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Abstract

Background: GBR is considered an effective tool for gaining mineralized tissue either at exposed implant surface or in deficient alveolar ridge areas prior to implant placement.

Material & Methods: Customized casts obtained following impression taking at surgery and re-entry allowed for morphometric assessment of alveolar ridge alterations 6 months after one-stage augmentation of bone dehiscences. In a randomized pilot study using biphasic calcium phosphate tests (n=17) received treatment with ribose cross linked collagen membranes whereas controls (n=20) received non-cross linked membranes. The primary endpoint was to quantify the effect of membrane type on dimensional changes in bone margins at crestal level of endosseous implants.

Results: Soft tissue dehiscencies occurred at 70.5% and 55% frequency for tests and controls, respectively. Gain in clinically hard newly mineralized tissue at the crestal level was significantly higher in test group in lateral (1.8mm vs. 0.7mm; *p*=.046) and in vertical dimensions (1.1mm vs. 0.2mm; *p*=.035) compared to controls. Second measurement obtained at the border of reflected flap revealed none-significant difference between groups (3.0mm vs. 2.1mm; *p*=0.57) for lateral dimension.

Conclusions: both collagen devices were effective in bone augmentation. RCLMs supported mineralization process and remodeling even in sites showing compromised healing as indicated by morphometric outcome.

Clinical relevance

Scientific rationale for the study: Limited data are available regarding morphometric outcome in terms of mineralized tissue gain if either cross linked or non-cross linked collagen membranes were used in lateral augmentation.

Principial findings: Results indicate both membranes having potential to effectively support GBR in dehiscence type of defect. Dehiscence of the soft tissue occurred in 70.5% of test and in 55% of control sites. However, significantly higher amount of newly mineralized tissue in a most critical zone argues for the use of cross linked collagen membranes although more exposures occurred in test sites.

Practical implications: Cross linked membranes combined with biphasic calcium phosphate are suitable for GBR and likely to support formation of significant amount of newly mineralized tissue under unlikely clinical conditions.

Introduction

Guided bone regeneration (GBR) is one of several well documented, evidence based augmentation techniques (Hammerle & Karring, 1998; McAllister & Haghighat, 2007). Several animal and clinical studies showed gain in marginal bone, using resorbable membranes in combination with an underlying, osteoconductive membrane-supporting material (Hammerle & Lang, 2001; Hockers, et al., 1999; Strietzel, et al., 2006; Zitzmann et al., 2001). Collagen membranes, as the most frequently used type of degradable membranes, lack enough stiffness for space maintenance and tend to collapse (Strietzel et al., 2006). Therefore, titanium re-inforced non-degradable e-PTFE membranes are still favored by some clinicians. Early exposure of barrier membranes to the oral environment jeopardizes the outcome due to infection, mostly manifested around non-resorbable membranes, or due to rapid disintegration in case of resorbable membrane (De Sanctis et al., 1996; Mayrand & Grenier, 1985; Nowzari & Slots, 1995; Sela, et al., 2003; Simion, et al., 1994; Tempro & Nalbandian, 1993).

Collagen cross-linking contributes to prolonged membrane barrier function (Bornstein et al., 2007; von Arx, et al., 2005). Barriers with high degradation rates could have a shorter-than-indicated effect (Moses, et al., 2008). Membrane degradation starts shortly after implantation (von Arx et al., 2005). The integration pattern of various collagen membranes into soft tissues were analyzed in recently published animal studies (Rothamel, et al., 2005; Schwarz, et al., 2006). A larger membrane porosity (less collagen contents per area) would allow for cell ingrowths within the membrane, resulting in better tissue (Rothamel et al., 2005; Schwarz et al., 2006), but may result in reduced barrier function (Rothamel, et al., 2004). Importantly, nutrient diffusion for cell proliferation and differentiation was not affected by collagen cross linking vs. non-cross linking in an in-vitro study (Friedmann, et al., 2008). Significantly more new

bone formation in animal defects augmented with biphasic calcium phosphate (BCP) together with either a non-degradable (e-PTFE) or a newly introduced slowly degrading polyethylene glycol membranes vs. controls grafted without membranes was recently confirmed by Jung, et al. (Jung, et al., 2006). Nevertheless, the discussion upon the benefits and disadvantages of cross-linked collagen material as slowly degradable vs. membranes from native collagen, a rapidly degrading type is still ongoing. In this respect, there is no data regarding the efficiency of resorbable membranes to support bone gain in cases in which bone augmentation is performed with simultaneous installation of implants with transgingival surgical elements.

Morphometric assessment of outcomes in bone augmentation in terms of volume gain has been the topic for in vitro and clinical studies (Kohles, et al., 2000; Llambes et al., 2007; Proussaefs & Lozada 2005; Proussaefs, et al., 2002; Studer, et al., 1997; Tai et al., 2000; Windisch, et al., 2007). Our group introduced a method to perform morphometric measurements on casts obtained from impressions of the residual alveolar ridge taken during surgery and of the post-augmented ridge taken during re-entry (Pitaru, et al., 2006).

The aim of the present randomized clinical trial was to test the efficiency of supporting bone gain and promoting soft tissue healing of a ribose cross-linked collagen membrane (RCLM) vs. a non-cross-linked collagen membrane (NCLM) during augmentation of bone dehiscences and fenestrations with biphasic calcium phosphate and concomitant implant placement using a new morphometric approach for human clinical trials.

Material and Methods

This study was a randomised controlled, single-blinded pilot clinical trial with an observation period of six months. All participants signed a written consent prior to the beginning of surgical procedures. The study was conducted in accordance with the guidelines of Good Clinical Practice (GCP-ICH) and the principles of the Declaration of Helsinki. The study was approved by the Ethics Committee of the Universitätsmedizin Charité, Berlin, Germany, under protocol number EA2/054/05 and registered at ClinicalTrials.gov under ID: NCT00835432. Patients were recruited from the pool of recall patients at the Department of Periodontology and Synoptic Dentistry or from referring dentists during the years 2005-2006. Included were partially edentulous patients in good general health with one or more teeth missing and requiring bone augmentation with placement of implants. There were no restrictions with regard to the location of the edentulous area, i.e. anterior and posterior regions of the maxilla and/or mandible were included. The study used a block randomization to randomize patients to either the cross-linked test (OSSIX, 3i, Palm Beach, FL, USA) or the non-cross-linked control (BioGide, Geistlich, Wohlhusen, Switzerland) membranes in a 1:1 ratio. This was a pilot study and no sample size calculation was performed. At the beginning of the study, treatment allocation for each patient was placed in a sealed envelope to be opened during the surgery. In patients who had two surgical sites that met the inclusion criteria, both sites were treated concomitantly and the first site received the membrane as per treatment allocation while the second site received the alternative treatment, facilitating comparisons within patients with two surgical sites.

Smokers consuming 10 or more cigarettes per day were excluded. All treatments were performed between November 2005 and May 2007. All surgeries were carried

out under local aneasthesia (Ultracain DS forte, Aventis, Germany) by a single surgeon (AF). All patients received a one-stage procedure including implant placement, concomitant augmentation, and primary wound closure. Defect extensions were recorded using periodontal probe (PCP 15, Hu-Friedy, Leimen, Germany) during surgery. While in vivo measurements were performed by the surgeon, morphometric analyses on the casts obtained were carried out by the Clinical Investigator (KG), who was blinded to the randomized patient assignment. In addition, impressions were taken for ex-vivo measurements by a blinded investigator (KG) using individualised plastic trays and a sterile A-silicone material (Elite® Implant, Zhermack, Germany). These impressions were taken before and after reflection of a muco-periosteal flap exposing the defect area. Straumann Soft Tissue Level implants with 4.1 mm in diameter and varying from 8 to 12mm in length (Institute Straumann AG, Basel, Switzerland) were used in accordance with established guidelines. In brief, recipient site was prepared for placing implant with it rough SLA surface at the crestal level of alveolar bone leaving the machined part of the implant neck above the bone level. Standard Plus (SP) implants with a machined neck of 1.8 mm were used. Biphasic calcium phosphate (BoneCeramic, Institute Straumann AG, Basel, Switzerland) was used for grafting dehiscences and fenestrations in alveolar bone in exposed implant areas. No autogenous bone was used. For easier application, a coagulum was formed by the calcium phosphate grafting material with 1 to 2 ml of the patients' own blood collected in the wound area after the incisions were carried out (Artzi, et al., 2005; Friedmann, et al., 2002); Friedman, et al., 2009). The composite grafting material was placed in the defect up to the level of the machined surface of the implant, in the vertical direction and up to the completion of the bony envelop in the lateral direction. After application of the augmentation material, envelopes containing the randomization code were opened

and membrane placement was performed as assigned. Each membrane was applied in a monolayer. All flaps were coronally advanced by periosteal release to achieve a tension free adaptation of soft tissue margins for complete closure of the wound. The post-operative regimen included twice daily mouth rinses with Chlorhexidine 0.2% (Chlorhexamed, Glaxo Smith Kline, Bühl, Germany). Systemic antibiotics, either amoxicillin 750mg 3xdaily (Amoxicillin-Ratiopharm, Ratiopharm, Germany) or clindamycine 300 mg 4xdaily (Clindamycin-Ratiopharm, Ratiopharm, Germany) were administered for 1 week; and ibuprofen (Ibuprofen-Ratiopharm 600mg, Ratiopharm, Germany) as necessary for postoperative analgesia. Sutures were removed after 14 days. Fixed partial dentures or semi-permanent splinting were used as temporary prosthetic devices only. In edentulous posterior regions, no dentures were applied during the study.

At re-entry after 6 months, an impression was taken to document tissue dimensions and full thickness flaps were then raised using similar incision extensions as during the first surgery, with the exception for lingual flaps which were not raised if the area augmented was sufficiently exposed (Fig. 2a-f). Following thorough removal of any remaining non-mineralized tissue with sterile curettes another impression was taken to document hard-tissue dimensions. In nine cases requiring additional augmentation, BCP and RCLM were used. All implants received gingival formers (Straumann AG, Basel, Switzerland) and the flap was sutured back by single sutures using Monocryl 6.0 suture (Ethicon, Hamburg, Germany).

Morphometric procedure

The primary objective of the study was to quantify the effect of the type of collagen membrane on the level of bone augmentation at the crestal level of endosseous implants. To do this the following morphometric procedure was undertaken. All

impressions were cast in stone rock plaster (Octa Stone CN, Hereus – Kulzer, Bensheim, Germany). Casts of impressions obtained at initial surgery and at re-entry (post-augmentation) are designated as casts-0 and casts-1, respectively. Negative templates of casts-1 were obtained by taking silicon (C-silicon, Silaplast®, Detax, Germany) impressions. Using landmarks as teeth adjacent to the augmented site and the implant neck the negative templates were adjusted upon the casts-1 (Fig. 3a+b). To determine reference points and to ascertain reproducibility in positioning one and the same template on casts obtained at both surgeries, the top aspects of the templates were trimmed parallel with the basis of cast 1; furthermore the side walls of templates were trimmed perpendicular to top and bottom aspect of the templates (Fig. 4a-d). While kept together, the casts-1 and their negative silicon templates were sectioned through bucco-lingual plans that mid-crossed in mesio-distal dimension of implants around which augmentation was performed. A perpendicular was dropped from the edge of template to the middle of the cover screw of a cross-sectioned implant to label central implant axis (Fig. 4a). To assess vertical dimension a parallel perpendicular was marked on the template at the crossing point of alveolar crest and implant surface and the distance between this point and the top plan of the silicon template was measured with a digitized calliper and termed - H1/1 (Fig. 3a; 4a). A perpendicular to H1/1 passing through the crossing point of alveolar crest and implant surface was drawn. The distance between the implant middle axis and the buccal aspect of the alveolar crest was measured on this perpendicular and termed - W1/1 (Fig. 3a; 4a). A second perpendicular, parallel to H1/1 was drawn at the level of most pronounced buccal aspect of augmented area and the distance from the middle of implant to this aspect was recorded and termed - W2/1 (Fig. 4a; 4b). The distance from this point to the top plan of the silicon template was measured with a digitized caliper and termed - H2/1 (Fig. 4a). Then, the cross sectioned silicon templates were

adapted to the casts-0 obtained during the augmentation procedure using the reference marks mentioned above (Fig. 4c+d). Using the templates as landmarks the casts-0 were sectioned in the same plan as described above for the casts-1. Using the landmark lines drawn on the silicon templates, now adapted to casts-0, the distances measured on casts-1 were measured for casts-0 and termed W1/0; H1/0; W2/0; and H2/0. This methodology ensured that casts-0 and casts-1 were sectioned in the same plans and exactly at the same site, that is a bucco-lingual plan crossing the central axis of the implants (Fig. 4b). Bone gain in width and height was calculated by:

- Crestal (coronal) width gain: $\Delta W1 = W1/1 - W1/0$

- Crestal (coronal) vertical gain: $\Delta H1 = H1/0 - H1/1$

- Apical width gain: $\Delta W2 = W2/1 - W2/0$

- Apical vertical gain: $\Delta H2 = H2/0 - H2/1$

Statistical analysis

Changes in hard and soft-tissue dimensions between baseline and re-entry were outcomes of interest. Data were analyzed in two different ways. Firstly, data of all 37 patients were analyzed using one randomly selected site of those patients with two surgical sites. Comparisons between groups and between baseline and re-entry within groups were made using t-tests and paired t-tests as appropriate. Further analyses used multiple linear regression adjusting for maxillary vs. mandibular defects, anterior and posterior sites, smoking, membrane exposure. Secondly, comparisons between groups were made limited to data of those patients who had two surgical sites (split-mouth comparison) using non-parametric Wilxocon sign rank

tests. All statistical tests were two-sided at α=0.05 and performed using statistical

software (STATA 11, Stata Corp, College Station, TX, USA).

Results

Patient recruitment involved 40 patients; three of them were excluded due to the extensive loss of alveolar bone making therefore the implant placement at one stage with augmentation not feasible (Fig. 1). All patients included completed the study, resulting in a total of 37 patients with 46 defect sites. All implants inserted (in total: 73) were well integrated after 6 months of healing. All implants received gingival formers for 4 to 6 weeks being loaded subsequently by single crowns or fixed partial dentures. There were 37 implants placed in 17 defect sites in the test group and 36 implants in 20 sites in the control group (Table 1). The overall survival rate at time point of loading was 100%.

Albeit patient assignment to the test and control groups was performed randomly, groups matched well in regard to patient's age, proportions between females and males and distribution of sites between maxilla and mandible (Table 1). In both groups not-smoking patients and smoking <10 cigarettes/day were represented in similar frequency. A group of nine patients formed a split mouth group and were treated at 2 sites each site with a different membrane. Analysis of the morphometric results within this group indicated not-statistically significant differences between the sites treated with the RCLM and those treated with NCLM. Therefore, only one site per patient has been chosen by secondary randomization assigning one study site and implant per patient, either to tests or to controls. Thus, Table 2 represents 37 patient data sets and the distribution among test and control group for 37 study sites randomly selected for analysis. The age ranged from 24 to 69 years with a median of 53 years (Table 2).

No adverse events were recorded but one participant in the control group showed hypersensitive reaction to Amoxicillin, which then was exchanged by Zithromax (Azithromycine, Pfizer, Germany).

Morphometric results

Statistical outcomes for all 37 sites including randomly selected one site per patient out of former split mouth randomization are given by Table 3. At reference point 1 (W1 / H1), indicating the most crestal bone-to-implant contact the median gain of mineralized tissue in the vertical dimension (vertical gain; $\Delta H1$) was 1.1mm in the test sites compared to 0.2 mm in the control sites (p = .0463). The median gain in the horizontal dimension (width gain; $\Delta W1$) was 1.8 mm in the test sites vs. 0.7 mm in the control sites (p = .0359). There were no statistically significant associations between the primary outcome and membrane exposure (p = .6845 for $\Delta H1$ and p = .2809 for $\Delta W1$, respectively).

At the second reference point ($\Delta W2$ / $\Delta H2$), the most apically accessible point for measurement, the median vertical gains were 2.5 mm and 2.7 mm for the test and control sites, respectively (p = 0.5674). The median width gains at this reference point were 3.0 mm and 2.1 mm for test and control sites, respectively (p = .1189).

In both groups of patients, test and control sites which exhibited soft tissue dehiscence required additional augmentation at exposed implant surface. There were 4 sites in the test group and 5 sites in the control group (23.5% vs. 20%, respectively) requiring additional treatment; implants involved received secondary application of BCP plus RCLM membranes at re-entry.

Discussion

The aim of the present randomized clinical trial was to test the effectivity of ribose-cross linked (RCLM; test) membrane vs. a non-cross linked (NCLM; control) membrane in GBR treatment using a new method for morphometric analysis. Generally, the results indicate that both membranes improved the bone volume and predictably supported GBR procedures at dehiscence-type and fenestration-type defects.

The rate of soft tissue dehiscences during healing was almost equally distributed for both groups. Over 50% of sites were exposed and underwent secondary epithelization. The figures are high compared to the data presented for the group of dehisence-type defects within the review by Jensen & Terheyden. They found rates of soft tissue dehiscences up to 14.5% for sites with resorbable and of 26.3% for those with non-resorbable mebranes (Jensen & Terheyden, 2009). Similar observations in regard to RCLM samples were reported previously by our group (Friedmann et al., 2001). Moses et al. found the RCLM membrane demonstrating a higher reduction of the bony defect area in cases of premature membrane exposure (Moses, et al., 2005). The history of premature membrane exposure may have a negative effect on new bone formation even if soft tissue dehiscence recovers by secondary epithelization. Although ribose-cross linked membranes might be associated with a higher incidence rate of soft tissue dehiscences (Moses et al., 2005; Tal, et al., 2008), the frequency of concomitant inflammatory reactions reported is almost zero (Friedmann et al., 2001). On the opposite, the histological report by Zubery et al. demonstrated nicely the ossification of ribose cross linked collagen membrane remnants facing underlying newly mineralized tissues. These observations support the idea that slow degradation of ribose-cross linked collagen

membranes is beneficial for mineralization process (Zubery, et al., 2007; Zubery et al., 2008).

In our study Soft Tissue Level Straumann implants were inserted in accordance with the ITI surgical protocol resulting in a position of the machined part of implant neck supracrestally. However, all implants and augmentation sites were planned to heal in the submerged mode according to the study protocol. Therefore complete flap closure required mobilization and coronal advancing of the flap to achieve tension free primary wound closure over the implant neck exceeding almost 2mm coronally to the crest. No grafting material was applied in the supracrestal area of bone dehiscencies laterally and therefore it is conceivable that flap stabilization was under optimal in this study. This lack of membrane support by grafting material might explain the unexpected high frequency of soft tissue dehiscence and premature membrane exposure. In a recent study by Burkhard and Lang tensions exceeding 0.1N determined before suturering the flap resulted in a wound dehiscence rate over 40% (Burkhardt & Lang, 2010). The high prevalence of dehiscences in our study may be a result of mechanical challenges due to masticatory movements as a complementary factor to membrane properties. According to the implant design secondary epithelialisation in this study did not always result in complete soft tissue closure over the cover screw. However, the difference in frequency of dehiscence onset following augmentation and the need of additional augmentation at re-entry was obvious.

The method used to assess bone gain was originally introduced by Pitaru et al. 2006 at Europerio in Madrid, Spain (Pitaru et al., 2006). Customizing each defect site before and after augmentation in plaster of paris allowed for determining identically positioned reference points on boths. A silikon template transfered the

reference points from one cast to the other. Implants inserted concomitantly with augmentation of dehiscence bone defects served as reference points. Albeit the implant necks were positioned supracrestally the equicrestal level of roughened sand blasted and acid-etched (SLA) surface on casts obtained at re-entry was clearly indicated. Therefore, measurements across alveolar crest perpendicular to the most coronal bony margin performed in this study can be considered standardized. In a previous publication our group demonstrated the degree of mineralization in newly formed tissues exceeding 40% in the area grafted laterally with BCP (Friedmann, et al., 2009). Since in this study biopsies for the histomorphometric analysis were harvested during re-entry surgeries from sites augmented in the present study, histologic outcome indicates an effective denudation of bony crest (Friedmann et al., 2009). Taking these observations into account and furthermore by removing all non-mineralized tissue from underneath the flap prior to impression we payed maximum attention to establish accuracy of the impressions. Since all surgeries were performed by one co-worker (AF) we consider the approach standardized for all sites. Our study presents for first time an accurate method for quantifying vertical and horizontal changes of the alveolar ridge in GBR. Furthermore this is first prospective report on efficacy of collagen membranes in one stage GBR with one stage Soft Tissue Level Straumann implants. Lang et al. reported successful implementation of Gore Tex membranes placing them around necks of Straumann implants which, however, healed in transmucosal mode (1994) (Lang, et al., 1994). The methods for tracking defect changes introduced in periodontal regeneration as standardized probing from the cemento-enamel junction (CEJ) to the deepest defect extension at baseline and at re-entry surgery (Yukna et al., 2000; Lekovic et al., 2002) are not applicable for purposes outlined in this study. Even in a situation illustrated by Fig. 2a – 2f

==probing across the ridge would result in significant variation in positioning any measuring device at baseline and the re-entry surgeries.==

Retrospective analyses presented by Jensen and Terhyeden at ITI consensus conference 2008 revealed an average fill of 85.5% together with 68.5% completely regenerated defects, respectively, calculated for the group of dehiscence-type of defects if a resorbable membrane was used. The rate of infectious complications was 13.75%. These data are based on a review of 20 studies (Jensen & Terheyden, 2009).

Our results did not evaluate the level of defect fill, but rather the change in the bone dimensions in the defect. Nevertheless, sites requiring additional augmentation can be considered showing incomplete regeneration. Implants exposed in the area to be grafted are generally considered seeking new bone formation. A failure in apposition of new bone results therefore in an unlikely contact of the implant surface with soft tissues bearing odds for onsetting peri-implantitis. Therefore, the gain in mineralized tissue at the crestal level of implant roughened surface is the crucial parameter in testing the efficacy of GBR procedure. The statistically significant differences in gain of clinically hard mineralized tissues at the crestal border of previously exposed SLA-surface (H1/W1) favors the use of the ribose-cross linked collagen test membrane. Clinically viable amounts of mineralized tissue was gained in the test group as indicated by without exception positive values for the difference between baseline and 6 months results in height and width parameters (ΔH1; ΔW1) of the bone covering previousely exposed implant areas (Tab. 3). There was none additional gain and even a slight loss of bone occurred obviously in some controls as expressed by negative differences in crestal height and width for this group. Taking into account similar frequencies of dehiscence onset in both groups, we had to assume that cases

treated with RCLM (tests) had a greater benefit in regard to primary outcome than those treated with NCLM (controls). This interpretation is supported by results of an animal study, which showed significantly greater membrane stability for the RCLM than for NCLM sutured onto oral mucosa in rats, both materials being exactly same as used in our study (Rothamel et al., 2005). The unpublished in vitro data by Pitaru et al. showed greater resistance of RCLM vs. NCLM against bacterial collagenases (personal communication, October 14, 2010). Evaluating at re-entry the degradation status of both collagen membranes histologically Tal et al. found that among 26 initially applied RCLMs 13 were prematurely exposed (50%). Five out of them appeared interrupted and four were completely degraded 6 months following placement, whereas all devices from none-exposed sites remained intact. On the contrary, none of 18 NCLM devices initially applied was detectible at re-entry histologically. The authors concluded RCLM being more resistant against tissue degradation and retaining its integrity for a longer period of time compared to NCLM (Tal et al., 2008).

Although none significant differences between both groups existed in regard to measurements at the second level addressed as $\Delta H2$ / $\Delta W2$, we conclude that the results are clearly superior for the use of RCLM material in lateral augmentation if compared to native collagen membranes, especially in regard to alterations in soft tissue healing.

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Legends:

Fig. 1: Flow diagram of study outline.

Fig. 2: clinical images of surgical procedure.

Fig. 2a: two Straumann Soft Tissue Level implants are placed displaying a dehiscence and a fenestration bone defects on the buccal aspect of the ridge. The necks of both implants are positioned supracrestally according to the protocol of use.

Fig. 2b: augmentation with biphasic calcium phosphate (BCP) is performed; the randomization assigned this site for test group (ribose cross-linked membrane).

Fig. 2c: primary closure by coronally advancing the flap tissue for submerged healing is achieved.

Fig. 2d: the site 6 months later prior to re-entry shows sufficient gain in width indicated by a perio probe.

Fig. 2e: re-opening demonstrates a complete fill of the defect extension by newly organized hard tissue in both, the area of former dehiscence and fenestration.

Fig. 2f: an example of intra surgical impression taking with sterile silicon and an individual tray.

Fig. 3: Schematic drawing of the principle for assessment of the parameters Width (W) and Height (H) at most crestal extension of augmented area on casts out of stone. The reflected portions of buccal flaps were reduced in stone for easier adaptation of the silicon template on both, cast 1 and cast 0.

Fig. 3a: mid-crestal section across alveolar ridge casted in plaster together with negative silicon template mounted on top shows position of implant neck and crestal extension of newly organized bone (cast 1). Perpendicular is marked on the

silicon template indicating the middle axis of the implant. A perpendicular to this one at the crestal level indicates width of the ridge in buccal direction termed as W1/1. H1/1 is the distance from the edge of silicon template down to the crossing point with the buccal proximity of the crest.

Fig 3b: mid-crestal section of the cast obtained at baseline surgery prior to implant positioning (cast 0) with the template mounted according to references determined by teeth adjacent to the gap thus reproducing the position previously achieved on cast 1. The perpendicular indicating the middle axis of the implant is the reference for assessment of Width 1/0 along the second perpendicular at the crestal level again. Assessment of the distance H1/0 repeats the measurement H1/1, however, the crossing point with alveolar crest is supposed to be more apical.

Fig. 4: illustration of morphometric steps performed on casts under laboratory conditions.

Fig. 4a: mid-crestal section of cast 1 (obtained after augmentation at re-entry) with mounted silicon template shows the implant neck casted in plaster and the perpendicular dropped from the edge of the template at the middle of cover screw indicating the middle axis of the implant. According to the scheme in the Fig. 3 H1/1 marks the distance from the edge of the template to the first crestal contact with the bone; W1/1 determines the distance from the mid-implant axis to the same crossing point, respectively. H2/1 and W2/1 reflect the distances in the same manner more apically.

Fig. 4b: mid-section of the cast 0 with the template transferred from cast 1 displaying the reference lines obtained from cast 1 post augmentation for assessment of baseline dimensions of the ridge. The gap between the ridge casted in plaster and

the edge of the template indicates bone deficiency in buccal–lingual direction. The labeled landmarks repeat those schematically drawn in Fig. 3.

Fig. 4c: silicon template shows parallel walls and perpendicularly arranged top plan and bottom for exact positioning transferring the template from cast 1 to cast 0.
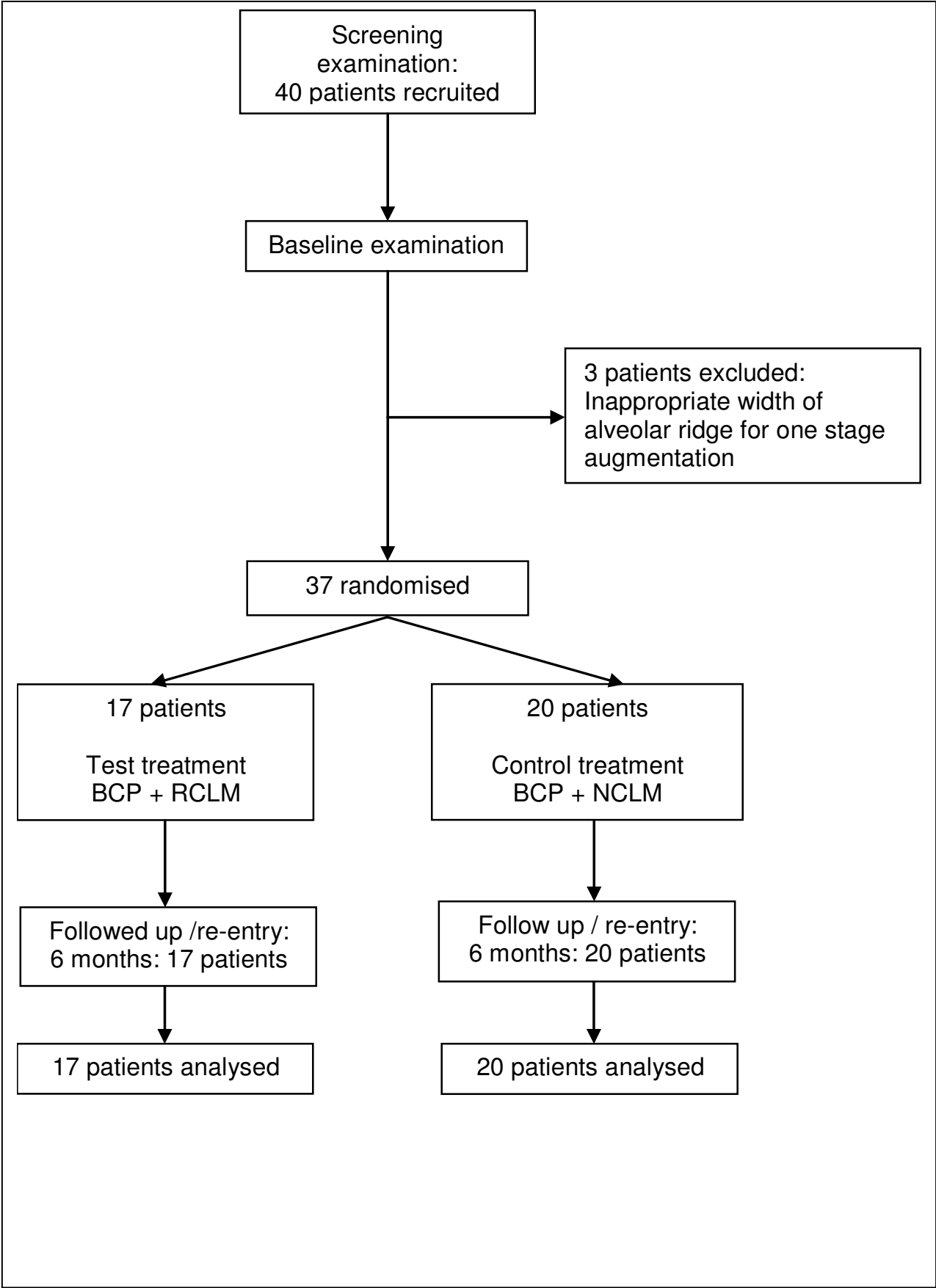
Fig. 4d: the image shows the tooth next to the area of interest from the opposite to the edentulous area site with the template being exactly adapted.

Table 1: Comprehensive patient data (n = 37). Patient*** indicates sites excluded from statistical analysis by secondary randomization.

Table 2: Baseline characteristics for patients and sites randomly selected for statistial analysis (n = 37).

Table 3: Median values and ranges of morphometric outcome (* p < 0.05).

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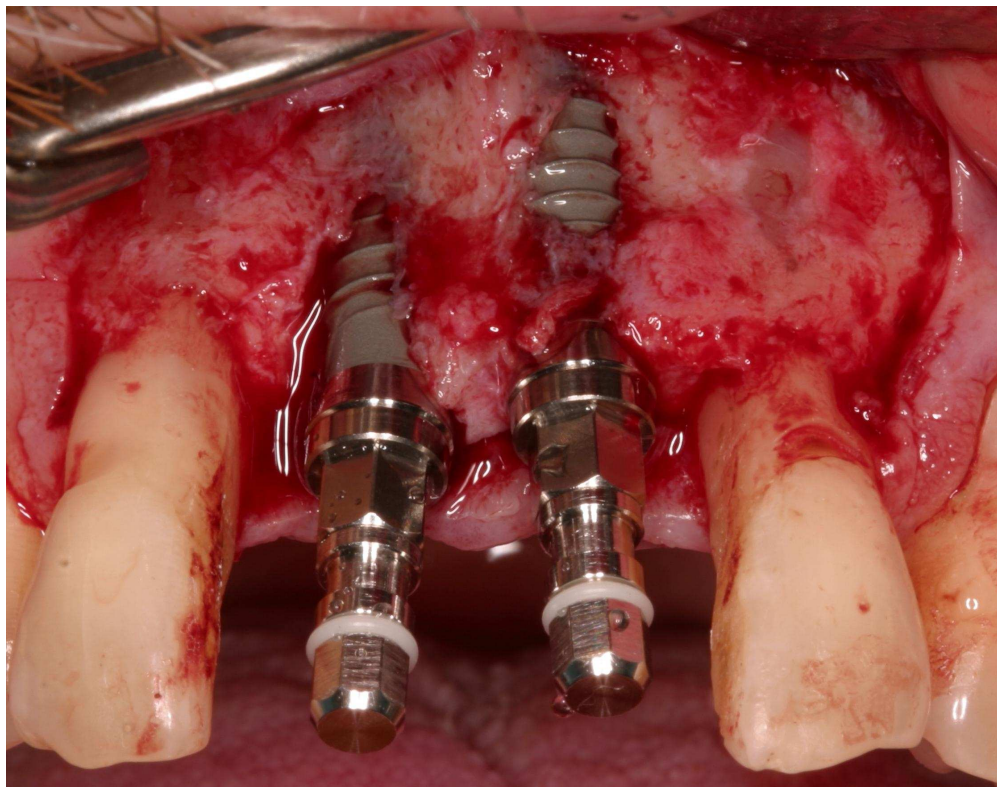51
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Fig. 1

Fig. 2a: Two Straumann Soft Tissue Level implants are placed displaying a dehiscence and a fenestration bone defects on the buccal aspect of the ridge. The necks of both implants are positioned supracrestally according to the protocol of use.
316x249mm (180 x 180 DPI)

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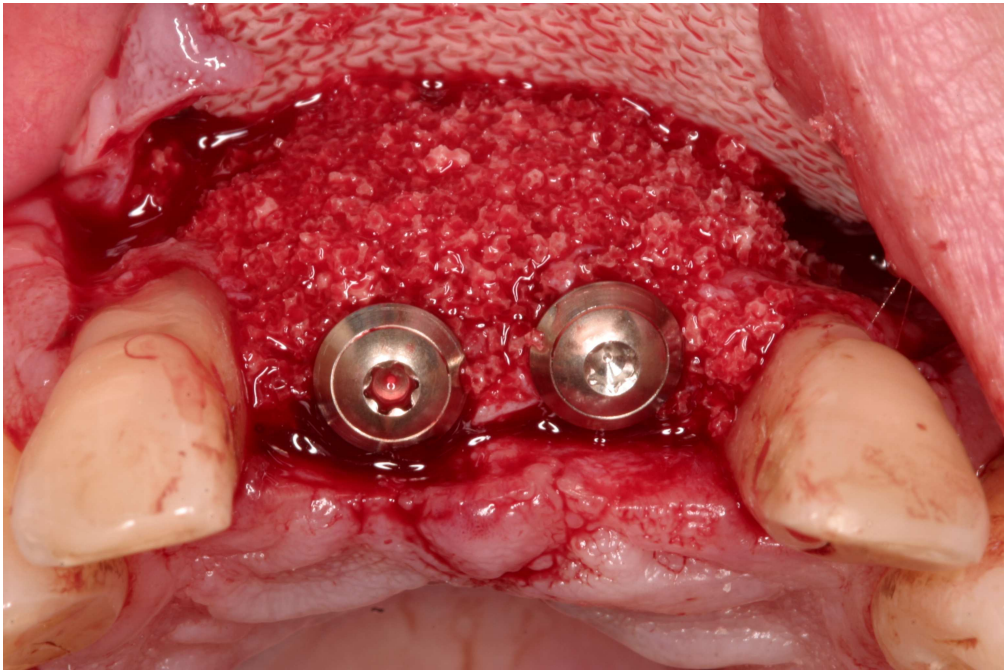43
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Fig. 2b: Augmentation with biphasic calcium phosphate (BCP) is performed; the randomization assigned this site for test group (ribose cross-linked membrane).
433x288mm (180 x 180 DPI)

Fig. 2c: Primary closure by coronally advancing the flap tissue for submerged healing is achieved.
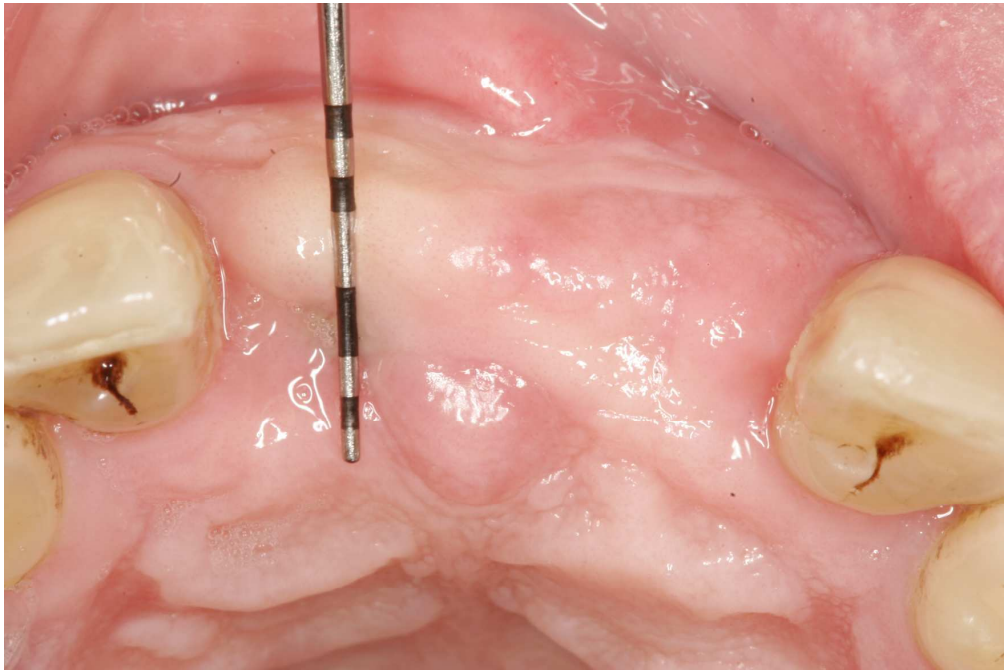433x288mm (180 x 180 DPI)

Fig. 2d: The site 6 months later prior to re-entry shows sufficient gain in width indicated by a perio probe.
1236x824mm (72 x 72 DPI)
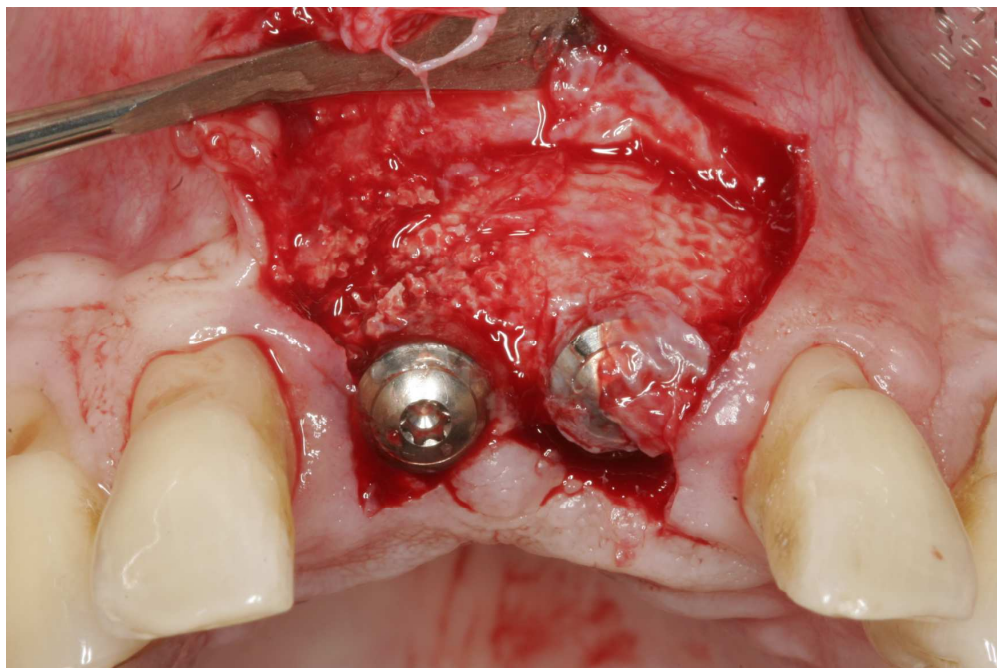
Fig. 2e: Re-opening demonstrates a complete fill of the defect extension by newly organized hard tissue in both, the area of former dehiscence and fenestration.
1236x824mm (72 x 72 DPI)

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Fig. 2f: An example of intra surgical impression taking with sterile silicon and an individual tray.
192x146mm (72 x 72 DPI)

Fig. 3a
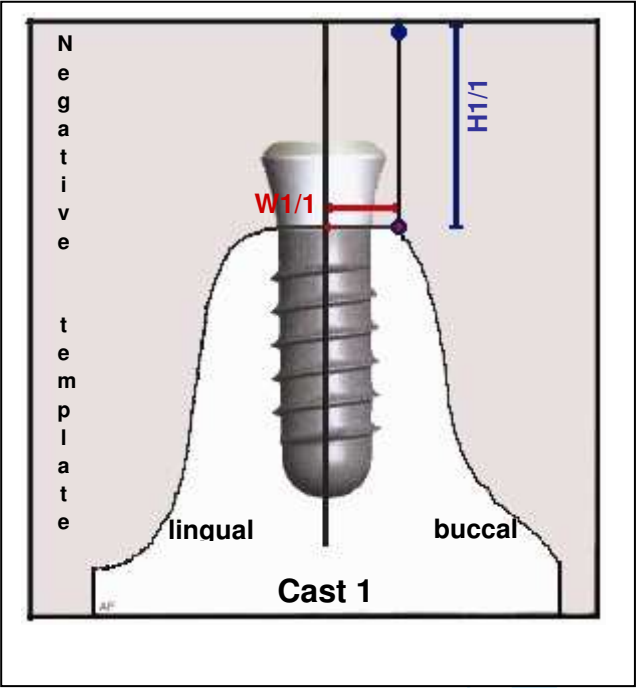
Fig. 3b

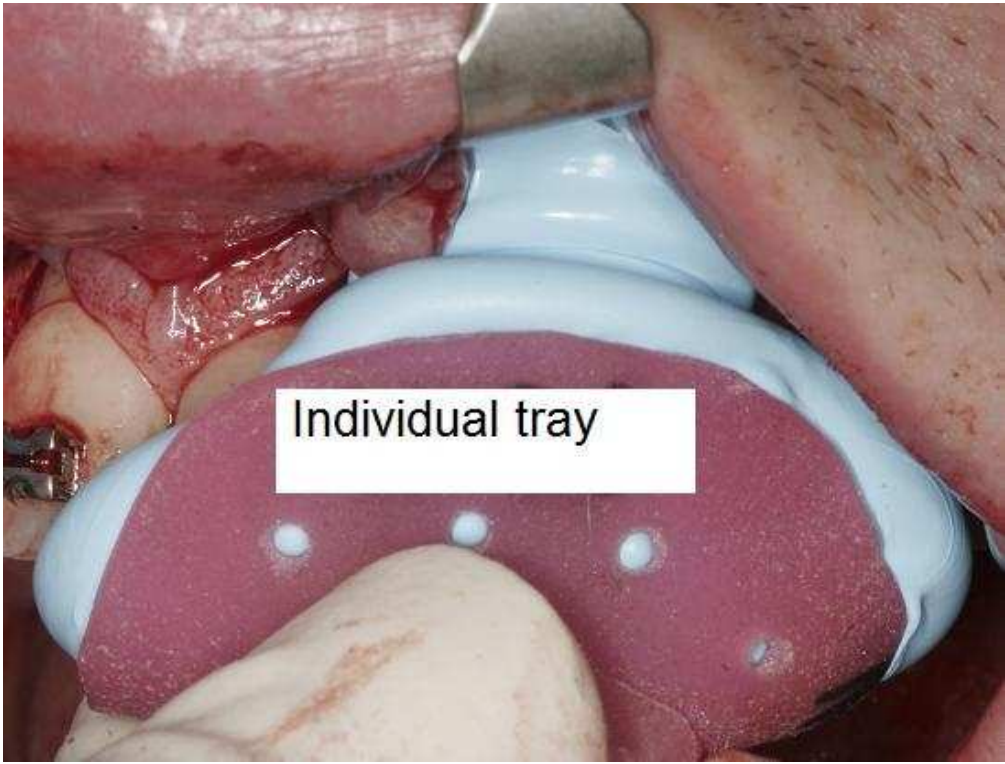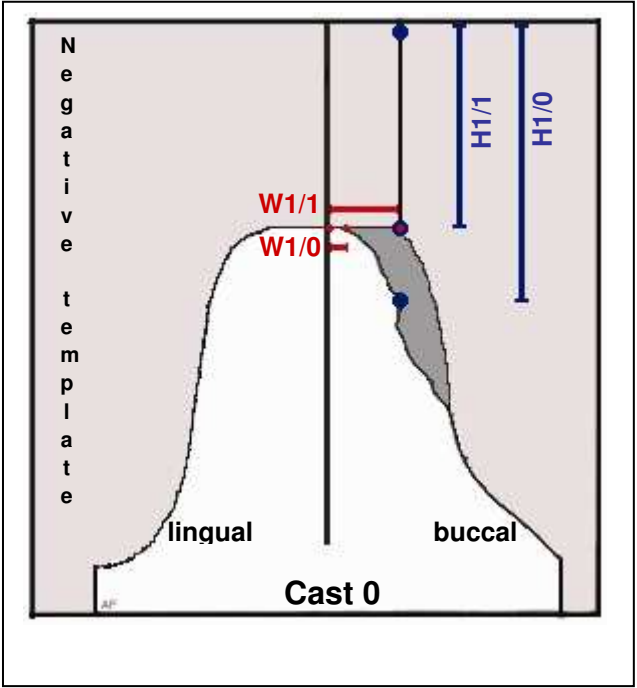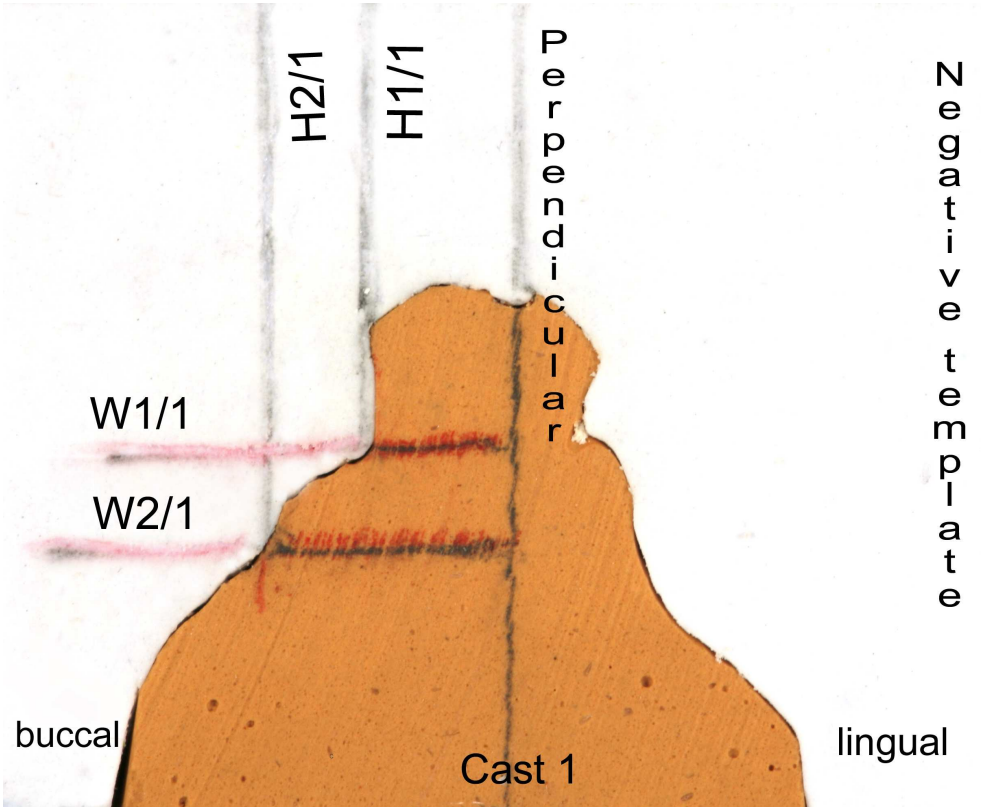Fig. 4a: Mid-crestal section of cast 1 (obtained after augmentation at re-entry) with mounted silicon template shows the implant neck casted in plaster and the perpendicular dropped from the edge of the template at the middle of cover screw indicating the middle axis of the implant. According to the scheme in the Fig. 3 H1/1 marks the distance from the edge of the template to the first crestal contact with the bone; W1/1 determines the distance from the mid-implant axis to the same crossing point, respectively. H2/1 and W2/1 reflect the distances in the same manner more apically.

868x698mm (72 x 72 DPI)
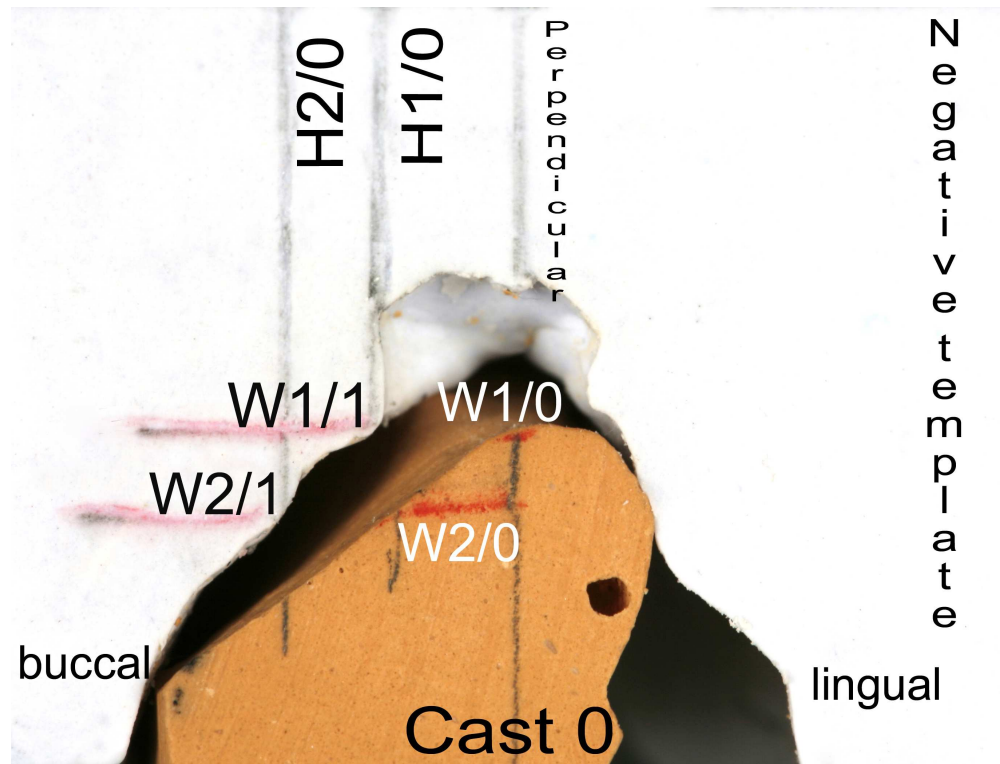
Fig. 4b: Mid-section of the cast 0 with the template transferred from cast 1 displaying the reference lines obtained from cast 1 post augmentation for assessment of baseline dimensions of the ridge. The gap between the ridge casted in plaster and the edge of the template indicates bone deficiency in buccal–lingual direction. The labeled landmarks repeat those schematically drawn in Fig. 3.
970x735mm (72 x 72 DPI)
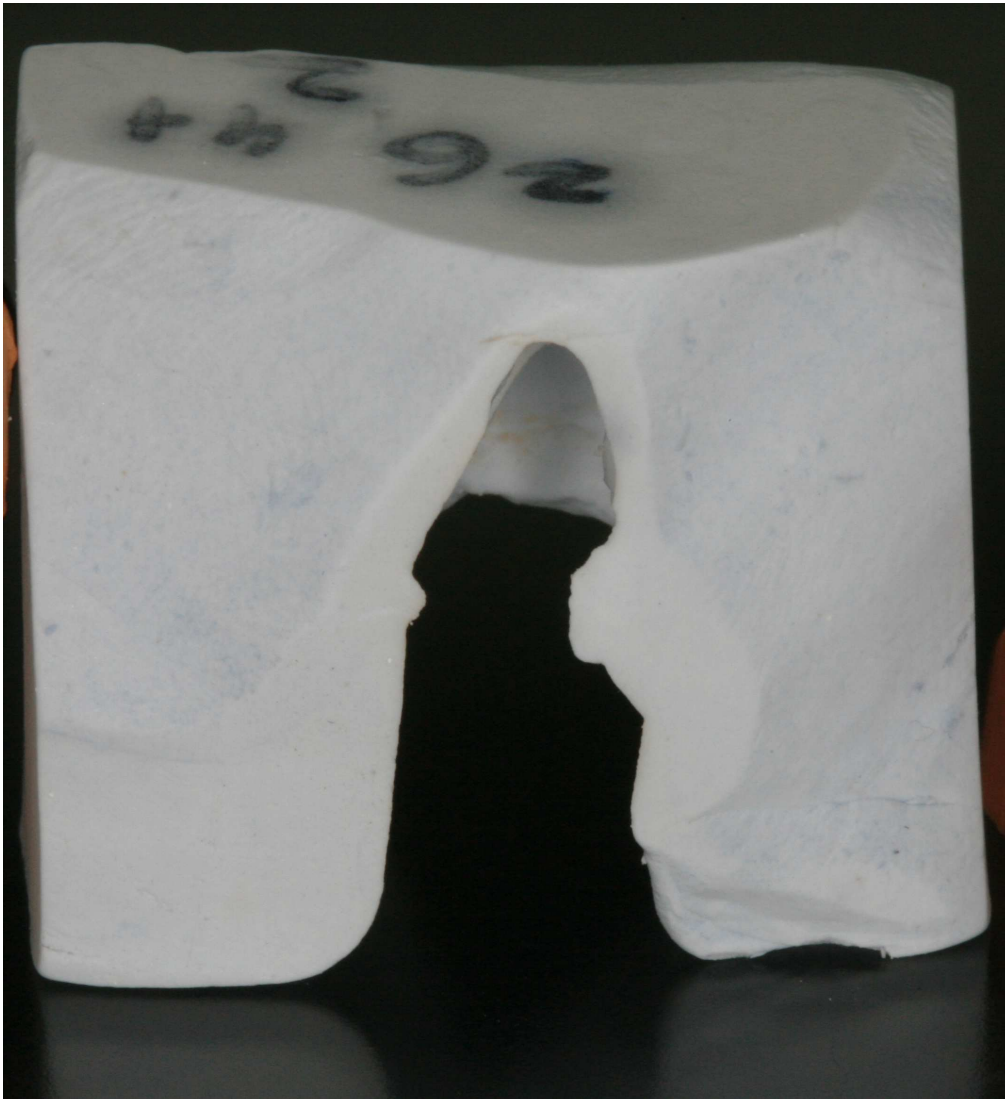
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Fig. 4c: Silicon template shows parallel walls and perpendicularly arranged top plan and bottom for exact positioning transferring the template from cast 1 to cast 0.
750x820mm (72 x 72 DPI)

Fig. 4d: The image shows the tooth next to the area of interest from the opposite to the edentulous area site with the template being exactly adapted.
518x1027mm (72 x 72 DPI)

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Tab. 1

Patient	Age	Sex F / M	Regio: 1=max.posterior 2=mand.posterior 3=max.anterior 4=mand.anterior	Defect size Baseline (mm) Depth / Width		N implants total	Test/Control 1 / 0	Exposure Yes/no 1 / 0
1	58	F	2	4	3	3	1	0
2	68	F	2	5	5	2	1	0
3	64	M	3	6	5	2	1	1
4	67	F	2	5	5	2	0	1
5	61	M	3	7	5	2	1	1
6***	47	F	2	4	5	1	1	1
6			2	4	8	1	0	1
7	59	F	2	5	4	1	0	1
7***			2	5	4	2	1	1
8	37	M	2	7	6	1	1	1
9	62	F	2	5	4	2	1	1
10***	52	F	2	8	4	2	0	1
10			2	5	4	2	1	1
11	64	F	3	8	6	1	0	1
12	44	F	2	2	4	1	0	0
13***	49	F	2	4	4	2	0	1
13			2	6	5	2	1	0
14	49	F	2	5	4	1	0	0
14***			2	5	5	1	1	1
15	40	M	2	5	6	1	0	0
16	69	M	3	10	6	1	1	1
17***	65	M	1	7	5	1	1	0
17			1	10	15	1	0	1

Patient	Age	Sex	Regio:	Depth	Width	N	Test/Control	Exposure
18	68	F	2	6	6	2	0	0
19	33	M	3	10	6	1	1	1
20	63	F	4	8	5	2	0	1
21	64	F	2	5	5	2	0	1
22	55	F	2	4	6	2	1	1
23	40	M	2	7	6	1	0	1
24	58	F	3	8	4	1	0	1
25	65	F	2	7	4	2	0	0
26	56	F	2	3	5	2	1	1
27	67	F	2	4	3	2	1	1
28	30	M	3	10	6	1	0	1
29***	67	M	2	4	4	1	0	1
29			2	3	3	2	1	0
30	69	F	2	5	4	2	1	1
31***	64	F	2	4	3	2	0	0
31			2	3	3	2	1	0
32	69	F	2	6	4	2	0	0
33***	24	M	3	7	4	1	1	0
33			3	6	4	1	0	1
34	44	F	1	8	10	1	1	1
35	49	F	2	5	7	2	0	0
36	62	F	2	7	5	2	0	0
37	59	F	1	1	1	2	0	0

Tab. 2

	Test (N = 17)	**Control (N = 20)**
Age: median (range)	61 years (33 – 69)	59 years (24 – 69)
Gender: **F : M**	11 : 6	15 : 5
Smoking: **- : +**	16 : 1	18 : 2
Soft tissue dehiscence: **- : + (%)**	5 : 12 (70.5)	9 : 11 (55.0)

Tab. 3

	Test (N = 17) (mm)	Control (N = 20) (mm)
Δ H1 (= H1/1 – H1/0)	1.1 (0.8 – 1.9)	0.2 (-0.2 – 1.8)
P =	0.0463*	
Δ W1 (= W1/1 – W1/0)	1.8 (1.0 – 3.0)	0.7 (-0.0 – 2.3)
P =	0.0359*	
Δ H2 (= H2/1 – H2/0)	2.5 (1.4 – 3.7)	2.7 (0.2 – +4.3)
P =	0.5674	
Δ W2 (= W2/1 – W2/0)	3.0 (2.2 – 3.3)	2.1 (0.8 – 3.0)
P =	0.1189	