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HUMAN RANDOMIZED CONTROLLED TRIAL

Effect of connective tissue grafting on buccal bone changes based on cone beam computed tomography scans in the esthetic zone of single immediate implants: A 1-year randomized controlled trial

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Abstract

Background: Connective tissue grafting has a beneficial effect on the peri-implant mucosa, but the effect of grafting the buccal mucosa on buccal bone thickness (BBT) has not been investigated, although BBT is proposed to be a key factor for the soft-tissue contour. The aim of this trial was to assess the outcome of a connective tissue graft (CTG) in the esthetic zone of single immediate implants on the change of BBT according to cone beam computed tomography (CBCT) scan analysis.

Methods: In a 1-year randomized controlled trial, 60 patients received an immediately placed implant and provisionalization, either combined with CTG (test group) or without CTG (control group). CBCTs were taken preoperatively (T_pre) and 1 year after definitive restoration (T_2). Any change in BBT was assessed at different implant levels. Additionally, the change in mid-buccal mucosal level (MBML) and approximal marginal bone level were assessed.

Results: Fifty-five patients were available for statistical analysis (test group, n = 28; control group, n = 27). At T_2, the average change in BBT was significantly larger in the test group (−0.84 ± 0.61 mm) than in the control group (−0.46 ± 0.54 mm, P = 0.02). A MBML gain of 0.07 ± 0.85 mm in the test and a MBML loss −0.52 ± 1.16 mm in the control group was observed at T_2. Average loss of marginal bone was 0.05 ± 0.33 mm and 0.01 ± 0.38 mm, respectively.

Conclusions: The application of CTG in the esthetic zone of immediately placed and provisionalized implants is accompanied with more loss of BBT, but at the same time better maintains the mid-buccal mucosal level.

KEYWORDS
cone-beam computed tomography, connective tissue, dental implants, single-tooth
Immediate implant placement and provisionalization (IIPP) in the esthetic zone has evolved into a viable opportunity for single-tooth replacement with esthetically acceptable results. However, the mid-buccal mucosa still often recedes. This recession is presumed to be most likely a result of the bone remodelling following tooth extraction, which cannot be prevented through an immediately inserted implant. Such a recession may lead to a less favourable esthetic result.

For reduction of the effects of bone resorption after tooth removal, it is recommended to position the implant at least 2 mm palatal from the internal buccal socket wall and the implant-socket gap should be grafted. The aim of the grafting procedure is to create additional amounts of peri-implant hard tissue and is presumed to have a beneficial outcome for the peri-implant soft tissues. In addition to grafting the implant-socket gap, thickening of the peri-implant soft tissues with a connective tissue grafting procedure combined with implant placement is suggested to reduce recession and volume loss of the mid-buccal mucosa. Some randomized controlled studies showed better preservation of the mid-buccal mucosa in immediate implant cases applying connective tissue grafting. Migliorati et al. even observed an increase in mucosal thickness on applying a connective tissue graft (CTG).

We showed a mid-buccal mucosal level preserving effect when applying a CTG simultaneously with an immediately placed and provisionalized implant, but no increase in buccal mucosal volume was observed. Measuring the change in mid-buccal mucosal volume does not provide accurate information on changes in the underlying buccal bone thickness (BBT). BBT is proposed to be a key factor that determines the overlying soft-tissue contour and changes in BBT can be considered an important outcome when predicting esthetic success. As far as we know, the effect of connective tissue grafting on the change in BBT in the esthetic zone when combined with immediately placed and provisionalized implants has not yet been investigated. Hence the present randomized controlled trial aims to assess the effect of connective tissue grafting on the change in BBT in the esthetic zone of single immediate implants.

Materials and Methods

Study design

Sixty patients were included in the randomized controlled trial to assess the effect of connective tissue grafting on peri-implant soft and hard tissues. Study set-up was described in detail by Zuiderveld et al. It was approved by the Medical Ethical Committee of the University Medical Center Groningen, The Netherlands, and registered in the trial register (NTR3815). This study was conducted in accordance with the requirements of the Helsinki Declaration of 1975 and revised in 2008. Outcomes were reported according to the CONSORT 2010 checklist. Written informed consent was obtained before enrolling the patients. All patients (aged ≥18 years) with a single non-restorable tooth in the maxillofacial esthetic zone (14 to 24) received an immediate implant-supported restoration. Then the patients were randomly allocated to one of the two study groups by sealed envelopes opened by a research nurse not involved in the study just prior to the surgery to either receive a CTG harvested from the tuberosity region or no graft at implant placement.

Patients

The following inclusion criteria were used:

- a post-extraction vertical bone defect of the buccal socket wall of <2 mm measured with a periodontal probe;
- adequate oral hygiene, that is modified plaque and sulcus bleeding score ≤1;
- sufficient mesial-distal (≥6 mm) and interocclusal space to place an implant-supported crown.

Exclusion criteria were:

- medical and general contraindications for the surgical procedure, according to the ASA score ≥ III;
- presence of periodontal disease, expressed by pocket probing depths of ≥4 mm and bleeding on probing (modified sulcus bleeding index score ≥2);
- smoking;
- history of radiotherapy to the head and neck region;
- pregnancy.

Intervention

One day preoperatively antibiotic prophylaxis started comprising of amoxicillin 500 mg, 3 t.i.d. for 7 days or clindamycin 300 mg, q.i.d. for 7 days in case of amoxicillin allergy. Furthermore, twice daily the patients had to take a 0.2% chlorhexidine mouthwash for 7 days.

All surgical procedures were done by one oral and maxillofacial surgeon (GMR). Local anaesthesia was applied before a flapless tooth extraction. Next, as defined by the
manufacturer, implant site preparation was done on the palatal side of the extraction socket using a surgical guide to secure the proposed implant crown position. Augmentation of the buccal implant socket gap was carried out with autogenous bone from the tuberosity or bone chips collected from the implant drills, and anorganic bovine bone*. Next, the implant† was inserted 3 mm apical of the most apical part of the prospective implant crown margin and primary stability was achieved with an insertion torque of ≥45Ncm. At this time point, the buccal wall, consisting of the original buccal bone wall and the newly augmented mixture of autologous bone and anorganic bovine bone in the socket gap, was at least 2 mm at every position at the buccal side of the implant. Afterwards, a non-occluding screw-retained provisional restoration was designed by taking an implant-level impression and a healing abutment was placed. The moist environment of physiologic saline solution and blood in which the particles are embedded prevents particles getting stuck in impression material.

The test group received a CTG taken from the maxillary tuberosity region, which was placed in a supraperiosteal envelope flap prepared at the buccal aspect and secured.§ The size of the graft was more or less standardized, being ≈8 mm in length, 6 mm in width and a thickness of 1.5 mm. In cases with a small bony defect of the buccal wall, not only the periosteum of the original bony layer was covered but also the added augmentation mixture of autologous bone and anorganic bovine bone. The wounds in both groups were closed with nylon sutures‖. The screw-retained provisional restoration was placed, with a torque of 20Ncm, on the same day as implant placement.

To fabricate the final implant crown with an individualized zirconia abutment¶ a definitive implant-level open-tray impression was produced 3 months later. The abutment screw was torqued with 35Ncm. Depending on the location of the screw access hole, the final crown was either screw-retained or cement-retained. All prosthetic procedures were accomplished by two experienced prosthodontists (HJAM, CS), and all crowns were fabricated by one dental technician (MvdV).

### 2.4 | Measurement of buccal bone thickness

Slagter et al.²⁴ showed that BBT changes can be measured in a reliable and reproducible way on cone beam computed tomography (CBCT) images. Accordingly, we measured BBT on T<sub>pre</sub>, T<sub>1</sub> (1 month after placement of the final implant crown) and T<sub>2</sub> (12 months after placement of the final implant crown) CBCT scans* using a designated program‖. The CBCT scanner was validated for measuring bone thickness²⁵ with a method error of 0.05 mm (95%CI 0.03 to 0.07). A standard voxel size of 0.30 and a FoV of 100 × 100 mm were used for all CBCTs. CBCT’s were made according the manufacturer’s instructions with head and chin support, and alignment lights.

First, the CBCT Digital Imaging and Communications in Medicine (DICOM) files from T<sub>1</sub> and T<sub>2</sub> were imported into a medical image computing program*. Second, the exact position of the implant was then determined with Multimodality Image Registration using Information Theory (MIRIT; Figure 1)²⁶ and a Maxilim file with the exact coordinates of the implant in the particular patient was created. Third, the planning software used these coordinates to align a planning implant onto the exact same position. Fourth, measurements of the buccal bone (in mm) could be done. The area of interest was the upper 5 mm section of the implant starting at the implant neck towards the apical point (location M<sub>0</sub>-M<sub>z</sub>, Figure 2). The distance of the buccal bone outline to the center of the implant was measured for each location. The radius of the interior contour of the implant, as provided by the manufacturer for each location, was then subtracted from this measurement to determine the distance of the outline of the implant to the buccal bone outline. This measuring method prevented measurements at the interface between implant and bone that are disturbed by scattering. The method applied results in measurements made at the most outer buccal contour of the implant relative to the dental arch. This means that at this sagittal plane the BBT is probably the thinnest and therefore the most predictive for the state of available buccal bone.

Fifth, the DICOM files of the T<sub>1</sub> and T<sub>pre</sub> buccal bone measurements were both imported into Maxilim and aligned (Figure 3). Sixth, the Maxilim file with the exact coordinates of the implant from the CBCT image taken at T<sub>1</sub> was inserted into a new DICOM file consisting of the combined T<sub>pre</sub> and T<sub>1</sub> DICOM files to enable placing a planning implant according to the coordinates (Figure 3). Buccal bone measurements could now be done for the prospective implant position on the T<sub>pre</sub> CBCT image. It must be realized that the measurement for BBT at T<sub>pre</sub> is actually the distance between a virtual implant and outer contour of the buccal bone plate. This distance may cross the tooth root.

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* Geistlich Bio-Oss, Geistlich Pharma AG, Wolhusen, Switzerland
† NobelActive, Nobel Biocare AB, Gothenburg, Sweden
‡ 4-0 vicryl, Johnson & Johnson Gateway, Piscataway, NJ.
§ Ethilon, Ethicon, Johnson & Johnson, Amersfoort, The Netherlands
¶ NobelProcera, Nobel Biocare AB, Gothenburg, Sweden
* iCAT 3D exam scanner, KaVo Dental GmbH, Biberach, Germany
‖ NobelClinician, version 2.1, Nobel Biocare-Guided Surgery Center, Mechelen, Belgium
§§ Maxilim, version 2.3, Medicim, Sint-Niklaas, Belgium
FIGURE 1 The planning implant is aligned with the implant in the CBCT image using MIRIT to obtain the exact coordinates for the procedure.

FIGURE 2 The planning implant is superimposed precisely over the implant in the CBCT image according to the previously obtained coordinates. Each millimeter measurement (M0-M5) is marked along 5 mm of the axis of the implant, starting at the neck of the implant.

All measurements were carried out by three operators (H.J.A.M., G.C.B., E.G.Z.) blinded for the specific groups and in a random order. Because inter-examiner reliability and intra-examiner reliability of the method was analyzed in an earlier manuscript, with partly the same examiners, and with a favorable outcome, it was decided not to explore these reliabilities again.

2.5 Measurement of approximal marginal bone level

Intraoral radiographs for analysis of approximal marginal bone level were made with an individualized lab-made acrylic splint for standardization at T_1 and T_2. Specifically designed software was applied for full-screen analysis of the radiographs. Bone exceeding the implant platform was scored as no bone loss. Change in marginal bone level at the mesial and distal side of the implant was averaged.

2.6 Measurement of mid-buccal mucosa level

The change in MBML was assessed at T_2 and compared with the preoperative MBML (T_{pre}) according to measurements from standardized intra-oral photographs. The photographs were calibrated by a periodontal probe held close to and parallel to the long axis of the tooth adjacent to the implant. The photographs were analysed using a digital picture editing program. Measurements were done between the reference line though the incisal edges of the natural adjacent teeth and the mucosal margin of the non-restorable teeth. There was no method applied to compensate for possible wear of the incisal edge of the neighboring teeth nor possible ongoing skeletal growth. MBML as well as volumetric changes in the tissue buccal from the implant have been reported before. The present study only used the MBML data from those patients who had CBCT scans available for BBT measurement from the preoperative situation and 12 months after placement of the final implant crown.

2.7 Assessment of gingival phenotype

The gingival phenotype (thin/thick) was assessed at T_{pre} by means of periodontal probe transparency through the gingival margin.
3 | STATISTICAL ANALYSIS

The original sample size calculation was based on change in MBML as primary outcome, as shown in the manuscript by Zuiderveld et al. At least 27 patients per group (significance level of 5%, power of 80%) had to be included and to compensate for withdrawals, 30 patients per group were included. The sample size calculation for the present study was done post factum and was done using an online sample size calculator according to an estimated change of the buccal bone between pre-extraction and 1 year after implant placement of 0.4 mm (SD = 0.7) for the test group and of 0.5 mm (SD = 0.6) for the control group. A minimum of 55 patients in total is needed (significance level of 5%, power of 80%). For this study, we had to exclude patients, but still have the required minimum number of patients needed for the analysis.

The normal distribution of the continuous data was assessed by Shapiro-Wilk tests together with normal Q-Q-plots. The normal distributed data, shown by means ± standard deviation (SD), were analysed using ANCOVA to detect differences between groups and to test the effect of gingival phenotype on BBT and the effect of the preoperative bone defect on BBT. The correlations between MBML and BBT, marginal bone level and BBT (locations M0-M5 combined) were tested by a Pearson’s test.

4 | RESULTS

The patient characteristics of the study groups at T_pre are depicted in Table 1. There was not a significant difference in patient characteristics between the test and control group. Of the original 60 patients, 55 patients had CBCT data available, from before and 1 year after implant placement, for the current analysis (Figure 4). One implant was lost in both groups because of failing osseointegration. In addition, one patient from the test group and two patients from the control group had to be excluded from the final analysis because of unclear landmarks caused by scatter artefacts in the CBCT.

During follow-up, no signs of soft tissue complications at the donor site, or extensive bleeding of or perforation through the maxillary sinuses after harvesting bone from the tuberosity region, were observed. Additionally, there were no objective signs of infection.

4.1 | Buccal bone thickness

The average BBT at T_pre was 2.38 ± 0.81 mm and 2.28 ± 0.92 mm for the test and control group, respectively. At T_1, the BBT in the test and control groups was on average 1.62 ± 0.74 mm and 2.00 ± 0.90 mm respectively. At T_2, the average BBT was 1.57 ± 0.80 mm in the test group and 1.83 ± 0.94 mm in the control group.
The average change in BBT between \( T_{\text{pre}} \) and \( T_2 \) for the test group and control group was \(-0.84 \pm 0.61\) mm and \(-0.46 \pm 0.54\) mm, respectively (\( P = 0.02 \)). The change in BBT at the M0-M5 locations between \( T_{\text{pre}} \) and \( T_2 \) is displayed in Table 2.

### Change in approximal marginal bone level

Between \( T_1 \) and \( T_2 \), the average loss of marginal bone was \(0.05 \pm 0.33\) mm and \(0.01 \pm 0.38\) mm in the test and control group, respectively, without a significant difference between the groups (\( P = 0.95 \)).

### Change in mid-buccal mucosal level

A MBML gain of \(0.07 \pm 0.85\) mm (95%CI –0.25 to 0.40) was observed at \( T_2 \) compared to \( T_{\text{pre}} \) in the test group, whereas the control group (\( P = 0.03 \)) had a loss of \(-0.52 \pm 1.16\) mm (95%CI –0.98 to –0.07).

### Effect of gingival phenotype on BBT

A thin or thick preoperative gingival phenotype showed a significant effect on the change in BBT between \( T_{\text{pre}} \) and \( T_2 \) (\( P = 0.04 \)). In a regression model it was shown...
that both gingival phenotype \((P = 0.04)\) and use of a CTG \((P = 0.006)\) significantly affected the change in BBT.

### 4.5 Effect of preoperative bone defect on BBT and MBML

The preoperative bone defect in the test group showed no significant correlation with the change in BBT between \(T_{\text{pre}}\) and \(T_2\) \((r = 0.08; P = 0.69)\) and with the change in MBML between \(T_{\text{pre}}\) and \(T_2\) \((r = -0.28; P = 0.15)\). And also in the control group the preoperative bone defect showed no significant correlation with the change in BBT between \(T_{\text{pre}}\) and \(T_2\) \((r = -0.29; P = 0.14)\) and with the change in MBML between \(T_{\text{pre}}\) and \(T_2\) \((r = 0.21; P = 0.29)\).

### 4.6 Correlation testing between MBML and BBT

No significant correlations were found between the changes in MBML and BBT \((r = -0.22\) and \(P = 0.26\) for the test group and \(r = -0.09\) and \(P = 0.67\) for the control group, respectively).

### 4.7 Correlation testing between approximal marginal bone level and BBT

No significant correlations was found between the changes in marginal bone level and BBT for the test group \((r = 0.14\) and \(P = 0.49)\); there was a significant correlation between the changes in marginal bone level and BBT for the control group \((r = 0.46\) and \(P = 0.015)\).

### 5 DISCUSSION

The results of the present study reveal that placement of a CTG, compared to no soft tissue graft, in a single immediate implant site results in a greater decrease in BBT after 1 year.

Significantly more buccal bone loss was noted in the group that received a CTG (test group). A possible explanation for the higher loss of BBT in the test group could be the surgical intervention used for the application of the CTG. A small envelope flap was prepared at the mid-buccal aspect, which disrupted the vascularization between the mucosa and periosteum. The disruption in the blood supply, together with the bone remodeling process after tooth extraction, could have induced further loss of mid-buccal bone. Moreover, adding a CTG seems to have a larger effect on loss of BBT than the gingival phenotype.

Because most teeth in the anterior maxilla display a thin (≤1 mm) buccal bone wall, the BBT measured at \(T_2\) and the amount of loss of BBT observed between \(T_{\text{pre}}\) and \(T_2\) could suggest that the entire buccal bone wall was lost as a consequence of the bone remodeling process following tooth extraction, as proposed earlier. However, according to the reported data on the average BBT 1 year after placement of the final implant crown, it can be suggested that using the grafting procedure with an implant-socket gap of at least 2 mm results in a new buccal bone wall with sufficient width. This suggestion is supported by the results of a recent cohort-study, which showed that a new buccal bone wall can be created when grafting the implant-socket gap buccal of the immediately placed implant. This wall buccal of the implant was well preserved for at least 1 year after immediate implant placement. The created buccal bone wall even had a sufficient width in the test group, which showed more pronounced bone resorption than in the control group, to support the overlying peri-implant soft tissues and to preserve the mid-buccal mucosal level. The greater decrease in BBT in the test group was not accompanied with a greater recession of the MBML when applying a CTG. This may suggest that connective tissue grafting can limit the amount of recession of the MBML, as already shown by the study of Zuiderveld et al., resulting in a beneficial effect for the esthetic outcome. However, this beneficial effect could not be confirmed by a better Pink Esthetic Score (PES) for the test group compared to the control group. It has to be mentioned that in both groups a high acceptable level of \(PES \geq 6\) was attained. A possible explanation for the better preservation of the MBML when applying a CTG could be thickening of the mid-buccal mucosa, as proposed earlier. However, the study by van Nimwegen et al. on the same study group could not confirm that applying a CTG results in a thickened mid-buccal mucosa, because a general loss of the mid-buccal mucosal volume was found. Another possible explanation for the better MBML in the test group could be that the CTG might not have been placed in its entirety into the prepared envelope, causing a small amount of the graft to be located coronal of the mucosal margin resulting in the graft adding to the mucosal level.

The short-term results of this study show that connective tissue grafting results in significantly more buccal bone loss, although the MBML is preserved better than when no CTG is applied. Therefore, based on these results, the clinical recommendation is that a CTG should only be considered concomitant with immediate implant placement in order to prevent asymmetry in facial mucosa levels between the peri-implant mucosa and the gingival contour of the neighboring teeth.

An important limitation of this study is that long-term results are not yet available. Such data could show whether
the BBT remains stable and whether MBML can be preserved. Furthermore, the patient inclusion and randomization procedure resulted in a skewed distribution of the implant location in the canine region, which could have had an influence on the evaluation of the BBT.

6 | CONCLUSION

Connective tissue grafting combined with immediate placement and provisionalization of single implants results in more buccal bone loss in the esthetic zone after an observation period of 1 year than when no CTG was applied. However, connective tissue grafting has been shown to have a beneficial effect on the esthetic outcome, viz., limiting the recession of the mid-buccal peri-implant mucosa.

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CONFLICT OF INTEREST

All authors report no conflict of interest. This study was supported by an unrestricted grant from Nobel Biocare Services AG, Gothenburg, Sweden (by means of implant materials, research grant: 2012-1135).

AUTHOR CONTRIBUTIONS

All authors have made substantial contributions to conception and design of the study, data interpretation, revising the manuscript critically and given final approval of the version to be published. Elise G. Zuiderveld, Wouter G. van Nimwege, Henny J.A. Meijer, and Gerry M. Raghoobar have been involved in data collection, data analysis, and drafting the manuscript.

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