Enhanced Implant Stability with a Chemically Modified SLA Surface: A Randomized Pilot Study

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Abstract

Chemical modification to a sand-blasted, acid-etched (SLA) implant surface has been shown to enhance the rate of osseointegration. The goal of the present study was to examine changes in stability for implants with the chemically modified surface, and to compare their outcome to control implants. A randomized controlled trial was conducted with 31 patients, each patient receiving two implants having the same physical properties, but with one having the standard SLA surface (control) and one with the modified surface (test). Resonance frequency analysis was assessed weekly over the first 6 weeks following implant placement. All implants proved clinically successful allowing for restoration. With most implants placed in the mandible (50 of 62), the shift in implant stability from one of decreasing stability to one of increasing stability ($p<0.0001$), occurred after 2 weeks for the test implants and after 4 weeks for the control implants. The findings from this pilot study provides clinical support for the potential for chemical modification of the SLA surface to alter biologic events during the osseointegration process, and demonstrated levels of short-term clinical success similar to implants with an SLA surface.

Key Words: Implant stability, clinical trial, resonance frequency analysis, implant surface chemistry

Introduction

Osseointegration of titanium implant surfaces is dependent upon both physical and chemical properties.[1] The influences of physical properties such as surface topography and roughness on osseointegration have translated to shorter healing times from implant placement to restoration.[2] The biologic basis underlying these clinical improvements continue to be explored.[3,4]

Surface chemistry has the potential to alter ionic interactions, protein adsorption and cellular activity to the implant surface.[5,6] These modifications may subsequently influence conformational changes in the structures and interactive natures of adsorbed proteins and cells. Furthermore, it must be considered within the complexities of an in vivo environment containing multiple protein and cellular interactions, that these alterations may differentially regulate biologic events within that environment. For example, the serum proteins albumin and fibrinogen showed less organized secondary structure upon adsorption onto a hydrophobic surface than a hydrophilic one.[7] Therefore, modifications to the implant surface chemistry may lead to alterations in the structure of adsorbed proteins, and have cascading effects, ultimately evident at the clinical level.

Recent in vivo evidence has supported the use of alterations in surface chemistry to modify osseointegration events. Specifically, an investigation utilizing two chemically distinct SLA surfaces, but having the same physical characteristics, was conducted to assess bone-to-implant contact as a measure of osseointegration. The chemically

enhanced SLA surface demonstrated significantly enhanced bone-to-implant contact during the first 4 weeks of bone healing, with 60% more bone than the standard SLA surface after 2 weeks.[8] The chemical modifications for the test SLA surface resulted in increased wettability, that is a hydrophilic surface rather than an hydrophobic one; water contact angles of 0° were seen with the chemically enhanced surface, compared to 139.9° for standard SLA, and the hydrophilicity was maintained after drying. The chemical composition of the surface is also altered, including a 50% reduction in carbon concentration compared with the control implant surface.[9]

The increase in bone-to-implant contact utilizing a chemically-modified SLA surface suggests the potential for enhancement in implant integration with the modified surface to be evident at the clinical level. In order to clinically assess implant integration, resonance frequency analysis (RFA) was used to measure implant stability. This technology has proven capable of characterizing alterations in implant stability during early healing, and sensitive enough to identify differences in longitudinal implant stability based on bone density at the implant recipient site.[10] Early investigations showed that RFA can also be related to the stiffness of an implant and the level of peri-implant bone.[11],[12] The technique has been shown to be more precise than damping capacity assessment for predicting implant stability,[13] and has also been demonstrated to be an accurate method for early assessment of osseointegration.[14]

The objective of the present investigation was to compare dental implant stabilization patterns over time for two SLA surfaces over the first 3 months following implant

placement, and to evaluate the short-term clinical experience of the implants with the modified surface. The study hypothesis was that there was a difference in patterns of implant stabilization between implants with test and control surfaces during the early healing period (6 weeks) following placement.

Materials and Methods

This two-center, randomized, controlled pilot trial was designed to prospectively evaluate implant integration of standard sand-blasted, acid-etched (SLA) implants (Straumann, Basel, Switzerland) relative to implants having the same physical properties, but with a chemically modified surface (SLActive). Clinical evaluation of implant integration over time was performed using resonance frequency analysis (RFA; Osstell, Integration Diagnostics, Savedalen, Sweden) and outcomes based on standard success criteria.[15]

Study population

The study population included thirty-one adult patients who were missing two or more posterior teeth in either the mandible or maxilla. Edentulous areas were required to have at least 4 months of healing following tooth extraction, no previous bone grafting, and indicated for implant-supported, fixed prosthetic single-tooth replacement. Informed consent was obtained from all patients in accord with the ethical policies and procedures for human research at both study centers (The University of Texas Health Science Center

at San Antonio and Clinique Dentaire, Vevey, Lausanne, Switzerland). Inclusion and exclusion criteria were the same as previously described.[2]

Treatment

Sixty–two implants having either a 4.1 mm diameter or 4.8 mm diameter and 8 or 10 mm in length were placed in 31 patients, Two implants were placed per patient, with one implant having a standard sandblasted and acid-etched surface (SLA, control) and the other implant having a chemically-modified SLA surface (SLActive, test). The dimensions of the test and control implants were matched on a per patient basis, with implants placed in the same arch. Test and control sites were determined using a blinded randomization scheme established prior to the start of the study and applied after implant osteotomies for both sites were prepared. Implants were placed in a non-submerged manner, with all implant procedures performed according to the manufacturer's guidelines.

Longitudinal RFA measurements and clinical success criteria were recorded at 0, 1, 2, 3, 4, 5, and 6 weeks following surgical implant placement. Each visit entailed removal of the healing cap or restorative abutment and standardized placement of the transducer perpendicular to the arch. The Implant Stability Quotient (ISQ) recorded in triplicate, measures clinical stiffness with a range from 1 to 100, and as implant stability increases ISQ values also increases. ISQ measurements show a high degree of repeatability (less than 1% variation for individual implants).[11] The transducers were calibrated using an implant fixed in a plaster block at the start and completion of each patient visit. In

addition, each implant was evaluated at all visits for mobility, and signs of infection, pain or suppuration.

The primary outcome value was the change in implant stability (ISQ,) from the mean baseline reading for each implant. Secondary outcome measures included the nature and frequency of adverse events or complications defined as persistent or irreversible pain, inflammation or parasthesia, peri-implant infection, peri-implant radiolucency or lateral or rotational implant mobility.

Statistical Analysis

The primary response variable, ISQ (with values between 0 and 100), is continuous and identified as normally distributed (Kolmogorov Smirnov test). To decrease the patient-specific variability and to adjust for patient specific situations, the response variable was transformed to normalize differences relative to baseline readings, as "observation minus baseline" (ISQ difference).

Two main fixed factors TREATMENT (test vs. control) and TIME (baseline through 6 weeks) with a possible interaction and the fixed factor ARCH and the random factor PATIENT (each patient received one test and one control implant) were evaluated. The linear mixed model was used to evaluate the significance of these overall effects. However, as has been previously identified ISQ values will first decrease and after some time period start to increase, the main statistical problem to be tested in this study was not amenable to a linear mixed model analysis. [10]

The analytic basis for this study was to determine if there is a difference in the time-dependent stability patterns for each of the implant types. Therefore, analysis was performed using a generalized linear model, the Chow test with secondary outcomes characterized by descriptive analyses.[16,17,18]

RESULTS

The study population consisted of 22 female patients (71%) and 9 male patients, ranging in age from 30 to 83 with a mean age of 61.1 $\pm$ 13 years. Of the 62 study implants placed in the 31 patients, fifty (in 25 patients) were placed in the mandible and 12 in the maxillary posterior sextants. Bone type scoring was equivalent at both sites in 25 of the patients, with 49 of the 62 implants placed in bone types 2 or 3, 10 of 62 implants placed in type 1 bone, and 3 implants (2 in test, 1 in control) placed in type 4 bone. Of the 31 patients enrolled in this study, 2 patients were excluded from RFA analysis due to protocol violations. In addition, two control implants in 2 patients were excluded from RFA analysis as 3 or more readings were not taken due to rotational movement. However, all 62 implants were included in secondary outcomes assessments.

Implant Stability

Overall, stability at the time of placement was not significantly different for the control implants (mean ISQ=63.7$\pm$6.9) than the test implants (mean ISQ=61.7$\pm$7.6). Both

implant types showed decreases in mean stability levels through the 2-week time point, and had similar levels of stability after 6 weeks (Table 1).

Initial evaluation of the effects of time, implant surface (test/control), and arch (maxilla/mandible) on ISQ levels showed that there was no significant interaction between these factors, allowing for independent assessment. Overall, implant surface (test vs. control) was not significant ($p=0.073$), while time ($p<0.017$) and arch (mandible vs. maxilla; $p<0.001$) were found to be significant factors in implant stability. Therefore changes in implant stability (primary outcome) were considered independently for each arch relative to time (Table 2). In addition, the study center was found to have no significant effect.

In the mandible, relative to baseline levels, control implants had decreased levels of stability throughout the 6-week evaluation period, whereas the test implants showed stability levels decreased below baseline levels through the first 5 weeks of evaluation. In the maxilla, both implant types had stability levels greater than baseline after 4 weeks (Table 2). Evaluation of the stabilization patterns over time for the mandibular implants showed that there was a significant ($p<0.0001$) change in the pattern of stability for the test implants at the 2-week time point from one of decreasing stability to one of increasing stability (Table 3). This is in contrast to the control implants, in which a similar ($p<0.0001$) change in the pattern of stability was identified at the 4-week time point (Figure 1). In the maxilla, there was a significant change in the pattern of stability

noted for the test implants at week 3, but no significant change in stabilization pattern for the control implants (Table 3).

Implant success rate/AEs and Complications

All 62 study implants were successfully integrated at the 6-week time point and restored. There were 20 adverse events reported related to the study. The most common adverse event was rotational movement of an implant during RFA assessments, identified for 7 of the 62 implants, with all occurrences in mandibular implants. The remainder of the adverse events were inconsequential to patient treatment or study results, for example post-operative discomfort, ulcerations, or loosened healing caps. Although implants were lost to analysis due to rotational mobility, none of the adverse events altered the clinical therapy for the implants.

Interestingly, 5 of the implants with rotational movement were found in the control group with 2 in the test group, with all occurrences between weeks 1 and 4, and most (4 of 7) occurring at week 3. While it is likely that the rotational movement and subsequent alterations in implant stability are reflective of overall differences between implant types, secondary analysis of the data was done excluding these implants. In contrast to the overall findings, significant effects were identified for arch ($p<0.001$) and for implant type ($p<0.001$), and the effects of time were notsignificance ($p=0.062$). Again separating the mandibular and maxillary implants for analysis, implant type was a significant factor in both the maxilla ($p<0.001$) and in the mandible ($p<0.01$). Time was found to be a significant factor in the mandible ($p<0.05$), but not in the maxilla ($p=0.329$).

Evaluation of the changes in implant stability, relative to initial stability and excluding the implants with rotational movement, showed that the test implants had a significant change in the pattern of stability at the 2-week time point in both the mandible ($p<0.01$) and in the maxilla ($p<0.001$). This is in contrast to the control implants, in which there was no significant change in the pattern of stability identified over the 6-week healing period (data not shown).

DISCUSSION

The objective of this investigation was to compare dental implant stabilization patterns over time for two SLA surfaces over the first 3 months following implant placement, and to evaluate the short-term clinical experience of the implants with the modified surface. The most interesting finding of this study was the earlier change in the pattern of stability with the modified SLA surface. That is, with the chemical modifications, the stability of the implants began to increase after the 2-week time point. While this was evident only for implants placed in the mandible, this finding is in contrast to the findings for the control implants in this investigation in which this transition from decreasing stability to increasing stability was evident after 4 weeks. This transition after the 2-week time point is also earlier than that reported in a previous investigation using the control surface implants, in which the transition was evident after 3 weeks.[10] Futhermore, the clinical success of the modified implant was similar to the control implant (SLA), with all implants resulting in clinical restoration and loading.

The changes in implant stabilization, when followed over time, are thought to be reflective of the biologic events associated with the bone-implant interface, i.e., increasing stability is associated with bone formation. The identification of a transition point from decreasing implant stability to increasing implant stability is suggestive of a change in the overall bone metabolism associated with the implant surface from one of predominantly resorptive to one predominantly formative in nature. These findings suggest an enhanced healing process associated with the modified implant surface, consistent with findings using an animal model.[8]

While the identified benefits of the modified implant surface demonstrate a shift in healing from 4 weeks to 2 weeks, these results must be considered within the broader scope of implant stabilization during the healing process. The difference in stability levels (implant stability quotient, ISQ) on a 100-point scale was approximately 2 points between the test and control surface. The clinical significance of the difference in stability between the two implant surfaces remains to be determined.

Overall, it is noteworthy that all implants were successful with no clinically significant effects of the rotational movement preventing implant restoration. It is interesting that of the 7 documented events of rotational movement, 5 of these events were evident in the control implants. This finding is consistent with an enhanced healing process for the modified surface implants.

The working hypothesis, therefore, was that the chemically-modified SLA implants heal more quickly than standard SLA implants. The challenge was to find an appropriate statistical model for evaluation. From repeated measures, the mixed model analysis appeared to be modeling an overall treatment effect of a structural change in the data over time. The Chow test is designed to be able to detect this special treatment effect (i.e. a decrease and subsequent increase in ISQ), so was therefore chosen as the most appropriate statistical model. Our findings from this analysis do identify differences in implant stability and healing based on placement of the implant in the maxilla or mandible. This finding is suggestive of differences in bone quality between arches affecting implant stability. Similar findings of interarch variations in implant stability, with greater changes in stability in the mandible than the maxilla, have been reported previously.[19] However, this is in contrast to previous investigations in which implants placed in less dense bone types tended to have greater changes in stability.[10,12,20,21] The contrasting findings between studies are suggestive of unique aspects of bone quality that impact on bone metabolism beyond clinical assessments of bone density or implant stability and remain to be elucidated.

In conclusion, this study supports the potential for chemical modifications in a roughened implant surface to alter biologic events during the osseointegration process. These alterations are suggestive of an enhanced healing process that may lead to alterations in clinical loading protocols for dental implant therapy.

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Table 1: Mean RFA values (ISQ) overall and by arch

			Overall		Maxilla		Mandible	
Visit		N	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std. Deviation
Baseline	control	27	63.6	6.6	55.4	3.8	65.5	5.5
	test	29	61.8	7.3	52.4	7.4	64.2	5.0
1 week	control	26	61.8	6.3	54.0	2.6	64.2	5.0
	test	28	60.7	6.7	51.9	5.2	63.1	4.9
2 weeks	control	27	61.2	7.6	55.1	4.5	63.0	7.4
	test	29	59.4	6.3	52.1	6.9	61.3	4.6
3 weeks	control	27	60.5	7.5	54.2	2.6	62.2	7.6
	test	28	60.1	6.8	51.7	5.4	62.4	5.2
4 weeks	control	27	60.2	7.6	56.3	3.0	61.3	8.1
	test	28	59.9	5.9	53.3	5.0	61.7	4.9
5 weeks	control	27	61.0	6.4	55.8	2.5	62.6	6.4
	test	29	61.2	6.6	53.3	4.3	63.3	5.5
6 weeks	control	24	61.3	5.5	57.0	2.8	62.8	5.4
	test	27	61.8	5.9	53.5	5.3	64.1	3.5

Table 2: Normalized mean RFA values (Difference from baseline)

		Maxilla			Mandible			Overall	
Visit		N	Mean	Std. Deviation	N	Mean	Std. Deviation	Mean	Std. Deviation
Baseline	control	6	0.0	0.0	21	0.0	0.0	.	.
	test	6	0.0	0.0	23	0.0	0.0	.	.
1 week	control	6	-1.4	3.5	20	-1.0	2.4	-0.7	2.4
	test	6	-0.5	2.8	22	-1.1	4.1	-1.1	4
2 weeks	control	6	-0.3	1.0	21	-2.5	3.8	-2.4	3.8
	test	6	-0.3	1.3	23	-2.9	4.8	-3.1	4.6
3 weeks	control	6	-1.1	1.6	21	-3.2	5.2	-3.1	5.1
	test	6	-0.7	4.2	22	-1.8	4.8	-2.2	4.8
4 weeks	control	6	0.8	1.9	21	-4.2	7.3	-4.2	7
	test	6	0.9	4.6	22	-2.5	5.2	-3.4	6
5 weeks	control	6	0.3	2.0	21	-2.9	4.6	-2.9	4.8
	test	6	0.8	5.2	23	-0.9	7.0	-0.9	6.9
6 weeks	control	6	1.5	1.1	18	-2.3	4.2	-2.4	4.3
	test	6	1.0	6.8	21	0.4	4.8	-0.1	5.5

Table 3: Changes in the patterns of stability (Chow test)

		Breakpoint	Significance
Test	**Maxilla**	**3 weeks**	**0.00078**
	Mandible	**2 weeks**	**0.00001**
Control	**Maxilla**	**3 weeks**	**0.64277 (n.s.)**
	Mandible	**4 weeks**	**0.00000**

Figure 1

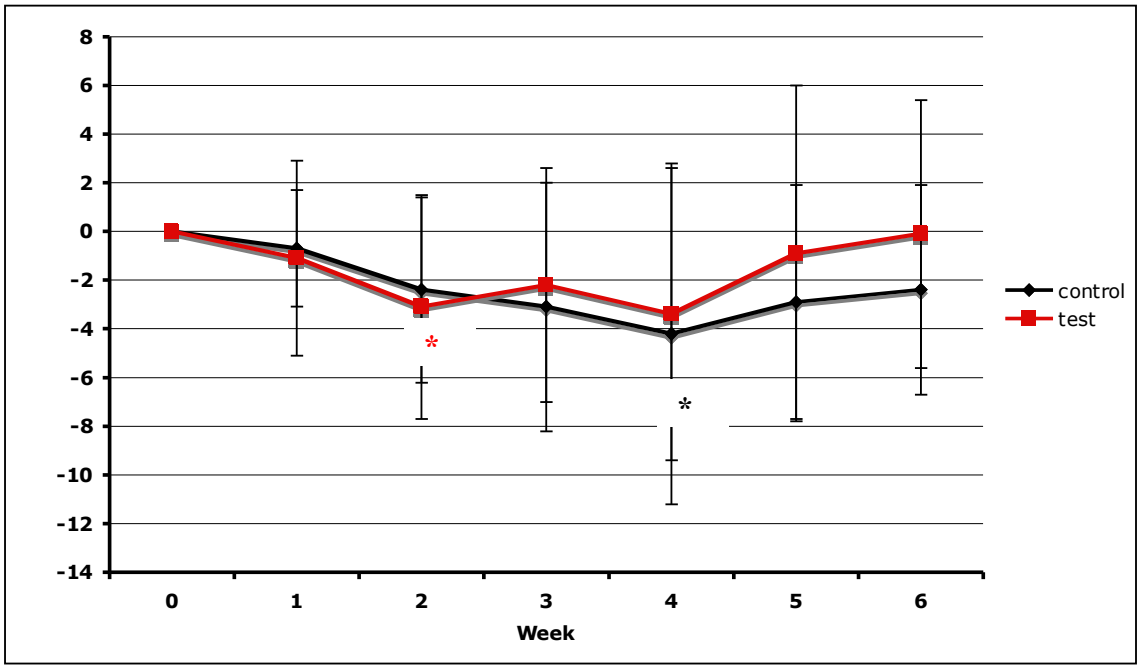

Figure 1. Mean differences in ISQ values from baseline for implants placed in the mandible, with (*) indicating significant ($p<0.00001$) breakpoints.