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Efficacy of plasma treatment for surface cleansing and osseointegration of sandblasted and acid-etched titanium implants

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PURPOSE. This study was conducted to evaluate the effects of plasma treatment of sandblasted and acid-etched (SLA) titanium implants on surface cleansing and osseointegration in a beagle model. **MATERIALS AND METHODS.** For morphological analysis and XPS analysis, scanning electron microscope and x-ray photoelectron spectroscopy were used to analyze the surface topography and chemical compositions of implant before and after plasma treatment. For this animal experiment, twelve SLA titanium implants were divided into two groups: a control group (untreated implants) and a plasma group (implants treated with plasma). Each group was randomly located in the mandibular bone of the beagle dog (n = 6). After 8 weeks, the beagle dogs were sacrificed, and volumetric analysis and histometric analysis were performed within the region of interest. **RESULTS.** In morphological analysis, plasma treatment did not alter the implant surface topography or cause any physical damage. In XPS analysis, the atomic percentage of carbon at the inspection point before the plasma treatment was 34.09%. After the plasma treatment, it was reduced to 18.74%, indicating a 45% reduction in carbon. In volumetric analysis and histometric analysis, the plasma group exhibited relatively higher mean values for new bone volume (NBV), bone to implant contact (BIC), and inter-thread bone density (ITBD) compared to the control group. However, there was no significant difference between the two groups ($P > .05$). **CONCLUSION.** Within the limits of this study, plasma treatment effectively eliminated hydrocarbons without changing the implant surface. [J Adv Prosthodont 2024;16:189-99]

KEYWORDS
Dental implant; Titanium; Plasma; Hydrocarbon; Osseointegration

INTRODUCTION

Dental implants are a commonly used treatment option for rehabilitating masticatory function and esthetics in cases of missing teeth.[1] Osseointegra-

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tion is an important factor for the success and long-term stability of implants.[2,3] Osseointegration can be influenced by various factors, including the biocompatibility of implant material, implant surface topography, bone quality and condition, and surgical procedure.[4] Titanium is widely used as an implant material due to its high biocompatibility, corrosion resistance, and adequate strength.[5] However, titanium, being a bioinert material, does not directly bind with bone perfectly, resulting in limitations such as a lack of osseointegration or the need for a longer time for osseointegration.[6-8] Therefore, numerous studies have been conducted on the mechanical and chemical surface treatment of implant surfaces in order to promote osseointegration of titanium implants and achieve early osseointegration.[9,10]

Sandblasted and acid-etched (SLA) implants, commonly used in clinic, are produced by sandblasting large grit particles such as alumina on titanium implants and then etching them with acid to create surface topography.[11] Microscale topography increases the surface contact area compared to machined surfaces, forming a mechanical connection that enhances the bone to implant contact (BIC).[12,13] In clinical studies, the healing period of titanium implants, which was more than 3 months, was reduced to 6 to 8 weeks for SLA implants and displayed good results even under unfavorable clinical conditions, such as implant placement in areas of poor bone quality or placement of short implants.[9,14,15] In this way, the surface topography formed through SLA improved the osseointegration ability of bioinert titanium implants,[16] but BIC was found to be approximately 50%, which is below the ideal 100%.[17,18]

Biological aging of commercially available titanium implants is inevitable due to the distribution period after manufacturing and the storage period prior to use.[19,20] Previous studies have reported that the biological aging of titanium is a cause of low BIC.[17-19] The biological aging of titanium is linked to the accumulation of hydrocarbons on the titanium surface over time.[19] The accumulation of carbon in the form of hydrocarbons causes the hydrophilic titanium surface to become hydrophobic and acts as a contaminant, reducing the biological abilities associated with osseointegration, such as protein adsorption and osteoblast attachment.[20] In a previous study using rat bone marrow-derived osteoblasts, it was found that protein adsorption, osteoblast attachment, and proliferation decreased over time after the processing of titanium discs.[17] In the same experiment, in which titanium implants were processed under identical conditions and then placed in the femurs of rats, the BIC of implants processed after 4 weeks was lower than that measured immediately after processing.[17]

Accordingly, several chemical modifications have been attempted on the titanium implant to enhance its biological capability, including hydroxyapatite coating, anodic oxidation, fluoride treatment, and ultraviolet (UV) irradiation.[11] Among these methods, UV irradiation was reported to be a method that could be applied without altering the surface of the implant.[21,22] Photofunctionalization, through UV irradiation, removes accumulated hydrocarbons and converts hydrophobic surfaces into hydrophilic ones.[21,22] Additionally, the negatively charged titanium surface becomes positively charged, thereby attracting the proteins and cells necessary for osseointegration.[22] However, due to its time-consuming and complicated operation, it had limitations that prevented its immediate application before implant surgery in a clinic.[23,24]

To address these limitations, plasma treatment, which can be applied in a relatively short time, has been introduced.[23,24] Plasma, which refers to the fourth state of matter, was described by Irving Langmuir.[25] Plasma, a gas consisting of electrons, ions, and neutral particles, can be classified in various ways based on its characteristics.[26,27] Plasma is generally classified into thermal plasma and non-thermal plasma.[26,27] Thermal plasma is an equilibrium state in which the temperatures of electrons and particles are nearly identical, and the temperature of the thermal plasma gas generally exceeds 5000 K.[26,28] Non-thermal or cold plasma is a non-equilibrium state in which the temperatures of electrons and particles are significantly different, and the plasma generated at atmospheric pressure, close to room temperature, is called non-thermal atmospheric pressure plasma (NTAPP).[26,28] NTAPP has the advantage of being applicable without causing thermal damage, so it is used in various medical fields such as sterilization of medi-

cal devices, wound healing, and surface modification of biomaterials.[28-30] There are several methods for generating NTAPP, including corona discharge, gliding arc discharge, and plasma jet.[26-28] Many studies have reported that non-thermal atmospheric pressure plasma jet (NTAPPJ) has improved the biological ability and hydrophilicity of titanium implants without altering their surface.[23,30-33]

However, to uniformly treat the entire implant surface using the plasma jet method, it is necessary to adjust the location of the implant and supply gases such as oxygen, nitrogen, helium, and argon for the plasma discharge.[24,26,31] Previously introduced plasma generators were difficult to utilize in the clinic due to requirements such as implant positioning and gas supply to achieve the desired outcome, but recently, a novel plasma generator was reported to improve existing shortcomings.[34,35] This device, which is commercialized for chairside use, utilizes a vacuum pump and a high-voltage power supply to apply cylindrical non-thermal plasma to the entire surface of the implant, distinguishing it from the jet method.[34,35] Plasma treatment takes 60 seconds and uses air as the gas for plasma discharge, thereby eliminating the need for any additional gas supply.[34,35] Previous studies using this device have reported that it removes carbon impurities from the implant surface and enhances biological capabilities.[34,35] However, research on the effectiveness of this device in improving osseointegration is still lacking because it was recently released. In this study, we aimed to evaluate the surface cleansing and osseointegration effects of SLA titanium implants through plasma treatment in a beagle dog mandible model using this plasma generator. The null hypothesis was that surface cleansing and osseointegration of plasma-treated and untreated implants would be similar.

MATERIALS AND METHODS

The animal experiment was approved and performed by the Chonnam National University Biomaterial R&BD Center Animal Experimental Ethics Committee (BMC-IACUC-2022-21).

Twelve SLA titanium implants (ADDplant ON, PNUADD, Busan, Korea, diameter: 3.5 mm, length: 8.5 mm) that are commercially available were prepared. Untreated implants were assigned to the control group, and implants treated with plasma were assigned to the plasma group. The plasma treatment was performed using the plasma generator (ACTILINK™ Reborn, Plasmapp, Seoul, Korea). Plasma treatment is performed for about 60 seconds, following the process of preparation, plasma surface activation, and purification. First, remove the implant's packaging, connect the mount driver to the implant hex, and attach it to the rocket holder. Place the rocket holder in the jig holder of the plasma generator. The implant connected to the rocket holder is electrically connected to the grounding electrode of the plasma generator. When the plasma surface activation process starts, the vacuum tube moves downward and maintains a vacuum state around the implant by a vacuum pump. The pressure inside the tube becomes approximately 5 torr within 30 seconds. In a vacuum state, plasma is generated and treated on the surface after applying power with a frequency of 100 kHz and a voltage of 3 kV to the power electrode. Finally, in the purification process, exhausting impurities are removed by a vacuum pump (Fig. 1).

For morphological analysis, the surface topography of the implant before and after plasma treatment was compared using a scanning electron microscope

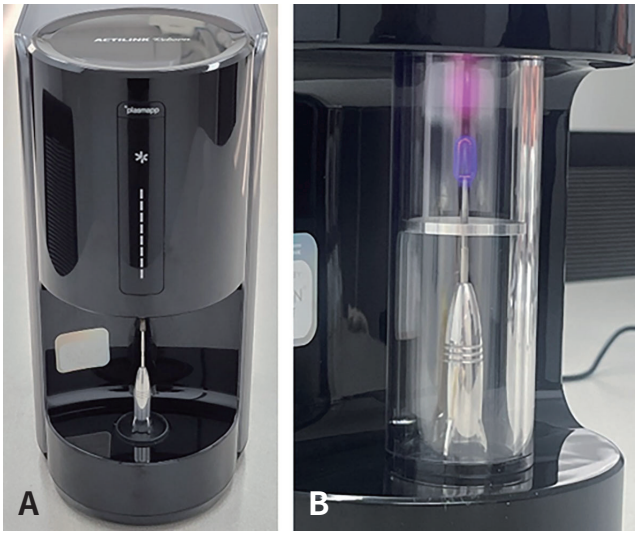

Fig. 1. Plasma surface activation using a plasma generator. (A) Location of the rocket holder, (B) Progress of plasma surface activation.

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(Phenom XL Desktop SEM, Thermo Fisher Scientific Inc., Waltham, MA, USA) at × 4000 magnification. SEM was activated at 15 kV to obtain surface images of implant.

The chemical composition of implant surface was determined using x-ray photoelectron spectroscopy (XPS, PHI Quantera II, ULVAC-PHI, Chigasaki, Japan) using a 25 W-15 kV monochromatic Al Kα x-ray source. Before and after plasma treatment, two identical inspection points were selected and analyzed for the implant surface.

Two beagles (male, up to 12 months old, 10-15 kg) were used in this experiment. For the sedation of beagles, medetomidine (Tomidin®, Provet Veterinary Products Ltd., Istanbul, Turkey) 0.005 to 0.02 mg/kg was injected intramuscularly. Intravenous injection of 1.5 to 2 mg/kg of alfaxalone (Alfaxan Multidose, JUROX Pty Ltd., Rutherford, Australia) was used to induce anesthesia. Inhalation anesthesia was performed by isoflurane (Hana Pharm Co., Ltd., Seoul, Korea). Bupivacaine (Myungmoon Pharm Co., Ltd., Seoul, Korea) 1 mg/kg was injected for local anesthesia. For pain control and infection prevention, carprofen (Rimadyl injectable 50, Zoetis Korea, Seoul, Korea) 2.2 mg/kg, tramadol hydrochloride (Tramadol HCl Huons Inj., Huonc Co., Seongnam, Korea) 5 mg/kg, cefazolin (CEFOZOL Inj., Hankook Korus Pharm. Co., Ltd., Seoul, Korea) 20 mg/kg were injected intravenously. After full mouth scaling, all mandibular premolars were extracted. Then, midcrestal incisions and vertical incisions were performed, and twelve implants were randomly located in the bone. The distance between the implants is more than 6 mm (Fig. 2).

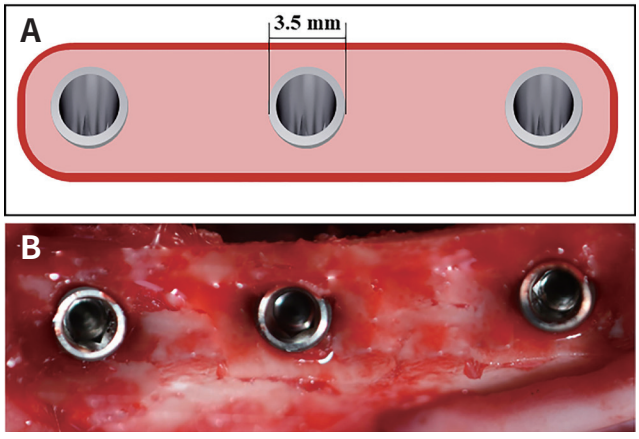

Fig. 2. Placement of implants (Implants with a diameter of 3.5 mm and a length of 8.5 mm, the distance between the implants is more than 6 mm). (A) Placement schematic image, (B) Placement of implant in the beagle mandible.

- Control group (n = 6): untreated implants
- Plasma group (n = 6): implants treated with plasma

After implant placement, the surgical site was sutured with poliglecaprone 25 (Monocryl, Ethicon Inc., Raritan, NJ, USA) 4-0. To relieve pain and prevent infection, famotidine (Gaster tab, Dong-A, Seoul, Korea) 1 mg/kg, carprofen (Rimadyl® Chewable Tablets 25 mg, Zoetis Korea, Seoul, Korea) 4.4 mg/kg, tramadol hydrochloride (Tramadol Retard Tab., Huonc Co., Seongnam, Korea) 5 mg/kg, gabapentin (Neurontin Cap 100 mg, Pfizer Biopharmaceuticals Korea Ltd., Seoul, Korea) 10 mg/kg, enrofloxacin (BaytrilFlavour Tablet, Bayer Korea Ltd., Seoul, Korea) 10 mg/kg were administered orally once daily for 7 days. After 8 weeks, anesthesia was performed using the same procedure, and the beagles were sacrificed by intravenous injection of potassium chloride (10 - 20 ml/body). The mandibles of beagles were collected and immersed in 10% neutral formalin for 14 days.

To analyze the new bone volume (NBV) of the area around the implant, micro-CT (SkyScan1173, Bruker corporation, Kontich, Belgium) was used. All the mandible specimens were scanned at 130 kV, 60 uA intensity, and 12.13 μm pixel resolution. Nrecon version 1.7.4.6 (Bruker corporation, Kontich, Belgium) was used for reconstructing images that were scanned by micro-CT. The region of interest (ROI) was 0.5 mm wide and 4 mm in height around the implant (Fig. 3).

For histometric analysis, specimens were dehydrated in concentrations of 70%, 95%, and 100% ethanol order. The specimens were infiltrated for 7 days using the Technovit 7200 VLC system (Heraeus KULZER, Hanau, Germany) and then embedded. The EXAKT 300 diamond band saw and EXAKT 400 CS micro grinder (EXAKT Advanced Technologies, Norderstedt, Germany) were used for sectioning specimens to 50 μm. The specimens were stained with Goldner's trichrome and images were obtained by optical microscope (Olympus BX, Evident Corporation, Tokyo, Japan). One trained person used the i-Solution (Image

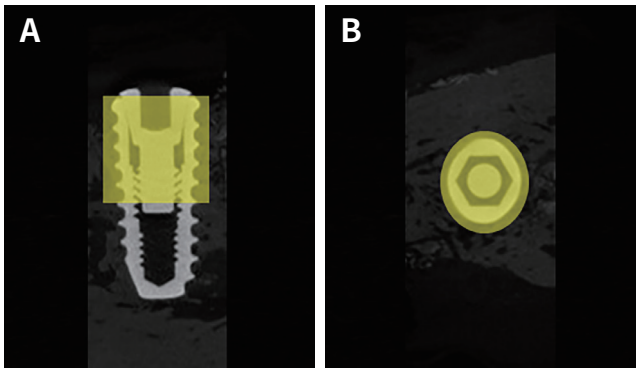

Fig. 3. Micro-CT image of the region of interest (yellow area, 0.5 mm wide and 4 mm in height around the implant). (A) Buccal view, (B) Occlusal view.

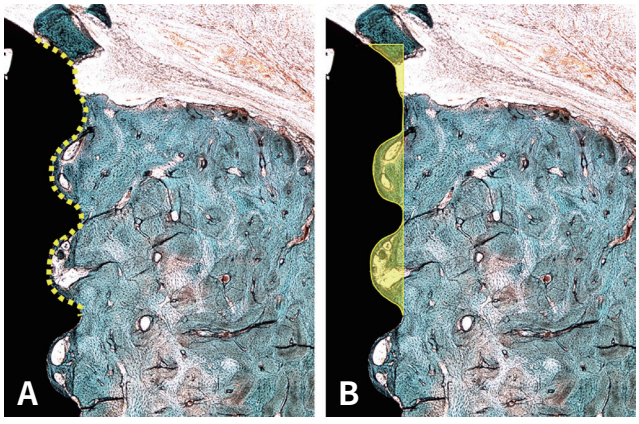

Fig. 4. Histometric parameters in region of interest. (A) Bone to implant contact (BIC, yellow dotted line, the implant platform to the third thread), (B) Inter-thread bone density (ITBD, yellow area, 0.5 mm around the implant, and the height from the implant platform to the third thread).

& Microscope Technology Inc., Daejeon, Korea) for the analysis of histometric parameters (Fig. 4). The region of interest (ROI) was set in the range of 0.5 mm around the implant, and the height from the implant platform to the third thread.

All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). A t-test was used to compare results. The significance level was set at $P = .05$.

RESULTS

In morphological analysis, after comparing the same area before and after plasma treatment, it was confirmed that plasma treatment did not alter the implant surface topography or cause any physical damage. The area of carbon impurities, which appeared black before plasma treatment, decreased after treatment, confirming that plasma treatment removes carbon (Fig. 5).

In XPS analysis, each constituent element of implant surface was identified at two identical inspection points, both before and after plasma treatment (Fig. 6). The atomic percentage of carbon at the inspection point before the plasma treatment was 34.09%. After the plasma treatment, it was reduced to 18.74%, indicating a 45% reduction in carbon. After plasma treatment, oxygen and titanium on the surface increased (Table 1).

After the surgical procedure, experimental animals recovered for 8 weeks. Four days after the procedure, two implants were respectively exposed in the control and plasma groups. Four exposed implants were excluded from the results data (n = 4 in each group).

In volumetric analysis, new bone volume (NBV) was 40.18 ± 4.65% in the control group, and 47.30 ± 2.44% in the plasma group. There was no significant difference between the control and plasma group ($P > .05$) (Fig. 7).

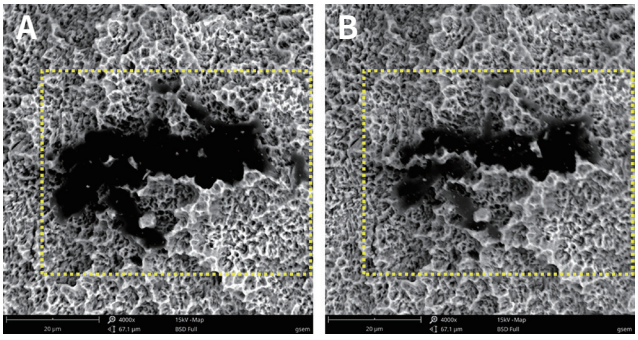

Fig. 5. SEM images of the same area before and after plasma treatment (rectangular box, carbon impurities). (A) Implant surface before plasma treatment, (B) Implant surface after plasma treatment.

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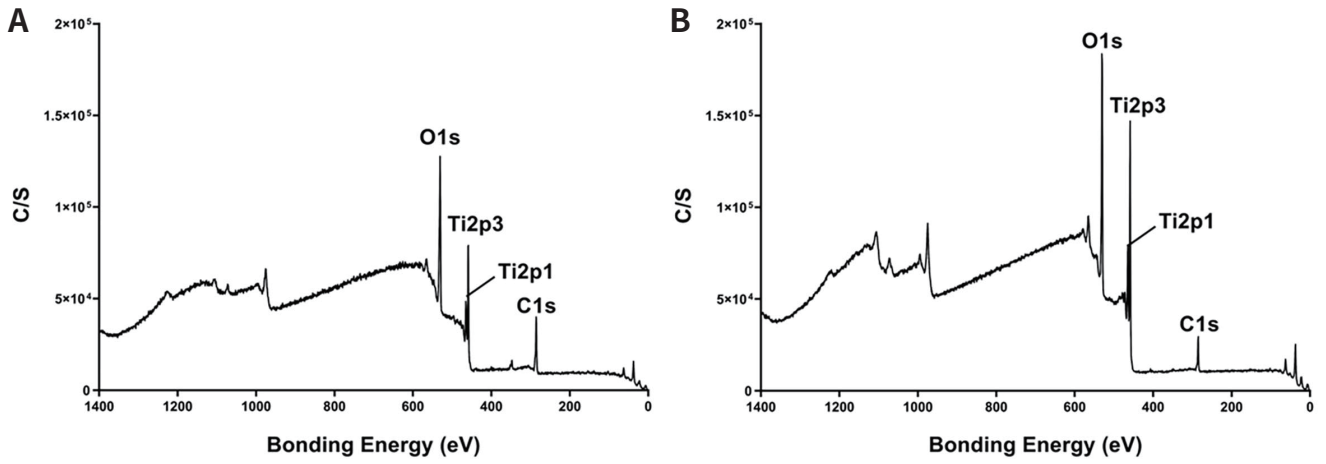

Fig. 6. Chemical compositions of implant surface. (A) XPS spectrum before plasma treatment, (B) XPS spectrum after plasma treatment.

Table 1. The atomic percentage of implant surface

		Implant surface before plasma treatment	Implant surface after plasma treatment
Elements	C	34.09	18.74
	O	50.58	57.96
	Ti	15.34	22.64

C, carbon; O, oxygen; Ti, titanium

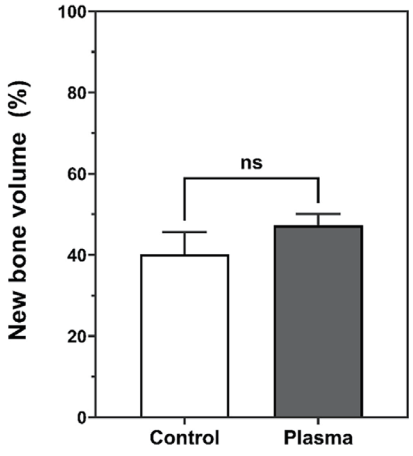

Fig. 7. New bone volume analysis in the region of interest (ns, not significant, $P > .05$).

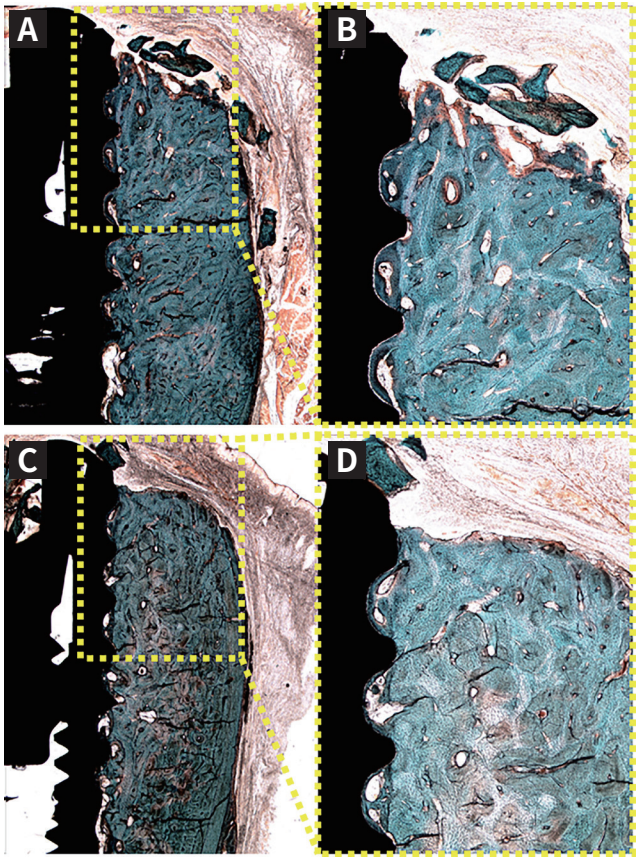

Fig. 8. Goldner's trichrome stained specimen at 8 weeks. (A) Control group at × 20 magnification, (B) Control group at × 40 magnification, (C) Plasma group at × 20 magnification, (D) Plasma group at × 40 magnification.

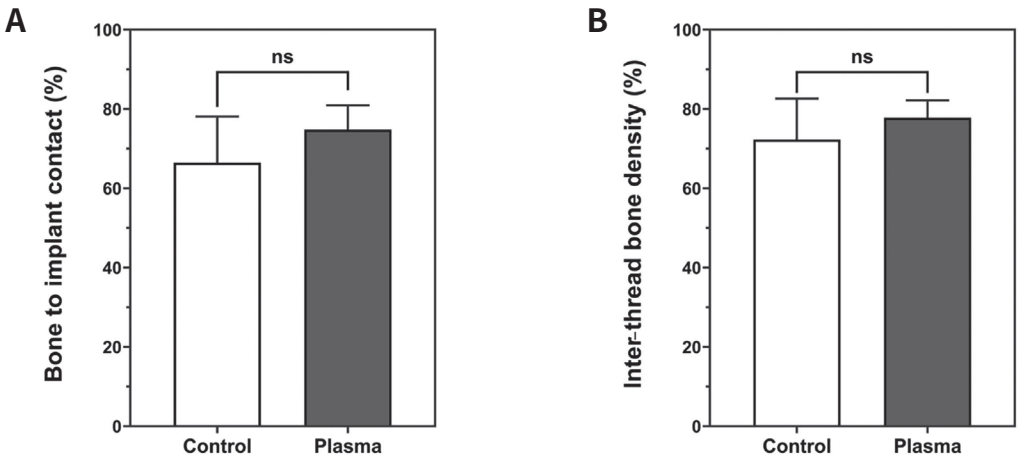

Fig. 9. Histometric analysis within the region of interest (ns, not significant, $P > .05$). (A) Bone to implant contact, (B) Inter-thread bone density.

Table 2. Mean values of histometric parameters

Group	Mean ± SD	
	BIC (%)	ITBD (%)
Control	66.48 ± 10.06	72.26 ± 8.99
Plasma	74.79 ± 5.30	77.82 ± 3.78
P value	.321	.188

BIC, bone to implant contact; ITBD, inter-thread bone density

Based on the histological image of the two groups, no abnormalities were found in the two groups (Fig. 8). In histometric analysis, bone to implant contact (BIC) was 66.48 ± 10.06% in the control group, and 74.79 ± 5.30% in the plasma group. Inter-thread bone density (ITBD) was 72.26 ± 8.99% in the control group and 77.82 ± 3.78% in the plasma group. Although BIC and ITBD were relatively higher mean values in the plasma group than control group, there was no significant difference between two groups ($P > .05$) (Fig. 9, Table 2).

DISCUSSION

This study aimed to confirm the surface cleansing and osseointegration effects of SLA titanium implants through plasma treatment on a beagle model. The null hypothesis was that surface cleansing and osseointegration of plasma-treated and untreated implants would be similar.

Twelve SLA titanium implants were divided into two groups: a control group (untreated implants) and a plasma group (implants treated with plasma). The plasma treatment was performed using a plasma generator based on non-thermal gas plasma.

Clinical success of implants is associated with wide bone to implant contact (BIC), and osseointegration is an important condition for stability after implantation.[3,36] Titanium implants are the most commonly used due to their biocompatibility and low cost among various other materials available in the market.[7] However, it has been reported that because titanium is a bioinert material, it lacks osseointegration, which may cause implant failure.[6,7] In many studies, the surface topography formed by SLA enhanced osseointegration.[11,12] However, BIC was still 50% to 60%, lower than the ideal 100%.[17,18,20] Implant failure can be caused by incomplete osseointegration or destructive changes in the bone-implant interface.[18] However, the reason why BIC does not reach 100% even with a sufficient healing period has not been mentioned.[20]

Several studies have reported on the biological aging of titanium, revealing a decrease in the biological abilities associated with osseointegration over time.[17,20,31,37] This is related to the deposition of atmospheric carbon in the form of hydrocarbons on the surface of titanium.[17,20] It has been shown that the higher the carbon accumulated, the lower the biological capability of titanium such as attracting osteoblasts and proteins.[17,20] A previous study demon-

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strated that the BIC obtained for newly processed titanium, which was 90%, can decrease to less than 60 % for aged titanium.[20] Titanium implants are provided to users in storable form.[17,37] The expiration date of implant is determined based on the sterilization date, ensuring its sterilization.[37] However, changes in the biological properties of titanium over time were not considered.[37] Commercially available titanium implant products are contaminated with carbon, so biological aging is inevitable.[38]

Ultraviolet irradiation and plasma treatment were suggested as methods to improve the biological abilities of titanium implants without altering their surface topography.[30,32,39-41] In comparative studies, both methods removed hydrocarbons on the titanium surface, increased hydrophilicity, and improved biological capabilities such as osteoblast attachment and protein adsorption.[31,42,43] However, it has been reported that plasma treatment can be applied in a relatively shorter time than UV irradiation to achieve an increase in biological abilities and hydrophilicity.[31,42,43] Choi *et al*.[31] found no difference in treatment effects on contact angle, atomic percentages of carbon, cell adhesion, and protein adsorption after ten minutes of non-thermal atmospheric pressure plasma treatment and after fifteen minutes of UV irradiation. According to Canullo *et al*.,[42] twelve minutes of non-thermal argon plasma treatment and three hours of UV irradiation had similar effects on cell adhesion and protein adsorption. Guo *et al*.[43] reported that one minute of non-thermal oxygen plasma treatment and twelve minutes of UV irradiation may be preferred for increasing cell adhesion of osteoblast-like cells (MC3T3-E1). The plasma generator used in this study utilizes a vacuum pump and a high-voltage power supply to apply cylindrical non-thermal plasma to the entire surface of the implant in 60 seconds.[35] In addition, this device uses air as the gas for plasma discharge, thereby eliminating the need for any additional gas supply.[35] This means that limitations for chairside use of existing plasma devices, such as implant positioning, additional gas supply for plasma discharge, and long application times, can be overcome. Additionally, several studies have suggested the possibility of applying plasma treatment to reduce bacterial contamination and infection by inhibiting the attachment of oral bacteria to titanium implants.[44-46]

In morphological analysis, plasma treatment did not alter the implant surface topography or cause any physical damage. In XPS analysis, the atomic percentage of carbon at the inspection point before the plasma treatment was 34.09%. After the plasma treatment, it was reduced to 18.74%, indicating a 45% reduction in carbon. This shows that plasma treatment can remove hydrocarbons without changing the implant surface and is consistent with previous studies.[34,35]

In volumetric analysis and histometric analysis, new bone volume (NBV) was 40.18 ± 4.65% in the control group and 47.30 ± 2.44% in the plasma group, bone to implant contact (BIC) was 66.48 ± 10.06% in the control group and 74.79 ± 5.30% in the plasma group, and inter-thread bone density (ITBD) was 72.26 ± 8.99% in the control group and 77.82 ± 3.78% in the plasma group. The plasma group exhibited relatively higher mean NBV, BIC, and ITBD compared to the control group. However, there was no significant difference between the two groups ($P > .05$).

Limitations described below are thought to be the reason for this result. The condition of the alveolar bone was checked before implantation in the mandibles of two beagles. The alveolar bone's thickness was insufficient on the buccal-lingual side. In particular, there have been observations of buccal bone resorption. Four days after the procedure, two implants were respectively exposed in the control and plasma groups. Four exposed implants were excluded from the results data (n = 4 in each group). Also, due to the difficulty in confirming the reference point of the buccal bone in the histometric analysis, the lingual bone was chosen as the reference point and analyzed instead. Therefore, despite the proven cleansing of implant surface through plasma treatment, further studies are required to confirm the clinical effectiveness of plasma treatment in improving osseointegration.

CONCLUSION

This study was conducted to evaluate the effects of plasma treatment of SLA titanium implants on surface cleansing and osseointegration in a beagle mod-

el. Within the limitations of this study, plasma treatment eliminated effectively hydrocarbons without changing the implant surface. However, further studies are required to confirm the clinical effectiveness of plasma treatment in improving osseointegration.

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