



Implant Stability Change and Osseointegration Speed of Immediately Loaded Photofunctionalized Implants

Senichi Suzuki, DDS, PhD,* Hiroyuki Kobayashi, MD, PhD,† and Takahiro Ogawa, DDS, PhD‡

Photofunctionalization of titanium implants, the 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 therapy.¹⁻⁶ Photofunctionalization of titanium implants increased the bone-implant contact from 55% to 98.2%, approximating an ideal level of 100%, in an animal model.⁵ Consequently, the strength of bone-implant integration increases more than 3 times at the early stage of healing.⁵ 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.

Objectives: This study evaluated the degree and rate of implant stability development for photofunctionalized dental implants in humans.

Materials and Methods: Thirty-three implants (7 patients) placed in the maxilla and immediate loaded were evaluated. Photofunctionalization was performed by treating implants with ultraviolet for 15 minutes 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 for various as-received implants after a longer healing time of 2 to 6 months. No stability dip was observed for photofunctionalized implants regardless of the initial ISQ values. The OSI for photofunctionalized implants was 6.3 and 3.1 when their initial ISQ was 65 to 70 and 71 to 75, respectively, whereas the OSI values for as-received implants calculated from literature ranged from -3.0 to 1.17 with an average of -0.10.

Conclusions: Photofunctionalization accelerated and enhanced osseointegration of dental implants, providing novel and practical avenues for further advancement in implant therapy. (Implant Dent 2013;22:481-490)

Key Words: ultraviolet, titanium, superhydrophilic, hydrocarbon, super osseointegration

*Director, Lion Implant Center, Kanagawa, Japan.

†Professor, Department of Hospital Administration, Juntendo University School of Medicine, Tokyo, Japan.

‡Professor, The Weintraub Center for Reconstructive Biotechnology, Division of Advanced Prosthodontics, University of California, Los Angeles, School of Dentistry, Los Angeles, CA.

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, University of California, Los Angeles, School of Dentistry, 10833 Le Conte Avenue (B3-081 CHS), Box 951668, Los Angeles, CA 90095-1668, Phone: (310) 825-0727, Fax: (310) 825-6345, E-mail: togawa@dentistry.ucla.edu.

Another study examined the effect of a periimplant gap in the cortical bone.⁸ The presence of a periimplant 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 microcomputed tomography analysis revealed that the effect can

be explained by an enhanced osteomorphogenesis around photofunctionalized implants.⁸ 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 3 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, this 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 sides.^{18–24} 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} Periimplant 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, respectively.^{31–33} 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 2 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,

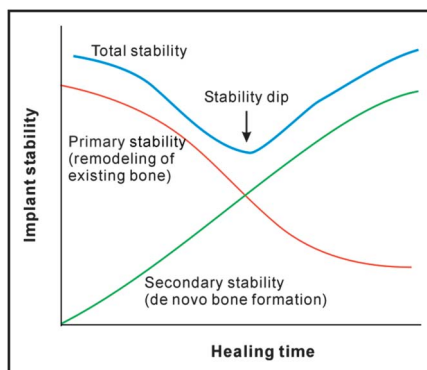


Fig. 1. A suggested mechanism of the occurrence of stability dip in dental implants. The total stability, as determined by the addition of primary stability and secondary stability, normally shows a merging gap, which is called the stability dip. The stability dip is considered unavoidable in current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

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 perspective 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, 7 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 7 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 6 implants were placed per edentulous maxilla. The implant neck was positioned at bone level. Multiunit straight abutments or 17-degree or 30-degree 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 minutes using a photo device (TeraBeam Affinity; Ushio, Inc., Tokyo, Japan) at the chair side immediately before implantation (Fig. 2, A). The photofunctionalization-induced change in surface property from hydrophobic to superhydrophilic (defined as a contact angle of water less than 5 degrees) was confirmed before patient visits by examining several implants for their wettability to double-distilled water (Fig. 2, B).

TABLE 1. Patient and Implant Data. All 33 Photofunctionalized Implants were Placed in the Maxilla and Immediately Loaded. The Distribution of Implant Length and Bone Type is Shown

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

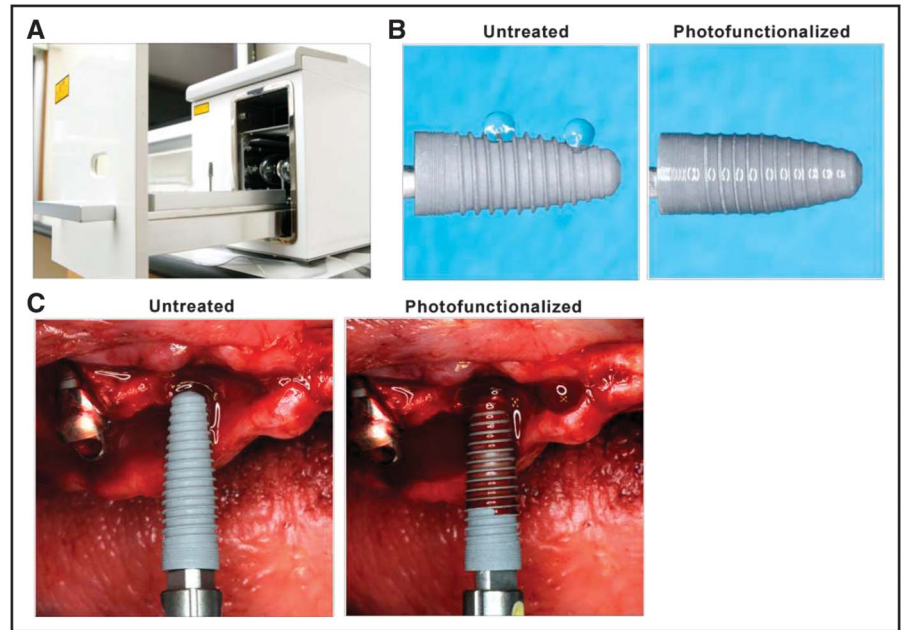


Fig. 2. Photofunctionalization of dental implants and its visualized effects on implant surface property. **A**, A photo device (TeraBeam; Affiny, Ushio, Inc.) used for photofunctionalization. Dental implants were treated for 15 minutes immediately before implantation. **B**, Implants, which were hydrophobic 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 (as-received) 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.

These tested implants were from a separate group of the same type of implants and not used for the patients. Furthermore, 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 Figure 2, C. Bone quality was categorized as type 1, 2, 3, or 4 during the surgery following the criteria proposed by Lekholm and Zarb.⁴⁰

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.

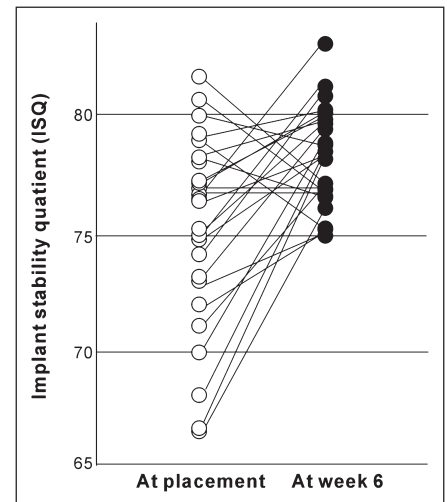


Fig. 3. The ISQ values at implant placement and week 6 of healing plotted for photofunctionalized implants. Note that all implants with an initial ISQ that was 75 or lower showed an increase at week 6, and consequently, the ISQ values at week 6 were all 75 or higher.

Implant Stability Measurement and Osseointegration Speed Index

Implant stability was evaluated by measuring the ISQ at implant

placement (ISQi) and during the healing period with a 1-week interval up to 11 weeks using Osstell ISQ (Osstell AB, Gothenburg, Sweden).

Furthermore, the rate of establishing implant stability was evaluated by the osseointegration speed index (OSI) defined as an ISQ increase per month, that is, $([ISQ \text{ at week 6}] - [ISQi])/1.5$.

Statistical Analysis

The effect of healing time on ISQ values was evaluated by ANOVA; $P < 0.05$ indicated statistical significance. When the effect was significant, further *post hoc* analysis of Bonferroni was performed to compare the ISQi with the ISQ at each of the subsequent time points. The ISQ values were compared among implants with different lengths using ANOVA. Furthermore, 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, whereas 24.2% and 18.2% implants were placed in the type 1 and type 3 bones, 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, ISQi values and the ISQ values at week 6 were individually plotted (Fig. 3). The ISQi 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, an increase, no change, or a decrease, for implants with ISQi that were 77 or higher. In contrast, all implants with ISQi 75 or lower showed an increase at week 6. There was a clear trend that lower the ISQi, 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 3 groups depending on the range of their ISQi (ISQi 65–70, ISQi 71–75, and ISQi ≥ 76), and the ISQ values

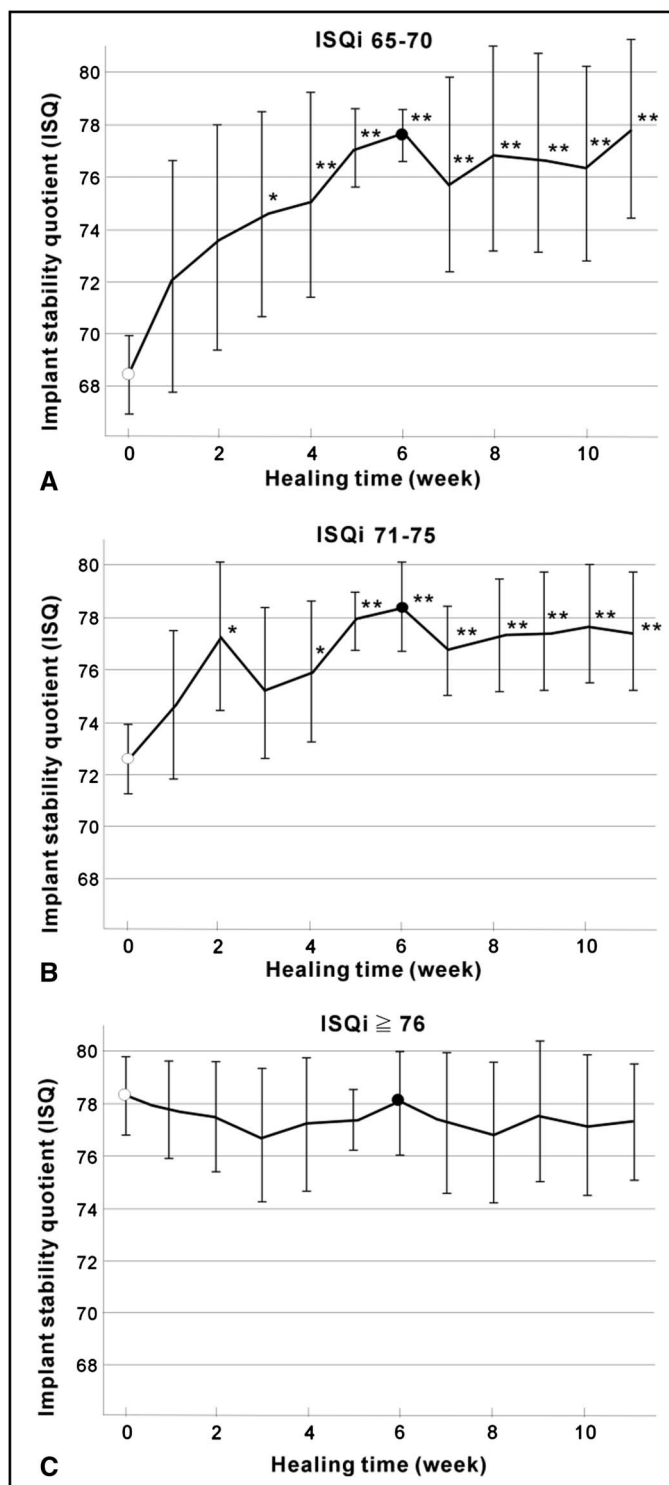


Fig. 4. Change in implant stability for photofunctionalized implants, evaluated by ISQ values at implant placement and subsequent healing time. Line graphs are drawn in 3 different groups depending on the initial ISQ values at implant placement (ISQi). **A**, ISQi 65–70; **B**, ISQi 71–75; and **C**, ISQi ≥ 76 . * $P < 0.05$, ** $P < 0.01$, statistically significant difference from the ISQi.

Table 2. ISQ Change and OSI in Photofunctionalized Implants

Primary Stability Range (ISQi)	ISQ			OSI
	At Placement	At Week 6	Change	
65–70	68.4 ± 1.5	77.5 ± 1.4	9.5 ± 1.3*	6.3 ± 0.9
71–75	73.0 ± 1.5	78.1 ± 2.3	4.6 ± 1.8*	3.1 ± 1.2
≥76	78.5 ± 1.6	78.1 ± 2.1	−0.3 ± 2.1†	NA

Implants were divided into 3 groups depending on the initial ISQ value at implant placement. This table shows mean ISQ values at implant placement and week 6 postimplantation as well as the ISQ change between the 2 time points for each group. Furthermore, the ISQ change divided by healing time of 1.5 months (6 weeks) is shown as the OSI value. The ISQ change was significant and positive when the initial ISQ was 75 and lower.

* $P < 0.01$; statistically significant change between 2 time points.

†Not significant.

NA, not applicable; ISQi, initial ISQ at implant placement; OSI, osseointegration speed index = ISQ increase per month.

starting from the implant placement up to 11th week were plotted in a line graph for each group (Fig. 4). When the ISQi values was 65 to 70, the ISQ line graph showed a rapid and continuous increase up to week 6, followed by the plateau at the increased level (Fig. 4, A). 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 ISQi, supporting the rapid increase and subsequent maintenance of ISQ. No significant ISQ decrease was found compared with the ISQi 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 ISQi 65 to 70 group, when the ISQi was 71 to 75, the subsequent ISQ showed an increasing course of change (Fig. 4, B). Although the rate of ISQ increase appeared less than that in ISQi 65 to 70 group because of the higher baseline, the ISQ values in the later time points appeared to be similar between the ISQi 71 to 75 and ISQi

65 to 70 groups. A significant ISQ increase compared with ISQi 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 2 results, there was no time-dependent ISQ increase, decrease, or dip when the ISQi was 76 or higher (Fig. 4, C). The mean ISQ values remained higher than 76 throughout the healing period without significant fluctuation in this group.

Osseointegration Speed Index

For each of the ISQi 65 to 70, ISQi 71 to 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 to 70 and ISQi 71 to 75 groups but not in ISQi ≥ 76 group. For the significant ISQ changes found, the osseointegration speed index (OSI) defined as the ISQ increase per month was calculated (Table 2). The OSI in ISQi 65 to 70 group was 6.3 ± 0.9 and approximately

2 times higher than that in ISQi 71 to 75 group. The OSI for ISQi 71 to 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 at placement. The interbone 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 2 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 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 that of the as-received untreated 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 2 time points

Table 3. 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

Implants were divided into 3 groups depending on the bone type in which implants were placed. This table shows mean ISQ values at implant placement and week 6 postimplantation for each group. The ISQ values in type 2 and 3 groups increased between the placement and week 6, and there were no significant difference among the 3 groups at week 6.

* $P < 0.05$; statistically significant difference among the three groups.

†Not significant.

Table 4. ISQ in Groups of Different Implant Length

Implant Length, mm	ISQ	
	At Placement*	At Week 6*
≤11.5	73.6 ± 3.6	77.5 ± 3.8
≥13	75.6 ± 4.2	78.1 ± 1.6

Implants were divided into 2 groups depending on the implant length. This table shows mean ISQ values at implant placement and week 6 postimplantation for each group. Both groups showed a significant increase between the placement and week 6 of healing. Therefore, there was no significant difference between the 2 groups at week 6, indicating that photofunctionalization was effective in increasing ISQ values regardless of the implant length.

*Not significant between the 2 groups.

Table 5. ISQ Change and Calculated OSI in the Literature and This Study

Implant Surface	Conditions	ISQ		Healing Time (mo)	OSI (ISQ increase/mo)
		Initial (at Placement)	Secondary*		
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†}	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 (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†}	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 and 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

The ISQ change during healing and calculated OSI are compared between untreated implants in literature and photofunctionalized implants. Note that 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.

*Some data were obtained at loading, whereas some at prescheduled follow-up time points.

†Values were read from the graph.

‡Data were provided only for ISQ difference between the implant placement and 3-month follow-up.

ISQi, initial ISQ at implant placement; OSI, osseointegration speed index = ISQ increase per month.

along with the calculated OSI in the literature.^{18,19,26,34–37,41–46} The OSI values from this study are also listed at the bottom of the table. Because the initial ISQ values were all higher than 65 in this 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 2 time points. The following were the 3 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 this 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 to 70 and the OSI of 3.1 even when the initial ISQ was 71 to 75 obtained in this study should be

considered remarkable. In fact, the calculated OSI for all as-received 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 this 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 this study at week 6 may imply the advantage of photofunctionalization to not only expedite the process but also

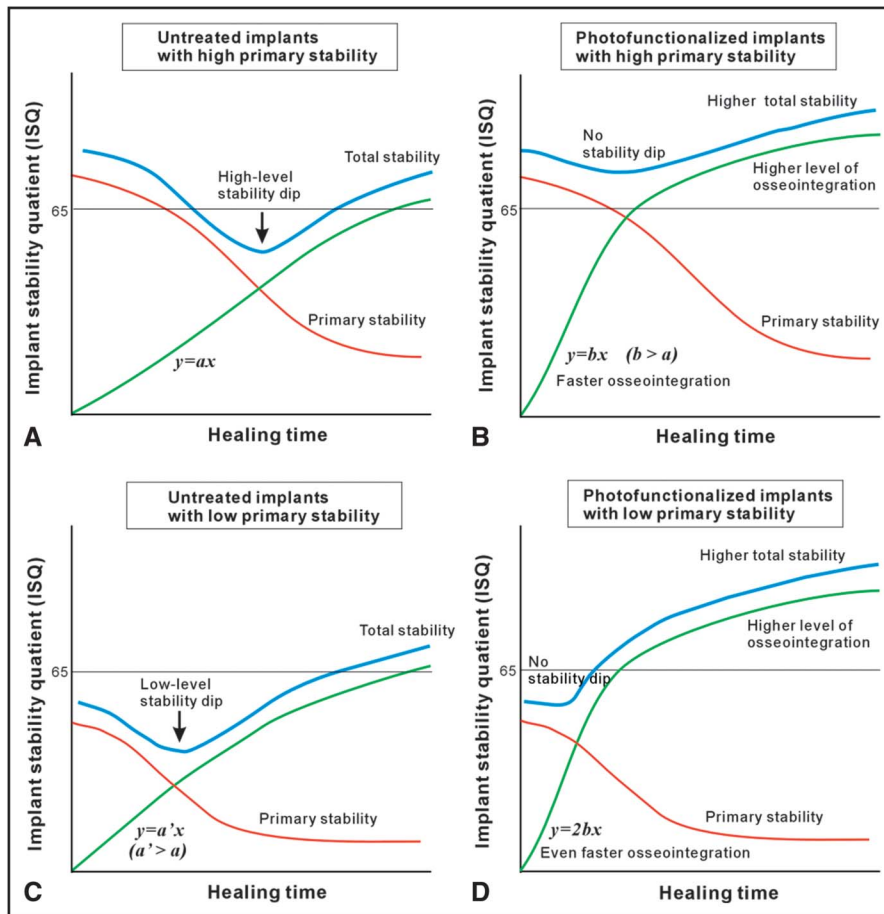


Fig. 5. Proposed mechanisms of appearance and disappearance of stability dip in schematic description. The stability dip is anticipated for as-received untreated implants as commonly understood whether the primary stability is high (**A**) or low (**C**). In contrast, the stability dip is eliminated by the use of photofunctionalization, regardless of the degree of primary stability (**B**, **D**), because of the faster (when the primary stability is high) 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.

achieve a higher level of osseointegration. The results were particularly surprising because of the following 2 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 current 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 periimplant 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.

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 to 9 days after implant placement to support a full-arch fixed bridge in the maxilla.⁴¹ A total of 61 oxidized implants (6 or 8 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 to 16 days after placement.⁴² 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 this study were remarkably greater. Knowing that these studies were carried out under a similar clinical protocol and host conditions to this study and with the implant texture being identical to an oxidized surface used in this study, the current results may genuinely demonstrate the effect of photofunctionalization in enabling a faster and more complete process of osseointegration. As mentioned in 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 this 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 to 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 this study, as shown in Table 2 and Figure 4, C, 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 current results will help explore a new strategy for early or immediate loading protocols. On the basis of the current 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 2 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 this study, an OSI with an initial ISQ of 65 to 70 was, in fact, 2 times greater than an OSI with an initial ISQ of 71 to 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; and (5) the rate of losing primary stability is assumed to be the same with or without photofunctionalization. In Figure 5, A and 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 Figure 5, C than in Figure 5, A, 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. 5, B). 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. 5, D). 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 minutes 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. Finally, the application of photofunctionalization should not be restricted to use in dental implants. Orthopedic implants face many, long-unresolved 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 minutes. 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 ISQ during the early stage of healing up to 3 months along with the rate of ISQ increase per month, defined as the 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 longer 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.

DISCLOSURE

The authors claim to have no financial interest, either directly or

indirectly, in the products or information listed in the article.

REFERENCES

- Ogawa T. UV photofunctionalization of titanium implants. *J Craniofac Tissue Eng*. 2012;2:151–158.
- 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.
- Lee JH, Ogawa T. The biological aging of titanium implants. *Implant Dent*. 2012;21:415–421.
- Ogawa T. Photofunctionalization of TiO₂ for optimal integration of titanium with bone. In: Kamat P, Anpo M, eds. *Benign Photocatalysts. Applications of Titanium Oxide-based Materials*. New York: Springer; 2010:699–713.
- Aita H, Hori N, Takeuchi M, et al. The effect of ultraviolet functionalization of titanium on integration with bone. *Biomaterials*. 2009;30:1015–1025.
- Tsukimura N, Yamada M, Iwasa F, et al. Synergistic effects of UV photofunctionalization and micro-nano hybrid topography on the biological properties of titanium. *Biomaterials*. 2011;32:4358–4368.
- Ueno T, Yamada M, Hori N, et al. Effect of ultraviolet photoactivation of titanium on osseointegration in a rat model. *Int J Oral Maxillofac Implants*. 2010;25:287–294.
- Ueno T, Yamada M, Suzuki T, et al. Enhancement of bone-titanium integration profile with UV-photofunctionalized titanium in a gap healing model. *Biomaterials*. 2010;31:1546–1557.
- Suzuki T, Hori N, Att W, et al. Ultraviolet treatment overcomes time-related degrading bioactivity of titanium. *Tissue Eng Part A*. 2009;15:3679–3688.
- Iwasa F, Tsukimura N, Sugita Y, et al. TiO₂ micro-nano-hybrid surface to alleviate biological aging of UV-photofunctionalized titanium. *Int J Nanomedicine*. 2011;6:1327–1341.
- Iwasa F, Hori N, Ueno T, et al. Enhancement of osteoblast adhesion to UV-photofunctionalized titanium via an electrostatic mechanism. *Biomaterials*. 2010;31:2717–2727.
- Hori N, Ueno T, Minamikawa H, et al. Electrostatic control of protein adsorption on UV-photofunctionalized titanium. *Acta Biomater*. 2010;6:4175–4180.
- Hori N, Att W, Ueno T, et al. Age-dependent degradation of the protein adsorption capacity of titanium. *J Dent Res*. 2009;88:663–667.
- Att W, Hori N, Takeuchi M, et al. Time-dependent degradation of titanium osteoconductivity: An implication of biological aging of implant materials. *Biomaterials*. 2009;30:5352–5363.
- Yamada M, Miyauchi T, Yamamoto A, 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.
- Miyauchi T, Yamada M, Yamamoto A, et al. The enhanced characteristics of osteoblast adhesion to photofunctionalized nanoscale TiO₂ layers on biomaterials surfaces. *Biomaterials*. 2010;31:3827–3839.
- Ueno T, Tsukimura N, Yamada M, et al. Enhanced bone-integration capability of alkali- and heat-treated nanopolymeric titanium in micro-to-nanoscale hierarchy. *Biomaterials*. 2011;32:7297–7308.
- Bischof M, Nedir R, Szmukler-Moncler S, et al. Implant stability measurement of delayed and immediately loaded implants during healing. *Clin Oral Implants Res*. 2004;15:529–539.
- Glauser R, Sennerby L, Meredith N, 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.
- 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.
- Makary C, Rebaudi A, Sammartino G, et al. 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.
- Javed F, Almas K, Crespi R, et al. Implant surface morphology and primary stability: Is there a connection? *Implant Dent*. 2011;20:40–46.
- Lee HJ, Aparecida de Mattias Sartori I, Alcántara PR, 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.
- Chan HL, El-Kholy K, Fu JH, et al. Implant primary stability determined by resonance frequency analysis in surgically created defects: A pilot cadaver study. *Implant Dent*. 2010;19:509–519.
- Gupta RK, Padmanabhan TV. An evaluation of the resonance frequency analysis device: Examiner reliability and repeatability of readings [published online ahead of print October 4, 2011]. *J Oral Implantol*. doi:10.1563/AALD-JOI-D-11-00099.
- Nedir R, Bischof M, Szmukler-Moncler S, et al. Predicting osseointegration by means of implant primary stability. *Clin Oral Implants Res*. 2004;15:520–528.
- 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.
- Huang HL, Tsai MT, Su KC, et al. Relation between initial implant stability quotient and bone-implant contact percentage: An in vitro model study [published online ahead of print August 23, 2012]. *Oral Surg Oral Med Oral Pathol Oral Radiol*. doi:10.1016/j.oooo.2012.01.037.
- Park KJ, Kwon JY, Kim SK, et al. The relationship between implant stability quotient values and implant insertion variables: A clinical study. *J Oral Rehabil*. 2012;39:151–159.
- Sennerby L, Meredith N. Implant stability measurements using resonance frequency analysis: Biological and biomechanical aspects and clinical implications. *Periodontol*. 2008;47:51–66.
- 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.
- 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.
- Atsumi M, Park SH, Wang HL. Methods used to assess implant stability: Current status. *Int J Oral Maxillofac Implants*. 2007;22:743–754.
- Barewal RM, Oates TW, Meredith N, et al. 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.
- Sengcimen M, Gülses A, Ozen J, 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.
- Oates TW, Valderrama P, Bischof M, et al. Enhanced implant stability with a chemically modified SLA surface: A randomized pilot study. *Int J Oral Maxillofac Implants*. 2007;22:755–760.
- Simunek A, Kopecka D, Brazda T, et al. Development of implant stability during early healing of immediately loaded implants. *Int J Oral Maxillofac Implants*. 2012;27:619–627.
- Maló P, de Araújo Nobre M, Lopes A, et al. “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–e150.
- Malo P, de Araújo Nobre M, Lopes A, et al. 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: Brånemark PI, Albrektsson T, eds. *Tissue Integrated Prostheses: Osseointegration in Clinical Dentistry*. Chicago, IL: Quintessence; 1985:199–209.

41. Olsson M, Urde G, Andersen JB, et al. 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, Bäckström 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. Sjöström M, Lundgren S, Nilson H, et al. 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, et al. 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, et al. Conventional SLA and chemically modified SLA implants in patients with poorly controlled type 2 diabetes mellitus—A randomized controlled trial. *Clin Oral Implants Res.* 2013;24:13–19.

48. Att W, Ogawa T. Biological aging of implant surfaces and its restoration with ultraviolet light treatment: A novel and breakthrough understanding of osseointegration. *Int J Oral Maxillofac Implants.* 2012;27:753–761.

49. Koppenburg P, Abe K, Abe K, 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, et al. The effect of UV-photofunctionalization on the time-related bioactivity of titanium and chromium-cobalt alloys. *Biomaterials.* 2009;30:4268–4276.