Science First

Volume 4, Issue 2 2017

TiUnite®

Setting the scientific standard. Again.



Cover

Nobel Biocare has set the scientific standard for high level evidence to back our moderately rough TiUnite implant surface. Background image left: red blood cells and fibrils of the fibrin meshwork over the titanium oxide surface of TiUnite. Image right: confocal microscopy z-stack projection shows fluorescent staining of fibrin (green), nuclei of white blood cells (blue) and platelets (red) on a TiUnite surface implant (NobelParallel CC).

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TiUnite[®] – osseointegration

TiUnite is a high performance implant surface that supports osseointegration – even under the most challenging conditions. It is characterized by a moderately rough thickened titanium oxide layer with high crystallinity and phosphorus content, with ceramic-like properties and micropores. The properties of TiUnite ensure osteoconductivity leading to fast apposition of newly formed bone.

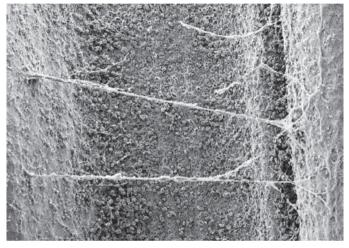
Developed for demanding situations

To address the challenge of increasingly demanding loading protocols, a surface that would speed up bone apposition was needed. The solution was TiUnite – an increased oxide layer formed by spark anodization of the cold-worked, commercially pure grade 4 titanium, altering the chemical composition of the surface and degree of crystallinity.¹ Containing anatase and rutile, TiUnite¹ is associated with greater bone growth compared to both the amorphous and rutile form², and TiUnite provides stronger bone anchorage compared to machined surfaces.^{3, 4}

Fast and strong osseointegration

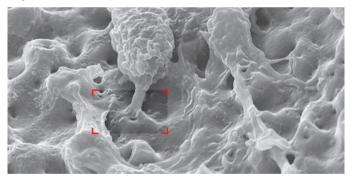
TiUnite's porous surface is an optimized substrate for the migration of osteogenic cells along the surface.⁵ Moreover, the osteoblasts, being polarized cells, secrete collagen matrix only perpendicularly to the surface – and thereby directly into the open TiUnite pores.⁵ This has been shown clinically in trephined-out mini implants in healed sites before placement of traditional implants and restoration.⁶

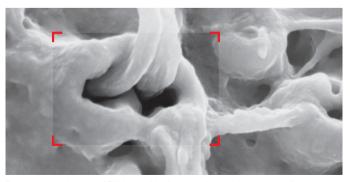
TiUnite influences the cascade of cellular and molecular processes promoting differentiation of stem cells into osteogenic cells and new bone growth.^{4, 7, 8} Through early induction of osteoclastic differentiation, TiUnite was shown to accelerate the maturation of the bone-to-implant interface.⁸ This, in turn, led to higher total bone area and bone to implant contact versus machined implants. Stronger upregulation of molecular pathways involved in osteogenesis mimic histological observations and further explain the osteoconductivity of TiUnite and its higher implant stability.^{7,8}



TiUnite is osteoconductive and new bone formation occurs rapidly and directly on and along the implant surface.

Image © 2017 Nobel Biocare Services AG





Bone grows into the pores of TiUnite, resulting in a strong interlock between its surface and bone. Images reproduced with permission. © Schüpbach Ltd, Switzerland.

TiUnite® - setting the scientific standard

TiUnite is one of the most clinically researched implant surfaces on the market. Since its launch in 2000, it has been clinically documented in more than 465 publications on 382 clinical studies evaluating more than 89,500 implants, over 22,600 patients, and 11.2 years of longest mean follow-up.^a Now, TiUnite is not only backed by a large quantity of evidence, it is also backed by the strongest evidence – a meta-analysis that confirms high implant survival and stable bone with TiUnite surface.⁹ The superiority of TiUnite compared with machined implants in terms of survival was documented in a previous meta-analysis. More than 19 million implants with TiUnite surface have been sold worldwide.^b Wide scientific and clinical documentation in peer-reviewed journals and the even wider clinical experience with TiUnite implants in patients globally is a testimony to its success.

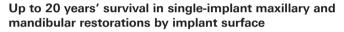
Key findings of prospective and retrospective clinical studies are:

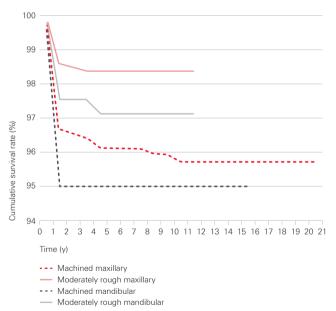
- Proven longevity with clinical follow-up of 10 or more years.¹⁰⁻¹⁴
- Significantly lowered early failure rates upon the introduction of TiUnite compared to historical survival data for machined implants.¹⁵
- Significantly lowered overall risk of failure^{16, 17} without compromise to hard tissue when compared to machined implants.¹⁷
- 97.1 % weighted mean survival in 6 studies with 10–11.2 years' mean follow-up, which compares well to a 97.4 % weighted mean for all studies regardless of follow-up.^a
- Stable marginal bone levels after the initial bone remodeling phase, over the medium and long-term.^{10, 14}

Introduction of TiUnite triggered reduction in early implant failures

In 2001 until 2004, the Brånemark Clinic, Göteborg, Sweden, gradually introduced moderately rough surface implants, primarily TiUnite. In their 28 years of clinical evaluation, 27,914 machined Brånemark implants and 11,163 predominantly TiUnite moderately rough surface implants were placed. Of the moderately rough implants, 10,744 were Brånemark System gradient TiUnite implants, with the remaining implants being an undisclosed number of NobelReplace TiUnite or other moderately rough surface implants.¹⁵ The authors observed that the mean incidence of early failures was 2.1% when implants with a TiUnite surface were used versus 2.4% for other moderately rough surface, e.g. TiUnite, was a key contributor to reducing rates of early failure.

Rates of implant failures decreased significantly in the period 2003–2012 compared with 1986–2002, reducing from 11.4% to 2.1% in the maxilla, and from 4.5% to 2.2% in the mandible (p<0.05).¹⁵ In the same clinic, patient cumulative survival rate (CSR) for maxillary implant placement was 95.8% for machined surfaces at 15 years' follow-up, and 98.5% for moderately rough surfaces at 10 years.¹⁶ The survival advantage of predominantly TiUnite moderately rough surfaces seems to continue over time (see figure).

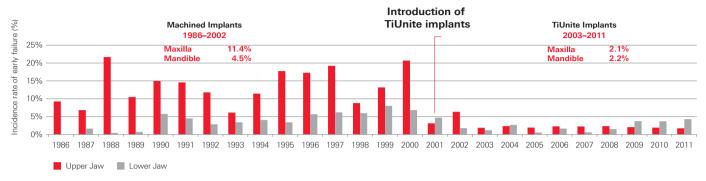




Data from studies comprising >25 patients at last follow-up.16 Figure reproduced with permission. Copyright © 2016 by Quintessence Publishing Co Inc.

^a TiUnite literature search. Nobel Biocare Services AG. July, 2017.

^b Sales data. Nobel Biocare AG. September, 2017.



Lower incidence of early failures upon the introduction of moderately rough surface, primarily TiUnite surface implants, was significant in both jaws (p<0.05). Figure courtesy of Professor Torsten Jemt, Sweden.

High survival without compromise to hard tissue

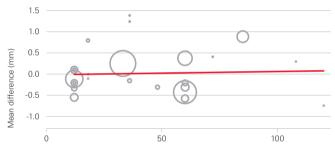
The advantage of TiUnite for implant survival has been continually confirmed over the full breadth of scientific evidence. Looking to a meta-analysis of 38 studies, the relative risk (RR) of implant failure was greater for machined implants versus TiUnite, statistically significant in both jaws: 2.54 times greater in the maxilla and 2.51 times greater in the mandible.¹⁷ There were no statistically significant effects of machined implants on the marginal bone loss (RR 0.02, p=0.82) compared to TiUnite surface implants over the long-term.¹⁷

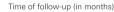
Stable marginal bone levels long-term

Glauser investigated 102 TiUnite surface implants placed predominantly in soft bone and immediately loaded. At 11 years of follow-up, 26 of 38 patients with 66 implants were available for clinical, radiographic and microbiological evaluations.¹⁴ The CSR was 97.1%, with all three implant failures occurring within the first 6 months. After initial bone remodeling during the first year, the mean marginal bone remodeling up to the 11-year follow-up was –0.47 mm, indicating stable bone levels over 10 years.¹⁴

Similarly, Östman et al. reports mean marginal bone change between -0.4 mm at one year, and only -0.3 mm additional bone loss during the subsequent 9 years, and >99% implant survival at 10 years of follow-up.¹⁰ Patients were partially and fully edentulous, 20% were immediately loaded and 80% followed a staged protocol.¹⁰ If needed, patients were enrolled in an oral hygiene program.

In fact, minimal marginal bone loss after the first year is shown in medium to long-term studies with TiUnite surface implants reporting mean bone level change both at 1 year and latest follow-up. In no studies (see table on page 7) did marginal bone loss exceed -0.1 mm per year, which is well within the established ranges of implant success that have been defined by expert consensus.^{18, 19} Scatter plot for meta-regression of mean difference in marginal bone loss between machined versus TiUnite surface implants according to follow-up time





Regression analysis shows no differences of marginal bone loss between machined and TiUnite surface implants.¹⁷ Differences were calculated for each study as mean marginal bone loss of machined implants minus mean marginal bone loss of TiUnite surface implants. The sizes of the circles indicates the relative weights of each included study.¹⁷

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Reference	Mean follow-up time [years] ^a	No. of implants	No. of patients	Implant survival rate [%]	Mean marginal bone level change at 1 year [mm]	Mean marginal bone level change at last radiological follow-up [mm]°
Glauser, 2016 ¹⁴	11.2	102	38	97.1	-1.16 (±0.9)	-1.66 (±1.0)
Mozzati et al., 2015 ¹²	11	209	90	97.1	NR	-0.60 (±1.2)
Östman et al., 2012 ¹⁰	10	121	46	99.2	-0.40 (±1.6)	-0.70 (±1.4)
Pozzi and Mura, 2014 ²⁰	8.8	167	73	100	NR	-1.58 (±1.6)
Imburgia et al., 2015 ²¹	8.8	205	41	96.1	NR	-0.43 (±1.2)
Froum and Khouly, 2017 ^{22, 23}	8.6	52	28	100	NR	-0.03 (±0.7)
Polizzi et al., 2013 ²⁴	7.5	243	96	96.6	NR	-1.55 (±1.8)
Wagenberg and Froum, 2015 ²⁵	7.4	312	312	100	NR	-0.40 (±0.8)
Gelb et al., 2013 ²⁶	7.3	107	57	100	NR	-1.49 (±1.0)
Turkyilmaz, 2012 ²⁷	7	52	26	100 в	NR	-1.31 (±0.2)
Meloni et al., 2017 ²⁸	6	356	66	98	-1.09 (±0.4)	-1.61 (±0.4)
Polizzi and Cantoni, 2015 ²⁹	5.1	160	27	97.33	NR	-1.39 (±1.9)
Alfadda et al., 2009 30	5	70	35	98.4	NR	-0.40 (±0.4)
Calandriello and Tomatis, 2011 ³¹	5	40	33	95	-0.98 (±0.4)	-1.17 (±0.9)
Cehreli et al., 2010 ³²	5	28	14	100 в	NR	-1.20 (±0.1)
Cosyn et al., 2016 ³³	5	22	22	95.5	-0.12 (±0.5)	-0.19 (±0.3)
Lopes et al., 2015 ³⁴	5	92	23	96.6	NR	-1.30 (±1.1)
Malo et al., 201435	5	380	103	99.4	NR	-0.71 (±0.4)
Mura, 2012 ³⁶	5	79	56	100	NR	-0.56 (±2.0)
Pettersson and Sennerby, 2015 ³⁷	5	271	88	99.6	-0.9 (±1.6)	-0.10 (±2.4)

Studies with 5 or more years of follow-up of TiUnite surface implants reporting mean bone level change

Source: Nobel Biocare data on file (TiUnite Rep 134625, last search December 15, 2016), updated with Nobel Biocare database and PubMed search results for publications in 2016-2017. A: Where the mean follow-up time was not available the reported follow-up time was used (minimum one-year follow-up).

B: The percentage of surviving implants was calculated.

C: Mean marginal bone level change as reported or calculated. Last radiological follow-up may differ from study follow-up.

NR: Not reported or no single figure could not be calculated from the paper.

Setting the scientific standard. Again.

In the largest ever meta-analysis of a single implant brand, the TiUnite surface has set the scientific standard again, with outcomes from 4,694 clinically evaluated patients treated with 12,804 TiUnite implants reported in 106 prospective studies being analyzed.⁹ The meta-analysis represents the highest-possible level of evidence and unequivocally confirms that the TiUnite implant surface supports peri-implant health, bone maintenance and overall success, long term.

Key findings of the TiUnite meta-analysis:

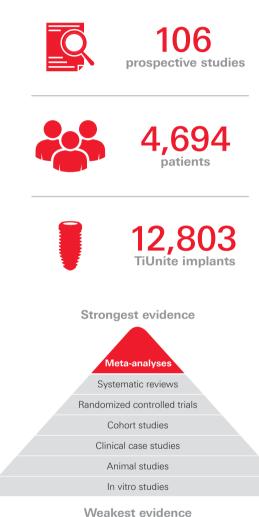
- Confirmed high early and late survival rates of TiUnite surface implants, exceeding 99% at 1 year and estimated at 95.1% after 10 years, at implant level.⁹
- Low prevalence of peri-implantitis⁹ at a rate comparable with other moderately rough implant surfaces.³⁸
- Estimated marginal bone level change from implant insertion to five-year follow-up is -0.9 mm at implant level and -1.0 mm at patient level.⁹

The highest-level evidence

Meta-analysis combines the results from multiple studies serving to improve the estimate of the size of an effect and to resolve uncertainty surrounding reports that disagree.³⁹ Meta-analysis is the most robust tool at our disposal to evaluate TiUnite implants. It far surpasses observational cohort studies, such as the *Effectiveness of implant therapy analyzed in a Swedish population* and animal studies, such as the *Ligature induced peri-implantitis at implants*, in terms of quality and reliability of evidence.⁴⁰⁻⁴²

Largest ever meta-analysis of a single brand

The study transparently reports patients with TiUnite surface implants prospectively evaluated in a clinical study. Studies reporting on a minimum of 20 patients with at least 12 months' follow-up post-loading were included regardless of protocol, patients' risk profile, or implant design, irrespective of whether or not the implant was still marketed. Prospective studies provide the advantage of proper baseline assessments, longitudinal follow-up and relatively fewer sources of bias. Thirty-two thousand, five hundred and nineteen publications reporting on clinical outcomes with dental implants were screened to ensure inclusion of all of the relevant studies. Of these studies, 106 met the inclusion criteria.⁹



32,519 publications screened

No cherry picking

Includes all patients with a TiUnite surface implant prospectively evaluated in a clinical study with a minimum of 20 patients and 12 months post-loading.

Low early failures and high long-term survival

The TiUnite meta-analysis applied regression analysis of survival outcomes of all studies at last available follow-up to create a meaningful projection of implant-level and patientlevel survival at multiple time points, as far out as 10 years. These results confirm that implants with the TiUnite surface have a remarkably low early failure rate and very good long-term survival.

One possible limitation of the survival analysis arises from the relatively limited number of studies with long-term survival data available. The quasi-linear shape of the survival curve may, in fact, overestimate the long-term trend in the rate of implant failure. As a result, the survival estimates reported are considered conservative.

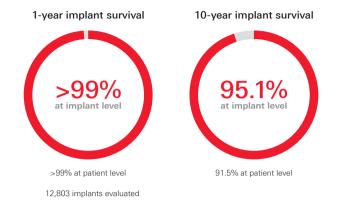
Stable marginal bone with all TiUnite surface implants in a wide set of indications

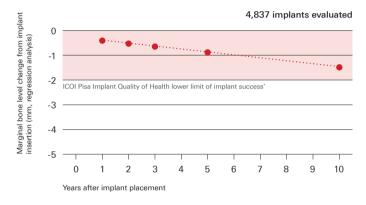
Marginal bone level change from implant insertion to 1, 2, 3, 5 and 10 years was also estimated using regression analysis. Estimates of bone level change from a baseline of implant insertion were –0.4 mm at 1-year follow-up and –0.9 mm at 5-year follow-up, and –1.5 mm at 10 years, at implant level (n=4,837).⁹ These estimates fall comfortably within the <2 mm range from implant insertion that was defined in the expert consensus from the 2008 International Congress of Oral Implantologists (ICOI) in Pisa, Italy, to be a condition of success (i.e. optimum implant health).¹⁸ Within studies, the rate of bone level change typically tapers off after a period of initial remodeling in the first year. As a result, one possible limitation of the meta-analysis may be that any long-term decreases in bone level are overestimated.

These results support TiUnite as a surface that promotes healthy bone response in the first year and stable bone levels long-term.

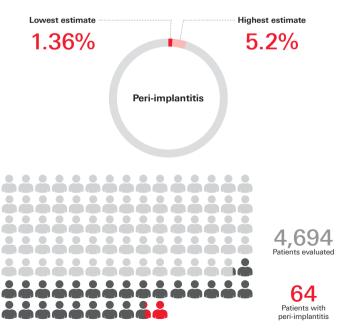
Low rates of peri-implantitis

Within the 106 studies, 47 evaluated biological complications, of which 19 studies reported directly cases of peri-implantitis in 64 patients. Using the patient population of the 19 studies as the denominator, the prevalence of peri-implantitis is 5.2% of patients treated with TiUnite surface implants.⁹ Professors Karl and Albrektsson postulated that the actual rate of peri-implantitis among the 4,694 patients in all 106 studies would be as low as 1.36% if peri-implantitis did not occur in studies where it was not reported.⁹ This would be the case supposing clinical investigators had assessed patients and would have reported any findings of peri-implantitis in the other examined studies. This estimate is in line with an earlier report by Albrektsson et al. of 1–2% among modern implants at 10 years.⁴³





* Misch CE, et al. Implant success, survival, and failure: the International Congress of Oral Implantologists ICOI) Pisa Consensus Conference. Implant Dent 2008 Mar;17:5–15.



1,229 patients in studies where peri-implantitis was directly reported

TiUnite® to the top

Clear evidence supports the clinical success of TiUnite to the top of the implant. Clinically, TiUnite supports not only osseointegration, high survival and stable bones long-term, but also soft tissue attachment and healthy soft tissue long-term.

TiUnite supports successful soft tissue integration

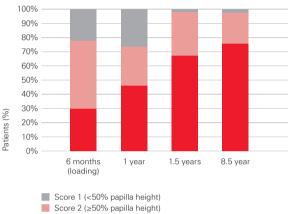
Providing protection to the underlying tissue structure, less epithelial downgrowth and a longer connective tissue seal was observed with TiUnite surface implants compared to machined surface.⁴⁴ In one paper, functionally oriented collagen fibers perpendicular to the implant surface were observed; this was unique to TiUnite compared to an acidetched and a machined surface and may result in a better interface between the implant and the connective tissue.⁴⁵

Successful soft and hard tissue outcomes with TiUnite in the soft tissue

While no longer marketed, results with a one-piece NobelDirect implant point towards favorable clinical outcomes, even when the moderately rough TiUnite surface is placed within the soft tissue. Overall bone level change was –0.3 mm at 8.5 years' mean follow-up. After initial remodeling in the first year, a significant bone gain of 0.6 mm was observed from the 1-year to the 8.5-year time point.²² Patients with Jemt papilla index scores of 2 and 3 increased from 6 months to 1.5 years. After 1.5 years, a greater proportion of patients exhibited scores of 3.²² Both soft and hard tissue responses over time showed healthy tissue development in the long run.²²



NobelDirect one-piece implants were placed with 1.5 mm to 2.0 mm of the moderately rough TiUnite surface coronal to the marginal bone. Proportion of patients with different interproximal papilla height (Jemt scores) over the course of the follow-up period



Score 3 (papilla fills entire proximal space)

Major improvements in papilla height occurred between 1 and 1.5 years after implant placement. $^{\rm 22}$

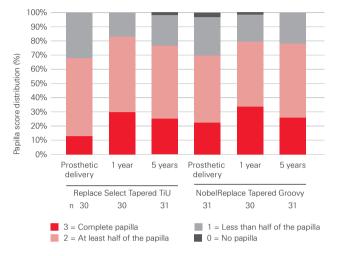
Implant neck design plays a role, but no difference between TiUnite surface implants with or without a machined collar

When TiUnite to the top with a groove (i.e. a textured collar) was compared to a 1.5 mm machined collar,⁴² the total amount of bone loss was $-1.26 (\pm 0.90)$ mm in the machined collar group (Replace Select Tapered TiU), $-1.20 (\pm 1.1)$ mm in the textured collar group (NobelReplace Tapered Groovy), showing no significant differences in the randomized control trial.⁴⁶ Furthermore, no differences were observed in soft tissue outcomes. A third arm of the study not reported here, with scalloped implants (that are no longer marketed) showed significantly poorer clinical outcomes in terms of both hard and soft tissue.

Determinants of bone remodeling

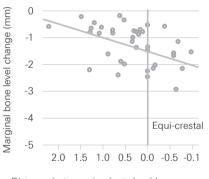
Whether the collar is TiUnite with grooves or machined, depth of implant placement relative to the crest of the bone may be the key determinant of bone remodeling.⁴⁷ In an observational pilot study with TiUnite surface implants, 20 patients received Replace Select Tapered TiU implants with a 1.5 mm machined collar, and 20 patients received NobelReplace Tapered Groovy, which has a textured collar, i.e. TiUnite to the top.⁴⁷ There were no differences in marginal bone change between the machined versus the textured collar group at 12–18 months. A power calculation determined that 2,064 patients would be required to embark on a full study, and would therefore not be feasible.⁴⁷ Only increased depths of implant insertion relative to the bone crest exhibited a statistically significant impact on the amount of bone remodeling surrounding the implants.

Papilla height (Jemt scores) from definitive crown placement to 1 and 5 years



No significant differences were observed in soft tissue outcomes, or in bone remodeling, with the textured collar compared to a 1.5 mm machined collar.⁴⁶

Relationship between depth of implant placement (supra-, equi- or sub-crestally) with marginal bone level change



Distance between implant shoulder and peri-implant bone crest at insertion (mm)

Greater implant insertion depths were associated with greater peri-implant marginal bone loss (rank correlation coefficient –0.46). $^{\rm 47}$

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Implants with an oxidized surface placed predominately in soft bone quality and subjected to immediate occlusal loading: results from an 11-year clinical follow-up

Glauser R

Clin Implant Dent Relat Res 2016;18(3):429-438.

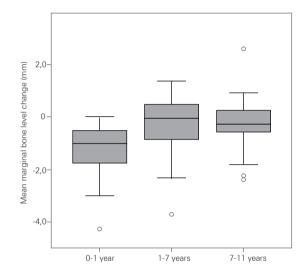
Describe of life table analysis

Results of life ta	Results of life table analysis					
Time period	Implants	Failed	Withdrawn	CSR (%)		
Implant insertion to 6 months	102	3	0	97.1		
6 months to 1 year	99	0	0	97.1		
1 year to 2 years	99	0	4	97.1		
2 years to 3 years	95	0	5	97.1		
3 years to 5 years	90	0	0	97.1		
5 years to 7 years	90	0	13	97.1		
7 years to 11 years	77	0	11	97.1		
11 years	66	-	-	-		

All three (3) failed implants were placed in the maxilla in one patient and were reported as failures at the same visit.

CSR = cumulative survival rate.

Marginal bone level changes (mm) between implant placement (loading) and 1 year, 1 and 7 years, and between 7 and 11 years' follow-up



Number of prostheses and implants per indication

			Indi	cation		
	Single anterior maxilla	Single posterior maxilla	Single posterior mandible	Partial posterior maxilla	Partial posterior mandible	Complete mandible
Reconstructions	5	7	8	10	20	1
Implants	5	7	8	26	51	5
Failures	-	-	_	3	-	-

Original abstract

Purpose: The purpose of this clinical follow-up was to document the 11-year outcome of implants with a moderately rough oxidized surface subjected to immediate occlusal loading.

Materials and methods: Twenty-six of 38 patients enrolled in a 5-year prospective study were available for this follow-up analysis, with 33 restorations supported by 66 slightly tapered implants (Brånemark System Mk IV, Nobel Biocare, Gothenburg, Sweden). The majority of implants were placed in posterior regions (88%) and into soft bone (76%). Parameters included cumulative survival rate, radiographic marginal bone level, bleeding on probing, intrasulcular counts of periopathogenic markers (DNA probes), and total bacterial load.

Results: The cumulative survival rate was 97.1% at 11.2 years' mean follow-up. Mean marginal bone remodeling was 0.47 mm (SD 1.09, n = 65) from 1 year postplacement to 11-year follow-up. Bleeding on probing was absent at most sites (63.6%). No statistically significant differences in total bacterial load or periopathogenic marker species were observed at implants and teeth.

Conclusion: The results of the present follow-up show high long-term survival, stable marginal bone levels, and soft tissue outcomes of oxidized surface implants placed predominately in posterior regions and soft bone. The quantity and quality of intrasulcular microbiota were comparable at implants and teeth.

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Ten years of clinical experience with NobelActive®

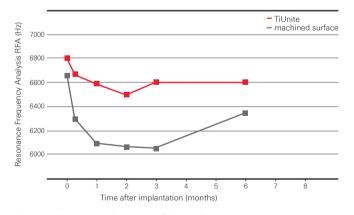
The innovation of NobelActive represented a breakthrough in implant design, harmonizing biomedical engineering expertise with the clinical needs and the wisdom of clinicians. NobelActive's expanding tapered implant body condenses bone gradually while the apex with drilling blades enables a smaller osteotomy. These features help to achieve high primary stability in demanding situations, such as soft bone or extraction sockets.

Perfect harmony of implant surface, drilling protocol and geometric design

The TiUnite surface combined with the NobelActive surgical protocol, tapered apex and threads from tip to platform are all designed to provide high primary stability and support immediate loading. Reverse-cutting flutes with drilling blades on the apex enable experienced clinicians to adjust the implant position during placement for an optimized restorative orientation, particularly in extraction sites. NobelActive's back-tapered coronal design and built-in platform shifting are designed to optimize bone and soft tissue volume for natural-looking esthetics.

The osteoconductive properties of TiUnite, supporting fast apposition of newly formed bone, helps ensure that high stability achieved at implant insertion can be maintained throughout the critical healing phase. Clinically, this relationship between the osteoconductive effect of the TiUnite surface and implant stability in patients with predominantly soft bone was confirmed by Glauser et al, with Brånemark IV implants.⁴⁸ Their study showed higher stability compared with machined implants of the same macro-geometry;⁴⁸ results were statistically significant at 1, 2 and 3 months following immediate loading after implant insertion.

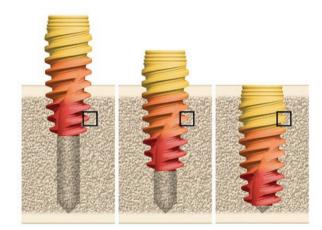
High stability in the critical healing phase allows for Immediate Function



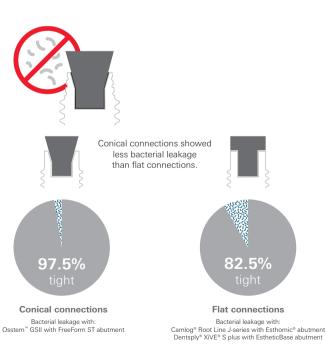
Higher stability with immediately loaded TiUnite surface implants (external hexagonal connection) than with the same implants with machined surface in the posterior maxilla.⁴⁴

The conical connection of NobelActive seems to have an advantage against leakage. Conical connection implants, including Nobel Biocare's conical connection, showed lower bacterial leakage compared to flat connections, in an in vitro model.⁴⁹

High primary stability in demanding situations, such as soft bone or extraction sockets



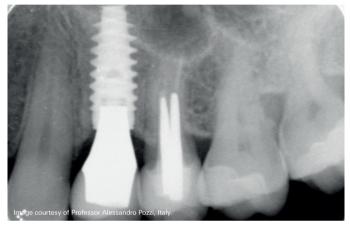
NobelActive's expanding tapered implant body condenses bone gradually while the apex with drilling blades enables a smaller osteotomy.



The included NobelActive Conical Connection implants with Snappy Abutment showed no leakage in this model. $^{\rm 49}$

Clinical case - NobelActive supporting hard and soft tissue for 10 years

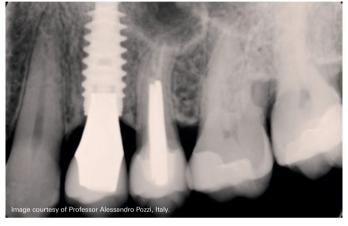
Immediate implant placement in a fresh extraction socket of a NobelActive RP implant 4.3 mm × 13 mm. Socket augmentation was performed, using xenograft and autogenous soft tissue grafting harvested from the tuberosity area, to close the socket and increase the amount of soft tissue at the recipient site. A cement-retained lithium disilicate crown was cemented onto an anatomically shaped zirconia abutment.



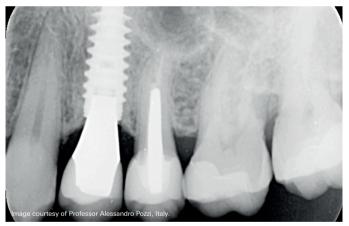
Radiological outcome with NobelActive at 1-year follow-up, showing stable bone.



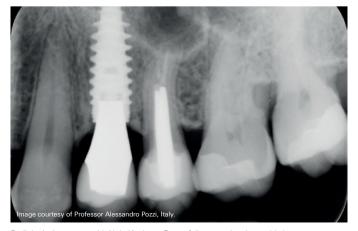
Radiological outcome with NobelActive at 3-year follow-up, showing stable bone.



Radiological outcome with NobelActive at 7-year follow-up, showing stable bone.



Radiological outcome with NobelActive at 9.5-year follow-up, showing bone overgrowth over time onto the implant platform.



Radiological outcome with NobelActive at 5-year follow-up, showing stable bone.



Clinical outcome with NobelActive at 1-year follow-up, showing healthy papilla.



Clinical outcome with NobelActive at 3-year follow-up, showing healthy papilla.



Clinical outcome with NobelActive at 5-year follow-up, showing healthy papilla.



Clinical outcome with NobelActive at 7-year follow-up, showing healthy papilla.



Clinical outcome with NobelActive at 9.5-year follow-up.

Scientific evidence backs conical connection implants with a TiUnite® surface

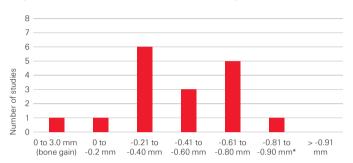
The conical connection is a strong connection designed to benefit the soft and hard tissue parameters. Nobel Biocare's conical connection was introduced with the NobelActive implant in 2008. Since then, over 14,000 NobelActive implants with conical connection and almost 500 NobelReplace Conical Connection implants in over 2,700 patients have been clinically evaluated in 45 clinical studies (see tables on pages 26 to 30).

Key findings of clinical studies with NobelActive are:

- Studies reporting mean marginal bone level change with NobelActive implants show minimal bone remodeling in the healing phase followed by stable or increasing bone levels.^{33,50-52}
- The implant design and conical connection with built-in platform shifting result in less crestal bone change.^{51, 52}
- Papilla size significantly improves during the first year, and from implant insertion until 3 and 5 years.^{33, 50}
- The unique implant design ensures high primary stability even in soft bone and fresh extraction sockets.^{33, 50, 52-54}
- Studies show that NobelActive is a reliable implant for Immediate Function protocols,^{50, 53, 55} as well as challenging cases such as severely atrophic maxilla.^{56, 57}
- NobelActive is also successful with full-arch restorations with the All-on-4[®] treatment concept.^{57, 58}

Nineteen studies with 1 to 5 years' follow-up have evaluated bone level change with NobelActive implants. There is a clear trend toward lower bone remodeling with NobelActive compared to historical data with TiUnite surface implants without a conical connection. No study with a minimum of 1-year and up to 5-years of follow-up had a bone remodeling of over –0.89 mm.^{59, 60} Thus, looking to the middle point in the graph, one may expect mean bone remodeling with NobelActive implants to be approximately –0.4 mm at up to 5 years of follow-up. This further speaks to the crucial interrelationship between implant surface, drill protocols and geometrical design and their synergistic effect on implant treatment outcomes.

Studies report mean marginal bone level change from implant insertion with NobelActive implants



* Excludes a single study that evaluated a predecessor NobelActive implant that was not made commercially available, which had a slightly different connection and back taper design.

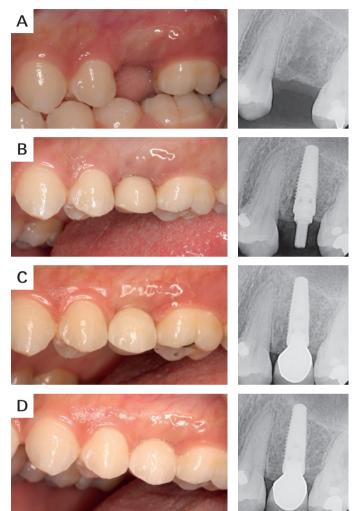
Key findings of clinical studies with NobelReplace Conical Connection are:

- High implant survival in single tooth, partially edentulous and fully edentulous indications.^{20, 61}
- Good performance in both healed and extraction sites.²⁰
- Stable bone levels after the initial bone remodeling of the healing period.⁶¹
- Good soft tissue outcomes and healthy papilla development over the first year.⁶¹

Data with NobelReplace Conical Connection implants has reached critical mass to evaluate clinical outcomes. Six clinical studies report survival rates between 98.3% and 100% at 1 to 3 years of mean follow-up. Weighted mean bone level change was –0.71 mm (see table on pages 26 to 30). In a study evaluating 72 patients, NobelReplace Conical Connection performed well in both healed (n=81) and post-extraction sites (n=67) with 99.3% implant and 100% prosthesis survival rates.²⁰ A multi-center prospective single-tooth study showed 99% cumulative survival rate at 1 year.⁶¹ Improving Jemt papilla index scores over time, partially or fully gained papilla was observed at 30.8% of sites at baseline, 87.2% at 6 months, and 90.5% at 1 year.⁶¹ After the initial 6-month remodeling period, bone gain observed until the 1-year follow-up of this study.⁶¹

Experience with NobelReplace Conical Connection covers a number of indications. For edentulous patients, four NobelReplace Conical Connection implants to support a CAD/ CAM NobelProcera bar supporting an overdenture has shown success.⁶² The bar was positioned with 1 mm clearance for easy oral hygiene maintenance and as a result, hygiene was maintained by patients with only slight plaque at 6.9% of implants.⁶² One year mean marginal, bone level change was low at –0.29 mm and patients experienced a significant improvement of quality of life.⁶²

A representative clinical case, position 25



Clinical view and periapical radiograph prior to surgery (a), at implant insertion (b), at final crown delivery (c), and 1 year after implant placement (d).

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Clinical case with the recently introduced NobelParallel CC implant



Radiograph of fully edentulous patient restored with NobelActive implants in the maxilla at 8 years and NobelParallel CC implants in the mandible at 2 years of follow-up.



The patient was restored with NobelProcera implant bridge zirconia.



Clinical image with NobelProcera implant bridge zirconia.

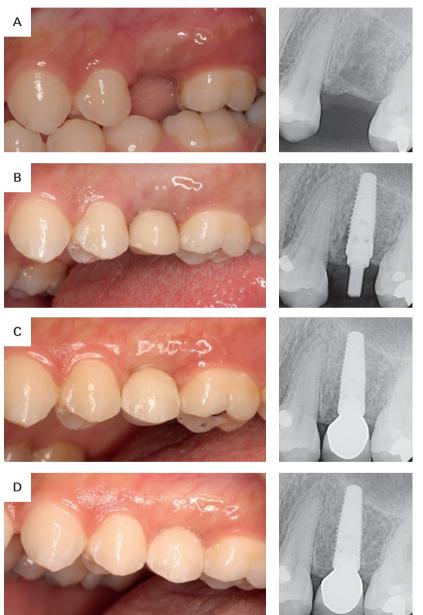


Excellent esthetic outcome.

An open prospective single cohort multicenter study evaluating the novel, tapered, conical connection implants supporting single crowns in the anterior and premolar maxilla: interim 1-year results

Fügl A, Zechner W, Pozzi A, Heydecke G, Mirzakhanian C, Behneke N, Behneke A, Baer RA, Nölken R, Gottesman E, Colic S Clin Oral Investig 2017;21(6):2133–2142

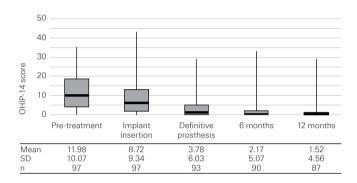
A representative clinical case, position 25



Clinical view and periapical radiograph prior to surgery (a), at implant insertion (b), at final crown delivery (c), and 1 year after implant placement (d).

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OHIP 14 scores throughout the study.



Marginal bone level changes throughout the study period

	Insertion to 6 months	Insertion to 1 year	6 months to 1 year
Mean (mm)	-0.94	-0.85	0.11
SD (mm)	1.32	1.37	1.06
n	84	80	83
р	<0.0001	<0.0001	0.0808

The black marker lines indicate the median and the boxes signify the first and third quartiles. Bars indicate minimum and maximum value. Mean, standard deviation (SD), and sample number per time point (n) are listed below the graph.

Original abstract

Objectives: The aim of this multicenter prospective clinical study was to evaluate anodized tapered implants with a conical connection and integrated platform shifting placed in the anterior and premolar maxilla.

Materials and methods: The study enrolled patients requiring single-tooth restorations in healed sites of maxillary anterior and premolar teeth. All implants were immediately temporized. Clinical and radiographic evaluations were conducted at implant insertion, 6 months, and 1 year. Outcome measures included bone remodeling, cumulative survival rate, success rate, soft-tissue health and esthetics, and patient satisfaction. Bone remodeling and pink esthetic score were analyzed using Wilcoxon signed-rank tests. CSR was calculated using life table analysis. Other soft-tissue outcomes were analyzed using sign tests.

Results: Out of 97 enrolled patients (102 implants), 87 patients (91 implants) completed the 1-year visit. Marginal bone remodeling was -0.85 ± 1.36 mm. After the expected initial bone loss, a mean bone gain of 0.11 ± 1.05 mm was observed between 6 months and 1 year. The cumulative survival rate was 99.0%, and the cumulative success rate was 97.0%. Partial or full papilla was observed at 30.8% of sites at baseline, 87.2% at 6 months, and 90.5% at 1 year. Soft-tissue response, esthetics, and patient satisfaction all improved during the study period.

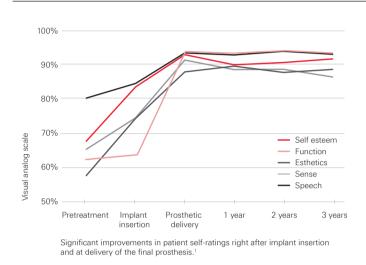
Conclusions: Bone gain was observed following the expected initial bone loss, and soft-tissue outcomes improved suggesting favorable tissue response using anotized tapered conical connection implants.

Clinical relevance: Rapid stabilization of bone remodeling and robust papilla regeneration indicate favorable tissue healing promoted by the conical connection, platform-shift design. Trial registration: clinicaltrials.gov NCT02175550.

Evaluation of a variable-thread tapered implant in extraction sites with immediate temporization: a 3-year multi-center clinical study

Kolinski ML, Cherry JE, McAllister BS, Parrish KD, Pumphrey DW, Schroering RL

J Periodontol 2014;85(3):386-394.



Summary of the study

Kolinski et al. (2014) report excellent results: high CSR, stable bone levels, good soft tissue health and patient satisfaction using NobelActive implants. A total of 60 implants were placed in 55 patients at 6 centers, all in extraction sites and subjected to Immediate Function. Patients requiring major bone augmentations were excluded, while minor augmentations were permitted. CSR after 3 years was 98.3%. Bone levels were exceptionally stable: Bone remodeling of a mere -0.2 mm during the first 6 months quickly stabilized and showed even a non-significant bone gain of 0.3 mm at 3 years. Papilla scores increased significantly (p < 0.001) from insertion to 3-year follow-up, with most of the increase occurring during the first year. The results on quality of life are also noteworthy, with significant improvements in patient self-ratings on esthetics, self-esteem, function, sense and speech. The authors therefore conclude that NobelActive can be used safely and effectively under demanding conditions such as immediate tooth replacement in extraction sites – not only with regards to CSR and hard- and soft-tissue health, but also in terms of patient satisfaction.

Clinical case - Excellent esthetic outcome at 8-year follow-up with Immediate Loading on a NobelActive implant



Clinical situation before treatment.



Clinical view of temporary after surgery (Immediate Loading).



Radiograph showing temporary after surgery (Immediate Loading).

Radiograph showing temporary after 3 months.



Clinical view of soft tissue before finalization.



Zirconia abutment in situ.



Clinical view following finalization.



Excellent esthetic outcome at 8 years' follow-up

Images courtesy of Dr. Giacomo Fabbri, Italy.



Radiograph following finalization.



Radiograph at 8 years' follow-up



Screw-retained crown

Three-year post-loading results of a randomised, controlled, split-mouth trial comparing implants with different prosthetic interfaces and design in partially posterior edentulous mandibles

Pozzi A, Tallarico M, Moy PK

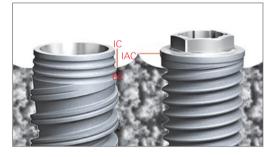
Eur J Oral Implantol 2014;7(1):47-61.



Clinical view of the two investigated implant designs.

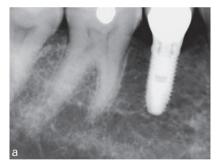


Characteristics of the two different implant designs and connections used in this study



Diagrams showing the measurement locations utilized in this investigation:

VMBL = the distance from the most coronal margin of the implant collar (IC) and the top of the bone crest (BC) HVBL = the distance from the internal aspect of the socket wall at the level of the alveolar crest (IAC) to the implant surface (I).



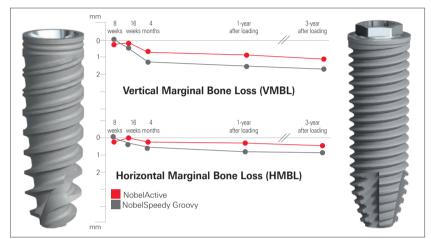


Periapical radiographs after 1 year in function: (a) NobelSpeedy Groovy implant (control group); (b) NobelActive implant (test group)





Periapical radiographs after 3 years in function: (a) NobelSpeedy Groovy implant (control group); (b) NobelActive implant (test group)



Graph showing the vertical and horizontal marginal bone loss from implant insertion to 3-year follow-up of all implants



Intraoral photographs after 3 years in function: (a) NobelSpeedy Groovy implant (control group); (b) NobelActive implant (test group).

Original abstract

Purpose: To compare the clinical and radiological outcomes of two implant designs with different prosthetic interfaces and neck configurations.

Materials and methods: Thirty-four partially edentate patients randomly received at least one NobelActive implant (Nobel Biocare, Goteborg, Sweden) with back-tapered collar, internal conical connection and platform shifting design, and one NobelSpeedy implant (Nobel Biocare) with external hexagon and flat-to-flat implant-abutment interface according to a splitmouth design. Follow-up continued to 3 years' post-loading. The primary outcome measures were the success rates of the implants and prostheses, and the occurrence of any surgical and prosthetic complications during the entire follow-up. Secondary outcome measures were: horizontal and vertical peri-implant marginal bone level (MBL) changes, resonance frequency analysis values at implant placement and loading (4 months), sulcus bleeding index (SBI) and plaque score (PS).

Results: No drop-out occurred. No implants and prostheses failures were observed to the 3-year follow-up. MBL changes were statistically significant different with better results for the NobelActive implants for both horizontal and vertical measurements (p = 0.000). After 3 years post-loading, the NobelActive implants underwent a mean vertical bone resorption of 0.66 mm, compared with 1.25 mm for the NobelSpeedy Groovy implants (p = 0.000); the mean horizontal bone resorption was 0.19 mm for the NobelActive implants and 0.60 mm for the NobelSpeedy Groovy implants (p = 0.000). A high ISQ value was found for both implants, and no statistically significant difference was found for ISQ mean values between interventions (p = 0.941 at baseline; p = 0.454 at implant–abutment connection; p = 0.120 at prosthesis delivery). All implants showed good periodontal health at the 3-year-in-function visit, with no significant differences between groups.

Conclusion: The results of this research suggest that in well-maintained patients, the MBL changes could be affected by the different implant design. After 4 months of unloaded healing, as well as after 3 years in function, both implants provided good results, however vertical and horizontal bone loss had statistically significant differences between the two groups (difference of 0.58 ± 0.10 mm for the vertical MBL, and 0.4 ± 0.05 mm for the horizontal MBL), with lower values in the NobelActive implants, compared to the NobelSpeedy Groovy implants.

TiUnite[®] implants with conical connection Overview of studies

The following overview includes clinical studies using TiUnite implants with conical connection. The studies are ordered by follow-up time.

Only peer-reviewed publications are listed. Meeting abstracts, reviews, single case reports, technique descriptions and animal and in vitro tests are excluded. The total number of implants and patients included in this overview is over 14,300 and 2,500 respectively, with mean implant survival rate of 98.6 %.^A

Only marginal bone level change of studies with implant level baseline are presented. For more information on these studies visit PubMed at pubmed.gov.

Reference	Mean follow-up time [years] ^B	Study type	Implant ^c	Indication/ study focus	No. of implants	No. of patients	Implant survival rate [%]	Mean change in marginal bone level (SD) [mm]
Jensen et al., 2016⁵ ⁷	5	Retrospective	NobelActive	Fully edentulous maxilla, Immediate-loading	158	39	94.9 ^D	NR
Li et al., 2017 ⁶³	5	Prospective	NobelActive	Fully edentulous maxilla & mandible, Extraction sites, All-on-4	28	NR	NR	NR
Cosyn et al., 2016 ³³ Cosyn et al., 2013 ⁶⁴	5	Prospective	NobelActive	Single tooth, Anterior & posterior maxilla, Cement- & screw-retained, Extraction sites, Immediate loading	22	22	94.1 ^D	-0.19 (0.3)
Passos et al., 2016⁵	5	Retrospective	NobelActive	Single tooth, Anterior maxilla & mandible	12	NR	100 D	NR
Babbush, 2015 ⁶⁶	4.5	Retrospective	NobelActive	Maxilla & mandible, Screw-retained, Healed & extraction sites, All-on-4	5002	NR	98.1	NR
Pozzi et al., 2015 ⁶⁷	4.1	Prospective	NobelActive	Fully edentulous maxilla & mandible, Screw-retrained, Healed sites, Immediate loading, Guided surgery	62	NR	100	NR
Pozzi and Moy, 2014 ⁶⁸	3.7	Prospective	NobelActive	Partially edentulous posterior maxilla, Immediate loading, Guided surgery	37	NR	97.3	NR
Pozzi et al., 2015 ⁶⁹	3.5	Retrospective	NobelActive	Fully edentulous maxilla & mandible, Healed & extraction sites, Immediate loading, Guided surgery	85	NR	100 D	NR

Reference	Mean follow-up time [years] ^B	Study type	Implant ^c	Indication/ study focus	No. of implants	No. of patients	Implant survival rate [%]	Mean change in marginal bone level (SD) [mm]
Babbush et al., 2014 ⁷⁰	3.4	Retrospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, Cement & Screw, fully- edentulous, Healed & Extraction, All-on-4	60	15	98.3 ^d	NR
Pozzi, et al., 2015 ⁷¹	3.2	Prospective	NobelReplace CC	Maxilla & Mandible, Anterior & Posterior, Cement & Screw, Healed & Extraction, 1-stage, Immediate- Loading	118	54	98.3 ^d	-0.68 (0.6)
Demanet, et al., 2011 ⁷²	3	Retrospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, Healed & Extraction, 1-stage & 2-stage	466	172	99.1	–0.39 (NR)
De Santis et al., 2016 ⁷³	3	Prospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, Screw, 2-stage, Delayed- Loading	144	62	98.6	-0.70 (0.5)
Arnhart et al., 2012 ⁵⁹ Kielbassa et al., 2009 ⁶⁰	3	Prospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, Cement & Screw, Healed, 1-stage, Immediate-Loading	117	117	96 ^D	–0.89 (1.7) ^D
Kolinski et al., 2014 ⁵⁰ McAllister et al., 2012 ⁷⁴	3	Prospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, Screw, Extraction, 1-stage, Immediate-Loading	60	55	98.3	+0.30 (1.6)
Pozzi et al., 2014 ⁵¹ Pozzi et al., 2014 ⁷⁵	3	Prospective	NobelActive	Mandible, Posterior, Cement, single-tooth, Healed, 2-stage, Early- Loading	44	34	100	-0.67 (0.4)
De Vico et al., 2011 ⁷⁶	2.1	Prospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, Screw, fully-edentulous, Healed & Extraction, 1-stage, Immediate- Loading, Guided-Surgery, All-on-4	140	35	100	–0.72 @ 1 year (NR) ^D
Babbush and Brokloff, 2012 ⁵⁸ Babbush et al., 2011 ⁷⁷	2	Retrospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, Healed & Extraction, 1-stage & 2-stage	1001	293	97.4	NR
Drago, 2016 ⁷⁸	2	Retrospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, screw, fully-edentulous, Healed & Extraction, 1-stage, Immediate- Loading	774	130	99.5	NR

Reference	Mean follow-up time [years] ^B	Study type	Implant ^c	Indication/ study focus	No. of implants	No. of patients	Implant survival rate [%]	Mean change in marginal bone level (SD) [mm]
Drago, 2016 ⁷⁹	2	Retrospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, Screw, fully-edentulous, Healed & Extraction, Immediate-Loading, All-on-4	770	128	99.5	NR
Drago, 2016 ⁸⁰	2	Retrospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, Screw, fully-edentulous, Healed & Extraction, 1-stage, Immediate- Loading, All-on-4	766	129	99.5	NR
Orentlicher et al., 2014 ⁸¹	2	Retrospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, Healed & Extraction, Guided-Surgery	121	NR	95.87	NR
Ganeles et al., 2017 ⁸²	2	Prospective	NobelActive	Single-arm, single center, Maxilla, Anterior & Posterior, Single-tooth, Extraction sites, 1-stage	15	15	100	+0.83 (2.73)
Pozzi and Mura, 2016 ⁸³	1.9	Retrospective	NobelReplace CC	Maxilla & Mandible, Anterior & Posterior, Cement & Screw, Healed & Extraction	148	64	99.3	-0.71 (1.5)
Aires and Berger, 2016 ⁸⁴	1.6	Retrospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, Screw, fully-edentulous, Healed & Extraction, 1-stage & 2-stage, Guided-Surgery	1657	228	99.4	NR
Younes et al., 2016 ⁸⁵	1.6	Retrospective	NobelActive	Maxilla, Posterior, Cement & Screw, 1-stage & 2-stage	165	57	98.2 ^D	NR
Wessing et al., 2016 ⁸⁶	1.53	Retrospective	NobelActive, NobelReplace CC	Maxilla & Mandible, partially-edentulous, Healed, 1-stage & 2-stage, Delayed-Loading	6	NR	100	NR
Pozzi et al., 2016 ⁶²	1.4	Prospective	NobelReplace CC	Maxilla & Mandible, Anterior & Posterior, Screw, fully-edentulous, Healed, Delayed-Loading, Guided-Surgery	72	18	100	-0.29 (0.2)
Babbush et al., 2016 ⁸⁷	1.3	Retrospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, fully- edentulous, Healed & Extraction, 1-stage, Immediate- Loading, All-on-4	856	169	99.8	-0.14 (0.6)
MacLean et al., 2016 ⁸⁸	1.3	Retrospective	NobelActive	Maxilla & Mandible, Anterior, Cement & Screw, single-tooth, Healed & Extraction, 1-stage & 2-stage	44	34	96.4	-0.36 (0.9)

Reference	Mean follow-up time [years] ^B	Study type	Implant ^c	Indication/ study focus	No. of implants	No. of patients	Implant survival rate [%]	Mean change in marginal bone level (SD) [mm]
Gultekin et al., 2013 ⁵²	1.25	Prospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, Cement, partially- edentulous, Healed, 2-stage, Delayed- Loading, Guided-Surgery	43	NR	100	-0.35 (0.1)
Polizzi G et al., 2016 ⁵³	2.4	Retrospective	NobelActive	Maxilla, Anterior & Posterior, Healed & Extraction, Immediate-Loading, Guided-Surgery	160	27	99.4	-0.58 (0.98)
Babbush and Kanawati, 2015 ⁸⁹	1.0	Retrospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, Healed & Extraction	262	65	98.1	NR
Yamada et al., 2015⁵⁵	1	Prospective	NobelActive (NP, RP)	Maxilla, Anterior & Posterior, Screw, fully- edentulous, Healed, 1-stage, Immediate-Loading, Guided-Surgery	290	50	98.6	-0.32 (0.4)
Babbush et al., 2013 ⁵⁶	1	Retrospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, fully-edentulous, Healed & Extraction, 1-stage & 2-stage	227	53	98.7	NR
Esposito et al., 2017 ⁹⁰	1	Prospective	NobelActive	Maxilla & Mandible, single-tooth Immediate-Loading, Immediate-delayed & delayed loading	210	210	95.4	-0.28 (0.16)
Fugl et al, 2016 ⁶¹	1	Prospective	NobelReplace CC	Maxilla, Anterior & Posterior, Cement & Screw, single-tooth, Healed, 1-stage, Immediate-Loading	102	97	99	-0.85 (1.4)
Galindo and Butura, 2012 ⁹¹	1	Retrospective	NobelActive	Mandible, Anterior & Posterior, Screw, fully-edentulous, Mixed, 1-stage, Immediate-Loading, Guided-Surgery, All-on-4	60	183	100 D	≤-1.0 (NR)
Meloni et al., 2017 ⁹²	1	Prospective	NobelReplace CC	Single-arm, Prospective, Single center, Maxilla & Mandible, Posterior, Single-tooth, partially edentulous & fully edentulous, Healed, 2-stage, Delayed loading	55	18	100	-1.03 (0.21)
Cosyn et al., 2015 ⁹³	1	Prospective	NobelActive	Maxilla, Anterior & Posterior, Screw, single-tooth, Healed, 1-stage, Delayed-Loading	47	47	100	-0.48 (0.5)

Reference	Mean follow-up time [years] ^B	Study type	Implant ^c	Indication/ study focus	No. of implants	No. of patients	Implant survival rate [%]	Mean change in marginal bone level (SD) [mm]
Slagter et al., 2015 ⁹⁴	1	Prospective	NobelActive	Maxilla, Anterior & Posterior, Cement & Screw, single-tooth, Extraction, 1-stage & 2-stage	40	40	100	–0.70 (NR) ^D
Slagter et al., 2016 ⁹⁵	1	Prospective	NobelActive	Maxilla, Anterior, Cement & Screw, single-tooth, Healed & Extraction, 2-stage, Delayed-Loading	40	40	100	–0.53 (NR) ^D
Cristalli et al., 2015 ⁹⁶	1	Prospective	NobelActive	Maxilla & Mandible, Anterior & Posterior, Cement, single-tooth, Extraction, 1-stage, Immediate-Loading	25	24	92	–0.33 (NR) ^D
Rokn et al., 2015 ⁹⁷	1	Prospective	NobelActive	Mandible, Posterior, single- tooth	25	NR	100 D	-0.68 (0.5)
Bruno et al., 2014 ⁹⁸	1	Prospective	NobelActive	Maxilla, Anterior & Posterior, single-tooth, Extraction, 1-stage, Immediate-Loading	5	3	100 D	NR

Source: Nobel Biocare data on file. TiUnite literature search. Clinical research department, July 31, 2017.

A: Arithmetic means weighted by number of initially placed implants (implant survival rate) or number of patients treated (prosthetic survival rate).

B: Where the mean follow-up time was not available the reported follow-up time was used (minimum one-year follow-up). Last radiological follow-up for mean marginal bone level change may differ from the overall study follow-up.

C: Minimum 10 implants, 1 year of follow-up.

D: The percentage of surviving implants/prostheses or MBL was calculated.

NR: Not reported.

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Notes

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