

Implant stability change and osseointegration speed of immediately loaded photofunctionalized implants

AUTHORS: Senichi Suzuki, DDS, PhD¹, Hiroyuki Kobayashi, MD, PhD¹, Takahiro Ogawa, DDS, PhD²

ABSTRACT: (186 WORDS)

Objectives: This study evaluated the degree and rate of implant stability development for photofunctionalized dental implants in humans. **Materials and Methods:** Thirty-three implants (seven patients) placed in the maxilla and immediate loaded were evaluated. Photofunctionalization was performed by treating implants with UV for 15 min immediately before placement. Implant stability was assessed by measuring the implant stability quotient (ISQ) weekly starting from implant placement up to 3 months. Osseointegration speed index (OSI), defined as ISQ increase per month, was also evaluated. **Results:** The average ISQ for photofunctionalized implants at week 6 was 78.0, which was considerably higher than the average ISQ of 66.1, reported in literature after a longer healing time of 2–6 months. No stability dip was observed regardless of the initial ISQ values. The OSI for photofunctionalized implants was 6.3 and 3.1 when their initial ISQ was 65–70 and 71–75, respectively, whereas the OSI values for untreated implants calculated from literature ranged from –3.0 to 1.17 with an average of –0.10. **Conclusion:** Photofunctionalization accelerated and enhanced osseointegration of dental implants, providing novel and practical avenues for further advancement in implant therapy.

KEYWORDS: Ultraviolet (UV); titanium; superhydrophilic; hydrocarbon; super osseointegration

¹ Private practice, Kanagawa, Japan

² Professor, Director The Weintraub Center for Reconstructive Biotechnology, Division of Advanced Prosthodontics, UCLA School of Dentistry, Los Angeles, California

Reprint requests and correspondence to: Takahiro Ogawa, DDS, PhD, Laboratory for Bone and Implant Sciences (LBIS), The Jane and Jerry Weintraub Center for Reconstructive Biotechnology Division of Advanced Prosthodontics, Biomaterials and Hospital Dentistry, UCLA School of Dentistry, 10833 Le Conte Avenue (B3-081 CHS), Box 951668, Los Angeles, CA 90095-1668

TEL:(310) 825-0727

FAX:(310) 825-6345

E-mail: togawa@dentistry.ucla.edu

Photofunctionalization of titanium implants, comprehensive physicochemical and biological effects of ultraviolet (UV)-light treatment, has earned considerable interest and attention in the fields of titanium science, biomaterials research, and implant therapy¹⁻⁶. Photofunctionalization of titanium implants increased the bone-implant contact from 55% to 98.2%, approximating an ideal level of 100%, in an animal model⁵. Consequently, the strength of bone-implant integration increases more than 3 times at the early stage of healing⁵. Subsequent *in vivo* animal studies further revealed the advantage of photofunctionalization to overcome challenging conditions. One of the studies showed that, when the implant was 40% shorter, the strength of bone-implant integration decreased by 50%⁷. More importantly, when 40% shorter implants were photofunctionalized, the strength of bone-implant integration was even greater than that of standard-length implants. Another study examined the effect of a peri-implant gap in the cortical bone⁸. The presence of a peri-implant gap, equivalent to half the implant diameter, resulted in significant reduction of the strength of bone-implant integration by 70% compared with the implants with cortical support. When photofunctionalized implants were placed in the same gap healing, the strength of bone-implant integration increased to the same level of the implants with cortical support. Detailed microCT analysis revealed that the effect can be explained by an enhanced osteomorphogenesis around photofunctionalized implants⁸. There was robust osteogenesis around photofunctionalized implants, which initiated at the implant interface and rapidly spread to and connected with the surrounding bone, whereas osteogenesis around untreated implants initiated at the surface of the remote cortical bone and slowly approached the implant interface.

The mechanism underlying the biological effects of photofunctionalization includes three property changes on titanium surfaces. Photofunctionalization converts titanium surfaces from hydrophobic to superhydrophilic, and from electronegative to electropositive^{2,3,5,9-13}. In addition, titanium surfaces, which are unavoidably covered by a significant amount of hydrocarbon during aging, can

be cleaned by photofunctionalization^{2,3,5,14}. Because of these surface changes, the recruitment, attachment, retention, spread, proliferation, and the expression of functional phenotypes of osteogenic cells are remarkably increased^{1,5,8,11,12,15,16}. Among cellular behavior and function, the present study paid attention to the potential benefits obtained by the enhanced attachment and retention of the cells. Mechanical stimulation, such as vibration of the titanium substrate, is known to detach a large number of cells from titanium surfaces even after the cells are adhered^{6,10,11,15,17}. When an immediate loading protocol is applied to dental implants, there is a reasonable concern that only a limited number of remnant cells could play a subsequent role in osseointegration. If photofunctionalization is proven to increase cellular attachment and retention, it may, in particular, help improve the process of osseointegration in immediately loaded dental implants.

Measuring implant stability at placement and its subsequent change during healing provides useful information for monitoring the process of osseointegration, planning a loading protocol, and evaluating various conditions of osseointegration on implant and host sides¹⁸⁻²⁴. The use of implant stability quotient (ISQ) values based on the resonance frequency analysis has been extensively reported for its reasonable reliability and validity^{20,25-30}. Peri-implant osteogenesis consists of postsurgical reaction and remodeling of the bone and the initiation and progression of *de novo* bone formation, which are represented as a reduction in primary stability and development of secondary stability, respectively³¹⁻³³. The rate of losing primary stability is known to be faster than the development of secondary stability and, thereby, causes a merging gap between the two processes to maintain overall implant stability, resulting in the occurrence of a stability dip^{32,33} (Fig. 1). The stability dip, including the progressive reduction of overall stability when the initial stability is high, is considered difficult to eliminate with current implants, and in fact, ISQ values are adequately sensitive to detect the stability dip between weeks 1 and 8 after implant placement^{19,21,26,34-37}. Because of the stability dip, there is a principle in clinical protocol that

implants should be kept unloaded until after the dip has passed, which limits the application of immediate and early loading.

Thus, an important question is whether photofunctionalization is effective in obtaining similar results in humans compared with animal studies and thereby providing clinical advantages or therapeutic significance. In particular, we hypothesized that photofunctionalization may affect the commonly understood time course of a change in implant stability because of its capability to expedite and enhance osseointegration as demonstrated in animal studies. This is a prospective cohort study to evaluate the change in stability of photofunctionalized dental implants placed in the edentulous maxilla and immediately loaded during their early healing time up to 3 months.

MATERIALS AND METHODS

Patients

Among the patients who visited Lion Implant Center during November 2011 and March 2012 for implant therapy and who provided consent for documentation and public presentation of their cases, seven male patients were selected consecutively for this study. Patients were included if they were at least 20 years old, if they complied with oral health care instructions and necessary visits, and if they showed indications for immediate loading in the edentulous maxilla. Patients with systemic or behavioral conditions that could potentially affect bone and soft tissue healing, such as osteoporosis, diabetes, radiation treatment, bruxism, or smoking, were excluded. In total, 33 implants were placed in the seven patients. The patient and implant information is provided in Table 1.

Surgical procedure and photofunctionalization of dental implants

Standardized consultation and diagnostic procedures were provided to all patients and a treatment plan was presented and approved by the patients. Following the routine procedures of local anesthesia and full-thickness flap reflection, implants were placed following the standard surgical procedure recommended by the manufacturer and described in-depth elsewhere^{38,39}. Four to six implants were placed per edentulous maxilla. The implant neck was positioned at bone level. Multiunit straight abutments, or 17° or 30° angulated abutments were used as appropriate to correct the fixture inclination. The soft tissues were readapted and sutured.

Implants used in this study had a tapered root form and identical surface microscale morphology by oxidation (TiUnite, NobelReplace Tapered Groovy RP, Nobel Biocare, Yorba Linda, CA). The dimensions of the implants are presented in Table 1. All implants were photofunctionalized by treating with UV light for 15 min using a photo device (TheraBeam® Affiny, Ushio Inc, Tokyo, Japan) at the chair side immediately before implantation (Fig. 2A). The photofunctionalization-induced change in surface property from hydrophobic to superhydrophilic (defined as a contact angle of water less than 5°) was confirmed prior to patient visits by examining several implants for their wettability to double-distilled water (Fig. 2B). These tested implants were from a separate group of the same type of implants and not used for the patients. Further, photofunctionalized surfaces were confirmed by watching the patient's blood spiral up the implant immediately after it was in contact with the drilled site, as typically seen in Fig. 2C. Bone quality was categorized as type 1, 2, 3, or 4 during the surgery following the criteria proposed by Lekholm and Zarb⁴⁰.

Immediate provisional restoration

Full-arch acrylic resin temporary prostheses were placed on the same day. The prostheses were fabricated following the manufacturer's instructions and as described elsewhere^{38,39} using autopolymerizing resin (Unifast II, GC, Tokyo, Japan) and temporary abutments (Nobel Biocare) in the in-house laboratory. Anterior occlusal contacts and canine guidance during lateral

movements were preferably established on the provisional prostheses. No cantilevers contact was given on the provisional prostheses.

Implant stability measurement and osseointegration speed index (OSI)

Implant stability was evaluated by measuring the ISQ at implant placement (ISQi) and during the healing period with a one-week interval up to 11 weeks using Osstell ISQ (Osstell AB, Göteborg, Sweden). Furthermore, the rate of establishing implant stability was evaluated by the osseointegration speed index (OSI) defined as an ISQ increase per month, i.e., $[(\text{ISQ at week 6}) - (\text{ISQi})]/1.5$.

Statistical analysis

The effect of healing time on ISQ values was evaluated by analysis of variance (ANOVA); $p < 0.05$ indicated statistical significance. When the effect was significant, further post-hoc analysis of Bonferroni was performed to compare the ISQ at placement (ISQi) with the ISQ at each of the subsequent time points. The ISQ values were compared among implants with different lengths using ANOVA. Further, the effect of different bone types where implants were placed was evaluated.

RESULTS

Implant dimensions and bone type

The diameter of all implants used in this study was 4.3 mm, whereas their length varied; 13 mm implants were used most often (Table 1). A majority of implants (57.6%) were placed in the type 2 bone, while 24.2% and 18.2% implants were placed in the type 1 and type 3 bone, respectively. There was no type 4 bone because the cases included in the study were selected for immediate loading.

Change in implant stability

To visualize the overall trend of change in implant stability, ISQ values at implant placement (ISQ_i) and week 6 were individually plotted (Fig. 3). The ISQ_i varied widely from 65 to 85, whereas the ISQ values at week 6 were converged to the higher level. There was a variation in ISQ fluctuation between the time of implant placement and week 6, either an increase, no change, or a decrease, for implants with ISQ_i that were 77 or higher. In contrast, all implants with ISQ_i that were 75 or lower showed an increase at week 6. There was a clear trend that the lower the ISQ_i, the greater the subsequent ISQ increase. As a result, the ISQ values at week 6 were all 75 or higher.

Next, the implants were divided into three groups depending on the range of their ISQ_i (“ISQ_i 65–70,” “ISQ_i 71–75,” and “ISQ_i ≥ 76”), and the ISQ values starting from the implant placement up to 11th week were plotted in a line graph for each group (Fig. 4). When the ISQ_i values was 65–70, the ISQ line graph showed a rapid and continuous increase up to week 6, followed by the plateau at the increased level (Fig. 4A). ANOVA showed a statistically significant effect of healing time on the ISQ values ($p < 0.05$). The post-hoc analysis showed that the ISQ values at week 3 and after week 3 were significantly higher than the ISQ_i, supporting the rapid increase and subsequent maintenance of ISQ. No significant ISQ decrease was found compared with the ISQ_i in the entire assessment period ($p > 0.05$). There also was no significant ISQ dip (a significantly lower ISQ value compared with neighbor time points) throughout the healing period ($p > 0.05$).

Similar to the “ISQ_i 65–70” group, when the ISQ_i was 71–75, the subsequent ISQ showed an increasing course of change (Fig. 4B). Although the rate of ISQ increase appeared less than that in “ISQ_i 65–70” group because of the higher baseline, the ISQ values in the later time points appeared to be similar between the “ISQ_i 71–75” and “ISQ_i 65–70” groups. A significant ISQ increase compared with ISQ_i was found starting at week 2 and continued until week 11, except at

week 3. Compared with ISQi, subsequent ISQ values did not show a significant decrease or a significant dip throughout the healing period. In contrast with these two results, there was no time-dependent ISQ increase, decrease, or dip when the ISQi was 76 or higher (Fig. 4C). The mean ISQ values remained higher than 76 throughout the healing period without significant fluctuation in this group.

Osseointegration speed index (OSI)

For each of the “ISQi 65–70,” “ISQi 71–75,” and “ISQi ≥ 76 ” groups, change in implant stability between the implant placement and week 6 was tallied in Table 2. A statistically significant ISQ increase was seen in “ISQi 65–70” and “ISQi 71–75” groups but not in “ISQi ≥ 76 ” group. For the significant ISQ changes found, the OSI defined as the ISQ increase per month was calculated (Table 2). The OSI in “ISQi 65–70” group was 6.3 ± 0.9 and approximately 2 times higher than that in “ISQi 71–75” group. The OSI for “ISQi 71–75” group was 3.1 ± 1.2 .

Effect of bone type and implant length

To find potential specificity or exclusivity of the effect of photofunctionalization, ISQ values were analyzed in different bone types. At implant placement, ISQi significantly varied with bone type (Table 3). The ISQ values were significantly lower for the type 2 and 3 groups than for the type 1 group. The inter-bone type difference became insignificant at week 6, indicating that photofunctionalization was effective in increasing the stability of implants with lower initial ISQ in the type 2 and 3 groups. Next, ISQ values were analyzed depending on the implant length (Table 4). The ISQi was not different between “ ≤ 11.5 mm” and “ ≥ 13 mm” groups. Although ISQ increased in both groups at week 6, there was no difference between the two groups, indicating the even effect of photofunctionalization regardless of the implant length.

DISCUSSION

By using ISQ values, this study quantitatively evaluated the level, change, and rate of osseointegration of photofunctionalized dental implants under the immediate loading condition. One of the hypotheses we tested was whether clinical effects of photofunctionalization similar to those found in animal studies can be obtained in humans. As mentioned in the Introduction, a series of animal studies demonstrated the accelerated and enhanced capability of osseointegration by photofunctionalization. To compare the osseointegration capability of photofunctionalized dental implants with one of the untreated conventional implants, we defined and calculated the OSI. The proposed OSI value represents a rate of developing implant stability standardized by healing time, providing more precise and reasonable information rather than the use of an ISQ *per se* at a certain time point or an ISQ increase during undefined period of time, and more importantly, allowing for a comparison among different sources of data. Table 5 lists ISQ values from two time points along with the calculated OSI in the literature^{18,19,26,34-37,41-46}. The OSI values from the present study are also listed at the bottom of the table. Because the initial ISQ values were all higher than 65 in the present study, we focused on the publications dealing with initial ISQ values higher than around 60 and at the same time, with data availability at least two time points. The following were the three major findings (Table 5); (1) a greater increase between the initial and secondary ISQ values in photofunctionalized implants than in literature; (2) the majority of OSI in literature was lower than 1.0 and the OSI of photofunctionalized implants was notably higher than those in literature; and (3) the ISQ values at secondary time points obtained in the present study between 77.5 and 78.1 were higher than any values in literature, even within a shorter healing time of 1.5 months.

The ISQ values are known to increase when the initial ISQ is lower than 60, whereas ISQ values mostly stay unchanged or decrease when the initial ISQ is higher than 60^{19,21,26,35,47}. This common understanding can be reaffirmed from the data in literature listed in Table 5 showing OSI of lower

than 1.0. or even in the negative range below 0. In this regard, the OSI of 6.3 when the initial ISQ was 65–70 and the OSI of 3.1 even when the initial ISQ was 71–75 obtained in the present study should be considered remarkable. In fact, the calculated OSI for all untreated conventional implants in Table 5 ranged from –3.0 to 1.17, with an average of –0.10. If only data with their initial ISQ being in a similar range to the present study (65–75) are selected, the OSI ranged from –1.8 to 1.17 with an average of 0.21. In both cases, the OSI values in literature were substantially low.

Although any interpretation should be carefully made because of the differences in macroscopic design and surface morphology among implants, considerably high ISQ values obtained in the present study at week 6 may imply the advantage of photofunctionalization to not only expedite the process but also achieve a higher level of osseointegration. The results were particularly surprising because of the following two reasons: initial ISQ values of 65 or higher are not expected to increase further, as reported in literature and high ISQ values were obtained after a healing time as short as 6 weeks. Future studies are needed to follow up on the subsequent change of the ISQ values of photofunctionalized implants. The higher level of osseointegration may lead to better success rates and long-term predictability of implant therapy, which will be a very interesting research topic in the future. Thus, the present ISQ data and its comparison with literature were indeed consistent with the results obtained from animal studies that showed highly increased implant fixation in the early and late stage of healing, accelerated rate of peri-implant bone formation, and the establishment of bone–implant contact nearing 100%⁵, supporting the hypothesis that photofunctionalized implants in humans are as effective as in animal experiments. Furthermore, we believe that photofunctionalization may have impacted the commonly understood time course of a change in implant stability in a positive way.

Discussing cases of immediate loading and with a similar type of implants would be of another particular interest. A study examined the stability change of implants loaded 1–9 days after implant placement to support a full-arch fixed bridge in the maxilla⁴¹. A total of 61 oxidized implants (six or eight implants per maxilla) were examined. The mean ISQ, which was 60.1 ± 3.6 at placement, increased to 62.8 ± 1.6 after 4 months, giving an OSI of 0.68. Another study evaluated implants placed in the partially edentulous maxilla and loaded 0–16 days after placement⁴². A total of 53 oxidized implants (16 for single tooth replacement and 37 for partial fixed bridges) were examined. The initial ISQ of 63.3 ± 6.1 slightly increased to 64.3 ± 5.3 after 3 months, giving an OSI of 0.33. Again, there is a general understanding regarding ISQ values that the lower the initial value the more increase is expected during the subsequent healing. Despite the initial ISQ being higher than these studies, OSI values obtained at week 6 in the present study were remarkably greater. Knowing that these studies were carried out under a similar clinical protocol and host conditions to the present study and with the implant texture being identical to an oxidized surface used in this study, the present results may genuinely demonstrate the effect of photofunctionalization in enabling a faster and more complete process of osseointegration. As mentioned in the Introduction, the clinical benefit of photofunctionalization was particularly anticipated in such early/immediate loading cases because of the increased attachment and retention of osteogenic cells, which indeed has been proven by the quantitative assessment of implant stability.

Another important result of the present study was the elimination of the stability dip or significant decrease of total stability throughout the healing period for photofunctionalized implants. High initial ISQ values of approximately 70–80 are bound to show a typical dip during the subsequent healing period or, if not a typical dip, a decrease and remain at the decreased level^{19,21,26,35,47}. In the present study, as shown in Table 2 and Fig. 4C, implants with very high initial ISQs (higher than 78) did not experience a stability dip or significant decrease during the healing period, providing

the compelling evidence to support immediate loading. Together with the rapid ISQ increase observed in the implants with lower initial ISQ, the present results will help explore a new strategy for early or immediate loading protocols. On the basis of the present results on ISQ dynamics combined with the common understanding on how the stability dip appears, we propose a mechanism underlying the disappearance of the stability dip by the use of photofunctionalized implants (Fig. 5). There are two scenarios to explain the phenomenon of stability dip, depending on the level of primary stability. The notions applied to construct the mechanism were as follows:

- 1) OSI for photofunctionalized implants was considerably higher than untreated implants reported in literature, which led to a rapid and steep secondary stability curve slope during the early healing period;
- 2) regardless of the use of photofunctionalization, implants with lower initial ISQ values tend to show higher OSI as understood commonly;
- 3) in the present study, an OSI with an initial ISQ of 65–70 was, in fact, two times greater than an OSI with an initial ISQ of 71–75;
- 4) not only the rate of implant stability but also the final level was increased by photofunctionalization, which indicates that the level of secondary stability could be higher with photofunctionalized implants than conventional implants;
- 5) the rate of losing primary stability is assumed to be the same with or without photofunctionalization. In the illustrations (Fig. 5A, C), high-level and low-level stability dips unavoidably take place in untreated conventional implants because of the quicker loss of primary stability than the development of secondary stability. The rate of secondary stability establishment, which is faster in Fig. 5C than in Fig. 5A, as indicated by " $a' > a$ ", is unlikely to help eliminate the stability dip. In contrast, because of the early shift of the secondary stability curve, as indicated by " $b > a$ ", the stability dip is effectively eliminated in photofunctionalized implants (Fig. 5B). The increased level of total stability by the increased degree of secondary stability should not be overlooked. In addition, because of further increased rate in the secondary stability, as indicated by " $y = 2bx$ ", the stability dip can be avoided even when the primary stability was low (Fig. 5D). We believe that the proposed schemes will help understand how the overall anchorage of photofunctionalized implants is uniquely established and

provide a novel platform to build a new strategy for future clinical protocols and the development of implant surfaces.

Although the interpretation should be limited to the results obtained during the initial period of osseointegration of up to 3 months, the quantitative analysis of implant stability by the consecutive measurement of ISQ values in a cohort design may have provided an invaluable data set to demonstrate the expedited and enhanced process of osseointegration in photofunctionalized dental implants and warrants further clinical studies to establish photofunctionalization as an effective measure to improve the current implant dentistry in multiple aspects. Photofunctionalization is a simple, practical, chair-side treatment of dental implants that requires only 15 min and has proven effective on all surface topographies of titanium-based materials tested, implying the versatile applicability in a wide range of dental and orthopedic implants^{9,48-50}. If future surface technologies are anticipated to expand the indications of implant therapy, shorten the healing time, increase the success rate for compromised bone conditions, and explore minimally invasive approaches, photofunctionalization as presented here may provide a novel insight and a practical avenue to pursue those goals. Lastly, the application of photofunctionalization should not be restricted to use in dental implants. Orthopedic implants face many, long-unsolved challenges. Photofunctionalization can be applied regardless of the shape and size of implants. Various orthopedic implants, including but not limited to spine screws, femoral stem, knee joint implants, plates, and pins, can potentially be enhanced for their osteoconduction.

Conclusions

This study reports a quantitative evaluation of the effect of photofunctionalization on clinical performance, specifically osseointegration capability, of dental implants. Photofunctionalization was conducted by treating implants with UV light for 15 min. The generation of

superhydrophilicity and hemophilicity was confirmed after photofunctionalization. The osseointegration capability of photofunctionalized implants placed in the maxilla and immediately loaded was assessed by consecutive measurements of implant stability (ISQ) during the early stage of healing up to 3 months along with the rate of ISQ increase per month, defined as the osseointegration speed index (OSI). Implants with their initial ISQ at placement between 65 and 70 showed a rapid and robust ISQ increase during the subsequent healing period. Implants with their initial ISQ between 71 and 75 also showed a rapid and significant increase. Implants with their initial ISQ of 76 or greater maintained a high level of ISQ throughout the healing period without showing any drop or progressive decrease in ISQ. Regardless of the initial ISQ, ISQ values were 75 or greater for all implants by week 6. The ISQ at week 6 for photofunctionalized implants ranged from 77.5 to 78.1 with an average of 78.0, whereas ISQ values after a decent healing period (mostly 2–6 months) observed in literature ranged between 60.2 and 74.8 with an average of 66.1. The OSI was considerably high for photofunctionalized implants (6.3 for implants with an initial ISQ of 65–70 and 3.1 for implants with an initial ISQ of 71–75) than for untreated conventional implants in literature ranging from –3.0 to 1.17 with an average of –0.10. In conclusion, photofunctionalization resulted in the acceleration and enhancement of osseointegration in commercial dental implants. As a result, the rate of establishing implant stability was substantially increased when initial stability was relatively low. When the initial stability was relatively high, the ISQ was maintained at a high value, eliminating the commonly accepted phenomenon of the stability dip. In both instances, the level of stability that implants may experience was considerably increased. These results imply that photofunctionalization may provide a novel and practical possibility to further advance implant therapy for its expanded indications, shortened healing time, improved predictability in challenging cases, and the exploration of minimally invasive approaches during the treatment.

REFERENCES

1. Ogawa T. UV photofunctionalization of titanium implants. *J Craniofac Tissue Eng* 2012;2:151-158.
2. Att W, Ogawa T. Biological aging of implant surfaces and their restoration with ultraviolet light treatment: a novel understanding of osseointegration. *Int J Oral Maxillofac Implants* 2012;27:753-761.
3. Lee JH, Ogawa T. The biological aging of titanium implants. *Implant Dent* 2012;21:415-421.
4. Ogawa T. Photofunctionalization of TiO₂ for optimal integration of titanium with bone. In *Benign Photocatalysts. Applications of titanium oxide-based materials*. Eds. Prashant Kamat and Masakazu Anpo. Springer US 2010:699-713.
5. Aita H, Hori N, Takeuchi M, Suzuki T, Yamada M, Anpo M, et al. The effect of ultraviolet functionalization of titanium on integration with bone. *Biomaterials* 2009;30:1015-1025.
6. Tsukimura N, Yamada M, Iwasa F, Minamikawa H, Att W, Ueno T, et al. Synergistic effects of UV photofunctionalization and micro-nano hybrid topography on the biological properties of titanium. *Biomaterials* 2011;32:4358-4368.
7. Ueno T, Yamada M, Hori N, Suzuki T, Ogawa T. Effect of ultraviolet photoactivation of titanium on osseointegration in a rat model. *Int J Oral Maxillofac Implants* 2010;25:287-294.
8. Ueno T, Yamada M, Suzuki T, Minamikawa H, Sato N, Hori N, et al. Enhancement of bone-titanium integration profile with UV-photofunctionalized titanium in a gap healing model. *Biomaterials* 2010;31:1546-1557.
9. Suzuki T, Hori N, Att W, Kubo K, Iwasa F, Ueno T, et al. Ultraviolet treatment overcomes time-related degrading bioactivity of titanium. *Tissue Eng Part A* 2009;15:3679-3688.

10. Iwasa F, Tsukimura N, Sugita Y, Kanuru RK, Kubo K, Hasnain H, et al. TiO₂ micro-nano-hybrid surface to alleviate biological aging of UV-photofunctionalized titanium. *Int J Nanomed* 2011;6:1327-1341.
11. Iwasa F, Hori N, Ueno T, Minamikawa H, Yamada M, Ogawa T. Enhancement of osteoblast adhesion to UV-photofunctionalized titanium via an electrostatic mechanism. *Biomaterials* 2010;31:2717-2727.
12. Hori N, Ueno T, Minamikawa H, Iwasa F, Yoshino F, Kimoto K, et al. Electrostatic control of protein adsorption on UV-photofunctionalized titanium. *Acta Biomater* 2010;6:4175-4180.
13. Hori N, Att W, Ueno T, Sato N, Yamada M, Saruwatari L, et al. Age-dependent degradation of the protein adsorption capacity of titanium. *J Dent Res* 2009;88:663-667.
14. Att W, Hori N, Takeuchi M, Ouyang J, Yang Y, Anpo M, et al. Time-dependent degradation of titanium osteoconductivity: an implication of biological aging of implant materials. *Biomaterials* 2009;30:5352-5363.
15. Yamada M, Miyauchi T, Yamamoto A, Iwasa F, Takeuchi M, Anpo M, et al. Enhancement of adhesion strength and cellular stiffness of osteoblasts on mirror-polished titanium surface by UV-photofunctionalization. *Acta Biomater* 2010;6:4578-4588.
16. Miyauchi T, Yamada M, Yamamoto A, Iwasa F, Suzawa T, Kamijo R, et al. The enhanced characteristics of osteoblast adhesion to photofunctionalized nanoscale TiO₂ layers on biomaterials surfaces. *Biomaterials* 2010;31:3827-3839.
17. Ueno T, Tsukimura N, Yamada M, Ogawa T. Enhanced bone-integration capability of alkali- and heat-treated nanopolymorphic titanium in micro-to-nanoscale hierarchy. *Biomaterials* 2011;32:7297-7308.
18. Bischof M, Nedir R, Szmukler-Moncler S, Bernard JP, Samson J. Implant stability measurement of delayed and immediately loaded implants during healing. *Clin Oral Implants Res* 2004;15:529-539.

19. Glauser R, Sennerby L, Meredith N, Ree A, Lundgren A, Gottlow J, et al. Resonance frequency analysis of implants subjected to immediate or early functional occlusal loading. Successful vs. failing implants. *Clin Oral Implants Res* 2004;15:428-434.
20. Han J, Lulic M, Lang NP. Factors influencing resonance frequency analysis assessed by Osstell mentor during implant tissue integration: II. Implant surface modifications and implant diameter. *Clin Oral Implants Res* 2010;21:605-611.
21. Makary C, Rebaudi A, Sammartino G, Naaman N. Implant primary stability determined by resonance frequency analysis: correlation with insertion torque, histologic bone volume, and torsional stability at 6 weeks. *Implant Dent* 2012;21:474-480.
22. Javed F, Almas K, Crespi R, Romanos GE. Implant surface morphology and primary stability: is there a connection? *Implant Dent* 2011;20:40-46.
23. Lee HJ, Aparecida de Mattias Sartori I, Alcantara PR, Vieira RA, Suzuki D, Gasparini Kiatake Fontao F, et al. Implant stability measurements of two immediate loading protocols for the edentulous mandible: rigid and semi-rigid splinting of the implants. *Implant Dent* 2012;21:486-490.
24. Chan HL, El-Kholy K, Fu JH, Galindo-Moreno P, Wang HL. Implant primary stability determined by resonance frequency analysis in surgically created defects: a pilot cadaver study. *Implant Dent* 2010;19:509-519.
25. Gupta RK, Padmanabhan TV. An Evaluation of the Resonance Frequency Analysis Device: Examiner Reliability and Repeatability of Readings. *J Oral Implantol* Epub ahead of print. doi: 10.1563/AAID-JOI-D-11-00099
26. Nedir R, Bischof M, Szmukler-Moncler S, Bernard JP, Samson J. Predicting osseointegration by means of implant primary stability. *Clin Oral Implants Res* 2004;15:520-528.

27. Meredith N, Alleyne D, Cawley P. Quantitative determination of the stability of the implant-tissue interface using resonance frequency analysis. *Clin Oral Implants Res* 1996;7:261-267.
28. Huang HL, Tsai MT, Su KC, Li YF, Hsu JT, Chang CH, et al. Relation between initial implant stability quotient and bone-implant contact percentage: an in vitro model study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endo* 2012 Epub ahead of print. doi.org/10.1016/j.oooo.2012.01.037
29. Park KJ, Kwon JY, Kim SK, Heo SJ, Koak JY, Lee JH, et al. The relationship between implant stability quotient values and implant insertion variables: a clinical study. *J Oral Rehabil* 2011 Epub ahead of print. doi: 10.1111/j.1365-2842.2011.02255.x
30. Sennerby L, Meredith N. Implant stability measurements using resonance frequency analysis: biological and biomechanical aspects and clinical implications. *Periodontology* 2000 2008;47:51-66.
31. Ogawa T, Nishimura I. Different bone integration profiles of turned and acid-etched implants associated with modulated expression of extracellular matrix genes. *Int J Oral Maxillofac Implants* 2003;18:200-210.
32. Aparicio C, Lang NP, Rangert B. Validity and clinical significance of biomechanical testing of implant/bone interface. *Clin Oral Implants Res* 2006;17 Suppl 2:2-7.
33. Atsumi M, Park SH, Wang HL. Methods used to assess implant stability: current status. *Int J Oral Maxillofac Implants* 2007;22:743-754.
34. Barewal RM, Oates TW, Meredith N, Cochran DL. Resonance frequency measurement of implant stability in vivo on implants with a sandblasted and acid-etched surface. *Int J Oral Maxillofac Implants* 2003;18:641-651.
35. Sencimen M, Gulses A, Ozen J, Dergin C, Okcu KM, Ayyildiz S, et al. Early detection of alterations in the resonance frequency assessment of oral implant stability on various bone types: a clinical study. *J Oral Implantol* 2011;37:411-419.

36. Oates TW, Valderrama P, Bischof M, Nedir R, Jones A, Simpson J, et al. Enhanced implant stability with a chemically modified SLA surface: a randomized pilot study. *Int J Oral Maxillofac Implants* 2007;22:755-760.
37. Simunek A, Kopecka D, Brazda T, Strnad I, Capek L, Slezak R. Development of implant stability during early healing of immediately loaded implants. *Int J Oral Maxillofac Implants* 2012;27:619-627.
38. Malo P, de Araujo Nobre M, Lopes A, Francischone C, Rigolizzo M. "All-on-4" immediate-function concept for completely edentulous maxillae: a clinical report on the medium (3 years) and long-term (5 years) outcomes. *Clin Implant Dent Relat Res* 2012;14 Suppl 1:e139-150.
39. Malo P, de Araujo Nobre M, Lopes A, Moss SM, Molina GJ. A longitudinal study of the survival of All-on-4 implants in the mandible with up to 10 years of follow-up. *J Am Dent Assoc* 2011;142:310-320.
40. Lekholm U, Zarb GA. Patient selection and preparation. In Branemark P.I., Albrektsson T. eds. *Tissue integrated prostheses: osseointegration in clinical dentistry* 1985;Chicago: Quintessence:199-209.
41. Olsson M, Urde G, Andersen JB, Sennerby L. Early loading of maxillary fixed cross-arch dental prostheses supported by six or eight oxidized titanium implants: results after 1 year of loading, case series. *Clin Implant Dent Relat Res* 2003;5 Suppl 1:81-87.
42. Fischer K, Backstrom M, Sennerby L. Immediate and early loading of oxidized tapered implants in the partially edentulous maxilla: a 1-year prospective clinical, radiographic, and resonance frequency analysis study. *Clin Implant Dent Relat Res* 2009;11:69-80.
43. Sjostrom M, Lundgren S, Nilson H, Sennerby L. Monitoring of implant stability in grafted bone using resonance frequency analysis. A clinical study from implant placement to 6 months of loading. *Int J Oral Maxillofac Surg* 2005;34:45-51.

44. Al-Khaldi N, Sleeman D, Allen F. Stability of dental implants in grafted bone in the anterior maxilla: longitudinal study. *Br J Oral Maxillofac Surg* 2011;49:319-323.
45. Karl M, Graef F, Heckmann S, Krafft T. Parameters of resonance frequency measurement values: a retrospective study of 385 ITI dental implants. *Clin Oral Implants Res* 2008;19:214-218.
46. Rasmusson L, Thor A, Sennerby L. Stability evaluation of implants integrated in grafted and nongrafted maxillary bone: a clinical study from implant placement to abutment connection. *Clin Implant Dent Relat Res* 2012;14:61-66.
47. Khandelwal N, Oates TW, Vargas A, Alexander PP, Schoolfield JD, Alex McMahan C. Conventional SLA and chemically modified SLA implants in patients with poorly controlled type 2 Diabetes mellitus - a randomized controlled trial. *Clin Oral Implants Res* 2011 Epub ahead of print. doi: 10.1111/j.1600-0501.2011.02369.x.
48. Att W, Ogawa T. Biological aging of implant surfaces and its restoration using UV light treatment: A novel and breakthrough understanding of osseointegration. *Int J Oral Maxillofac Implants* 2012; 27: 753-61.
49. Koppenburg P, Abe K, Abe T, Adachi I, Aihara H, Akatsu M, et al. Inclusive measurement of the photon energy spectrum in $b \rightarrow s\gamma$ decays. *Phys Rev Lett* 2004;93:061803.
50. Att W, Hori N, Iwasa F, Yamada M, Ueno T, Ogawa T. The effect of UV-photofunctionalization on the time-related bioactivity of titanium and chromium-cobalt alloys. *Biomaterials* 2009;30:4268-4276.

LEGENDS

Fig. 1 A suggested mechanism of the occurrence of a stability dip in dental implants. The total stability, as determined by the addition of primary stability and secondary stability, normally shows an merging gap, which is called the stability dip. The stability dip is considered unavoidable

in current dental implants because the rate of losing primary stability is faster than the development of secondary stability.

Fig. 2 Photofunctionalization of dental implants and its visualized effects on implant surface property. (A) A photo device (TheraBeam® Affiny, Ushio Inc, Tokyo, Japan) used for photofunctionalization. Dental implants were treated for 15 min immediately before implantation. (B) Implants, that were hydrophobic as received, were converted to superhydrophilic after photofunctionalization. Photographic images of 3 μ l of ddH₂O droplets placed on implant surfaces are shown. Two droplets (6 μ l) were sufficient to entirely cover a photofunctionalized implant. (C) Clinical images of untreated and photofunctionalized dental implants when they were in contact with an implant site. A hemophilic conversion of the implant surfaces is evidently seen after photofunctionalization. The generated hemophilicity was robust enough to soak up blood along the implant thread.

Fig. 3 The implant stability quotient (ISQ) values at implant placement and week 6 of healing plotted for photofunctionalized implants. Note that all implants with an initial ISQ that was 75 or lower showed an increase at week 6 and consequently, the ISQ values at week 6 were all 75 or higher.

Fig. 4 Change in implant stability for photofunctionalized implants, evaluated by implant stability quotient (ISQ) values at implant placement and subsequent healing time. Line graphs are drawn in three different groups depending on the initial ISQ values at implant placement. * $p < 0.05$, ** $p < 0.01$, statistically significant difference from the ISQ at placement (ISQi).

Fig. 5 Proposed mechanisms of appearance and disappearance of stability dip in schematic description. The stability dip is eliminated by the use of photofunctionalization, regardless of the

degree of primary stability, because of faster and even faster (when the primary stability is low) development of secondary stability. Note that photofunctionalization did not only expedite the rate of establishing the total stability but also increased the degree of the total stability. Refer to the main text for detailed explanation.

LEGENDS TO TABLES

Table 1.

All 33 photofunctionalized implants were placed in the maxilla and immediately loaded in this study. All implants were 4.3 mm in diameter, and most often used length was 13 mm. Approximately 60% implants were placed in the type 2 bone.

Table 2.

When the initial ISQ was 75 or lower, there found a significant increase in the subsequent ISQ value at week 6. The OSI values, defined as the ISQ increase divided by healing time of 1.5 month (6 weeks), allowed for evaluating a standardized rate of establishing implant stability. Implants with an initial ISQ of 76 or greater maintained a high ISQ at week 6 without showing significant change.

Table 3.

The ISQ values in type 2 and 3 groups increased between the placement and week 6, indicating that photofunctionalization is particularly effective in enhancing osseointegration in weak bone types. As a result, there was no significant difference in ISQ values among the three groups at week 6.

Table 4.

There were no significant difference between the two groups at week 6 of healing, indicating that photofunctionalization was effective in increasing ISQ values regardless of the implant length.

Table 5.

The OSI values for photofunctionalized implants are considerably higher than those from literature. In addition, the ISQ values achievable at week 6 of healing (1.5-month healing) in photofunctionalized implants are higher than those in any untreated implants even after longer healing time.

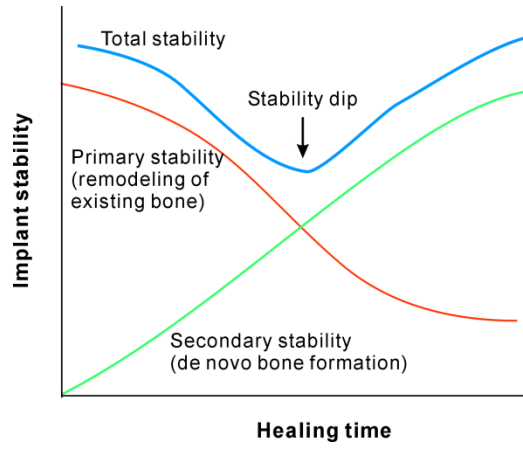


Fig. 1

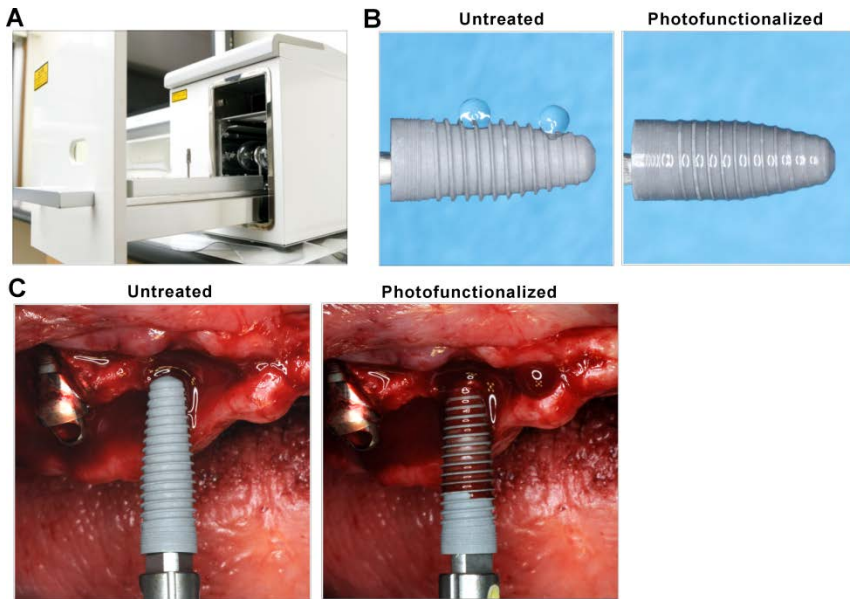


Fig. 2

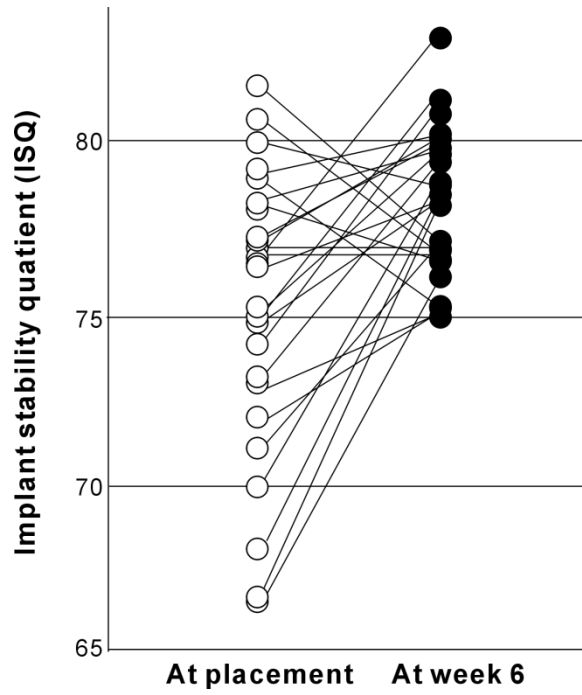


Fig. 3

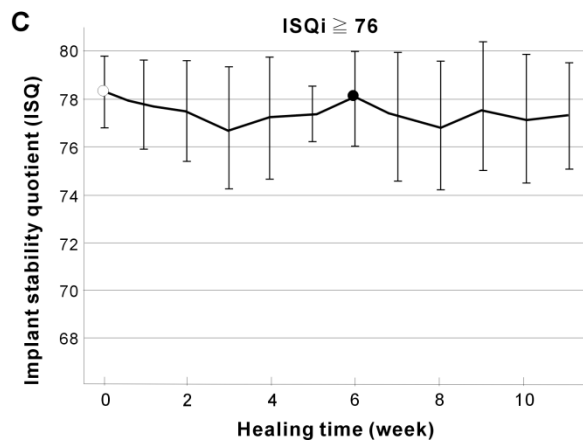
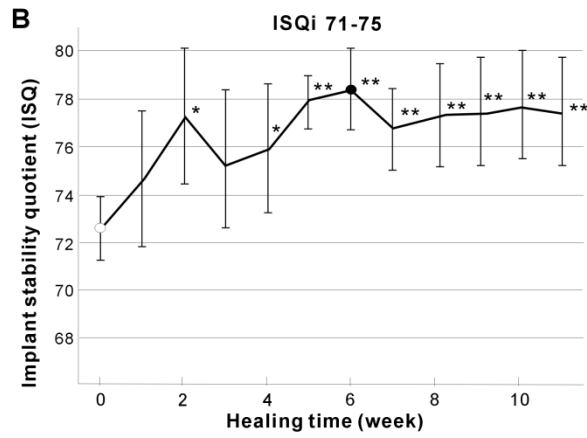
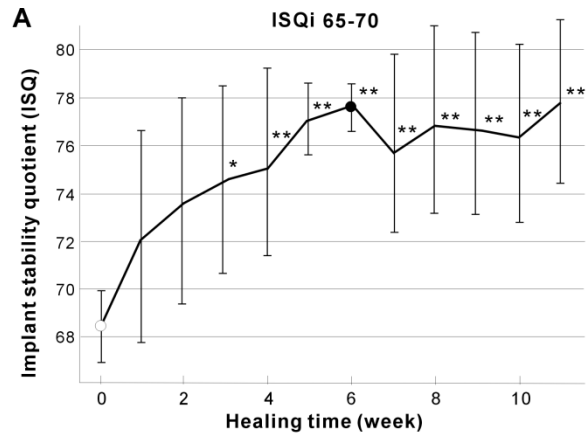


Fig.4

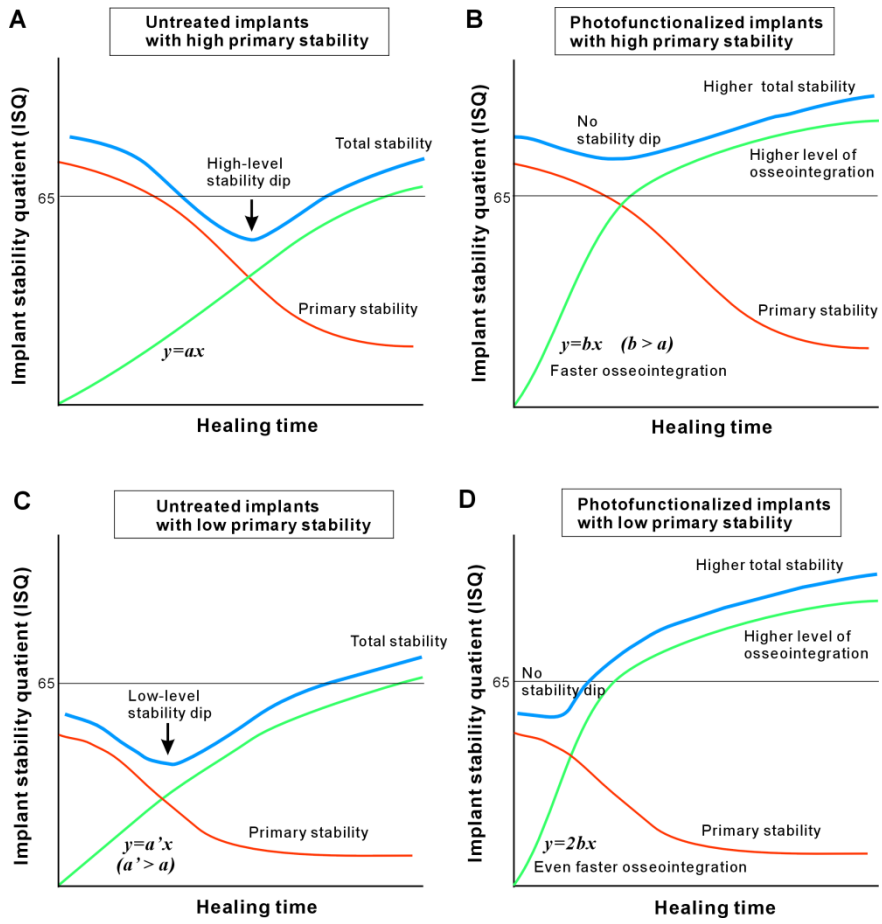


Fig.5

Table 1. Patient and implant data.

Patients			Implants								
Number	Age	Age range	Total number	Diameter	Length			Bone type			
					10 mm	11.5 mm	13 mm	16 mm	Type 1	Type 2	Type 3
7	59.0±5.8	53—66	33	4.3 mm 33 (100%)	2 (6.1%)	5 (15.2%)	23 (69.7%)	3 (9.1%)	8 (24.2%)	19 (57.6%)	6 (18.2%)

Table 2. Implant stability quotient (ISQ) change and osseointegration speed index (OSI) in photofunctionalized implants.

Primary stability range	ISQ			Osseointegration speed index (OSI)
	At placement	At week 6	Change	
ISQi 65–70	68.4 ± 1.5	77.5 ± 1.4	9.5 ± 1.3**	6.3 ± 0.9
ISQi 71–75	73.0 ± 1.5	78.1 ± 2.3	4.6 ± 1.8**	3.1 ± 1.2
ISQi ≥ 76	78.5 ± 1.6	78.1 ± 2.1	−0.3 ± 2.1 ^{NS}	NA

Statistically significant change between two time points, **p<0.01

NS, not significant

NA, not applicable

ISQi: initial ISQ at implant placement

OSI: ISQ increase per month

Table 3. Implant stability quotient (ISQ) in different bone types

Bone type	ISQ	
	At placement	At week 6
Type 1	78.6 ± 2.0	77.0 ± 0.0
Type 2	74.1 ± 4.5	78.2 ± 1.6
Type 3	74.0 ± 2.5	78.2 ± 3.2

Statistically significant difference among the three groups, *p<0.05

NS, not significant

Table 4. Implant stability quotient (ISQ) in groups of different implant length

Implant length	ISQ	
	At placement	At week 6
≤ 11.5 mm	73.6 ± 3.6	77.5 ± 3.8
≥ 13 mm	75.6 ± 4.2	78.1 ± 1.6

] NS

] NS

NS, not significant between the two groups

Table 5. Implant stability quotient (ISQ) change and calculated osseointegration speed index (OSI) in the literature and the present study.

Implant surface	Conditions	ISQ		Healing time (month)	OSI (ISQ increase/month)
		Initial (at placement)	Secondary ^{#3}		
TiUnite ⁴¹⁾ (oxidized)	Immediate/early loading maxilla	60.1 ± 3.6	62.8 ± 1.6	4	0.68
TiUnite ⁴²⁾	Immediate/early loading maxilla	63.3 ± 6.1	64.3 ± 5.3	3	0.33
TiUnite ¹⁹⁾ #1	Includes GBR and extraction socket	68.0	63.0	3	-1.67
TiUnite ⁴³⁾	Anterior maxilla	58.5 ± 4.7	60.9 ± 4.3	6	0.4
	Grafted anterior maxilla	61.5 ± 9.0	60.2 ± 6.9	6	-0.2
TiUnite ⁴⁴⁾	Grafted anterior maxilla	61.9 ± 6.6	63.5 ± 5.7	6	0.26
SLA ²⁶⁾ #2 (sandblasted, acid-etched)	ISQi 65–69			3	-1.8
	ISQi ≥ 70			3	-3.0
SLA ⁴⁵⁾	Anterior maxilla	69.4 ± 9.3	73.4 ± 6.6	3.4	1.17
	Posterior maxilla	69.9 ± 8.5	74.4 ± 6.9	4	1.12
SLA ¹⁸⁾	Type 1 bone	62.8 ± 7.2	60.7 ± 3.6	3	-0.7
SLA ³⁴⁾ #1	Mandible	60.0	62.7	2.5	1.1
SLA ³⁶⁾	Mandible	65.5 ± 5.5	62.8 ± 5.4	1.5	-1.8
SLActive ³⁶⁾ (sandblasted, acid-etched, chemically modified)	Mandible	64.2 ± 5.0	64.1 ± 3.5	1.5	-0.06
Impladent ³⁷⁾ (sandblasted, acid- & alkali-treated)	ISQi 68–72	70.2 ± 1.5	71.5 ± 1.3	2.5	0.52
	ISQi ≥ 72	76.7 ± 3.1	74.8 ± 1.3	2.5	-0.76
SPI ³⁵⁾ (sandblasted, acid-etched)	Type 3 bone	73.6 ± 5.8	74.8 ± 5.4	2	0.6
	Type 4 bone	68.9 ± 4.3	69.9 ± 4.3	2	0.51
TiOblast ⁴⁶⁾ (sandblasted)	Maxilla	62.3 ± 5.1	63.9 ± 5.5	6	0.27
	Grafted maxilla	60.7 ± 6.1	61.4 ± 5.2	6	0.12
Photofunctionalized surface (TiUnite, oxidized)	Immediate loading, maxilla				
	ISQi 65–70	68.4 ± 1.5	77.5 ± 1.4	1.5	6.3
	ISQi 71–75	73.0 ± 1.5	78.1 ± 2.3	1.5	3.1

#1 Values were read from the graph.

#2 Data were provided only for ISQ difference between the implant placement and 3-months follow-up.

#3 Some data were obtained at loading, while some at pre-scheduled follow-up time points.

ISQi: Initial ISQ at implant placement