Effects of Ultraviolet Photoactivation on Osseointegration of Commercial Pure Titanium Dental Implant After 8 Weeks in a Rabbit Model

Arturo Sanchez-Perez, MD, PhD[1]*
Carlos Cachazo-Jiménez, DDS[2]
Carmen Sánchez-Matás, MD[3]
José Javier Martín-de-Llano, BDS, PhD[4]
Scott Davis, MDSc[5]
Carmen Carda-Batalla, MD, PhD[4]

This study investigated whether a 6-Watt ultraviolet C-lamp was capable of producing photofunctionalization on commercial implants during a medium observation term of 8 weeks. A total of 20 implants were inserted in 5 New Zealand rabbits, with each animal receiving 2 implants per tibia (one photofunctionalized and one untreated), according to a previously established randomization sequence. All implants were inserted by a single surgeon following the manufacturer's instructions. Histological analysis was performed by an evaluator who was blinded to the treatment condition. After 8 weeks of healing, the 2 groups showed no statistically significant differences in terms of bone-to-implant contact. Compared to control implants, the photofunctionalized implants showed improved wettability and more homogenous results. Within the limits of the present study, the use of this 6-W ultraviolet C-lamp, for an irradiation time of 15 minutes at a distance of 15 cm, did not improve the percentages of bone-to-implant contact in rabbits at an osseointegration time of 8 weeks.

Key Words: dental implants, osseointegration, photocatalysis, ultraviolet, titanium dioxide

INTRODUCTION

Titanium is an excellent material for dental implants.[1] Various surface modifications with macro-, micro-, and nanodesign features have improved the predictability of osseointegration,[2,3] yielding improved response of bone to implants and reduced healing times.[4,5] These improvements seem linked to properties of the modified titanium surface,[6] which increase the absorption of ions, lipids, carbohydrates, and proteins,[7] thus stimulating cell attraction, proliferation, and expansion.[8] The ultimate result is a greater proportion of contact between bone and the implant (BIC).[9]

Importantly, titanium is altered by aging[10–13] due to the deposition of atmospheric hydrocarbons existing within the sterile packaging of the implant.[11,13,14] These accumulated hydrocarbons cover titanium oxide atoms, causing the titanium surface to become progressively more hydrophobic.[8,11,15,16] Such aging has been detected as soon as 4 weeks after manufacture.[8] Aged titanium surfaces exhibit 50% lower absorption of proteins and osteoblasts compared to newly manufactured titanium surfaces.[12,13] This alteration is considered unavoidable and is dependent on storage time.[17,18]

The use of ultraviolet light has been proposed as a means of removing hydrocarbon components from the implant surface.[16] This procedure, termed "photofunctionalization," creates a superhydrophilic surface[19] without altering any other characteristics of the titanium surface.[20,21] Photofunctionalization was initially introduced in 1997 as a means of creating an antifog coating for titanium oxide, and its effect can be explained by the generation of Ti^{3+}, which absorbs hydroxyl groups.[22,23]

Photofunctionalization reportedly improves both the percentage of BIC and the counter-torque strength required to disrupt osseointegration in animal experiments.[24,25] Some authors have called this phenomenon "superosteointegration."[10] Optimal photofunctionalization effects have been obtained using a ultraviolet-C (UVC) spectrum with a wavelength of 254 nm.[26,27] However, it remains unknown what irradiation distance, minimum power in watts, and minimum irradiation time are required to obtain a clinically appreciable effect.

In the present study, we aimed to determine the effects of UVC light (254 nm applied for 15 minutes at a distance of 15 cm) on dental implants that were inserted in rabbit tibiae after 8 weeks of healing, with comparison between treated and nontreated implants.

[1] Periodontics Unit, Medicine and Dentistry, University of Murcia, Spain.
[2] Private practice in Murcia, Spain.
[3] Virgen del Rocio Hospital, Seville, Spain.
[4] Department of Pathology, Medicine and Dentistry, University of Valencia, Spain; INCLIVA, Valencia, Spain.
[5] Private practice in Port Macquarie and Coffs Harbour, NSW Australia.
* *Corresponding author,* e-mail: arturosa@um.es
https://doi.org/10.1563/aaid-joi-D-19-00122

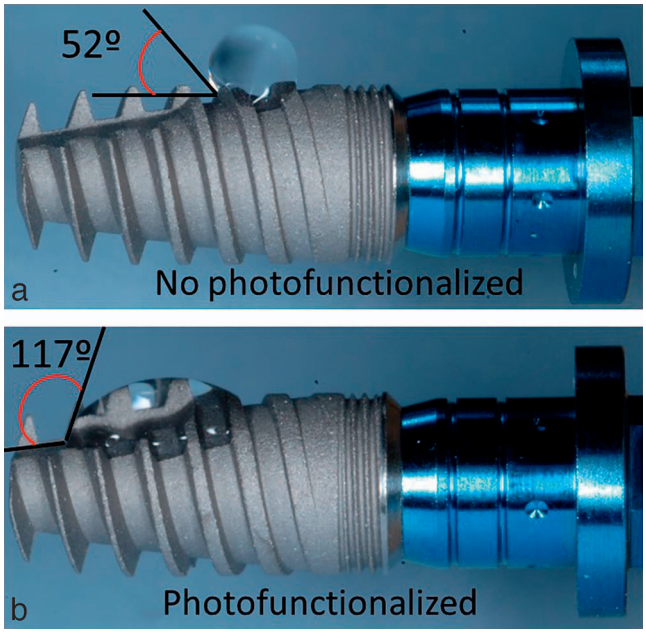

Figure 1. A micro-pipette was used to place 10-μL drops of bidistilled water on untreated and photofunctionalized implants. (a) Poor wettability (<90°) on the untreated implant. (b) Good wettability (>90°) on the photofunctionalized implant.

Material and Methods

Checking the ability to improve wettability by the UVC lamp

To determine the effect of the UVC lamp on the implants' surfaces, we followed the methodology described by Flanagan.[28] We used 2 commercial implants Ticare Quattro Inhex of 3.75 × 8 mm (Mozo Grau, Valladolid, Spain): One implant was used as a control without UVC irradiation, and the other as a test with UVC irradiation. These implants were not used in animal experiments. Both were maintained under the same conditions as the implants used in animal experiments. On both implants, a drop of double-distilled sterilized water (10 μL) was deposited using a micropipette. The contact angle was 52° with the non-photofunctionalized implant, versus 117° with the photofunctionalized (hydrophilic) implant (Figure 1). These findings demonstrated that the UVC lamp could improve wettability. This effect was further verified when the implants were inserted in the experimental animals, based on the more rapid extension of blood on the photofunctionalized implants compared to the control implants (Figure 2).

To avoid introducing another variable, contact angle testing was not performed using any of the 20 implants utilized in the animal experiments.

Animals used in the experiments

Animal experiments were conducted with 5 adult New Zealand rabbits weighing 3–3.5 kg from animal housing facilities (University of Murcia, Spain). Each rabbit was given an identifying number on an ear tab. This study was conducted in strict accordance with the guidelines for the use of animals for experimentation purposes (Spanish Royal Decree 53/2013 of February 1, as published in the Official State Bulletin no. 34 of February 8, 2013). The study was approved by the ethics committee of the University of Murcia (Spain). The principles of replacement, reuse, and reduction were observed, and all personnel in charge of the experimental work were vetted for their qualifications.

Randomization

Prior to surgery, a randomization sequence was performed using a computer app (https://www.random.org), and the results were concealed in envelopes until surgery. After an animal was anesthetized, an envelope was randomly chosen, and the implants were placed following the indicated order.

Implants

We used a total of 20 implants (3.75 × 8 mm) with no modifications, as provided by the manufacturer for clinical use. All implants were subjected to surface treatment with resorbable blast media and had an internal conical connection. The control implants were inserted just as the manufacturer distributes them for clinical use. The photofunctionalized implants were photoactivated prior to osteotomy, using 15 minutes of irradiation with a 6-W UVC source at 254 nm, at a distance of 15 cm (VL-6C model; Analyzer, Murcia, Spain).

Surgical procedures

First, the animals were anesthetized with medetomidine (0.15 mL/kg, intramuscular) and ketamine hydrochloride (0.35 mL/kg, intramuscular), and the fur was removed (teichoic acid) to generate adequate skin exposure. Then antiseptic cleaning was performed using 70% ethanol and chlorhexidine. The animals were additionally anesthetized with a local injection of 1% lidocaine-adrenaline.

To access the bone surface, a 3-cm incision was made on the interior side of the tibia. The implants were set following a surgical guide, and drilling was performed following the manufacturer's recommendations. There was a 7-mm distance between the centers of the implants. During drilling, the housing area was abundantly irrigated with room temperature saline solution. The drilling speed was 800 rpm, and the torque was 20 N. After this preparation, the implants were inserted according to the sequence indicated in the envelope assigned to each animal (Figure 3). Finally, the surgical site was sutured with Vicryl 4/0 in the muscular and subcutaneous planes, and the surgical site was disinfected.

Fentanyl patches were applied on the inside of the ear as a slow-liberating analgesic and were changed daily. Each day, the wounds were washed, and the animals were given antibiotics (60 000 IU/kg daily). Healing occurred with no incidents. For 8 weeks, the animals were kept in the animal experimental facilities and given a standard diet.

Histomorphometry

At 8 weeks after surgery, the animals were sacrificed with an overdose of pentobarbital sodium with ketamine-xylazine. The tibias were retrieved by sharp dissection. An electrical saw was used to obtain sections that included the implants. Then the implants were dehydrated by sequential passes of 70% ethanol,

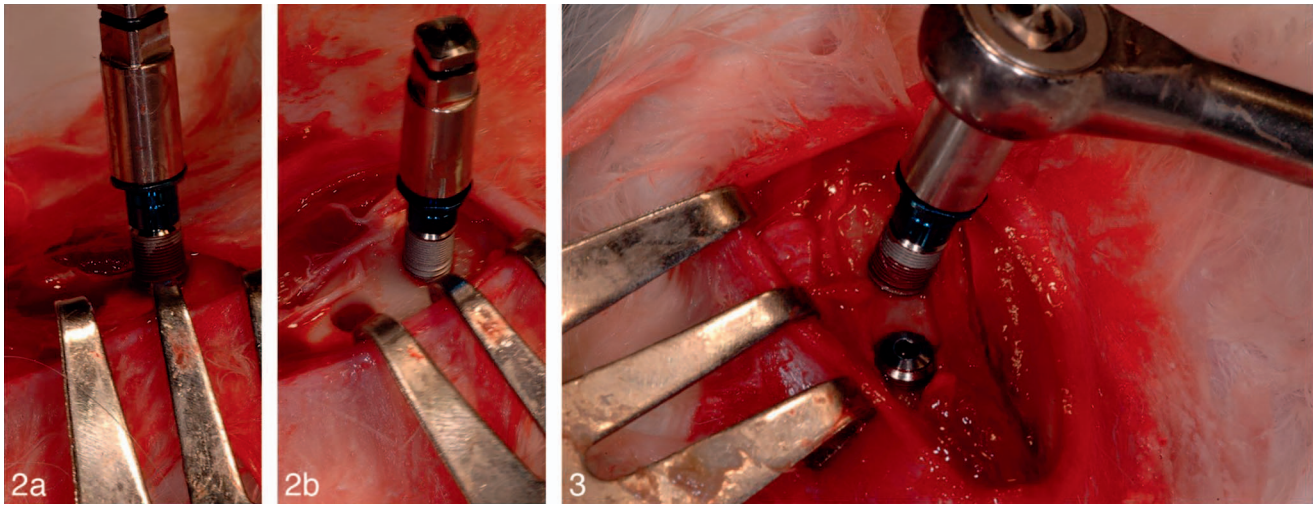

Figure 2 and 3. (a) Upon insertion of a photofunctionalized implant, blood rapidly reached the coronal zone. (b) Upon insertion of an untreated implant, blood only moisturized the area in contact with the cortical bone. **Figure 3.** Insertion of a photofunctionalized implant, along with a non-photofunctionalized implant. The hydrophilicity of the photofunctionalized implant can be observed.

pure ethanol, and xylol every 24 hours. Next, they were placed for 5 days into methyl methacrylate and then for 5 days in poly(methyl methacrylate) 5 g/100 mL. Finally, we added benzoyl peroxide (1 g/100 mL), and the samples were left to polymerize at room temperature for several days.

The polymerized samples were sectioned using a diamond disc mounted on a precision cutter (Accutom-5; Struers, Inc, Cleveland, Ohio), and these preparations were ground down and polished (LaboPol 21; Struers). Upon exposing the middle part of the implant, the preparation was polished again using diamond pastes of decreasing grain size. The sections were dyed with toluidine blue (0.1 M in sodium phosphate, pH 3.5) for 30 minutes at 55°C. The preparations were digitalized with a bright-field Leica DM4000 B microscope and photographed using a 10× lens and a DFC420 camera. The BIC was measured using the image program ImageJ 1.48 (ImageJ, National Institutes of Health, htttp://omagej.nih.gov/ij) (Figure 2). The evaluator was blinded to whether a sample belonged to the test or control condition.

Statistical analysis

The obtained BIC values were expressed as means and standard deviations. Statistical analyses were performed using SPSS version 19 for Windows. Data were presented as descriptive statistics (mean and I.C.) using Tukey's exploratory analysis. The adjustment to normality was determined using the Shapiro-Wilk test, and between-group comparisons were performed using the Mann-Whitney *U* test. We considered a *P* value of $<.05$ to indicate significance. The results were reviewed by an independent statistician (http://estadisticamurcia.com/web/#2).

Results

The histometric analysis results are summarized in Table 1 and Figure 4. The average percentage of BIC for photoactivated implants was 24.225%, with a standard error of 2.249991%, and a 95% confidence interval of 19.13517 to 29.31483 and a standard deviation of 7.115095. The average BIC for untreated implants was 26.835%, with a standard error of 4.037271, a 95% confidence interval of 17.70206 to 35.96794, and a standard deviation of 12.766972 (Figure 5). Additionally, the photofunctionalized implants showed less heterogeneity than the untreated implants.

Discussion

Biological aging of titanium is associated with the disappearance of hydrophilicity, progressive contamination with hydrocarbons, and changes in the electrostatic status of titanium surfaces.[8,11,15,16] Titanium aging slows the cellular response, with clinical consequences up to 50% decrease of BIC and 3-fold lower biomechanical resistance for implants.[16,25]

We performed an electronic and manual search of the literature regarding the effects of photofunctionalization and identified a total of 73 articles. The previously reported findings indicate that photofunctionalization accelerates the osseointegration process.[15,16,25,29–36] This effect has been achieved using various UV wavelengths, including ultraviolet A light (UVA), ultraviolet B (UVB) light, and ultraviolet C light (UVC), as well as combinations of these wavelengths. Decontamination leads to increased adhesion of organic and cellular components,[7,14,37–39] resulting in increased bone formation and a greater percentage of BIC, with no impact on the titanium surface, its alloys, or other materials.[20,30,40–44] UVC is the most commonly used wavelength due to its higher power (Table 2).

Photofunctionalization can reportedly shorten healing time while improving prognosis through a minimally invasive approach.[45] Thus, it may be highly useful in certain clinical situations, such as short implants, immediate implants, situations involving low primary stability, and systemic diseases.[43,45–54] Prior studies show that this response is significant in animal models at 2–4 weeks of osseointegra-

TABLE 1

Main histometric results of photofunctionalized implants and controls after 8 weeks of healing*

	BIC			
	Mean	SD	CI	Median
Control implants	26.83	12.76	17.70–35.96	24.02
Photofunctionalized implants	24.22	7.11	19.13–29.31	23.97

*BIC indicates bone to implant contact.

tion,[24,55–57] and its effect seems to weaken after 12 weeks as non-photofunctionalized implants reach the same BIC level.[55] An investigation in a minipig animal model demonstrated that photofunctionalization yields no significant difference in terms of osseointegration at 9 months.[58] However, no prior studies have examined the medium-term effect of photofunctionalization.

Our present findings indicate that there was no significant difference between photofunctionalized and untreated implants after 8 weeks of healing in a rabbit model. Notably, the BIC results with photofunctionalized implants were more homogeneous. It is possible that the results may have indicated a difference if we had used a lamp with a higher power, a longer irradiation time, or a combination of both factors. Our results are in concordance with the findings of Yamazaki et al[59] with respect to the cortical zone, although that group identified significant differences in the apical and middle zones.

Our study completes the in vivo sequence for commercial titanium implants inserted in New Zealand rabbit tibiae at 8 weeks. Other investigations in this sequence include the works of Sawase et al[56] in rabbits at 2 weeks, Ikeda et al[57] in rats at 2–4 weeks, Pyo et al[24] in dogs at 4 weeks, Park et al[60] in rabbits at 4–12 weeks, and Mehl et al[58] in minipigs at 9 months. Based on the available literature, the effects of photofunctionalization seem to occur rapidly and can be observed during the first 4 weeks. However, non-treated commercial implants have achieved similar results in New Zealand rabbit tibiae and minipig jaws at 8 and 12 weeks and at 9 months. Although our present method generated a hydrophilic surface, both in vitro and in vivo, it did not lead to a statistically significant improvement in BIC at 8 weeks.

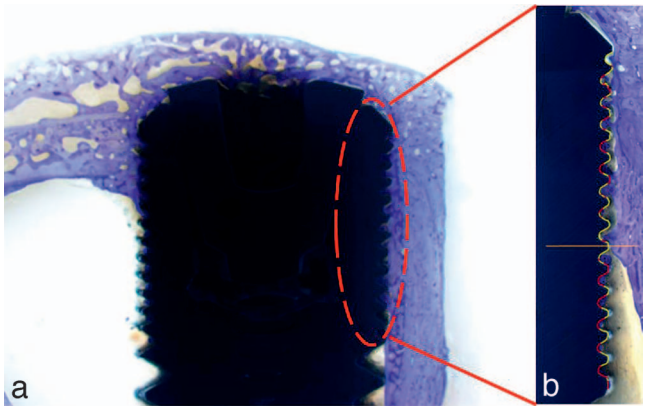

FIGURE 4. (a) Sagittal section of the implant. (b) ×10 magnification image. Red lines indicate bone-implant contact, yellow line indicates the area without contact, and orange horizontal line indicates the separation between the cortical and medullar bone.

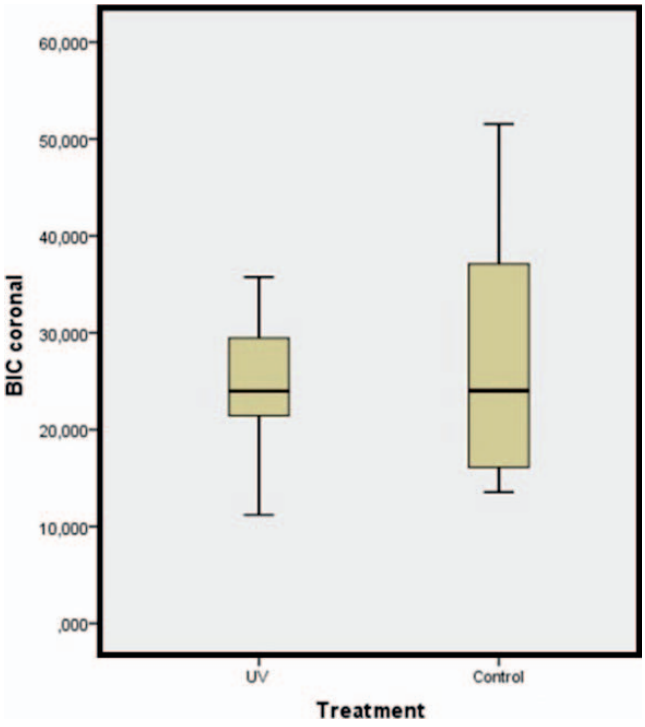

FIGURE 5. Box plot of the total bone-to-implant contact obtained with control and ultraviolet-C-treated surfaces. Plots show the lower (Q1), median (Q2), and upper (Q3) quartiles. The whiskers indicate the highest and lowest observations. BIC indicates bone to implant contact.

The present study had several limitations. First, the available evidence indicates that data regarding the implant response to long bones in animal models cannot easily be transferred to clinical practice. Moreover, implants placed in long bones might not behave like implants placed in jawbones. Secondly, we made our observations at 8 weeks after surgery, which could be considered a medium-term observation time. It would be interesting to see the results of our photofunctionalization method at an earlier time-point. Finally, in our study, we used a 6-W UVC lamp for 15 minutes. It is possible that we may have achieved different results with a higher power lamp and/or a longer irradiation time. Most experiments performed

TABLE 2

Nomenclature, characteristics and different types of ultraviolet light (UV) energy (according to International Organization for Standardization ISO 21348)

Name	Abbreviation	Wavelength (nm)	Photon Energy (eV)
Near UV	NUV	400–200	3.10–6.30
UV long wave	UVA	400–320	3.10–3.87
UV middle wave	UVB	320–280	3.87–4.43
UV short-wave	UVC	280–200	4.43–6.20
Far UV	FUV	200–10	6.20–124

with low-power lamps have involved surface irradiation for 48 hours. However, our method was sufficient to generate a hydrophilic surface.

Conclusions

Photofunctionalization of a titanium implant using a UVC lamp (wavelength of 254 nm, power of 6 W, for 15 minutes, at a distance of 15 cm) did not result in a higher BIC at 8 weeks after implantation in rabbits. Although there were no significant differences between photofunctionalized and non-treated implants, the photofunctionalized implants showed more homogenous BIC values. Future studies should be performed using higher irradiation power, longer irradiation times, or a combination of both to determine the best photofunctionalization protocol.

Abbreviations

BIC: bone-to-implant contact
FUV: far ultraviolet
NUV: near ultraviolet
UV: ultraviolet
UVA: ultraviolet A (long wave)
UVB: ultraviolet B (middle wave)
UVC: ultraviolet C (short-wave)

Acknowledgments

This study was funded by a contract between the Office of Transfer of Research Results and the company Mozo Grau. We thank Dr Belen Cano-Tovar for assisting in the completion of surgeries. We also would like to thank to Mr Antonio Fco, Bravo-Cantero (Director, Estadística Murcia) for performing the statistical analysis.

Notes

The authors have no conflicts of interest to declare.

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