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A multi-level analysis of platform-switching flapless implants placed tissue-level: 4-year prospective cohort study

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ABSTRACT

Purpose: To evaluate the factors affecting peri-implant marginal bone level of single platform-switch implants placed with smooth neck at gingival level (tissue level) by using a flapless technique.

Material and Methods: 76 consecutive patients received 128 titanium implants with a zirconium-oxide blasted surface (ZirTi) and a platform-switching neck tulip-configuration. Implants were loaded 3 months after insertion with a provisional resin crown and after approx. 15 days with a definitive ceramic crown. Peri-implant marginal bone level (MBL) was measured on periapical radiographs at 1,3,6,12,24, 36 and 48 months by blinded assessor. The following parameters were evaluated: Implant placement groups (immediate, early, delayed), location (maxillary/mandibular), gingival thickness (thin/thick), sex (male/female), endodontically treated adjacent teeth (yes/no). Multilevel analyses exploring factors associated to MBL at 36 and 48 months were performed.

Results: The survival rate was 98.4**%.** Mean MBL at 36 and 48 months was 0.95mm ± 0.85 and 0.99 ± 0.68 respectively, not statistically different from the values at 24 months ($p>0.05$).

Mandibular location, delayed implants and presence of adjacent endodontic treated teeth showed significantly higher bone loss at 36 months ($p< 0.05$). Interestingly, at 48 months only implant placement timing showed statistically significant differences. Delayed implants showed increased bone loss when compared to both early and immediate groups ($p<0.05$).

Multilevel analysis confirmed the statistical significance of implant location (p=0.031; 95%CI:0.031-0.659), endodontically treated adjacent teeth (p= 0.001; 95%CI:-1.228-0.859) and implant placement group (p=0.045; 95%CI:0.003-0.337) as factors affecting MBL at 36 months. All the investigated parameters, with the only exception of implant placement group (p=0.020; 95%CI:0.334-1.432) were not statistically significant at 48 months ($p>0.05$).

Conclusion: Platform-switch implants placed nonsubmerged with a flapless approach showed a reduced bone loss progression in the first 4 years from insertion, as MBL remained stable at longer times (36 and 48 months). Implants placed after 10-12 months after extraction showed a higher bone loss when compared to early and immediate implants.

Keywords: MBL, dental implants, flapless surgery, best clinical practice, platform-switch.

INTRODUCTION

Although submerged dental implants show high and predicable long-term success, [1,2] a growing interest in less invasive protocols is reported in literature.[3]

Placement of implants in a **nonsubmerged tissue-level approach** has been proposed in different studies as a predictable technique with similar risks compared to traditional submerged technique[4,6] and high long term survival.[7] Nonsubmerged healing is usually achieved placing a bone level implant and immediately positioning a healing screw which remain exposed to the oral environment.[8] Key factors to preserve marginal bone level (MBL) are implant abutment connection, implant neck configuration and surgical techniques.[9-11]

Platform switch concept has been reported by Lazara and Porter in 2006.[12] Through the repositioning of a cylindrical implant abutment junction far from the crestal bone, platform switch demonstrated reduced bone loss values.[12,13]

Implants with this configuration are usually positioned at bone level (submerged), with the neck at crestal bone height (equicrestally) or 1mm under (subcrestally).[14]

Histological findings, however, revealed that when tapered platform-switch implants are positioned subcrestally, greater bone remodeling may be expected, as the removal of a great portion of the coronal bone during site preparation could compromise blood supply of the remaining cortical bone.[14,15]

A low invasive approach could be placing a flapless switching platform implant in a supracrestal position, with the rough surface positioned at the bony crest and the smooth machined neck at tissue level, allowing the implant cover screw to be exposed at the oral environment.

MBL differences represent an important analysis which may provide information on peri-implant bone health/disease.[16] Indeed, the radiographic assessment of MBL at different endpoints gives important information regarding the hard and soft tissues modification which occurs in the early healing phases (pre-loading period)[17,18] or after the definitive restoration (post-loading period).[19] Numerous other conditions, as well as pre, intra and post-operative parameters may affect peri-implant marginal bone morphology/environment and clinical-radiographic aspects.

Different **statistical methodologies**, such as multilevel analysis[20] or linear logistic regressions[21,22] have been proposed and used to evaluate and correlate strategic-technical (i.e. surgical) decision with many factors associated to MBL such as bone quality, implant diameter, implant surface, and type of prosthetic prosthesis.[21]

To the best of our knowledge, no studies have ever analysed multiple operative factors associated to MBL modifications around nonsubmerged tulip-shaped platform-switch flapless implants.

Therefore, the aim of this consecutive, non-randomized prospective cohort study was to investigate factors which may affect MBL around implants placed nonsubmerged. Different pre-operative, intra and post-operative clinical parameters have been analyzed at 1, 3 (preloading time) and at 6, 12, 24, 36 and 48 months.

MATERIALS AND METHODS

Study setting and patient selection

The study design was a single-blind human longitudinal prospective cohort study comparing the clinical and radiographic outcome after 4 years for the treatment of patients who had been lost one or more teeth for endodontic, root fracture and deep-carious lesions.

The study was conducted in one University Endodontic Clinical Department and in two private dental offices between January 2011 and January June 2018 by the same clinical team.

Recruitment of patients was performed from October 2009 to June 2014.

Once included in the study, patients were treated from January 2010 to July 2014.

All patients included in this investigation were treated according to the principles established by the Declaration of Helsinki as modified in 2013.[23]

Before enrolment, written and verbal information were given by the clinical staff and each patient gave a written consent according to the above-mentioned principles. An additional signed informed consent was obtained from all patients stating that they accepted the treatment plan and agreed to cover the costs and follow the maintenance hygiene program. This report was written according to the Consolidated Standards of Reporting trials guidelines for reporting clinical trials (STROBE)[24] and respecting the guidelines published by Dodson in 2007.[25]

The patients were considered eligible or non-eligible for inclusion in the clinical protocol based on the following criteria:

<u>Inclusion criteria</u>

- 18-75 years of age at the time of implant placement
- partially dentate requiring dental implants
- possibility to be included in a hygiene recall program and implant control for at least 4 years

<u>Exclusion criteria</u>

- Medical and/or general contraindications for the surgical procedures (ASA score $\geq$3)
- poor oral hygiene and lack of motivation
- active clinical periodontal disease in the dentition expressed by probing pocket depth >4 mm and bleeding on probing
- smoking more than 20 cigarettes by day
- uncontrolled diabetes mellitus
- systemic or local diseases that could compromise post-operative healing and osseointegration
- alcohol and/or drug abuse
- pregnancy or lactating

- malocclusion and other occlusal disorder (bruxism)
- bisphosphonate therapy

Clinical evaluations of periapical status were made by three experienced operators included as Authors.

Treatment procedures

Choice of the surgical approach and timing of implant placement, (immediate, early, delayed according to the timing classification proposed by the Third ITI Consensus Conference)[26] was not determined randomly as the purpose of the study was to use well-defined clinical parameters for the "best clinical practice".[27]

Therefore, the choice of the different surgical approach and the consequent clinical decision and implant placement timing (immediate, early and delayed) was made on the basis of the following clinical criteria: presence of acute endodontic periapical lesion (with pain, fistula, exudate/pus, tenderness and radiographic apical translucency or all of them) and/or the presence of chronic periapical disease (Periapical Index or PAI 3-4).[28]

The three surgical timings were defined as follow:

- Immediate post-extraction implant (Type 1 for ITI)[26]: when the implant was placed into fresh extraction socket immediately after extraction of root affected by chronic periapical disease and/or seriously damaged hopeless (or fractured) teeth were assigned to this group. Only chronic periapical lesions were present and identified by periapical radiolucency.
- Early implant (Type 2 for ITI)[26]: when the implant was placed in healed bone after 8-12 weeks after extraction of root affected by acute periapical lesion and/or abscess, pus and clinical symptoms.
- Delayed implant (Type 4 for ITI)[26]: when the implant was placed in edentulous mature bone 10-12 months after the tooth extraction for different reasons,

Surgical procedures

Cylindrical implants (SP Premium, Sweden & Martina, Padova, Italy) with zirconium-oxide blasted (ZirTi) surface, smooth machined collar 0.5 mm, tulip-shape profile switching platform emergence profile 0.3 mm, hexagonal internal connection and 3.8 or 4.25 or 5.0 mm diameter (10.0 mm or 11.5 mm length) were used.

One single experienced surgeon performed all surgeries.

A careful occlusal and periodontal examination was performed on each patient, including presence of plaque, gingivitis, pocket depth and radiographic bone loss of all remaining teeth. Oral hygiene instruction and periodontal therapy were performed when and where indicated.

Two days prior to the intervention, all patients were asked to comply with a pharmacological regime that included amoxicillin/clavulanic acid 1 gr tablet and application of chlorhexidine digluconate 0.20% gel (Corsodyl Gel, GlaxoSmithKline UK, Brentford, UK) twice a day, according with a previous study.[29]

Antibiotic administration continued during 5-6 days after surgery.

All surgical procedures were conducted under local anesthesia with mepivacaine chlorhydrate 30mg/ml (Carboplyina, Dentsply Italia srl, Roma, Italy). No computer-aided guide was used.

Implants were placed in order to obtain transmucosal nonsubmerged tissue level position healing. The smooth machined collar of the implant platform was placed in the thickness of gingival tissue while the divergent rough implant portion was lean/nested at the bony crest (using standard protocol). In all implants an adequate primary stability was obtained. The final insertion torque value ranged between 20-70 N/cm^2 and was recorded. Considering the thickness of the mucosa, a 1 mm or 2-3 mm high cover-healing screw, that emerged just over the gingival level, was applied.

Immediate implant placement

For immediate post-extractive insertion an atraumatic flapless root extraction was performed and a careful inspection of the socket site was made. All granulation tissue was gently debrided from the apical portion of the socket.

Then a 1.2 mm drill was used to prepare the intra-socket place, following the palatal bony walls as a guide. Twist and calibrated drills at 225 rpm were then used and irrigated with sterile saline solution.

Primary implant stability was obtained by anchoring the implant in the remaining apical portion of the socket at least 3 mm beyond the root apex area.

When necessary, (4 cases) a porcine corticocancellous bone substitute (Osteobiol MP3, Tecknoss Dental, Coazze, Italy) was applied into the surgical site to fill the socket and to reduce any gaps between the implant and the residual bone.

Considering the thickness of the mucosa, a 1 mm or 2-3 mm high cover-healing screw, that emerged just over the gingival level, was applied, following a nonsubmerged healing approach (as above mentioned).

Early and delayed implant placement

The surgical procedures were similar for the Early and Delayed placements. No flaps were reflected. An initial 1.2 mm diameter drill was used to mark the position, angle and depth. The drill passed through the mucosa (transmucosal), cortical bone and cancellous bone under copious saline irrigation. A twist and calibrated drill at 225 rpm was used and a site of the adequate depth and diameter was created whilst irrigating with sterile saline solution.

The entire rough surface region of implants was positioned approx. 1 mm under the cortical bone level and smooth machined collars of the implant platform were placed in the thickness of gingival tissue. The cover screw was at tissue level exposed.

Considering the thickness of the mucosa, a 1 mm or 2-3 mm high cover-healing screw, that emerged just over the gingival level, was applied, following a nonsubmerged healing approach (as above mentioned). No computer-aided surgical guides were used.

Post-operative procedures

A surgical dressing (Coe-Pak, GC, Tokyo, Japan) was placed on the wound in all patients and removed at the first clinical control after one week

Patients were instructed to follow a soft diet regime for one week, to rinse 3 time/day with 0.12% chlorhexidine gel for 3 weeks and to perform oral hygiene on the Coe-Pak using a normal-medium toothbrush for the first week and for 2 weeks after surgical pack removal. Thereafter, conventional brushing and flossing were permitted.

Prosthetic rehabilitation

Prosthetic phases started after 3 months from implant insertion. No second surgeries to expose the implant neck were performed. Briefly, cover screws were removed, impression posts were placed and impressions made with polyether materials (Permadyne™ and Garand™, 3M ESPE, St Paul, MN, USA) in customized trays for pick up technique.

Customized definitive abutments were screwed on the implants after approx. 15 days and provisional resin crowns cemented with temporary zinc-oxide eugenol cement (Temp Bond, Kerr, Scafati, Italy).

Definitive prosthetic metal-ceramic rehabilitation, made by two equally experienced prosthodontists, were positioned on definitive abutments and fixed with polycarboxylate cement (Heraeus Kulzer GmbH, Hanau, Germany) 12-15 days later.[30]

The quantity of the extruded cement was reduced by filling the occlusal half of the crown and maintaining an occlusal space of the abutment screw channel as internal venting to minimize the hydraulic pressure through slowing cement escape. Patients were instructed to continuously bite on a cotton roll for 5 minutes. Subsequently dental floss was used to remove the cement flow.

Follow-up implant evaluation

Active periodontal therapy consisting of motivation, instruction in oral hygiene practice, scaling and root planning was performed during the entire time of observation, no bleeding on probing and pocket probing depth ≥ 3 mm were detected during the follow-up procedures. Routinary follow-up visits were performed every 6 months from implant loading. Occurrence of endodontic treatments on implant adjacent teeth was also recorded.

Gingival thickness evaluation

The soft tissue thickness around implants and their corresponding mesial neighboring teeth was determined at 4 year follow-up. The soft tissue was pierced mid-facially at three millimeters apical to the gingival margin with an endodontic file. (K-file Nr. 20; Dentsply-Maillefer, Switzerland). Gingival biotype was defined thick (soft tissue thickness > 2mm) or thin (soft tissue thickness ≤ 2mm).[31-33]

Radiographic assessment

Intraoral periapical radiographs of all implants were taken using a paralleling technique with Rinn-holders and analog films (Kodak Ektaspeed Plus, Eastman Kodak Co., Rochester, NY, USA) after implant placement (baseline) and at 1, 3, 6, 12 and 24 months after implant insertion.

All X-rays were scanned with a slide scanner with a resolution of 968 dpi and a magnification factor of x20. Length and diameter of implants were used to calibrate the measurement.

The crestal marginal bone and the bone-implant interface were examined to evaluate the marginal bone morphology. MBL was assessed at the mesial and distal implant surfaces by measuring the distance between the reference point of the implant platform to the most coronal bone-to-implant contact level using a scale divided into 0.1 mm steps according to previous studies[34,35] and corrected according to the know height and width of each implant.[36]

Radiographic evaluation was performed in single-blind by one additional examiner. Before evaluating the radiographs, the examiner was calibrated by using well-defined instructions and reference radiographs with different marginal bone level measures.

Evaluated Variables

MBL was measured and evaluated according to the following variables:

1) Preoperative parameters: Implant location (maxilla/mandible), Implant position (anterior/posterior) Gender (male/female), Endodontically treated adjacent teeth (yes/no), Smoke (yes/no), Implant placement timing (immediate/early/delayed)
2) Intra operative parameters: Implant diameter (3.8/4.25/5.0)
3) Post-operative parameters: Gingival thickness (yes/no)

Statistical analysis

Statistical analyses were performed using Stata 13.1 (StataCorp, College Station, TX). Linear regression models were fitted to evaluate the existence of any significant difference regarding endodontically treated adjacent teeth (yes/no), times (one month, 3 months, 6 months, 12, 24, 36 and 48 months), and the interactions between endodontically treated adjacent teeth and time. To take into account the correlation in the data due to the presence of multiple implants per subject, the abovementioned regression models were estimated following a generalized estimating equation (GEE) approach. The estimates of coefficients' standard errors and confidence intervals were adjusted by using a robust variance-covariance estimator.[37] The same analysis was performed for all the operative variables.

A multiple linear regression with stepwise selection was fitted to evaluate the relationship between MBL at 36, 48 months and the following variables: gender (male/female), smoke (yes/no), location (mandible/maxilla), implant position (anterior/posterior), endodontic adjacent teeth (yes/no), adjacent teeth coronal restoration (direct/indirect/no restoration), implant placement timing (immediate/early/delayed), implant diameter (3.8/4.25/5.0), gingival thickness" (thin/thick).

Box plots were created by using Sigma plot 12 software (Systat, Usa) to show the range and distribution of MBL (mm) as a function of implant placement timing (immediate, early delayed) at at 1, 3, 6, 12, 24, 36 and 48 months from implant insertion.

RESULTS

Study population and demographic data

According to the inclusion/exclusion criteria, 76 patients (128 implants) were studied with a mean age of 55.6 ± 10.7 years (42 women and 34 men). Eight patients (17 implants) were identified as smokers, consuming between 10 to 20 cigarettes/day and included in the study; these patients were distributed evenly across the three groups (3 in immediate, 2 in early and 3 in delayed group).

The survival rate was 98.4% as 2 delayed implants failed during the observational time.

Two non-smoker patients dropped out after 6 and 36 months, respectively. Total drop out was 2.58%.

No wound infection, osteitis and bone graft sequestration occurred during follow-up period.

Mucositis was observed in one patient after 3 months caused by a recurrent unscrewing of the implant abutment. The abutment was removed and the area was carefully treated with chlorhexidine 0.12%. After 1 month, a new abutment was screwed and a new metal-ceramic crown was cemented.

Two series of periapical radiograph is reported in **Figs 1,2.**

Radiographic and clinical assessment

Mean MBL did not significantly change from T_{24} to T_{36} and T_{48} ($p>0.05$). The values were 0.89 0.95 and 0.99 mm, respectively.

MBL of implants placed according to all the evaluated parameters is reported in **Table 1.**

Regarding pre-operative parameters, no statistical differences were observed for **implant position**, **gender** and **smoke** at T_{36}. Differently, i**mplant location**, **presence of endodontic adjacent teeth** and **implant placement timing significantly affected MBL,** revealing the most considerable variations at T_{36}.

Concerning **implant diameter** as intra-operative and **gingival thickness** as post operative parameter, no MBL significant differences were present at both T_{36} and T_{48} ($p>0.05$).

Significant differences were present considering **implant location** at T_{36} (maxilla/mandible) ($p=0.004$). Implant placed in the maxilla showed reduced bone loss when compared to that placed in the mandible.

Implants placed in sites with no **adjacent endodontically treated teeth** shows a more stable MBL at T_{36} (mean MBL was 0.70mm vs 1.16mm, respectively), the differences were statistically significant ($p<0.001$).

Considering **implant placement timing**, MBL increased significantly with time (from 1 month and 3-month pre-loading evaluation to the 24-36 month post-loading evaluation) in all the three groups (immediate, early and delayed). Early implants showed the lowest bone loss at all the evaluation times. Immediate implants demonstrated a similar behavior up to T_6.

Interestingly, when considering MBL at **T_{48}**, only **implant placement timing** shows statistically significant differences. Delayed implants shows a higher MBL variation (mean value was 1.22± 0.69) mm when compared to both immediate and early implants (values were 0.76± 0.58 and 0.73±0.57, respectively).

Multilevel mixed logistic regression analysis at T_{36} is reported in **Table 2a.**

The analysis confirms the significant influence of **endodontically treated adjacent teeth** ($p<0.0001$), **implant placement timing** ($p=0.044$) and **implant location** (maxilla/mandible) ($p=0.019$). No statistical differences were observed for the other parameters ($p<0.05$**)**,

Multiple linear regression after stepwise selection (**Table 2b**) additionally confirms that all the 3 variables statistically affected MBL at T_{36} (p value was 0.001 for endodontic treated adjacent teeth, 0.031 for implant location and 0.044 for implant placement timing).

Multilevel mixed logistic regression analysis at T_{48} is reported in **Table 3a**. Interestingly, none of the evaluated parameters appears to significantly affect MBL at this time. Implant placement group appears to be a factor which significantly affects implant MBL only after stepwise logistic regression, confirming data shown in Table 1 (p=0.020). (**Table 3b**)
Box plots representations concerning implant placement timing are showed in **Figure 3.** Delayed group showed the highest presence of outliers, in particular after T_6 from insertion (post loading period). Early group showed the most stable MBL values (less wide distributions) up to T_6 (preloading time) and at T_{48}.

DISCUSSION

This is the first 4-year study where platform-switch implants were used with an enlarged implant neck positioned following a nonsubmerged healing. The results obtained confirms previously reported 2-year prospective study.[30]

The enlarged neck resulted partially immersed along the soft tissues thickness, the entire 0.50 mm smooth machined neck surface close to the most superficial gingiva and the rough surface close to the deeper gingival tissues.
Several benefits may be provided following this protocol. As cover screws (or healing screws, depending on the soft tissue thickness) resulted exposed at soft tissue levels, additional surgeries before the prosthetic phases could be avoided. The **implant-abutment connection**, as well as the crown margins, resulted more distant from bone tissues, allowing a better control of cement flowing from the restoration and avoiding the risks for **cement overflow** and cement retention in proximity with the bone tissues.[38]
This risk was reported in studies where subcrestal or equicrestal implants have been performed, conditions where cement excess cannot be adequately controlled[39-41] or when methacrylate based cements are used.[42] A recent study evaluated clinical radiographic and immunologic parameters

around platform switch dental implants with cement retained or screw retained restorations.[43] Conclusions were that the type of crown retention does not affect BoP, Pocket depth, MBL and levels of IL-1B. In the present study a polycarboxylate cement was used as luting agent.

MBL values follow a similar trend when compared to previously reported with other implant brands,[44] neck,[45]insertion depth,[5] and surgical interventions.[18] A previous randomized clinical trial evaluating bone level implants placed submerged or with a transmucosal approach found similar MBL values at 36 months.[5] Likewise, MBL remained stable after the first 12 months from insertion, where the greater bone level changes occurred.[5] A recently published randomized clinical trial comparing flared tissue level versus platform-switch bone level implants found lower MBL values at 5 years (mean MBL of tissue level implant was 0.61± 0.75)[44] than that reported in our study (0.99 ± 0.68). However, pre-loading MBL changes were not considered in that study as the MBL evaluation started from the delivery of the definitive crown.

Significant bone level changes/remodeling during the **pre load period occurs**. This concept has been also reported with other implants and surgical approaches.[17,18]

Indeed, in the present study, mean MBL at 3 months (pre-load) was statistically different to 6 months MBL (post load) (p=0.001), the values being 0.28 ± 0.56 and 0.47 ± 0.57 respectively, thus corroborating this hypothesis.

Data on implant depth insertion, are mostly from histological studies (45-Romanos 2015). Implants with a tulip-shaped (flared) neck placed in a most apical position revealed more bone loss when compared to the same implants placed supracrestally. This was attributed to the removal of a great portion of the coronal bone, thus potentially compromising blood supply of the remaining cortical bone.[14,15]

In accordance with these histological findings, a recent randomized clinical trial concluded that the preparation of the implant site following a subcrestal approach may induce more stress on marginal bone, which can turn into greater bone resorption after implant placement.[46]

Different operative variables have been analyzed in this study, which found to be important in on bone level changes. Some of them revealed to greatly affect MBL.

Implant location, **presence of endodontic adjacent teeth and implant placement timing** were significantly related to MBL at T_{36}.

Delayed group (implant placement timing) revealed significant differences from T_3 to T_{48}, showing greater bone loss compared to both immediate and early implants. Indeed, box plots (**Figure 3**) clearly evidences that delayed implants presented a wider distribution of implant with MBL values > 1.0 mm at T_{48}.

Implant position parameter did not significantly influence MBL at T_{36} and at T_{48}($p>0.05$). The group discrepancies may have influenced this result.

Presence of endodontically treated adjacent teeth close to peri-implant site are rarely reported even though among all causes of implant failures, retrograde peri-implantitis or endodontic peri-implantitis may have a central role.[47,48]

In the present study, the presence of one or more **endodontic treated teeth** adjacent to the implant site (**Endodontic adjacent teeth** parameter) appears to affect MBL only at T_{36} ($p=0.042$): mean MBL of implants with no adjacent endodontic treated teeth varied from 0.82mm ± 0.73 at T_{24} to 0.72mm ± 0.68 at T_{36} **($p>0.05$)**.

Retrograde peri-implantitis may be an important cause of implant failures, the infection triggered by bacteria present in an adjacent (generally) active periapical lesion.[47]

In some cases, dormant bacteria may remain silent around asymptomatic endodontic treated teeth.

[49-51]

A radiological follow-up of endodontic treated teeth might be important to identify this critical condition.

Considering **gender**, female patients showed an increased MBL after 3 years, compared to males (mean MBL was 1.08mm vs 0.83mm respectively). These differences, however, were not statistically significant (p=0.157). From literature, male patients seem to have higher risks of implant failure however these data are controversial as it is difficult to correlate peri-implant bone loss and patient gender. [52]

In the present study **smoke** was found to not significantly affect MBL in the medium-term. The small sample size of smoking patients and the groups discrepancies (17 implants in 8 patients vs 92 implants in 57 patients) may justify this finding.

Gingival thickness was evaluated in all patients at 48-month follow-up. Interestingly, even though thin biotype showed higher values of MBL this parameter appears not to influence MBL at 36 and 48 months(p>0.05).

Implants placement timing was found to be the most significant factors affecting MBL on nonsubmerged platform-switch tulip-shaped implants. In particular delayed implant groups showed the greatest bone loss. Differences were statistically significant at all the evaluation times. Drilling procedures at the implant site may be responsible for bone necrosis and bone smear layer formation, inducing the activation of osteoclasts and vascularization damage. Both these conditions may be responsible for higher bone resorption of the mature cortical bone.[53,54]

It should be underlined that the reduced bone loss values reported in this study may be influenced by the operator expertise who performed the surgeries and the possibility of patients to be included in a hygienic recall programme. This protocol should be further validated with long term follow-up.

Conclusions

Conclusion may be summarized as follows:

- Tulip-shaped neck platform switch implants may be placed at tissue level (nonsubmerged) with a minimally invasive flapless technique.
- The present protocol demonstrated a reduced bone loss in the early phases from implant placement and a MBL stability at 36 and 48 months.
- Among all the evaluated parameters, only implant placement timing appears to significantly affect MBL before loading and during the entire period of observation.
- Delayed implant placement was responsible for higher bone loss when compared to early and immediate implants

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FIGURES:

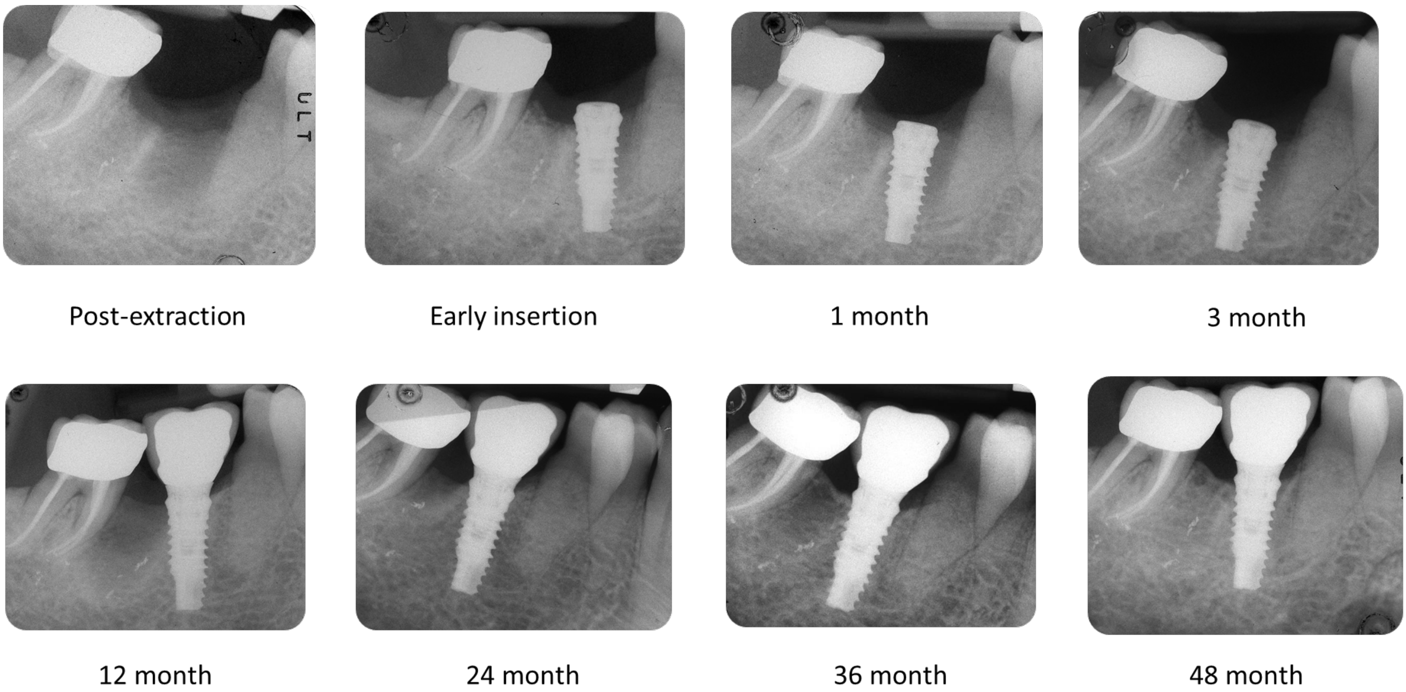

Figure 1: 49-year old female nonsmoker patient with early post-extractive site (first lower right root treated molar was extracted for root fracture 2 months before). A 4.25x 11.5 mm platform switch implants was placed nonsubmerged by using flapless technique. No complications were observed. After 3 months an impression was taken without second stage surgeries. MBL resulted stable at preloading time (1,3 months from implant insertion) and at 12 and 24 months (post-loading time). Please note that the crown margin ends approx. 2mm from the alveolar bone. In this way, cement excesses may be more easily removed. Crestal bone loss has been evidenced at 36 and 48 months.

Figure 2: 42 year old female patient with upper right premolar presenting a vertical root fracture and active periapical lesion (periapical fistula). Extraction was performed and implant insertion was scheduled 3 months after **(**early insertion). A 4.25x10mm implant was inserted with a flapless technique. Impression were taken after 3 months and a provisional crown cemented. Initial bone loss have been observed during pre-loading period. MBL remained stable up to 48 months. Note the presence of 2 endodontic treated teeth 10-12 months from implant insetion. Bone loss was observed.

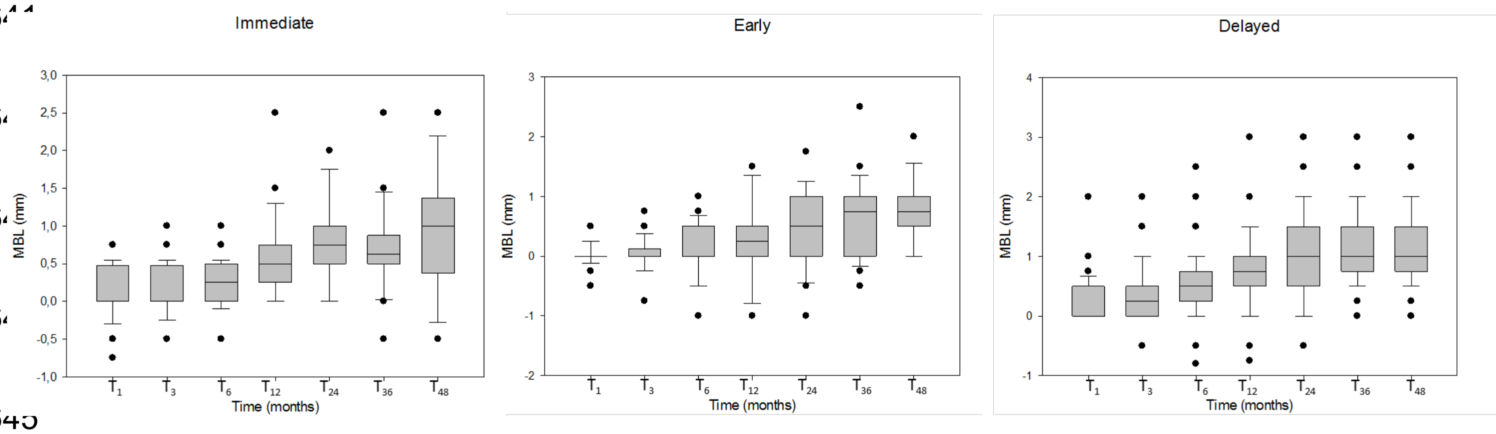

Figure 3 Boxplot representation of placed implants at different evaluation times. Outliers are represented by circle points.

TABLES

Table 1. MBL (Mean ± SD) of the placed implants according to the operative parameters

		n	T_1	T_3	T_6	T_{12}	T_{24}	T_{36}	T_{48}
Pre-operative parameters									
Implant location	Maxilla	70	0.15 ± 0.38^{Aa}	0.23 ± 0.65^{Aa}	0.32 ± 0.51^{ABb}	0.50 ± 0.61^{Bb}	0.72 ± 0.76^{Ca}	0.75 ± 0.75^{Cb}	0.86 ± 0.69^{Ca}
	Mandible	58	0.29 ± 0.44^{A}	0.36 ± 0.49^{Aa}	0.63 ± 0.67^{Ba}	0.90 ± 0.75^{Ca}	1.05 ± 0.80^{Ca}	1.20 ± 0.87^{Ca}	1.19 ± 0.71^{Ca}
Implant position	Anterior	16	0.20 ± 0.39^{Aa}	0.22 ± 0.60^{Aa}	0.39 ± 0.57^{Ba}	0.50 ± 0.69^{Ba}	1.18 ± 0.77^{Ca}	0.91 ± 0.89^{Ca}	0.80 ± 0.64^{Ca}
	Posterior	112	0.22 ± 0.40^{Aa}	0.29 ± 0.57^{Aa}	0.48 ± 0.52^{Ba}	0.65 ± 0.70^{Ca}	0.87 ± 0.76^{Da}	0.95 ± 0.81^{Da}	1.03 ± 0.68^{Da}
Gender	Male	57	0.12 ± 0.36^{Aa}	0.15 ± 0.41^{Aa}	0.29 ± 0.54^{Ba}	0.52 ± 0.68^{Ca}	0.74 ± 0.66^{Da}	0.83 ± 0.71^{Da}	0.85 ± 0.64^{Da}
	Female	71	0.27 ± 0.49^{Aa}	0.39 ± 0.65^{Ab}	0.59 ± 0.61^{Bb}	0.82 ± 0.69^{Cb}	1.05 ± 0.82^{Da}	1.08 ± 0.91^{Da}	1.21 ± 0.68^{Da}
Endodontic adjacent teeth	No	59	0.19 ± 0.38^{Aa}	0.25 ± 0.56^{Aa}	0.42 ± 0.61^{Ba}	0.56 ± 0.69^{Ba}	0.82 ± 0.73^{Ca}	0.70 ± 0.68^{BCa}	0.88 ± 0.68^{Ba}
	Yes	69	0.23 ± 0.39^{Aa}	0.28 ± 0.51^{Aa}	0.49 ± 0.56^{Ba}	0.76 ± 0.68^{Ca}	0.95 ± 0.65^{Da}	1.16 ± 0.69^{Eb}	1.17 ± 0.68^{Ea}
Smoke	Smokers	17	0.11 ± 0.42^{Aa}	0.12 ± 0.52^{Aa}	0.19 ± 0.56^{Aa}	0.57 ± 0.75^{Ba}	0.81 ± 0.86^{Ca}	0.82 ± 0.96^{Ca}	0.84 ± 0.67^{Ca}
	Non smokers	111	0.22 ± 0.41^{Aa}	0.27 ± 0.53^{Aa}	0.46 ± 0.52^{Ba}	0.69 ± 0.35^{Ba}	0.88 ± 0.75^{Ca}	0.97 ± 0.89^{Ca}	1.07 ± 0.65^{Ca}
Implant placement	Immediate	24	0.09 ± 0.30^{Aa}	0.14 ± 0.35^{Aa}	0.23 ± 0.27^{Ba}	0.61 ± 0.59^{Ca}	0.80 ± 0.62^{Ca}	0.73 ± 1.07^{Ca}	0.76 ± 0.58^{Ca}
	Early	21	0.01 ± 0.18^{Aa}	0.03 ± 0.29^{Aa}	0.10 ± 0.47^{Aa}	0.22 ± 0.66^{Bb}	0.53 ± 0.67^{Ba}	0.66 ± 0.71^{Bab}	0.73 ± 0.57^{Ba}
	Delayed	83	0.29 ± 0.45^{Ab}	0.39 ± 0.62^{Ab}	0.62 ± 0.66^{Bb}	0.82 ± 0.68^{Ca}	1.02 ± 0.76^{Da}	1.16 ± 0.81^{Db}	1.22 ± 0.69^{Db}
Intra-operative parameter									
Implant Diameter	3.8	53	0.27 ± 0.30^{Aa}	0.34 ± 0.33^{Aa}	0.43 ± 0.27^{ABa}	0.60 ± 0.69^{Ba}	0.76 ± 0.70^{Ba}	0.99 ± 0.70^{Ca}	0.95 ± 0.67^{Ca}
	4.25	56	0.22 ± 0.19^{Aa}	0.33 ± 0.29^{Aa}	0.56 ± 0.47^{Ba}	0.76 ± 0.64^{Ba}	1.07 ± 0.72^{Ca}	0.96 ± 0.72^{Ca}	1.08 ± 0.67^{Ca}
	5.0	19	0.11 ± 0.41^{Aa}	0.08 ± 0.62^{Aa}	0.24 ± 0.64^{Ba}	0.57 ± 0.84^{Ca}	0.75 ± 1.01^{Da}	0.83 ± 1.01^{Da}	0.91 ± 0.65^{Da}
Post-operative parameter									
Gingival thickness	Thin	73	0.19 ± 0.34^{Aa}	0.27 ± 0.39^{Aa}	0.53 ± 0.58^{Ba}	0.75 ± 0.66^{Ba}	0.97 ± 0.77^{BCa}	1.06 ± 0.82^{Ca}	1.16 ± 0.72^{Ca}
	Thick	55	0.25 ± 0.48^{Aa}	0.31 ± 0.75^{Aa}	0.38 ± 0.64^{ABa}	0.53 ± 0.75^{Ba}	0.78 ± 0.79^{BCa}	0.81 ± 0.81^{Ba}	0.80 ± 0.65^{Ba}
Total		128	0.21 ± 0.38^{A}	0.28 ± 0.56^{A}	0.47 ± 0.57^{B}	0.67 ± 0.78^{C}	0.89 ± 0.81^{D}	0.95 ± 0.85^{D}	0.99 ± 0.68^{D}

Table 2a.	Multilevel-mixed logistic regression exploring factor associated to MBL at 36 months			
Groups	Coefficent	Robust SE	95% CI	p-value
Pre-operative parameters				
Gender	0.204	0.144	(-0.079; 0.487)	0.158
Location	0.373	0.159	(0.061; 0.685)	**0.019**
Smoke	0.252	0.146	(-0.034; 0.137)	0.084
Position	-0.276	0.169	(-0.609; 0.056)	0.104
Endodontically treated adjacent teeth	0.501	0.143	(0.219; 0.780)	**<0.0001**
Implant placement group	0.181	0.089	(0.005; 0.357)	**0.044**
Intra-operative parameters				
Implant Diameter	0.052	0.118	(-0.179; 0.283)	0.659
Post-operative parameters				
Gingival biotype	-0.128	0.135	(-0.394; 0.137)	0.343

Table 2b	Multiple linear regression after stepwise selection			
Groups	Coefficient	Robust SE	95% CI	p-value
Implant placement group	0.168	0.083	(0.003; 0.337)	**0.045**
Location	0.335	0.155	(0.031; 0.639)	**0.031**
Endodontically treated adjacent teeth	-0.57	0.335	(-1.228; 0.859)	**0.001**

Table 3a.	Multilevel-mixed logistic regression exploring factor associated to MBL at 48 months			
Groups	Coefficent	Robust SE	95% CI	p-value
Pre-operative parameters				
Gender	0.226	0.190	(-0.146; 0.598)	0.234
Location	0.138	0.237	(-0.326; 0.604)	0.559
Smoke	0.252	0.146	(-0.034; 0.137)	0.084
Position	-0.186	0.308	(-0.792; 0.419)	0.546
Endodontically treated adjacent teeth	0.329	0.172	(-0.009; 0.668)	0.056
Implant placement group	0.180	0.150	(-0.113; 0.475)	0.229
Intra-operative parameters				
Implant Diameter	0.075	0.121	(-0.161; 0.31)	0.532
Post-operative parameters				
Gingival biotype	-0.224	0.186	(-0.254; 0.432)	0.227

Table 3b	Multiple linear regression after stepwise selection			
Groups	Coefficient	Robust SE	95% CI	p-value
Implant placement group	0.231	0.998	(0.362; 0.427)	**0.020**
Thickness	-0.291	0.280	(0.334; 1.432)	0.076