Clinical Performance of Dental Implants with a Moderately Rough (TiUnite) Surface: A Meta-Analysis of Prospective Clinical Studies

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Purpose: *A moderately rough anodized titanium implant surface (TiUnite) was introduced in 2000. This review and meta-analysis aimed to assess implant survival and marginal bone level (MBL) changes documented in the literature.* ***Materials and Methods:*** *Repeated literature searches on dental implants were conducted, with the final search on October 7, 2016. The inclusion criteria were: prospective study, minimum of 20 patients, at least 12 months follow-up postloading, and TiUnite implant survival reported. Regression analysis was performed on implant survival and MBL change from implant surgery. Peri-implantitis as defined by the primary authors was reported at the patient level.* ***Results:*** *One hundred six out of 32,519 publications on dental implants met the inclusion criteria. Implant survival rates at 1 year were 99.50% at the implant level and 99.12% at the patient level, and survival rates at 10 years were 95.14% at the implant level and 91.50% at the patient level. Mean MBL change at 1 year was –0.409 mm at the implant level and –0.413 mm at the patient level, and at 5 years, it was –0.886 mm at the implant level and –1.029 mm at the patient level. Nineteen studies (18%) specifically reported peri-implantitis in 64 out of 1,229 patients with a mean follow-up of 47.89 months, indicating a prevalence of 5.20% at the patient level.* ***Conclusion:*** *Based on a meta-analysis of prospective studies, implants with the TiUnite surface provide a predictable treatment modality in a variety of indications.* Int J Oral Maxillofac Implants 2017;32:717–734. doi: 10.11607/jomi.5699

Keywords: *implant surface, implant survival rate, marginal bone level change, meta-analysis, moderately rough, prospective clinical study*

At the outset of modern implant dentistry, implant surfaces were not altered following the machining process, which today is referred to as "turned" or "machined" surfaces.[1] Realizing that the surface characteristics of dental implants are important determinants of short-term and long-term clinical performance,[2] implant manufacturers focused their research and development efforts on optimizing the implant-bone interface. According to several authors, an optimal implant surface would at least exhibit osteoconductive properties,[3] facilitate a strong mechanical and biologic fusion with alveolar bone in shorter periods of time through increased surface roughness,[1,4–6] and ultimately lead to a lower incidence of implant failure within the first year after placement compared with machined surface implants.[7]

A number of surface modifications have been introduced with varying success. Plasma spraying has been applied for coating implants with titanium[8,9] or with osteoconductive materials such as hydroxyapatite[3,10] and other calcium phosphates.[11] The major shortcoming of these additive implant surfaces was delaminations during clinical use. Consequently, subtractive surface modifications involving blasting and acid etching[4] as well as advanced fabrication methods such as anodic oxidation have been applied.[12] These modifications improve osseointegration because they result in moderately rough implant surfaces[13]; however, there is no consensus on the degree of surface roughness that is optimal for bone cell attachment (Table 1).[2]

It was the aim of this meta-analysis to assess the clinical performance of TiUnite, including implant failures, marginal bone level (MBL) changes,[14] and prevalence of peri-implantitis by summarizing data from prospective clinical reports.

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Table 1 Characteristics of Different Implant Surfaces with Respect to Roughness Over a Surface (Sa value) and Surface Area Ratio (Sdr) as Derived from Wennerberg and Albrektsson[31]

Implant surface	Sa [µm]	Sdr [%]
Moderately rough (theoretical)	1.5	50
Machined (original Brånemark implant)	0.9	34
TiUnite	1.1–1.3	37

Table 2 Parameters Derived from Primary Publications

Endpoint	Remark
No. of patients included	Initial no. of patients used for weighting were those included in each study according to an intention to treat approach.
No. and type of implants placed	One-piece, two-piece, and two-piece scalloped implants were included. Zygoma implants were excluded, while regular implants used in combination with Zygoma implants were included.
Follow-up period postloading	Only mean values were recorded; SDs were omitted.
Implant failures at implant and patient level	Only failed implants were considered as failures. Implants lost to follow-up were not considered as failures.
Implant survival rate	The cumulative survival rate (CSR) was used whenever reported. If the publication stated that no implant was lost, a survival rate of 100% was assumed. Survival rates calculated from raw data are marked with an asterisk in the results section (Table 3)
No. of implants and no. of patients assessed for calculating marginal bone level change	Calculating MBL change requires repeated standardized radiographs; consequently, these numbers may differ from the no. of patients and implants included in a study.
Marginal bone level changes with bone levels at implant insertion used as baseline	No calculations were carried out for this parameter.
Biologic complications including peri-implantitis	Peri-implantitis was noted only when explicitly stated in the primary publication and included the following alternative terms: peri-implant infection and peri-implant pathology. Peri-implant mucositis was not scored as peri-implantitis, with two exceptions (Table 8).

MATERIALS AND METHODS

Data Collection

PubMed was repeatedly searched applying the basic search string (implant* OR implants OR implantat* OR fixture) AND (("start date"[PDat] : "end date"[PDat]) AND (jsubsetd[text])) NOT (Animals[Mesh:noexp]) NOT (Review[ptyp]). This search was done for the following time periods: 1995/01/01 to 2009/07/01, 2009/05/01 to 2011/05/15. In May 2011, the search was then switched to a daily alert using the same search string. The resulting hits are fed into a database that also collects references found within other activities and is subject to audit by the manufacturer's notified body (British Standards Institute). The last search date included is 2016/10/07. These searches are required for the Clinical Evaluation of the devices according to MEDDEV 2.7.1 rev 3, which is part of the CE-marking and subsequent Post-Market Surveillance activities. In addition to PubMed, the Cochrane library, the Web of Science, and Google Scholar databases were searched.

Two reviewers independently evaluated all articles identified in the initial search and then discussed whether or not a specific paper should be included. The inclusion criteria were: prospective study design; minimum of 20 patients treated with TiUnite implants; a mean follow-up of at least 12 months postloading; and implant survival reported, or included data sufficient to calculate the implant survival rate. After the titles and abstracts of the initial search results were screened for relevance, the full text of the relevant publications was assessed. Any disagreement was resolved by discussion until a consensus was reached. The clinical outcomes derived from the primary publications are described in Table 2.

Numerical data from primary publications were extracted independently by the two reviewers. In cases of publications with incomplete data, the corresponding authors were contacted by email and requested to provide missing information. If incomplete or no data were available for a particular study, either the missing variable or the entire publication was excluded from analysis.

Statistical Analysis

Given that response to implants at various sites within a given patient may be considered interdependent,[15] data for implant survival and marginal bone level changes were analyzed both at the implant and patient level as reported or calculated where sufficient information was available. If a publication reported more than one treatment group, the groups were considered as separate populations for statistical analysis. For cohorts reported in more than one publication, only the longest follow-up results were included in the analysis. All calculations were carried out using the R software for statistical computing, version 3.0.2 with packages car, metaphor, and lattice.[16]

For estimating a survival function for the included implants, a regression analysis on a parametric class of possible hazard functions reflecting the bathtub curve from reliability theory was performed. The survival function S at time t was defined as $S(t) = Pr(T > t)$, ie, the probability for the lifetime of the object under observation exceeding length t. It is completely determined by the so-called hazard function or hazard rate $\lambda(t) = -S'(t)/S(t)$, where $S'(t)$ is the time derivative of $S(t)$. Considering the large standard deviations of the data available, it was not possible to detect regions where the hazard function was falling or rising. Hence, a constant hazard rate $\lambda(t) = \lambda$ with the negative exponential survival function $S(t) = \exp(-\lambda * t)$ was assumed. The relative frequency of remaining implants after a follow-up time t may be seen as estimates of the survival function $S(t)$ at time t. After applying a logarithmic transformation, the cumulative hazard function $\Lambda(t) = \lambda * t$ was fitted to the logarithmic frequencies using the weighted least-squares method using the treatment group sizes as weights.

To determine the MBL change at different observation periods, metaregression with follow-up time as covariate and inverse variances as weights was applied with negative values for bone loss and positive values for bone gain.

For both implant survival and MBL change, studentized residuals were computed to detect outliers at a level of significance of $\alpha = .05$ with Bonferroni correction for sample size effects.

To score the number of peri-implantitis cases, no common definition was applied, and only author-defined and observed instances were noted. For calculating the prevalence of peri-implantitis, the cases reported in the different studies were counted and related to the total number of patients treated in these populations.

RESULTS

Overall, 32,519 articles were identified, and 106 met the inclusion criteria. Clinical data derived from these publications forming the basis for this review are summarized in Table 3.

Implant Survival

The data derived from the primary publications did not allow computation of a survival function of the Kaplan-Meier type, since in each study, failure counts were available only for a single time interval from the start to the end of the respective observation period. Primary survival data included the cumulative survival rates according to Kaplan-Meier statistics, if available, and otherwise simple arithmetic survival rates at a fixed time point. The statistical analysis revealed maximum deviations of 1.3% between these two types of survival rates. Implant survival rates at the implant level were calculated based on 115 patient populations with a total of 12,803 implants. A total of 98 patient populations with 4,694 patients could be used for determining implant survival rates at the patient level. Following a loading period of 1 year, implant survival was 99.50% at the implant level and 99.12% at the patient level. At 10 years, the rates were 95.14% and 91.50%, respectively (Table 4). The lower survival rates at the patient level were because patients often received more than just one implant. Given the interdependency between both rates, statistical difference between the implant level and patient level could not be tested.

At both the implant and patient levels, two studies[17,18] qualified as outliers with studentized residuals > 2 and P values < .01 after Bonferroni correction (Table 5). Excluding these outliers from the calculation of implant survival, a maximum increase in survival rate at the implant level of 0.16% at 10 years was noted. Similarly, at the patient level, a maximum increase in survival rate of 0.84% at 10 years was calculated.

Marginal Bone Level Change

A total of 62 studies with 4,837 implants and 39 studies with 1,393 patients provided data to calculate MBL change from insertion as the baseline at the implant level and patient level, respectively. Using implant insertion as the baseline and following a loading period of 1 year, MBL change was –0.409 mm at the implant level and –0.413 mm at the patient level. These numbers changed to –0.886 mm and –1.029 mm at 5 years (Table 6). Two patient populations from one study[19] showed positive bone level changes and qualified as outliers with studentized residuals > 2 and P values < .01 after Bonferroni correction at the implant level (Table 7).

Peri-implantitis

Biologic complications associated with implant treatment were reported in 47 publications. Peri-implantitis, peri-implant infection, or peri-implant pathology were reported in 19 studies affecting a total of 64 out

Table 3 List of Included Publications and Data Used for Statistical Analyses

Publication	No. patients (initial)	No. of implants (initial)	Implant type	Mean follow-up (mo)	Implant failures	Implant failures: patient level	Implant survival rate (%)
Achilli et al (2007)[51]	51	120	Replace Select Tapered	12	0	0	100
Agliardi et al (2008)[52]	21	126	Brånemark MkIV; NobelSpeedy Groovy	20	0	0	100
Agliardi et al (2010)[53]	173	692	Brånemark Mk IV; NobelSpeedy Groovy	32	5	5	99.19
Agliardi et al (2014)[54]	32	192	Brånemark Mk IV; NobelSpeedy Groovy	55.53	2	2	98.96
Alfadda (2014)[55]	42	160		12	5	4	96.88
Alvira-González et al (2015)[56]	26 26	54 15	MkIII Shorty MkIII	47.72 47.72	7 0	 0	87 100
Antoun et al (2016)[57]	48	53	NobelSpeedy Groovy	12	1	1	98.1
Aparicio et al[a] (2010)[49]	25	129		24[a]	1	1	99.2
Aparicio et al (2010)[50]	20	104		41	0	0	100
Arnhart et al (2012)[38]	177 	117 82 126	NobelActive NobelActive modified NobelReplace Tapered Groovy	36	5 3 4	5 3 3	95.7 96.3 96.6
Baer et al (2013)[58]	84	115	NobelDirect Groovy, NobelDirect Oval, NobelDirect Posterior	36	2	2	98.3
Bahat (2009)[59]	126	290	Replace Tapered, Replace Select Tapered	36	2	1	99.3
Becker et al (2009)[60]	57	79		24	1	1	98.7
Browaeys et al (2015)[61]	20	80	MkIII; NobelSpeedy	36	0	0	100
Bruno et al (2014)[62]	28	36	NobelActive, NobelReplace Select, NobelPerfect	12	0	0	100
Calandriello and Tomatis (2004)[36]		66	Brånemark Standard, Mk III, Mk IV	12	0	0	100
Calandriello and Tomatis (2011)[63]	33	40	Brånemark Mk III	60	2	2	95
Cooper et al (2015)[64]	49	53	NobelSpeedy Replace	12	7	7	85.7
Cosyn et al (2011)[65]	30	30	NobelReplace Tapered	36	1	1	96
Cosyn et al (2012)[66]	48	49	NobelReplace Tapered	30	3	3	94
Cosyn et al (2016)[67]	22	22	NobelActive	60	1	1	95.45
Cricchio et al (2011)[68]	84	239	Brånemark Mk III, Brånemark Groovy	25.68	3	3	98.7
Cristalli et al (2015)[69]	24	25	NobelActive	12	2	2	92
Davó et al (2013)[70]	40	140	Brånemark, Replace	60	6	4	94.9
de Araújo Nobre et al (2015)[71]	40	88	NobelSpeedy Groovy/Shorty	12	3	2	97
De Rouck et al (2009)[72]	24 25	24 25	NobelReplace Tapered	12	1 2	1 2	96 92
De Santis et al (2015)[73]	55	120	Brånemark Mk III Shorty, NobelSpeedy Shorty	46.8	4	4	96.1
De Santis et al (2016)[74]	62	144	NobelActive	36	0	0	100
den Hartog et al (2011)[47]	31 31 31	31 31 31	Replace Select Tapered, NobelReplace Tapered Groovy, NobelPerfect Groovy	18	1 0 0	1 0 0	96.8 100 100

[a]Baseline radiographs obtained at 8 or 9 days after implant insertion. [b]Baseline radiographs obtained at a later stage, but values were included because all implants were placed at clinical bone level and authors reported implant-bone distance. [c]Baseline radiographs reported to be taken prior to re-entry surgery; however, no exact time is provided.
*Values marked with an asterisk were calculated. ISQ = implant stability quotient.

Patients MBL change	Implants MBL change	Follow-up MBL change (mo)	MBL change (mm)	Biologic complications
	68		–1.24 ± 0.88	1 edema and pain, 1 edema and dysesthesia, 1 bleeding on superficial probing
	42		–1.19 ± 1.01	
	84	12	–0.87 ± 0.47	
51	204		–0.9 ± 0.7	
73	292		–1.2 ± 0.9	
32	64	36	–1.55 ± 0.31	
	126		–1.46 ± 0.19	
				3 implants had bone loss of > 2 mm and suppuration
	34	12	–0.17 ± 1.84	> 95% of the sites showed no bleeding on probing and no visual signs of inflammation
				Some postoperative pain and swelling
				Some postoperative pain and swelling
39	63		–0.89 ± 1.65	1 hypaesthesia, 6 mobile implants, 4 pain, 3 swelling/sore gingiva, 2 peri-implantitis, 1 soft tissue recession, 1 buccal exostosis, 1 sinus perforation
37	58		–0.16 ± 1.06	
34	63		–0.85 ± 1.32	
70	85		–1.07 ± 1.40	1 pain, 1 gingival hyperplasia
	61	36	–1.61 ± 1.40	
	66		–0.59 ± 0.4	
33	38		–1.17 ± 0.90	
40	40		–1.2 ± 0.64	
25			–1.00	
17	17	60	0.19 ± 0.30	
6	14	72	–2.0	2 temporarily mobile implants
23	23		–0.31 ± 0.64	
				“2 implants failed due to excessive bone resorption”; these were not counted as implant loss
30	30		–1.19 ± 0.82	
31	31		–0.9 ± 0.57	
31	31		–2.01 ± 0.77	

Table 3 List of Included Publications and Data Used for Statistical Analyses (cont.)

Publication	No. patients (initial)	No. of implants (initial)	Implant type	Mean follow-up (mo)	Implant failures	Implant failures: patient level	Implant survival rate (%)
den Hartog et al (2011)[75]	31	31	NobelReplace Tapered Groovy	18	1	1	96.8
Di et al (2013)[76]	69	344	Brånemark MK III, NobelSpeedy Groovy	33.7	13		96.2
Ekfeldt et al (2013)[77]	27	75	Brånemark Mk III, Mk IV, Replace Select, Speedy Groovy Tapered	86.4	9		88*
Famili and Zavoral (2015)[78]	30	31	NobelReplace Tapered Groovy	36	1	1	96.7
Finne et al (2012)[79]	56	82	NobelDirect, NobelPerfect One-Piece	36	1	1	98.8
Fischer et al (2009)[80]	32	53	Replace Select	12	1	1	98.1
Francetti et al[a] (2012)[81]	47	196	Brånemark Mk IV, NobelSpeedy Groovy	46.6[a]	0	0	100
Francetti et al (2014)[82]	22	54	NobelReplace Straight, NobelReplace Tapered	81.8	1	1	97.96
Friberg et al (2005)[83]	187	478	Brånemark Mk III, Brånemark Mk IV	12	5	5	98.9
Friberg and Jemt (2015)[84]	165	750	Brånemark	60	9	2	98.55
Froum et al (2011)[85]	60	60	NobelDirect	12	0	0	100
Glauser (2016)[86]	38	102	Brånemark Mk IV	134.4	3	1	97.1
Göthberg et al (2016)[87]	50	150	Brånemark Mk III	36	6		95.7
Gultekin et al (2013)[88]	27	52 52	NobelActive NobelReplace Tapered Groovy	15	0	0	100
Hahn (2011)[89]	30	47	NobelDirect; NobelPerfect	48	1	1	97.9
Hernández et al (2012)[90]	36	118	Brånemark Mk III, NobelDirect	52.96	2	2	98.2
Huber et al (2012)[91]	35	65	Replace Tapered	35	0	0	100
Johansson et al (2009)[24]	52	312	Brånemark Mk III	12	2		99.4
Jokstad and Alkumru (2014)[92]	42	168	Brånemark Mk III, Mk IV	60	4	4	97.6*
Kaminaka et al (2015)[93]	33	34	NobelSpeedy Groovy, NobelReplace, NobelActive	12	0	0	100
Kan et al (2007)[94]	29	38	NobelPerfect	12	0	0	100
Kan et al (2007)[95]	23	23	Replace Select, NobelPerfect	12	0	0	100
Kan et al (2009)[96]	20	20	NobelReplace Tapered Groovy, NobelPerfect Groovy	25.8	0	0	100
Khoo et al (2013)[97]	43	86	Brånemark Mk III	12	0	0	100
Khraisat et al (2013)[98]	24	24	NobelPerfect, Brånemark Mk III	36	0	0	100
Kolgeci et al (2014)[35]	127	289	NobelReplace Tapered	39.6	3	3	99*
Kolinski et al (2014)[26]	55	60	NobelActive	36	1	1	98.3
Kronstrom et al (2014)[17]	36	55	Brånemark TiUnite	36	10	9	81.8
Liddelow and Henry (2010)[99]	25	25	Brånemark Mk III	36	0	0	100
Lopes et al (2014)[100]	23	92	NobelSpeedy Groovy	60	3	3	96.6

[a]Baseline radiographs obtained at 8 or 9 days after implant insertion. [b]Baseline radiographs obtained at a later stage, but values were included because all implants were placed at clinical bone level and authors reported implant-bone distance. [c]Baseline radiographs reported to be taken prior to re-entry surgery; however, no exact time is provided.
*Values marked with an asterisk were calculated. ISQ = implant stability quotient.

Patients MBL change	Implants MBL change	Follow-up MBL change (mo)	MBL change (mm)	Biologic complications
30	30		–0.91 ± 0.61	
47	63		–1.17 ± 1.43	1 abscess, 1 bleeding after removal of excess cement, 1 failure of soft tissue attachment, 2 soft tissue recession, 1 peri-implantitis, 3 discoloration of soft tissue
	48		–1.1 ± 1.0	
36	144	36	–0.97 ± 0.31	3 peri-implantitis
19	49	72	–0.76 ± 0.47	1 transient ipoaesthesia, 1 postoperative swelling, 1 peri-implantitis causing implant failure, 3 peri-implant mucositis, 1 advanced marginal bone resorption
				1 each: altered sensation of lower lip, allergic reaction to gold restoration, phonetic problems, fistula and pus formation, exposed cover screw, hyperplastic gingiva
95	426		–0.6 ± 0.98[a]	12 hyperplasia/inflammation, 3 peri-implantitis surgery, 28 increased bone loss
	65	134.4	–1.66 ± 0.98	Peri-implantitis at 5/102 implants (4/38 pts); 13 implants had non-serious biologic complications
	144	247	–1.67 ± 0.79	
25	43		–0.35 ± 0.13	
	50		–0.83 ± 0.16	
				1 swelling around implant
				28 peri-implant mucositis, 9 peri-implantitis
48			–1.3 ± 1.28	Postoperative swelling and bleeding, 66 inflamed mucosa, 10 local pain
35	140		–1.7 ± 0.81	4 transient pain, 4 transient swelling, 13 bleeding on probing, 3 loose implants
	11	12	–1.85 ± 0.90	No signs of peri-implant inflammation
	11	12	–1.00 ± 1.08	
	12	12	–0.21 ± 0.28	
28	37		–0.1 ± 3.3	1 gingival graying
20	20		–0.505 ± 0.43*	
				4 mucosal inflammation, 5 peri-implant infection
	35		Gain 0.30 ± 1.62	2 recession, 1 swelling, 1 drainage
19	27		–0.86	
12	12		–0.89 ± 0.66	
21	63		–1.9 ± 1.1	2 peri-implant pathology

Table 3 List of Included Publications and Data Used for Statistical Analyses (cont.)

Publication	No. patients (initial)	No. of implants (initial)	Implant type	Mean follow-up (mo)	Implant failures	Implant failures: patient level	Implant survival rate (%)
Maló et al (2007)[101]	23	92	NobelSpeedy	13	2	2	98
Maló et al (2008)[102]	24	57	NobelSpeedy	13	0	0	100
Maló and Nobre (2008)[103]	41	72	NobelSpeedy Groovy	12	1	1	98.6
Maló et al (2011)[104]	127	217	NobelSpeedy Shorty	12	10	6	95
Maló et al (2012)[105]	142	227	Brånemark Mk III, Mk IV, NobelSpeedy	26	7	6	96.7
Maló et al (2014)[106]	103	380	Brånemark Mk III, Mk IV, NobelSpeedy Groovy	60	2	2	99.4
Maló et al (2016)[107]	41	72	NobelSpeedy	36	1	1	98.6
Marra et al (2013)[108]	30	312	NobelSpeedy Groovy, Brånemark Mk III	36	7		97.9
Meloni et al (2012)[109]	20	40	NobelReplace Tapered Groovy	12	0	0	100
Montebugnoli et al (2015)[110]	26	57	NobelReplace Tapered Groovy	17	0	0	100
Nickenig et al (2013)[111]	34	70 63	Replace Straight Groovy Replace Select Straight	62.4	0	0	100
De Araújo Nobre et al (2015)[112]	40	79	NobelSpeedy Groovy NobelSpeedy Shorty	12	3	2	97
Östman et al (2005)[37]	20	123	Brånemark Mk III, Brånemark Mk IV, Replace Select Tapered	12	1	1	99.2
Östman et al (2007)[113]	48	115	NobelDirect, NobelPerfect	12	6		94.8
Östman et al (2008)[114]	77	180	Brånemark	12	1	1	99.4
Östman et al (2012)[115]	46	121	Brånemark Mk III, Mk IV	120	1	1	99.2
Parel and Schow (2005)[116]	35	45	NobelDirect	14	1	1	97.8
Pozzi et al (2012)[117]	27	81	NobelSpeedy Replace, NobelSpeedy Groovy	43.3	3	1	96.3
Pozzi et al (2014)[118]	34	44 44	NobelActive NobelSpeedy Groovy	16	0	0	100
Pozzi and Moy (2014)[119]	66	136	NobelSpeedy Replace, NobelSpeedy Groovy, NobelActive	43.96	2	2	98.53
Pozzi et al (2014)[120]	51	202	NobelSpeedy Groovy	12	1	1	99.5*
Pozzi et al (2014)[121]	34	44 44	NobelActive NobelSpeedy Groovy	40	0	0	100
Pozzi et al (2015)[122]	54	118	NobelReplace Conical Connection	38.5	2	2	98.3
Rao and Benzi (2007)[123]	46	51	Replace Select Tapered	12	0	0	100
Rocci et al (2013)[124]	22	66	Brånemark Mk II, Mk III, Mk IV	108	3		95.5
Rompen et al[a] (2007)[125]	41	54	Replace Select Groovy	19.6[a]	0	0	100
Sato et al (2014)[27]	63	93	NobelDirect	36	0	0	100
Schincaglia et al (2008)[126]	30	30	Brånemark Mk III	12	1	1	97
Shibly et al (2010)[19]	30 30	30 30	NobelReplace Straight Groovy	24	2 1	2 1	93.3 96.7
Slagter et al (2016)[127]	40	40	NobelActive	18			100

[a]Baseline radiographs obtained at 8 or 9 days after implant insertion. [b]Baseline radiographs obtained at a later stage, but values were included because all implants were placed at clinical bone level and authors reported implant-bone distance. [c]Baseline radiographs reported to be taken prior to re-entry surgery; however, no exact time is provided.
*Values marked with an asterisk were calculated. ISQ = implant stability quotient.

Patients MBL change	Implants MBL change	Follow-up MBL change (mo)	MBL change (mm)	Biologic complications
9	36		–1.9 ± 1.5	2 peri-implant pathology
	48	12	1.6 ± 1.1	peri-implant pathology (3 implants in 3 patients)
108	172		–1.27 ± 0.67	
				6 peri-implant pathology
50	260		–0.71 ± 0.42	13 peri-implant pathology
	53	36	–1.37 ± 0.94	Peri-implant infection at 3 implants (3 patients); presence of peri-implant pockets > 4 mm, with concurrent presence of bone loss and bleeding on probing
				2 peri-implant mucositis
34	70 63		–0.7 –1.4	
				No suppuration
				1 extensive gingivitis and candidiasis
				Frequently: gray coloring of gingiva, exposure of TiUnite surface, radiographic bone loss
				1 anesthesia of inferior alveolar nerve
				1 mucositis and bone loss due to allergic reaction to superstructure, 11 bleeding on probing, 2 pus
	78		–0.6 ± 0.3	
34	44 44		–0.51 ± 0.34 –1.10 ± 0.52	
26 25			–0.80 ± 0.29 –0.71 ± 0.25	2 pain; 1 pain, swelling and suppuration
34	44 44		–0.67 ± 0.39 –1.24 ± 0.47	6 exposure of cover screw, 1 peri-implant mucositis
52	116		–0.68 ± 0.59	1 peri-implantitis
				3 reduction of ISQ and regain
				Minor or no postsurgical swelling
	62		Gain 0.40 ± 1.46	
29	29		–0.98 ± 0.52	Healing with minor discomfort
49	49		Gain 1.00 ± 0.20 Gain 1.19 ± 0.26	
				1 pt with bone sequestrum, no complications during follow-up

Table 3 List of Included Publications and Data Used for Statistical Analyses (cont.)

Publication	No. patients (initial)	No. of implants (initial)	Implant type	Mean follow-up (mo)	Implant failures	Implant failures: patient level	Implant survival rate (%)
Stephan et al (2007)[128]	26	78	Brånemark Mk III	19	0	0	100
Tallarico et al (2015)[129]	40	200	NobelSpeedy Groovy	63.8	7		96.5
Tallarico et al (2016)[130]	40	116	NobelReplace	36	1	1	98.98
Thoma et al[b] (2014)[131]	30	94	Brånemark Mk III, Mk IV	12	0	0	100
Turkyilmaz et al (2007)[132]	19 10	36 23	Brånemark Mk III	48	2 1	2 1	94.4 95.7
Turkyilmaz et al (2012)[133]	26	52	Brånemark Mk III	84	0	0	100
Urban and Lozada (2010)[134]	79	245	Brånemark Mk IV, Brånemark Mk III, NobelReplace, NobelSpeedy	60	1	1	99.6
Urban et al (2011)[135]	22	58	Brånemark System	45.88	0	0	100
Urban et al[c] (2012)[18]	92	92	Brånemark Mk III Groovy	12	15	15	82.6
Urban et al (2013)[136]	25	76	Brånemark System	20.88	0	0	100
van Steenberghe et al (2005)[25]	27	184	Brånemark Mk III	12	0	0	100
Van Nimwegen et al (2015)[137]	40	80	NobelPerfect Groovy NobelReplace Groovy	60	2	1	97.5
Villa and Rangert (2007)[138]	33	76	Brånemark Mk III, Brånemark Mk IV, NobelSpeedy	12	2	2	97.4
Yamada et al (2015)[139]	50	290	NobelActive	12	4	2	98.6
Zembić et al (2012)[140]	47	57	NobelDirect	12.8	1	1	98
Zembić et al (2013)[141]	22	40	Brånemark	67.2	3	2	89.3

[a]Baseline radiographs obtained at 8 or 9 days after implant insertion. [b]Baseline radiographs obtained at a later stage, but values were included because all implants were placed at clinical bone level and authors reported implant-bone distance. [c]Baseline radiographs reported to be taken prior to re-entry surgery; however, no exact time is provided.
*Values marked with an asterisk were calculated. ISQ = implant stability quotient.

Table 4 Results of Implant Survival Regression Analysis

	Years				
	1	2	3	5	10
Implant level	99.50	99.01	98.52	97.54	95.14
Patient level	99.12	98.24	97.37	95.66	91.50

Results are reported as estimated survival rates at implant and patient levels based on 115 study populations having received a total of 12,803 implants (implant level) and 98 study populations comprising 4,694 patients (patient level).

Table 5 Outliers for Implant Survival at Implant and Patient Levels

Publication	Implant survival rate (%)	Implant level analysis			Patient level analysis		
		Studentized residuals	Unadjusted *P* value	Corrected *P* value	Studentized residuals	Unadjusted *P* value	Corrected *P* value
Kronstrom et al (2014)[17]	81.8	–4.924	< .01	< .01	–5.539	< .01	< .01
Urban et al (2012)[18]	82.6	–4.312	< .01	< .01	–5.843	< .01	< .01

Patients MBL change	Implants MBL change	Follow-up MBL change (mo)	MBL change (mm)	Biologic complications
20		63.8	–1.71 ± 0.42	Pain and swelling in 2 pts (without suppuration) who had 10 implants; PI in three patients
20		63.8	–1.51 ± 0.36	
32		36	–1.35 ± 0.21	No major biologic complications; 3 pts had mucositis with BoP after 6 months, which was resolved upon oral hygiene improvement
30	94		–0.05 ± 0.32	
26	56		–1.11	
24	48		–1.31 ± 0.2	
				1 increased bone loss
92	92		–0.48[d]	
	125		–1.15 ± 1.15	4 inflamed gingiva, 4 postoperative pain, 1 marginal fistula
16	32	60	–3.2 ± 1.1	2 implants were lost in the scalloped group due to ongoing bone loss peri-implantitis after 4 years
19	38	60	–1.5 ± 0.8	
32	73		–0.91 ± 1.50	
48	278		–0.32 ± 0.43	1 minor postoperative bleeding
40	50		–1.6 ± 1.2	1 fistula, periodical pain of the peri-implant mucosa

Table 6 Marginal Bone Level Change (mm) at Different Time Points at Implant (62 Studies with 4,837 Implants) and Patient Level (39 Studies with 1,393 Patients)

	Years				
	1	2	3	5	10
Implant level	–0.409	–0.529	–0.649	–0.886	–1.487
Patient level	–0.413	–0.567	–0.720	–1.029	–1.800

Table 7 Outlier for MBL at Implant Level

Publication	Population (n = 49 patients)	Implant level analysis			Patient level analysis		
		MBL change (mm)	Unadjusted *P* value	Corrected *P* value	Studentized residuals	Unadjusted *P* value	Corrected *P* value
Shibly et al[19]							
Delayed loading	1.00 ± 0.20	5.418	< .01	< .01	9.044	< .01	< .01
Immediate loading	1.19 ± 0.26	4.334	< .01	< .01			

Table 8 Studies Reporting Peri-implantitis

Publication	Patients initial	Implants initial	Follow-up (mo)	Peri-implantitis – description	Peri-implantitis – patients
Arnhart et al (2012)[38]	177	325	36	Peri-implantitis: 2 patients	2
Finne et al (2012)[79]	56	82	36	Peri-implantitis: 1 patient	1
Francetti et al (2014)[82]	22	54	81.8	Peri-implantitis: 1 patient/1 implant; periimplant mucositis: 1 patient/3 implants	1
Francetti et al (2012)[81]	47	196	46.6	Peri-implantitis: 2 patients/3 implants	2
Friberg and Jemt (2015)[84]	165	750	60	Peri-implantitis: 3 patients	3
Glauser (2016)[86]	38	102	134.4	5 implants with peri-implantitis in 4 patients	4
Hernández et al (2012)[90]	36	118	52.96	Peri-implantitis: 9 patients; peri-implant mucositis: 28 patients (5 and 12 with oral lichen planus)	9
Kolgeci et al (2014)[35]	127	289	39.6	Peri-implant infection: 5 restorations	5
Lopes et al (2014)[100]	23	92	60	Peri-implant pathology: 2 patients/2 implants	2
Maló et al (2007)[101]	23	92	13	Peri-implant pathology: 2 patients/2 implants	2
Maló and Nobre (2008)[103]	41	72	12	Peri-implant pathology (3 implants in 3 patients)	3
Maló et al (2012)[105]	142	227	26	Peri-implant pathology: 6 patients/6 implants	6
Maló et al (2014)[106]	103	380	60	Peri-implant pathology: 13 patients/13 implants	13
Maló et al (2016)[107]	41	72	36	Peri-implant infection at 3 implants (3 patients)	3
Meloni et al (2012)[109]	20	40	12	Peri-implant mucositis: 2 patients/4 implants	2[a]
Pozzi et al (2014)[121]	34	44	40	Peri-implant mucositis: 1 patient/1 implant	1[a]
Pozzi et al (2015)[122]	54	118	38.5	Peri-implantitis: 1 patient/1 implant	1
Tallarico et al (2015)[129]	40	200	63.8	Peri-implantitis in 3 patients	3
Van Nimwegen et al (2015)[137]	40	80	60	2 implants lost in 1 patient after ongoing bone loss as a result of peri-implantitis	1
Total	1,229	3,333	Mean: 47.89		64

[a] Peri-implant mucositis counted as peri-implantitis. In Meloni et al,[109] the two patients were described as having "peri-implant inflammation." In Pozzi et al,[121] the treatment of the patient was a disassembly of the reconstruction, and therefore, the patient was counted as having peri-implantitis.

of 1,229 patients, indicating a prevalence of 5.20% at the patient level (Table 8).

DISCUSSION

This meta-analysis intended to provide a comprehensive overview on the clinical performance of dental implants with a moderately rough anodized (TiUnite) surface with respect to implant survival, marginal bone level change, and prevalence of peri-implantitis. Since market launch 15 years ago, a broad variety of clinical studies with substantial design differences have been conducted using this implant surface. To provide an unbiased analysis, only prospective studies were considered, statistical outliers were not excluded, and no interpretation of primary data was performed.

Implant Survival

The implant survival rates were 99.50% at the implant level and 99.12% at the patient level after 1 year and 95.14% and 91.50%, respectively, after 10 years of loading. The general trend toward lower survival rates at the patient level compared with the implant level was expected, as patients frequently received more than one implant. The differing behavior of the implant level and patient level survival rates may have partly resulted from this fact; in addition, data available and used to calculate either survival function were not identical. From a prosthodontist perspective, however, implant loss may not necessarily affect the survival and success of a specific restoration.[20]

As pointed out in a recent review, implant success not only constitutes a function of the surface but also depends on treatment planning, surgical skills, patient behavior, and prosthetic design.[2] The high survival rates 12 months postloading reported in the identified studies are indicative of the predictive nature of the osseointegration of TiUnite implants independent of the clinical indication and the chosen implant design. It may be argued that late failures are primarily related to patient characteristics such as insufficient hygiene

measures and to prosthetic limitations. Indeed, Roccuzzo and coworkers showed in a 10-year clinical study that the patients' periodontal condition had an effect on implant survival rates, with compromised patients achieving survival rates of approximately 97%, whereas 100% survival was reached for periodontally healthy subjects.[21] However, periodontitis and peri-implantitis are not the same disease. On the contrary, Becker and coworkers showed that periodontitis and peri-implantitis have a significantly different gene expression pattern, and thus, are likely to involve a separate and distinct set of molecular pathways.[22]

Two studies qualified as statistical outliers with respect to the implant survival rate at both the implant and patient levels. A very low 1-year survival rate of 82.6% was reported for implants immediately placed in molar sites associated with various bone augmentation procedures,[18] while mandibular overdentures supported by one or two implants achieved an 81.8% survival rate after 3 years in the study of Kronstrom et al.[17] Both studies may be considered as having a high risk due to limited bone quality and/or quantity and a challenging treatment concept, respectively.

It is difficult to properly compare the findings of this work with summaries on other current implant surfaces because results from similar-sized patient cohorts have not been published so far, and, according to a recent review, there are no well-documented studies showing the superiority of a specific implant surface.[2] One prospective[15] and one retrospective[23] clinical study on the 10-year performance of SLA (Straumann), a specific sand-blasted, large-grit, acid-etched implant surface, were found in the literature. These investigations were based on comparably small patient cohorts of 374 and 511 implants and showed implant level survival rates of 99.7% and 98.8%, respectively. Furthermore, TiUnite implants are often associated with more demanding treatment protocols: Two studies were based on the now-abandoned "teeth in an hour" protocol,[24, 25] while 55 studies used an immediate placement and/or loading concept.

A retrospective patient chart-based analysis recently compared the performance of different implant brands in a Swedish cohort of 11,311 implants placed in 2,765 patients.[20] The authors described an early implant failure rate (prior to prosthetic reconstruction) of 1.4% and a late failure rate of 2.0% after 8.9 years. While the failure rate for late failures seems to be realistic on an implant level basis, the initial failure rate reported by Derks and coworkers appears to be considerably higher than that demonstrated in this review.

Marginal Bone Level Change

Using implant insertion as the baseline, a mean bone loss of –0.409 mm at the implant level and –0.413 mm at the patient level was found after 1 year of loading. These values were –0.886 mm at the implant level and –1.029 mm at the patient level at 5 years postloading, which is in accordance with widely accepted implant success criteria.[14] In light of these findings, future assessments of bone remodeling should use bone level at implant insertion as a reference, as otherwise the most relevant time period may be missed.

Three publications reported marginal bone level gain ranging from 0.30 to 1.19 mm,[19,26,27] which is contrary to the negative bone level changes observed in all other studies. In two cases,[26, 27] the standard deviations of these measurement values were at least three times higher compared with the absolute value, which may be indicative of measurement errors potentially due to radiographic inconsistencies. Shibly and coworkers, however, reported a consistent bone gain 24 months after implant placement with moderate standard deviations, indicating a real effect that may be explained by the bone regeneration procedures that were performed.[19] Based on the statistical analysis performed in this review, only the latter publication qualified as an outlier.

Peri-implantitis

Although peri-implantitis is frequently reported to affect the success and survival rates of implant-supported reconstructions, to date, no uniformly applied definition exists with respect to clinical symptoms leading to its diagnosis.[28–31] As increasing evidence emerges indicating that marginal bone loss is dependent on complications to treatment and on immunologic reactions, it seems questionable whether or not peri-implantitis constitutes a disease at all. Out of all studies selected in this review, only 19 comprising a total of 1,229 patients who had been followed for a mean period of 47.89 months explicitly mentioned the occurrence of peri-implantitis in a total of 64 patients resulting in a prevalence of peri-implantitis of 5.20%. However, it may also be argued that peri-implantitis simply did not occur in the remaining studies, which would consequently yield a prevalence of 1.36%. The prevalence of peri-implantitis calculated in this analysis is similar to the range of 2%, which has previously been suggested for TiUnite.[32,33]

Cautious interpretation of this finding is mandatory, as peri-implantitis was only scored when reported by the authors of primary publications despite the fact that they acted on different scales. Furthermore, although most papers included in this meta-analysis had defined peri-implantitis as an increase in probing depth or bleeding on probing, these diagnostic parameters have themselves been questioned.[34] In addition, two potential sources of error relate to the numbers given earlier. Kolgeci and coworkers focused on prosthetic restorations as a statistical unit, and it was assumed

that each of the affected patients had only one restoration.[35] Similarly, Calandriello and Tomatis did not include the number of patients treated in their study, but used implants as a unit for reporting and analysis.[36]

This prevalence of peri-implantitis with TiUnite implants reported here is comparable to the rates reported for the sand-blasted, large-grit, acid-etched implant surface, which in a retrospective analysis showed the prevalence of peri-implantitis to be 1.8% in a cohort of 303 orally healthy patients with 511 implants.[23] By contrast, titanium plasma-coated implants seem to be more susceptible to peri-implantitis, reaching a prevalence of 9.7% of the surviving implants after a follow-up time of 12 to 23 years, and seemed to be more susceptible to marginal bone loss compared with modern implant surfaces.[8]

Specifics of TiUnite Implants

Several factors have to be taken into account when interpreting the presented data. Because the focus of this report was the implant surface, all conventional implant types of the broad portfolio associated with the TiUnite surface were included. However, the small number of outliers indicates that TiUnite implants perform consistently in all clinical indications and independently of the chosen macrodesign.

Nevertheless, differences in implant geometry (parallel-walled, root-form, conical), thread design, implant-abutment connection (trichannel, external hexagon, internal conical hexagon), and cervical texture (polished, moderately rough) may have resulted in a selection bias. Conical implants, for instance, are preferred in low-quality bone,[37] and implants with more aggressive threads are frequently chosen for immediate loading protocols.[26,38] These selection processes may be considered problematic in prospective clinical trials since clinicians do not use the entire implant portfolio in a single study; nevertheless, such decision-making best reflects daily clinical practice.

Another factor to be taken into consideration when interpreting these results is that some of the studies included in the analysis were carried out in patients with advanced bone resorption and a combination of conventional and zygomatic implants. The restorations in these patients may be considered at greater risk of failure due to the compromised anatomical situation, and to the tilted and strongly palatal positioning of the zygomatic implants. Specifically, unfavorable biomechanical loading causing technical complications such as screw loosening[39] and compromised access for hygiene measures[40] may ultimately lead to increased failure rates for the conventional implants.[41]

Inclusion of one-piece implants in this analysis may be considered as another confounding variable. Initially, one-piece implants had been anticipated to show less marginal bone loss compared with two-piece implants due to elimination of the micromotion at the implant-abutment interface.[27,42] However, several studies showed that the clinical use of one-piece implants led to higher bone loss,[43,44] possibly due to the detrimental effect of the intraoral implant preparation.[45]

Furthermore, this analysis included dental implants with a unique scalloped shoulder design originally developed for maintaining interdental bony peaks and for optimizing esthetics.[46] Not surprisingly, as this specific implant type requires advanced surgical skills as well as proper patient selection and preparation, greater bone loss was reported for this implant design when these prerequisites were not met.[47,48]

Another very specific treatment modality associated with TiUnite implants are immediate restorations following pure digital planning according to the teeth-in-an-hour concept.[25] Inevitable discrepancies between the prefabricated prostheses and the actual implant positions led to considerable misfit stresses, causing severe prosthetic complications and increased marginal bone loss.[24] Because of its poor performance, the teeth-in-an-hour concept has been abandoned by the manufacturer.

Limitations

The validity of any meta-analysis largely depends on the quality of reporting in the included primary publications. In order to gather robust data, strict inclusion criteria were applied; unclear data were discussed internally prior to contacting corresponding authors, and ultimately, uncertain data were excluded. While implant survival constituted a reliably reported parameter, reporting marginal bone level changes and biologic complications revealed uncertainties.[49,50] In light of a variety of methods applied by authors for calculating MBL change, no calculations beyond linear regression with time as covariate were carried out.

Similarly, peri-implantitis was noted as a biologic complication only if explicitly mentioned. Technical complications were not considered, as the focus of this review was on the performance of the implant surface.

Based on the data derived from the primary publications, a regression analysis was performed. Alternatively to this approach, the relative frequency of remaining implants or patients over all studies ending at a specific time point as well as confidence intervals could have been computed and interpolated linearly for estimating a survival function.

The quasi-linear shape of the survival function estimates is partly due to mathematics, as the exponential curve is approximately linear near the argument zero. In addition, an eventual flattening of the slope could not be detected by statistical means because of the scarcity of available data for the years 6 to 10. Consequently,

cautious interpretation of data beyond 5 years of follow-up is mandatory. Nevertheless, the applied exclusion criteria and the small number of data sets available to extrapolate the results constitute an inherent risk of bias.

CONCLUSIONS

This meta-analysis, exclusively based on prospective clinical reports on dental implants with a TiUnite surface, demonstrates high implant survival and good marginal bone level maintenance. The prevalence of peri-implantitis is low and similar to results reported with other moderately rough surface implant brands. The results of this analysis indicate that implants with a TiUnite surface provide a predictable treatment modality in a variety of indications.

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