Increased corrosion resistance of stent materials by converting current surface film of polycrystalline oxide into amorphous oxide

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Abstract: Current efforts of new stent technology have been aimed largely at the improvement of intravascular stent biocompatibility. Among the chemical characteristics of metallic stents, surface oxide corrosion properties are paramount. Using our unique technique, the currently marketed 316 L stainless steel and nitinol stent wires covered with polycrystalline oxide were chemically etched and then passivated to form amorphous oxide. Excellent metallic-stent corrosion resistance with an amorphous oxide surface was demonstrated in our previous in vitro study. For in vivo validation, we compared the corrosion behavior of different oxide surfaces on various forms of test wires in the abdominal aorta of mongrel dogs using open-circuit potential and cyclic anodic polarization measurements. After conduction, the retrieved test wires were observed under scanning electron microscope. No passivity breakdown was found for wires covered with amorphous oxide, while wires with polycrystalline oxide showed breakdown at potentials between +0.2 to +0.6 V. It has been proven that severe pitting or crevice corrosion occurred on the surface of polycrystalline oxide, while the surface of amorphous oxide was free of degradations in our experiment. We have demonstrated that this amorphous oxide coating on metallic material provides better corrosion resistance, not only in vitro but also in vivo, and it is superior not only in strength safety but also in medical device biocompatibility. © 2000 John Wiley & Sons, Inc. J Biomed Mater Res, 52, 323–332, 2000.

Key words: corrosion; nitinol; 316 L stainless steel; polycrystalline oxide; amorphous oxide

INTRODUCTION

Coronary stenting has been widely used clinically for the treatment of atherosclerotic coronary artery disease. Recent research progress in intravascular stents, grafts, and other implantable devices has been aimed largely at improving blood and tissue biocompatibility. Since the interface between the host tissue and foreign biomaterial plays an important role in stent biocompatibility, most of these advancements in stent design focused on modifications in surface properties, including surface energy or “wettability,” electrical surface charge, surface texture, and surface chemistry.1,2 The constitution and surface characteristics of a biomaterial may determine the nature of the host response and the immediate and long-term stent patency rate.2,3

When metals are exposed to a reactive milieu, corrosion, mainly electrochemical in nature, occurs on the surface. Most metals and alloys form a protective oxide film on the surface, which retards further dissolution of the metal ions into the environment. Some metals such as titanium and chromium form a coherent thin oxide film. This oxide film is highly corrosion-
resistant despite the relative position of the electrode potentials. The formation of a protective oxide layer is called “passivation.” Under certain circumstances, the passivation film can be broken down, and corrosion takes place at that point.

The final finishing process during manufacturing determines the chemical composition of the surface. In all intravascular devices, a layer of metal oxide provides the ultimate interface with the host after implantation. The type of metal oxide depends on the composition of the metal or alloy material and the industrial process used in surface finishing. Since heat treatment is involved during current manufacturing processes, most oxides formed on 316 L stainless steel and nitinol have a polycrystalline nature. Only after a special procedure is the polycrystalline oxide removed and reformed with a layer of amorphous oxide.4

A variety of intravascular metallic devices have been in clinical use since 1988. The most popular materials currently used in intravascular stenting are 316 L stainless steel and nitinol. Chemical and electrochemical reactions are initiated and accelerated when these devices are implanted and contact with the aggressive in vivo environment. These reactions are dependent on the nature of the physiological fluid, which contains a high concentration of chloride ions.5 Chloride ions have been proven to be aggressive and are responsive for the pitting and crevice corrosion of various metals in aqueous environments.6–8 Degradation follows immediately after these reactions. To reduce the corrosion rate in implanted materials, metallic stents are passivated (inactive, quiescent) before implantation.

The rate of chemical and electrochemical reactions is strongly dependent upon the properties of the passive layer on the surface of these stents. This passive layer is metallic oxide, whose constitution is a function of the passivation process and metallic corrosion. The oxide structure can be either polycrystalline, amorphous, or a combination of both, depending on the properties of the passive layer. This passive layer is the ultimate interface with the host after implantation. The type of metal oxide depends on the composition of the metal or alloy material and the industrial process used in surface finishing. Since heat treatment is involved during current manufacturing processes, most oxides formed on 316 L stainless steel and nitinol have a polycrystalline nature. Only after a special procedure is the polycrystalline oxide removed and reformed with a layer of amorphous oxide.4

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Both in vivo and in vitro studies of both 316 L stainless steel and nitinol implanted alloys with polycrystalline oxide exhibited a huge hysteresis loop with pit-

### Table I

<table>
<thead>
<tr>
<th>Elements</th>
<th>Polycrystalline Oxide</th>
<th>Amorphous Oxide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromium</td>
<td>5.8</td>
<td>13.0</td>
</tr>
<tr>
<td>Nickel</td>
<td>2.1</td>
<td>5.9</td>
</tr>
<tr>
<td>Molybdenum</td>
<td>1.6</td>
<td>15.6</td>
</tr>
<tr>
<td>Oxygen</td>
<td>32.7</td>
<td>31.6</td>
</tr>
<tr>
<td>Iron</td>
<td>57.8</td>
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</tr>
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</table>

### Table II

The Nitinol Surface Oxide Composition Weight Percentage

<table>
<thead>
<tr>
<th>Elements</th>
<th>Polycrystalline Oxide</th>
<th>Amorphous Oxide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Titanium</td>
<td>84.0</td>
<td>26.0</td>
</tr>
<tr>
<td>Nickel</td>
<td>Nil</td>
<td>25.0</td>
</tr>
<tr>
<td>Oxygen</td>
<td>16.0</td>
<td>49.0</td>
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</table>

The as-received marketed wires with existing polycrystalline oxide film were converted into an amorphous oxide coating (Fig. 2) according to our previously developed technique.4

For smooth insertion into the abdominal aorta of dogs and protection of the wire tip, a special wire electrode set was designed (Fig. 3). Each set consisted of a 0.25 mm-diameter platinum wire as a counter electrode, a test wire of 316 L stainless steel (0.16 mm) or nitinol (0.05 mm) as a working electrode, and a AgCl wire (0.25 mm) as a reference electrode. These three wire electrodes were mounted and sealed in a glass tube supporter, except for the tip and tail portions,

### MATERIALS AND METHODS

#### Sample wire preparation

Both 316 L stainless steel and nitinol wires with polycrystalline oxide or amorphous oxide film were used for corrosion studies.

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and tied together with insulation. The outer protector was made with plastic intravenous cannula. Passing through a 1.7 × 50-mm intravenous cannula, all the wire electrode tips were confined and protected before insertion.

**In vivo animal experiment**

Forty assembled wire electrode-cannula sets were inserted into the abdominal aorta of 15 mongrel dogs with a mean body weight of 16.7 ± 1.4 Kg (range, 14.1–18.5 kg). Ten sets for each surface oxide-treated group of 316 L stainless steel or nitinol wires were studied. NIH guidelines for the care and use of laboratory animals (NIH Publication #85-23 Rev. 1985) were observed.

Anesthesia of the dogs was induced by inhalation of halothane in oxygen. After endotracheal intubation, the animals’ lungs were mechanically ventilated to achieve normocapnia and the anesthesia was maintained with 1.5% halothane in oxygen for the remainder of the experimental period. In addition, animals were paralyzed with an infusion of succinylcholine and kept warm with blanket heater. Blood gas analysis was performed every 2 h. After median laparotomy, the wire electrode-cannula set was inserted into the abdominal aorta of the animals. The cannula was withdrawn out of the aorta and the wire electrodes remained intact and detained inside the aorta (Fig. 3). The aortotomy site was sealed securely with two purse-string 5-O proline sutures in fastened tourniquet tubes. Patent distal aortic blood flow with prominent pulsation and no blood leakage were assured. The body temperature of the animals (around 37°C) and intra-arterial blood pH (value between 7.35–7.45) was maintained during the whole procedure. The wire electrodes were connected to a Potentiostat (model 273, EG & G PARC, USA) and electrochemical corrosion tests were conducted. All data were recorded using a computer program.

**In vivo electrochemical corrosion tests**

Two types of electrochemical tests, including open-circuit potential measurement and cyclic anodic polarization measurement, were conducted using a Potentiostat.

Open-circuit potential was measured with respect to the standard AgCl wire electrode. The potential was recorded as a function of time.

After the open-circuit potential was measured and stabilized for 6 h, the cyclic anodic polarization measurement was then conducted for 3–6 h at a scan rate of 0.6 V/h, beginning at −0.4 V with respect to the AgCl reference electrode in the noble direction. The vertex reverse potential was set at +1.0 V, and final stop potential at 0 V. Samples of 316 L stainless steel or nitinol wire were retrieved after the in vivo experiment. The characterization of the degradation on the wire surface was scrutinized.

**Surface morphology analysis**

Degradation of the wires was examined with scanning electron microscopy (SEM, Hitachi model S-800, San Jose, CA). To prevent a charge problem, samples were sputtered with a thin layer of gold, and SEM was operated at 15 kV to characterize the stent surface and determine the degree of degradation or corrosion.

**Statistical analysis**

Data were expressed as mean ± SEM (standard error of mean). The Mann–Whitney test was used to compare the
The difference in baseline open-circuit potential and the difference in cyclic anodic polarization conduction time between amorphous and polycrystalline oxide groups. Comparative analyses of corrosion after open-circuit potential and cyclic anodic polarization tests were performed by Chi-Square test. Differences between groups were considered significant at a probability value of less than 0.05. All statistical work was done with SPSS 8.0 (Microsoft).

**RESULTS**

Seven test wire samples were damaged during insertion. Only 33 effective wire samples with complete and readable electrochemical tests were analyzed. The cyclic anodic polarization processes were recorded with a mean duration of 261 ± 11 min for 316 L stainless steel wire and 245 ± 13 min for nitinol wire.

Most of 316 L stainless steel (9/9) and nitinol (7/8) wires with amorphous oxide surfaces showed a stable open-circuit potential during the 6 h exposure to circulatory blood, as shown in Fig. 4, Tables III and IV. Due to the different chemical compositions, the baseline open-circuit potential of the amorphous oxide (AO) groups were significantly lower than the polycrystalline oxide (PO) groups [−0.37 ± 0.03 V (AO) vs. −0.02 ± 0.07 V (PO), p < 0.05, for 316 L stainless steel wire; −0.33 ± 0.07 V (AO) vs. −0.03 ± 0.05 V (PO), p < 0.05, for nitinol wire]. However, some of polycrystalline oxide group (4/8 for 316 L stainless steel wire and 5/8 for nitinol wire) showed unstable deep concave curves, which might indicate the possibility of crevice or pitting corrosion occurring during the cyclic polarization measurement, as shown in Fig. 4, Tables III and IV.

Both the 316 L stainless steel and nitinol wires with polycrystalline oxide also showed a poor corrosion resistance (Figs. 5 and 6) with significantly shorter conduction time during cyclic anodic polarization than those with amorphous oxide [239 ± 15 min (PO)

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**Figure 2.** The morphology of amorphous oxide observed under transmission electron microscope. (a) Amorphous oxide converted from the underlying layer of polycrystalline oxide. (b) The selected area diffraction (SAD) of the amorphous oxide structure of the upper layer, which displays the typical diffuse ring style. (c) The SAD of the matrix area of the underlying layer, which displays the typical ring-and-spot style of polycrystalline oxide structure. Original magnification: × 120,000.
vs. 281 ± 12 min (AO), \( p < 0.05 \), for 316 L stainless steel wire; 204 ± 11 min (PO) vs. 286 ± 13 min (AO), \( p < 0.05 \), for nitinol wire). Breakdown usually occurred at the potential between 0.2–0.6 V vs. AgCl reference electrode, and they exhibited a huge hysteresis loop (Figs. 5 and 6). Severe pitting of the typical degradation on the wire surface was seen under SEM, as shown in Figs. 5, 6, and 7. Furthermore, the corrosion breakdown was vigorous with elevated current density higher than \( \log^{-3} \) A/cm\(^2\). The entire tips of four nitinol and two 316 L stainless steel test wires with polycrystalline oxide surface were totally dissolved.

On the contrary, no passivity breakdown was found for the wires of both 316 L stainless steel and nitinol covered with amorphous oxide. These test samples exhibited no hysteresis loop after a cyclic potentiodynamic test, as shown in Figs. 5, 6, and 7. The surface of these wires was clean and free of any degradation such as pits.

**DISCUSSION**

Metals have been used as biomaterial for several hundred years. There are several basic requirements for a successful implantable material. The first, and the most important, is that the material must have corrosion endurance in physiological fluids. Second, the material must be strong enough to withstand cyclic and high static forces. Third, the material must resist stress corrosion and corrosion fatigue. Finally, the material must own high formability for various applications.

The biocompatibility of metals, including noncarcinogenic and nontoxic effects as well as least tissue response, is also highly considerable, because they can be implanted in the hostile environment of the body, especially in blood circulation. As a consequence of corrosion, the material itself wears away and thus weakens the implant. More importantly, the released corrosion products may cause harmful effects to the surrounding tissues.

All metallic implants suffer chemical and/or electrochemical destruction to a certain degree, depending upon the surface treatment prior to the implant. This destruction is due to the nature of the body fluid, which contains high concentrations of chloride ions. Chloride ion has been confirmed to be an active ion, which is responsible for the pitting and crevice corrosion of various metals in aqueous circumstances.\(^6\)–\(^8\)

The synergistic effect of mechanical forces, chemical and electrochemical reactions could jeopardize the implanted materials, result in a short service life, and compromise the patent rate and patent duration of intravascular stents.

**Surface defects**

The manufacture of 316 L stainless steel or nitinol wires through conventional hot and cold deformation could generate several defects on the finished products. The presence of surface defects could dramatically change the corrosion resistance and significantly alter the mechanical properties of a component.\(^{14}–^{19}\)

Therefore, a combination of corrosion and cyclic loading could destroy the wire, resulting in an unpredictably short service life and enormous release of harmful corrosion products.

**Surface oxides**

When a bare metallic surface reacts with the environment, a layer of oxide can form on the surface to protect the matrix and prevent further corrosion dam-
depending on the chemical composition of the wire and the oxidation environment, a dense oxide layer can form on the metallic surface through a traditional thermal treatment that has typical polycrystalline oxide properties.

The structure of amorphous oxide was examined by transmission electron microscopy (TEM) at an acceleration voltage of 200 kV. The TEM morphology of a layer of amorphous oxide in Fig. 2 showed that this layer was free of grain boundaries, particles, and segregation. This amorphous oxide was also characterized by electron diffraction on the selected area with diffuse rings. These important features can prevent chloride penetration. Quantitative analysis by Energy Dispersion X-ray analysis (EDXA), in combination with the high resolution of a TEM (Hitachi model HF-2000), showed a high atomic concentration of oxygen as well as an abnormally high molybdenum concentration in amorphous oxide compared to polycrystalline oxide, as shown in Tables I and II.

**Figure 4.** The change in open-circuit potential of 316 L stainless steel and nitinol wires with various surface treatments: (a) 316 L stainless steel with polycrystalline oxide (PO) film; (b) 316 L stainless steel with amorphous oxide (AO) film; (c) nitinol with PO layer; (d) nitinol with AO layer. Arrowheads indicated the possibility of crevice or pitting corrosion.

<table>
<thead>
<tr>
<th>Corrosion</th>
<th>No</th>
<th>Yes</th>
<th>Total</th>
<th>( p )</th>
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<td>Open-circuit</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amorphous oxide 9</td>
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<td>0.015a</td>
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<tr>
<td>Polycrystalline oxide 4</td>
<td>4</td>
<td>4</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Cyclic anodic polarization 9</td>
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<tr>
<td>Polycrystalline oxide 0</td>
<td>8</td>
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</tr>
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</table>

*Pearson Chi-Square (two sided).

**TABLE IV**

The Results of Electrochemical Corrosion Tests of Nitinol Wires

<table>
<thead>
<tr>
<th>Corrosion</th>
<th>No</th>
<th>Yes</th>
<th>Total</th>
<th>( p )</th>
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<tbody>
<tr>
<td>Open-circuit</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amorphous oxide 7</td>
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<tr>
<td>Polycrystalline oxide 3</td>
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<tr>
<td>Cyclic anodic polarization 8</td>
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<tr>
<td>Polycrystalline oxide 0</td>
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</tr>
</tbody>
</table>

*Pearson Chi-Square (two sided)
Electrochemical measurements in vivo

For evaluating the corrosion behavior, two standard electrochemical tests can be conducted.

Open-circuit potential

The open-circuit potential reflects the balance of oxidation and reduction on the same surface. Both of these processes involve the transfer of electrons, and the net sum of the electron transfer must be zero. Therefore, the open-circuit potential is established at such a value that the total rate of oxidation equals the total rate of reduction.

Cyclic potentiodynamic measurement

Cyclic potentiodynamic measurement is a test designed to detect the relative susceptibility to localized pitting or crevice corrosion of the metallic wires in the electrolyte. The onset of localized corrosion is usually marked by rapid increase in the anodic current density at a potential below the oxygen-evolution poten-
When the current density reaches $5 \times 10^{-3}$ amp/cm$^2$, the potential (Eb) is reversed toward the more active potential until the hysteresis loop closes. The hysteresis loop dimension represents the degree of metallic wire suffering localized corrosion in the body fluid. This has been used to rank the metallic wire relative to the resistance to crevice and pitting corrosion in a chloride-containing environment such as body fluid.$^4$

The cyclic polarization type of polycrystalline oxide shows high susceptibility to pitting corrosion due to its huge hysteresis. On the contrary, there is no pitting corrosion in amorphous oxide, where almost no hysteresis loop was formed during the cyclic polarization measurement. Since molybdenum has been cited as the most effective element for reducing pitting corrosion in stainless steel in chloride-containing electrolyte, the extraordinary high concentration of molybdenum and chromium in the amorphous oxide film (Table I) could provide higher corrosion resistance to body fluid.$^{20-22}$ The high oxygen concentration in the nitinol amorphous oxide film (Table II) could also provide excellent oxidation and passivation environment to the corroded metallic ions released from inner matrix. Thus, both amorphous oxides have proven their strong immunity to body fluid during in vivo tests, indicating that amorphous oxide could be the best candidate with the required surface properties for implantable metallic materials (Tables III and IV).

**Surface analysis**

The composition of a passive layer could be either $M_xO_y$ or $M_x(OH)_y$ or a combination of these two...
compounds on the surface of the wire to prevent further wire dissolution. However, this passivated layer might be penetrated by the chloride ion to form corrosion pits. The surface morphologies of the wires were examined with SEM after the cyclic potentiodynamic test. Severe pitting is the typical wire degradation having a polycrystalline oxide as the protective coating. In an amorphous oxide layer that does not show any hysteresis loop after a cyclic potentiodynamic test, the surface is clean and free of any degradation such as pits.

A number of physical characteristics of a prosthetic surface such as net electrical charge, surface texture, and free surface energy, determine its reactivity with circulating blood. Surface charge is relevant, as most metallic intravascular devices are electropositive and all biological intravascular surfaces are electronegative. The positive surface charge of metals is one of the primary reasons that stents attract plasma proteins, which cover the stent surface within seconds. The resultant proteinaceous layer neutralizes the metal surface charge, decreasing its thrombogenicity and creating favorable conditions for tissue colonization. This phenomenon could not be duplicated in vitro in Ringer’s solution.

CONCLUSION

Using our unique technique, 316 L stainless steel and nitinol stent wires covered with polycrystalline oxide were removed and reformed with a layer of amorphous oxide. The absence of crystalline defects such as grain boundaries, crystalline particles, and segregation makes the electrochemical breakdown of

Figure 7. The features of wires with polycrystalline oxide structure after cyclic anodic polarization test observed under scanning electron microscope: (a)-(b) 316 L stainless steel wire with corrosion; (c)-(d) nitinol wire with corrosion. Original magnification: (a) × 100; (b) × 150; (c) × 800; (d) × 400.
amorphous oxide film difficult. These important features can prevent chloride penetration in body fluid. The surface elemental compositions of amorphous oxide with an extraordinarily high atomic concentration of oxygen in nitinol, as well as molybdenum and chromium in 316 L stainless steel have provided the best corrosion resistance, not only in vitro but also in vivo. Since the ion release from metallic cardiovascular stents is strongly dependent on its corrosion behavior, the extraordinary properties of amorphous oxide-coated wire has proven its superiority, not only in safety but also in medical device biocompatibility.

References