Improvement of corrosion resistance and biocompatibility of medical nickel–titanium alloys through forming TiO₂ thin film

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Abstract

Nickel–titanium alloys have been investigated for applications to various surgical procedures. However, little is known about the toxicity of Ni-elements and the actual conditions of surface modification of Ni-Ti alloy for preventing the toxicity of Ni. In this study, the corrosion resistance of Ni-Ti alloys was improved through producing a thin TiO₂ film by conducting in-air oxidation and reactive sputtering. These thin films were characterized using field emission type scanning electron microscopy, X-ray diffraction, X-ray photoelectron spectroscopy and atomic force microscopy. Using the polarization curves obtained by electro-chemical measurements in quasi-living body environment, the corrosion resistance of Ni-Ti super elastic alloy was evaluated. In addition, the effect of an air-oxidized Ni-Ti alloy specimen upon cell multiplication and morphological change of cell were investigated by culturing cells for 72 hrs on a Ni-Ti alloy specimen surface with TiO₂ thin film. From these considerations, some trials for establishing a method for TiO₂ thin film formation on the surface of Ni-Ti alloy were conducted from the view point of improving biocompatibility.

Keywords: nickel–titanium alloy, corrosion resistance, biocompatibility, surface modification, TiO₂ thin film, reactive sputtering, air oxidation – suppressed partial pressure, cell multiplication – morphological change.

1 Introduction

In recent years, some concern has been raised about the corrosion resistance of implant alloys within an aging society. Implant materials have been required to exhibit biocompatibility in the long term without a re-operation. The biocompatibility of implant materials means they should not adversely influence the living body nor lead to loss of function of the materials of interest. Especially,

the strength degradation by corrosion and elution of a toxic metallic ion by corrosion in the severe living body environment has attracted growing interest. The shape memory effect and super elasticity effect of Ni-Ti alloys [1, 2] have received considerable attention in the medical domain [3–6]. The Ti-Ni alloy has been increasingly applied to medical and dental devices, such as coronary stents and orthodontic wires. Thus, the application of Ni-Ti alloys in medical and dental devices has been the subject of many research papers. However, in practical cases, the presence of Ni element (Ni ion) in Ni-Ti alloys for such applications has been a cause for apprehension due to carcinogenicity and allergic reaction [7]. In the present state of affairs, the view about the use of Ni-Ti alloys in the medical domain is negative. A comprehensive understanding of the surface modification of Ni-Ti alloys for use under quasi-living body environment is still lacking.

Therefore, in this paper, the corrosion resistance of Ni-Ti alloys was improved through the production of a thin TiO_2 film. The TiO_2 thin film has been studied for photocatalysis and a lot of production methods have been developed. In this study, the TiO_2 thin film was produced by air oxidation and reactive sputtering. Air oxidation is a comparatively simple thin film production method and thin films made by this method do not easily exfoliate. Reactive sputtering is the film production method that can control the forming condition precisely and thin films made by this method are highly coherent. These thin films were characterized using field emission type scanning electron microscopy (FE-SEM), X-ray diffraction (XRD), X-ray photoelectron spectroscopy (XPS) and atomic force microscopy (AFM). Using the polarization curves obtained by electro-chemical measurement in quasi-living body environment, the corrosion resistance of Ni-Ti super elastic alloy was evaluated. In addition, the effect of an air-oxidized Ni-Ti alloy specimen upon cell multiplication and morphological change of cell were investigated by culturing cells for 72 hrs on Ni-Ti alloy specimen surface with TiO_2 thin film.

From these considerations, some trials for establishing a method for TiO_2 thin film formation on the surface of Ni-Ti alloy were conducted from the view point of improving biocompatibility.

2 Experimental procedures

2.1 Test specimen

Plate specimens with sizes of $11.5 \times 11.5 \times 2.5\text{--}3.0 \text{ mm}^3$ were cut from a block of Ni-Ti alloy (44% titanium, 56% nickel by weight). The samples were finished by mechanical abrasion and then polished to a mirror finish. The test specimen was ultrasonically cleaned in ethanol. Air oxidation treatments were performed in an electric furnace in oxidizing atmosphere. Four kinds of samples (A1–A4) were prepared through changing the heat treatment temperature and heating time (A1: 673 K, 30 min, A2: 773 K, 30 min, A3: 773 K, 60 min, A4: 1073 K, 30 min) [8].

A DC reactive sputtering system (MPS-2000-HC3, ALVAC) was employed for forming the TiO_2 thin film [9]. The target is titanium with purity of 99.99%. The distance between target and substrates was fixed at 200 mm. After the

chamber was evacuated to a vacuum lower than $\times 10^{-6}$ Pa, argon was introduced into the chamber. The input power was fixed at 200 W and the substrate temperature was not controlled. After the discharge colour was confirmed, oxygen was introduced into the chamber. Three kinds of samples were prepared through changing the ratio of argon and oxygen flow rate (S1: Ar:O₂ = 5:10 [sccm], S2: Ar:O₂ = 20:10 [sccm], S3: Ar:O₂ = 50:10 [sccm]).

2.2 Anodic polarization measurement and immersion test

The corrosion resistance was evaluated employing an anodic polarization measurement method based on JIS T 0302 (testing method for corrosion resistance of metallic biomaterials by anodic polarization measurement). The electro-chemical measurement was conducted using a three-electrode method (HZ-3000 Hokutodenkou Japan) composed of the specimen (working electrode), Pt (counter electrode) and the saturated calomel electrode (SCE) (reference electrode). The electro-chemical measurement was conducted using a plate specimen in lactated Ringer's solution at 310 K. The test solution was de-aerated by extra-high purity nitrogen for 20 minutes before testing to suppress dissolved oxygen at a level similar to that of the living body. The potentio-dynamic corrosion test was conducted with the sweep rate of 20 mV/min from -1000 mV to 2000 mV (vs. SCE).

Immersion tests were conducted as follows. The specimens were put into polyethylene vessels with 20 ml of 1.0% lactic acid (JIS T 0304). After immersion at 310 K for 30 days, quantification of released ions was carried out by means of an inductively coupled plasma emission spectrometer ICP-AES: SPS7700 (Seiko Instruments Inc.). Three specimens were tested for each condition. Amounts of released component ions per unit surface area of the specimens were then calculated.

2.3 Evaluation of bio-compatibility of air oxidized Ni-Ti alloy

As a final goal of biocompatibility evaluation, it was planned to employ the inflammatory response of macrophage. In previous research, U937 (Human Leukemic Monocyte Lymphoma Cell) was used to differentiate into macrophage [10, 11]. In this study, however, an osteoblast-like cell line MC3T3-E1 was applied because of improvement in reproducibility of test results due to its having no ability to differentiate into other cell systems.

At first, a pure Ni square plate specimen (27 mm) whose thickness is 1.0 mm was dissolved in 1.0 M phosphate buffer whose temperature is 310 K employing three-electrode anodic polarization measurement method under the constant current density of 130 mA/cm². Then through analysing it by ICP, test solutions with various Ni ion concentrations from 0.125 to 2.0 ppm were prepared.

The effect of Ni ion concentration upon cell multiplication and morphological change of cell was investigated. Also, the effect of air oxidized Ni-Ti alloy specimen upon cell multiplication and morphological change of cell were investigated by culturing cells for 72 hrs on Ni-Ti alloy specimen surface with TiO₂ thin film.

3 Experimental results and discussion

3.1 Characterization of modified surface

In Fig. 1, the FE-SEM morphology of Ni-Ti specimen surface, the film thickness determined by FIB processing and SIM (Scanning Ion Microscopy) observation and the structure of thin film determined by XRD are summarized.

Then, the structural analysis of the thin film layer was conducted by sputtering and XPS [12]. From the results of compositional analysis toward the depth direction by XPS shown in Fig. 2, the composition of extreme thin surface of specimen was understood. A thin TiO_2 layer exists in the vicinity of film surface.

On the surface of the thin film formed by air oxidation, a peak of Ni was observed, and it is considered that a Ni-free layer was not present on the surface of the specimen. On the other hand, a peak of Ni was not observed on the surface of the film formed by reactive sputtering; thus, it is considered that a Ni-free layer was provided on the surface of sputtered specimen.

Sugawara *et al.* [8] investigated the effect of thermal oxidation treatment on the surface characteristic and corrosion resistance of a Ni-Ti shape memory alloy.

In this study, a mechanically polished Ni-Ti alloy was subjected to isothermal oxidation (TO) in N_2 -20vol.% O_2 at temperatures ranging from 300 to 800°C. TO-treated surfaces were then characterized by FE-SEM, energy dispersive X-ray spectrometer (EDX), XPS and XRD. The results showed that the Ni-Ti alloy exhibited different oxidation behaviour depending on the treatment temperatures. A Ni-free layer was observed in the oxide layer for the specimen TO-treated at temperatures 500°C and above. Element concentration and chemical binding condition from the surface to interior were investigated using XPS. As a result, oxygen diffusion was detected in the surface layer and the depth of this layer increases with increasing treatment temperature.

3.2 Evaluation of corrosion resistance by electro-chemical measurement

Figs. 3 and 4 show the polarization curves obtained in lactated Ringer's solution at 310 K using in air oxidized and reactive sputtered Ni-Ti alloy. From the polarization curves obtained from in air oxidized specimen, it can be understood that the passivation current density was extremely suppressed compared with that of non-treated materials, and improvement of corrosion resistance was confirmed. As in-air oxidation heat treatment temperature increases, film thicknesses increase and corrosion resistance improved from the view point of passivation current density. It is considered that corrosion resistance rather depends on film thickness than on crystal structure. However, the potential width of passive state remains approximately equal to that of virgin materials.

Sugawara *et al.* also carried out electrochemical corrosion tests using a three-electrochemical cell connected to a computer-driven potentiostat [8]. TO-treated specimens at temperatures ranging from 300 to 500°C showed higher corrosion resistance compared to that of the surface finished by polishing. This was because

Figure 1: Morphology, film thickness and structure of surface-modified specimens.

Figure 2: Analysis of composition toward depth direction by XPS.

Figure 3: Polarization curves of surface-modified Ni-Ti alloy (in-air oxidation) in lactic Ringer's solution of 310 K.

Figure 4: Polarization curves of reactive sputtered modified Ni-Ti alloy in lactic Ringer's solution of 310 K.

the TO-treatment created a thick oxide layer with an amorphous structure. TO-treated specimens at above 600°C showed very low passive current densities, but lower pitting potential. This was because these samples were covered with crystalline oxide. Consequently, the TO-treatment at 500°C produced a smooth protective nickel free oxide layer, which contributes to good biocompatibility of Ni-Ti implants. As a result, it was made clear that TO-treatment applied to Ni-Ti alloy can drastically suppress Ni ion elution from the alloy surface.

From polarization curves of a reactive sputtered specimen, it can be stated that the passivation current density was significantly improved compared with that of non-treated ones, and the improvement of corrosion resistance was thus confirmed.

As Ar flow rate increases, film thicknesses increase and corrosion resistance improve. The potential width of the passive state is wider than that of the virgin material, thus biocompatibility without re-operation in the long term is expected.

3.3 Bio-compatibility of air oxidized Ni-Ti alloy specimen

At first, the effect of Ni ion concentration upon cell multiplication was investigated in this section. Fig. 5 shows the number of adhered cells after cultured 72 hrs in 1.0 M phosphate buffer with various Ni ion concentrations under 2 ppm or cultured 72 hrs on Ni-Ti alloy specimen surface with TiO₂ thin film. The solid line shown in this figure indicates sowed cell density, that is, 5600 cells/cm². From these results, cell multiplication occurred under each ion concentration condition in the same manner as control. Therefore, no significant difference in the number of adhered cells was recognized. As a result, there is no effect of Ni ion upon cell multiplication within ion concentration below 2 ppm. Also, in case of Ni-Ti alloy with TiO₂ thin film formed by air oxidation, no effect of Ni ion dissolution from extreme thin surface layer upon cell multiplication was detected.

Figure 5: Number of adhered cells after cultured 72 hrs in 1.0 M phosphate buffer.

Also in Fig. 6, the number of adhered cells after cultured 24–72 hrs in 1.0 M phosphate buffer with various Ni ion concentrations under 0–100 ppm are indicated. Cell multiplication characteristics were suppressed with Ni ion concentration increasing. Then, cells died out under the Ni ion concentration condition of 100 ppm.

Figure 6: Changes in number of adhered cells in 1.0 M phosphate buffer with different Ni ion concentration (MC3TA-E1).

Mizutani *et al.* also investigated the effects of thermal oxidation on the biocompatibility of a Ni-Ti shape memory alloy [13]. They conducted cell culture tests with L929 fibroblast cells to examine the cell proliferation. The amount of Ni ions elution in the culture medium used during the cell proliferation test was analysed by atomic absorption photometer. As a result, all TO-treated samples

showed good biocompatibility after 3 days of immersion tests as shown in Fig. 7, and released Ni ions were significantly reduced by TO-treatment as shown in Fig. 8. These results are caused by the generated thick and stable surface-modified layer on the alloy surface by TO-treatment. In addition, the wear resistance of the Ni-Ti alloy also improved by TO-treatment. After the wear test, biocompatibility was evaluated by cell proliferation tests, and the results showed that the surface damage on the TO-treated sample did not affect the attachment cells. From these results, it was concluded that the isothermal oxidation treatment is effective as a surface modification method for a Ni-Ti alloy.

Figure 7: Results of cell proliferation tests ($n = 4$, mean $\pm$ SD) [14].

Figure 8: Comparison of released Ni ion ($n = 4$, mean $\pm$ SD) [14].

Then, the effect of Ni ion concentration upon morphology change of cell was investigated. In Fig. 9, the cell morphology after cultured 72 hrs on Ni-Ti alloy specimen surface with TiO_2 thin film is indicated. Fig. 9(a) shows the cell morphology obtained after fluorescent stain, and (b) shows the cell morphology obtained after Giemsa stain. Also, in Fig. 10(b), the fluorescent stain cell

morphology after cultured 72 hrs in 1.0 M phosphate buffer with 0.5 ppm Ni ion concentration is indicated and in Fig. 10(a) that of control is indicated. In the case of cell after cultured 72 hrs in 1.0 M phosphate buffer with Ni ion concentration of 0.5 ppm, some morphological change, that is, linearization of cell was recognized. In contrast, in the case of cell after cultured 72 hrs on Ni-Ti alloy specimen surface with TiO₂ thin film, no remarkable change in cell morphology was generated just like the case of control.

Figure 9: Cell morphology after cultured 72 hrs on Ni-Ti alloy specimen surface. (a) Fluorescent stain; (b) Giemsa stain.

From these observed results, TiO₂ thin film formed by air oxidation also significantly contributes to improved biocompatibility of the Ti-Ni alloy.

Figure 10: Cell morphology after cultured 72 hrs in 1.0 M phosphate buffer with 0.5 ppm Ni ion. (a) Ni ion: 0 ppm; (b) Ni ion: 0.5 ppm.

At the same time, the effect of Ni ion concentration upon the morphology change of cell was investigated under the Ni ion concentration conditions from 0–100 ppm. As a result, some morphological change, that is, linearization of cell was recognized in phase-contrast micrographs under the Ni ion concentration conditions of 10 ppm and above as shown in Fig. 11. Then, the cells almost died out under the Ni ion concentration condition of 100 ppm. This morphological change was also detected by the change in aspect ratio of cells as show in Fig. 12.

Figure 11: A phase-contrast micrograph of cells (MC3T3-E1, 72 h).

Figure 12: Aspect ratio (determined by image J) dependency of cell upon ion concentration (MC3T3-E1).

3.4 Biocompatibility improvement through optimal TiO₂ thin film

In this section, other trials of surface modifications were conducted.

Fukushima *et al.* discussed corrosion resistance and surface characterization of an electrolyzed Ti-Ni alloy [14]. This alloy contains nickel, which is known to

give rise to cytotoxicity, metal allergy and carcinogenicity. Therefore, the purpose of that study was to improve the corrosion resistance of Ti-Ni alloy by electrolytic treatment; thus, an investigation was carried out using different acidic electrolyte compositions. As a result, specimens electrolyzed with lactic acid, water and glycerol were found to show higher corrosion potential and release lower amount of titanium and nickel ions than mechanically polished specimens ($p < 0.05$). With the electrolytic treatment, nickel concentration in the surface oxide layer of Ti-Ni alloy decreased and the thickness of the surface oxide layer increased. Based on the results of that study, it was shown that electrolytic treatment with suitable electrolyte could improve the corrosion resistance of Ti-Ni alloy, which is effective to produce medical and dental devices that utilize the shape memory effect or super elasticity with better biocompatibility.

On the other hand, Mizutani *et al.* examined the creation of bioactive surface by nanosecond-pulsed laser irradiation of commercially pure titanium [15]. In that paper, nanosecond-pulsed laser irradiation was conducted under various conditions, and then morphologies, chemical compositions and crystal structure of irradiated titanium surface were examined. As a result, it was made clear that nanosecond-pulsed laser irradiation can give bioactive properties on commercially pure titanium surface.

Therefore, in the present paper, the following two kinds of methods were employed. The first one is in-air oxidation under suppressed partial pressure oxygen condition using sputtering equipment. Judging from above mentioned results [15], another method is the sequential combination of electro-polishing and air oxidation. Figs. 13 and 14 show the polarization curves obtained in lactated Ringer's solution at 310 K using these two kinds of surface-modified

Figure 13: Polarization curves of Ni-Ti alloy oxidized in suppressed partial pressure air obtained in lactated Ringer's solution of 310 K.

Figure 14: Polarization curves of complexly surface-modified Ni-Ti alloy obtained in lactic Ringer's solution of 310 K.

Ni-Ti alloy. From these figures, remarkable improvement in corrosion resistance was recognized in both the abovementioned surface-modified specimens compared with a simply air oxidized specimen. This remarkable improvement in corrosion resistance may be brought about through eliminating the Ni element in the extreme surface layer. Therefore, XPS analysis in the extreme surface layer has to be conducted in the near future. At the same time, more improvement in biocompatibility may also be accomplished judging from the abovementioned results.

4 Conclusions

The corrosion resistance of Ni-Ti alloys was improved through forming TiO_2 thin film by air oxidation and reactive sputtering. Surface morphology, crystal structure and composition of films were characterized by FE-SEM, XRD and XPS. Then, electro-chemical measurements in quasi-living body environment were conducted. In addition, the biocompatibility of air oxidized Ni-Ti alloy was evaluated by cell multiplication and morphological change of cell. The results obtained are summarized as follows.

A specimen with TiO_2 film whose thickness is more than 100 nm showed sufficient corrosion resistance in quasi-human body environment. The corrosion resistance in quasi-human body environment was influenced more by the film thickness and film defects than by the crystal structure of TiO_2 .

In the case of cell after cultured 72 hrs in Ni ion concentration of 0.5 ppm, some morphological change, that is, linearization of cell was recognized. In contrast, in the case of cell after cultured 72 hrs on Ni-Ti alloy specimen surface with TiO_2 thin film, no remarkable change in cell morphology was generated. From these

observed results, TiO₂ thin film formed by air oxidization also significantly contributes to improved biocompatibility of a Ti-Ni alloy.

The corrosion resistance of surface-modified Ni-Ti alloy may be significantly improved when air oxidization is conducted under the condition of suppressed partial pressure oxygen and the sequential combination of electro-polishing and air oxidation. In these cases, also remarkable improvement in biocompatibility of Ni-Ti alloy may be expected.

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