1. TITLE

Interproximal implant thread exposure after initial bone remodeling as a risk indicator for peri-implantitis

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None

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6. RUNNING TITLE

Implant-thread exposure as a peri-implantitis risk indicator

7. ONE SENTENCE SUMMARY

Implants with radiographically assessed exposed interproximal threads one year after implant restoration had 8 times greater risk for peri-implantitis than implants without such exposure and the risk increased 4 times with each exposed thread.

8. ABSTRACT

Background: Due to the clinical challenges involved in successfully treating peri-implantitis, it is imperative to identify patient- and implant-level risk factors for its prevention. The main goal of this retrospective longitudinal radiographic and clinical study was to investigate whether interproximal radiographic implant thread exposure after physiological bone remodeling may be a risk factor for peri-implantitis. The secondary goal was to evaluate several other potential risk indicators.

Methods: Of 4,325 active dental school patients having implants placed, 165 partially edentulous adults (77 men, 88 women) aged 30 – 91 with $\geq$2 years of follow-up upon implant restoration were included. Implants with $\geq$1 interproximal thread exposed (no bone-to-implant contact) (n=98, 35%) constituted the test group and those without exposed threads (n=182, 65%) the control group. Descriptive and binary and multivariate regression analyses were evaluated for goodness of fit. Wald's tests evaluated for significance set at 0.05.

Results: Of the 280 implants (98 test, 182 control), 8 (2.9%) failed over a mean follow-up period of 7.67 ($\pm$2.63) years, and 27 implants (19 test, 8 control) developed peri-implantitis, with the exposed group having 8-fold (7.82 times) adjusted greater odds than the non-exposed. The risk increased 4-fold (3.77 times) with each thread exposed. No other patient or implant related potentially confounding risk factors were identified.

Conclusions: Exposed interproximal implant threads after physiologic bone remodeling may be an independent risk indicator for incident peri-implantitis. Hence, clinicians should closely monitor patients with implant threads that have no bone to implant contact for incident peri-implantitis.

9. KEY WORDS

1. INTRODUCTION

Peri-implantitis (PI) is defined as an inflammatory lesion in the tissues surrounding the implant with progressing of bone loss beyond the expected physiologic bone remodeling. [1, 2]. PI is the most common complication in implant dentistry, [3, 4] affecting around 20% of patients[5-7] and 13% of implants, [6, 7] with study results ranging widely.

Because successful treatment of peri-implantitis (PI) is so challenging and the outcome unpredictable, [4, 8] it is imperative to prevent PI from developing, which necessitates identification of its local and systemic risk factors [3] for potential mitigation.

According to the 2017 World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions ("2017 World Workshop"), a history of periodontitis, poor plaque control, and lack of regular maintenance therapy might be considered risk indicators of PI; however other

factors such as smoking, diabetes, width of keratinized tissue, titanium particles, and prosthesis design need to be further evaluated. [1]

It is currently accepted that PI is caused by bacterial challenge in a susceptible host, [9] possibly in combination with a foreign body immune reaction. [10]

Several studies have focused on the roles of the patient (plaque control and compliance with professional maintenance visits) and of the provider (non-surgical or surgical therapies and maintenance) in the development of PI. [8, 11-18] Implant design has been discussed extensively regarding osseointegration, but few studies have explored its role in disease onset, [19, 20] so the role of the implant topography in PI requires further investigation. [21] Implant topography can be categorized as macro- and micro-design, respectively. The macro-design pertains to the shape of the implant body as well as the design and number of threads, and is an established key factor for osseointegration as a crucial element for primary implant stability and possibly for bone-to-implant contact (BIC). [22-24] Implant macro-design has also been hypothesized to be a possible factor contributing to peri-implant disease. [21, 25-27] In support of this hypothesis, greater PI prevalence was found in implants with triple-thread, with a micro-threaded collar, and with a cylindric shape. [27]

The micro-design concerns the chemically or mechanically treated implant surface, such as by acid etching, sandblasting, titanium plasma spraying, and hydroxyapatite coating. [28-30] Moderately rough implant surfaces were associated with lower prevalence rates of PI, [7] but due to the limited quality of evidence on the topic, more studies are necessary to evaluate the relationship between implant micro-design and PI. [31] As a potential risk for PI, [32] bone graft was also recorded.

A clinical study observed that small bony buccal dehiscence defects developed greater than expected vertical bone loss 6 months post implant placement. [33] However, no study has explored the impact of the interproximal thread exposure on the development of PI.

Thus, the main aim of this retrospective longitudinal study was to investigate whether radiological interproximal implant thread exposure after physiological bone remodeling may be a potential risk indicator for incident PI. The secondary goal was to identify other potential patient- or implant-related risk factors for incident PI.

2. MATERIALS AND METHODS

The study protocol was approved by the University of Michigan Medical School Institutional Review Board (Study #HUM00194509) and was conducted in accordance with the Helsinki Declaration adopted in 1964 and 1975, [34, 35] as revised in 2013. [36] This retrospective investigation included implants placed and restored by graduate students or faculty at the University of Michigan School of Dentistry between January 2000 and September 2017. Eligible participants needed to fulfill the following inclusion criteria: 1) partially edentulous area restored with >1 implant with a documented follow-up period of ≥2-years after implant loading; 2) clinical data and high-quality periapical radiographs available at the time of implant placement (T0), prosthetic restoration (T1), 1 year after prosthetic restoration (T2, radiograph exposed at that time as per institutional protocol), and at

follow-up of ≥2 years after prosthetic restoration (T3); 3) available information about the implant brand as well as the surface micro- and macro-structure; 4) presence of opposing teeth/restored implants (occlusion): 5) no active periodontitis at the time of implant placement (T0). Exclusion criteria were a) presence of PI in the test group at T2; b) potentially confounding comorbidities, such as a history of uncontrolled diabetes mellitus, radiation or chemotherapy, psychologic or psychiatric issues); and c) receipt of treatment or maintenance visits external to the study institution. Physical and digital records for potentially eligible patient were screened and evaluated by four examiners (AS, MQ, MS, LW) who subsequently extracted the data. Any disagreement that arose during the screening for eligibility and data collection process was resolved through discussion with the principal investigator (AR).

a. Data collection and classification

Relevant patient information was extracted, including age at the time of implant placement (T0), sex, smoking habit (≥1 cigarette/day), diabetes mellitus (validated via the patient's medical records), history of periodontitis, and number of maintenance appointments. A positive history of periodontitis was determined following the case definition for periodontitis proposed by the 2017 World Workshop[37] based on periodontal charts and radiographs. Detailed implant specific data collected included the number of implants and their positions (location in the edentulous jaw area, implant design [bone or soft tissue level], brand, length, diameter, neck design, retention type of restoration (cement or screw), and splinting. Bone grafting (yes/no) was recorded, and the type of implant-abutment connection, and neck designs was also collected. Moreover, data were collected on the distance between threads (pitch) and the implant macro-surface, such as thread design (buttress, reverse buttress, square, progressive square, V shaped that are schematically illustrated in Figure 3.[24] Details about the micro-surface recorded included type of surface (microtextured and sandblasted, large grit, acid-etched). The implants were divided into four different categories according to their roughness (S_a): smooth (S_a <0.5 μm); minimally rough (S_a 0.5 - 1.0 μm), moderately rough (S_a >1.0-2.0 μm) and rough (S_a >2.0 μm).[38, 39]

Implants were divided by radiographic evaluation of interproximal (mesial/distal) bone-to-implant contact (BIC) 1 year after prosthetic restoration (T2): 1) absence of BIC with ≥1 proximal implant thread (test group, "exposed"), 2) no thread without BIC (control group, "non-exposed"). A thread was regarded radiographically exposed when the adjacent bone did not completely cover its surface. [40] Exposed and non-exposed implant threads are illustrated conceptually (Fig. 2) and radiographically (see Figures S1 and S2 in online Journal of Periodontology).

b. Definition of outcomes

Based on our predefined outcomes, data analyses for implant failure, prevalence of PI, marginal bone loss, and numbers of thread exposed was performed. Two distinct follow-up periods were defined prior to data acquisition: a) follow-up to assess implant survival, and b) follow-up to assess occurrence of PI, marginal bone loss, and number of interproximal (mesial or distal) threads exposed (with no BIC). The follow-up duration based on implant survival was defined as the time between implant placement (T0) and T4, defined as the last visit, during which each implant was classified as

present or explanted. The follow-up based on the occurrence of PI, marginal bone loss, and number of threads exposed, was defined as the duration of time between T2 and exposure of the last radiograph on which peri-implant bone could be clearly visualized (T3). The time between T2 and T3 is referred to as the "radiograph period." In case of concomitancy between T3 and T4 (the last x-rays available and the last patient visit), the 2 follow-up durations were identical.

Implant failure was defined as a removed, lost, mobile, or fractured implant. [41] Peri-implantitis was defined as proposed by the 2017 World Workshop[2] and was used to classify cases in a binary fashion as either positive (1) or negative (0) for PI. Because baseline data were available, a PI diagnosis was based on 1) progressive bone loss beyond initial bone remodeling, 2) increased probing depth, and 3) presence of bleeding and/or suppuration on gentle probing. Marginal bone level (MBL) was defined as the distance between the most coronal portion of the implant expected to present radiographic bone contact (for tissue level implants: the interface between the polished collar and rough surface, and for bone level implants: the platform level) to the most coronal point of the implant body in contact with bone. The MBL and the count of the exposed threads at T2 and T3 were radiographically assessed by two authors (AR, MS) at the mesial and distal aspects of the affected implants using commercially available image software.* If significant differences arose (>0.5mm for bone loss and >1 thread for the threads count), a third reviewer (HLW) was included for reassessing the radiographs in a joint session to reach a final judgment. Repeated measurements of 15 implants were initially conducted to quantify mean inter-examiner agreement measurement errors for MBL: 0.32 (± 0.2) mm.

c. Statistical analysis

The statistical analysis included descriptive analyses of categorical (absolute and relative frequencies) and continuous (mean, standard deviation, range and median) variables for the total sample and stratified by study group (exposed/non-exposed threads) using dedicated statistical software.[†] The outcome PI diagnosis (yes/no) was related to all independent variables using multi-level binary logistic regression with generalized estimation equations (GEE). Raw odds ratios and 95% confidence intervals (95% CI) were obtained from the Wald´s Chi^2 statistic. Then, multivariate models were applied to adjust by potential confounding factors. The goodness of fit of different GEE estimates (for different matrix correlations) was assessed by QIC (Quasi likelihood under the Independence model Criterion) statistic. Significance level in all analysis was set to 5% (α=0.05). A post-hoc power analysis was conducted. A sample size of 280 independent implants would provide 90.9% power with a confidence of 95% to detect an odds ratio (OR) of 3 as significant, using logistic regression models. Since the implants were not independent due to the two-level (patient and implant) data structure, this power needed correction. With each patient providing 1.75 implants on average and assuming a within-subject correlation of 0.5 (moderate), the correcting coefficient (D) was 1.35. Therefore, 280 dependent implants provide the same power as 207 independent implants, estimated at 80.4% under the mentioned conditions.

3. RESULTS

a. Clinical characteristics and demographic profiles

Records from a total of 4,325 active patients who had received implant therapy at the university of Michigan School of Dentistry were screened for potential inclusion. A total of 1,287 patients were excluded due to <2 years post-implant restoration follow-up period, 2,423 patients due to absence of ≥1 radiographs or periodontal charts, 352 patients due to lack of information about brand and other implant characteristics, 53 patients due to presence of fixed full-arch restorations, and 45 due to ambiguous or incomplete charts. Hence, 165 patients were included in the study, including 77 males (46.7%) and 88 females (53.3%) with a mean age of 62.5 (± 11.7) years ranging from 30 to 91 years at baseline (T0). A total of 280 implants were included (n = 98 test group, n = 182 control group). Characteristics of the sample at patient and implant levels are displayed in Table 1.

b. Peri-implantitis and marginal bone loss

Overall, the PI rate was 9.6% (27/280) in the total sample of implants. About one-fifth (19.4%) of the implants in the test group and 4.4% in the control group developed PI. Results from simple binary logistic regression using GEE (Table 2) show that an increasing number of threads exposed, and the square thread design significantly increased the probability of developing PI. Moreover, increasing patient age significantly decreased this probability. No other confounder obtained statistically significant effect in the bivariate analyses.

A multi-variate model (Table 3) considering these findings and adjusting for potential confounders (duration of and mean annual number of maintenance visits during the radiographic period (T2 to T3)) showed that thread exposure remained a significant factor for increasing the likelihood of PI, with the risk of PI increasing almost 8-fold with each additional exposed thread (OR=7.82; 95% CI: 1.91 – 32.03; p=0.004). Splinting was also associated with greater risk for PI (OR=3.49; 95% CI: 1.02 – 12.05; p=0.047). Each year of increased age was associated with 5% lower risk of a PI diagnosis (OR=0.95; 95% CI: 0.92 – 0.99; p=0.016).

No association was found between PI and any other implant macro- or micro-surface design nor a history of periodontitis. The mean annual crestal bone loss between T2 to T3 was 0.26 (± 0.65) mm in the exposed (test group) versus 0.11 (± 0.31) mm per year in the non-exposed (control) group (P=0.05). Each additional exposed thread significantly increased the odds of PI almost 4-fold (OR=3.77; 95% CI: 1.82 – 7.82; p<0.001) (Fig. 1 Panel A, see also Table S1 in online Journal of Periodontology).

c. Implant failure

Each group lost 4 implants. The failure rate was at 2.9% (8/280) in the total sample (4.1% in the test group and 2.2% in the control group), a statistically non-significant difference (p=0.470) (see Table S2 in online Journal of Periodontology). The probability of failure increased with the number of exposed threads, with each additional thread increasing the probability of failure about 3 times (OR=3.13; 95% CI: 1.01 – 9.66; p<0.001) (Fig. 1 Panel B; see also Table S3 in online Journal of Periodontology). Other than older age (OR: 0.97; 95% CI: 0.94 – 1.00; p=0.049), there were no other variables identified to potentially prevent implant failure.

4. DISCUSSION

Because PI is difficult to arrest once established, identification of its modifiable risk factors is key for prevention. In implant treatment planning, execution, and maintenance, all possible measures to prevent development of exposed threads must be taken. Indeed, the results demonstrated an 8-fold increased risk for PI in implants with exposed threads than those with non-exposed threads. The risk increased 4-fold with each additional thread exposed, and splinting was associated with 3.49 times greater risk for incident PI, whereas no other confounding patient-level factor (except for age), or implant macro- or micro-design feature was identified.

The reasons for exploring other potential risk factors were to not only identify them, but to ensure statistically that such confounders might not actually be causing the incident PI instead of the thread exposure. Successful treatment of PI is very demanding. Retaining such success through maintenance proved to be challenging as well as shown by a systematic review and meta-analysis, where there was merely <5% reduction in the risk of implant loss for patients undergoing periodic maintenance therapy, compared to those who did not. [42] In a recent study, patients without maintenance therapy had 4.25 times greater risk for PI. [16] Nonetheless, in the present study, the mean number of annual maintenance visits was found to not be associated with incident PI.

Splinting was found to present a 3.49 times greater risk for PI in multivariate analyses adjusted for duration and mean annual number of maintenance visits (Table 3). This finding is in contrast to the conclusions of a systematic review that a) there was no difference in marginal bone level between splinted and non-splinted implant restorations[43] and b) splinting was associated with lower risk for implant failure. [43] On the contrary, our finding was in agreement with another study that also found greater risk of PI in splinted individual implant restorations, although 3-unit bridges supported by 2 implants had significantly less risk for PI. [44] It should be noted that our study was not able to assess the accessibility for cleaning the implants and their restorations."

Our findings suggest that apart from splinting, the only modifiable statistically significant patient- and implant-related risk factors for incident PI was and the number of implant threads exposed 1 year after prosthetic implant restorations, and the latter impact was dose-dependent. To the best of our knowledge, this is the first time such conclusion has been demonstrated by rigorous research, even though this result seems intuitive. Since the body of literature appears to be void of relevant findings regarding the number of exposed threads, we cannot compare this main finding to prior research results.

Interestingly, severity of periodontitis was not a significant factor for incidence of PI, which is in accord with our group's earlier findings in another study population among patients at the same institution, where only periodontitis Grade C was associated with incident PI. [15] This finding is also in line with the results of the meta-analysis published in 2016, which obviously could not have applied the 2017 World Workshop case definitions for either disease. [42] A systematic review by Doornewaard and co-workers supports our findings that implants surface roughness was not a significant factor in PI. [39] It is noteworthy that we applied the current classification of both periodontitis and PI defined by the 2017 World Workshop, and therefore, any direct comparison to prior research would benefit from reassessing the classification of both diseases in the older studies.

Despite the multitude of operators and potentially changing protocols related to implant placement and restoration at a dental school over a period of 18 years, only 8 (2.9%) implants, from this series, failed. The overall implant level PI rate was 9.6% (and only 4.4% of the implants that did not have any interproximal threads exposed after the initial physiologic bone remodeling), which is well within, actually at the lower end of, the reported range between 0.4% and 85%. [5, 7, 40, 45-47] Importantly, almost one-fifth (19.4%) of the implants with such thread exposure developed PI. This is the same overall rate as that found for implant placed by general practitioners. [48]

Our stringent eligibility criteria were selected to create the test and comparison groups for comparisons as precise and valid as possible. It requires a large source population to conduct such a study, which can be deducted from including only 165 patients from a pool of 4,325 active patients whose charts were screened. The low eligibility rate of 3.8% also leads to potential bias in representing any real-life population. Hence, this study could be perceived as a proof of concept study, although the prevalence of PI corresponds to findings from non-academic studies. The paucity of such large, well-documented source populations may be a reason for the lack of studies like this. A main limitation of this study is the high number and great diversity in skill levels of various categories of providers as well as the variety of implant systems used, some of which have been associated with the prevalence of PI. [26] The same applies to the various prosthetic designs included, some of which may be considered risk indicators for PI. [49]

Furthermore, with this study being primarily based on radiographic assessment, the observed correlation between implant threads not embedded in bone and an increased risk for the onset of PI could not consider soft tissue variables, such as keratinized mucosa width, mucosal thickness, or peri-implant soft tissue height. Moreover, we could not assess the presence/absence of buccal thread exposure due to the utilization of 2-dimensional radiographs allowing only assessment of the interproximal aspects. Finally, inherent in the study design are the limitations of any retrospective study, such as no new data being collected and the data having been recorded for purposes other than this study with no possibility for randomization and recording of prospective observations.

5. CONCLUSION

Within the limitations of this retrospective study, and age being the only non-modifiable risk factor identified, splinting and implant thread exposure (no bone-to-implant contact) after the expected

initial bone remodeling were the only statistically significant potentially modifiable risk indicators for incident PI that were identified in this study. Implants with $\geq$1 thread exposed 1 year after implant restoration were 7.82 times more likely to develop PI than those with no exposed threads. This impact occurred in a dose-response manner, as the risk for PI increased with increasing number of exposed threads, with each additional exposed thread increasing the risk of PI almost 4-fold.

CONFLICT OF INTEREST

All authors declare that they have no conflict of interest related to this manuscript.

AUTHOR CONTRIBUTIONS

Study conception and design: AR, HLW, PGM

Data collection: AR, AS, MQ, LW

Analysis and interpretation of the data: HLW, PGM, WSB, MHAS

Drafting of the manuscript: AR, LW, WSB, MHAS

All authors gave their final approval and agreed to be accountable for all aspects of the work.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

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PRODUCT FOOTNOTES

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FIGURE LEGENDS

Figure 1. Predicted probability of peri-implantitis (Panel A) and of implant failure (Panel B) by the number of exposed threads (N=280 implants).

Footnotes: implant failure, removed or lost or mobile or fractured implant; [41] PI, peri-implantitis; T2, 1 year after implant prosthetic restoration.
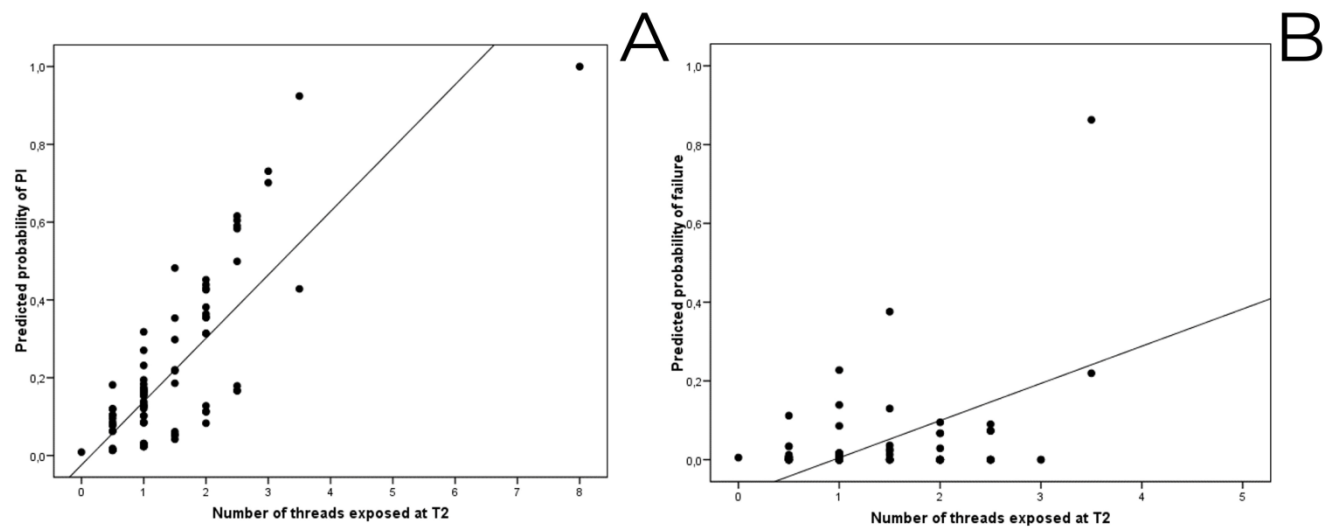
Figure 2. Development of marginal bone loss leading to exposed implant thread (no bone-to-implant contact). Implant placed at bone level (T1) (Panel A). Bone loss after remodeling 1 year after implant prosthetic restoration (T2) (Panel B). Close-up from Panel B showing the most coronal implant thread exposed (Panel C). (Conceptual model not showing any prosthetic restoration.) (Please also see radiographs from study patients with and without interproximal thread exposure in See Supplemental Figures 1 and 2 in online Journal of Periodontology)
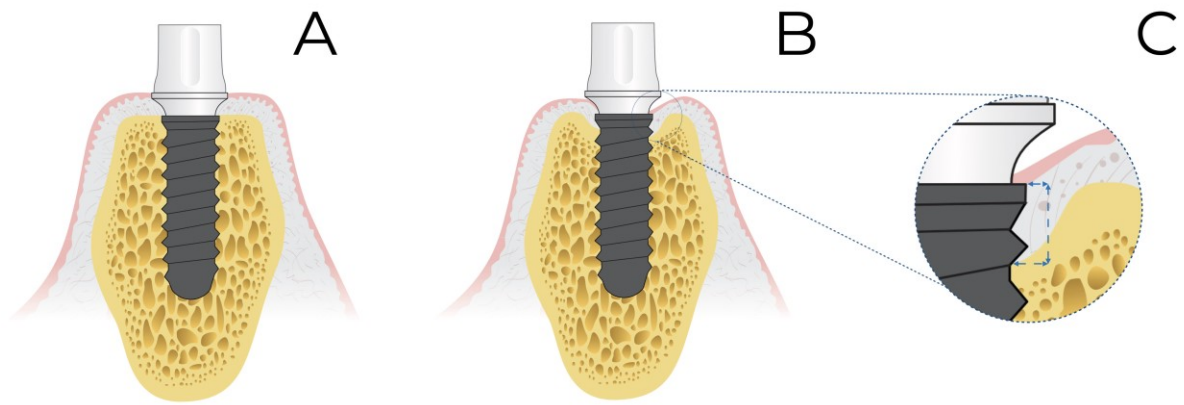
Figure 3. Implant thread pattern types: V-thread, square thread, buttress thread, reverse buttress thread and spiral thread. *Reprinted with permission from Ref.#24 (Fig. 2).*
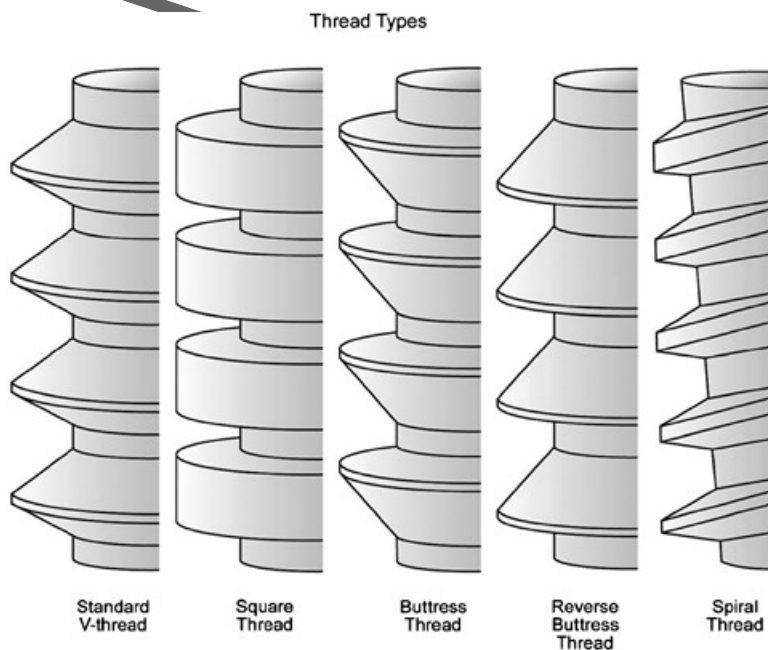
SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

Table 1. Patient- and implant-level characteristics of the implants placed in the165 patients (N=280 implants).

Characteristic	Total Mean ±*SD* or n (%)	Non-exposed (0 Threads Exposed) Mean ±*SD* or n (%)	Exposed (≥1 Thread Exposed) Mean ±*SD* or n (%)
Number of Implants	280	182 (65.0)	98 (35.0)
Patient Age at T0, years	63.0 ± 11.3	62.7 ± 11.1	63.3 ± 11.5
Sex			
Male	123 (43.9)	76 (41.8)	47 (48.0)
Female	157 (56.1)	106 (58.2)	51 (52.0)
Smoking (≥1 cigarette/day)			
No	241 (86.1)	161 (88.5)	80 (81.6)
Yes	39 (13.9)	21 (11.5)	18 (18.4)
Diabetes			
No	245 (87.5)	155 (85.2)	90 (91.8)
Yes	35 (12.5)	27 (14.8)	8 (8.2)
History of Periodontitis			
No	185 (66.1)	122 (67.0)	63 (64.3)
Yes	95 (33.9)	60 (33.0)	35 (35.7)
Duration of Follow-up Period			
T0-T1, months	8.81 ± 4.72	8.41 ± 4.57	9.55 ± 4.94
T2-T3 (radiograph period),years	4.60 ± 2.52	4.51 ± 2.66	4.78 ± 2.25
T0-T4 years	7.67 ± 2.63	7.53 ± 2.45	7.91 ± 2.93
Edentulous Site			
Incisor/Canine (I/C)	20 (7.2)	12 (6.6)	8 (8.2)

Premolar (PM)	110 (39.3)	70 (38.5)	40 (40.8)
Molar (M)	150 (53.6)	100 (54.9)	50 (51.0)
Arch			
Maxilla	99 (35.4)	65 (35.7)	34 (34.7)
Mandible	181 (64.6)	117 (64.3)	64 (65.3)
Bone graft			
No	212 (76.0)	138 (76.2)	74 (75.5)
Yes	67 (24.0)	43 (23.8)	24 (24.5)
Implant Surface			
MTX	105 (37.5)	87 (47.8)	18 (18.4)
TiUnite[TM]	103 (36.8)	32 (17.6)	71 (72.4)
SLA	43 (15.4)	42 (23.1)	1 (1.0)
SLA active	2 (0.7)	2 (1.1)	0
Friadent[®] plus	7 (2.5)	7 (3.8)	0
Nanotite[®]	9 (3.2)	6 (3.3)	3 (3.1)
RBT	10 (3.6)	6 (3.3)	4 (4.1)
CMI	1 (0.4)	0 (0.0)	1 (1.0)
Roughness (S_a)			
Smooth /Minimally rough ($S_a \leq 1.0$ µm)	7 (2.5)	7 (3.8)	0
Moderate (S_a >1.0-2.0 µm)	170 (60.7)	143 (78.6)	27 (27.6)
Rough (S_a >2.0 µm)	103 (36.8)	32 (17.6)	71 (72.4)
Connection			
Internal hexagon	124 (44.4)	99 (54.4)	25 (25.8)
External hexagon	52 (18.6)	8 (4.4)	44 (45.4)
Mores taper	45 (16.1)	44 (24.2)	1 (1.0)
Internal hexagon with Morse taper	20 (7.2)	12 (6.6)	8 (8.2)
Internal tri-lobe	31 (11.1)	12 (6.6)	19 (19.6)
Morse taper cone connection	7 (2.5)	7 (3.8)	0

Neck Design

0.5 Machined collar (Zimmer)	25 (9.0)	17 (9.3)	8 (8.2)
0.5 MTX collar	67 (24.0)	58 (31.9)	9 (9.3)
1.0 Machined collar (Zimmer)	13 (4.7)	12 (6.6)	1 (1.0)
Fine micron feature	9 (3.2)	6 (3.3)	3 (3.1)
Laser-Lok® collar	10 (3.6)	6 (3.3)	4 (4.1)
Misc. Machined collar (Nobel)	22 (7.9)	8 (4.4)	14 (14.4)
Micro-rough shoulder	7 (2.5)	7 (3.8)	0
Micro-threads	29 (10.4)	16 (8.8)	13 (13.4)
Smooth collar	44 (15.8)	43 (23.6)	1 (1.0)
Threaded	53 (19.0)	9 (4.9)	44 (45.4)
Thread Design			
Buttress	46 (16.4)	44 (24.2)	2 (2.0)
Progressive square	7 (2.5)	7 (3.8)	0
Reverse buttress	93 (33.2)	26 (14.3)	67 (68.4)
Square	20 (7.1)	12 (6.6)	8 (8.2)
V-shaped	114 (40.7)	93 (51.1)	21 (21.4)
Implant level			
Bone level	197 (70.6)	110 (60.4)	87 (89.7)
Tissue level	82 (29.4)	72 (39.6)	10 (10.3)
Length			
<11mm	79 (28.3)	52 (28.6)	27 (27.8)
11 - 12mm	131 (47.0)	88 (48.4)	43 (44.3)
>12mm	69 (24.7)	42 (23.1)	27 (27.8)
Diameter			
<4mm	52 (22.4)	34 (20.0)	18 (29.0)
4 - 4.5mm	81 (34.9)	63 (37.1)	18 (29.0)
>4.5mm	99 (42.7)	73 (42.9)	26 (41.9)
Retention			
Cemented	201 (72.0)	134 (73.6)	67 (69.1)
Screwed	75 (26.9)	45 (24.7)	30 (30.9)

Overdenture	3 (1.1)	3 (1.6)	0		
Splinted					
No	204 (72.9)	144 (79.1)	60 (61.2)		
Yes	76 (27.1)	38 (20.9)	38 (38.8)		
Number of Annual Maintenance Visits during Radiograph Period (T2 to T3)					
≤ 1	63 (23.1)	41 (22.8)	22 (23.7)		
$>1 - \leq 2$	104 (38.1)	73 (40.6)	31 (33.3)		
$>2 - \leq 3$	77 (28.2)	47 (26.1)	30 (32.3)		
>3	29 (10.6)	19 (10.6)	10 (10.8)		
Number of Annual Maintenance Visits (T0 to T4)					
≤ 0.5	61 (22.4)	43 (24.0)	18 (19.4)		
$>0.5 - \leq 1$	59 (21.7)	45 (25.1)	14 (15.1)		
$>1 - \leq 1.5$	91 (33.5)	54 (30.2)	37 (39.8)		
>1.5	61 (22.4)	37 (20.7)	24 (25.8)		

Number of or N or number*;* MTX, MicroTextured surface; *SD,* standard deviation; SLA, Sand blasted Large grit Acid etched; T0, time of implant placement; T1, time of prosthetic restoration; T2, 1 year after prosthetic restoration; T3, time of exposure of last radiograph on which peri-implant bone could be clearly visualized; T4, time of last patient visit.

Table 2. Risks of incident peri-implantitis by patient, implant, and prosthesis characteristics during the total study period (T0 to T4): Results from unadjusted binary logistic regression analyses with generalized estimation equations (GEE) (N=2 implants)..

Characteristic	Total Mean ±*SD* or n (%)	Peri-implantitis n (%)	OR	95% CI	*p*-value
Number of implants	280	27 (9.6)			
Study group					
Non-exposed (0 thread exposed)	182 (65.0)	8 (4.4)	1		
Exposed (≥1 thread exposed)	98 (35.0)	19 (19.4)	5.23	2.10 – 13.0	**<0.001*****

Patient age at T0, years	63.0 ± 11.3		0.95	0.92 – 0.99	**0.008****
Sex					
Male	123 (43.9)	16 (13.0)	1		
Female	157 (56.1)	11 (7.0)	0.50	0.18 – 1.40	0.190
Smoking (≥1 cigarette/day)					
No	241 (86.1)	26 (10.8)	1		
Yes	39 (13.9)	1 (2.6)	0.22	0.03 – 1.77	0.154
Diabetes					
No	245 (87.5)	23 (9.4)	1		
Yes	35 (12.5)	4 (11.4)	1.25	0.26 – 5.93	0.783
History of periodontitis					
No	185 (66.1)	15 (8.1)	1		
Yes	95 (33.9)	12 (12.6)	1.64	0.61– 4.43	0.331
Duration of follow-up period					
T0-T1, months	8.81 ± 4.72		1.05	0.93 – 1.18	0.458
T2-T3 (radiograph period), years	4.60 ± 2.52		1.08	0.84 – 1.39	0.546
T0-T4, years	7.67 ± 2.63		1.03	0.79 – 1.33	0.841
Edentulous site					0.552
Incisor/Canine (I/C)	20 (7.2)	1 (5)	1		
Premolar (PM)	110 (39.3)	12 (10.9)	2.33	0.42 – 12.9	0.334
Molar (M)	150 (53.6)	14 (9.3)	1.96	0.26 – 15.0	0.519
Arch					
Maxilla	99 (35.4)	9 (9.1)	1		
Mandible	181 (64.6)	18 (9.9)	1.10	0.38 – 3.21	0.856
Bone graft					
No	212 (76.0)	22 (10.4)	1		
Yes	67 (24.0)	5 (7.5)	0.70	0.23 – 2.13	0.525
Implant surface					0.194
MTX	105 (37.5)	6 (5.7)	1		

TiUniteTM	103 (36.8)	15 (14.6)	2.81	0.82 – 9.61	0.099
SLA	43 (15.4)	2 (4.7)	0.81	0.15 – 4.37	0.801
SLA active	2 (0.7)	0	n/a	n/a	n/a
Friadent® plus	7 (2.5)	0	n/a	n/a	n/a
Nanotite®	9 (3.2)	1 (11.1)	2.06	0.18 – 23.9	0.563
RBT	10 (3.6)	3 (30.0)	7.07	0.77 – 64.9	0.084
CMI	1 (0.4)	0	n/a	n/a	n/a
Roughness (S_a)					
Smooth/Minimally rough (S_a <1.0 μm)	7 (2.5)	0	n/a	n/a	n/a
Moderate (S_a 1.0-2.0 μm)	170 (60.7)	12 (7.1)	1		
Rough (S_a >2.0 μm)	103 (36.8)	15 (14.6)	2.24	0.82 – 6.13	0.115
Connection					0.275
Internal hexagon	124 (44.4)	10 (8.1)	1		
External hexagon	52 (18.6)	6 (11.5)	1.49	0.40 – 5.47	0.550
Mores taper	45 (16.1)	2 (4.4)	0.53	0.11 – 2.62	0.437
Internal hexagon with Morse taper	20 (7.2)	5 (25.0)	3.80	0.82 – 17.7	0.089
Internal tri-lobe	31 (11.1)	4 (12.9)	1.69	0.37 – 7.72	0.499
Morse taper cone connection	7 (2.5)	0	n/a	n/a	n/a
Neck design					0.308
0.5 Machined collar (Zimmer)	25 (9.0)	3 (12.0)	1		
0.5 MTX collar	67 (24.0)	3 (4.5)	0.34	0.04 – 2.78	0.317
1.0 Machined collar (Zimmer)	13 (4.7)	0	n/a	n/a	n/a
Fine micron feature	9 (3.2)	1 (11.1)	0.92	0.06 – 13.5	0.317
Laser-Lok® collar	10 (3.6)	3 (30.0)	3.14	0.27 – 36.9	0.362
Machined collar (Zimmer)	22 (7.9)	2 (9.1)	0.73	0.10 – 5.62	0.765
Micro-rough shoulder	7 (2.5)	0	n/a	n/a	n/a
Micro-threads	29 (10.4)	7 (24.1)	2.33	0.37 -14.9	0.309
Smooth collar	44 (15.8)	2 (4.5)	0.35	0.05 – 2.65	0.309
Threaded	53 (19.0)	6 (11.3)	0.94	0.16 – 5.66	0.943

Thread design					0.080
Buttress	46 (16.4)	2 (4.3)	1		
Progressive square	7 (2.5)	0	n/a	n/a	n/a
Reverse buttress	93 (33.2)	13 (14.0)	3.58	0.77 – 16.6	0.105
Square	20 (7.1)	5 (25.0)	7.33	1.16 – 46.4	**0.034***
V-shaped	114 (40.7)	7 (6.1)	1.44	0.28 – 7.39	0.663
Implant level					
Bone level	197 (70.6)	22 (11.2)	1		
Tissue level	82 (29.4)	5 (6.1)	0.52	0.16 – 1.69	0.274
Length					0.280
<11mm	79 (28.3)	5 (6.3)	1		
11 - 12mm	131 (47.0)	17 (13.0)	2.21	0.76 – 6.41	0.146
>12mm	69 (24.7)	5 (7.2)	1.16	0.29 – 4.67	0.838
Diameter					0.978
<4mm	52 (22.4)	4 (7.7)	1		
4 - 4.5mm	81 (34.9)	7 (8.6)	1.14	0.19 – 6.63	0.888
>4.5mm	99 (42.7)	9 (9.1)	1.20	0.21 – 6.81	0.837
Retention					0.409
Cemented	201 (72.0)	22 (10.9)	1		
Screwed	75 (26.9)	5 (6.7)	0.58	0.16 – 2.11	0.409
Overdenture	3 (1.1)	0	n/a	n/a	n/a
Splinted					
No	204 (72.9)	14 (6.9)	1		
Yes	76 (27.1)	13 (17.1)	2.80	0.98 – 8.02	0.055
Number of annual maintenance visits during radiograph period (T2 to T3)					0.079
≤1	63 (23.1)	5 (7.9)	1		
>1 - ≤2	104 (38.1)	4 (3.8)	0.46	0.11 – 1.96	0.296
>2 - ≤3	77 (28.2)	12 (15.6)	2.14	0.56 – 8.22	0.267
>3	29 (10.6)	5 (17.2)	2.42	0.44 – 13.2	0.309
Number of annual maintenance visits (T0 to T4)					0.280

	Total Mean (±SD) or n (%)	Peri-implantitis n (%)	OR	95% CI	p-value
≤0.5	61 (22.4)	5 (8.2)	1		
>0.5 - ≤1	59 (21.7)	4 (6.8)	0.82	0.17 – 3.92	0.798
>1 - ≤1.5	91 (33.5)	6 (6.6)	0.79	0.16 – 3.95	0.775
>1.5	61 (22.4)	11 (18.0)	2.46	0.64 – 9.44	0.188

N or n, number; CI, confidence interval; MTX, MicroTextured surface; OR, odds ratio; SLA, Sand-blasted Large-grit Acid-etched; T0, time of implant placement; T1, time of prosthetic restoration; T2, 1 year after prosthetic restoration; T3, time of exposure of last radiograph on which peri-implant bone could be clearly visualized; T4, time of last patient visit.

p-value by Wald´s test.

*p<0.05; **p<0.01; ***p<0.001.

Table 3. Risk of incident peri-implantitis by patient, implant, and prosthesis characteristics during the radiograph period (T2 to T3): Results from multi-variate logistic regression with generalized estimation equations (GEE) adjusting for duration and mean annual number of maintenance visits (N=280 implants).

Characteristic	Total Mean (±SD) or n (%)	Peri-implantitis n (%)	OR	95% CI	p-value
Number of implants	280	27 (9.6)			
Study group					
Non-exposed (0 threads exposed)	182 (65.0)	8 (4.4)	1		
Exposed (≥1 thread exposed)	98 (35.0)	19 (19.4)	7.82	1.91 – 32.0	**0.004****
Patient age at T0, years	63.0 ± 11.3		0.95	0.90 – 0.99	**0.016***
Thread design					0.205
Buttress	46 (16.4)	2 (4.3)	1		
Progressive square	7 (2.5)	0	n/a	n/a	n/a
Reverse buttress	93 (33.2)	13 (14.0)	0.35	0.04 – 3.11	0.348
Square	20 (7.1)	5 (25.0)	2.02	0.26 – 15.9	0.506
V-shaped	114 (40.7)	7 (6.1)	0.23	0.20 – 2.28	0.211
Splinted					
No	204 (72.9)	14 (6.9)	1		

Yes	76 (27.1)	13 (17.1)	3.49	1.02 – 12.0	**0.047***
Duration of radiograph period (T2 to T3), years	4.60 ± 2.52		1.19	0.95 – 1.50	0.136
Number of annual maintenance visits during radiograph period (T2 to T3)					0.052
≤1	63 (23.1)	5 (7.9)	1		
>1-≤2	104 (38.1)	4 (3.8)	0.84	0.20 – 3.52	0.811
>2-≤3	77 (28.2)	12 (15.6)	3.23	0.57 – 13.9	0.114
>3	29 (10.6)	5 (17.2)	5.16	0.73 – 36.4	0.101

N or n, number; CI, confidence interval; OR, odds ratio; T2, 1 year after prosthetic restoration; T3, time of exposure of last radiograph on which peri-implant bone could be clearly visualized.

p-values by Wald´s test.

*p<0.05; **p<0.01

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found Pag 1 and 4
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Pag 6-7
Objectives	3	State specific objectives, including any prespecified hypotheses PAG 8
Methods		
Study design	4	Present key elements of study design early in the paper PAG 8-9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection PAG 8
Participants	6	(*a*) Cohort study—Give the eligibility criteria, and the sources and methods

of selection of participants. Describe methods of follow-up

Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls

Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants PAG 8-9-10

		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable PAG 10-11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group PAG 10-11
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at PAG 11
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why PAG 11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy. PAG 11-12
		(*e*) Describe any sensitivity analyses

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. PAG 12
		(b) Give reasons for non-participation at each stage PAG 12
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) PAG 12
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period. PAG 12-13
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

Discussion

Key results	18	Summarise key results with reference to study objectives PAG 13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. PAG 15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. PAG 14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results PAG 14-15

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based. PAG 3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.