CHAPTER 4

Effect of connective tissue grafting on level and volume of the mid-buccal mucosa and change of buccal bone thickness of single immediate implants in the aesthetic zone

This chapter is an edited version of the manuscript:
Zuiderveld, E.G., van Nimwegen, W.G., Meijer, H.J.A., Jung, R.E., Mühlemann, S., Vissink, A., Raghoebar, G.M.
Effect of connective tissue grafting on level and volume of the mid-buccal mucosa and change of buccal bone thickness of single immediate implants in the aesthetic zone.
Submitted for publication, 2018

Abstract

Aim:

To assess the effect of a connective tissue graft on the preservation of the mid-buccal mucosal level (MBML), change in mid-buccal mucosal volume (MBMV) and buccal bone thickness (BBT) of single immediate implants in the aesthetic zone.

Materials & Methods:

The study consisted of 49 patients, who received an immediately placed implant and non-occluding provisional restoration, either combined with a connective tissue graft (test group, n=25) or without a connective tissue graft (control group, n=24). CBCTs were taken before removal of the tooth (T_{pre}) and twelve months (T_{12}) after final crown placement. MBML, MBMV and BBT were assessed at T_{pre} and T_{12}.

Results:

At T_{12}, change in MBML was 0.20±0.70 mm and -0.51±1.15 mm in the test and control group, respectively (p=0.01). The change in MBMV was -0.68±0.59 mm (test group) and -0.49±0.55 mm (control group, p=0.25). The average change in BBT was -0.81±0.66 mm (test group) and -0.47±0.55 mm (control group, p=0.05).

Conclusion:

These findings suggest that a connective tissue graft can reduce the recession of the mid-buccal mucosa, whilst it was accompanied with a loss in mucosal volume and buccal bone thickness, however.

Introduction

Single-tooth replacement by immediate implant placement and provisionalisation (IIPP) in the aesthetic zone has evolved into a viable treatment option with aesthetically acceptable results (Slagter et al. 2014, Del Fabbro et al. 2015, Khzam et al. 2015). Recession of the mid-buccal mucosa still commonly occurs, however (Chen & Buser 2014, Cosyn et al. 2016). This recession is most likely a result of the bone remodelling following tooth extraction, which cannot be prevented by immediate implant placement (Araújo et al. 2006, Vignoletti et al. 2012, Merheb et al. 2014). It is presumed that such a recession may lead to a less favourable aesthetic outcome.

To reduce the effects of bone resorption after tooth extraction, it is recommended that an implant should be positioned at least 2 mm palatal from the internal buccal socket wall and that the implant-socket gap should be grafted. The grafting procedure helps to create additional amounts of peri-implant hard tissue (Araújo et al. 2011) and is presumed to have a beneficial effect on the peri-implant soft tissues (Merheb et al. 2014, Lin et al. 2014, Cardaropoli et al. 2015).

In addition to grafting of the implant-socket gap, it has been proposed to thicken the peri-implant soft tissues with a connective tissue graft combined with implant placement in order to reduce recession and volume loss of the mid-buccal mucosa (Levine et al. 2014, Lee et al. 2016). Two randomized clinical trials (RCTs) observed less recession of the mid-buccal mucosa in immediate implant cases when combined with connective tissue grafting (Yoshino et al. 2014, Migliorati et al. 2015). Additionally, Migliorati et al. (2015) observed an increase in mucosal thickness when a connective tissue graft was applied.

Changes in mucosal volume of large areas of peri-implant soft tissues can be objectively measured using the volumetric analysis of Windisch et al. (2007). This analysis allows us to objectively measure the change in mid-buccal mucosal volume (MBMV) after implant placement either combined or not with a connective tissue graft. It has to be mentioned, however, that this analysis does not provide accurate information on the changes of the underlying buccal bone thickness (BBT). BBT is proposed to be a key factor that determines the overlying soft-tissue contour (Merheb et al. 2014). Therefore, changes in BBT can be considered an important outcome to aesthetic success. Slagter et al. (2015a) concluded that changes in BBT can be measured in a reliable and reproducible way on cone beam computed tomographic (CBCT) images. Therefore, we used both the volumetric analysis according to Windisch et al. (2007) and the CBCT analysis according to Slagter et al. (2015a).

As far as we know, no literature is available on assessing the effect of connective tissue grafting on the mid-buccal mucosal level (MBML), MBMV and BBT in the aesthetic zone when combined with immediate placed and provisionalised implants. Therefore, the aim of this study was to assess the effect of connective tissue grafting on the preservation of MBML, change in MBMV and change in BBT of single immediate implants in the aesthetic zone.

Materials & Methods

Study design

Sixty patients were included in a RCT assessing the effect of connective tissue grafting on peri-implant soft and hard tissues (Zuiderveld et al. 2018), approved by our Medical Ethical Committee (NL43085.042.13) and registered in a trial register (www.trialregister.nl: NTR3815). Written informed consent was obtained before enrollment of patients. All patients (aged ≥18 years) with a single failing tooth in the maxillofacial aesthetic zone (14-24) received an immediately installed implant-supported restoration. After immediate implant placement, patients were randomly allocated to one of the two study groups by sealed envelopes, opened by an independent research-assistant, either receiving a connective tissue graft harvested from the tuberosity region or no graft at implant placement. The present study investigates data regarding MBML presented by Zuiderveld et al. (2018) and data regarding MBMV presented by van Nimwegen et al. (2018) (Fig. 1), combined with data of CBCT scans taken before implant placement (T_{pre}), one month (T_1) and one year after final crown placement (T_{12}).

Patients

The following inclusion criteria were used:

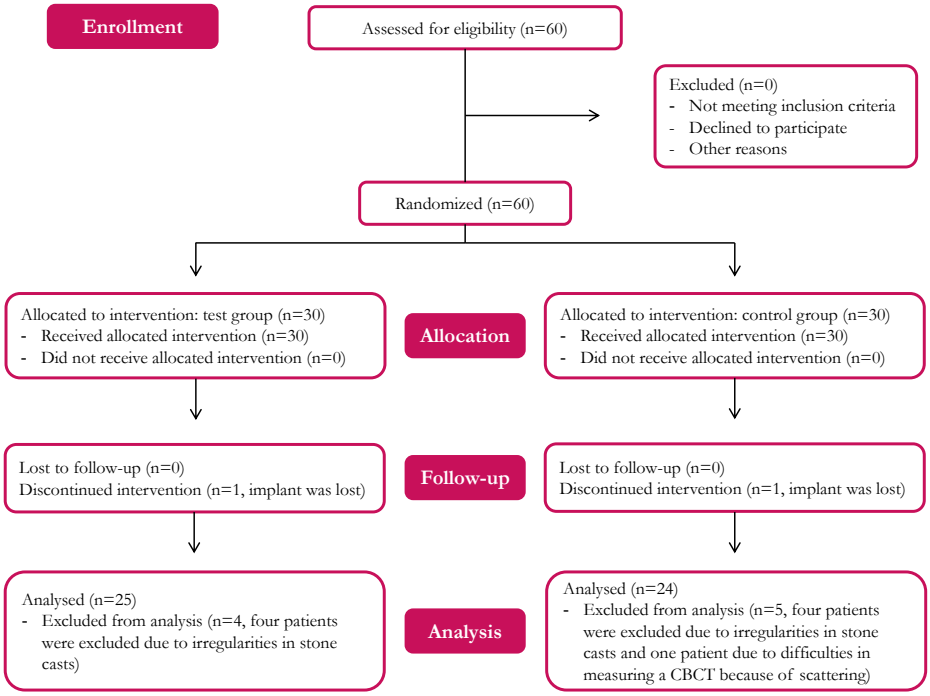
- a post-extraction vertical bone defect of the buccal socket wall of <5 mm measured from the bony defect to the buccal marginal mucosa using a periodontal probe (Williams Color-Coded probe; Hu-Friedy Chicago, IL, USA; Slagter et al. 2015b);
- adequate oral hygiene, i.e., modified plaque and sulcus bleeding score ≤1 (Mombelli et al. 1987);
- sufficient mesial-distal (≥6 mm) and interocclusal space for placement of an implant supported implant crown.

Exclusion criteria were:

- medical and general contraindications for the surgical procedure, expressed by ASA score ≥ III (Smeets et al. 1998);
- 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.

Fig. 1 – Cohort flow diagram



Intervention

One day prior to surgery, patients started taking antibiotics (amoxicillin 500mg, 3 times daily for 7 days or clindamycin 300mg, 4 times daily for 7 days in case of amoxicillin allergy) and using a 0.2% chlorhexidine mouthwash (2 times daily for 7 days). After administration of local anaesthesia the failing tooth was removed without raising a flap. Next, the implant site was prepared on the palatal side of the extraction socket according to the manufacturer's manual with the aid of a surgical template representing the ideal position of the prospective implant crown. Augmentation of the buccal implant-socket gap was carried out with a 1:1 mixture of autogenous bone, harvested from the maxillary tuberosity region or bone chips collected from the implant drills, and anorganic bovine bone (Geistlich Bio-Oss®, Geistlich Pharma AG, Wolhusen, Switzerland). Following, the implant (NobelActive, Nobel Biocare AB, Gothenburg, Sweden) 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. The

horizontal distance between buccal socket wall and the outer implant contour was at least 2 mm. Afterwards, an implant-level impression was taken for the fabrication of a non-occluding screw-retained provisional restoration and a healing abutment was placed. In the test group, a connective tissue graft was harvested from the maxillary tuberosity region. The graft was placed in a supraperiosteal envelope flap prepared at the buccal aspect and secured with vertical and horizontal mattresses (4-0 vicryl, Johnson&Johnson Gateway, Piscatatway, USA). The wounds in both groups were closed with Ethilon 5-0 nylon sutures (Johnson&Johnson). The same day as implant placement, the screw-retained provisional restoration was placed with a torque of 20Ncm.

After three months, a final implant-level open-tray impression was taken for fabrication of the final implant crown with an individualized zirconia abutment (NobelProcera, Nobel Biocare AB). 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 (H.J.A.M. and C.S.), and all crowns were fabricated by one dental technician (M.v.d.V.).

Outcome measures

MBML, MBMV (transformed to a linear distance according to the technique described by Schneider et al. (2011)) and BBT were assessed before extraction of the failing tooth (T_{pre}) and 12 months after placement of the final implant crown (T_{12}).

Measurement of mid-buccal mucosal level

Change in MBML was assessed at T_{12} and compared to pre-operative MBML (T_{pre}) as measured on standardized intra-oral photographs (camera: Canon EOS 650D with ring flash; Meijndert et al. 2004). For calibration of the photographs, a periodontal probe (Williams Color-Coded probe; Hu-Friedy) with known dimensions was held in close contact and parallel to the long axis of the tooth adjacent to the implant. Photographs were analysed using Adobe Photoshop (Adobe Photoshop CS5.1, Adobe Systems Inc., San Jose, USA). A horizontal line through the incisal edges of the natural neighbouring teeth was drawn (reference line). Next, the distance between the reference line and the mucosal margin of the failing tooth was measured (Zuiderveld et al. 2018).

Measurement of mid-buccal mucosal volume

Full-arch alginate impressions (Cavex, Cavex Holland BV, Haarlem, The Netherlands) were taken at T_{pre} and T_{12}. Afterwards, the impressions were poured in dental stone type IV (Sherahard-rock, Shera Werkstoff-Technologie, Lemförde, Germany) and the gypsum casts were optically scanned with a laboratory optical scanner (IScan D301i, Imetric, Courgenay, Switzerland) resulting in digital STL files (Standard Tessellation Language). For each patient

the digital surface models representing T_{pre} and T_{12} were imported into the volume analysis software (Swissmeda/SMOP, Zürich, Switzerland). A best-fit algorithm was then used to superimpose the digital surface models based on unchanged neighbouring tooth surfaces as reference. The study-relevant area of interest for the volumetric measurements was defined as described in previous volumetric studies (Thoma et al. 2010, Schneider et al. 2011). The mesial and distal papilla, the mucogingival line, and the crown margin served as anatomical reference structures to define the area of interest. If necessary, the coronal area of interest was shifted 1-2 mm more apical to avoid non-readable measurements because of an invalid superimposition. As a result, the area of interest was of variable size between patients. In order to allow for a direct comparison in volumetric changes between patients, the mean dimensional change per area was calculated and transformed to a mean linear buccal distance in millimetres (Schneider et al. 2011).

Measurement of buccal bone thickness

Change in BBT from T_{pre} to T_{12} was measured on CBCT scans (iCAT 3D exam scanner, KaVo Dental GmbH, Biberach, Germany) taken at T_{pre}, T_1 and T_{12} using NobelClinician (version 2.1, Nobel Biocare-Guided Surgery Center, Mechelen, Belgium). The CBCT scanner was validated for measuring bone thickness (Fourie et al. 2012) with a method error of 0.05 mm (95% CI 0.03-0.07). A standard voxel size of 0.30 and a FoV of 100x100 mm were used for all CBCTs. A new measuring method was used to measure changes in BBT (Slagter et al. 2015a).

First, the CBCT Digital Imaging and Communications in Medicine (DICOM) files of T_1 and T_{12} were imported into a medical image computing program (Maxilim, version 2.3, Medicim, Sint-Niklaas, Belgium). The exact position of the implant was then determined with Multi-modality Image Registration using Information Theory (MIRIT; Figs. 2a-d; Maes et al. 1997) and a Maxilim file with the exact coordinates of the implant in this particular patient was created. Then, these coordinates were used to align a planning implant on the exact same position with planning software (NobelClinician, NobelBiocare AB). Next, 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 apical (location M_0-M_5, Fig. 3). For each location, the distance of the buccal bone outline to the center of the implant was measured. 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, which are disturbed by scattering.

For buccal bone measurements in CBCT images taken at T_{pre}, DICOM files of T_1 and T_{pre} were both imported into Maxilim and aligned (Fig. 4a). Next, the Maxilim file with the exact coordinates of the implant in the CBCT image taken at T_1 was inserted in a new DICOM

file consisting of the combined DICOM files of T_{pre} and T_1 to place a planning implant according to the coordinates (Fig. 4b). Now, buccal bone measurements could be done on the prospective implant position in the T_{pre} CBCT image.

All measurements were done (with time interval to prevent recollection) by three independent operators (H.J.A.M., G.C.B. and E.G.Z.) in a random order.

Assessment of gingival biotype

The gingival biotype (thin/thick) was assessed at T_{pre} by means of transparency of a periodontal probe (Williams Color-Coded probe; Hu-Friedy) through the gingival margin (Kan et al. 2010).

Statistical analysis

Normal distribution of continuous data was assessed with Shapiro-Wilk tests together with normal Q-Q-plots. Normal distributed data are shown with means±standard deviation (SD) and were analysed using independent t-test to detect differences between groups. Non-normal distributed data are depicted with median and interquartile range (IQR) and were evaluated with Mann-Whitney tests.

The influence of gingival biotype on MBML, MBMV and BBT was assessed by a multiple variance analysis (MANOVA). Furthermore, a Pearson's test was carried out to test for correlations between MBML and MBMV, MBML and BBT (locations M0-M5 combined) and MBMV and BBT (locations M0-M5 combined).

Fig. 2a – CBCT image of the implant and the planning implant aside.

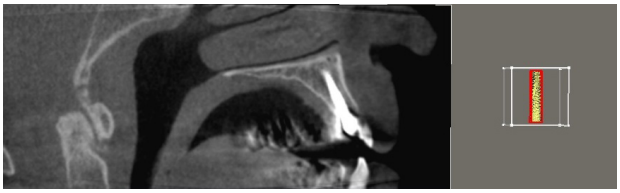


Fig. 2b – Manual alignment of the planning implant with the implant in the CBCT image.

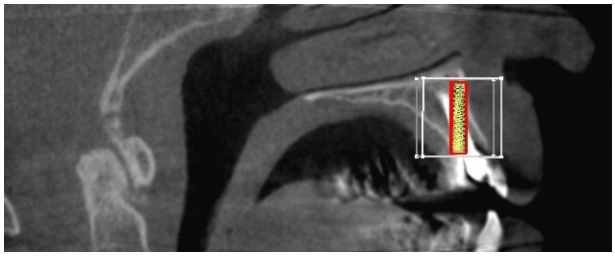


Fig. 2c – Further manual alignment of the implant with the implant in the CBCT image.

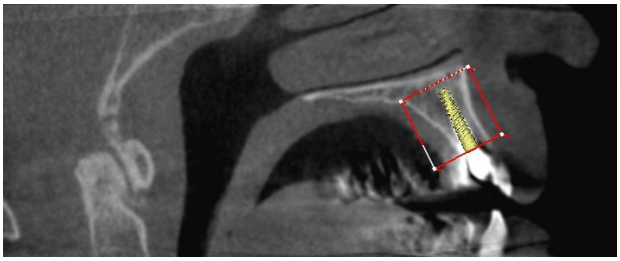


Fig. 2d – Last part of alignment done with MIRIT to obtain the exact coordinates of the implant in the CBCT image.

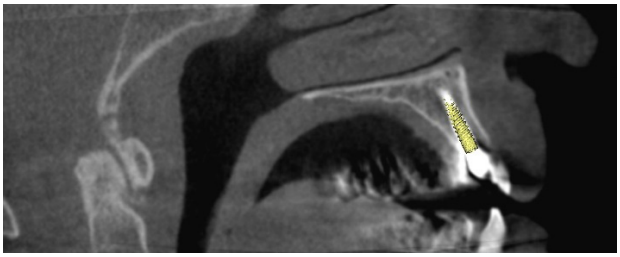
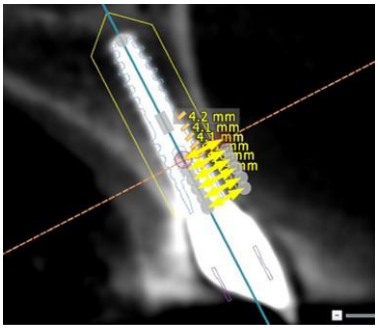


Fig. 3 – Planning implant superimposed over the implant in the CBCT image according to the exact coordinates obtained.



Measurements were done at each millimetre (M0-M5) along the axis of the implant for 5 mm, starting at the neck of the implant.

Fig. 4a – Alignment of DICOM files of CBCT images taken at T_{pre} and T_1.

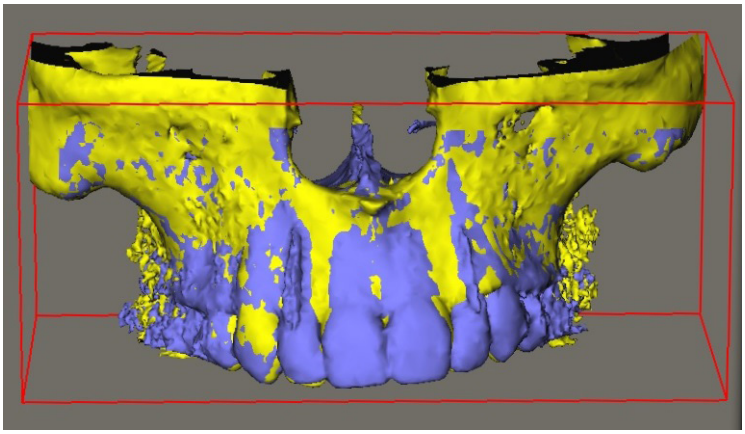
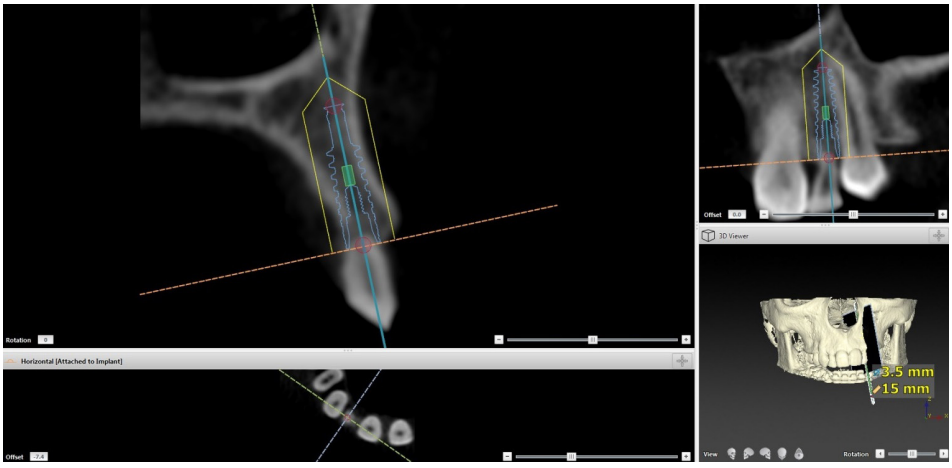


Fig. 4b – Alignment of planning implant according to the coordinates of the prospective position of the implant in the CBCT image taken at T_{pre} with the failing tooth still in place.



Results

Patient characteristics of the study groups at T_{pre} are depicted in Table 1. The distribution of gingival biotype was comparable between both groups (p=0.49). Of the original 60 patients, data of 49 patients were available for the current sub-analysis (Fig. 1): two implants were lost due to failing osseointegration (one implant in both groups), a total of nine patients (five from the control group and four from the test group) were excluded from final analysis due to irregularities in eight cast models and difficulties measuring one CBCT because of scattering.

Table 1 – Patient characteristics per study group at baseline (T_{pre}).

Variable	Test group (n=25)	Control group (n=24)
Male/female ratio	12/13	11/13
Age (years) mean±SD (range)	44.9±15.1 (19-67)	47.8±16.5 (20-82)
Gingival biotype thin/thick	16/9	13/11
Implant site location $I_1/I_2/C/P_1$	13/9/1/2	8/8/7/1
Implant length (mm) 15/18	4/21	4/20
Implant diameter (mm) 3.5/4.3	11/14	12/12

Change in mid-buccal mucosal level

At T_{12}, a MBML gain of 0.20±0.70 mm (95% CI -0.09 - 0.49) was observed in the test group, while a loss of -0.51±1.15 mm (95% CI -0.99 - -0.02) was seen in the control group (p=0.01).

Change in mid-buccal mucosal volume

At T_{12}, MBMV showed a comparable loss of volume in the test (-0.68±0.59 mm, 95% CI -0.92 - -0.44) and control (-0.49±0.55 mm, 95% CI -0.72 - -0.26) group (p=0.25).

Change in buccal bone thickness

The change in BBT at locations M0-M5 between T_{pre} and T_{12} is displayed in Table 2. No statistical differences in buccal bone loss were found between both groups, except for the measurement 2 mm apical of the implant neck (M_2, p=0.04). Nevertheless, at all locations (M0-M5) a slight tendency of more bone loss in the test group was measured.

Influence of gingival biotype on MBML, MBMV and BBT

At T_{12}, a significantly higher loss of MBMV was found in the control group in the presence of a thick pre-operative gingival biotype than in the presence of a thin gingival biotype (-0.74±0.66 mm versus -0.28±0.46 mm, p=0.04). In contrast, no significant differences in

loss of MBMV were found in the test group between a thin or thick gingival biotype. Furthermore, no significant differences in MBML and BBT were found between a thin or thick pre-operative gingival biotype, regardless of study group.

Correlation testing between MBML, MBMV and BBT

At $T_{12,}$ a significant correlation was found between the change in BBT (M0-M5) and change in MBMV in the control group (0.517, p=0.01). This implicated that a higher loss of BBT correlated with a higher loss of MBMV. This significant correlation was not found in the test group. Additionally, no significant correlations were found between change in MBML and MBMV and change in MBML and BBT, regardless of study group.

Table 2 – Change in buccal bone thickness between T_{pre} – T_{12}.

Location	Test group (n=25) mean±SD (mm)	Control group (n=24) mean±SD (mm)	p-value
M_0	-1.19±1.12	-0.81±0.67	0.15
M_1	-0.80±0.90	-0.48±0.54	0.13
M_2	-0.84±0.81	-0.40±0.63	0.04*
M_3	-0.72±0.65	-0.35±0.65	0.05
M_4	-0.69±0.59	-0.40±0.71	0.13
M_5	-0.63±0.64	-0.39±0.66	0.21
Total	-0.81±0.66	-0.47±0.55	0.05

*p <0.05 inter-group comparison.

Abbreviations: T_{pre}, pre-operative state; T_{12}, twelve months after crown placement.

Discussion

The results of the present study revealed that placement of a connective tissue graft compared to no soft tissue grafting in single immediate implants results in less recession of the mid-buccal mucosal level after one year and leads to a comparable change in mid-buccal mucosal volume and buccal bone thickness.

Less recession of the MBML when applying a connective tissue graft is in line with what has been reported by two earlier RCTs (Yoshino et al. 2014, Migliorati et al. 2015). This may suggest that connective tissue grafting can limit the amount of recession of the MBML through thickening of the mid-buccal mucosa, as proposed earlier (Levine et al. 2014, Lee et al. 2016). This study could not confirm that applying a connective tissue graft resulted in a thickened mid-buccal mucosa, since on average a loss of MBMV was found in both groups. The better preservation of the MBML in the test group, when there was no thickening found of the MBMV, could also not be explained by less resorption of BBT when applying a connective tissue graft.

A tendency of more buccal bone loss was noted in the test group compared to the control group. A possible explanation for the higher bone loss in the test group could be the surgical intervention used for application of the connective tissue graft. A small envelope flap had to be prepared, which is accompanied by disruption of the vascularization between mucosa and periosteum. In addition to the bone remodelling process after tooth extraction (Araújo et al. 2006, Vignoletti et al. 2012), this disruption of the blood supply could have induced further loss of buccal bone (Cosyn et al. 2013, Mazzocco et al. 2017).

As most teeth in the anterior maxilla display a thin (≤1 mm) buccal bone wall (Huynh-Ba et al. 2010, Januario et al. 2011, El Nahass & Naiem 2015), the BBT measured at T_{12} and the amount of loss of BBT observed between T_{pre}-T_{12} could suggest that most of the buccal bone wall was lost as a consequence of the bone remodelling process following tooth extraction, as proposed earlier (El Nahass & Naiem 2015, Morimoto et al. 2015). In addition, since it was stressed to place the implant at least 2 mm from the internal buccal socket wall and to graft the remaining gap (Merheb et al. 2014, Lin et al. 2014), which was done in the present study, it can be suggested that despite the more pronounced bone resorption in the test group a sufficient width of buccal bone and bone grafting material for the support of the MBML was left.

In the present study a significant correlation between change in BBT and change in MBMV in the control group was observed. This indicates that together with buccal bone loss also a loss of MBMV occurred. When a connective tissue graft was used, no correlations were found. This observation might be explained by the possibility that the additional thickness

of a connective tissue graft can mask changes in BBT. This is in line with what has been observed by Schwarz et al. (2016), viz. an inverse correlation between mucosal thickness and buccal bone thickness. However, because of their very short follow-up of 8 weeks, the true nature of this correlation is questionable.

The higher loss of MBMV in the control group in the presence of a thick pre-operative gingival biotype cannot be fully explained by existing literature, as no comparable studies are available. An earlier study of Cook et al. (2011) concluded that a thin gingival biotype is significantly correlated to a thinner BBT, which might be more prone to bone remodelling and bone loss. In contrast, this correlation was not found by La Rocca et al. (2012). As it is unknown whether the gingival biotype correlates with the thickness of the labial bone plate in the current study, no conclusions can be drawn on this finding.

Conclusion

Connective tissue grafting combined with immediate placement and provisionalisation of single implants in the aesthetic zone results in a better preservation of MBML, however, it did not contribute to a volume gain of the mid-buccal mucosa and buccal bone thickness.

References

Araújo, M.G., Linder, E. & Lindhe, J. (2011) Bio-Oss collagen in the buccal gap at immediate implants: a 6-month study in the dog. *Clinical oral implants research* 22, 1–8.

Araújo, M.G., Sukekava, F., Wennström, J.L. & Lindhe, J. (2006) Tissue modeling following implant placement in fresh extraction sockets. *Clinical oral implants research* 17, 615–624.

Cardaropoli, D., Tamagnone, L., Roffredo, A. & Gaveglio, L. (2015) Soft tissue contour changes at immediate postextraction single-tooth implants with immediate restoration: a 12-month prospective cohort study. *The International journal of periodontics & restorative dentistry* 35, 191–198.

Chen, S.T. & Buser, D. (2014) Esthetic outcomes following immediate and early implant placement in the anterior maxilla-a systematic review. *The International journal of oral & maxillofacial implants* 29 Suppl, 186–215.

Cook, D.R., Mealey, B.L., Verrett, R.G., Mills, M.P., Noujeim, M.E., Lasho, D.J. & Cronin, R.J. (2011) Relationship between clinical periodontal biotype and labial plate thickness: an in vivo study. *The International journal of periodontics & restorative dentistry* 31, 345–354.

Cosyn, J., De Bruyn, H. & Cleymaet, R. (2013) Soft tissue preservation and pink aesthetics around single immediate implant restorations: a 1-year prospective study. *Clinical implant dentistry and related research* 15, 847–857.

Cosyn, J., Eghbali, A., Hermans, A., Vervaeke, S., De Bruyn, H. & Cleymaet, R. (2016) A 5-year prospective study on single immediate implants in the aesthetic zone. *Journal of clinical periodontology* 43, 702–709.

Del Fabbro, M., Ceresoli, V., Taschieri, S., Ceci, C. & Testori, T. (2015) Immediate loading of postextraction implants in the esthetic area: systematic review of the literature. *Clinical implant dentistry and related research* 17, 52–70.

Fourie, Z., Damstra, J., Schepers, R.H., Gerrits, P.O. & Ren, Y. (2012) Segmentation process significantly influences the accuracy of 3D surface models derived from cone beam computed tomography. *European journal of radiology* 81, e524–530.

Huynh-Ba, G., Pjetursson, B.E., Sanz, M., Cecchinato, D., Ferrus, J., Lindhe, J. & Lang, N.P. (2010) Analysis of the socket bone wall dimensions in the upper maxilla in relation to immediate implant placement. *Clinical oral implants research* 21, 37–42.

Januario, A.L., Duarte, W.R., Barriviera, M., Mesti, J.C., Araújo, M.G. & Lindhe, J. (2011) Dimension of the facial bone wall in the anterior maxilla: a cone-beam computed tomography study. *Clinical oral implants research* 22, 1168–1171.

Kan, J.Y., Morimoto, T., Rungcharassaeng, K., Roe, P. & Smith, D.H. (2010) Gingival biotype assessment in the esthetic zone: visual versus direct measurement. *The International journal of periodontics & restorative dentistry* 30, 237–243.

Khzam, N., Arora, H., Kim, P., Fisher, A., Mattheos, N. & Ivanovski, S. (2015) Systematic review of soft tissue alterations and esthetic outcomes following immediate implant placement and restoration of single implants in the anterior maxilla. *Journal of periodontology* 86, 1321–1330.

Lee, C.T., Tao, C.Y. & Stoupel, J. (2016) The effect of subepithelial connective tissue graft placement on esthetic outcomes after immediate implant placement: systematic review. *Journal of periodontology* 87, 156–167.

Levine, R.A., Huynh-Ba, G. & Cochran, D.L. (2014) Soft tissue augmentation procedures for mucogingival defects in esthetic sites. *The International journal of oral & maxillofacial implants* 29 Suppl, 155–185.

Lin, G.H., Chan, H.L. & Wang, H.L. (2014) Effects of currently available surgical and restorative interventions on reducing midfacial mucosal recession of immediately placed single-tooth implants: a systematic review. *Journal of periodontology* 85, 92–102.

Maes, F.F., Collignon, A., Vandermeulen, D., Marchal, G., Suetens, P. (1997) Multimodality image registration by maximization of mutual information. *Medical Imaging, IEEE Transactions on Medical Imaging* 16, 187–198.

Mazzocco, F., Jimenez, D., Barallat, L., Paniz, G., Del Fabbro, M. & Nart, J. (2017) Bone volume changes after immediate implant placement with or without flap elevation. *Clinical oral implants research* 28, 495–501.

Meijndert, L., Meijer, H.J.A., Raghoebar, G.M. & Vissink, A. (2004) A technique for standardized evaluation of soft and hard peri-implant tissues in partially edentulous patients. *Journal of periodontology* 75, 646–651.

Merheb, J., Quirynen, M. & Teughels, W. (2014) Critical buccal bone dimensions along implants. *Periodontology 2000* 66, 97–105.

Migliorati, M., Amorfini, L., Signori, A., Biavati, A.S. & Benedicenti, S. (2015) Clinical and aesthetic outcome with post-extractive implants with or without soft tissue augmentation: a 2-year randomized clinical trial. *Clinical implant dentistry and related research* 17, 983–995.

Mombelli, A., van Oosten, M.A., Schurch Jr, E. & Lang, N.P. (1987) The microbiota associated with successful or failing osseointegrated titanium implants. *Oral microbiology and immunology* 2, 145–151.

Morimoto, T., Tsukiyama, Y., Morimoto, K. & Koyano, K. (2015) Facial bone alterations on maxillary anterior single implants for immediate placement and provisionalization following tooth extraction: a superimposed cone beam computed tomography study. *Clinical oral implants research* 26, 1383–1389.

El Nahass, H. & Naiem, S.N. (2015) Analysis of the dimensions of the labial bone wall in the anterior maxilla: a cone-beam computed tomography study. *Clinical oral implants research* 26, e57–61.

Van Nimwegen, W.G., Raghoebar, G.M., Zuiderveld, E.G., Jung, R.E., Meijer, H.J.A., Mühlemann, S. (2018) Immediate placement and provisionalization of implants in the aesthetic zone with or without a connective tissue graft: A 1-year Randomized Controlled Trial and Volumetric Study. *Clinical oral implants research*, doi:10.1111/clr.13258.

La Rocca, A.P., Alemany, A.S., Levi, P., Juan, M.V., Molina, J.N. & Weisgold, A.S. (2012) Anterior maxillary and mandibular biotype: relationship between gingival thickness and width with respect to underlying bone thickness. *Implant dentistry* 21, 507–515.

Schneider, D., Grunder, U., Ender, A., Hämmerle, C.H.F. & Jung, R.E. (2011) Volume gain and stability of peri-implant tissue following bone and soft tissue augmentation: 1-year results from a prospective cohort study. *Clinical oral implants research* 22, 28–37.

Schwarz, F., Sager, M., Golubovic, V., Iglhaut, G. & Becker, K. (2016) Horizontal mucosal thickness at implant sites as it correlates with the integrity and thickness of the buccal bone plate. *Clinical oral implants research* 27, 1305–1309.

Slagter, K.W., den Hartog, L., Bakker, N.A., Vissink, A., Meijer, H.J.A. & Raghoebar, G.M. (2014) Immediate placement of dental implants in the esthetic zone: a systematic review and pooled analysis. *Journal of periodontology* 85, e241–250.

Slagter, K.W., Raghoebar, G.M., Vissink, A. & Meijer, H.J.A. (2015a) Inter- and intraobserver reproducibility of buccal bone measurements at dental implants with cone beam computed tomography in the esthetic region. *International journal of implant dentistry* 1, 8. doi:10.1186/s40729-015-0007-1.

Slagter, K.W., Meijer, H.J.A., Bakker, N.A., Vissink, A. & Raghoebar, G.M. (2015b) Feasibility of immediate placement of single-tooth implants in the aesthetic zone: a 1-year randomized controlled trial. *Journal of clinical periodontology* 42, 773–782.

Smeets, E.C., de Jong, K.J. & Abraham-Inpijn, L. (1998) Detecting the medically compromised patient in dentistry by means of the medical risk-related history. A survey of 29,424 dental patients in The Netherlands. *Preventive medicine* 27, 530–535.

Thoma, D.S., Jung, R.E., Schneider, D., Cochran, D.L., Ender, A., Jones, A.A., Gorlach, C., Uebersax, L., Graf-Hausner, U. & Hämmerle, C.H.F. (2010) Soft tissue volume augmentation by the use of collagen-based matrices: a volumetric analysis. *Journal of clinical periodontology* 37, 659–666.

Vignoletti, F., Discepoli, N., Muller, A., de Sanctis, M., Munoz, F. & Sanz, M. (2012) Bone modelling at fresh extraction sockets: immediate implant placement versus spontaneous healing: an experimental study in the beagle dog. *Journal of clinical periodontology* 39, 91–97.

Windisch, S.I., Jung, R.E., Sailer, I., Studer, S.P., Ender, A. & Hämmerle, C.H.F. (2007) A new optical method to evaluate three-dimensional volume changes of alveolar contours: a methodological in vitro study. *Clinical oral implants research* 18, 545–551.

Yoshino, S., Kan, J.Y., Rungcharassaeng, K., Roe, P. & Lozada, J.L. (2014) Effects of connective tissue grafting on the facial gingival level following single immediate implant placement and provisionalization in the esthetic zone: a 1-year randomized controlled prospective study. *The International journal of oral & maxillofacial implants* 29, 432–440.

Zuiderveld, E.G., Meijer, H.J.A., den Hartog, L., Vissink, A. & Raghoebar, G.M. (2018) Effect of connective tissue grafting on peri-implant tissue in single immediate implant sites: a RCT. *Journal of clinical periodontology* 45, 253–264.