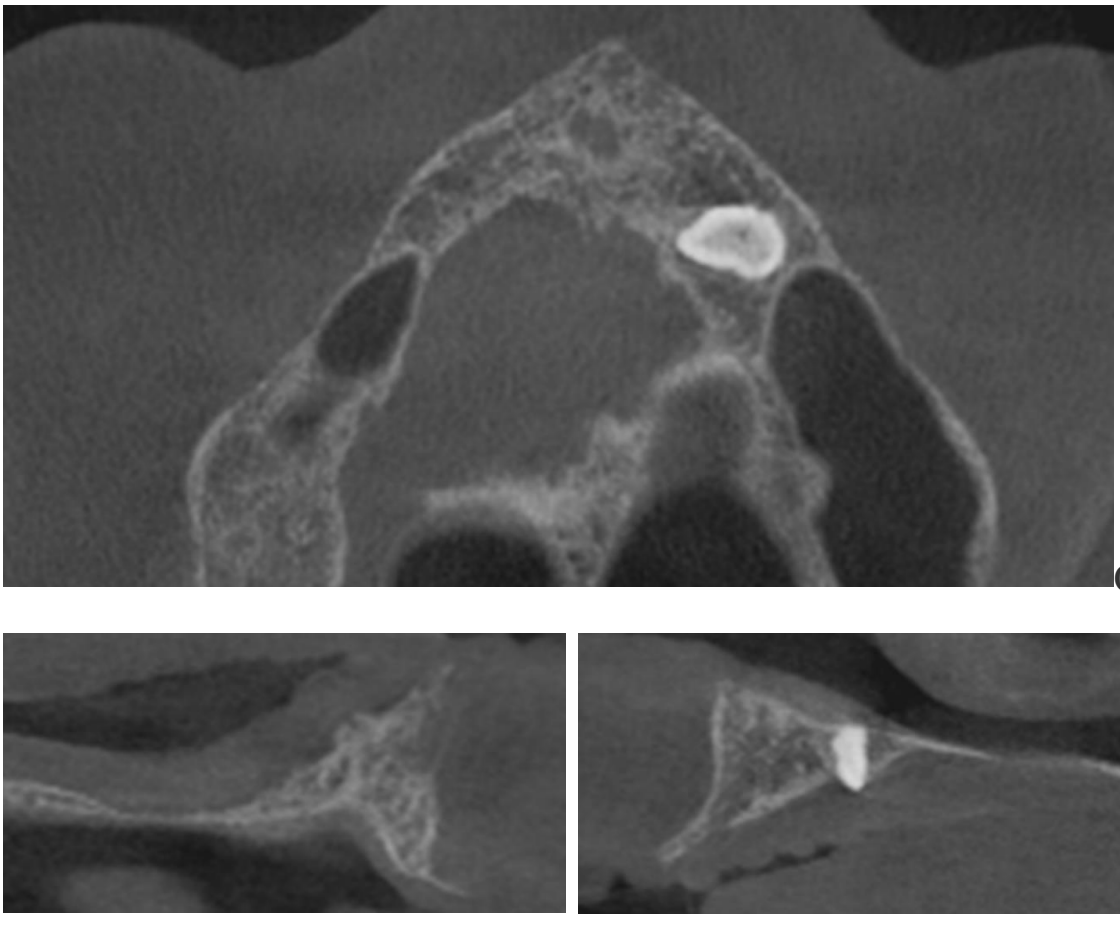
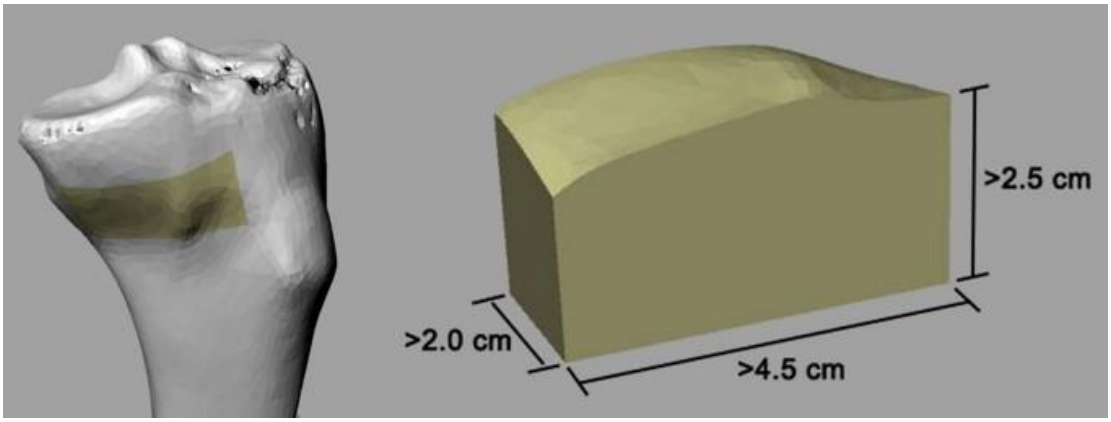


Figure 1. Preoperative anatomic situation on CBCT axial (a) and cross-sectional (b 1-2) images.

After a threshold setting for the automatic selection of the areas delimiting the cortical bone, a manual analysis for each slice was performed to correct potential errors. Starting from the selected areas, an automatic procedure generated the 3D model as STL file.

The graft design was performed by Rhinoceros ver. 4 (www.rhino3d.com) following these steps: a) placement of a parallelepiped in the position where the volume increase was required; b) Boolean subtraction between the parallelepiped and the STL model of the patient's anatomy; c) revision of the model for the manufacture by a 3-axis milling machine to obtain a L–shape section. This procedure was performed for each graft.

The design of the grafts has been repeatedly validated and subsequently corrected following the surgeon's indications, up to the final model [Figure 2].



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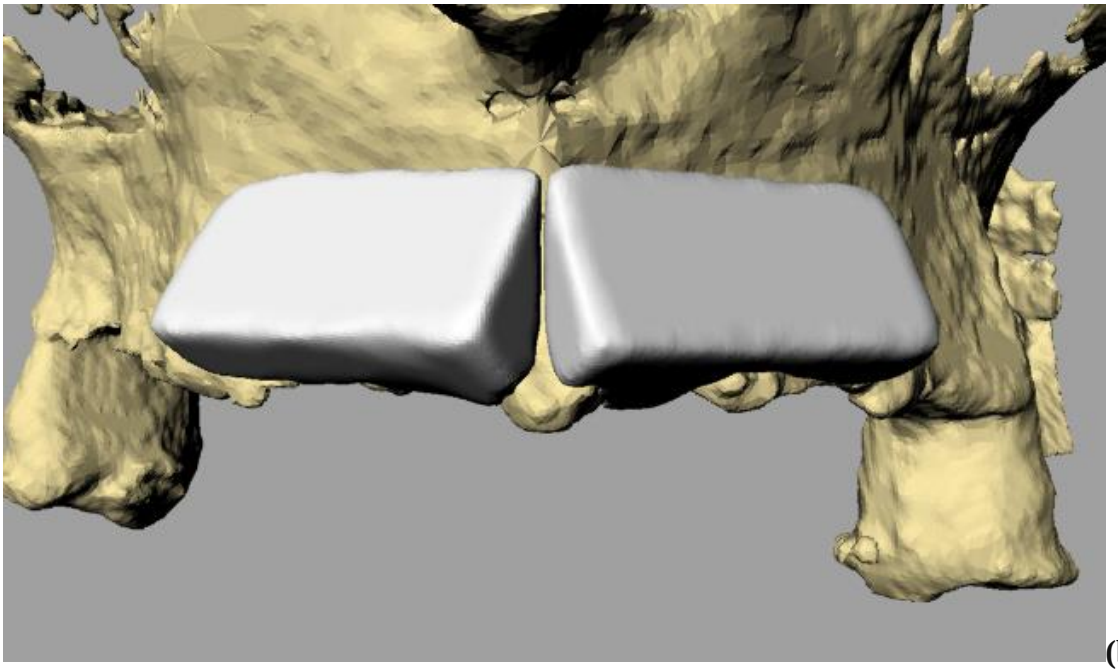

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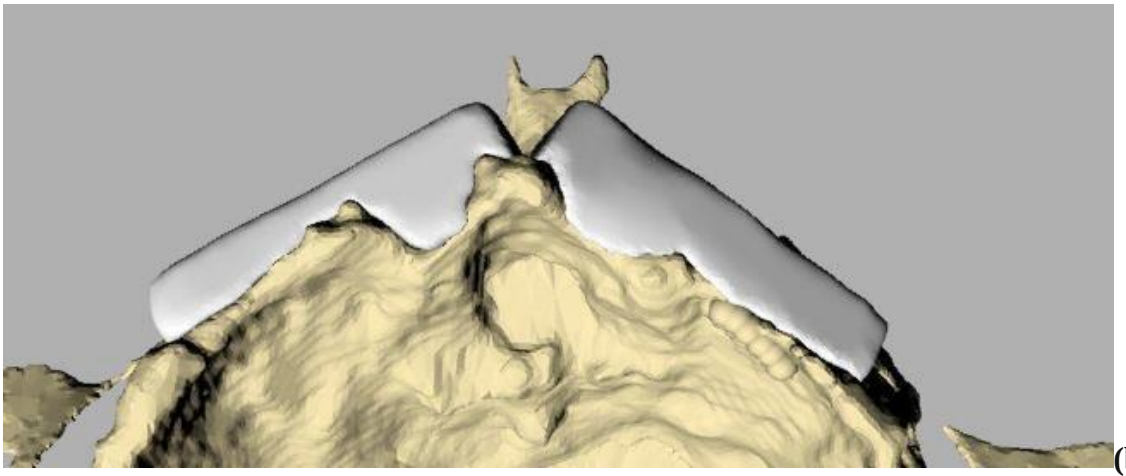

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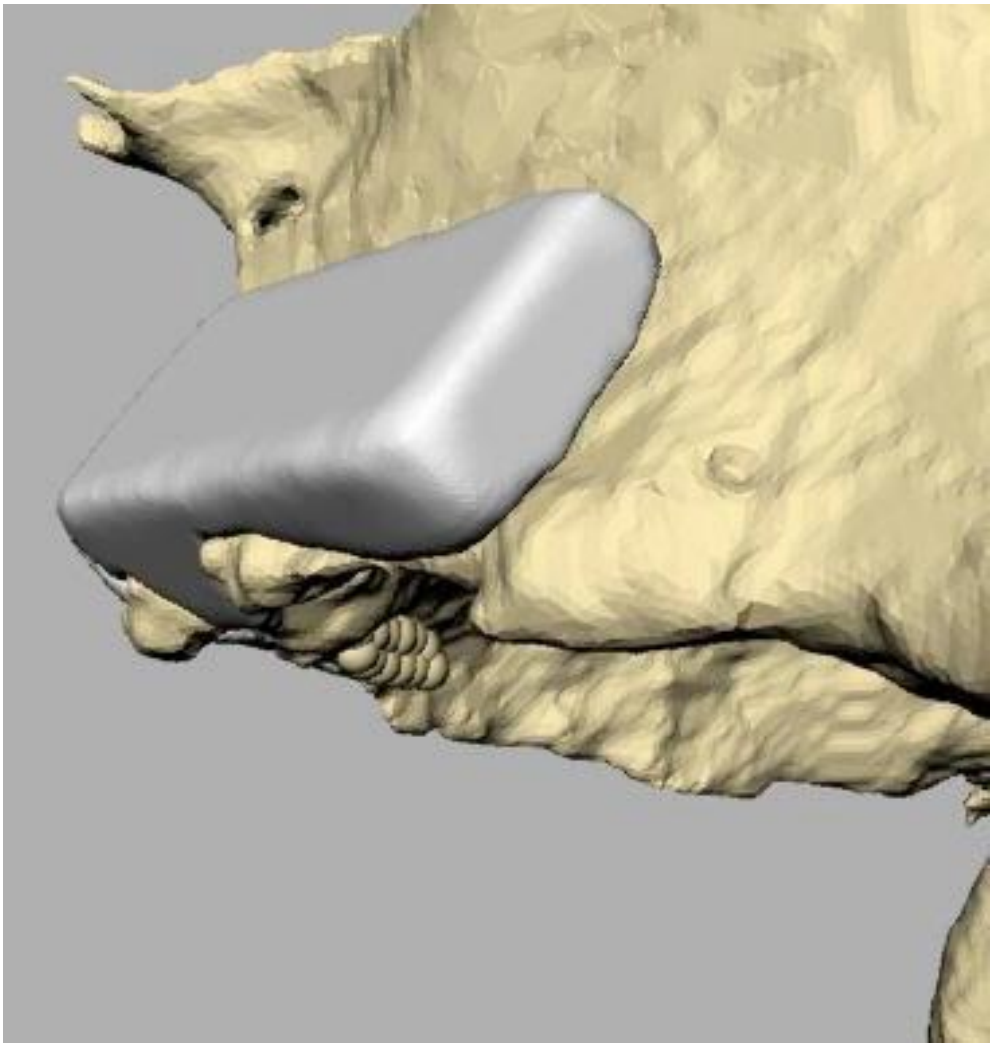

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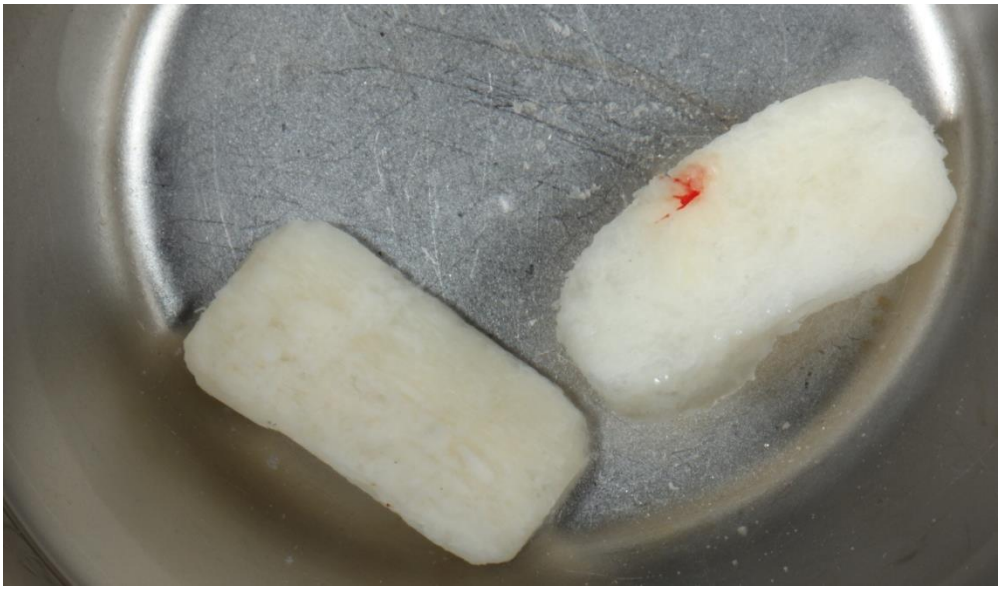


(c-)

Figure 2. Render of 3D bone donor site harvested from cadaver tibial hemiplateau (a). Render of 3D reconstruction of patient's anatomy (yellow) and designed bone grafts (white) (b). Final block for clinical use (c).

Trajectory planning and graft manufacturing

The planning of machining trajectories was performed using Rhinoceros by the Rhino-CAM 2 plug-in (MecSoft Corporation, Irvine, CA, USA). Each graft was positioned in the center of the machining CAM area with the larger flat area facing down to preserve the cortical portion of the tissue intact, in order to enhance the graft resistance during processing and avoid breaking during implantation. Bone bridges have been added to the CAD design to maintain fixation during processing and removed by hand at the end of the graft manufacturing procedure. The working area was defined according to the design' dimensions and the diameter of the milling tool (3 mm).

The tool-path trajectories have been programmed, subsequently simulated and modified to obtain the best result [Figure 3]. Then, the definitive trajectories have been exported as G-CODE coding specific for the milling machine used.

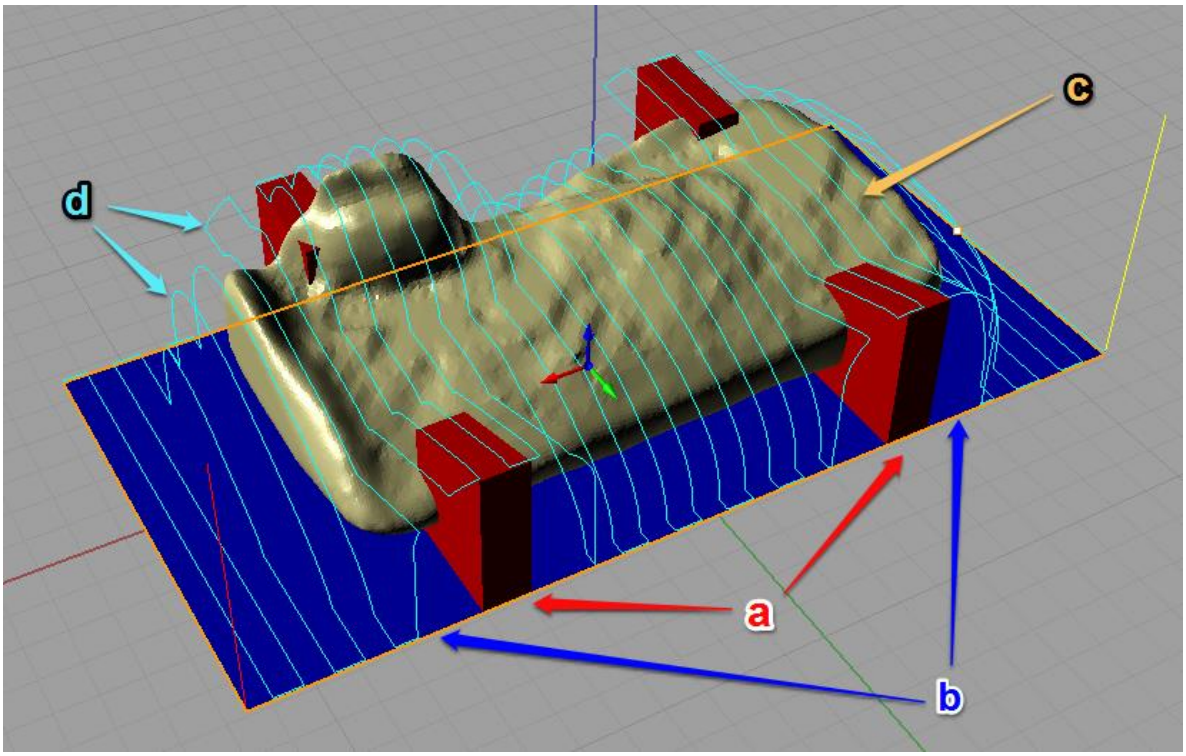


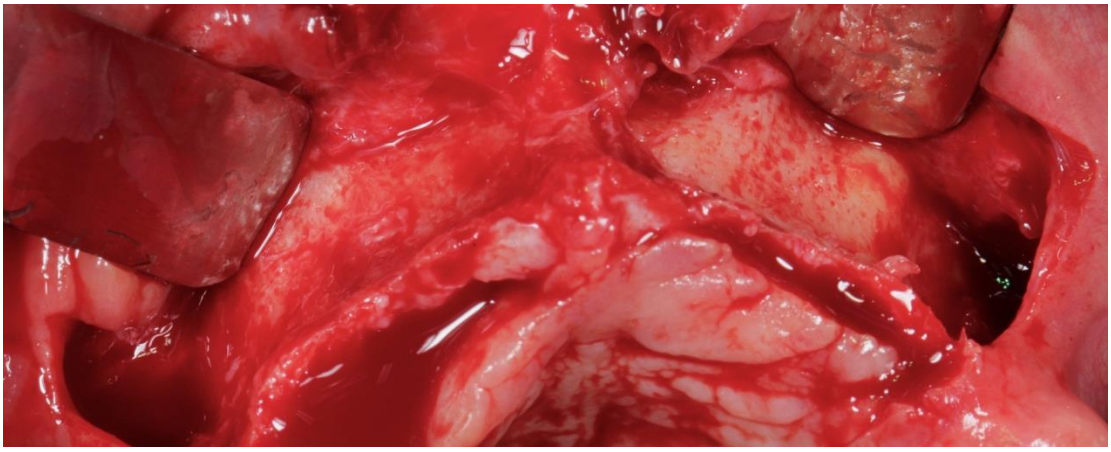
Figure 3. Tool-path trajectory planning: (a) added bone bridges; (b) work area; (c) graft design; (d) tool-path.

Surgical procedure

Local anesthesia was obtained by infiltrating articaine (4% containing 1:100 000 adrenaline). To expose the three-dimensional aspect of the bone defects was achieved a full-thickness crestal incision with two vertical releasing incisions [Figure 4-a].

The clinically sized, anatomically shaped custom-made bone block was placed in position strictly overlapping the underlying alveolar crest and fitted securely to the residual bone [Figure 4-b1]. The recipient site was weakened with multiple micro-holes to enhance bleeding from the trabecular bone [19-21]. Rigid fixation of the scaffold to the residual crest was obtained by means of a 1,5Wx8L titanium mini-screw (Tekka by Global-D Lyon, Fr) [Figure 4-b2] [20].

The grafted area was closed with a pulley suture for proper flap adaptation and to avoid any tissue strangulation by an absorbable 4.0/5.0 suture material. Sutures were removed 14 days postoperatively [Figure 4-c]. No removable prosthesis was allowed for 3 months. Patients were enrolled in an oral hygiene programme with recall visits every month for the entire duration of the study.



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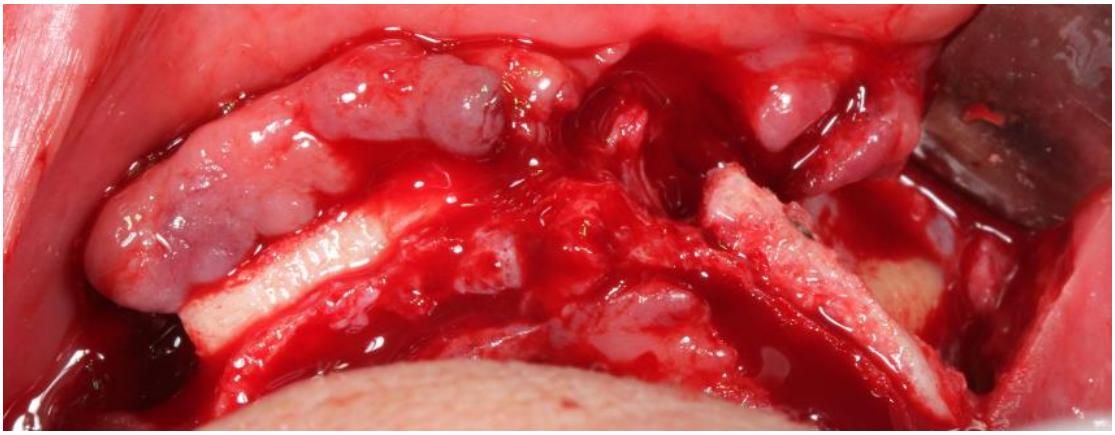

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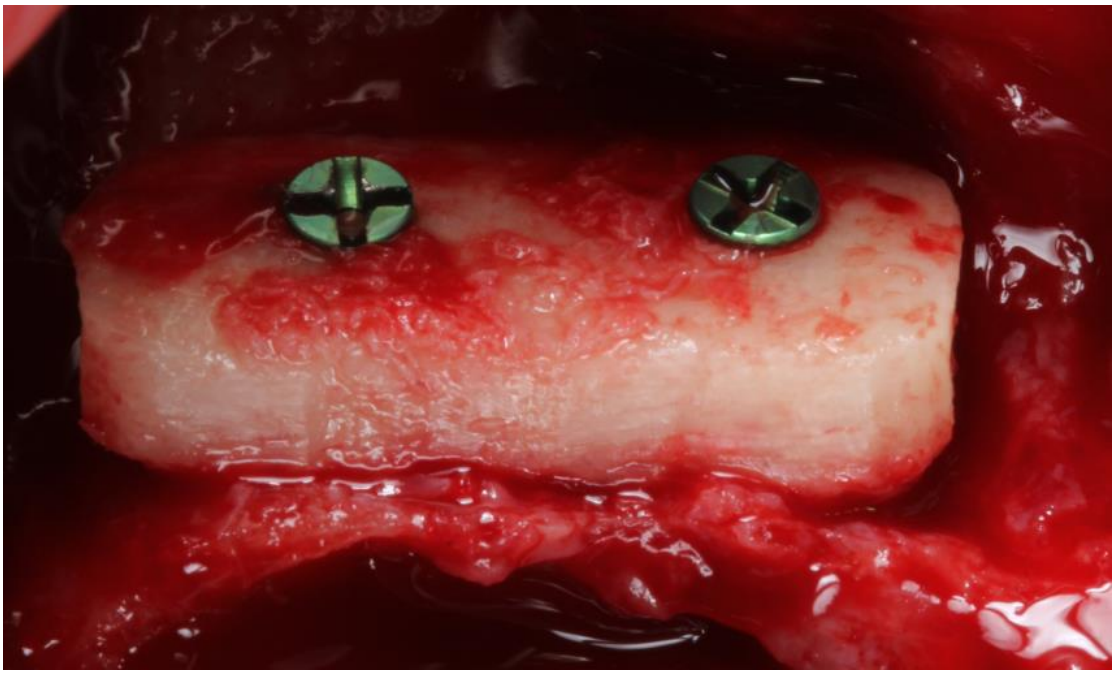

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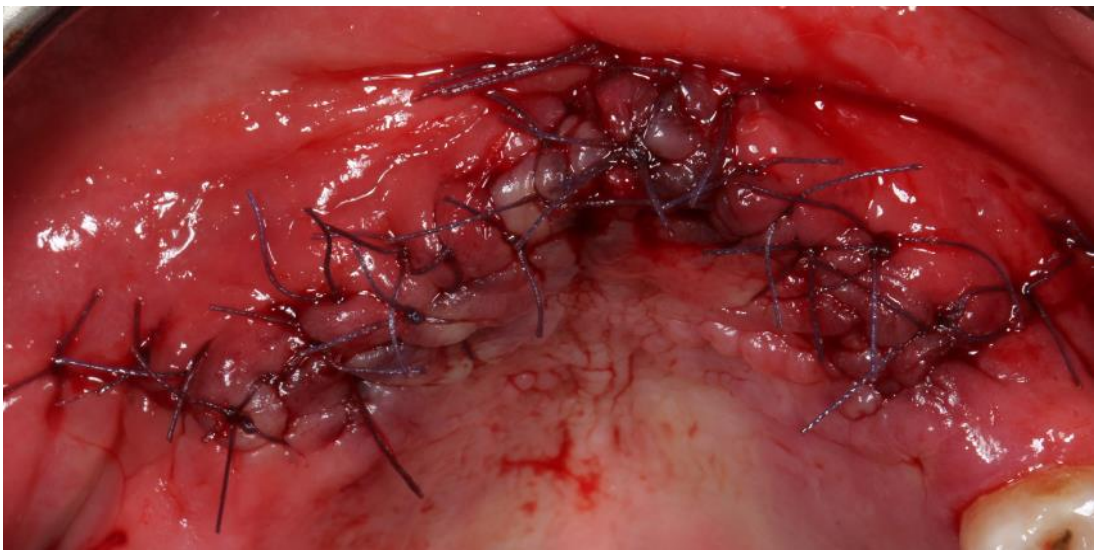
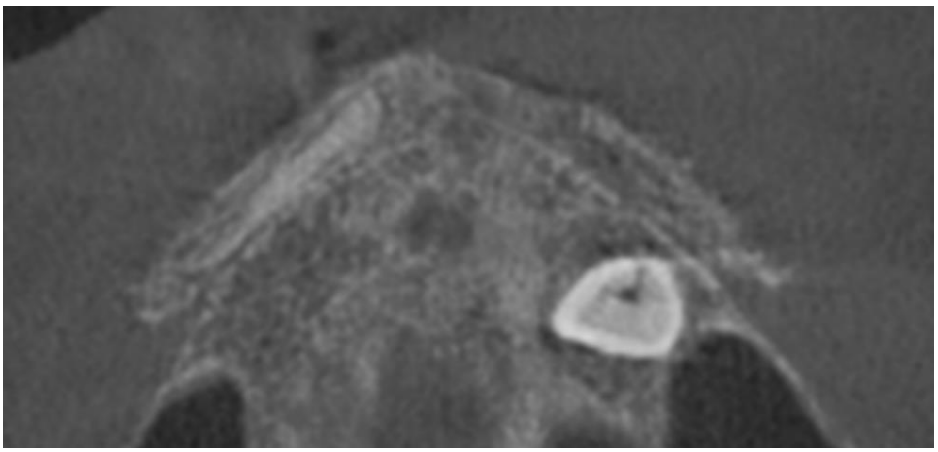


(c)

Figure 4. The allograft block is placed in the defect area through the tunnel and stabilized with a screw so that the screw head perfectly fits the cortical plate of the block. a) Site before intervention and clinical view of the defect. b1-2) Bone block with screw. c) Sutures.

Preceding to the second phase, supplementary CBCT scans were taken in in order to evaluate grafts gain [Figure 5].



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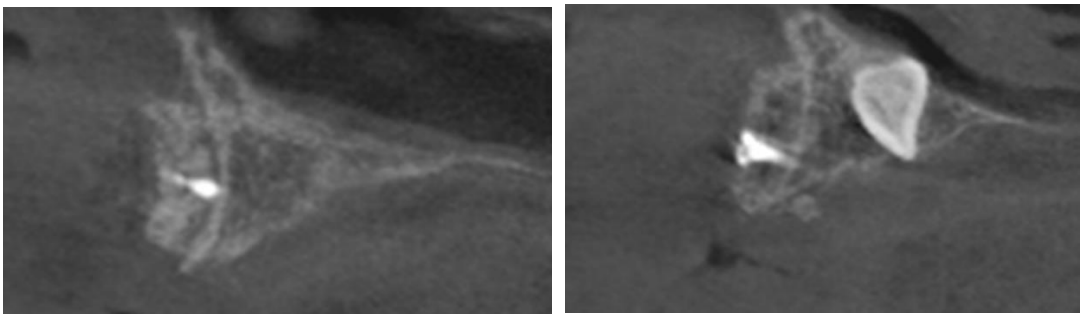

(b-)

Figure 5. CBCT scans were obtain after 9 months to determine implant width and length, on axial (a) and cross-sectional (b) images-

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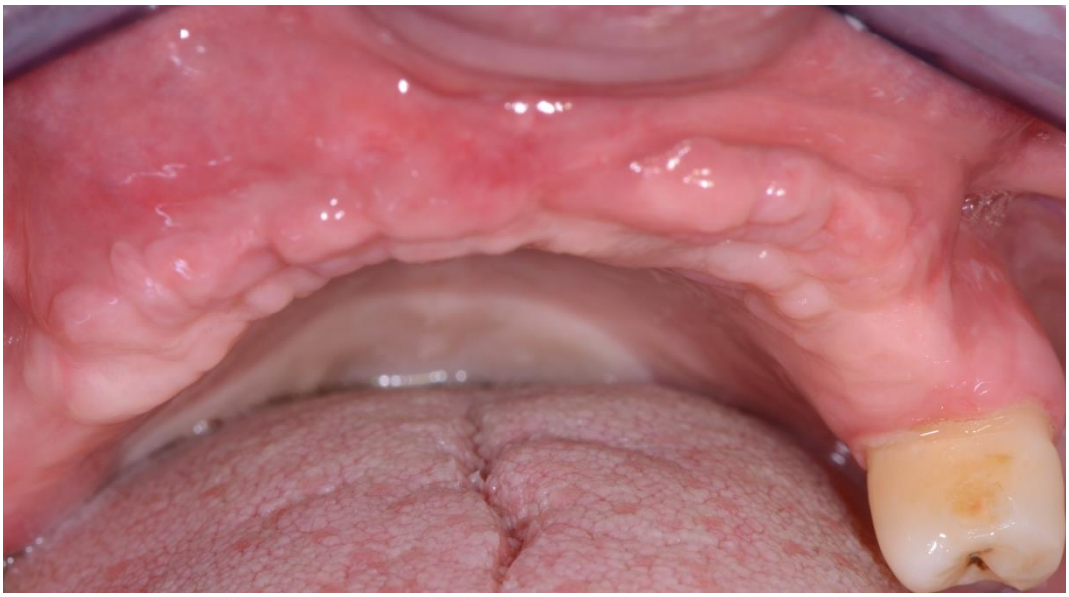
After a 9-month healing period, implant placement was performed, with the surgical exposure of the augmented sites [Figure 6-a;b].

The micro-screws were removed and 3.7 mm in diameter for a 10 mm in length dental implants (iRES SAGL, Mendrisio, CH) were placed and sutures performed [Figure 6-c]. No supplementary grafting procedure was required in the current investigation [21].



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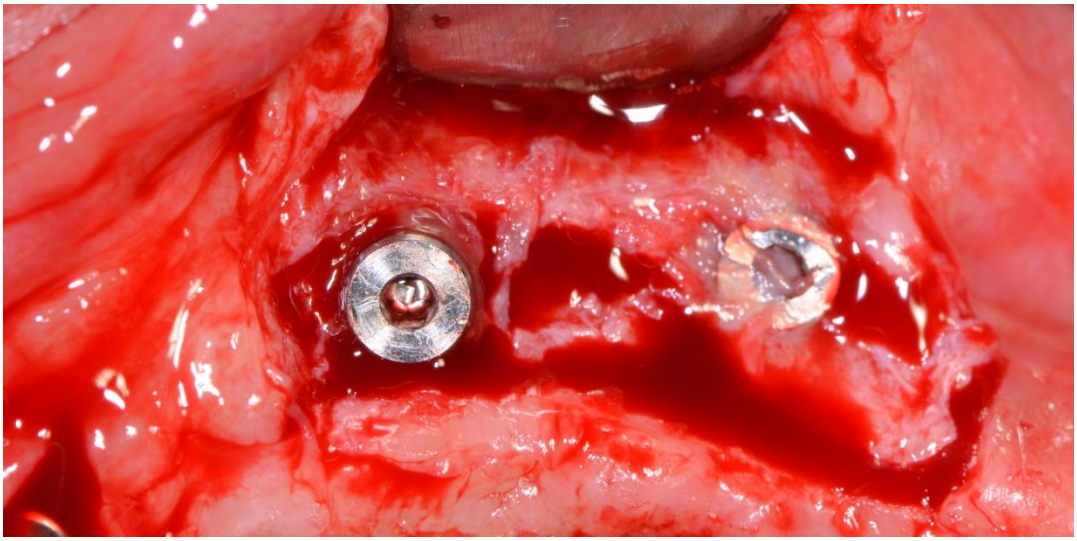

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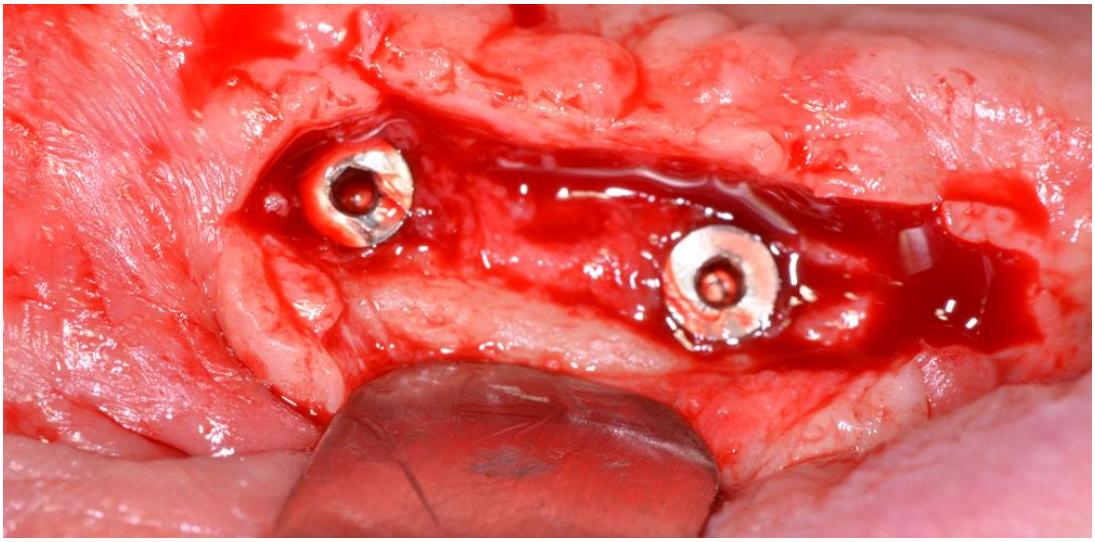

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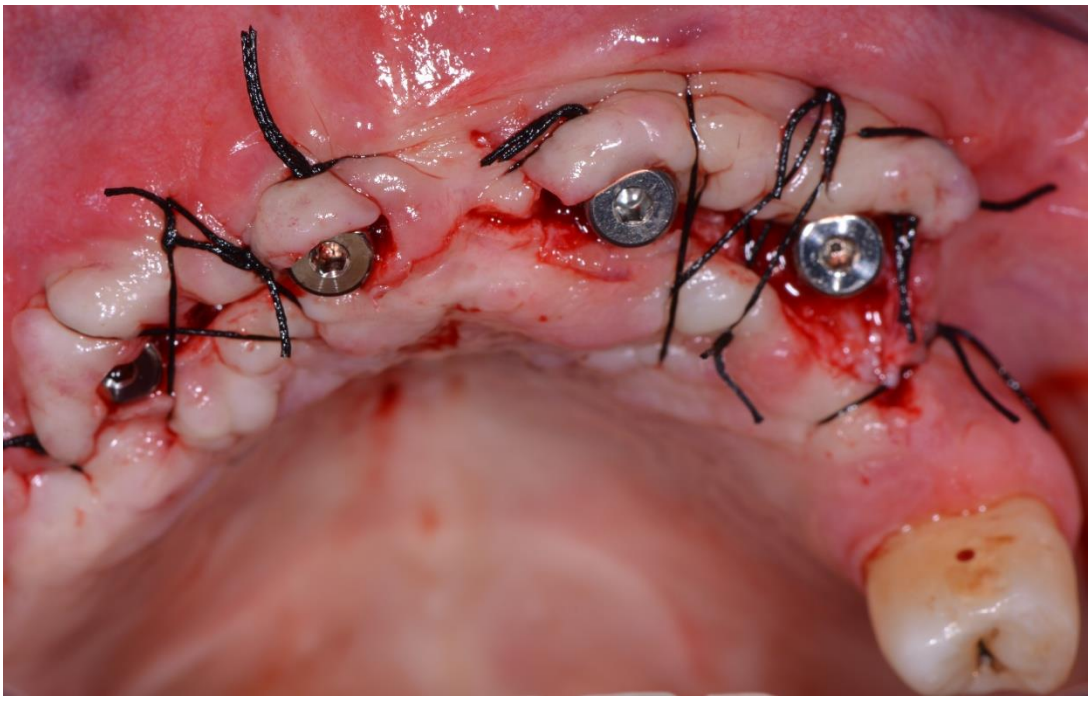

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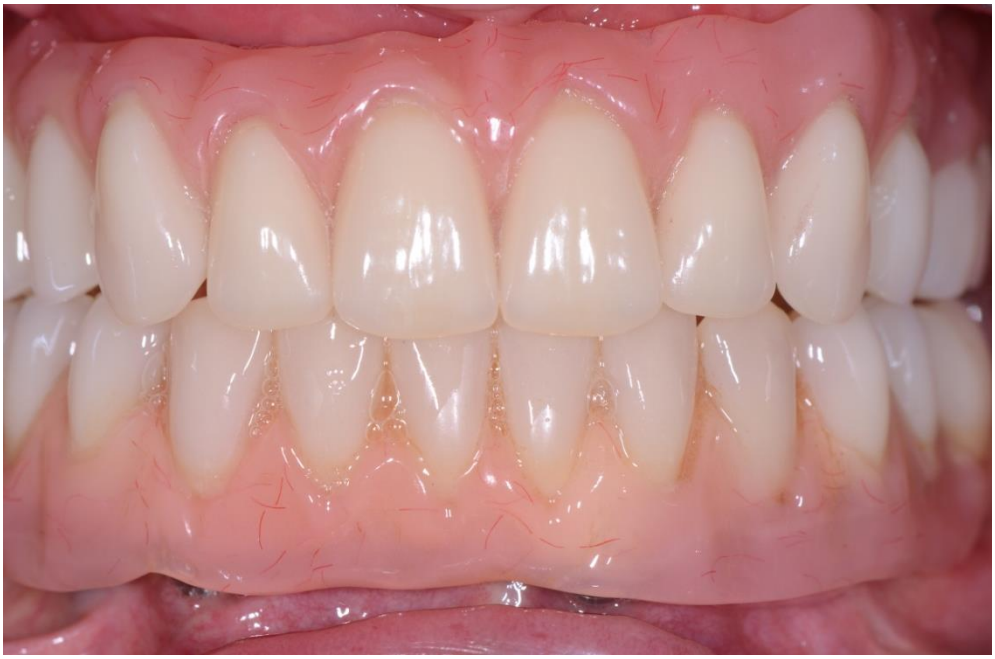

(d)

Figure 6. At 9 months after the reconstructive surgery, the implant was placed in position. (a) Site before intervention. (b) Surgical flap is raised. (c1) The implant is placed and (c2) sutures performed. (d) Frontal view of the final rehabilitation.

Statistical evaluation

The outcome values were analyzed using the *t-test* for paired samples for pre–post differences with time as the factor and IBM Statistical Package for the Social Sciences (SPSS Inc. Version 21.0, Chicago, IL, USA) software to detect significant differences between pre-test and post-test scores.

3. Results

A patient presenting atrophic anterior maxillae was selected to participate in the study. The patient received 2 corticocancellous allograft onlay bone blocks. The healing period was uneventful.

At the crestal level, the patient met the inclusion criteria of ridge width around 2 mm [21]. The titanium fixation mini-screws were detached and bleeding from the bone graft was detected, demonstrating revascularization of the site.

Moreover, the regenerative surgical procedure went well. In fact, the custom-made allograft scaffolds perfectly fitted in the bone anatomy and were therefore easily adapted to the bone defects during surgery, secured by titanium mini-screws [Figures 4, 5 and6]. This excellent matching of the size/shape helped the surgeon to reduce the operation time [22]. Moreover, all implants were inserted with fitting primary stability [Figure 6-d].

Paired comparisons revealed a significant mean increase in ridge thickness of 5.0 ± 0.55 mm from the preoperative measurement to the immediate postoperative measurement ($p < .01$).

The bone resorption that occurred during the incorporation period corresponds to 7,8% (95% confidence interval [CI]: [6.4%, 9.2%]) of the measured postoperative ridge thickness.

4. Discussion

Maxillary ridge augmentation states to procedures designed to correct a thin alveolar ridge. For dental implant placement, adequate bone volume is necessary; unfortunately, bone volume is not always adequate, particularly in elderly patients.

Bone regenerative techniques, although successful in many cases, entail an infection risk, may involve complications, and certainly increase cost and duration of therapy [23]. In some elderly patients with severe bone atrophy, performing bone regeneration can be risky, due to compromised general health, overly invasive procedures and higher costs [24].

With the increasing popularity of CBCT, digital planning software for implant placement, and manufacturing of surgical guides for fully guided implant placement, the complete digital workflow is a reality in everyday clinical practice and is rapidly becoming the standard of care in implant dentistry [25]. With regards to alveolar ridge augmentation in preparation for implant placement, the concept of preparing block graft materials extra-orally and pre-operatively has always been quite attractive due to the potential for reduction in surgical time and for more precise adaptation of graft materials [25].

The reduction of risk factors as infections caused by contamination of surgical site or contamination of graft during preoperative preparation, can be obtained with the manufacturing of custom sterile graft [22]. The correct design of a custom graft with also a reduction of surgical time, can be obtained with a proper planning of surgical procedure.

With the recent advances in planning and manufacturing software and hardware, graft customization can be integrated with the implant dentistry digital workflow with the potential to become part of everyday clinical practice [25].

Apart from the surgical management of CAD/CAM design for bone grafts, the biological properties of the biomaterial itself are of great importance. Some of the characteristics of the bone substitutes that should be analysed prior to clinical use are biocompadibility, osteoconductivity, surface porosity, surface chemistry, tissue bonding, material strength and degradation rate [26]. Nevertheless the sterile manufacturing of bone in a GMP-Class A environment, without the need of terminal sterilization via gamma radiation, guarantees the safety of graft in terms of sterility and the quality of tissue in terms of biological properties [27-28].

Among bone replacement grafts, autograft is considered the gold standard [29]. However, owing to the low level of patient acceptance of autografts, allografts (grafts from the same species) have become the most popular bone grafts in oral surgery. Allografts are being processed as fresh-frozen or freeze-dried [29].

Freeze-dried bone allograft (FDBA) is a type of allograft requested in clinical practice to be superior because of the osteoconductive and osteoinductive properties. The findings of our study showed, with a high success rate, that FDBA allogeneic bone grafts represent a reliable treatment option for extensive rehabilitation of atrophic maxillae, consistent with findings reported with the use of autologous bone.

The success rate of the block grafts was very effective and comparable with those reported by other authors [30-32]. Besides, the augmentation procedure permitted the insertion of implants in the grafted area 9 months next surgery. The clinical and radiographic observations showed a very low rate of bone resorption of the graft material, improving the ability to place endosseous implants.

Our data shown that custom-made FDBA can be used as successful graft material for the treatment of bone maxillary ridge defects. If adequate surgical techniques are adopted, this type of

bone graft can be safely used in regions of implant placement as a suitable alternative to autogenous grafts.

5. Conclusions

This pilot study has demonstrated the possibility to fabricate customized CAD/CAM grafts from the tibial hemiplateau of cadaver donors. The grafts were digitally designed based on CBCT scans of partially dentate patients using a set of 3D software, showing that grafts dimensions were correlated to the defect type. The sterile manufacturing of grafts showed a correct reproduction of designed graft, leading to a correct matching with the bone surface of patient. Additional *in vivo* studies with custom-made bone allografts are required for the validation of this digital workflow for maxillary bone augmentation.

Author Contributions: All authors made substantial contributions to the present study. FRG, RG and GMN contributed to conception and design, ZK to acquisition of data and statistical evaluation, AB and LV to analysis and interpretation of data; they were, moreover, involved in writing and editing the manuscript. LV, DD, MG performed the 3D reconstructions and volume renderings. F.R.G. and A.B. supervised the manuscript and gave the final approval of the version to be published. All authors read and approved the final manuscript.

Conflicts of Interest: The authors declare no conflict of interest.

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