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Original Research

Assessment Of Soft Tissue Around Healing Abutments Placed Via Platform-Matched And Platform-Switched In Dental Implant Cases: An Original Research

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ABSTRACT:
Background: It has been shown that platform-switching implants minimize marginal bone loss. The impact on the soft tissue healing around the implant is uncertain, though. This study was created to look into how implant uncovery affected the healing of the soft tissue surrounding the implant. **Methods:** In the present study, non-smokers who required two implants in various quadrants were included. The two-stage approach was used to implant one platform switching and one platform matching implant for each person. All implants were exposed and linked to the corresponding healing abutments after 2 to 8 months of healing. After the second step of surgery, clinical measures and crevicular fluid around the implant were collected at 1, 2, 4, and 6 weeks. The levels of cytokines in PICF were examined. For the investigation of gene expression at uncovery and six weeks after uncovery, peri-implant mucosa (1×2×2 mm) was taken around the healing abutment. **Results:** 32 total participants were enrolled, out of which 18 were male and 18 were female. In comparison to platform matching, platform switching demonstrated significantly decreased 1- and 2-week probing depths (PD) and 1-, 4-, and 6-week modified sulcus bleeding indices (mSBI) (P< 0.05). Osteoprotegerin and interleukin-1 concentrations in PICF decreased over time, while periostin, peroxidasin, and receptor activator of unclear factor kappa B ligand gene expression in the peri-implant mucosa increased (P 0.05), with no discernible intergroup differences. **Conclusion:** Within the limitations, implants with platform switching design outperformed PM design in terms of reducing PD and mSBI during the course of a 6-week healing. However, molecular alterations brought on by platform matching and platform switching appear to be minimal in PICF and peri-implant mucosa.
Keywords: cytokines, dental implant-abutment design, dental implants, gene expression

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INTRODUCTION

Dental implant therapy is a widely accepted option for partially or fully edentulous patients with restorative demands. Early marginal bone loss (MBL), particularly in the first year following functional loading of implants, is a typical occurrence. [1] After years of extensive research, the causes of MBL can be broadly classified as mechanical, biological, or mixed. [2] While bacterial pathogens are the primary cause of MBL, [3-5] it has been shown that implant surface features and implant structure can produce MBL independently of biological challenges.[6]

Implant-abutment junction (IAJ) is a feature that comes with a typical two-piece implant installation. Nonetheless, IAJ contains a little but necessary junctional space known as a "microgap."[7] Certain

research indicates a potential connection between microgap and MBL, particularly in cases where an IAJ is situated sub-crestal. [8,9,10] The concentration of stress along the implant-crestal bone contact during axial force loading on the abutment provides an explanation for the microgap-MBL association.[11] In addition to stress, MBL may also be caused by bacterial accumulation [7,13] and improved microgap-enabled abutment micromovement [12].

Platform switching, an implant-abutment connection architecture, has been developed to address biological issues associated to microgaps and has shown promise in reducing MBL. In 2006, Lazzara and Porter [15] presented the idea of platform switching. In an in vitro investigation, the inward movement of platform switching 's healing abutment contour greatly decreased the concentration of stress on the nearby crestal bone during force loading. [11] The design in question facilitates the growth of biological width by providing greater surface area, while simultaneously restricting the infiltration of inflammatory cells to a narrower area. [15] Some studies show that platform switching can dramatically minimize vertical crest bone loss by 0.3 to 0.5 mm when compared with normal implant-abutment connections, while the precise process is still unclear. [14,16-18]

A meta-regression analysis indicated that MBL might be lowered by 0.0907 mm for every 0.1 mm increase in mismatch.[17] To further enhance the danger of abutment fracture, the platform switching design should be used cautiously since the stress may focus more on the abutment [11,19]

In addition to using radiography to evaluate MBL, peri implant health can also be evaluated using peri-implant crevicular fluid analysis (PICF).[20] Significant variations in PICF components between healthy and diseased implants, as well as before and after treatment for peri-implant disorders, have been shown in certain investigations.[21,22] Therefore, it stands to reason that examining the inflammatory biomarkers in PICF will also help determine the inflammatory condition of peri-implant tissue.

Compared to regular platform matching design, platform switching abutment design provides greater stability of the marginal bone level after functional loading; its impact on the healing of the peri-implant mucosa following the second stage of the surgery is uncertain, though. In order to examine the healing of the peri-implant soft tissue around platform switching and platform matching abutments following implant uncovery in a variety of ways, including clinical metrics, PICF biomarker profiles, and gene expressions in the peri-implant mucosa, this study set out to do just that. The study's null hypothesis states that, during the early healing period, platform switching and platform matching implants have the same biomarker profiles in PICF and gene expressions in peri-implant tissue. The results of this study may explain if platform switching design affects peri-implant mucosa healing in a different way than platform matching.

MATERIALS AND METHODOLOGY

Study population and study design

The eligibility of patients seeking implant-supported restorations at Department of Periodontology was assessed and included in the study based on the following criteria. The following criteria were required for inclusion: (1) age between 18 and 70 years old; (2) non-smokers or former smokers who have abstained from smoking for more than five years; (3) patients classified as Class-I or Class-II by the American Society of Anesthesiologists;23 (5) diabetic patients with self-reported HbA1c 7.0; (6) patients with two similar single edentulous sites at two different quadrants and where treatment plan is carried out to have implant-supported restorations, (7) patients being able and willing to provide informed consents..

The following patients were excluded from the study: (1) current smokers; (2) pregnant or nursing women; (3) patients with active periodontal diseases; (4) patients with a history of using bisphosphonates; radiotherapy for the head and neck region; or chemotherapy for malignant tumours; and (5) patients who were taking inflammatory drugs, prophylactic antibiotics, or were undergoing hormone replacement therapy.

A screening was done during the first visit to determine each patient's eligibility in accordance with the inclusion and exclusion criteria. Using a questionnaire, the medical and dental histories of each patient were examined. Following the completion of the questionnaire, the qualified participants were also given a detailed explanation of the research methodology, and the consent papers were signed before scheduling the implant operation. In the second visit, each subject got two implants in accordance with the normal two-stage protocol: one platform switching and one platform matching implant (same diameter, different platform sizes) were randomly implanted in two distinct quadrants, along with a concurrent bone grafting process, if necessary.

A few months were given for implants to heal before being exposed (longer healing times were chosen for implant locations that received bone grafts at the time of implantation). The implants were then exposed, and they were joined to their corresponding healing abutments. From that point on, the PICF collection and clinical parameter measurements were done at 1, 2, 4, and 6 weeks after uncovery.

Additionally, at uncovery (0-week) and 6 weeks following uncovery, a little fragment of peri-implant mucosa (1.2 x 2.2 x 2.2 mm) was taken from the sidewalls of the platform matching and platform switching implants. A periapical radiograph was also performed after the surgery to ensure the tight fit between the healing abutment and the implant fixture.

Randomization during the surgical placement of implant fixtures

As per conventional clinical protocol, all patients took 2 g of prophylactic amoxicillin 1 hour before implant surgery. Patients who were allergic to Penicillin could instead take clindamycin (600 mg). Local anaesthetic was applied using 1-2 cartridges of lidocaine with 1:100,000 epinephrine for each implant site. On the edentulous ridge, a crestal incision was created, and the intrasulcular incision was extended to the buccal and lingual surfaces of the neighbouring teeth. For the implant site osteotomy, a full thickness flap was lifted in accordance with the manufacturer's recommendations. Using a two-stage technique, one platform switching implant and one platform matching implant with the same diameter but distinct platform designs were randomly implanted into each patient. For the purpose of allocating platform switching and platform matching implants randomly, the simplest and most often used form of randomization was coin flipping.

When the torque value of the implants' primary stability reached 35 Ncm, it was deemed satisfactory. A simultaneous bone grafting operation, such as guided bone regeneration or indirect sinus augmentation, was carried out when it was essential in addition to implant implantation. The flap was then relocated and predominantly stitched with a size 4-0 suture. The subjects were instructed to hold off on brushing and flossing until the sutures were removed (1-2 weeks after surgery). Each patient also received a prescription for analgesics, an antibacterial rinse, and antibiotics (for those getting bone grafts) in addition to oral and written postoperative instructions.

A second surgery to uncover an implant

2–8 months following implant implantation, implant uncovery was carried out. An H-incision with a width just large enough to reveal the cover screw made up the flap design. The lingual and buccal flaps were raised, and a healing abutment was used in place of the cover screw: The healing abutments for platform switching and platform matching implants with a diameter of 5 mm and 4 mm were respectively 4.1 mm and 5 mm, and for platform switching and platform matching implants with a diameter of 4 mm, 3.4 mm and 4.1 mm. An instantaneous periapical radiograph was taken to verify a solid connection between the implant and abutment.

A tiny portion of keratinized gingival tissue (1 mm x 2 mm x 2 mm) was removed from each implant site prior to suturing. For future gene expression study, gingival samples were preserved in a vial, shipped in a container containing liquid nitrogen, and kept in a freezer at -20 °C. A 4-0 suture was used to seal the wound. All patients were advised not to brush the surgery site for a week, and an antibacterial rinse was administered.

Post-uncovery visits and sample collections

One qualified examiner completed the clinical measures and collected the PICF samples at 1, 2, 4, and 6 weeks following the second stage operation. After performing an intra-examiner calibration, the Kappa value for the intra-examiner agreement was 0.78.25

Modified plaque index (mPI), modified sulcus bleeding index (mSBI), and probing depth (PD) were the clinical assessments. Following PICF sample, these measurements were made at six sites/implant using a coloured periodontal probe. The abutment was gently irrigated with saline water for PICF collection, and the plaque was scraped off with a piece of cotton pellet. A sterilized paper strip was carefully placed there and left there for 30 seconds.

The volume of the captured PICF was then determined by instantly transferring the strip to an electronic volume quantification machine that had been calibrated. After that, this strip was put in a vial* with ice and moved to a freezer at -20°C for later protein analysis. For the protein assays, four PICF strips from each implant were gathered and combined.

Sandwich enzyme-linked immunosorbent assay (ELISA)

Interleukin-1 (IL-1), IL-10, tumour necrosis factor (TNF), osteoprotegerin (OPG), and vascular endothelial growth factor (VEGF) concentrations in PICF were measured using ELISA kits in accordance with the manufacturer's instructions. At a wavelength of 450 nm, all proteins were identified using an array reader and expressed as pg/mL.

Reverse transcription-quantitative polymerase chain reaction (RT-qPCR)

Dry ice was used to ship the gingival samples to the clinical medical laboratory for RT-qPCR analysis. Analysis was done on the peri-implant mucosa's gene expression levels for IL-6, CRP, connective tissue growth factor (CTGF), OPG, receptor activator of nuclear factor kappa-B ligand (RANKL), periostin, and peroxidasin. [27] Following the manufacturer's instructions, total RNAs were isolated from the peri-implant mucosa using an RNA isolation kit. Reverse transcription was performed using a cDNA Synthesis Kit# in accordance with the manufacturer's instructions on 250 ng of total RNA.

A reaction mixture containing 4 litres of reaction solution, 2 litres of reverse transcriptase mixture, 500 ng of total RNA, and nuclease-free water were combined and incubated in a thermocycler under the following conditions: 10 minutes at 25 °C, 60 minutes at 42 °C, and 5 minutes at 85 °C. Following a 1/5 dilution, the cDNA mixture was utilized for RT-qPCR. Two housekeeping genes, human ribosomal protein L30 (RPL30) and ATP synthase subunit six (ATP-6), as well as the previously listed seven target genes, had their primers ordered from the company. The following conditions were used for quantitative PCR:

95 °C for 20 seconds for one cycle, 95 °C for 1 second, and 60 °C for 20 seconds for 40 cycles.
The three individual data from each reaction were averaged, standardized to housekeeping genes (RPL30 and ATP-6), and each reaction was carried out in triplicate. The levels of target gene expression were measured by comparative Ct. Target gene and housekeeping gene mean Ct values were calculated using PM and platform switching samples (Ct mean = [(Target Gene Ct mean - ATP-6 Ct mean) + (Target Gene Ct mean - RPL30 Ct mean)]/2). The formula below was used to calculate Ct values: Ct is calculated as (Ct mean target gene in PM or platform switching sample) minus (Ct mean target gene from typical PM samples). The levels of gene expression for each sample (platform matching versus platform switching) were calculated using the relative quantification (RQ) of fold-change in mRNA levels using the 2 Ct method.

Statistical analysis

Power analysis was used to determine that 16 samples per group would have at least 95% power to detect one SD change for each group at a significant threshold of 0.05 using paired t-tests. Using common statistical software, the statistical analysis for the clinical parameters was carried out. At four separate time points, data were compared within and between groups. Protein concentration was used in the PICF analysis. The levels of cytokine production and significant inter- and intragroup differences were examined using a paired samples t-test and Pearson correlation. Statistics were considered significant for P values below 0.05. The P values of the RQ between platform switching and platform matching groups at the same time point and within the platform switching or platform matching groups at two distinct time points were determined for RT-qPCR data using the conventional t-test. Standard error of RQ values were used as the mean and error bars to illustrate the data for each gene and each treatment.

RESULTS

The study population

Fourty patients who met the inclusion criteria were chosen from a pool of 64 patients who were screened from June 2014 to December 2016 for this clinical trial. 32 participants eventually came back to complete the data collection.

Table 1 Demographic data, intra-oral distribution and dimensions of implants

Number of subjects (n) = 36 (72 implants)			
Sex distribution F/M = 18/18			
Age range and mean = 23-70 (51.7 years old)			
	Control side (PM)	**Test side (platform switching)**	**Total (n = 72)**
Distribution in oral cavity	Maxilla: 12 (33.3%) Mandible: 24 (66.7%)	Maxilla: 16 (44.4%) Mandible: 20 (55.6%)	Maxilla: 28 (38.9%) Mandible: 44 (61.1%)
Tooth type	Incisor: 4 (11.1%) Canine: 2 (5.6%) Premolar: 10 (27.8%) Molar: 20 (55.6%)	Incisor: 4 (11.1%) Canine: 2 (5.6%) Premolar: 10 (27.8%) Molar: 20 (55.6%)	Incisor: 8 (11.1%) Canine: 4 (5.6%) Premolar: 20 (27.8%) Molar: 40 (55.6%)
Implant diameter	5 mm: 18 (50.0%) 4 mm: 18 (50.0%)	5 mm: 18 (50.0%) 4 mm: 18 (50.0%)	5 mm: 32 (50.0%) 4 mm: 32 (50.0%)
Implant length	8.5 mm: 2 (5.6%) 10 mm: 20 (55.6%) 11.5mm: 12 (33.3%) 13 mm: 2 (5.6%)	8.5 mm: 2 (5.6%) 10 mm: 20 (55.6%) 11.5mm: 10 (27.8%) 13 mm: 4 (11.1%)	8.5 mm: 4 (5.6%) 10 mm: 40 (55.6%) 11.5mm: 22 (30.6%) 13 mm: 6 (8.3%)
Simultaneous procedure	BG: 8 (22.2%) GBR: 4 (11.1%)	BG: 14 (38.9%) Indirect SL: 2 (5.6%)	with: 28 (38.9%) without: 44 (61.1%)

Abbreviations: BG, bone grafting; GBR, guided bone regeneration; SL, sinus lift.

Table 1 provides an overview of the demographic information, intraoral distribution, and implant dimensions in this investigation. Equal numbers of implants with a diameter of 4 and 5 mm were used, and 86.2% of implants had a length between 10 and 11.5 mm. When it comes to implant placement, the majority (61.1%) were installed in the mandible, and more than 80% were positioned in the posterior edentulous ridge. Furthermore, more than 60% of the implants were inserted into areas that had already received bone grafts or in areas where no further bone augmentation was required. While lengthier healing times were permitted for sites that received either bone grafting or indirect sinus augmentation at the time of implant placement (5.77 ± 2.78 months), the average implant healing time for all implants was 4.44 ± 2.07 months.

Clinical measurements

From week 1 to week 6, both groups mPI, mSBI, PD, and PICF volume generally shown a definite time-dependent decline. With regard to mSBI, noteworthy, significant intergroup differences between platform switching and PM were seen at weeks 1, 4, and 6 ($P<0.05$), as well as during weeks 1 and 2 for PD ($P<0.001$). However, there were no appreciable variations in mPI and PICF volume between the platform switching and platform matching groups

(P>0.05). Multiple pairwise comparisons across two time intervals between the time-dependent intragroup comparisons showed statistically significant changes in all 4 clinical indicators (P<0.05).

Levels of inflammatory cytokine in PICF

Not all of the cytokines examined in this study shown a substantial time-dependent shift during the 6-week healing period, in contrast to the findings of clinical assessment. In actuality, only IL-1 and OPG in PICF showed a time-dependent decline over the course of six weeks, with the exception of the OPG at week six. With the exception of IL-1 at week 2 for both groups and OPG at week 6 for the platform switching group, these decreases were statistically significant within the platform switching and platform matching groups. Except for TNF- at week 2 against week 6 (P<0.05) in platform matching and VEGF at week 1 versus week 2 (P< 0.001) in platform switching, intragroup differences for the other three cytokines (IL-10, TNF-, and VEGF) were not statistically significant (P >0.05).

Levels of gene expression in peri-implant mucosa

Three distinct patterns were seen in terms of intragroup comparisons. There were no discernible differences for CTGF and OPG in the platform switching and platform matching groups between weeks 0 and 6. In all the platform switching and PM groups, RANKL, periostin, and peroxidasin gene expression levels were noticeably increased at week 6 compared to week 0 levels. As a result, the OPG/RANKL ratio was significantly greater in both groups at week 0 than at week 6. However, only in the platform switching group did levels of IL-6 and CRP gene expression differ significantly between week 0 and week 6, while there were no such alterations between week 0 and week 6 for the platform matching group. No significant differences were seen for any of the targeted genes in either groups at either the week 0 or week 6 time points (P >0.05).

DISCUSSION

By examining changes in clinical parameters, profiles of biomarkers in PICF, and gene expressions in peri-implant mucosa, this study aimed to examine the preloading implant soft tissue healing around platform switching and platform matching abutments after implant uncovery. Our findings showed that compared to platform matching locations, platform switching sites displayed considerably lower SBI and shallower PD. Although time-dependent alterations were found within both groups, there were no differences between the two groups in terms of PICF protein concentration or peri-implant mucosa gene expression. In spite of better changes shown in several clinical measures, platform switching implant does not appear to affect cellular responses relevant to early stages of recovery.

The study was able to examine the soft tissue reaction to platform switching and contrast it with that to platform matching using a study group that included 36 patients with 72 implant fixtures of particular platform designs. Similar distributions of systemic and local variables, such as gender, age, systemic health problems, periodontal health, and dental plaque accumulation over the course of the observation period, were made possible by the cross-sectional study design. Clinical recovery went smoothly, taking an average of 4.44 ± 2.07 months. Only one patient's cover screw became prematurely exposed, necessitating further surgical care to coronally place the gingival tissue and avoid the necessity for an early uncovery procedure. When the implants were placed, bone grafting or indirect sinus augmentation was done simultaneously at 28 of the 72 implant locations (38.9%).

The second surgical procedure had no impact on PICF volume. This study's PICF volume and inflammatory cytokine concentration were lower than those of our prior study [23]. The implants utilized in this study were specially created to match their associated healing abutments and to create either a platform matching or platform switching setting, therefore this could be related to the implant platform design. The clinical data revealed considerable intergroup variations in PD and mSBI during the initial phase of healing. Clinically, it seemed that the peri-implant mucosa around the platform matching implant was less swollen than the one around the platform matching implant.

The biological roles and functions of the cytokines and target genes evaluated in this study have been examined. PICF cytokine alterations have been seen under a variety of circumstances. Emecen Huja et al. [24] studied the recovery of peri-implant tissue following one-stage implant implantation and discovered that after 12 weeks of non-loaded settings, both the total quantities and concentrations of IL-1 and VEGF reduced.

Over the course of the observation period, the mean volume of PICF also decreased. The cytokine profile variations in PICF before and after the therapy of sick implants were examined by Renvert et al. [25] After six months, the stable treatment outcome group had a considerable reduction in IL-1, but there was no such reduction in TNF- or OPG levels.Guncu et al [26] contrasted the cytokines in PICF between implants with and without illness. In comparison to the control group, the sick implant group's levels of IL-1, IL-10, and OPG were shown to be noticeably higher. The level of IL-1 in PICF reduced concurrently with the reduction of peri-implant tissue inflammation, despite the fact that the results of the current investigation were not entirely compatible with those from the aforementioned studies. The variances in study designs may be the primary cause of the results disparities between studies.

In peri-implant tissue from healthy, mucositis- and peri-implantitis-infected implants, Duarte et al. [27] compared the gene expressions. According to their

findings, healthy peri-implant tissue had much greater levels of OPG mRNA than did tissue from implants with mucositis and peri-implantitis. Additionally, the level of RANKL mRNA dramatically rose as the severity of the peri-implant infection increased. The RANKL and OPG gene expressions seem to be related to the level of infection or inflammation in the peri-implant tissue. In the current study, RANKL gene expression decreased 6 weeks after implant uncovery, whereas OPG gene expression did not alter significantly over time. The lack of peri-implant infection in our investigation may have prevented OPG gene expression from reaching statistically significant levels. However, it is interesting in the current study that at week 6 RANKL, periostin, and peroxidasin gene expressions significantly increased in both groups compared to baseline. This might be connected to the establishment of biological width during the early stages of soft tissue healing and peri-implant bone remodelling.

This study has several limitations, which are as follows. This investigation couldn't be done using a double-blind approach since the surgeon could easily tell the difference in the corresponding healing abutment. Additionally, because the healing abutment on the platform switching implant was smaller than that on the platform matching implant, data collection throughout the 6-week healing period was also not blinded. The abutment dimension variable was controlled in this study using manufacturer-designed platform switching and platform matching abutments. The findings of this study therefore do not apply to the long term with the final prosthesis and are only applicable to the transitional stage with healing abutments. Moreover, due to the small quantity of PICF that could be collected each time, only a select few cytokines were examined in this investigation. To better understand the role of inflammatory cytokines in the peri implant mucosa during early wound healing after uncovery of dental implants placed with a two-stage surgical technique, more research on other inflammatory cytokines is required.

CONCLUSION

Within the limitations of this investigation, dental implants with platform switching design offered substantial advantages over those with platform matching design in terms of shallower PD and less bleeding over a 6-week healing period. The levels of cytokine production and gene expression between platform switching and platform matching, however, were not shown to be significantly different. During the first healing phase, it seems that the peri-implant soft tissue response to platform matching and platform switching implants is biologically mostly comparable.

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