Surface analysis of titanium disks with strontium coating

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Peri-implantitis is one of the most common complications after dental implant placement. Researchers have demonstrated that the peri-implantitis tends to occur around dental implants with a rough surface rather than those with a smooth surface. We aimed to investigate the ability of a smooth titanium (Ti) surface containing strontium (Sr) to enhance bone formation as a result of strontium’s capacity to support osteoblast proliferation and differentiation. A thin titanium oxide film was formed on an as-mirror polished Ti surface by dipping in 5% sodium hypochlorite (NaOCl) solution for 24 h, followed by thermal treatment at 350°C. The Ti surface was then treated with 1% strontium nitrate (Sr(NO₃)₂) solution and turned in spin coater. The surface morphology, chemical composition, and release of strontium ions (Sr²⁺) were evaluated. The results demonstrate that strontium in the form of Sr²⁺ was successfully doped into the titanium dioxide (TiO₂) film by this simple chemical treatment.

Keywords: Titanium disk, Strontium nitrate, Hydrophilic, Smooth surface, Sodium hypochlorite

INTRODUCTION

The aim of dental implant treatment is to achieve optimal functional and aesthetic outcomes; however, a range of long-term complications are sometimes encountered. Such complications include peri-implant diseases such as peri-mucositis and peri-implantitis. Peri-implantitis is usually initiated by accumulation of bacterial biofilm around the implant surface⁹. Numerous etiological factors also play a decisive role in the progress of peri-implant infection. The implant design, the degree of roughness, and the external morphology are all related to the disease⁵,⁶,⁷. Our focus was on the prevention of peri-implant disease, through factors related to the surface morphology. The success of the implant treatment depends on an osseointegration, which is defined as a direct histological bone-implant contact. Osseointegration allows the functional loading of dental implants to occur¹. A rough surface enhances mechanical loading and bone formation around the implant. However, a rough surface also increases the incidence of peri-implantitis and an ionic leakage⁵,⁶,⁷, because bacterial accumulation is greater on implants with a rough surface than on those with a smooth surface⁵,⁶,⁷. Moreover, a smooth surface is accessible for treatment during peri-implantitis once it has occurred. Thus, there is a need for the development of a smooth surface capable of increasing osseointegration. Some studies have revealed that unfavorable osseointegration is related to biological aging of titanium⁸, caused by the loss of hydrophilicity and the progressive contamination of the titanium surface by hydrocarbons⁹. We used a sodium hypochlorite (NaOCl) solution based on its previously reported oxidizing properties and an antimicrobial and organic decomposition effects, which clean organic contaminants and hydrocarbons from the titanium surface⁸,¹⁰.

Bone formation and osseointegration around titanium implants can be increased by various methods, such as acid or alkali treatment, chemical vapor deposition, anodization, plasma spraying, sputtering, ion deposition, and sol-gel and dip coating¹¹. A smooth surface can be created by the sol-gel coating process; however, it is labor-intensive and time-consuming, and requires special equipment. In the present study, we aimed to create a smooth surface that enhances osseointegration by using a simple chemical treatment.

Strontium (Sr) has been attracting the attention of scientists for many years because of its beneficial biological role. It is an essential trace element for human skeletal components and works effectively to both promote bone formation and inhibit bone resorption¹². Many researchers have been investigated Sr coatings on titanium (Ti) implants with a rough surface. The Sr-coated Ti implants inserted in ovariectomized rat tibiae promoted bone formation, and osteoblast proliferation and function, and inhibited osteoclast function in the case of osteopenia¹³. An in vitro study also found that the Sr coating on titanium plates promoted osteoblastic cell adhesion and proliferation¹⁴. A series of studies revealed that a coating of magnesium ions on the titanium surface promoted bone formation¹⁵,¹⁶; however, the capability of Sr for enhancing bone formation has been reported to be superior to that of Mg¹⁷. Therefore, the present study

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aimed to create a smooth Ti surface containing Sr ions using a simple chemical treatment.

**MATERIALS AND METHODS**

**Surface modification**
Commercially pure grade-2 Ti disks (JIS, Specification H 4600, 99.4 mass% Ti; T-alloy M, GC, Tokyo, Japan), 14 mm in diameter and 3 mm thick, and 5 mm in diameter and 1 mm thick were mechanically polished (ECOMET 3, Buehler, Lake Bluff, IL, USA) to a mirror finish using a colloidal silica suspension (Master Met™, Buehler). The specimens were subsequently cleaned ultrasonically in distilled and deionized water for 15 min, followed by immersion in acetone and then ethanol for 1 min each to remove contamination related to handling. The specimens were classified into the control group (as-mirror polished), and the test group. Each group included four specimens.

The test groups were prepared in two different ways:
1) The NaOCl-Sr group was prepared by immersion in the 5% NaOCl solution for 24 h at room temperature, followed by ultrasonic cleaning (2510-J-MT, Branson, Danbury, CT, USA) in distilled and deionized water for 10 min, rinsing and drying. Samples were subsequently dipped in 1% Sr(NO₃)₂ for 30 s, and were turned in spin coater (ACT-220D, Active, Saitama, Japan) at 7,000 rpm for 60 s

2) The NaOCl-Sr-washed group was prepared in the same way as the NaOCl-Sr group, but were additionally ultrasonically cleaned in distilled and deionized water for 5 min and dried with oil-free compressed air.

3) The Thermal-Sr-washed was treated at 350°C for 45 min in a furnace (MS-1200 Jelenko Cerafusion VPF, Morita, Tokyo, Japan). The specimens were cooled to room temperature and were immersed in 1% Sr(NO₃)₂ solution for 30 s. The specimens were turned in a spin coater at 7,000 rpm for 60 s, ultrasonically cleaned in distilled and deionized water for 5 min, and dried with oil-free compressed air.

**Surface analysis**
1. Surface characterization
The elemental composition of the surface was analyzed with an X-ray photoelectron microscope (XPS; ESCA-850, Shimadzu, Kyoto, Japan) using 5 mm in diameter and 1 mm thick specimens. The Ti 2p, O 1s, C 1s, and Sr 3d spectra were obtained with Mg Kα radiation operated at 7 kV accelerating voltage and 30 mA current under a vacuum of 1×10⁻⁶ Pa. The surface was subjected to argon ion (Ar⁺) etching at 2 kV and 20 mA under a pressure of 5×10⁻⁴ Pa in the spectrometer. The etching rate was approximately 0.1 nm/s.

The surface roughness (arithmetic average roughness, Ra) was measured on the 10×10 μm-area images (n=10), using the roughness measurement tool of the scanning probe microscope (SPM) image analyzing software (SPM Off-line ver. 2.12, Shimadzu).

2. Strontium ion release
The specimens were soaked in 5 mL of saline in sealed bottles for 1, 3, and 7 days respectively at 37°C in an incubator. The Sr²⁺ concentration was measured on days 1, 3, and 7, using inductively coupled plasma optical emission spectroscopy (ICP-OES; Optima 5300 DV, PerkinElmer precisely, Waltham, MA, USA). After each measurement, the specimens were moved to new bottles with distilled and deionized water. Standard solutions containing Sr concentrations of 0.1, 0.5, 1, and 10 ppm adjusted using strontium standard solution (Wako Pure Chemical, Osaka, Japan) were used to obtain a standard calibration curve.

3. Analysis of surface wettability
From a 1 cm distance 10 μL of distilled water was dropped on the surface of the specimens. Side images of the specimens were captured and measured with an automatic contact angle measuring device (Phoenix Alpha, Surface Electro Optics, Suwon, Korea) immediately after preparation of the specimens, and at 1 and 2 weeks.

4. Statistical analysis
The groups were compared with one-way ANOVA followed by the Tukey HSD post-hoc test. All tests were conducted with a significance level of 5% (p<0.05) using statistical software (SPSS version 26, IBM, Armonk, NY, USA).

**RESULTS**

**Surface morphology and composition**
Figure 1 shows SPM images of the NaOCl-Sr and NaOCl-Sr-washed specimens. Three dimensional SPM images showed that the surface of both the NaOCl-Sr and the NaOCl-Sr-washed specimens was quite smooth with an Ra of 0.003 (0.0006) μm for the NaOCl-Sr (Fig.1a) and 0.004 (0.0003) μm for the NaOCl-Sr-washed (Fig.1b). There were no significant differences in the surface morphology before and after ultrasonic cleaning in distilled and deionized water for 5 min.

The results of XPS surface analysis of the NaOCl-Sr group revealed a Ti 2p peak at 458.7 eV corresponding to TiO₂, and a high Sr 3d peak at 134.7 eV corresponding to Sr²⁺. A N 1s peak at 408 eV corresponding to NO₃⁻ also appeared on the surface (Fig. 2a), suggesting that crystals composed of Sr(NO₃)₂ precipitated on the NaOCl-Sr surface. On the NaOCl-Sr-washed surface, a peak of Sr 3d was still detected, but the N 1s peak corresponding to NO₃⁻ had disappeared (Fig. 2b). This result suggested that the remaining Sr²⁺ that remained after cleaning in distilled and deionized water was successfully doped in the oxide after spin coating. A C 1s peak at 285.0 eV corresponding to hydrocarbon contamination was observed for both the NaOCl-Sr and the NaOCl-Sr-washed specimens (Figs. 2a and b). A O
1s peak at 530.0 eV corresponding to TiO$_2$ was observed for both the NaOCl-Sr and the NaOCl-Sr-washed specimens, while a O 1s peak at 533.3 eV corresponding to NO$_3^-$ (Sr(NO$_3^-$)$_2$) was observed only for the NaOCl-Sr specimens (Figs. 2a and b).

Figure 3a shows the XPS depth analysis of the NaOCl-Sr-washed group. The Ti 2p peak corresponding to TiO$_2$ disappeared after Ar$^+$ etching for 360 s, indicating that an oxide film approximately 0.036 µm thick was formed on the Ti surface with NaOCl solution treatment. This result suggests that a relatively thick oxide film was formed as a result of the NaOCl solution treatment, as compared with the passive film on titanium (1–2 nm). The Sr 3d peak also disappeared after Ar$^+$ etching for 360 s, however, no N 1s peak was observed before or after Ar$^+$ etching (Fig. 3a).

In the group that underwent thermal treatment at 350°C for 45 min (Fig. 3b), a Ti 2p peak corresponding to TiO$_2$ was detected and disappeared after 240 s of Ar$^+$ etching treatment, indicating that a 0.024 µm thickness of TiO$_2$ film was formed. A N 1s peak was observed at 397 eV after Ar$^+$ etching for 240 s, corresponding to nitride, but no Sr 3d peak was detected. A small amount of nitrogen contained in pure titanium as an impurity might have formed clusters of nitrides on the titanium surface and become embedded in the oxide film during the heat treatment.

**Strontium ion release**

The concentration of Sr$^{2+}$ released from the NaOCl-Sr group was 5.69 ppm at day 1, 0.05 ppm at day 3, and 0.001 ppm at day 7 (Fig. 4a). In the NaOCl-Sr-washed group, Sr$^{2+}$ concentration was 0.64 ppm at day 1 (one order of magnitude lower than the NaOCl-Sr group), 0.05 ppm at day 3, and 0.01 ppm at day 7 (Fig. 4b).

**Surface wettability**

The water contact angle on the NaOCl-Sr-washed surface was 2.03±0.6° just after coating, which was significantly lower (p<0.05) than that of the as-mirror polished...
Fig. 3 The spectra of XPS depth analysis of NaOCl-Sr-washed (a) and Thermal-Sr-washed (b) surfaces.

Fig. 4 Sr2+ release from NaOCl-Sr (a) and NaOCl-Sr-washed (b) groups into the saline at days 1, 3, and 7, analyzed by ICP-OES.

Fig. 5 The results of water contact angle of as-mirror polished titanium and NaOCl-Sr-washed groups at different time intervals. Asterisks indicate statistically significant differences relative to each group (p<0.05).

DISCUSSION

The Ti implant bodies with micro rough surfaces induced by sandblasting and acid-etching have commonly been used because of their enhanced endosseous integration and bone formation11). However, a smooth surface is more suitable for the prevention and treatment of peri-implantitis. Three types of surfaces were evaluated in this study. Both the NaOCl-Sr surface and the NaOCl-Sr-washed surface took up the Sr2+ via a simple chemical treatment, according to the XPS analysis (Fig. 2). After 1 and 2 weeks, the water contact angle of the as-mirror polished surface became 51.06±2.8° and 55.3±2.4°, while that of the Sr-doped surface became 4.3±0.8° and 5.3±0.9°. The water contact angle was significantly higher on the as-mirror polished surface than on the Sr-doped surface (p<0.05) after 1 and 2 weeks.
However, the NaOCl-Sr surface released more Sr\(^{2+}\) than the NaOCl-Sr-washed surface, due to the excess Sr(NO\(_3\))\(_2\) precipitated on the surface. The peaks corresponding to Sr 3d, N 1s, and O 1s spectra revealed that Sr(NO\(_3\))\(_2\) precipitation had formed on the NaOCl-Sr surface (Fig. 2a). These Sr(NO\(_3\))\(_2\) precipitates could not be observed clearly in the SPM image at this magnification for the NaOCl-Sr-washed surface (Fig. 1a) probably because of their small size.

The N 1s peak disappeared and the Sr 3d peak was still detected on the NaOCl-Sr-washed surface, which suggested that the Sr(NO\(_3\))\(_2\) precipitation was removed and Sr\(^{2+}\) was successfully doped into the TiO\(_2\) layer (Fig. 2b). The XPS depth analysis detected the Sr\(^{2+}\) doped into the TiO\(_2\) film from the uppermost surface to the interface between the oxide film on the Ti substrate of the NaOCl-Sr-washed specimens (Fig. 3a). The Sr 3d peak was not detected in the Thermal-Sr-washed surface, indicating that the high temperature oxidation film could not take up any Sr\(^{2+}\) (Fig. 3b) in the way that the oxide film was formed by 5% NaOCl treatment. The NaOCl-treated Ti surface is favorable to the uptake of Sr\(^{2+}\), probably as a result of the relatively coarse structure of the thick oxide film, as compared with the thick and dense oxide film formed during the heat treatment at 350\(^{\circ}\)C (Thermal-Sr-washed).

The Ra of Straumann, Basel, Switzerland (acid etched surface) was 1.5 \(\mu\)m, that of GEASS, Pozzuolo Del Friuli, Italy (machined surface) was 0.75 \(\mu\)m, and that of GEASS (laser treated surface) was 0.37 \(\mu\)m.\(^{18}\) The roughness obtained in the present study for the NaOCl-Sr-washed surface was 0.004 \(\mu\)m — much smoother than the surfaces of the dental implants in clinical use. A smoother surface (Ra≤0.2 \(\mu\)m) has been shown to result in significant reductions in the periodontal pathogenicity of adhering bacteria. When the roughness is above 0.2 \(\mu\)m, bacterial adhesion cannot be further reduced.\(^{7}\) Thus, the NaOCl-Sr-washed surface has the capability of releasing Sr\(^{2+}\) without increasing the surface roughness, which leads to better healing after implant placement and also reduces the risk of peri-implantitis by inhibiting bacterial attachment and subsequent biofilm formation.

Strontium has been shown to beneficial biological effects. Sr-modified Ti6Al6V alloy fabricated by hydrothermal treatment was capable of releasing Sr\(^{2+}\) (0.135 ppm) for up to 7 days, which enhanced alkaline phosphatase activity and gene expression of osteoblastic cells.\(^{19}\) Sr-modified pure Ti, which released Sr\(^{2+}\) (0.407–0.409 ppm) at day 1, improved the adherent number, spreading, and growth of osteoblastic cells.\(^{14}\) In the present study, NaOCl-Sr group released 5.69 ppm Sr\(^{2+}\) and NaOCl-Sr-washed group released 0.64 ppm Sr\(^{2+}\) at day 1. These results show that the NaOCl-Sr-washed surface probably enhances the early behavior of osteoblastic cells. Moreover, as reported previously, the number of hydroxyl groups on the titanium surface increases after 5% NaOCl treatment, which accounts for the enhanced cell attachment.\(^{20}\) Future studies should investigate osteoblastic cell responses on the new surfaces created in this study.

Surface wettability is one of the most important indices for the understanding the interfacial characteristics between a solid surface and a liquid, especially such physicochemical properties as hydrophilicity and water repellency. The water contact angle of the NaOCl treated as-mirror polished Ti surface was previously reported to be 10\(^{\circ}\), but that of the NaOCl-Sr-washed surface evaluated in the present study was 2.03\(^{\circ}\). The NaOCl is a strong oxidant, and has an antimicrobial and organic decomposition effect, which cleans organic contaminants from the surface. In this study, we employed the standard concentration of NaOCl\(^{21}\) to remove organic contaminants and hydrocarbons from the titanium surface before coating. The absorbed amines and amides from the atmosphere can react with ClO\(^-\) of NaOCl to yield chloramines and chloramides, and desorb from the Ti surface.\(^{20}\) The results of XPS depth analysis showed that the specimens treated with 5% NaOCl took up some Sr ions to the surface of the oxide layer, but this did not occur after thermal oxidation at 350\(^{\circ}\)C. As mentioned above, the ability to take up Sr\(^{2+}\) to the thick oxide film of NaOCl-Sr was due to its coarse structure, which enhanced the migration of Sr\(^{2+}\) into the oxide film. In contrast, the dense oxide film formed after heat treatment at 350\(^{\circ}\)C for 30 min probably inhibited the migration of Sr\(^{2+}\) into the film. A recent study investigated a super-hydrophilic (<5\(^{\circ}\)) surface containing Sr\(^{2+}\), which is highly likely to exhibit excellent biocompatibility through enhanced cell attachment and osteoblastic gene expression.\(^{22}\) Numerous studies have examined methods for coating Ti with Sr, such as electrochemical deposition of Sr-substituted hydroxyapatite coating, sol-gel dip coating, and soaking.\(^{25}\) These studies investigated Sr coatings on rough surfaces or produced a rough surface by Sr coating. This is the first study to create a functional smooth titanium surface with the ability to release Sr\(^{2+}\) through a simple chemical treatment.

CONCLUSIONS

1. Strontium ions were doped into the TiO\(_2\) film after 5% NaOCl treatment, but not into the high temperature oxidation film on the smooth surface of Ti disks.

2. Sr\(^{2+}\) was doped into the surface of the NaOCl-Sr and NaOCl-Sr-washed groups, and was released when the specimens were immersed in distilled and deionized water for up to 7 days, which may have a beneficial effect on the early behavior of osteoblastic cells.

3. The surface of the NaOCl-Sr-washed Ti is able to maintain its super-hydrophilicity.

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CONFLICT OF INTEREST
The authors declare that they have no conflicts of interest.

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