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Influence of loading and grafting on hard- and soft tissue healing at immediately placed implants. An experimental study in minipigs.

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The authors contributions of the present research were the following: F.S., D.B., BE.P., B.B. and C.J. conceived the ideas; P.P, D.B., JC.I., A.S., B.P., and F.S. collected and analyzed the data; F.S. and D.B. led the writing. All authors critically revised the manuscript and agreed to the final version.

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The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Conflict of Interests

Dr. Schwarz reports Grants, Personal fees and Other from Institut Straumann AG, grants and personal fees from Geistlich Biomaterials, grants and personal fees from Osteology Foundation, grants and personal fees from International Team for Implantology ITI, outside the submitted work. Dr. Buser reports consulting and lecture fees from Institut Straumann AG, outside the submitted work. Dr. Parvini reports lecture fees from Institut Straumann AG, outside the submitted work. Dr. Imber reports Grants the Osteology Foundation, outside the submitted work. Dr. Stavropoulos reports Grants the Osteology Foundation and the ITI foundation outside the submitted work. Dr. Pippenger, Mr. Bellon and Dr. Jarry are employees of Institut Straumann AG.

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Abstract

Objectives: To histologically evaluate the influence of i) loading and ii) grafting on osseointegration and peri-implant soft tissue healing at immediately placed, self- cutting progressive tissue- level implants (TLX) in a minipig model.

Material & Methods: TLX implants (n=56) were immediately placed following the extraction of the mandibular first and second premolars, bilaterally, in a total of n=14 minipigs. In each animal, the implant sites were allocated to the following four groups: 1. unloaded with simultaneous grafting using a bovine bone mineral; 2. unloaded without grafting; 3. loaded with simultaneous grafting; 4. loaded without grafting. Histomorphometrical assessments at 4 and 12 weeks (n=7 animals each) included primary (i.e. bone-to-implant contact - BIC) and secondary outcome measures (e.g. first bone-to-implant contact – fBIC, junctional epithelium length– JE, connective tissue contact length – CTC, biological width – BW = JE + CTC).

Results: At 4 weeks, mean BIC values ranged from 74.5 ± 11.6% in group 2 to 83.8 ± 13.3% in group 1, and, at 12 weeks, from 75.5% ± 7.9% in group 2 to 79.9 ± 8.6% in group 1, respectively. Multivariate linear mixed regression did not reveal any associations between BIC and implant loading or grafting at 4 and 12 weeks. At 12 weeks, significantly higher fBIC values were noted in group 2 when compared with group 1. All groups showed comparable JE, CTC and BW values.

Conclusions: Implant loading and grafting had no major effects on osseointegration and peri-implant soft tissue healing at TLX implants.

Clinical Relevance

Scientific rationale for the study: The effects of loading and grafting on the osseointegration of immediately placed implants is unclear.

Principal findings: Mean BIC at 4 and 12 weeks were similar in all groups investigated. At 12 weeks under unloaded conditions, grafting resulted in lower fBIC values when compared with nongrafted sites. Similarly, all groups were associated with comparable JE, CTC, and BW values.

Practical implications: Grafting may reduce the risk for an exposure of the endosseous micro-rough implant surface.

Introduction

Immediate implant placement has evolved to an evidence based intervention for the replacement of non-retainable teeth (Tonetti et al., 2019). In fact, a recent systematic review and meta-analysis comparing the efficacy of immediate and delayed implant placement revealed high overall implant survival rates in both groups, which were also associated with comparable clinical (i.e. probing depths) and esthetic outcomes (i.e. pink esthetic scores) (Cosyn et al., 2019). However, it was also noted that immediate implant placement tended to be associated with a greater risk for an early implant loss amounting to about 4% (Cosyn et al., 2019; Tonetti et al., 2019). While the latter observation derived particularly from studies which did not include administration of postoperative antibiotics, it has to be realized that the rate of early implant losses reported for various timing protocols ranges between 0 and 6% (Tomasi & Derks, 2022).

Nevertheless, the specific configuration of extraction sockets may challenge the achievement of a sufficient primary stability during immediate placement, thus potentially contributing to a compromised secondary implant integration (Monje et al., 2019). The latter cascade may be further challenged by an immediate provisonalization, which is commonly applied following immediate implant placement (Parvini et al., 2020). Accordingly, external implant geometries and thread designs were modified to improve the primary stability of the implant. Particularly progressive thread designs proved to be associated with a bone-condensing effect and may therefore be of particular benefit for immediate placement protocols (Romanos et al., 2020). Even though immediate placement is commonly associated with grafting of the circumferential defect component without the addition of a barrier membrane (Cosyn et al., 2019), the overall effect of grafting on biological implant integration, particularly under loading conditions, remains rather unknown.

Therefore, the present study aimed at evaluating histologically the influence of i) loading and ii) grafting, on osseointegration and peri-implant soft tissue healing at immediately placed self-cutting progressive one- piece tissue-level implants (TLX) in a minipig model, based on a histometric analysis.

Material and Methods

Animals

A total of n=14 female Ellegaard Goettingen Minipigs (A/S, Dalmose, Denmark) (age between 22 and 29 months, bodyweight of about 40 kg) were used. The animals were housed in standard boxes in groups of 3 and provided a standard diet (soft food) expanded for Minipigs (SDS Standard Service, UK # 801586). Housing started at least 10 days before the first surgical intervention to adapt the animal to the experimental environment. All animals were fasted overnight before surgeries to prevent vomiting. All surgeries were conducted at the Biomedical Department of Lund University, Lund, Sweden, and were previously approved by the local Animal Experiment Ethics Committee (approval number 5.8.18-15672/2019). This study respected the Swedish Animal Protection Law and was designed and performed under consideration of the 3R (Replace, Reduce, Refine) guidelines for animal experimentation. The following reporting adhered to the ARRIVE Guidelines 2.0, for relevant items (Percie du Sert et al., 2020).

Study Design

In all animals, the following four treatment regimens were applied immediately following tooth extraction and immediate implant placement in the lower jaws:

1. Unloaded with simultaneous grafting (Group 1)

2. Unloaded without grafting (Group 2)

3. Loaded with simultaneous grafting (Group 3)

4. Loaded without grafting (Group 4)

Loading and non-loading was allocated in a split-mouth design, such that each group was equally spread across implantation site an equal number of times across the animals. Accordingly, each animal had received four implants, resulting in a total of n=56 implants placed in n=14 animals. Seven animals each were allocated to healing periods of 4 and 12 weeks, respectively. A schematic overview of the surgical outline and timeline can be found in Figure 1.

Anesthesia protocol and animal care

All surgical interventions were carried out under general anesthesia, including an intramuscular injection of dexmedetomidine (25-35 µg/kg i.m., Dexdomitor; Orion Pharma Animal Health) and tiletamine-zolazepam (50-70 mg/kg i.m., Zoletil 100 Vet, Virbac) and maintained with intravenous infusion until effect with propofol (PropoVet multidose, Orion Pharma Animal Health) and fentanyl (Fentanyl B. Braun). Carprofen (4mg/kg, s.i.d., i.m., Rimadyl vet., Orion Pharma Animal Health) was given as a preemptive dose for up to 4 days with buprenorphine (0,03mg/kg, i.m., Vetergesic vet, Orion Pharma Animal Health). Local anesthesia was provided intraoperatively via infiltrative injection with 1.8 ml of Xylocaine (Xylocaine, Dental adrenalin, 20 mg/ml, and 12.5 µg/ml; Astra AB) per hemi-mandible. Antibiotic prophylaxis was administered using bensylpenicillinprokain-dihydrostreptomycin (25 mg/kg+20 mg/kg, s.i.d, i.m., Streptocillin vet., Boehringer Ingelheim Vetmedica). During anesthesia, the animals were intubated and breathing withheld by a ventilator. Vital parameters were monitored continuously (pulse oximetry, rectal temperature, blood pressure, CO_2). All anesthetics, analgesics, and other medications were administered in doses and intervals following standard veterinary practice and according to the study objectives.

Surgical procedures

The surgical procedure is illustrated in Figure 2a-h. In particular, the mandibular premolars (P2-P4) and first molars (M1) were bilaterally extracted under general anesthesia without flap elevation. In detail, dental luxation devices together with extraction forceps were used to loosen the periodontal ligaments and finally extract the whole teeth at once. Particular care was taken to preserve the buccal and lingual bone. Subsequently, immediate implant site preparation was accomplished in regions P3 and P4 following the manufacturers' recommendation (Ø 2.2mm needle drill followed by a Ø2.8 mm drill; VeloDrill, Straumann, Switzerland). Two implants with a 2.8 mm machined surface in the neck area (Straumann® TLX RT Roxolid®, SLActive®, Ø 3.75 x 6mm) and a fully tapered endosseous design with progressive threads exhibiting a hydrophilic, sandblasted, acid-etched surface were placed in each hemimandible using a motorized handpiece. In particular, each implant was positioned in the center of the residual, shallow alveolar septum at a distance of 2.0 to 2.5 mm to the buccal and lingual bone, respectively. The insertion depth considered the smooth-rough border being located at the level of the buccal bone crest. Insertion torques were limited to 80 Ncm by in- and outward placement of the implant using a ratchet.

Grafting of the resulting peri-implant gap at both buccal and lingual aspects, as well as the adjacent mesial and distal extraction sockets by means of a bovine bone mineral (Cerabone®, 0.5-1.0 mm, Straumann, Switzerland) was accomplished in one hemimandible, thus leaving the contralateral implant sites nongrafted. In the subsequently treated animals, grafting was consecutively alternated between the left and right hemimandibles.

In each hemimandible, each implant was either furnished with a closure (RT, TLX, height: 1.5 mm, Straumann) or a healing cap (RT, TLX, height: 4.5 mm, Straumann) to ensure unloaded or loaded healing conditions, respectively. In the subsequently treated animals, the connection of closure and healing caps was consecutively alternated between the anterior and posterior implants. It was ensured that the healing caps were not in occlusal contact with the opposing dentition. The mucosal margins were fixed with resorbable sutures (Vicryl 4-0) to allow for a transmucosal healing.

In regions M1, experimental large diameter implants were inserted and analyzed separately. The postoperative care included administration of antibiotics (3-4 mL/pig i.m., Streptocilin vet, Boehringer Ingelheim, Germany) for 7 days post surgery as well as analgesics (Carprofen (4mg/kg, i.m., Rimadyl vet., Orion Pharma Animal Health, Espoo, Finland and buprenorphine 0.03mg/kg, i.m., Vetergesic vet, Orion Pharma Animal Health) for 4 days post-surgery. Experienced animal care takers evaluated the condition of the animals twice daily and further analgesia was administered if necessary. The animals were housed in pens in groups of 3 or 4 animals under controlled environmental conditions and received standard diet expanded for Minipigs (soft food) and water ad libidum. No oral hygiene protocol was provided during the whole duration of the study.

All surgical procedures were performed by experienced surgeons (P.P., A. S., D.B.).

Power calculation

For the given sample size of n=7 animals per observation period, a power of 0.893 was calculated. This considered a Type I error of 0.05 and an effect size d (1.25) that was calculated based on the means and standard deviations of BIC values noted following immediate placement of TLX implants in minipigs (El Chaar et al., 2021) (t-test; G*Power 3.1).

Retrieval of specimens

Seven animals each were terminated at 4 and 12 weeks after surgery, respectively. An intra-cardiac arrest was induced by injecting a 20% pentobarbital solution (Pentobarbitalnatrium, Apoteket AB; Stockholm, Sweden, 60 mg/ml). Block sections of the mandibular implantation sites were prepared using an oscillating autopsy saw under perseveration of the soft tissues. Sections were fixed in formalin (4 % formaldehyde solution) for at least 2 weeks before histological processing.

Histological preparation

Block sections were immersed in formalin buffer solution, dehydrated using ascending grades of alcohol and xylene, and subsequently infiltrated and embedded in methyl methacrylate for non-decalcified sectioning. Bucco-lingual sections of 200 µm were prepared by cutting and grinding and stained with paragon (toluidin blue and basic fuchsin).

Histomorphometrical analysis

The light-microscopic histometric evaluation was performed on the most central bucco-lingual section of each implant. The following parameters were measured or calculated (Figures 3a and b):

1. Total bone-to-implant contact (BIC): percentage of implant surface in contact with bone in the region of interest defined in Fig. 2.
2. First bone to implant contact (fBIC): the vertical distance between the most coronal BIC to the implants' smooth to rough transition line.
3. Sulcular epithelium (SE): distance between the mucosal margin and the most coronal aspect of the junctional epithelium (JE).
4. JE: vertical distance between the most coronal and apical aspect of JE.
5. Connective tissue contact (CTC): the distance between the apical aspect of JE and fBIC.
6. Biological width (BW) = JE + CTC.

   fBIC, SE, JE and CTC, values were measured at both buccal and lingual aspects.

All measurements were performed by one previously calibrated examiner (S.O.). Masking of the examiner was not feasible due to obvious macroscopic (i.e. presence of healing cap) and microscopic (i.e. presence of bone filler particles) characteristics noted in different groups. Calibration was accepted when repeated measurements of n=5 different sections were similar at >95% level.

Statistical analysis

Descriptive statistic parameters comprised means, standard deviations, medians, and interquartile ranges. Paired comparisons of the respective groups were accomplished individually for both healing periods using the Wilcoxon signed-rank test. Values reported in this manuscript correspond to adjusted mean values and corresponding confidence intervals (95% CI) as derived from multivariate mixed linear regression models. Models were set up separately for the 4- and 12-week timepoints and adjusted for the effect of the individual animal, side of the mandible, and anterio-posterior implant position. The animal was considered in the model as a random effect. All other factors were set as fixed effects. P-values were adjusted for multiple comparisons according to Dunnett-Hsu. A p-value of <0.05 was considered statistically significant.

Results

Clinical observations

Postoperative healing following implant placement was uneventful in all animals. Seven implants were excluded from the analysis due to the loss of the healing abutment at some point during the healing phase (dropouts were as follows: Group 1: 4 weeks = 1/ 12 weeks = 1; Group 2: 4 weeks = 0/ 12 weeks = 0; Group 3: 4 weeks = 1/ 12 weeks = 1; Group 4: 4 weeks = 1/ 12 weeks = 2. One additional implant (Group 3: 4 weeks) failed to osseointegrate and resulted in a fibrous encapsulation as identified histologically. Accordingly, a total of n=48 implants were available for the histomorphometrical analysis.

Histomorphometrical analysis - osseointegration and crestal bone formation

The adjusted mean BIC and fBIC values as a function of healing time, loading, and grafting are illustrated in Figure 4.

At 4 and 12 weeks, between group comparisons of BIC values revealed no significant differences, irrespective of the loading regime, or grafting. In particular, BIC values ranged between 74.5 ± 11.6% in group 1 to 83.8 ± 13.3% in group 3 after 4 weeks of healing and between 75.5% ± 7.9% and 79.9 ± 8.6% in group 2 and group 1 after 12 weeks of healing, respectively (Figure 4a).

In most of the specimens evaluated, mean fBIC values at 4 weeks tended to be highest at the buccal when compared with the corresponding lingual aspects, respectively. At 12 weeks, fBIC values commonly decreased in groups 1 (buccal and lingual), 3 (buccal and lingual) and partially in 4 (buccal), whereas group 2 revealed marked increases of mean fBIC values at both buccal and lingual aspects (Figures 4b and c). Mean total fBIC (averaged buccal and lingual) values did not significantly differ between groups at 4 weeks. At 12 weeks, significant differences were noted when comparing grafted and non-grafted groups under unloaded conditions (i.e. groups 1 and 2) ($p=0.0107$).

At grafted implant sites, loading tended to decrease buccal (182 ± 878 µm vs. 269 ± 954 µm) and lingual (257 ± 505 µm vs. 414 ± 504 µm) fBIC values (Figure 4b and c; Supplementary Tables 1 and 2). However, the differences in total fBIC values to unloaded implants did not reach statistical significance.

Histomorphometrical analysis - peri-implant soft tissue dimensions

The adjusted mean JE, CTC and BW values as a function of healing time, loading, and grafting are illustrated in Figure 5.

In all groups investigated, mean JE values at both 4 and 12 weeks commonly tended be higher at the buccal when compared with the corresponding lingual aspects (Figure 5a). As opposed to mean JE values, all groups investigated revealed higher CTC values at the lingual, when compared with the corresponding buccal aspects after 4 and 12 weeks of healing (Figure 5b). The resulting BW values at 4 weeks ranged from 4091 ± 1077μm at the buccal aspect of group 4 to 2481 ± 721μm at the lingual aspect of group 2, respectively. At 12 weeks, BW values ranged from 3802 ± 858μm at the buccal aspect of group 3 to 2501 ± 691μm at the lingual aspect of group 2, respectively (Figure 5c). Between group comparisons failed to reveal any significant differences in the total (averaged buccal and lingual) JE, CTC and BW values, respectively.

Representative histological views in different groups at 4 and 12 weeks are summarized in Figure 6 and Supplementary Tables 1 and 2.

A schematic drawing of the proportional extensions of SE, JE and CTC in different groups along with representative histological views are depicted in Figure 7.

Discussion

The present study aimed at evaluating the influence of i) loading and ii) grafting on osseointegration and peri-implant soft tissue healing at immediately placed TLX implants in minipigs.

The selected animal model is a commonly used and well established standard to investigate the osseointegration and soft tissue healing at dental implants (Buser et al., 2004; Caballe-Serrano et al., 2019; Liñares, et al., 2011). The specific surgical procedure (i.e. implant placement in the center of the residual septum at P3 and P4) was chosen to mimic the clinical approach commonly associated with an immediate implant placement at molar sites.

Basically, the histomorphometrical analysis revealed that mean BIC values were similar at loaded and unloaded, as well as grafted and non-grafted implants. In particular, mean BIC values at 4 weeks ranged from 74.5 ± 11.6% in group 2 to 83.8 ± 13.3% in group 1, and, at 12 weeks, from 75.5% ± 7.9% in group 2 to 79.9 ± 8.6% in group 1, respectively. The BIC values noted in groups 1 and 2 are within the range of those experimental data reported following a delayed transmucosal placement of unloaded hydrophilic, one-piece titanium implants exhibiting a conventional (i.e. non-progressive) thread design (refers to as TL) (Schwarz et al., 2007; Schwarz et al., 2015). In particular, after 4 weeks of healing in the canine, mean BIC values ranged from 72.3±2.9% in the upper- to 79.8±12.1% in the lower jaws, respectively (Schwarz et al., 2007). At 16 weeks, mean BIC values in the upper jaws amounted to 87.88±6.73% at titanium-, and to 92.69±1.87% at titanium-zirconium alloy implants, respectively (Schwarz et al., 2015).

The results of a previous animal study also pointed to comparable BIC values at immediately placed loaded and unloaded hydrophilic TL implants in a canine model. At 3 months, mean BIC calculated just for the endosseous portion of the implant amounted to 82.72% and 76.96%, respectively (Blanco et al. 2010). Likewise, immediate- or delayed loading (i.e. after 4 weeks) also resulted in a comparable osseointegration of TL implants, even though the reported mean BIC values were markedly lower than those noted in the present analysis (Liñares et al., 2011). In particular, after 8 weeks of healing in minipigs, mean BIC values amounted to 65.1±6.2% in the immediately- and to 66.1±1.3% in the delayed loaded groups, respectively. When evaluating these data, it must however be noted that the latter study included the transmucosal (i.e. 1.8 mm) area of TL implants for the calculation of BIC, whereas the present analysis just considered the endosseous portion of TLX implants.

Another recently published study indicated that mean BIC values at 12 weeks following delayed placement of TLX implants were comparable and non-inferior to conventional TL implants in a minipig model (61.30 ± 10.63% vs. 54.46 ± 18.31%) (El Chaar et al., 2021). However, TLX implants revealed higher maximum insertion torque values when compared with TL implants (El Chaar et al., 2021).

There is evidence that the specific progressive thread design of TLX implants results in a higher primary stability than the conventional thread design of TL implants (Emmert et al., 2021). While primary stability has been correlated with an improved biological implant integration, the associated higher insertion torques may also have a detrimental effect on marginal bone levels (Monje et al. 2019). Nevertheless, the resulting immediate implant-bone contact and associated bone-condensing effect (Romanos et al., 2020) may have contributed to the relatively high BIC values at immediately placed TLX implants after 4 and 12 weeks, as noted in the present analysis. In this context, it must be emphasized that the present BIC values at 12 weeks were also within the range of those values reported 12 weeks following delayed placement of a bone-level implant featuring a similar progressive thread design (i.e. BLX) (Francisco et al., 2021). Likewise, the latter study also failed to reveal any significant differences between loaded (i.e. transmucosal) and unloaded (submerged) BLX implants. Similar to the present study, loading was accomplished by healing abutments, which may however not entirely reflect the clinical scenario following the connection of a temporary restoration. In fact, Blanco et al. (2010) had provided a provisional resin bridge with a proof of contact points, thus clearly verifying loading of the respective implants. Accordingly, the present study may rather mimic an immediate non-functional provisionalization than loading of the implants.

When further analyzing the present data, it was also noted that under unloaded conditions, grafting had an apparent effect on crestal bone level values at 12 weeks, as evidenced by significantly lower fBIC values in group 1 when compared with group 2. Furthermore, at grafted sites, implant loading also tended to further decrease fBIC values over unloaded conditions, event though these differences did not reach statistical significance. A major methodological drawback of the present study was the lack of an exact assessment of the sizes and extensions of the initial circumferential defects as well as the thickness of the buccal and lingual bone plates. Accordingly, potential differences in the initial defect sizes and bone thicknesses between groups may have confounded the histological outcomes assessed and need to be carefully considered in future studies. In this context, it must also be emphasized that the circumferential defects associated with immediate implant placement at molar sites commonly reveal a wider interproximal component. Accordingly, grafting is predominant at both mesial and distal aspects. Since the present analysis had a focus on the clinically more relevant buccal and lingual aspects, it is impossible to estimate to what extend grafting may have influenced interproximal bone remodeling. However, it is assumed that changes in peri-implant soft- and hard tissue dimensions at either mesial- and or distal aspects may also have influenced the outcomes assessed in the bucco-lingual hard tissue sections.

Previous experimental data have also pointed to the high potential of hydrophilic over hyprophobic implant surfaces to promote BIC values and defect fill in circumferential-type defects at TL implants without grafting (Lai et al., 2009). Similarly, hydrophilic BLX implants were also commonly associated with improved fBIC values over hydrophobic control implants following grafting of 2-mm circumferential defects using two different types of bone fillers (El Chaar et al., 2019). When evaluating the results of the latter studies, it must be realized that acute-type circumferential defects may not entirely reflect the configuration of extraction sockets as employed in the present study. Moreover, it must be emphasized that fBIC values are also influenced by peri-implant soft tissue wound healing, and in particular the associated establishment of BW values.

While the present analysis did not reveal any marked differences in JE or CTC values between either grafted and nongrafted, or loaded and unloaded implants, the respective values tended to vary between buccal and lingual aspects at the respective implant sites.

Basically, the noted JE and CTC values and variations noted between buccal and lingual aspects were within the range of those values reported for TL implants following delayed or immediate placement (Linares et al., 2011; Schwarz et al., 2007; Schwarz et al., 2014). In particular, following delayed implant placement in the canine, mean JE and CTC values amounted to 1.7±0.5mm and 0.9±0.3mm at 4 weeks, and to 2.71±1.10mm and 1.04±0.55mm at 16 weeks, respectively (Schwarz et al., 2007; Schwarz et al., 2014).

In conclusion, and within the limitations of a preclinical study, implant loading and grafting had no major effects on the osseointegration and peri-implant soft tissue healing at TLX implants.

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Figure legends

Fig. 1. Illustration of the study design and outline.

Fig. 2. Surgical procedure

a) Hemi-mandible before tooth extraction

b) Situation after gentle tooth extraction

c) Implant bed preparation in the shallow septum area of P3.

d) Immediate placement of TLX resulting in a circumferential defect area.

e) Insertion torques were limited to 80 Ncm.

f) Situation after placement of both implants. The anterior implant was restored with a closure cap (non-loaded groups). A healing abutment (loaded group) was connected to the distal implant

g) The circumferential gaps between the implant and the alveolar crest were augmented using a xenogenic bone graft material (only in the grafted groups).

h) Situation after wound closure to allow for a transmucosal healing.

Fig. 3. Landmarks defined for the histomorphometrical analysis (scale bar = 1 mm).

a) Bone- related measurements:

First bone-to-implant contact (fBIC): the vertical distance between the most coronal bone-to-implant contact (BIC) to the reference line (RL; i.e. implants' smooth to rough transition line).

BIC: percentage of implant surface in contact with bone measured from RL to the onset of the apical curvature (OAC).

b) Soft tissue- related measurements:

Sulcular epithelium (SE): distance between the mucosal margin and the most coronal aspect of the junctional epithelium (JE).

JE: vertical distance between the most coronal and apical aspect of JE.

Connective tissue contact (CTC): the distance between the apical aspect of JE and fBIC.

BW = JE + CTC

Fig. 4. Adjusted mean BIC and fBIC values at 4 and 12 weeks as a function of loading and grafting. Error bars designate the 95% confidence intervals.

a) Bone-to-implant contact (BIC) (%)

b) First bone-to-implant contact (fBIC) buccal

c) First bone-to-implant contact (fBIC) lingual

Fig. 5. Adjusted mean junctional epithelium (JE), connective tissue contact (CTC) and biological width (BW) values at 4 and 12 weeks as a function of loading and grafting.

a) JE buccal

b) CTC buccal

c) BW buccal

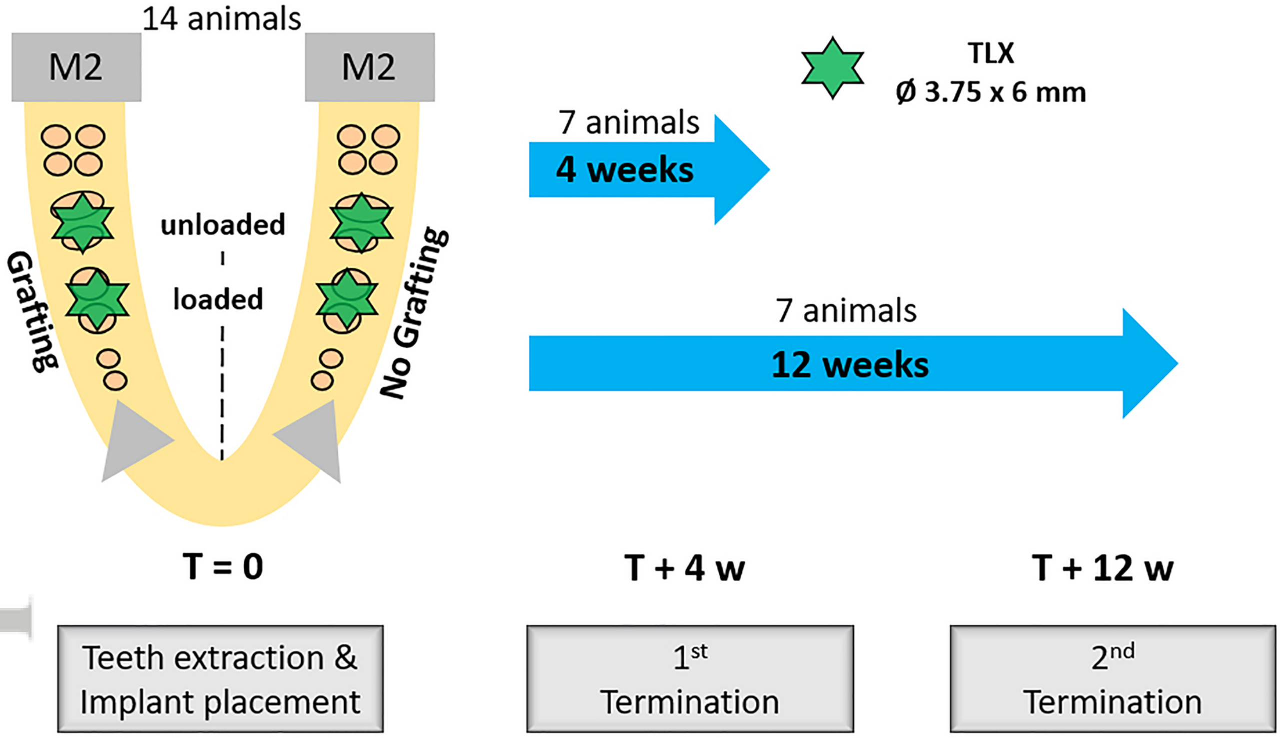
d) JE lingual

e) CTC lingual

f) BW lingual

Fig. 6. Representative paragon-stained bucco-lingual sections at 4 and 12 weeks of healing in different groups. Grey particles in the crestal (yellow asterisks) and supracrestal regions relate to integrated and dispersed bone filler particles at grafted implant sites (scale bar = 1 mm).

Fig. 7. Visualization of the relative crestal bone levels and soft tissue dimensions in relation to the rough to smooth transition between the endosseous implant segment and the machined implant neck equaling the placement level of the implant (dotted black line).



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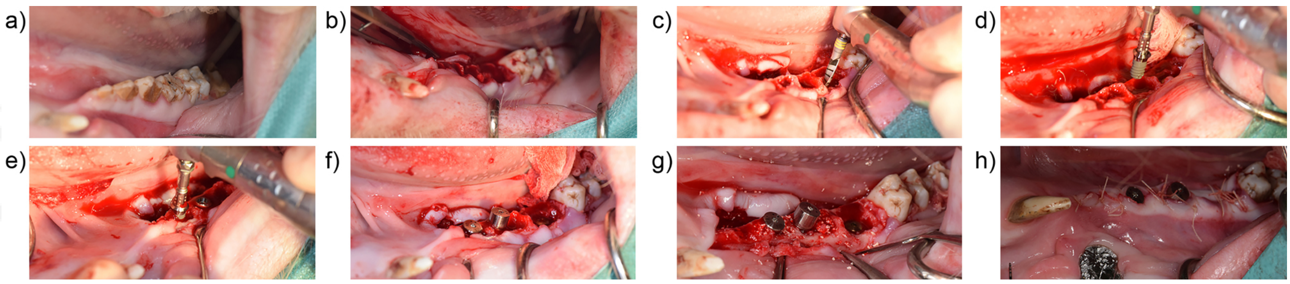

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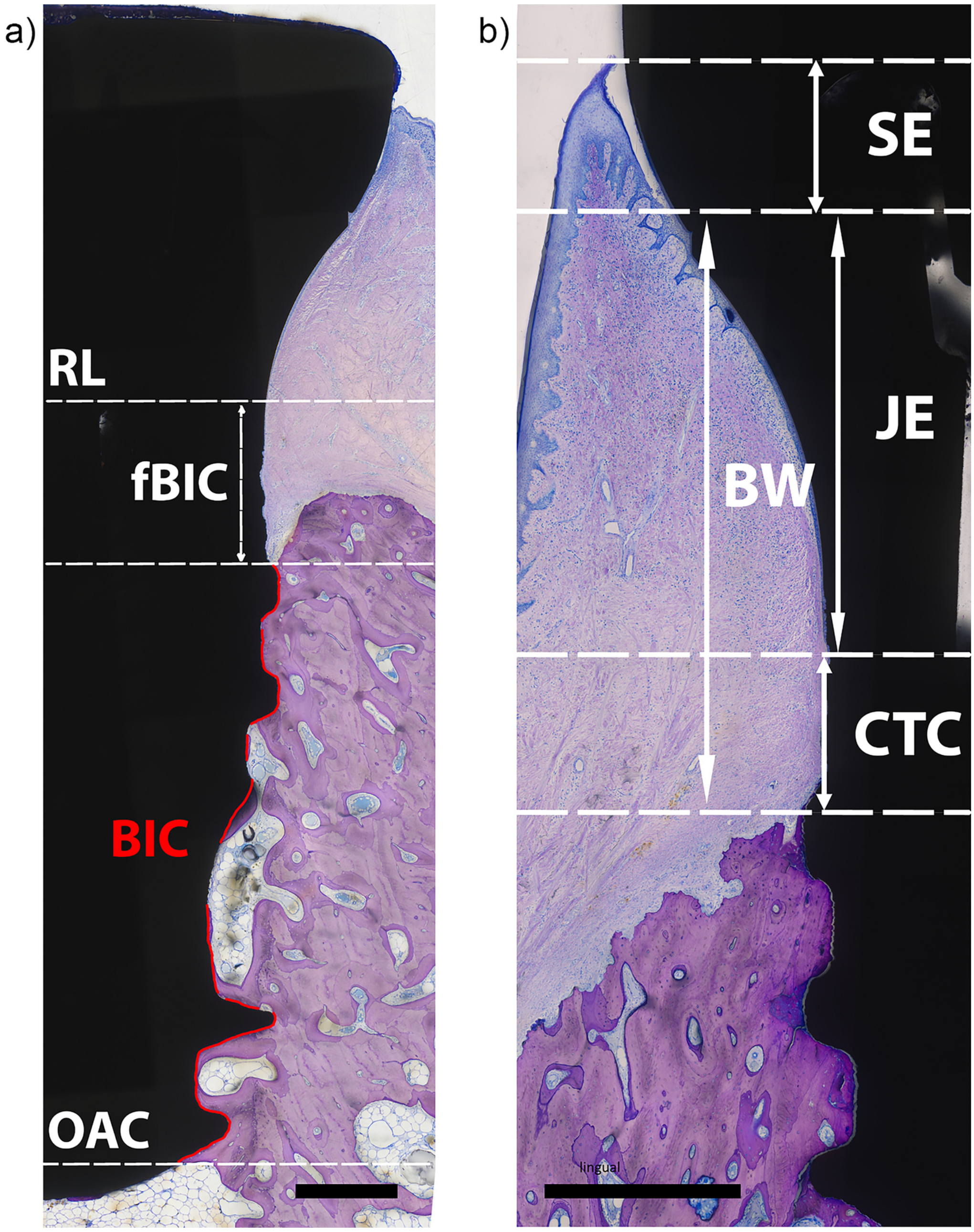

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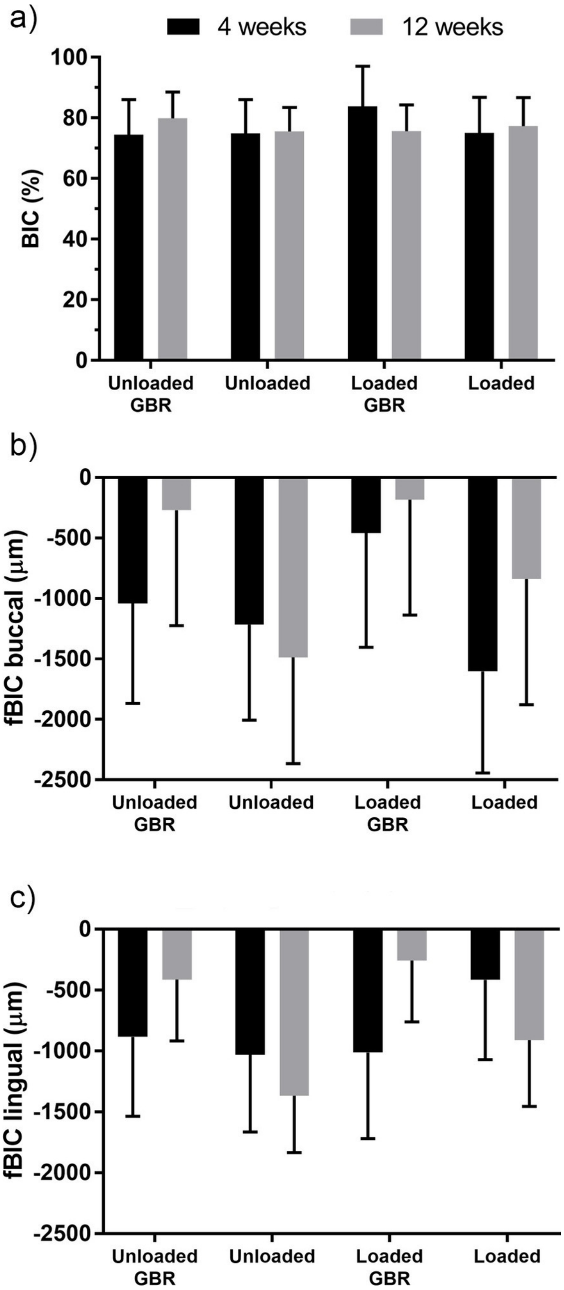

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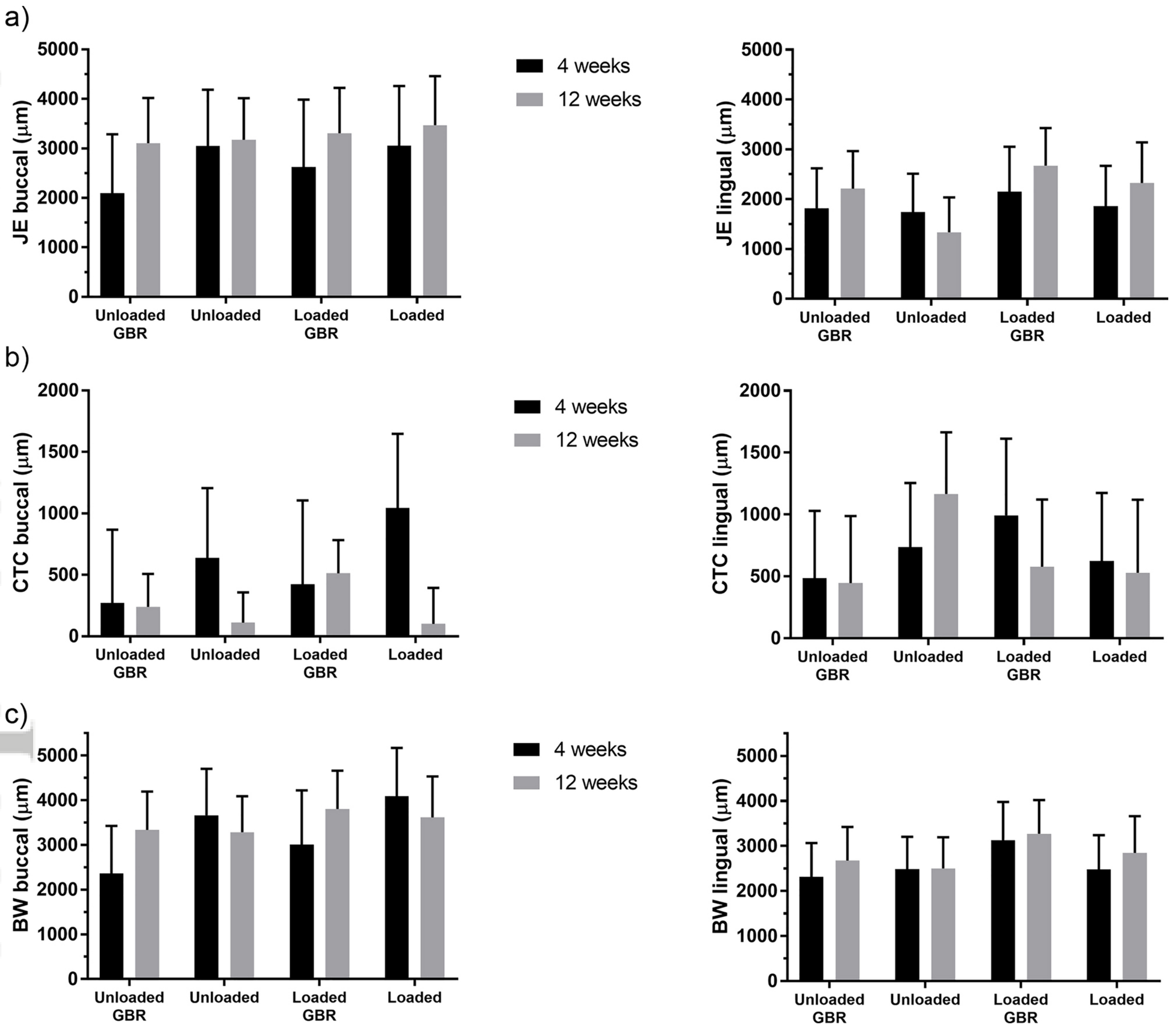

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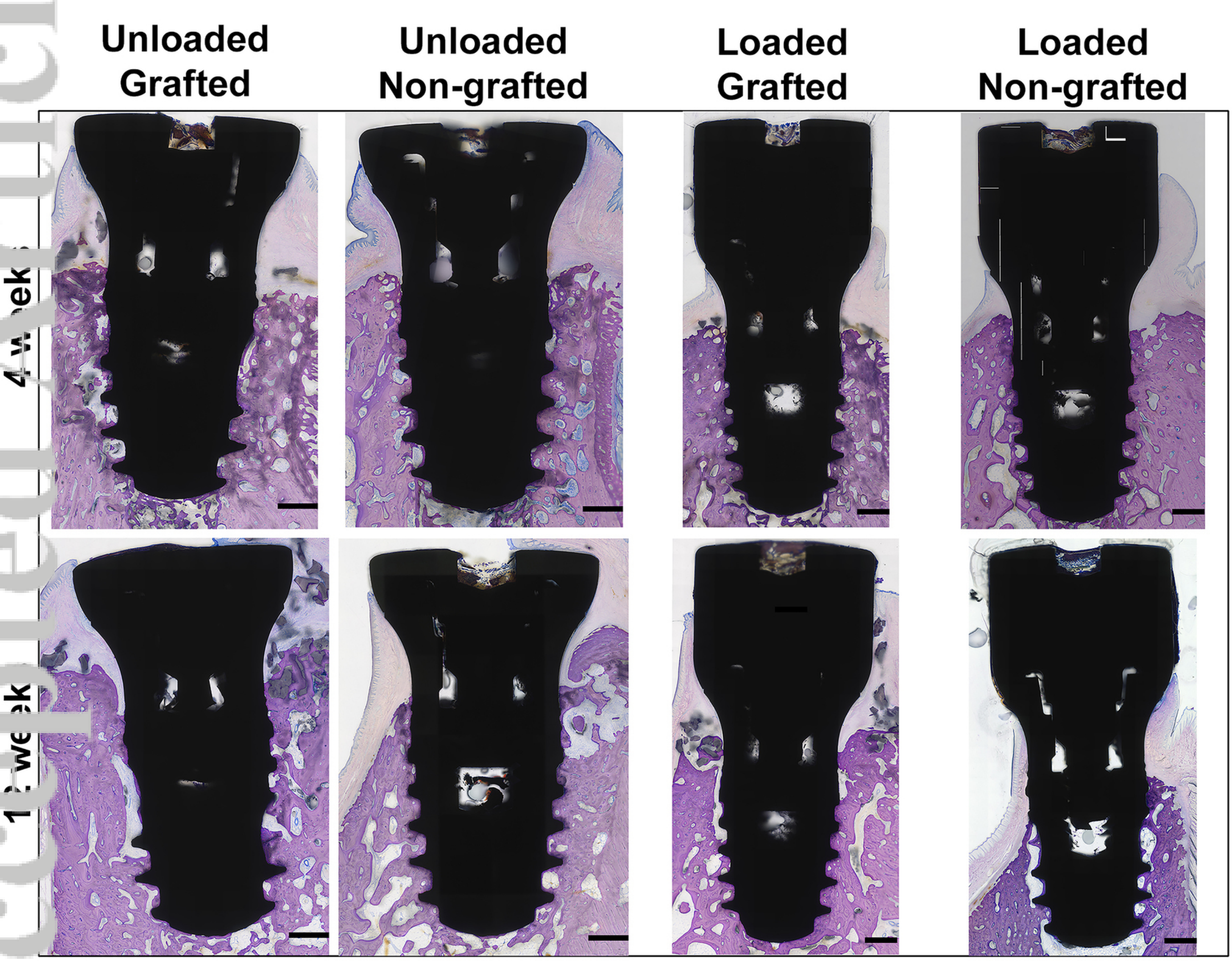

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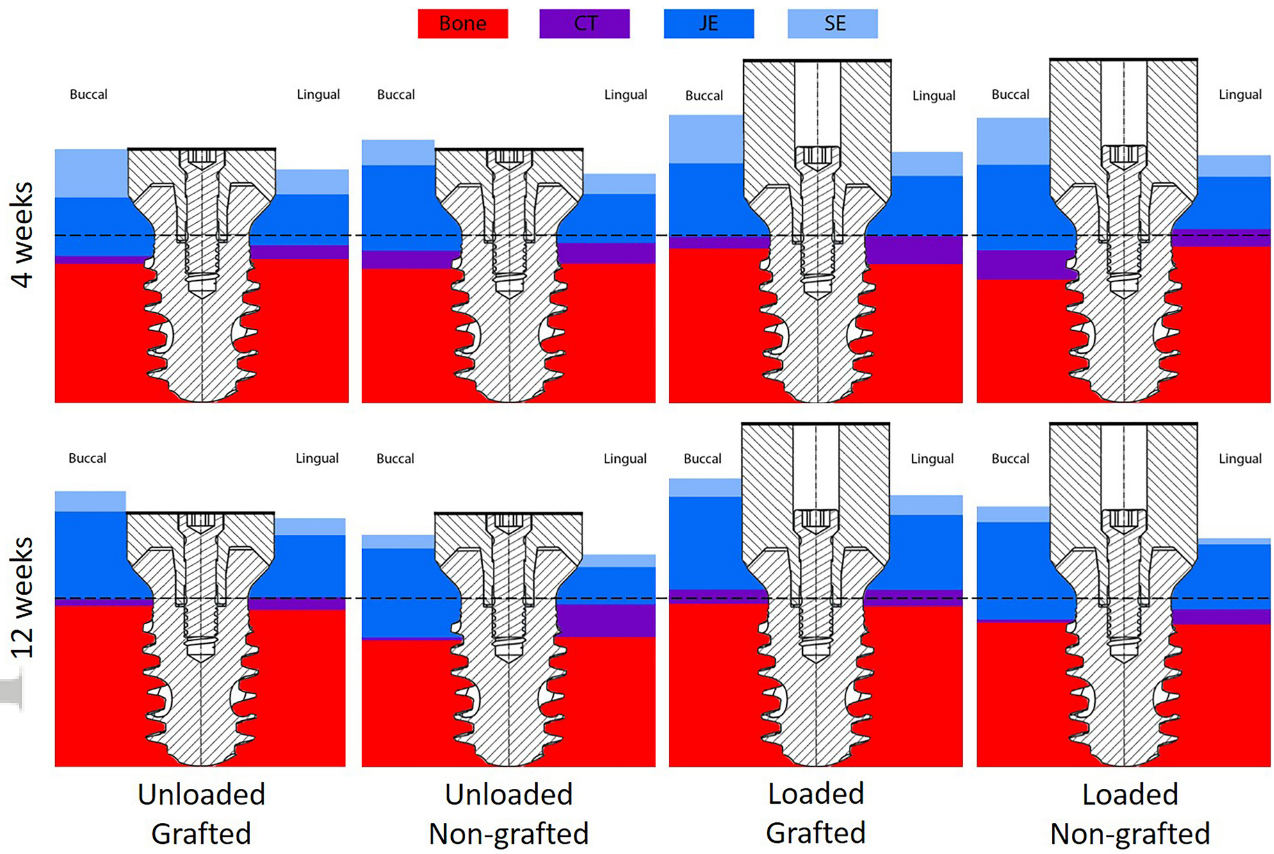

JCPE_13734_Figure 7.jpg