

## Effect of ultraviolet photofunctionalization of dental titanium implants on osseointegration\*

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**Abstract:** Objective: The aim of the current study was to evaluate the effect of ultraviolet (UV) photofunctionalization of dental titanium implants with exposure to the oral cavity on osseointegration in an animal model. Methods: Forty-eight titanium implants (Camlog® Conelog® 4.3 mm×9.0 mm) were placed epicrestally into the edentulous jaws of three minipigs and implant stability was assessed by measuring the implant stability quotient (ISQ). Prior to implantation half of the implants were photofunctionalized with intense UV-light. After three months, the implants were exposed and ISQ was measured again. After six months of implant exposure, the minipigs were sacrificed and the harvested specimens were analyzed using histomorphometric, light, and fluorescence microscopy. Main results: Forty-two of 48 implants osseointegrated. The overall mean bone-implant contact area (BIC) was (64±22)%. No significant differences were found in BIC or ISQ value (multivariate analysis of variance (MANOVA),  $P>0.05$ ) between implants with and without exposure to UV photofunctionalization. Conclusions: No significant effects were observed on osseointegration of dental titanium implants nine months after exposure of UV photofunctionalization.

**Key words:** Dental implant; Osseointegration; Photofunctionalization

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### 1 Introduction

Replacing missing teeth with dental titanium implants has a positive impact on the quality of oral health (Zarb and Schmitt, 1990; Aita et al., 2009). Titanium implants significantly improve masticatory function (van Kampen et al., 2004), speech (Heydecke et al., 2004), and the overall quality of life (Melas et al., 2001), compared to conventional removable dental prostheses (Melas et al., 2001; Aita

et al., 2009). However, long implant healing time of at least six months is recommended, until the implant can be loaded (Adell et al., 1981; Urban et al., 2009). Thus, osseointegration and safe restoration of the implant are critical (Adell et al., 1981). In recent years, the demands on implants and associated surgery have shifted significantly towards implant placement combined with immediate function (Abboud et al., 2005; Tealdo et al., 2008; Bergkvist et al., 2009; Maló et al., 2012). Successful osseointegration of dental implants depends on the amount of bone directly contacting the titanium surface without soft tissue intervention (Aita et al., 2009). Incomplete or destructive changes at the bone-implant contact area (BIC) can lead to implant failure (Chuang et al., 2002; Moy et al., 2005; Aita

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et al., 2009). The BIC is estimated to be (45±16)% without any implant surface modifications for conventional implant procedures (Weinlaender et al., 1992). With additional surface modifications, e.g. acid-etching, fluoride-apposition, or carbon-oxygen applications, BIC values between 50% and 75% can be achieved (Ogawa and Nishimura, 2003; Berglundh et al., 2007; de Maeztu et al., 2008). However, this is still much lower than a BIC of 100%. One problem recently associated with a reduced BIC is the shelf life of implants after production (Att and Ogawa, 2012; Ogawa, 2014). It is assumed that the biological characteristics and the resulting ability of titanium implant surfaces to bond to bone remain stable over time (Att and Ogawa, 2012). In recent reports, four-week-old titanium surfaces needed twice the healing time to achieve similar osseointegration levels and exhibited less BIC than newly prepared titanium surfaces (Aita et al., 2009; Att and Ogawa, 2012).

Ultraviolet (UV)-light-induced superhydrophilicity of titanium dioxide ( $TiO_2$ ) was discovered in 1997. UV photofunctionalization is defined as the phenomenon of titanium surface modification after intense UV treatment, including the change in the physicochemical properties and the improvement in biological features. UV-light treatment of titanium surfaces creates surface oxygen vacancies at bridging sites, converting  $Ti^{4+}$ -ions to  $Ti^{3+}$ -ions. This, in turn, increases dissociative water adsorption (Wang et al., 1997; Aita et al., 2009). Several studies reported an accelerated implant stability, an increase in cell proliferation, a higher BIC value of up to 98%, and a reduced clinical implant healing time (Aita et al., 2009; Att and Ogawa, 2012; Funato and Ogawa, 2013; Funato et al., 2013; Park et al., 2013; Pyo et al., 2013; Suzuki et al., 2013).

Three of these studies measured histomorphometric values in rats, rabbits, and dogs (Aita et al., 2009; Park et al., 2013; Pyo et al., 2013). However, the animal models used in these particular studies could not be directly compared to humans with regards to the bone formation rate (Eriksen et al., 1984; Mosekilde, 1995). The three human studies only measured the implant stability quotient (ISQ) (Funato and Ogawa, 2013; Funato et al., 2013; Suzuki et al., 2013) and could not provide any histomorphometric data, for obvious reasons. Furthermore, the investigation period/implant healing time was set at four

weeks and the implants were placed into compact bone with submerged healing (Aita et al., 2009; Park et al., 2013; Pyo et al., 2013).

Therefore, the aim of this study was to evaluate the effect of UV photofunctionalization of dental titanium implants on osseointegration over a longer period, in an animal model with bone formation rates comparable to human beings, in a location that provided partially cancellous bone exposed to the oral cavity.

## 2 Materials and methods

### 2.1 Surgical procedures

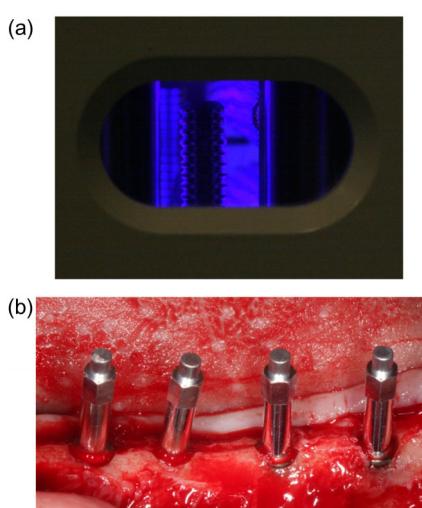
A list of the materials used can be found in Table 1. Three minipigs (2 males, 1 female, average body weight (BW) (56.8±3.5) kg) were used in this study. The study procedures were in accordance with the German and European Animal Welfare Act (Animal Experiment Permit V-242.7224.121-14 (49-4/14)). All animals received food and water ad libitum.

During all surgical interventions, the animals were initially sedated with an intramuscular injection of 4% (0.04 g/ml) azaperone (4 mg/kg BW of the minipigs, Stresnil, Jannsen-Cilag, Neuss, Germany), followed by an intramuscular injection of 10% (0.1 g/ml) ketamine (10 mg/kg BW, Bremer Pharma, Warburg, Germany) and 0.5% (5 g/L) midazolam (1.8 mg/kg BW, Braun, Melsungen, Germany). Intubation anesthesia was conducted using Isoflurane (Isofluran CP, CP Pharma GmbH, Burgdorf, Germany) (Mehl et al., 2013). After applying a local anesthetic in the upper and lower jaw (Ultracain DS forte, Hoechst, Frankfurt a. M., Germany), a dental cleaning was performed and all premolars and the first molars were removed. After a healing period of three months, four implants per quadrant were placed epicrestally in each minipig, according to the manufacturers' instructions (Camlog® Conelog®, 4.3 mm×9.0 mm, Camlog Biotechnologies, Basel, Switzerland). Prior to implant placement, half of the implants were photofunctionalized for 15 min with a commercially available UV-light-producing device, which was especially designed for dental implant surface modification (TheraBeam® Super Osseo, Ushio, Tokyo, Japan; Fig. 1a). Although the company provided the machine, no information was given upon request regarding the UV-light intensity,

**Table 1 Materials used in this study**

Proprietary material	Lot No.	Type	Manufacturer
TheraBeam® Super Osseo	URC0016	AKM 004	USHIO, Tokyo, Japan
Camlog® Conelog® implant	0020052224	9.0 mm×4.3 mm	Camlog Biotechnologies, Basel, Switzerland
Conelog® abutment screw	0000054456	Titanium abutment screw	Camlog Biotechnologies, Basel, Switzerland
Multilink® implant	U27197	Adhesive resin	Ivoclar Vivadent, Schaan, Liechtenstein
Abutments	D0065.6305	Hybrid abutments	CamlogDedicam, Wimsheim, Germany
	D0065.6347		
	C2242.4308		
Conelog® titanium base	0000056093	Link abutment	Camlog Biotechnologies, Basel, Switzerland
Calcein-blue	SLBJ7607V	Fluorescent dye	Sigma-Aldrich, Schnelldorf, Germany
Xylenol-orange	BCBN7544V	Fluorescent dye	Sigma-Aldrich, Schnelldorf, Germany
Terramycin® LA	A437810	Antibiotic/fluorescent dye	Zoetis, Berlin, Germany
Epoxy Resin Stycast®	47458	Epoxy resin	Emerson Cuming, Westerloo, Belgium
Loctite® 493	49333	Instant adhesive	Loctite UK Ltd., Hemel Hempstead, UK

Data are provided by the manufacturers



**Fig. 1 Photofunctionalization and stability measurement**  
 (a) Photofunctionalization of four implants with high energy UV-light. (b) Placed implants screwed with SmartPegs (Osstell) ready for resonance frequency measurement (implant stability quotient (ISQ))

ozone ( $O_3$ ) concentration and other important data. In a “split mouth” design, eight implants per minipig were photofunctionalized and eight untreated implants served as controls (four per jaw). Overall, 48 implants were placed. Directly after placement, the ISQ was measured mesially/distally and buccally/orally (Osstell, Gothenburg, Sweden; Fig. 1b). ISQ is measured on a scale from 1 to 100 and is a measure of the stability of an implant. The ISQ scale has a non-linear correlation to micro-mobility: high stability if ISQ values  $>70$ ; medium stability if values between 60 and 69; and low stability if values  $<60$ .

The wound was closed with absorbable sutures and implants were allowed to heal for three months.

To mimic the clinical situation, all implants were exposed and platform-switched conical abutments, with 4 mm height and 3.7 mm diameter, were inserted. Antibiotics (10 mg/kg BW, Enrofloxacin, 10% (0.1 g/ml) Baytril®, Bayer, Leverkusen, Germany) and painkillers (4 mg/kg BW, Rimadyl, Carprofen, Pfizer, Berlin, Germany) were injected directly after the surgery (Mehl et al., 2013).

Although the initial front of bone mineralization after a trauma starts within the first 4–6 d (Eriksen et al., 1984), fluorochrome labeling was initiated one week after implant exposure. This was done to determine longer-term effects of photofunctionalization on implant bone interaction and to reduce animal suffering.

Labeling was repeated every two weeks by intraperitoneal injections as follows: (1) oxytetracycline (30 mg/kg BW, Terramycin®, Zoetis, Berlin, Germany) (Becker et al., 2009; Mehl et al., 2013); (2) xylenol-orange (6% in 2% (0.02 g/ml) NaHCO<sub>3</sub>, 90 mg/kg BW, Sigma-Aldrich, Steinheim, Germany) (Lentrot and Bull, 1976; Mehl et al., 2013); (3) calcein-blue (1% in 2% NaHCO<sub>3</sub>, 15 mg/kg BW, Sigma-Aldrich, Schnelldorf, Germany) (Lentrot and Bull, 1976; Mehl et al., 2013); (4) start again with (1).

All minipigs simultaneously received fluorochrome injections and a professional dental cleaning, with an electrical toothbrush and plastic curettes (universal implant deplaque; KerrHawe, Bioggio, Switzerland) under sedation. The animals were sacrificed after overall nine months (six months: implant healing time), and the jaws harvested. The minipigs were initially anesthetized by an intramuscular injection of azaperone (2 mg/kg BW), midazolam (1.8 mg/kg

BW), and 10% (0.1 g/ml) ketamin (10 mg/kg BW). They were then euthanized by an intravascular injection of 40 mg/kg pentobarbital (Narcoren®, Merial, Hallbergmoos, Germany) via an ear flexure.

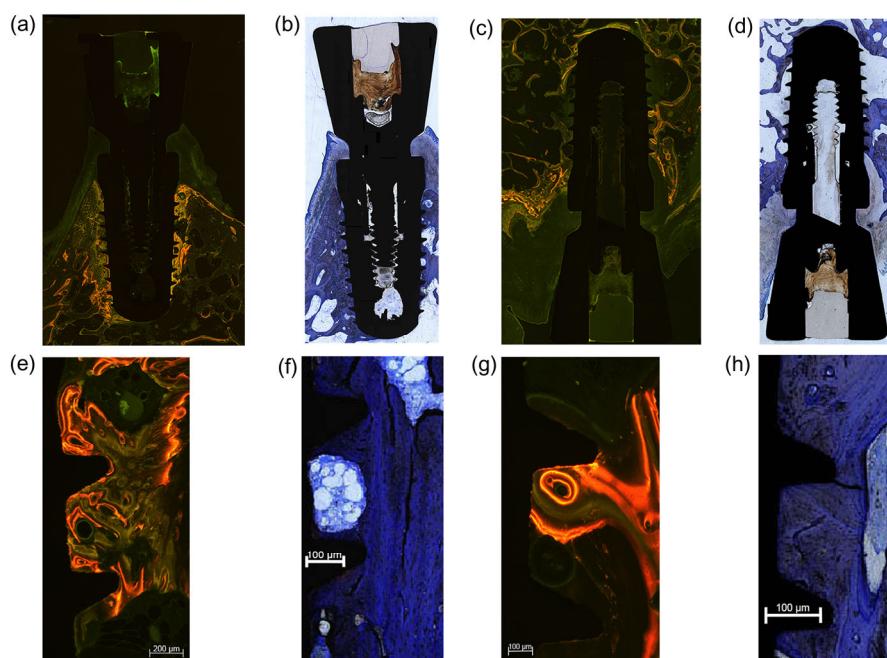
## 2.2 Preparation of the specimens

The preparation of the specimens has been described in detail by Mehl et al. (2013). In short, after sacrificing the animals, the harvested jaws were immediately placed in freshly mixed and weekly replaced 4% paraformaldehyde at 4 °C (Mehl et al., 2013). After fixation, the specimens were dehydrated and embedded (Type 1.412.00, Pool of Scientific Instruments Grünwald GmbH & Co., KG, Laudenbach, Germany) (Mehl et al., 2013). The embedding procedures were conducted using a technique described by Donath and Breuner (1982). Following polymerization, the jaws were cut (Metabo, Wiesmoor, Germany) according to the experimental groups, and then

further sliced to 100 µm in the anterior-posterior direction (Exakt Apparatebau, Norderstedt, Germany) (Mehl et al., 2013).

## 2.3 Light and fluorescence microscopy, and histomorphometry

Light and fluorescence microscopy procedures have been described in detail by Mehl et al. (2013). In short, half of each specimen was ground into polished undecalcified sections of 30–40 µm, which were then stained with toluidine blue solution (Donath and Breuner, 1982; Mehl et al., 2013). The stained sections were examined under a light or fluorescence microscope (Mikrophot-FXA, Nikon, Tokyo, Japan) and digital photographs were taken (Q500MC, Leica Cambridge Ltd., Cambridge, England, UK). The BIC area was calculated using computer software (Photoshop Version 12.0, Adobe Systems, San Jose, USA; Fig. 2).



**Fig. 2 Histomorphometric measurements and fluorescence microscopy**

(a) Exemplary fluorescent-dyed merged photograph of a photofunctionalized implant in the lower jaw (original magnification 2.5×); (b) showing (a) with toluidine blue staining used for bone-implant contact area measurement (original magnification 2.5×). (c) Exemplary fluorescent-dyed merged photograph of a non-photofunctionalized implant in the upper jaw (original magnification 2.5×); (d) showing (c) with toluidine blue staining used for bone-implant contact area measurement (original magnification 2.5×). The difference in the cancellous bone proportions between upper and lower jaw specimen can be seen. In the visual analysis, no differences between photofunctionalized and non-photofunctionalized implants could be evaluated. (e)–(h) are 10× magnification of (a)–(d), respectively, with two implant screw turns seen on the left side and bone and bone marrow adjacent to the implant surfaces. The sequential succession of newly formed bone adjacent to the implant is shown with brown/yellow (oxytetracycline staining), bright yellow (xylene-orange staining) and to a lesser degree blue (calcein-blue staining) colors. This newly formed bone possibly developed during the loading period of the implants (tertiary stability) (Note: for interpretation of the references to color in this figure legend, the reader is referred to the web version of this article)

The calculation of the BIC area was performed as a percentage of the implant surface area where the bone could have been in direct contact with the implant (overall bone area) and the area where bone actually deposited on the implant (measured bone area; Fig. 2). The BIC was calculated: BIC=measured bone/overall bone area×100%. The photographs of the fluorescence microscopy were visually inspected.

#### 2.4 Statistical analysis

Data were statistically analyzed using SPSS for Windows (Version 23.0; SPSS Inc., Chicago, USA). The data for overall implant surface area, BIC in mm, and BIC in percentage were distributed normally (Kolmogorov-Smirnov and Lilliefors test) and parametric

tests were employed (multivariate analysis of variance (MANOVA), analysis of variance (ANOVA)). ISQ data were not distributed normally (Kolmogorov-Smirnov and Lilliefors test) and hence a non-parametric test was used (Kruskal-Wallis tests). All tests were performed at a confidence level of 95%.

### 3 Results

A summary of the data and the statistical analysis can be found in Tables 2–4. Overall, six implants were lost (12.5%), five until exposure (10.4%) and one until sacrifice of the animals (2.1%) (exemplarily Fig. 3).

**Table 2 Implant stability quotient (ISQ) value at implantation and implant exposure**

Group	ISQ at implantation				ISQ at exposure			
	PF		No PF		PF		No PF	
	U	L	U	L	U	L	U	L
Minipig 1	77 (77; -/3)	77 (74; 79/4)	71 (66; 74/4)	80 (79; 80/4)	80 (76; -/3)	80 (78; 82/4)	74 (73; 75/4)	80 (80; 81/4)
Minipig 2	78 (77; 80/4)	76 (71; 78/4)	74 (73; -/3)	75 (66; 79/4)	78 (76; 80/4)	76 (73; 78/4)	75 (75; -/3)	80 (78; 81/4)
Minipig 3	72 (65; 72/3)	74 (72; -/2)	69 (61; 73/4)	78 (76; -/3)	76 (72; -/3)	81 (77; -/2)	75 (75; 81/4)	69 (69; -/3)
Data pooled								
Upper jaw			75 (70; 77/21)				76 (75; 79/21)	
Lower jaw			77 (74; 79/21)				80 (77; 80/21)	
PF			77 (73; 78/20)				78 (76; 83/20)	
No PF			76 (70; 79/22)				77 (74; 80/22)	
Overall			76 (72; 78/42)				78 (75; 80/42)	

Mesial/distal and buccal/oral values were averaged for calculation purposes. Median (25th; 75th percentile/number) is shown. PF: photofunctionalization; U: upper jaw; L: lower jaw; -: no

**Table 3 Overall implant surface area and bone-implant contact (BIC)**

Group	Overall implant surface area (mm)				BIC (mm)				BIC (%)			
	PF		No PF		PF		No PF		PF		No PF	
	U	L	U	L	U	L	U	L	U	L	U	L
Minipig 1	23.8 (3.3/3)	22.0 (3.8/4)	21.6 (5.9/4)	23.9 (3.5/4)	9.3 (5.3/3)	14.3 (5.4/4)	12.8 (3.6/4)	16.2 (3.3/4)	38.2 (18.5/3)	63.3 (16.9/4)	60.2 (16.9/4)	68.4 (13.1/4)
Minipig 2	22.7 (2.3/4)	23.5 (6.6/4)	21.5 (2.2/3)	23.2 (2.8/4)	14.1 (4.4/4)	16.4 (4.6/4)	15.1 (7.9/3)	19.1 (1.9/4)	61.5 (16.8/4)	71.3 (19.5/4)	69.7 (34.9/3)	84.3 (5.9/4)
Minipig 3	23.9 (3.7/3)	26.3 (0.8/2)	24.4 (2.1/4)	20.9 (3.9/3)	11.2 (6.5/3)	24.8 (1.1/2)	13.4 (4.3/4)	12.0 (8.1/3)	47.4 (28.9/3)	94.1 (1/2)	55.3 (17.8/4)	54.0 (27/3)
Data pooled												
Upper jaw			23.0 (2.8/21)				12.8 (4.9/21)			55.9 (21.7/21)		
Lower jaw			23.2 (3.9/21)				16.7 (5.4/21)			71.4 (18.6/21)		
PF			23.5 (3.7/20)				14.5 (5.0/20)			61.5 (22.9/20)		
No PF			22.7 (3.1/22)				14.9 (5.1/22)			65.7 (20.4/22)		
Overall			23.1 (3.4/42)				14.7 (5.5/42)			63.7 (21.4/42)		

Mean (standard deviation/number) is shown. PF: photofunctionalization; U: upper jaw; L: lower jaw

**Table 4 Statistical analyses of the influences of the three experimental factors minipig, jaw, and photofunctionalization on overall implant surface area and bone-implant contact (BIC) using MANOVA**

Factor	Parameter	Mean square	F	P
Minipigs compared	Overall implant surface area	4.951	0.371	0.693
Minipig 1 ( <i>n</i> =15);	BIC in mm	36.846	1.492	0.241
Minipig 2 ( <i>n</i> =15);	BIC in %	757.938	1.974	0.157
Minipig 3 ( <i>n</i> =12)				
Upper jaw vs. lower jaw	Overall implant surface area	1.211	0.091	0.765
Upper jaw ( <i>n</i> =21);	BIC in mm	205.078	8.306	<b>0.007</b>
Lower jaw ( <i>n</i> =21)	BIC in %	2977.683	7.755	<b>0.009</b>
PF vs. no PF	Overall implant surface area	13.609	1.020	0.321
PF ( <i>n</i> =20);	BIC in mm	0.364	0.015	0.904
No PF ( <i>n</i> =22)	BIC in %	74.868	0.195	0.662
Interactions				
Minipigs×jaw ( <i>n</i> =42)	Overall implant surface area	2.615	0.196	0.823
	BIC in mm	6.244	0.253	0.778
	BIC in %	90.267	0.235	0.792
Minipigs×PF ( <i>n</i> =42)	Overall implant surface area	3.850	0.288	0.752
	BIC in mm	59.776	2.421	0.106
	BIC in %	811.822	2.114	0.138
Jaw×PF ( <i>n</i> =42)	Overall implant surface area	0.380	0.028	0.867
	BIC in mm	57.935	2.346	0.136
	BIC in %	998.159	2.600	0.117
Minipigs×jaw×PF ( <i>n</i> =42)	Overall implant surface area	20.001	1.498	0.240
	BIC in mm	62.155	2.517	0.098
	BIC in %	553.560	1.442	0.252

MANOVA: multivariate analysis of variance; PF: photofunctionalization. Values of *P*<0.05 are bold



**Fig. 3 A failed implant due to an inflammatory response**  
A bacterial colonization caused the implant to be repelled by the host as a foreign body

Individual ISQ data between the minipigs were not significantly different at the implantation stage or at the exposure stage. Consequently, the data were pooled (Kruskal-Wallis test; *P*>0.05). No significant differences in ISQ values were observed for the experimental factors minipig and photofunctionalization at the implantation stage, exposure stage, or between the implantation and exposure stage (Kruskal-Wallis test; *P*>0.05). The lower jaw showed significantly

higher ISQ values at the implantation and exposure stage than the upper jaw (Kruskal-Wallis test; *P*≤0.05).

The overall median BIC was (64±22)%. No statistically significant difference was observed between the individual overall implant surface area in mm, BIC in mm and BIC in percentage of the minipigs (ANOVA, *P*>0.05). Thus, the data were pooled. No significant differences in overall implant surface area in mm, BIC in mm or BIC in percentage were observed for the experimental factors minipig and photofunctionalization (MANOVA; *P*>0.05). BIC between upper and lower jaw implants was statistically significantly different (MANOVA; *P*≤0.05). No difference was detected by visual inspection of the fluorescent microscopy pictures.

#### 4 Discussion

Overall, six implants lost osseointegration. Of the 48 implants, 42 were evaluated. A test for periodontitis was performed at the implant exposure stage (Hain Lifescience, Nehren, Germany). All minipigs exhibited gingival pockets above 6 mm around the

remaining second molars. For all of the minipigs, bacteria responsible for periodontitis were found that included *Treponema denticola*, *Fusobacterium nucleatum*, *Tannerella forsythia*, *Porphyromonas gingivalis* (Nibali, 2015). The proposed treatment (Hain Lifescience) incorporated a deep scaling in all three cases and an adjuvant antibiotic therapy for two minipigs. The bacterial infection was most likely the reason for the implant losses and for the marginal bone reduction at the implant shoulders. Other possible explanations for the marginal bone reduction and inflammation seen around the implants could be due to unfinished bone remodeling three months after the extractions, especially in animals with periodontitis (Elsubeihi and Heersche, 2004; Covani et al., 2011) or highly cancellous bone, especially in the upper jaw (Figs. 2c and 2d) (Mosekilde et al., 1987; Mosekilde, 1995). Lastly, a very unlikely reason could also be titanium-induced immune reactions (Nishimura et al., 2014).

Although the company provided the machine, even upon request (probably due to industrial confidentiality), no information was given regarding the UV-light intensity, O<sub>3</sub> concentration, or other relevant data, which could have helped in identifying the biological effects. Additionally, we did not find any publications that could give us more information in this context (Aita et al., 2009; Park et al., 2013; Pyo et al., 2013). However, according to the knowledge of the authors, this is the only commercially available device, which enables implanting dentists to modify the implant surface using UV-light. Since literature on this topic exists, we aimed at finding out if these data justify the use of such a device in every implanting practice/clinic. As mentioned before, the operating parameters of the USHIO TheraBeam® device are unavailable for the general public. One important parameter is the processing time of 15 min, which cannot be changed. Hence, we were only able to test a UV-light processing time of 15 min. Testing more time brackets would maybe have benefits in understanding the potential of UV-light photofunctionalization better. However, longer photofunctionalization time is clinically very difficult to establish, as no surgeon would wait a long time during an operation until an implant is ready to be placed.

In contrast to other studies (Aita et al., 2009; Park et al., 2013; Pyo et al., 2013), UV-treatment did

not substantially impact BIC in our study. The reported BIC of up to 98% after four weeks of healing (Aita et al., 2009) was not achieved after the nine-month observation period. The current study had a BIC of about 64%, which is within the range of typical BIC values, between 50% and 75%, observed in “conventional studies” using surface modifications (Ogawa and Nishimura, 2003; Berglundh et al., 2007; de Maeztu et al., 2008). Animal studies that used photofunctionalization, inserted small-diameter implants into rat tibia (Aita et al., 2009), rabbit tibia (Park et al., 2010), or dog jaw bone (Pyo et al., 2013; Ishii et al., 2016). The tibia model is of limited value, since BIC is evaluated circumferentially in compact bone. In contrast, implants placed in the jaw bone and evaluated by the longitudinal axis contain contact areas in cancellous bone, particularly in the upper jaw (Figs. 2c and 2d). This results in a lower BIC and is probably why no statistically significant differences were observed between photofunctionalized and non-photofunctionalized implants.

In instances where histomorphometric values cannot be measured, e.g. in human trials, ISQ values have been used (Funato and Ogawa, 2013; Funato et al., 2013; Suzuki et al., 2013; Ishii et al., 2016). ISQ values measured mesially/distally and buccally/orally provide the advantage of a near 360° evaluation compared to a two-dimensional histomorphometric analysis. The ISQ values in the current study are comparable to the values reported in the literature (human trials, ISQ between 40 and 81, ISQ increase of 2.0–8.7 between insertion and after implant exposure measurement) (Funato and Ogawa, 2013; Funato et al., 2013; Suzuki et al., 2013). Although implant cavities were tapped, before implant placement, the high initial ISQ values in this study can very likely be linked to the hard compact surface layer of the minipigs’ jaw bones. Hence, no statistically significant difference was detected between implant placement and exposure ISQs (Funato and Ogawa, 2013; Funato et al., 2013; Suzuki et al., 2013). The major aim of the study was to evaluate if patients would benefit from additional intense UV-light treatment of their implants being placed, to receive restorations earlier and help speed up the healing process. We speculate that the stability of the implant at exposure, compared to a later stage, is more important as the implant will have to carry an expensive restoration a

few weeks later. It is therefore critical to know if the restoration can be placed. Additionally, the chewing and the tertiary stability might have falsified the results of the ISQ stability measurements at a later stage. Hence, we decided to focus mainly on the ISQ values at a time when it mattered most clinically. However, the tertiary stability might also have influenced the histomorphometric measurements taken half a year after exposure, and is a limitation to the histological analysis. However, we did not observe any differences in the images evaluated and tertiary stability was equal in all implants.

It would be beneficial for further research in this area to place implants with ISQ values about 60. This would result in measuring the improvement of the implant-bone bond and not measuring the primary stability of the implants. This idea is consistent with the fact that implants placed in the upper jaw did not show statistically significantly higher ISQ values at exposure compared to the placement. However, the investigation period/implant healing time of the current study was set at nine months, while other groups evaluated the specimens after four weeks (Aita et al., 2009; Park et al., 2013; Pyo et al., 2013), making it difficult to compare the results directly to one another.

## 5 Conclusions

The UV photofunctionalization of dental titanium implants in the current study did not have a significant impact on osseointegration after a period of nine months.

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## Compliance with ethics guidelines

Christian MEHL, Matthias KERN, Friederike NEUMANN, Telse BÄHR, Jörg WILTFANG, and Volker GASSLING declare that they have no conflict of interest.

All institutional and national guidelines for the care and use of laboratory animals were followed.

## References

- Abboud M, Koeck B, Stark H, et al., 2005. Immediate loading of single-tooth implants in the posterior region. *Int J Oral Maxillofac Implants*, 20(1):61-68.  
<https://doi.org/10.1016/j.prosdent.2005.04.021>
- Adell R, Lekholm U, Rockler B, et al., 1981. A 15-year study of osseointegrated implants in the treatment of the edentulous jaw. *Int J Oral Surg*, 10(6):387-416.  
[https://doi.org/10.1016/S0300-9785\(81\)80077-4](https://doi.org/10.1016/S0300-9785(81)80077-4)
- Aita H, Hori N, Takeuchi M, et al., 2009. The effect of ultraviolet functionalization of titanium on integration with bone. *Biomaterials*, 30(6):1015-1025.  
<https://doi.org/10.1016/j.biomaterials.2008.11.004>
- Att W, Ogawa T, 2012. Biological aging of implant surfaces and their restoration with ultraviolet light treatment: a novel understanding of osseointegration. *Int J Oral Maxillofac Implants*, 27(4):753-761.  
[https://doi.org/10.1016/S0022-3913\(12\)60182-6](https://doi.org/10.1016/S0022-3913(12)60182-6)
- Becker ST, Bolte H, Krapf O, et al., 2009. Endocultivation: 3D printed customized porous scaffolds for heterotopic bone induction. *Oral Oncol*, 45(11):e181-e188.  
<https://doi.org/10.1016/j.oraloncology.2009.07.004>
- Bergkvist G, Nilner K, Sahlholm S, et al., 2009. Immediate loading of implants in the edentulous maxilla: use of an interim fixed prosthesis followed by a permanent fixed prosthesis: a 32-month prospective radiological and clinical study. *Clin Implant Dent Relat Res*, 11(1):1-10.  
<https://doi.org/10.1111/j.1708-8208.2008.00094.x>
- Berglundh T, Abrahamsson I, Albouy JP, et al., 2007. Bone healing at implants with a fluoride-modified surface: an experimental study in dogs. *Clin Oral Implants Res*, 18(2):147-152.  
<https://doi.org/10.1111/j.1600-0501.2006.01309.x>
- Chuang SK, Wei LJ, Douglass CW, et al., 2002. Risk factors for dental implant failure: a strategy for the analysis of clustered failure-time observations. *J Dent Res*, 81(8):572-577.  
<https://doi.org/10.1177/154405910208100814>
- Covani U, Ricci M, Bozzolo G, et al., 2011. Analysis of the pattern of the alveolar ridge remodelling following single tooth extraction. *Clin Oral Implants Res*, 22(8):820-825.  
<https://doi.org/10.1111/j.1600-0501.2010.02060.x>
- de Maeztu MA, Braceras I, Alava JI, et al., 2008. Improvement of osseointegration of titanium dental implant surfaces modified with CO ions: a comparative histomorphometric study in beagle dogs. *Int J Oral Maxillofac Surg*, 37(5):441-447.  
<https://doi.org/10.1016/j.ijom.2008.01.010>
- Donath K, Breuner G, 1982. A method for the study of undecalcified bones and teeth with attached soft tissues. The Säge-Schliff (sawing and grinding) technique. *J Oral Pathol*, 11(4):318-326.  
<https://doi.org/10.1111/j.1600-0714.1982.tb00172.x>
- Elsubeihi ES, Heersche JN, 2004. Quantitative assessment of post-extraction healing and alveolar ridge remodelling of the mandible in female rats. *Arch Oral Biol*, 49(5):

- 401-412.  
<https://doi.org/10.1016/j.archoralbio.2003.12.003>
- Eriksen EF, Gundersen HJ, Melsen F, et al., 1984. Reconstruction of the formative site in iliac trabecular bone in 20 normal individuals employing a kinetic model for matrix and mineral apposition. *Metab Bone Dis Relat Res*, 5(5):243-252.  
[https://doi.org/10.1016/0221-8747\(84\)90066-3](https://doi.org/10.1016/0221-8747(84)90066-3)
- Funato A, Ogawa T, 2013. Photofunctionalized dental implants: a case series in compromised bone. *Int J Oral Maxillofac Implants*, 28(6):1589-1601.  
<https://doi.org/10.11607/jomi.3232>
- Funato A, Yamada M, Ogawa T, 2013. Success rate, healing time, and implant stability of photofunctionalized dental implants. *Int J Oral Maxillofac Implants*, 28(5):1261-1271.  
<https://doi.org/10.11607/jomi.3263>
- Heydecke G, McFarland DH, Feine JS, et al., 2004. Speech with maxillary implant prostheses: ratings of articulation. *J Dent Res*, 83(3):236-240.  
<https://doi.org/10.1177/154405910408300310>
- Ishii K, Matsuo M, Hoshi N, et al., 2016. Effect of ultraviolet irradiation of the implant surface on progression of periimplantitis—a pilot study in dogs. *Implant Dent*, 25(1):47-53.  
<https://doi.org/10.1097/ID.0000000000000322>
- Lentrodt J, Bull HG, 1976. Animal experimental studies on bone regeneration following drilling of the bone. *Dtsch Zahnärztl Z*, 31(2):115-124 (in German).
- Maló P, de Araújo Nobre M, Lopes A, et al., 2012. ‘All-on-4’ immediate-function concept for completely edentulous maxillae: a clinical report on the medium (3 years) and long-term (5 years) outcomes. *Clin Implant Dent Relat Res*, 14(Suppl 1):e139-e150.  
<https://doi.org/10.1111/j.1708-8208.2011.00395.x>
- Mehl C, Becker ST, Acil Y, et al., 2013. Impact of vertical loading on the implant-bone interface. *Clin Oral Implants Res*, 24(8):949-956.  
<https://doi.org/10.1111/j.1600-0501.2012.02487.x>
- Melas F, Marques W, Wright PS, 2001. Oral health impact on daily performance in patients with implant-stabilized overdentures and patients with conventional complete dentures. *Int J Oral Maxillofac Implants*, 16(5):700-712.
- Mosekilde L, 1995. Assessing bone quality—animal models in preclinical osteoporosis research. *Bone*, 17(4 Suppl):S343-S352.  
[https://doi.org/10.1016/8756-3282\(95\)00312-2](https://doi.org/10.1016/8756-3282(95)00312-2)
- Mosekilde L, Kragstrup J, Richards A, 1987. Compressive strength, ash weight, and volume of vertebral trabecular bone in experimental fluorosis in pigs. *Calcif Tissue Int*, 40(6):318-322.  
<https://doi.org/10.1007/BF02556693>
- Moy PK, Medina D, Shetty V, et al., 2005. Dental implant failure rates and associated risk factors. *Int J Oral Maxillofac Implants*, 20(4):569-577.
- Nibali L, 2015. Aggressive periodontitis: microbes and host response, who to blame? *Virulence*, 6(3):223-228.  
<https://doi.org/10.4161/21505594.2014.986407>
- Nishimura K, Kato T, Ito T, et al., 2014. Influence of titanium ions on cytokine levels of murine splenocytes stimulated with periodontopathic bacterial lipopolysaccharide. *Int J Oral Maxillofac Implants*, 29(2):472-477.  
<https://doi.org/10.11607/jomi.3434>
- Ogawa T, 2014. Ultraviolet photofunctionalization of titanium implants. *Int J Oral Maxillofac Implants*, 29(1):e95-e102.  
<https://doi.org/10.11607/jomi.te47>
- Ogawa T, Nishimura I, 2003. Different bone integration profiles of turned and acid-etched implants associated with modulated expression of extracellular matrix genes. *Int J Oral Maxillofac Implants*, 18(2):200-210.
- Park DS, Kim IS, Kim H, et al., 2010. Improved biocompatibility of hydroxyapatite thin film prepared by aerosol deposition. *J Biomed Mater Res B Appl Biomater*, 94(2):353-358.  
<https://doi.org/10.1002/jbm.b.31658>
- Park KH, Koak JY, Kim SK, et al., 2013. The effect of ultraviolet-C irradiation via a bactericidal ultraviolet sterilizer on an anodized titanium implant: a study in rabbits. *Int J Oral Maxillofac Implants*, 28(1):57-66.  
<https://doi.org/10.11607/jomi.2638>
- Pyo SW, Park YB, Moon HS, et al., 2013. Photofunctionalization enhances bone-implant contact, dynamics of interfacial osteogenesis, marginal bone seal, and removal torque value of implants: a dog jawbone study. *Implant Dent*, 22(6):666-675.  
<https://doi.org/10.1097/ID.0000000000000003>
- Suzuki S, Kobayashi H, Ogawa T, 2013. Implant stability change and osseointegration speed of immediately loaded photofunctionalized implants. *Implant Dent*, 22(5):481-490.  
<https://doi.org/10.1097/ID.0b013e31829deb62>
- Tealdo T, Bevilacqua M, Pera F, et al., 2008. Immediate function with fixed implant-supported maxillary dentures: a 12-month pilot study. *J Prosthet Dent*, 99(5):351-360.  
[https://doi.org/10.1016/S0022-3913\(08\)60082-7](https://doi.org/10.1016/S0022-3913(08)60082-7)
- Urban IA, Jovanovic SA, Lozada JL, 2009. Vertical ridge augmentation using guided bone regeneration (GBR) in three clinical scenarios prior to implant placement: a retrospective study of 35 patients 12 to 72 months after loading. *Int J Oral Maxillofac Implants*, 24(3):502-510.
- van Kampen FM, van der Bilt A, Cune MS, et al., 2004. Masticatory function with implant-supported overdentures. *J Dent Res*, 83(9):708-711.  
<https://doi.org/10.1177/154405910408300910>
- Wang R, Hashimoto K, Fujishima A, 1997. Light-induced amphiphilic surfaces. *Nature*, 388:431-432.  
<https://doi.org/10.1038/41233>
- Weinlaender M, Kenney EB, Lekovic V, et al., 1992. Histomorphometry of bone apposition around three types of endosseous dental implants. *Int J Oral Maxillofac Implants*, 7(4):491-496.
- Zarb GA, Schmitt A, 1990. Terminal dentition in elderly patients and implant therapy alternatives. *Int Dent J*, 40(2):67-73.

## 中文摘要

**题 目:** 牙钛种植体的紫外线光化功能对骨整合的影响

**目 的:** 通过在动物模组上植入钛种植体，测量紫外线光化功能对于骨整合的作用和影响。

**方 法:** 在三只小型猪的无牙颌中植入共 48 个钛种植体 (Camlog® Conelog® 4.3 mm×9.0 mm)，测量其植体稳定度数值 (ISQ)。在植入手术前，用强紫外光对一半的种植体进行光化处理。植入手术三个

月后，暴露种植体，再次测量 ISQ。在暴露种植体六个月后，处死动物，通过组织形态学、光学和荧光显微镜对采样标本进行分析。

**结 论:** 在 48 个种植体中，42 个完成骨整合。总平均骨-植人物的接触面积 (BIC) 为 (64±22)%。作为实验因素的小型猪及紫外线光化功能没有造成 BIC 和 ISQ 值的显著差异 ( $P>0.05$ ，多元方差分析)。九个月后，对钛种植体进行紫外线光化处理，没有对骨结合产生显著的影响。

**关键词:** 种植牙；骨结合；光化功能