Journal of Dental Sciences (2020) **15**, 294–301

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-jds.com

Original Article

A four-year prospective study of self-assembling nano-modified dental implants in patients with type 2 diabetes mellitus

Cui-Xia Li [a], **Feng Wang** [b], **Zuo-Lin Jin** [a*]

[a] *State Key Laboratory of Military Stomatology and National Clinical Research Center for Oral Diseases and Shaanxi Clinical Research Center for Oral Diseases, Department of Orthodontics, School of Stomatology, Fourth Military Medical University, Xi'an, PR China*

[b] *Department of Stomatology, The 546th Hospital of People's Liberation Army, Malan, PR China*

Received 2 September 2019; Final revision received 25 March 2020
Available online 20 May 2020

KEYWORDS
Marginal bone loss (MBL);
Nano-modified (NM);
Resonance frequency analysis (RFA);
Type 2 diabetes mellitus

Background/purpose: Dental implantation has become an efficient and important method of replacing lost teeth. However, the success rate of dental-implant treatment in diabetics is higher than patients without diabetes. The aim of this study was to prospectively evaluate long-term marginal bone loss (MBL) and the stability of a self-assembling nano-modified implant in patients with type 2 diabetes mellitus compared with a conventional implant.

Materials and methods: Twenty-five patients with type 2 diabetes were recruited for this study. Through a random selection process, one site in each patient received a conventional implant and the other site received a nano-modified implant. The implant stability quotient was measured using resonance frequency analysis (RFA), and MBL was measured using panoramic radiography from uncovering to four-year follow-up.

Results: No significant difference in implant stability quotient was found between the two groups ($P > 0.05$), except for the time at implant insertion ($P < 0.05$). MBL in the nano-modified implant group exhibited a decreasing change compared with the conventional implant group, between the uncovering and the loading stage ($P < 0.05$), while there was no significant difference in other stages ($P > 0.05$).

Conclusion: There was potentially increased implant stability and diminished MBL around the self-assembling nano-modified implant in the uncovering-loading stage of early osseointegration in patients with type 2 diabetes.

---

* Corresponding author. Department of Orthodontics, School of Stomatology, Fourth Military Medical University, No. 145 Changle West Road, Xi'an, PR China.
E-mail address: Jinzuolindh@hotmail.com (Z.-L. Jin).

https://doi.org/10.1016/j.jds.2020.03.013

Introduction

Over the past few decades, dental implants have become an efficient and important method of replacing lost teeth.[1] However, diabetes mellitus is considered to be a relative contraindication to dental implant therapy because of the slightly higher failure rate compared to populations without diabetes.[2] Individuals with diabetes, especially those with poorly controlled hyperglycemia, have usually exhibited increased susceptibility to infection, impaired wound healing, and microvascular complications.[3] Moreover, diabetic patients also have an increased risk for oral diseases such as gingivitis, periodontitis, gradual loss of tooth attachment to the alveolar bone, and tooth loss.[4] Therefore, dental clinicians are usually wary about the effect of hyperglycemia on bone metabolism and the outcomes for diabetic patients receiving dental implants. Previous studies using animal models with poorly controlled diabetes have demonstrated alterations in osseointegration around dental implants and reduced bone-to-implant contact.[5,6] Our research team has been searching for new ways to improve osseointegration and counteract the adverse effects of hyperglycemia in diabetic patients.[7,8]

In 1980, Albrektsson et al. suggested six factors that influence the osseointegration of dental implants: implant material; implant design; implant finish; status of the bone; surgical technique; and implant loading conditions.[9] These factors can be categorized into three groups: patient-related factors; factors related to clinical procedures; and factors related to the implant surface design.[10] Modifications to the implant surface provide the potential to alter the bone turnover process and enhance implant integration.[11] Several previous studies have focused on micro-pits and nanoporous titanium oxide (TiO_2) layers generated via grit blasting, acid etching, anodization, and electrochemical functionalization methods to mimic the natural bony environment.[12,13] Consequently, special consideration should be given to the surface properties of titanium implants, which may have a positive influence on bone healing in diabetic patients with poorly controlled hyperglycemia.

The aim of this study was to evaluate the long-term clinical performance of nano-modified (NM) titanium implants in patients with type 2 diabetes in mandibular posterior region single-unit restoration, and to compare the results with a control group (conventional implant) followed for a minimum of 4 years.

Materials and methods

Material preparation

50 bone-level dental implants (MIS, Jerusalem, Israel), 5 mm in diameter and 10 mm in length with a SLA (Sandblasted with Large grit and Acid-etched) surface, were used in this study. For special nanotechnology processing, the MIS implants were treated using optimal anodizing at a constant potential of 10 V. Thus, the well-organized TiO_2 nanotubes were fabricated on the SLA surface of the MIS implants. A platinum (thickness, 0.1 mm; purity: 99.99%) electrode (Alfa Aesar, Ward Hill, MA, USA) was used as the cathode. The green calomel (Kangning, Shanghai, China) was used as a reference electrode in the anodizing process, and the MIS dental implants served as the working electrode (anode). After the above special modification, the NM dental implants were ultrasonically cleaned in acetone for 20 min at 25 °C, followed by air-drying before use.

Surface characterization

Field-emission scanning electron microscope (model: QUANTA FEG-250) (FEI, Eindhoven, Netherlands) was used to analyze the surface morphology of the SLA and the NM + SLA MIS dental implants at an accelerating voltage of 15 kV in the high vacuum mode. The constituent elements of the surface of the MIS dental implants were measured using an energy dispersive spectrometer (Ametek, Berwyn, PA, USA) at an accelerating voltage of 30 keV. The contact angles were measured using a video system (model: OCA 20) (Dataphysics, Regensburg, Germany) at room temperature in 5 μL of ultra-pure water.

Patient inclusion and exclusion

This study was approved by the Ethics and Research Committee, according to the Helsinki Declaration of 1994. All participants signed a consent form and agreed to participate in the entire clinical trial. Twenty-five patients with type 2 diabetes mellitus seeking dental treatment were recruited between January 2012 and June 2014. Inclusion criteria were as follows: age between 41 and 60 years; bilateral first molar loss in mandible for at least 5 months; uncontrolled type 2 diabetes mellitus of at least 2 years, and glycated hemoglobin values between 8% and 10.5% at the time of implant placement. (The American Association of Clinical Endocrinologists considers an HbA1c level $\leq$7% as a goal for controlled type 2 diabetes and $\geq$7% as a threshold for uncontrolled type 2 diabetes.) Throughout the whole experiment, there was no medical measures adopted to all participants. Type 2 diabetes status was confirmed and documented by a professional physician. Patients with a history of treatment for microvascular or macrovascular complications of diabetes, those who did not attend annual follow-up visits, those taking medications, those with bleeding disorders, metabolic bone disorders, alcoholism or drug abuse, or smoked >10 cigarettes per day, individuals who required complex guide bone regeneration procedures, and those with allergic diseases or poor oral hygiene were excluded from this study.

Implant placement

All implant surgeries were performed by a specialized surgeon with >10 years' experience in implant surgery. Each implant placement satisfied the standard surgical technique and process without additional bone grafting. For each included patient, the bilateral mandibular first molar implant sites were randomized per patient to receive one each of either a 5.0*10 mm MIS SLA implant or an NM counterpart (SLA + NM) (Fig. 1). The implant position was determined with a permuted block randomization plan

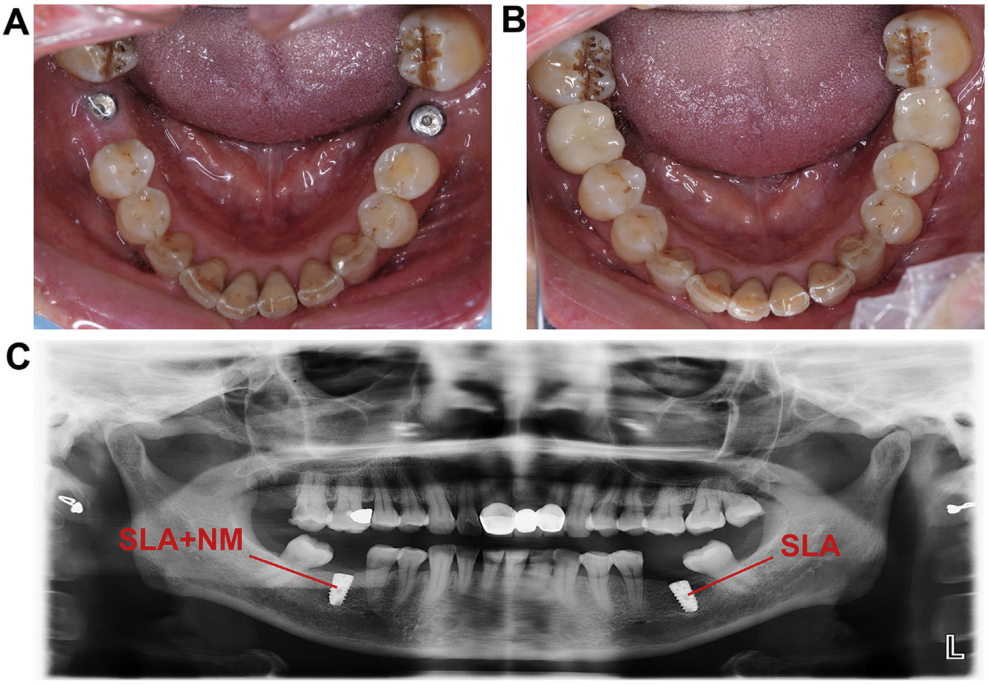


Figure 1 The classical restoration process of a type 2 diabetic patient with bilateral mandibular first molar loss. A The healing abutments were mounted in oral cavity in 4 months after implant placement. B The zirconia all-ceramic crown was fixed using the central screw after one additional month. C The one implant site receive SLA implant and the other site receive an NM + SLA counterpart.

developed using an online pseudo-random number generator (http://www.randomization.com).

Patients rinsed with 0.12% chlorhexidine mouthwash 10 min before the surgery. After conventional disinfection of the implant sites, 4% articaine (ACTEON, Bordeaux, France) was used with local anesthesia of the implant area. An H-shape incision was made on the alveolar ridge, followed by mucoperiosteal flap elevation to bone tissue, the area was irrigated with a 4 °C sterile physiological saline solution to keep the implant site from overheating. The implant site was prepared using a standard MIS systematic drilling, the platform of implant was immersed 0.5 mm below the alveolar bone level. The submerged healing screw was attached to implant and closely sutured using 4/0 silk. Prophylactic antibiotics were used in type 2 diabetic patients for 8 days post-surgically (amoxicillin 250 mg every 8 h, ornidazole capsule 400 mg every 12 h), and 0.12% compound chlorhexidine oral rinse was applied by the patients three times per day for 2 weeks. After 4 months, the healing abutments were mounted (Fig. 1A) and a zirconia all-ceramic crown was fixed using the central screw after one additional month (Fig. 1B).

Measurement of marginal bone loss

Marginal bone loss (MBL) was defined as the average distance from the first bone-implant contact to the implant shoulder between two time points, measured mesially and distally to the implant on digitized panoramic radiographs. The change in marginal bone loss with time was defined according to the following equation: $MBL = 2c - a - b/2$ (Fig. 2).

Resonance frequency analysis

Resonance frequency analysis (RFA) values were evaluated using the Osstell Mentor (Osstell, Goteborg, Sweden). Implant stability (implant stability quotient [ISQ]) was determined in duplicate with a third reading recorded if there was greater than a 2 ISQ unit difference between readings. Each implant's ISQ was calculated according to the average of two independent readings recorded from the buccal and proximal direction. The ISQ value and expulsion rate of two group (SLA and NM + SLA) was observed at insertion, uncovering, loading, 1 year, 2 years, and 4 years.

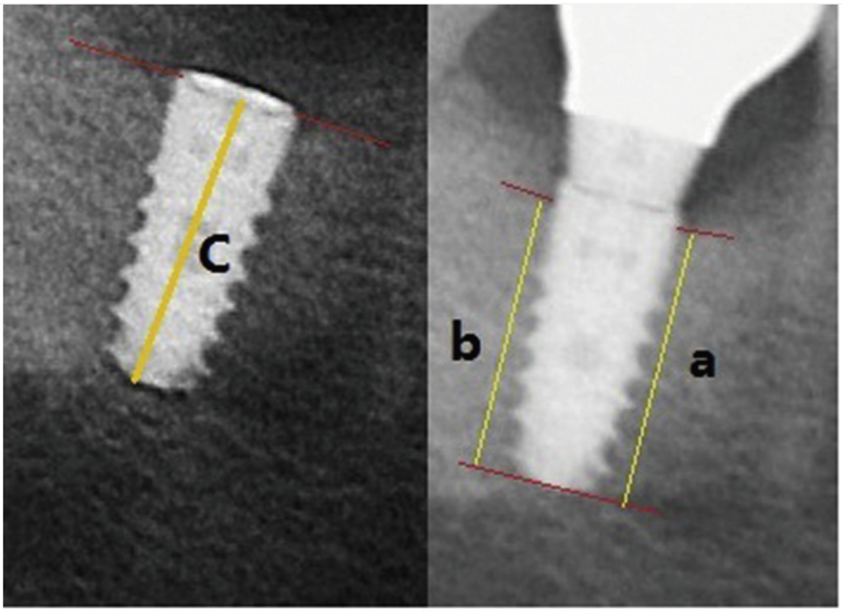
Statistical analysis

The contact angle, MBL, and ISQ were expressed as mean ± standard deviation (SD) from at least XY independent readings. The significance of differences between the two groups (SLA and NM + SLA) was assessed using the paired *t*-test. Statistical analysis was performed using SPSS version 18 (IBM, Armonk, NY, USA); $P \leq 0.05$ was considered to be statistically significant.

Results

Characteristics of implants with NM surfaces

The geometric morphology of the SLA surface of the MIS implants was composed of regularly aligned micro-pit units (Fig. 3A). On the surface of the NM MIS implants (NM + SLA), it was clear that the vertically arranged TiO_2 nanotubes,



$$\text{MBL (Marginal Bone Loss)} = \frac{2c\text{-}a\text{-}b}{2}$$

Figure 2 The measurement of MBL between two time points. The illustration diagram of marginal bone loss (MBL) was presented as a equation: $\mathrm{MBL} = 2c - a - b/2$ (a and b is the distance from first bone-implant contact thread to apex of the implant in mesial and distal direction respectively; **c** is the length of Mis implant).

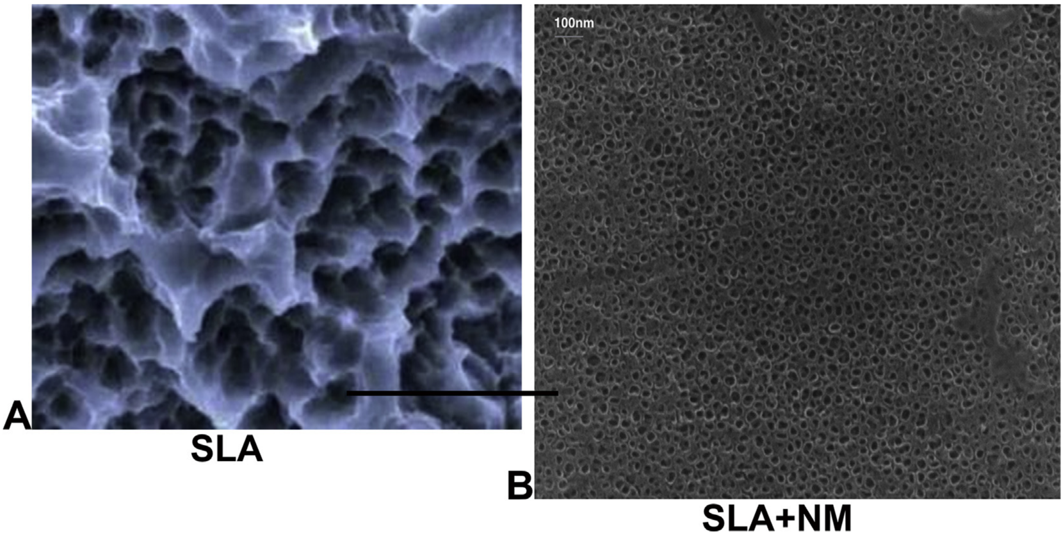


Figure 3 The SEM images of two different Mis implants' surface. A (magnification: 5000×) is the micro-pits like architecture on SLA surface. B (magnification: 100,000×) is the TiO_2 nanotubes on SLA + NM surface.

30–50 nm in diameter (Fig. 3B), were orderly aligned into the micro-pit structure (Fig. 3A). Representative energy dispersive X-ray detector (EDX) spectra are illustrated in Fig. 4. The elemental weight percentage of the NM + SLA surfaces (Fig. 4B) revealed a corresponding change compared with their SLA counterparts (Fig. 4A). The weight percentage of oxygen demonstrated a 9.84% increase, while titanium simultaneously demonstrated a 10.34% decrease.

In vitro hydrophilicity assay

The appearance of a drop of ultra-pure water on the surface of the titanium implants is shown in Fig. 5A. The water contact angle of the SLA surface and NM + SLA surface was $56.2 \pm 2.2°$ (Fig. 5B) and $22.5 \pm 1.3°$ (Fig. 5C), respectively. As shown in Fig. 5D, there was a significant difference between the SLA surface and the NM + SLA surface of the MIS

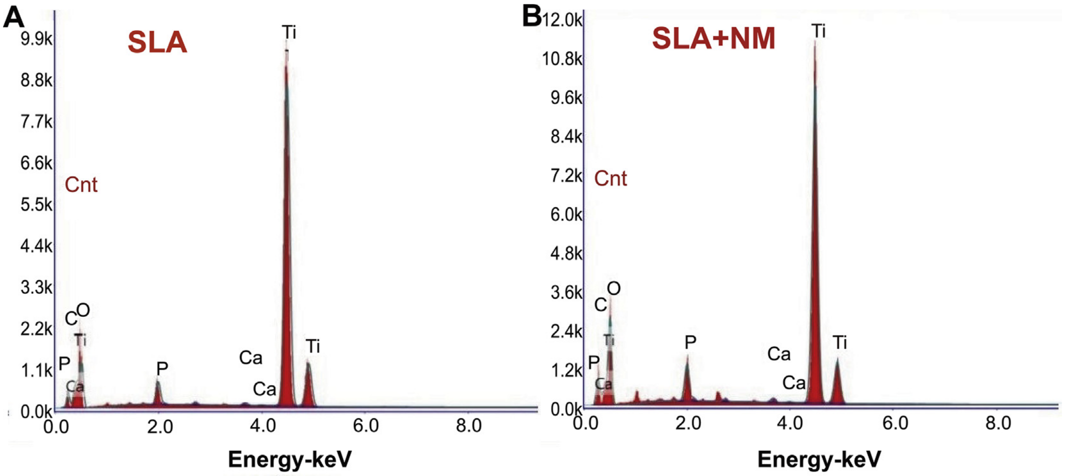


Figure 4 The X-ray EDS spectra of the threaded parts of two different Mis implants A SLA B SLA + NM.

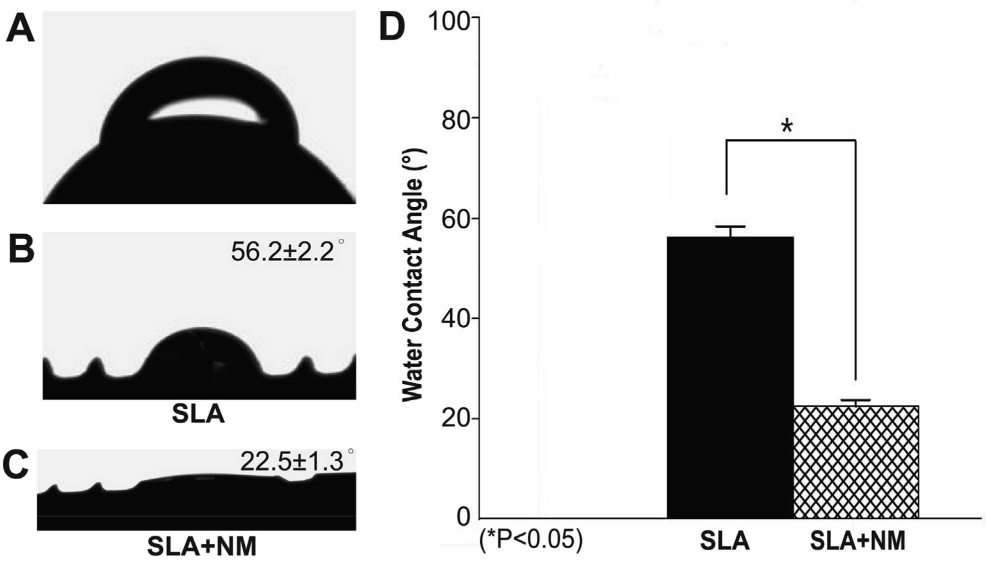


Figure 5 The hydrophily of two different implants' surface. A. The status of the ultra-pure water was dropped on the titanium implants' surface. B and C is the measuring results of statical water contact angle (°) on two different Mis implants' surface (SLA and SLA + NM). D is the statistical analysis of the water contact angle on SLA and SLA + NM surface.

implants ($P < 0.05$). The self-assembling NM surface of the dental implants were relative more hydrophilic than the conventional SLA surface. These characteristics are beneficial for blood adsorption, which may promote better primary osseointegration around the alveolar bone in patients with type 2 diabetes.

Patient characteristics

Characteristics of the 25 type 2 diabetic patients in this study are given in Table 1. Fourteen (56%) of participants were female. The average age was 51.5 years, and the average BMI was 33.5 kg/m^2. During the whole experiment, participants had HbA1c levels between 8% and 10.5% (Table 1). The average HbA1c did not differ significantly among the measurements made at insertion, uncovering, loading,

Table 1 Patient characteristics.

Variable	Number (%)
Female sex	14 (56)
Age (years)	51.5 ± 7.6 (41–60)
BMI (kg/m^2)	33.5 ± 6.8 (25.4–47.8)
HbA1c (%)	
Insertion	9.4 ± 0.8 (7.9–10.2)
Uncovering	9.5 ± 1.0 (8.1–10.5)
Loading	9.1 ± 1.3 (8.3–10.4)
One-year follow-up	8.9 ± 1.6 (8.7–10.6)
Two-year follow-up	9.6 ± 0.7 (8.9–10.3)
Four-year follow-up	9.3 ± 1.1 (8.2–10.4)

one-year follow-up, two-year follow-up and four-year follow-up.

MBL and implant stability

All 25 type 2 diabetic patients received an SLA implant and an SLA + NM implant restoration in bilateral mandible first molar, respectively. After implant-supported ceramic crown loading, one patient did not return for the one-year follow-up visit and further observation. Data from the remaining 24 patients and panoramic radiographs were analyzed. There were no significant differences in MBL change between the SLA group and the NM + SLA group during the entire recording term after loading ($P > 0.05$). The SLA group demonstrated a greater change than the NM + SLA group from uncovering to loading (SLA, 0.35 ± 0.25 versus SLA + NM, 0.11 ± 0.18; $P < 0.05$) (Table 2).

The mean ISQ for each type implant according to time following implant insertion is shown in Fig. 6. It was clear that the NM + SLA group demonstrated higher immediate ISQ values than the SLA group after implant placement ($P < 0.05$), while no significant difference was identified between the two groups from uncovering to four-year follow-up visit.

Discussion

A recent systematic review of 16 longitudinal studies involving diabetic patients reported an implant failure rate of 0%—14.3%,[14] without a clear association with glycemic control. Furthermore, a previous study also revealed that the success rate in type 2 diabetic patients with poor glycemic control was similar to those in both well-controlled and non-diabetic patients.[15] In contrast, patients with uncontrolled diabetes present a contraindication to implant treatment, as established in the 1996 World Workshop in Periodontics.[16] Some authors have also found that implant stability and osseointegration were compromised during the metabolically active healing period following placement, which was directly related to poor control of glycemic levels.[17] Therefore, the long-term performance and survival rate of dental implants in patients with type 2 diabetes remains controversial.

In the present study, the results did not reveal a clear difference in stability between the two patterns of different implant surfaces (i.e., SLA and SLA + NM) most of the time, except for the insertion-uncovering term (Fig. 6). Our study demonstrated high clinical success rates over a four-year period for both implant types in patients with uncontrolled type 2 diabetes, who have traditionally been considered to have contraindications to implant therapy.[18] A hyperglycemic state increases the formation and accumulation of advanced glycation end-products in periodontal tissue, which impair the chemotactic and phagocytic function of polymorphonuclear leukocytes and induce the production of destructive inflammatory cytokines in the serum and gingival crevicular fluid.[19] These adverse effects can also impair primary bone healing around dental implants; therefore, poor glycemic control in patients with type 2 diabetes was a relative contraindication. However, recent relative reports indicated an increasing implant survival rate in type 2 diabetic patients with elevation in glycemic levels.[20,21] The above findings are highly consistent with the present study over the four-year clinical success of 48 dental implants in 24 type 2 diabetic patients with glycated hemoglobin ranging from 8.0% to 10.5% over the entire study period.

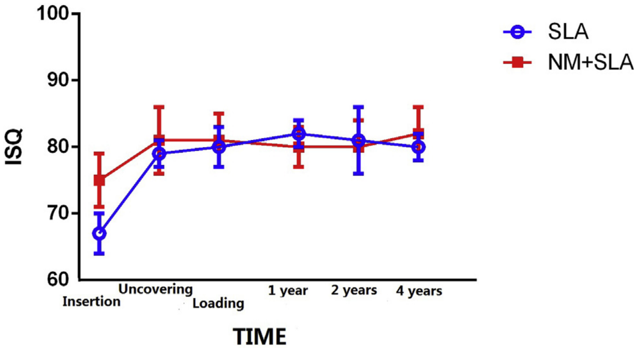


Figure 6 The stability of two different implants from insertion to 4 years follow-up. The mean ISQ (Implant Stability Quotient) value for each Mis implant type by time, following implant placement.

Table 2 The marginal bone loss of two type Mis implants of different surface (mean ± SD).

Treatment term	MBL (mm)	
	SLA	SLA + NM
Uncovering-loading	0.35 ± 0.25	0.11 ± 0.18*
Loading-one-year follow-up	0.16 ± 0.1	0.12 ± 0.08
One-year to two-year follow-up	0.12 ± 0.08	0.1 ± 0.06
Two-year to four-year follow-up	0.11 ± 0.05	0.1 ± 0.06

MBL, marginal bone loss; SLA, sand blasted-large grit-acid etched; NM, nano-modified. *means $P < 0.05$.

In the present study, the total MBL was 0.74 ± 0.48 mm in the SLA group and 0.43 ± 0.38 mm in the SLA + NM group (Table 2). A 5-year follow-up study examining MBL from the moment of implant placement reported values of 1.06 ± 0.19 mm to 1.98 ± 0.21 mm, depending on the implant system and the arch in which the implants were placed.[22] Coincidentally, our results were also close to this range, this similar MBL level indicated that placing dental implants in patients with uncontrolled type 2 diabetes can result in acceptable clinical outcomes compared with nondiabetic patients. However, in a retrospective study with a mean 60.7 months' follow-up, 85% of all implants exhibited MBL ≤1 mm.[23] After a special nano-modification to the surface of the SLA implant, the MBL of the SLA + NM group (0.43 ± 0.38 mm) decreased to approach the criterion for normal individuals (≤1 mm). Another explanation for our results was that the dental implants placed were located in the posterior region, which is a region of MBL less than the anterior region.[24] Therefore, placing dental implants in the molar area of patients with type 2 diabetes usually leads to the desired restoration result.

A previous study reported that dental implants with hydrophilic surfaces induce greater bone-to-implant contact than implants with a hydrophobic surface during early bone formation.[25] Our results confirmed the above point: the SLA + NM group exhibited a hydrophilic properties than the SLA group (22.5 ± 1.3° versus 56.2 ± 2.2°) (Fig. 5). This hydrophilic surface decreased MBL in type 2 diabetic patients from uncovering to loading (early bone healing, 0.11 ± 0.18 mm versus 0.35 ± 0.25 mm) (Table 2). The hydrophilic properties of the SLA + NM surface were attributed to the orderly arrangement of TiO_2 nanotubes, 30–50 nm in diameter (Fig. 3B). Porous surfaces not only improve hydrophilicity, but also enhance surface roughness compared with nonporous surfaces.[26] The more appropriate element component on the SLA + NM surface (oxygen content increase, titanium decrease) (Fig. 4), leading to the increasing CaP precipitation on the surface of the titanium implants, affecting protein adsorption and subsequent cell response.[27] Another previous study confirmed that the nanotopography of modified titanium implants can mimic the extracellular matrix, the components of which are generally nanometer in size.[28] These characteristics enhance the rate of osseointegration, favoring a direct bone-implant without the presence of an interfering connective tissue layer, which tends to appear in type 2 diabetic animal models.[29] The results of the present study imply that NM implant surfaces may produce a positive effect on early bone healing in patients with uncontrolled type 2 diabetes.

This prospective study had limitations, the first of which was the small sample size and limited follow-up term. Twenty-four patients with uncontrolled type 2 diabetes and an average 4.6 years of follow-up is not likely to be representative of the entire diabetic population. A greater sample size and a longer follow-up period are required to fully determine the long-term effect on patients with type 2 diabetes. Nano-modification was affected by many factors, including ambient humidity, the environment and constant room temperature, among others. Therefore, future studies exploring specified standards and operating details are warranted.

In this study, within the limits of 4.6 years of follow-up study on 24 patients with type 2 diabetes, both the SLA and NM + SLA implants achieved the desired clinical results in the mandible first molar site. However, our self-assembling NM + SLA implants demonstrated preferable implant stability and diminished MBL in the uncovering-loading stage of early osseointegration. This performance may be attributed to hydrophilicity and an optimal chemical composition of the surface. Therefore, these findings indicated that the special consideration of nano-modification maybe is a potential strategy for dental implantation on type 2 diabetics.

Conflicts of interest statement

The authors declare that there is no conflict of interest regarding the publication of this paper.

Author contribution

Conception and design of study: Z.L. Jin.
Acquisition of data: C.X. Li, F. Wang and Z.L. Jin.
Analysis and/or interpretation of data: C.X. Li and F. Wang.
Drafting the manuscript: C.X. Li and F. Wang.
Revising the manuscript critically for important intellectual content: Z.L. Jin.

Acknowledgments

This work was supported by the project of preeminent youth fund of the General Armament Department of People's Liberation Army [grant number ZZQP003] and the National Natural Science Foundation of China [grant number NSFC 81701002, NSFC 81571000, NSFC 81970960]. The authors acknowledge Prof. Zexu Gu for helpful discussions and Mr. He for technical support. Finally, the authors thank Prof. Peizhong Wang's research team from the Northwest Institute of Nuclear Physics for their assistance.

References

1. Moraschini V, Poubel LA, Ferreira VF, Barboza Edos S. Evaluation of survival and success rates of dental implants reported in longitudinal studies with a follow-up period of at least 10 years: a systematic review. *Int J Oral Maxillofac Surg* 2015;44:377–88.
2. Marchand F, Raskin A, Dionnes-Hornes A, et al. Dental implants and diabetes: conditions for success. *Diabetes Metab* 2012;38:14–9.
3. Courtney MW, Snider TN, Cottrell DA. Dental implant placement in type II diabetics: a review of the literature. *J Mass Dent Soc* 2010;59:12–4.
4. Salvi GE, Carollo-Bittel B, Lang NP. Effects of diabetes mellitus on periodontal and peri-implant conditions: update on associations and risks. *J Clin Periodontol* 2008;35:398–409.
5. McCracken M, Lemons JE, Rahemtulla F, Prince CW, Feldman D. Bone response to titanium alloy implants placed in diabetic rats. *Int J Oral Maxillofac Implants* 2000;15:345–54.
6. Siqueira JT, Cavalher-Machado SC, Arana-Chavez VE, Sannomiya P. Bone formation around titanium implants in the rat tibia: role of insulin. *Implant Dent* 2003;12:242–51.
7. Wang F, Song YL, Li CX, et al. Sustained release of insulin-like growth factor-1 from poly(lactide-co-glycolide) microspheres improves osseointegration of dental implants in type 2 diabetic rats. *Eur J Pharmacol* 2010;640:226–32.
8. Wang B, Song Y, Wang F, et al. Effects of local infiltration of insulin around titanium implants in diabetic rats. *Br J Oral Maxillofac Surg* 2011;49:225–9.
9. Albrektsson T, Branemark PI, Hansson HA, Lindstrom J. Osseointegrated titanium implants. Requirements for ensuring a long-lasting, direct bone-to-implant anchorage in man. *Acta Orthop Scand* 1981;52:155–70.
10. Chen Y, Kyung HM, Zhao WT, Yu WJ. Critical factors for the success of orthodontic mini-implants: a systematic review. *Am J Orthod Dentofac Orthop* 2009;135:284–91.
11. 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;22:755–60.
12. Huang CF, Chiang HJ, Lin HJ, Hossein H, Ou KL, Peng PW. Comparison of cell response and surface characteristics on titanium implant with SLA and SLAffinity functionalization. *J Electrochem Soc* 2014;161:G15–20.
13. Lin YH, Peng PW, Ou KL. The effect of titanium with electrochemical anodization on the response of the adherent osteoblast-like cell. *Implant Dent* 2012;21:344–9.
14. Oates TW, Huynh-Ba G, Vargas A, Alexander P, Feine J. A critical review of diabetes, glycemic control, and dental implant therapy. *Clin Oral Implants Res* 2013;24:117–27.

15. Oates TW, Dowell S, Robinson M, McMahan CA. Glycemic control and implant stabilization in type 2 diabetes mellitus. *J Dent Res* 2009;88:367—71.
16. Blanchaert RH. Implants in the medically challenged patient. *Dent Clin N Am* 1998;42:35—45.
17. Fiorellini JP, Chen PK, Nevins M, Nevins ML. A retrospective study of dental implants in diabetic patients. *Int J Periodontics Restor Dent* 2000;20:366—73.
18. Beikler T, Flemmig TF. Implants in the medically compromised patient. *Crit Rev Oral Biol Med* 2003;14:305—16.
19. Gurav AN. Advanced glycation end products: a link between periodontitis and diabetes mellitus? *Curr Diabetes Rev* 2013;9:355—61.
20. Tawil G, Younan R, Azar P, Sleilati G. Conventional and advanced implant treatment in the type II diabetic patient: surgical protocol and long-term clinical results. *Int J Oral Maxillofac Implants* 2008;23:744—52.
21. Turkyilmaz I. One-year clinical outcome of dental implants placed in patients with type 2 diabetes mellitus: a case series. *Implant Dent* 2010;19:323—9.
22. Astrand P, Engquist B, Dahlgren S, Grondahl K, Engquist E, Feldmann H. Astra Tech and Branemark system implants: a 5-year prospective study of marginal bone reactions. *Clin Oral Implants Res* 2004;15:413—20.
23. Krebs M, Schmenger K, Neumann K, Weigl P, Moser W, Nentwig GH. Long-term evaluation of ANKYLOS(R) dental implants, part i: 20-year life table analysis of a longitudinal study of more than 12,500 implants. *Clin Implant Dent Relat Res* 2015;17(Suppl 1):e275—86.
24. Dam HG, Najm SA, Nurdin N, Bischof M, Finkelman M, Nedir R. A 5- to 6-year radiological evaluation of titanium plasma sprayed/sandblasted and acid-etched implants: results from private practice. *Clin Oral Implants Res* 2014;25:e159—65.
25. Lang NP, Salvi GE, Huynh-Ba G, Ivanovski S, Donos N, Bosshardt DD. Early osseointegration to hydrophilic and hydrophobic implant surfaces in humans. *Clin Oral Implants Res* 2011;22:349—56.
26. Yan Y, Sun J, Yong H, Li D, Kai C. Microstructure and bioactivity of Ca, P and Sr doped TiO_2 coating formed on porous titanium by micro-arc oxidation. *Surf Coat Tech* 2010;205:1702—13.
27. Kim MH, Lee SY, Kim MJ, Kim SK, Heo SJ, Koak JY. Effect of biomimetic deposition on anodized titanium surfaces. *J Dent Res* 2011;90:711—6.
28. Tomisa AP, Launey ME, Lee JS, Mankani MH, Wegst UG, Saiz E. Nanotechnology approaches to improve dental implants. *Int J Oral Maxillofac Implants* 2011;26(Suppl):25—44.
29. Le Guehennec L, Soueidan A, Layrolle P, Amouriq Y. Surface treatments of titanium dental implants for rapid osseointegration. *Dent Mater* 2007;23:844—54.