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- 36 **Abstract:** The objective of this case report is to introduce a customized CAD/CAM freeze-
- dried bone allograft (FDBA) block for its use in Guided Bone Regeneration (GBR) procedures
- 38 for severely deficient maxillary bones. Additionally, a special newly developed remote incision
- 39 technique is presented to avoid wound dehiscence. The results show an optimal integration
- 40 behaviour of the FDBA block after six months and the formation of new vital bone. Thus, the
- results of the present case report confirm the use of the customized CAD/CAM bone block for
- 42 augmentation of complex defects in the maxillary aesthetic zone as a successful treatment
- 43 concept.

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- 44 Keywords: bone block; allograft; tissue reaction; Guided Bone Regeneration (GBR);
- 45 CAD/CAM

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47 INTRODUCTION

- 48 To date the treatment of complex alveolar bone defects, especially within the aesthetic zone,
- 49 remains challenging even with respect to both functional and aesthetic restoration. The
- 50 clinician's options for treating such defects used to be limited to the use of autologous bone
- grafts (ABG), with its known drawbacks of increased operation time, costs and complications;
- 52 increased donor site morbidity and unpredictable resorption. 1,2,3 In recent years, the advancing

development of bone substitute materials created a set of alternatives with which comparably predictable clinical outcomes can be achieved,⁴ as they maintain comparable osteoconductive properties to ABG.⁵ Freeze-dried bone allografts (FDBA) represent the most promising option because of low block graft failure rate, minimal resorption, and high implant survival rates.^{6,7,8} Interestingly, the computer-aided design/computer-aided manufacturing (CAD/CAM) technology nowadays allows for patient customized manufacturing of allogenic bone blocks for complex ridge augmentation. Since there is limited literature addressing the feasibility of this class of customized allogenic bone blocks, the objective of this case report is to introduce its use in Guided Bone Regeneration (GBR) procedures for severely deficient maxillary bones. Additionally, a special newly developed remote incision technique is presented to avoid wound dehiscence. Established histological and histomorphometrical analyses of the tissue reactions and the integration pattern of the FDBA material are included to show its remodelling capacities.⁹

CASE REPORT

A 43-year-old woman presented with the wish for a fixed prosthetic rehabilitation of the maxillary aesthetic zone. Preliminary clinical and radiographic evaluations showed periimplantitis related to three dental implants with massive bone resorption and partial loss of the buccal wall within the maxillary aesthetic zone, tooth #7-#10 (ADA Dental Terminology 2011-2012) (Fig. 1). Treatment plan for this complex and spacious bone defect was agreed to be a customized CAD/CAM freeze-dried bone allograft (maxgraft® bonebuilder, botiss biomaterials GmbH, Zossen, Germany). After implant extraction and a healing period of three months, a cone beam computed tomography (CBCT) scan was taken and submitted in Digital Imaging and Communications in Medicine (DICOM) format to virtually design the allogenic bone block on a three-dimensional reconstruction of the patient's defect (Fig. 2). After review of the block design and approval by the surgeon, the customized FDBA block was milled from

79 processed (Allotec® process, Cells + Tissuebank Austria (C+TBA), Krems, Austria) cancellous

bone of femoral heads of living donors.

Surgical procedure

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Six months after extraction of the failing implants, GBR procedure was performed under general anesthesia including processing of autologous platelet-rich fibrin (PRF) matrices from patient's blood and perioperative antibiotic prophylaxis. After making a full-thickness remote 'pillar incision' (Fig. 3), raising a vestibular flap with distal relief incisions on adjacent tooth #6 and #11, the buccal tissue was carefully dissected, protecting the neurovascular structures, and mobilized in palatinal direction for proper soft tissue management. The cortical layer of the recipient site was perforated using a diamond bur to promote bleeding. Afterwards, the FDBA block was obtained sterile from the double blister package and rehydrated in exudate serum obtained during the PRF process by creating a vacuum in a disposable syringe. The block fitted exactly onto the recipient site and was rigidly fixed on the maxillary ridge with 1.25 mm-diameter titanium osteosynthesis screws. Before fixation, a countersink for the screw heads was created using a diamond ball mill to avoid soft tissue perforation. Small residual volume on mesial and distal areas was filled using allogenic cancellous bone substitute material (Human-Spongiosa CHB, botiss biomaterials GmbH, Zossen, Germany) and xenograft material (cerabone®, botiss biomaterials GmbH, Zossen, Germany) and sharp edges were smoothed. The surgical site area was covered with a resorbable barrier membrane of native pericardium (Jason® membrane, botiss biomaterials GmbH, Zossen, Germany), which was fixed to the local bone using titanium pins, followed by one layer of PRF matrices. The grafted area was closed with a pulley suture for proper flap adaptation and to avoid any tissue strangulation by using absorbable 4.0/5.0 suture material. Sutures were removed in part 7 days and entirely 14 days postoperatively.

Six months after the GBR procedure, at re-entry, fixation screws were removed and bone core 104 biopsies were taken for histological and histomorphometrical analysis based on previously 105 described methods. In brief, the biopsies were fixed in 4% neutral buffered formalin for 24 106 hours, decalcified in 10% Tris-buffered EDTA (Carl Roth, Karlsruhe, Germany) at 37° C for 107 15 days and passed through a series of increasing alcohol concentrations followed by xylol. 108 After embedding of the biopsies in paraffin, cutting was conducted using a microtome (Leica 109 RM2245, Wetzlar, Germany) in sections of 3-5 µm thickness. Slides were stained with Masson-110 Goldner, Toluidin blue and a combinatory Safranin / Toluidin blue staining. 111 The histological examination included analysis of the following histological parameters: 112 Integration pattern of the implant, fibrosis, hemorrhage, necrosis, vascularization and the 113 presence of neutrophils, lymphocytes, plasma cells, macrophages and multinucleated giant cells 114 (MNGCs). The histological images were recorded by means of an Axiocam 105 color digital 115 camera (Carl Zeiss AG, Oberkochen, Germany) connected to a computer system running the 116 Zen software (version 2.3, blue edition, Carl Zeiss AG, Oberkochen, Germany). The 117 histomorphometrical analysis included the following steps: Initially, the histological slides 118 were digitized using a light microscope (Axioscope 40, Carl Zeiss AG, Oberkochen, Germany) 119 connected with a scanning table (EK 14 mot, Merzhauser, Wetzlar, Germany), a digital camera 120 (AxioCam MRc 5, Carl Zeiss AG, Oberkochen, Germany) and a computer running the Zeiss 121 AxioCam software (AxioVs40, version 4.8.2.0, Carl Zeiss AG, Oberkochen, Germany) at a 10x 122 magnification. Total scans were used for histomorphometric measurements by means of the 123 NIS Elements software (Basic Research, version 4.51, Nikon, Tokyo, Japan). Finally, the 124 software GraphPad Prism (Version 6.01, GraphPad Software Inc., La Jolla, USA) was used for 125 the statistical analysis and graph drawing. 126 Four implants (Straumann Bone Level Roxolid®, Basel, Switzerland) were inserted under 127 general anaesthesia in locations #7, #8,#9 and #10 by the same surgeon who had performed 128 the grafting procedure with a torque value of 25-50 N cm using a drill guide. Vestibuloplasty 129

was performed using a 3D stable soft tissue collagenous graft (mucoderm®, botiss) and a radiograph was taken after implant insertion to confirm the correct implant position (Fig. 5). Implants were uncovered three months after placement and again a radiograph was taken. The patient received temporary restoration and is awaiting final prosthetics sixteen months after grafting procedure.

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Results

The post-operative recovery and healing process was uneventful and six months after GBR 138 surgery the grafted area showed sufficient bone volume and vital tissue for implant placement 139 (Fig. 2). Histologically vital new formed bone was found in the augmentation area at re-entry 140 and the FDBA material was completely integrated within this new built bone tissue showing its 141 optimal osteoconductive properties (Fig. 4b). While most distances of the material surfaces 142 were covered by new built bone tissue, at the surface areas covered by connective tissue 143 144 multinucleated giant cells were observed involved in the incorporation of the grafting material (Fig. 4c). However, no histological signs of implant-related inflammatory tissue reactions were 145 observed (Fig. 4c). 146 Histomorphometrical analysis showed an amount of new bone of 52 %, which was statistically 147 higher (** p > 0.01) compared to the amounts of connective tissue (25 %) and residual grafting 148 material (23 %), respectively (Fig. 4a). Radiographs and clinical examinations at re-entry and 149 during implant uncovering six and nine months after augmentation surgery indicated 150 continuous remodeling of the allogenic bone block and hence stable osseointegrated implants 151 providing an optimal result (Fig. 2c and 5). 152

DISCUSSION

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Allogenic bone blocks have several advantages over autologous bone blocks, namely, (1) no donor site morbidity, (2) no second surgical site, (3) less patient discomfort and (4) reduced surgery time. 10 The added value of a precise fit gains importance for complex bone defects, as the space between residual bone and bone graft can be reduced to a minimum to enhance the physical contact between the graft and the recipient site to allow for FDBA revascularization through integration/replacement (creeping substitution) at the recipient site. 11,12 Moreover, this direct contact with the neighbored bone tissue allows for a fast bony integration. Furthermore, the application of customized CAD/CAM allogenic blocks brings the surgery time reduction to a new level, as shaping of the block is no longer necessary, and chair time can be significantly reduced for both the patient and the surgeon. Moreover, surgery time reduction positively influences the complication rate and the infection rate of the recipient site and the graft, which is one major complication reported for the use of allografts. 13 In this context, the decrease of graft infection is based on the fact that CAD/CAM designed bone blocks are no longer subjected to numerous possible sources of contamination during manual adjustment deriving from prolonged contact with the gloves of the surgeon, the oral fluids of the patient, the burs, and other environmental factors.¹⁴ The present results show an optimal integration behavior of the FDBA block after six months and the formation of new vital bone, which is comparable to values found in case of other treatment options for such kind of defects. 15,16 Thus, the analyses of the present case report confirm the use of the customized CAD/CAM bone block for augmentation of a complex defect in the maxillary aesthetic zone as a successful treatment concept. The rationale behind using a remote 'pillar incision' technique described herein is aiming for a complete tension-free primary closure, because inability to obtain tension-free closure of the advanced flap can encourage incision line opening and membrane exposure, which are common complications following augmentations with cancellous block allografts.¹³ Advantages of this

remote technique are the following: (1) incision is positioned far away from graft (2) intact keratinized mucosa on the alveolar ridge and intact papillae (3) no visible scars because incision lies in the flexible mucosa in the vestibular fold. To deepen the understanding of this incision technique for GBR procedures using the customized bone block, two different cases (single tooth gap and free end situation in the maxilla) have been included to highlight the therein performed alternative incision line.

Although there are some reports on midcrestal incisions having the most anatomic potential for success in GBR procedures due to the features of mucosal vascularization of the alveolar ridge, 17,18 the remote incision technique introduced in this case report has proven to be a valuable alternative assuring sufficient mobilization of the overlying soft tissue to cover the graft, resulting in uneventful wound healing with no aesthetic impairment in the maxillary aesthetic zone. However, further studies involving more cases are necessary to verify the reliability and validity of this technique.

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Captions to figures

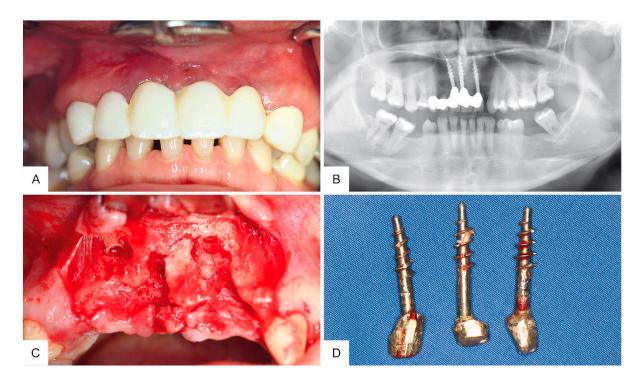


FIGURE 1. Clinical and radiographic examination of the maxillary defect. (a) Clinical preoperative examination revealed changed color in the gingiva on site #7-10. (b) Radiographic preoperative film demonstrated massive bone loss surrounding the three failing implants. (c) Complex bone defect and partial loss of the buccal wall within the maxillary aesthetic zone after extraction of failing implants. (d) Extracted implants causing peri-implantitis.



FIGURE 2. CAD/CAM block design and real bone allograft. (a) Virtual three dimensional reconstruction of the defect and bone block design (blue). (b) Customized CAD/CAM bone block. (c) Grafted area showed sufficient bone volume and vital tissue for implant placement six months after GBR procedure.

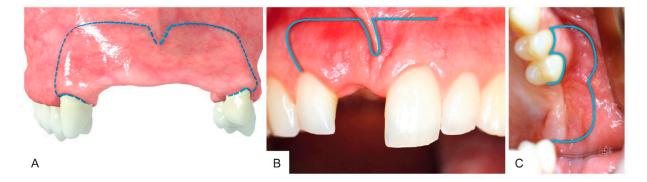


FIGURE 3. Remote incision techniques for augmentation procedures using a customized allogenic bone block. (a) Pillar incision performed as reported in this case. The horizontal part of the incision is positioned far up in the flexible mucosa in the vestibular fold and relief incisions are positioned in the posterior third of the adjacent teeth. (b) Semi pillar incision in case of a single tooth gap in the maxilla. (c) Lateral incision in case of a free end situation in the posterior maxilla.

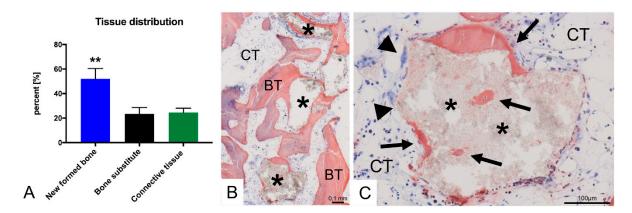


FIGURE 4. Results of the histological and histomorphometrical analyses. (a) Tissue distribution six months post-OP (** p > 0.01). (b) Integration of the FDBA material (asterisks) surrounded by vascularized connective tissue (CT) and new formed bone (BT). (c) Both the material-mediated bone growth (arrows) in combination with the multinucleated giant cells (arrowheads) resemble the ongoing remodeling processes.

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FIGURE 5. Four implants were placed in locations #7, #8, #9 and #10. (a) Buccal view after implant placement. (b) Radiograph taken immediate after the procedure. (c) Temporary restoration.