Photofunctionalization of Dental Implants

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After dental implants are manufactured there can be a loss of biological activity that may be reactivated by exposure to ultraviolet (UV) radiation, that is, photofunctionalization. The titanium surface is energy conditioned by UV radiation. This imparts a slight positive surface energy and hydrophilicity to the titanium dental implant surface. This conditioning renews biological activity lost after a shelf life of as little as 2 weeks. The UV radiation has chemical and biological effects on the osseous-implant interface. Photofunctionization for as little as 15 minutes accelerates healing and increases bone to implant contact. The most effective time exposure and UV wave length are in need of identification to produce a surface most conducive for osseointegration.

Key Words: dental implant, hydrophilic, osseointegration, titanium, zirconia, surface energy

INTRODUCTION

Ultraviolet (UV) radiation has been used for many years to disinfect surfaces in industrial and medical technologies as well as in titanium dental implants.[1,2] The passified titanium surface is primarily titanium dioxide (TiO); TiO, or titania, is used in a multiplicity of applications in technology, sunscreen products, paints, food, and nanotechnology (Figure 1). TiO is the primary surface composition of dental implants after manufacture. After manufacture, surface passification occurs where elemental titanium is oxidized to TiO in a fraction of a second.[1]

The TiO surface is capable of osseointegrating with bone. However, the TiO of manufactured implants may lose some ability to bioactively integrate with bone after a storage time of as little as 2 weeks,[3] during which time there is a degradation of bioactivity. However, the bioactivity can be regained with exposure to UV. This is a non–surface-altering conditioning known as photofunctionalization.[3]

The objective of this article is to review UV conditioning of dental implant surfaces and subsequent bioactivity related to dental implant osseointegration.

MATERIALS AND METHODS

An online search of Medline PubMed was done on March 20, 2016, using the term "photofunctionalization."

RESULTS

Forty-three articles were retrieved, reviewed, and included in this report.

A demonstration of photofuncionalization

An inexpensive UV fingernail drier was purchased (Salon Edge, Palm Gardens, Fla). Two 5.7 × 10 mm (Implant Direct, Ventura, Calif) implants were used to test the UV time exposure. A bead of water was gingerly placed on one implant surface (Figure 1). Hydrophobic surface tension maintained the bead at an approximate contact angle of 45°. After 15 minutes of UV exposure, the bead collapsed and spread over the implant surface for a 0° contact angle (Figure 2). This indicates surface hydrophilicity. Another control bead was placed on an implant in ambient light (Figure 3). After 15 minutes the control water bead did not change (Figure 4). The unconditioned TiO surface maintained the hydrophobic property. This hydrophobic property may affect the initiation of osseointegration.[4,5] This induced surface change may increase initial blood contact with the implant surface and facilitate cellular ingrowth.[4,5]

Ultraviolet radiation and titanium

Humanly visible light has 400–700 nm wavelength range; UV radiation (10–400 nm) is classified as UVA (320–400 nm), UVB (290–320 nm). and UVC (10–290 nm) wavelengths.[5] These divisions are made to classify the dermal biological actions of UV radiation. Most solar UVC does not enter the earth's atmosphere because it is blocked by the ozone layer in the stratosphere. Most solar UV radiation that reaches earth is UVA. UV radiation is non-ionizing radiation that is generated by the sun, electrical arcs, and mercury lamps. UV photons can alter chemical bonds but cannot ionize atoms and is capable of inducing an electronic energy change in molecules.[5,6] UV is invisible to the human eye and induces the metabolic production of human vitamin D. UVA and UVB can act to degrade skin elastin and form eye cataracts, melanomas, and basal and squamous cell carcinomas.[5] UV acts mainly photochemically.[6] UVA may be most active in altering TiO for increased bioactivity. The range used in biological investigations is generally 200–400 nm, which encompasses all UVA, all UVB, and some UVC.[7]

Titanium dental implants osseointegrate with bone, and this is termed "bioactivity." Some postmanufacture bioactivity study of dental implants has been done. One found that after 4 weeks of manufacture, dental implants can lose significant bioactivity.[3] A 4-week-old implant may need twice the healing time to reach the same bone to implant contact (BIC) as a newly manufactured implant.[3] It was found that implants more

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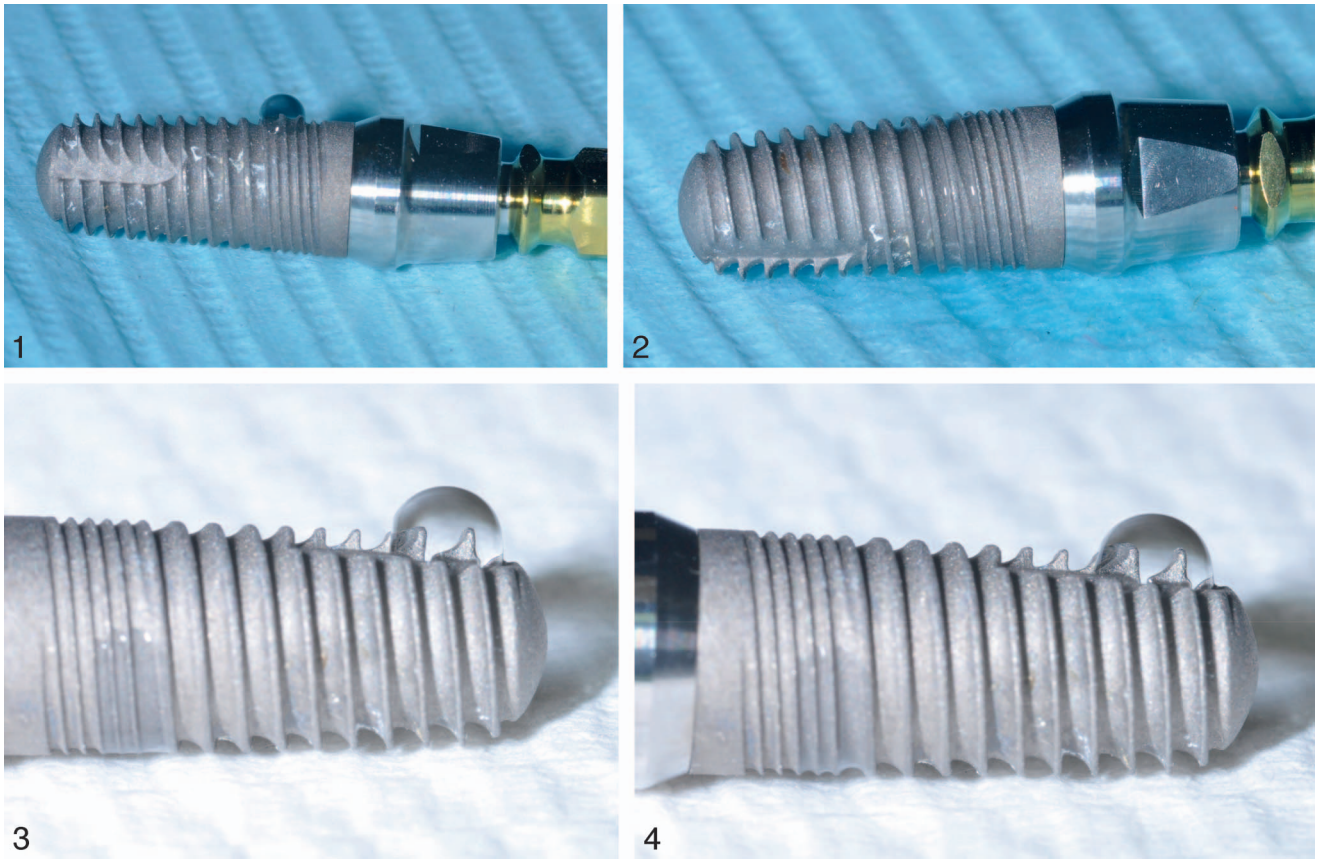

Figures 1–4. Figure 1. A bead of water was gingerly placed on the test implant. **Figure 2.** After 5 minutes of ultraviolet treatment the water bead spread across the implant surface. **Figure 3.** A control was made by gingerly placing a water bead on an implant and not applying ultraviolet light. **Figure 4.** After 5 minutes the bead did not spread across the implant surface.

than 4 weeks old had a BIC of 60%, while newly manufactured implants had a BIC of 90%.[3] Four-week-old implants were found in vitro to have only 20% osteogenic cell recruitment, attachment, settlement, and proliferation compared with the 50% levels of new implant surfaces.[3] There is bioactive aging of TiO within a short period of time after manufacture and this may be as short as 1 week.[7]

Recent publications in the dental implant literature have indicated that treating dental implant TiO surfaces with UV radiation 200–400 nm may increase BIC after the usual healing time.[3,5,6] The UV radiation induces energy into the surface electrons of the TiO.[6] The electron energy may induce reactions to increase cell attachment and osteocyte contact by influencing the interaction with hemidesmosomal chemistry.[5,7] UV radiation acts mainly photochemically on titanium surfaces to increase hydrophilicity.[7,8] The exact mechanism of this phenomenon is not fully understood. UV radiation may induct energy into the TiO molecular electron structure to increase biological reactivity and make the TiO surface attractive to cellular attachment.

Biomaterials research has found that UV radiation increases by 10 times the field emission electronic current in TiO compared with before UV treatment.[5] However, this increase subsequently decreases with exposure to air.[3] Thus, there may be a shelf life for titanium dental implants, which are usually stored in non–air-tight containers.[3] However, in the past one implant company did deliver implants in an aqueous solution (Thommen Medical, Cleveland, Ohio). No comparison studies of storage methods have been done. Nonetheless, biological activity of a newly machined and passified TiO surface apparently degrades in as little as 7 days.[3] Nonetheless, UV treatment may reactivate this biological activity.[8–12] This photofunctionalization treatment converts hydrophobic surface conditions to a superhydrophilic surface.[3,4,12] It removes any contaminating hydrocarbons and increases direct cell attractiveness.[3,12,13] This imparts biofunctionality to TiO, a conceptually bioinert material.[10–13]

In a common tetragonal form, the crystalline anatase form, TiO can be bioactively reactivated by a photocatalyst such as UV or visible light.[13] Exposure to UV radiation induces a surface energy to the TiO surface.[13–15] The surface energy creates an oxidative potential that converts water to hydroxyl radicals, effectively breaking water into hydrogen and oxygen.[13–15] Visible light may also induce an electrical current in the TiO nanoparticle.[14–16] This activated TiO can act as a catalyst to split protein at the proline amino acid unit, thereby creating a bioactive locus.[17] The UV radiation causes a succinimidyl ester bond to be formed between protein and hydroxyl groups created on the oxide on the irradiated metal.[18] In these studies, UV treatment was found to enhance osseointegration on acid-etched and anodized porous dental implants in rats and rabbits.[16,17]

In an in vitro study, layers of TiO in various thicknesses were treated with UV radiation, and hydrophilic changes were measured by x-ray diffraction and scanning electron microscopy.[18,19] The biological activity of the TiO surfaces was then observed by proliferation of human periodontal ligament fibroblasts. Fibroblastic initial proliferation was found to be dramatically increased after UV treatment.[20]

The UV radiation acts on the TiO surface to make it hydrophilic. It decomposes and removes hydrocarbons and induces the surface to a positive charge.[3,4,6,12] The TiO surfaces degrade with time so that hydrocarbons accumulate.[6,7] This was true for machined smooth surface implants and rough, acid-etched blasted surfaces.[6,7]

TiO is responsive to any visible light that has a UV component.[21] This was first referred to as the Honda-Fujishima effect.[13] Photocatalysts can disinfect, clean, and deodorize substrate surfaces. Though TiO is inert it can be antimicrobial when UV radiation is illuminated to become a photocatalyst.[21] For this particular effect, UVC appears to be the primary wavelength range that can excite TiO. The TiO impurities, such as tungsten trioxide, nitrogen ions, or calcinations, may extend the TiO wavelength absorption spectrum.[21]

Photofunctinalization and osseous activity

A study by Funato et al[22] found that the implant stability quotient (ISQ) for UV-treated dental implants increased during monthly testing to 8.0 ISQ units compared with literature reports of increases of −1.8 to 2.8 of untreated implants. The work of Suzuki et al[23] confirmed the increased stability of UV-treated implants had enhanced and accelerated osseointegration.

A study of UVC-treated implants in rabbits found that after 4 months of healing there was a higher BIC than with the untreated implants.[24] These authors also found that carbon surface impurities were decreased and water contact angles were lower, indicating hydrophilicity. Hydrophicity can enhance initial attachment of osteoblast-like cells to the implant surface.[25]

In rats with UV-treated dental implants, BIC has been reported to be as high as 100%.[6] Thus, UV treatment causes a reported threefold increase of protein adsorption, osteoblast spread, attachment, proliferation, and differentiation.[6]

An increase of 57% BIC was found after 24 hours of UV treatment of a series of branded dental implants in rabbit tibias.[9,10] The UV treatment increased the hydrophilicity of the TiO surface by dramatically decreasing the water contact angle from 43.5° to 0.5° (Figure 2). During bone integration an elongation of cellular lamellipodia preceded increased cell attachment, flattening, and proliferation. The control trial cells were round and spherical, indicating less attachment and hydrophilicity.[9,10] Interestingly, on only one proprietary brand implant surface was the BIC not increased after UV treatment.[10]

In a recent study in rats, Hirota and coworkers[26] found that a 12-minute UV conditioned, machined, titanium mesh had a superhydrophilic surface. The conditioning also produced a significant reduction of surface carbon from 15% to 8%.[26] They also found that the photofunctionalization produced a 2.5 times adsorption of albumin protein on the UV-conditioned TiO surface.[26] After 3 hours of incubation testing, the osteoblasts that attached to the conditioned surface were larger and had clear lamellipodia-like cytoplasmic elongations with cytoskeletal fibers. This activity may be related to resolution of the hydrophobic surface by the UV conditioning.[4,5] The untreated surfaces had osteoblasts that were rounded and rarely showed any elongations or cytoskeletal fibers.[26] After 24 hours the cells on the conditioned surfaces were even larger and had extensive actin fibers.[26] After 4 days there was a significantly greater number of conditioned surface cells with increased calcium deposition.[26] At 3 weeks the surface conditioned cellular layers were thickened and dense with mineralized bone. This was 2.5 times the bone generation as that of the unconditioned surfaces.[26] There was an increased alkaline phosphatase activity, which indicates increased osteoblastic activity with bone formation.[26] Because cells are negatively charged there is little direct interaction with an untreated TiO surface.[26] Photofunctionalized TiO, which is electropositive, causes direct cell contact and increases cellular recruitment and attachment.[26] Thus, the photofunctionalized surfaces had an osteoconductivity that produced enhanced bone formation with deep 3-dimensional bone growth.[26] However, this study was done in rats and may not be extrapolated to a human physiological situation. Additionally, this study was done with machined titanium mesh. Most implants are now rough surfaced, and this may produce different results. Nonetheless, photofunctionalization should be tested credibly in human subjects.

Kitajima and Ogawa[27] recently found that photofunctionalization for 15 minutes produced a rapid increase in stability for implants placed with low or no primary stability. Photofunctionalization was more effective for improving stability for implants with lower initial stability and demonstrated a high success rated after 2 years.[27] The average ISQ for all implants tested was 50.4, but after an average of 7 months of healing they averaged 74.3. Implants that had no primary stability on placement attained an ISQ of 75 or greater.[27] Thus, photofunctionalization is particularly effective for implants with compromised initial stability.[27]

Initial osteoblast attachment and osseointegration capacity are enhanced by UV treatment of the TiO surface.[28] In a study of rat marrow osteoblasts by Iwasa and coworkers,[28] osteoblasts were cultured on new, 4-week-old, and UV-treated TiO. The new and UV-treated surfaces were found to be superhydrophilic, but the more than 4-week-old surfaces were hydrophobic. [28] The protein adsorption of the new and UV-treated surfaces was higher than that of the 4-week-old surfaces.[28] The UV-treated surfaces had more numerous attached cells and enhanced spreading behavior.[28] Additionally, the cells of the UV-treated surfaces had an upregulation of switching genes for organelle development, cytoskeletal development, cell movement, and other cellular functions.[28]

In a study by Saita and associates,[29] photofunctionalization enabled faster TiO surface deposition of nanoscale biomimetic apatite. They found that there was an improved biological capability compared with similarly prepared apatite-deposited titanium without photofunctionalization.[29] Biomimetic apatite deposition of UV-treated TiO may effectively enhance micro-roughened titanium surfaces without altering their microscale morphology.[29]

Qin and Teng[30] found that photofunctionalization for 48 hours promotes protein adsorption on TiO.

In a study by Shen and associates,[31] osteoblasts were cultured on UV-treated and untreated TiO plates. The surfaces were examined with x-ray photoelectron microscopy, and it was found that the UV treatment effectively removed hydrocarbons and increased cell proliferation, alkaline phosphatase activity, and osteocalcin release.[31] Additionally, it was found that when the new TiO was stored in water, the bioactivity loss was attenuated. Nonetheless, the UV-treated TiO had a much higher bioactivity than the TiO stored in water.[31]

Osteogenic cells on photofunctionalized TiO have increased cell attachment, retention, and expression of vinculin, an adhesion protein.[32]

UV radiation exposure time

While time exposures of 12 minutes to 48 hours have been used for surface treatment of implants, it may be that as little as 16 seconds is the minimum effective exposure time.[33,34] Nonetheless, the most appropriate UV time exposure has yet to be determined.[33,34] Tabuchi and coworkers[35] photofunctionalized titanium alloy orthodontic mini screws for 12 minutes immediately before placement in rat femurs. The implants were assessed after 3 weeks of healing, and the researchers found 30% to 40% less movement to lateral displacement loading, more robust bone formation and anchorage, and enhanced bone attachment.[35]

A recent study used commercially available dental implants in dogs.[36] These implants were treated with UV for 15 minutes just before placement. The exact wavelength used was not stated. After 4 weeks of healing, the BIC was found to be about 95% as opposed to about 70% in untreated implants. Another animal study found BIC of 53% and 98.2%, respectively, in untreated and UV-treated implants.[30]

Though UVA penetrates clouds and glass to alter chemical bonds, UVB does not significantly pass through glass, so implants should be removed from glass or plastic containers before UV irradiation to ensure exposure to all of the wavelengths. It may be that the most biologically effective UV wavelength is about 250 nm.[6,33] A spectrometer can be used to ensure that any generator is operating in a range of 10–400 nm. Nonetheless, the exact therapeutic wavelength range and time exposure have not yet been determined.

A UV generator, that is not yet approved for sale in the United States, is available internationally that conditions dental implants for 12 minutes (TheraBeam, SuperOsseo, Ushio, West Lothian, UK).

Antibacterial properties of UV radiation

UV is antibacterial. An in vitro study found that a UV radiation at 470 nm at 55 J/cm^2 generated from a superluminous diode source is lethal for more than 90% of methicillin-resistant *Staphylococccus aureus* (MRSA) colonies.[37] Other studies confirm the antibiotic properties of UV against *Clostridium difficile*, *Clostridium difficile* spores, *Giardia intestinalis*, MRSA, and vancomycin-resistant *Enterococcus*.[38–40] It must be noted that UV acts as a disinfectant and not a sterilizing agent. Though UV irradiation does not alter human cell adhesion, it will reduce bacterial adhesion rates and the bacterial retention to TiO surface.[41] In vitro studies indicated poor adhesion and retention of *Staphylococcus aureus* and *Staphylococcus epidermidis* on TiO surfaces in static, dynamic and shearing forces.[42]

The UV radiation activation of TiO can produce activity against *Escherichia coli* and human pathogens by significantly reducing their surviving numbers and spores.[42] The activated TiO may act to disrupt the bacterial cell membrane and oxidize cellular debris. Clinically, the presence of bacteria on the TiO surface may inhibit healing of the implant; thus, their elimination may enhance healing. Bacterial spores, however, may retain germination abilities.[40–42] The UV treatment reduces bacterial adhesion to TiO dental implant surfaces and may enhance the epithelial cell attachment to TiO.[37,41] Since dental implants are delivered sterile to the clinician, the value of UV treatment may be in the enhanced surface integration healing prospects.

Bacterial activity is a major cause of implant failure.[43] Bacteria do attach and colonize TiO surfaces.[43] The UV treatment surface alteration to superhydrophilic causes a significant reduction of bacterial attachment and biofilm formation.[43] Nonetheless bacterial viability is not affected.[43] The reduction of bacterial colonization can be maintained by storing the TiO in liquid.[43] Thus, UV treatment is potentially antimicrobial.[43]

UV radiation and peri-implantitis

UV radiation may be useful in treating peri-implantitis. A 15-minute UV exposure in a study on dogs produced some resolution of the infection.[44] Low power laser and UV radiation may be effective in treating periimplantitis.[45,46] Bacteria in peri-implantitis may be difficult to detoxify due to the implant rough surface, which may protect the bacteria from chemical treatment.[19] The UV radiation may be effective in surface treatment because it may reach most, if not all, of the rough surface due to reflection off of the titanium surface irregularities. However, sometimes an infected or ailing implant surface is located on the lingual surface and is obstructed by the lingual cortical bone. In the future, the UV radiation may be applied via small emitters that may reach some parts of the otherwise inaccessible surface. UV treatment may be effective for peri-implantitis by enhancing epithelium to attach to the TiO.[33,36] The UV treatment of TiO decomposes organic compounds and decreases the bacterial adhesion of *Streptococcus sanguinis*.[1] This may enhance osseous healing and epithelial attachment to the TiO.[46,47]

UV radiation and zirconia

Zirconia, that is, zirconium oxide (ZiO), is not considered to be biologically active.[48,49] However, micro-arc oxidation treatment may impart bioactivity to zirconia.[48] Subsequent UV radiation treatment of ZiO implants causes increased bone formation and significant bonding with bone compared with untreated ZiO surfaces.[48] Thus, UV radiation may act on some metal oxides that absorb activating band wavelengths, thereby imparting or improving bioactivity.[48–51]

A study in rats found that UV-treated zirconium implants

had increased alkaline phosphatase activity and mineralization.[14] The UV treatment converted the ZiO surface from being hydrophobic to hydrophilic.[48,49] Cell attachment, proliferation, and mineralization were increased in UV-treated ZiO implants.[49]

On ZiO, UV treatment does not induce any topographical changes but does change the physiochemical properties of ZiO.[50] It reduces carbon content by 43% to 81%, increases oxygen content by 19% to 45%, and increases the hydrophilic status of ZiO surfaces.[50]

Hazards of UV radiation

During clinical treatments a lower wavelength range of 390–420 nm may be injurious to the clinician and staff.[38,51,52] Thus, ocular protective measures should be instituted to prevent occupational injuries.

Conclusions

UV radiation has chemical and biological effects on TiO that enhance osseointegration. UV radiation may impart a slight positive surface energy and hydrophilicity to titanium and zirconia dental implants. This renews biological reactivity of titanium implants lost after manufacture and storage in air. The UV treatment results in accelerated healing and increased BIC. Nonetheless, most evidence has been done in animal or in vitro studies, which may not be extrapolated to human clinical usage. The astute clinician may seriously consider 15 minutes of photofunctional treatment of implants before placement. The most effective time exposure and wave length need to be identified. Long-term randomized blinded trials are needed to find if this treatment is truly effective.

Abbreviations

BIC: bone to implant contact
ISQ: instability quotient
MRSA: methicillin-resistant *Staphylococcus aureus*
TiO: titanium dioxide
UV: ultraviolet
ZiO: zirconium oxide

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