Original Article

The stability of tetracalcium phosphate/titanium implants: A short-term follow-up study

Pawhat Nimmawitt a, Paknisa Sittikornpaiboona, Svas Jaemsuwan a, Sirida Arunjaroensuk a, Jen-Chyan Wang b, Chun-Cheng Hung b, Boosana Kaboosaya a, Atiphan Pimkhaokham a*

a Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand
b Department of Prosthodontics, Kaohsiung Medical University Hospital, School of Dentistry, College of Dental Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

Received 31 January 2022; Final revision received 3 February 2022
Available online 23 February 2022

KEYWORDS
Tetracalcium phosphate; Surface modification; Resonance frequency analysis; Implant stability

Background/purpose: Bioceramic tetracalcium phosphate (TTCP) is used as a surface modifier on the implant surface and the clinical studies on this surface modification are still limited. The objective of this clinical study was to investigate short-term implant stability of titanium implant surfaces being modified through sandblasting and acid etching (SLA), followed by TTCP sintered bioceramic anchoring.

Materials and methods: A total of 20 patients who had single tooth space were included in this study. Surface modification by SLA plus with TTCP on Ti implants with a diameter of 4.0 mm and lengths of 10 and 11.5 mm were placed. Implant stability quotient (ISQ) value was measured immediately (ISQ0) and one month (ISQ1), two months (ISQ2), three months (ISQ3), and four months (ISQ4) after implantation. Subgroup analysis was defined to location (maxilla, mandible) and bone density (soft or hard bone). Statistical analysis was performed using Friedman test and Mann–Whitney U test.

Results: The mean ISQ values with standard deviation at the different time points of ISQ0 to ISQ4 were 60.03 ± 14.12, 53.48 ± 15.24, 58.91 ± 14.43, 63.14 ± 12.22, and 63.50 ± 13.61, respectively. The results showed significant differences between the ISQ1 and ISQ3 groups and between the ISQ1 and ISQ4 groups. On the other hand, there was no statistical differences between the maxilla and mandible as well as between soft and hard bone types in all implant groups.

* Corresponding author. Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Chulalongkorn University, 34 Henri Dunant Road Wangmai, Patumwan, Bangkok, 10330, Thailand.

E-mail address: atiphan.p@chula.ac.th (A. Pimkhaokham).

https://doi.org/10.1016/j.jds.2022.02.003
1991-7902/© 2022 Association for Dental Sciences of the Republic of China. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Conclusion: TTCP/titanium implant showed favorable stability in short-term ISQ values over 4 months. The locations and bone types demonstrated no effect on implant stability.

Introduction

Dental implants are constantly evolving in order to provide better effective treatment outcomes. The chemical composition and surface treatment of implant materials can affect early bone healing after implant placement due to implant-associated protein adsorption and conformational changes. With the well-known concept of sandblasting and acid etching (SLA) surface treatment, the titanium machine surface is modified by coarse grit-blasting using 0.25–0.5 mm corundum grit at air pressure of five bars, followed by acid-etching. Recently, the newly developed titanium implant surface treated with SLA and anchored with sintering tetracalcium phosphate (TTCP) can promote osseointegration by forming a mechanical granular interlocking film. About 70% of the minerals in human bone are calcium phosphates (CaPs), therefore, the CaPs on the implant surface can conduct and promote bone healing, thereby causing the biointegration of the implant. Ca₄(PO₄)₂O is the chemical formula for TTCP with a high atomic Ca/P ratio of 2.0 in a calcium phosphate compound. When TTCP is dissolved in an aqueous solution, a large amount of calcium cations (Ca²⁺) and phosphate anions (PO₄³⁻) are spontaneously generated. Furthermore, in addition to ion release, the residual phase of TTCP is generally converted to hydroxyapatite (HA) with the molecular formula Ca₁₀(PO₄)₆(OH)₂, and appropriately affects early bone formation and healing. HA is a naturally occurring calcium phosphate mineral at neutral pH with good biocompatibility and an excellent candidate for bone repair with a Ca/P atomic ratio of 1.67. The SLA plus with TTCPs on implant surfaces can accelerate and mineralize progenitor Ca/P atomic ratio of 1.67. The SLA plus with TTCPs on implant surfaces treated with SLA and anchored with sintering tetracalcium phosphate (TTCP) can promote osseointegration by forming a mechanical granular interlocking film. About 70% of the minerals in human bone are calcium phosphates (CaPs), therefore, the CaPs on the implant surface can conduct and promote bone healing, thereby causing the biointegration of the implant.

Dental implants are constantly evolving in order to provide better effective treatment outcomes. The chemical composition and surface treatment of implant materials can affect early bone healing after implant placement due to implant-associated protein adsorption and conformational changes. With the well-known concept of sandblasting and acid etching (SLA) surface treatment, the titanium machine surface is modified by coarse grit-blasting using 0.25–0.5 mm corundum grit at air pressure of five bars, followed by acid-etching. Recently, the newly developed titanium implant surface treated with SLA and anchored with sintering tetracalcium phosphate (TTCP) can promote osseointegration by forming a mechanical granular interlocking film. About 70% of the minerals in human bone are calcium phosphates (CaPs), therefore, the CaPs on the implant surface can conduct and promote bone healing, thereby causing the biointegration of the implant.

Materials and methods

This prospective cohort study was approved by the Human Research Ethics Committee of the Faculty of Dentistry Chulalongkorn University (study code: HREC-DCU 2018–114) and registered at the Thai Clinical Trials Registry database (study code: TCTR20190423001). All patients participating in this clinical trial were voluntary and have signed informed consent.

All surgeries were performed at Department of Oral and Maxillofacial Surgery, Chulalongkorn University between May 2019 and January 2020 by one surgeon. The 20 patients who followed the inclusion criteria: (a) single tooth space on upper or lower arch, and require single restoration, (b) adults aged 20–75 years. The exclusion criteria were as followed: (a) uncontrolled diabetes, and chronic diseases, (b) cerebrovascular accident patients or the patients taking anti-rejection medicine and osteoporosis drugs for long-term, (c) the case with filled bone graft, (d) the case of other missing teeth, (e) the case of dental bridge or dentures equipment required, (f) the health condition is not well after health education and physical therapy.

Patients were examined at the first visit for screening by periapical film to include in this study. Impression was taken with irreversible hydrocolloid for making diagnostic model. The conventional acrylic stent with radiopaque marker was produced and inserted, then a cone-beam computed tomography image was done using 3D Accuitomo 170 machine (J. Morita Inc., Kyoto, Japan).

In the surgical stage, the surgery was performed under local anesthesia. Full thickness mucoperiosteal flap was elevated after sulcular and crestal incision. AnkerII dental implant system (Alliance Global Tech Inc., Kaohsiung, Taiwan) with diameter of 4.0 mm and length of 10 and 11.5 were selected in this study. Resonance frequency analysis (RFA) presented as ISQ (Ostell, Gothenburg, Sweden) value was measured immediately after implants placement (ISQO). Implants that insertion torque less than 25 Ncm were excluded. Healing abutments that higher than gingival margin were inserted. Briefly, the surgical procedure was shown in Fig. 1.

The postoperative medications were administered included systemic antibiotics (amoxicillin one gram, twice a day) and analgesic (mefenamic acid 500 mg, three times a day) for five days. In patients allergic to penicillin, clindamycin 300 mg was administered three times a day. Periapical film was taken immediately after the surgical intervention.
Two weeks after surgical intervention, the patients were followed up for checking wound healing at implant sites. Patients were followed up for examining the implant sites, taking periapical radiographs and RFA measurements on one month (ISQ1), two months (ISQ2), three months (ISQ3), and four months (ISQ4). Subgroup analysis was defined to location (maxilla, mandible) and bone density (soft bone: bone type I, II; hard bone: bone type III, IV). Four months after surgical intervention, the patients were referred to prosthodontist for supra-structure construction.

Statistical analysis was using SPSS 22.0 software (SPSS Inc., Chicago, IL, USA). The normality of data distribution of ISQ was calculated using Shapiro–Wilk test. ISQ between different time points were compared using Friedman test. Mann–Whitney U test was using to compared mean ISQ between different bone type and location. P-value < 0.05 was considered as statistically significant.

Results

Twenty patients received single implant placement with no bone graft. All samples included 6 males and 14 females with mean age of 48.05 years (range 30–74). Locations of implant were maxilla (9 patients) and mandible (11 patients). Bone types of patients were soft bone (11 patients) and hard bone (9 patients). All implants achieved 25 Ncm insertion torque or more. The implant size and basic information of the patients were detailed in Table 1.

The mean ISQ values and standard deviations at different time points were 60.03 ± 14.12 (ISQ0), 53.48 ± 15.24 (ISQ1), 58.91 ± 14.43 (ISQ2), 63.14 ± 12.22 (ISQ3), and 63.50 ± 13.61 (ISQ4). Statistical analysis showed that there were significant differences between ISQ1 and ISQ3 groups (p = 0.027) and ISQ1 and ISQ4 groups (p < 0.001). However, the others ISQ values were no statistically significant differences between groups as shown in Fig. 2.

There were no statistically significant differences in the paired ISQ0, ISQ1, ISQ2, ISQ3, ISQ4 values, when the implants were placed either in the maxilla or in the mandible (Fig. 3). The p-values of ISQ0 to ISQ4 were 0.849, 0.790,

![Fig. 1](image)

**Fig. 1** Representative images of implant placement (a) Pre-operative (b) Full-thickness flap operation (c) Implant placement (d) Suturing.
Moreover, no statistically significant differences in the paired ISQ0, ISQ1, ISQ2, ISQ3, ISQ4 values were found, when the implants were placed either in the soft bone or in the hard bone (Fig. 4).

The $p$-values of ISQ0 to ISQ4 were 0.676, 0.909, 0.676, 0.543 and 0.970, respectively.

**Discussion**

Resonance frequency analysis (RFA) is extensively utilized procedures in clinical practice for assessing implant stability.\textsuperscript{15,16} The RFA technique measures implant stability by continuously exciting the implant interface through dynamic vibration analysis (piezo effect). The ISQ measured by the RFA technique is calculated on a scale of 1–100, with a range of 60–70 indicating successful dental implantation.\textsuperscript{17}

Titanium implant containing CaPs is an alternative modification for improved osseointegration.\textsuperscript{12} The efficient incorporation of cell-secreted organic and inorganic substances on the implant surface is the primary mechanism for subsequent function and biological efficacy, resulting in osseointegration. The surface of the bioceramic TTCP-modified titanium implants released a large amount of Ca\textsuperscript{2+} cations to promote the growth of epitaxial apatite, thereby inducing binding to the extracellular matrix proteins. It is well known that nano-films of TiO\textsubscript{2} with thickness reaches 10 nm are spontaneously formed on the surface of titanium. In addition, Ca\textsuperscript{2+} ions show high affinity for TiO\textsubscript{2}, so they are largely adsorbed on the oxide layer on the surface of titanium, adhering extracellular matrix proteins and induces migration of progenitor bone cells. In this study, we investigated the clinical application in term of stability of CaPs implant with ISQ. The results showed statistical differences between groups of ISQ1 and ISQ3 and groups of ISQ1 and ISQ4, in accordance with previous studies that ISQ values decreased significantly after three to four weeks of implant placement and subsequently increased after 5–8 weeks.\textsuperscript{18–20}

Some studies investigated the effect of implant location to ISQ.\textsuperscript{21,22} The results showed that there were no significant different between mandible and maxilla which also showed the same results as our study. Nevertheless, Bischof et al., 2004 reported that ISQ value of mandible was higher than maxilla.\textsuperscript{23}

Alsabeeha et al., 2010 showed that the primary stability of implants measured using RFA was not affected by bone quality, which is consistent with our study.\textsuperscript{24} On the contrary Hieu et al., 2013 evaluated RFA in magnesium ion-incorporated titanium implant at 0, 2, 4, 8, and 12 weeks after implant placement, they found significant different in type II and type IV bone.\textsuperscript{25} Barewal et al., 2003 investigated RFA in SLA surface implants and found significant difference between groups for each bone type at three weeks post-healing. Nevertheless, five weeks after implant placement, there were no significant differences in all bone types.\textsuperscript{18} Thongborisoot et al., 2017 compared the implant stability between SLA and SLA active surfaces, the results demonstrated that the SLA active might play an important role in type IV bone due to the higher significant differences of ISQ than SLA surface after 1–2 months of placement. However, both groups had RFA values higher than 60 after 1 month.\textsuperscript{26} Thus, the titanium implant containing CaP achieve sufficient stability as the ISQ of both soft and hard bone types reached 60 or above from 3 months.
The limitations of this study are the relatively small sample size and minimal number of subjects involved. Large sample sizes of other implant surface modifications with stability should be compared in further studies. Moreover, the long-term follow up is required for TTCP/titanium implant.

In accordance with this study, titanium implant surface treated by SLA plus with TTCP achieved desirable stability. The ISQ value was decreased at the one month after implant placement, subsequently it was increased over the initial stability. Moreover, this TTCP surface implant can be apply at any locations and bone types.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

Acknowledgements

This study was supported by Southern Taiwan Science Park Bureau, Ministry of Science and Technology [grant number BX-02-02-02-110 and BX-03-06-09-108].

References

1. Gotfredsen K, Berglundh T, Lindhe J. Anchorage of titanium implants with different surface characteristics: an experimental study in rabbits. Clin Implant Dent Relat Res 2000;2:120–8.
2. Buser D. Titanium for dental applications (II). Implants with Roughened Surfaces, 2001:875–88.
3. Albrektsson T, Wennerberg A. Oral implant surfaces: Part 2: review focusing on clinical knowledge of different surfaces. Int J Prosthodont (IJP) 2004;17:544–64.
4. Esposito M, Coulthard P, Thomsen P, Worthington HV. The role of implant surface modifications, shape and material on the success of osseointegrated dental implants. A Cochrane systematic review. Eur J Prosthodont Restor Dent 2005;13:15–31.
5. Puleo DA, Thomas MV. Implant surfaces. Dent Clin 2006;50:323–8.
6. Le Guehennec L, Soueidain A, Layrolle P, Amouriq Y. Surface treatments of titanium dental implants for rapid osseointegration. Dent Mater 2007;23:844–54.
7. Wennerberg A, Galili S, Albrektsson T. Current knowledge about the hydrophilic and nanostructured SLActive surface. Clin Cosmet Invest Dent 2011;3:59–67.
8. Wennerberg A, Albrektsson T. Effects of titanium surface topography on bone integration: a systematic review. Clin Oral Implants Res 2009;20:172–84.
9. Moseke C, Gbureck U. Tetracalcium phosphate: synthesis, properties and biomedical applications. Acta Biomater 2010;6:3815–23.
10. Klein CPAT, de Blieck-Hogervorst JMA, Wolke JGC, de Groot K. A study of solubility and surface features of different calcium phosphate coatings in vitro and in vivo: a pilot study. In: Vincenzini P, ed. Ceramics in substitutive and reconstructive surgery. Amsterdam: Elsevier, 1991:363–73.
11. Ko CL, Chang YY, Liou CH, Chen WC. Characterization of the aspects of osteoprogenitor cell interactions with physical tetracalcium phosphate anchor on titanium implant surfaces. Mater Sci Eng C Mater Biol Appl 2015;49:7–13.
12. Chen JC, Ko CL, Lin DJ, Wu HY, Hung CC, Chen WC. In vivo studies of titanium implant surface treatment by sandblasted, acid-etched and further anchored with ceramic of tetracalcium phosphate on osseointegration. J Australas Ceram Soc 2019;55:799–806.
13. Sennerby L, Meredith N. Implant stability measurements using resonance frequency analysis: biological and biomechanical aspects and clinical implications. Periodontal 2008;47:51–66.
14. Lekholm U, Zarb GA. Patient selection and preparation. In: Branemark PI, Zarb GA, Albrektsson T, eds. Tissue Integrated prostheses: osseointegration in clinical Dentistry. Chicago: Quintessence Publishing Company, 1985:199–209.
15. Resnik RR, Misch CE. Periodontal and maintenance complications. In: Misch’s avoiding complications in oral implantology. St. Louis, Missouri: Elsevier, 2018:771–826.
16. Janyaphadungpong R, Serichetaphongse P, Pimkhoakham A. A clinical-resonance frequency analysis of implants placed at dehiscence-type defects with simultaneous guided bone regeneration during early healing. Int J Oral Maxillofac Implants 2019;34:772–7.
17. Sennerby L, Roos J. Surgical determinants of clinical success of osseointegrated oral implants: a review of the literature. Int J Prosthodont (IJP) 1998;11:408–20.
18. 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;18:641–51.
19. Portmann M, Glauser R. Report of a case receiving full-arch rehabilitation in both jaws using immediate implant loading protocols: a 1-year resonance frequency analysis follow-up. Clin Implant Dent Relat Res 2006;8:25–31.
20. Stacchi C, Vercellotti T, Torelli L, Furlan F, Di Lenarda R. Changes in implant stability using different site preparation techniques: twist drills versus piezosurgery. A single-blinded, randomized, controlled clinical trial. Clin Implant Dent Relat Res 2013;15:188–97.
21. Guler AU, Sumer M, Duran I, Sandikci EO, Teliçoglu NT. Resonance frequency analysis of 208 Straumann dental implants during the healing period. J Oral Implantol 2013;39:161–7.
22. Zix J, Kessler-Liechti G, Mericske-Stern R. Stability measurements of 1-stage implants in the maxilla by means of resonance frequency analysis: a pilot study. Int J Oral Maxillofac Implants 2005;20:747–52.
23. 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;15:529–39.
24. Alsabeha NH, De Silva RK, Thomson WM, Payne AG. Primary stability measurements of single implants in the midline of the edentulous mandible for overdentures. Clin Oral Implants Res 2010;21:563–6.
25. Hieu PD, Baek DH, Park DS, Park JT, Hong KS. Evaluation of stability changes in magnesium-incorporated titanium implants in the early healing period. J Craniofac Surg 2013;24:1552–7.
26. Thongborisoot S, Serichetaphongse P, Dard MM, Pimkhoakham A, Janissyanont P. The comparison of implant stability between two dental implant surfaces using resonance frequency analysis: a pilot study. J Implant Adv Clin Dent 2017;9:26–37.