TOPICAL REVIEW

Nickel-free austenitic stainless steels for medical applications

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Abstract
The adverse effects of nickel ions being released into the human body have prompted the development of high-nitrogen nickel-free austenitic stainless steels for medical applications. Nitrogen not only replaces nickel for austenitic structure stability but also much improves steel properties. Here we review the harmful effects associated with nickel in medical stainless steels, the advantages of nitrogen in stainless steels, and emphatically, the development of high-nitrogen nickel-free stainless steels for medical applications. By combining the benefits of stable austenitic structure, high strength and good plasticity, better corrosion and wear resistances, and superior biocompatibility compared to the currently used 316L stainless steel, the newly developed high-nitrogen nickel-free stainless steel is a reliable substitute for the conventional medical stainless steels.

Keywords: medical stainless steel, austenitic stainless steel, high-nitrogen steel, nickel-free, biocompatibility

1. Introduction
Metals are by far the oldest materials used in surgical procedures. Because of crucial and detrimental effects of metal corrosion on human body, the history of implant metals development has been largely focused on seeking better corrosion-resistant materials. Today, the widely used metallic biomaterials mainly include stainless steels, titanium and its alloys, cobalt-chromium-based alloys, as well as tantalum, niobium and gold.

Stainless steels, AISI 316L as a representative, are conventionally used in orthopedics, with main advantages of low cost, good mechanical properties and easy processing. However, problems were found with medical stainless steels during the last decades of clinical applications. Firstly, the medical stainless steels are denser, stronger and have higher elastic modulus than bones, so this incompatibility of strength or modulus can cause the shielding effect of stress [1] and worsen the bone healing processes. Secondly, there is inevitable corrosion and wear of the medical stainless steels in body fluid environment, such as crevice corrosion, intergranular corrosion, pitting corrosion and fretting corrosion [2–5]. These factors probably lead to an early fracture or failure of the implants, and corrosion of the implanted devices may result in release of harmful products into the body [4–6]. Finally, the most important problem is the negative effect of metal ions or fretting debris [6–11], which can be released from the stainless steel implant devices because of corrosion, wear or other reasons. Nickel and chromium are known as potentially harmful elements in the medical stainless steel [7, 11]. Nickel ions act as the allergens, which may cause cutaneous inflammations such as swelling, reddening, eczema and itching on skins, and may also lead to allergy reactions, teratogenicity and carcinogenicity in human body [10–20].

Because of the harmful effect of nickel ions from the austenitic stainless steels, such as AISI 316L, to human body, the high-nitrogen nickel-free austenitic stainless steels, generally the Fe–Cr–Mn–Mo–N system, are thought as a...
potential replacement in recent years [21, 22]. Nitrogen is a strong austenite formation element and has been successfully used to replace nickel that largely improved the mechanical properties and corrosion resistance of steel [23, 24]. Considering the potentially detrimental effect of nickel-containing stainless steels on the human body, experts suggested to forbid or restrict the nickel content in the medical stainless steel products, such as medical implants, dental materials, ornaments and so on. Therefore, the medical grade high-nitrogen nickel-free austenitic stainless steels are becoming an important medical metal material.

2. Harmful effects of nickel ions and their release from stainless steels

2.1. Harmful effect of nickel

Nickel is a metallic element that is naturally present in the Earth’s crust. Because of unique physical and chemical properties, nickel and its compounds are widely used in modern industry. Nickel and its alloys, in particular nickel-containing austenitic stainless steels, have been indispensable for technological progress during the past decades [24]. Nickel alloys are often used as prosthetics and implants in medical fields, as well as many items in daily life, such as coins, kitchen utensils, watches, style jewelry, buckles, etc. Fe-18Cr-14Ni-2Mo austenitic stainless steel is a typical and the most commonly used medical stainless steel. Its application for implants has been standardized in ISO 5832-1 and ASTM F138 or F139 [25–27].

It has been recognized that exposure to nickel compounds can have adverse effects on human health, among which nickel allergy in form of contact dermatitis is the most common and well-known reaction [9, 15]. Nickel ions are the most widespread skin contact allergen in Europe that has become a serious medical problem. The number of women affected by nickel allergy has doubled every year of the last few decades. Dermatologists assumed about 20% of young women and 4% of young men are suffering from the nickel allergy. Figure 1 indicates that this trend was increasing recently both for men and women [28]. The allergic effect of nickel and nickel alloys originates from their easy ionization by human sweat upon contact with the skin. The higher prevalence of nickel allergy in women is not genetically determined, but could be related to more frequent daily use of nickel-containing utensils and jewelry [15]. Moreover, the overall environmental pollution may also be a significant reason for the ever-increasing number of affected people.

In trace amounts, nickel is necessary for normal function of the human organism, but its too high concentration can cause health problems. Nickel at high doses and in certain forms is toxic to both humans and animals. For example, the oral LD50 (median lethal dose) of nickel acetate is 350 mg kg$^{-1}$ of body weight for rats and 420 mg kg$^{-1}$ for mice; the intraperitoneal LD50 for rats is 23 mg kg$^{-1}$ [16, 29]. The intraperitoneal LD50 values for nickel chloride are 11 and 48 mg kg$^{-1}$ in rats and mice, respectively [16, 29]. Although the accumulation of nickel in the body through chronic exposure can lead to lung fibrosis, cardiovascular and kidney diseases, the most serious concerns are related to the carcinogenic activity of nickel [16]. Epidemiological studies have clearly implicated nickel compounds as human carcinogens based upon a higher incidence of lung and nasal cancer among nickel mining, smelting and refinery workers. Experiments with high nickel intake have shown that nickel is teratogenic and has carcinogenic potential. The International Agency for Research on Cancer (IARC) evaluated the carcinogenicity of nickel in 1990 [30] and all nickel compounds, except for metallic nickel, are classified as carcinogenic to humans.

Because of the above problems, legislation has been established in some countries of the European Community and in the US to restrict the use of nickel-containing materials on and in the human body. In 1989, Denmark and Sweden limited the use of nickel in some applications, aiming at reducing nickel allergy [15]. Consequently, legislations and directives aiming at restricting the use of nickel-containing parts in human body are also in place in US and some European countries. In 1994, the European Parliament and Council adopted the Nickel Directive (the European Directive 94/27/EC of 30 June 1994) [31], which entered into full force in 2001. The Nickel Directive limits the nickel content in items used for epithelization after piercing (limit 0.05%), and the nickel release from objects intended for use in direct and prolonged contact with skin (limit 0.5 µg cm$^{-2}$ week$^{-1}$).

2.2. Release of nickel from stainless steel

Nickel-containing stainless steels are only potential allergen or carcinogen, they are safe unless they are corroded and the high doses of nickel ions interact with body tissues. However, corrosion of nickel-containing stainless steel is unavoidable in the body fluid [4, 32]. As the implanted stainless steels degrade or corrode in such environment (and all the implanted metals degrade to some degree), the reaction
products, i.e., particulates, oxides, insoluble salts and free metal ions, especially nickel ions, can rapidly interact with the host proteins in a process known as haptenization, and combinations of the protein and the degradation products may become immunogenic, eliciting the hypersensitivity reaction [20].

It has been reported that 316L orthopedic implants would corrode in body environment and release iron, chromium and nickel [5, 8, 13, 33]. When used as implants, 316L stainless steel is not resistant to localized corrosions such as pitting, crevice corrosion and stress corrosion cracking [5, 13], although it contains 2.0–3.0% of molybdenum and the carbon content is reduced to less than 0.03%. Moreover, it contains 12.0–15.0% of nickel, which can be harmful if released into the human body. For example, the corrosion products of 316L stainless steel are toxic to the primary culture of vascular smooth muscle cells when the released nickel concentration is higher than 11.7 ppm. The toxicity effects include inhibiting the growth, changing the cell morphology and inducing the cell necrosis [19, 20, 33].

A particularly contentious area is use of those nickel-containing stainless steels in surgical and dental prosthetics. Although these steels are in general resistant to homogenous corrosion, they are prone to localized corrosion such as pitting, crevice corrosion and stress corrosion. Corrosion of medical stainless steels in body fluid environment usually includes intergranular corrosion, pitting and crevice corrosion. Intergranular corrosion is generally associated with precipitation of chromium carbides at grain boundaries, inducing depletion of chromium in their vicinity and thus decreasing the corrosion resistance. Pitting is induced by cold working which promotes formation of second-phase constituents along strain lines. Crevice corrosion is the most common corrosion damage; in some cases, corrosion starting at the junction between the steel plates and nails may be induced by fretting corrosion damage [4]. Crevice corrosion is often associated with adverse tissue reaction and pain in the patient, requiring removal of the implant. Clinical experience revealed that severe and prolonged corrosion processes can lead to toxic reactions and tissue alterations with resultant clinical failure of the implant [32, 33].

Inflammatory and allergic reactions to metal, particularly to nickel, occurred in patients with orthopedic, dental and other stainless steel implants [19, 20]. Within orthodontics, nickel is one of the most commonly used metals, and is included in stainless steel and other alloys. It has been shown that the level of nickel in saliva and serum increases significantly after insertion of fixed orthodontic appliances. The potential for orthodontic metals to cause allergic reactions is related to the pattern and the mode of corrosion, with subsequent release of metal ions, such as nickel, into the oral cavity. Nickel is the most common metal to cause contact dermatitis in orthodontics, with more cases of allergic reactions than for all the other metals combined.

The first report of an allergic reaction to an orthopedic implant described an eczematous rash over a stainless steel fracture plate [34]. Numerous similar observations were documented later, with symptoms of discomfort, erythema, swelling and skin changes in the area of the implant [35]. In addition, some patients exhibited general discomfort, fatigue or weakness. Most cases involved the implants manufactured from alloys containing nickel and cobalt [36].

Stainless steel implants can cause inflammatory hypersensitivity reactions and allergic reactions which lead to a fibro-proliferative response around the implant [19]. A fibro-proliferative and inflammatory response has also been characteristically seen in restenotic tissue within coronary stents [9]. Most cardiovascular and peripheral vascular stents are made from 316L stainless steel which contains strongly sensitizing metals such as nickel and chromium. Nickel, chromium and molybdenum ions can be eluted from the stainless steel stents [37], and the action of blood, saline, proteins and mechanical stress can facilitate the release of these ions, which is probably associated with inflammatory and allergic reactions around the metal [38]. It is uncertain whether similar reactions occur around stents and trigger restenosis in patients with allergy to metal; however, Köster et al. found a higher frequency of in-stent restenosis in patients with delayed-type hypersensitivity to metals [39], particularly to nickel, than in patients without sensitization to metals. These findings support the hypothesis that contact allergies to nickel and molybdenum trigger the in-stent restenoses to a clinically relevant degree [39].

A typical medical stainless steel 316L or 317L contains strongly sensitizing metals, including 13–15% of nickel, 17–19% of chromium and about 2% of molybdenum [25–27]. Because of corrosion of the implants, small amounts of metal ions may be released into surrounding organs. Systemic toxicity may be caused by the accumulation, processing and subsequent reaction of the host to corrosion products [40]. When high doses of nickel salts are injected into mice, accumulation and some deleterious effects could be seen in their liver, kidney and spleen [41]. The normal nickel concentration in human liver is 10–50 mg kg$^{-1}$ (wet weight), while the values vary within 1–5 mg L$^{-1}$ in serum and blood [42]. In tissues adjacent to 316L stainless steel plates and screws, the nickel concentration ranges between 116 and 1200 mg L$^{-1}$ [43]. The maximum rate of nickel release, due to corrosion in patients who have implants made of nickel alloys, is estimated as 20 mg kg$^{-1}$ day$^{-1}$ [44].

The best method to limit nickel allergy or other adverse effects is to avoid direct contact of human body with any nickel containing material. Considering the potential danger of nickel and the wide applications of stainless steel in medical fields, development of nickel-free stainless steels for medical application is of great importance, which should meet the following requirements: absence of nickel, good biocompatibility, no ferromagnetism, high corrosion resistance and good combination of mechanical properties, including strength, ductility, fatigue endurance, wear resistance, and so on.

3. Development of nickel-free medical stainless steels

Nickel-free corrosion-resistant steels have been developed for several decades, but nickel-free ferritic or martensitic stainless
steels are ferromagnetic and have poor ductility. Nickel-free austenitic stainless steel is non-ferromagnetic, and the nickel in steels can be replaced by either nitrogen or manganese or both. From the modified Schiziffer diagram, the direction for development of the biocompatible nitrogen-containing austenitic stainless steels is presented schematically in figure 2 [21]. Owing to the strong effect of nitrogen to increase the austenite stability, mechanical properties and corrosion resistance of steels, as well as to prevent the formation of ferritic phase, high-nitrogen nickel-free stainless steel can solve the ‘nickel problem’ in medical stainless steels.

3.1. Roles of nitrogen in medical stainless steels

Corrosion-resistant nickel-free austenitic stainless steel can be produced if high amounts of chromium, molybdenum and nitrogen are alloyed in the steel. Both nitrogen and carbon are potent and effective stabilizers of austenite structure; however, small addition of carbon can decrease the corrosion resistance of steel and also enhance its tendency to form precipitates. Therefore, the carbon content in medical stainless steel is restricted to less than 0.03%. The best and only acceptable element to stabilize the austenitic phase in nickel-free steels should be nitrogen. Thus, nickel-free austenitic stainless steels have been developed in which nickel is completely replaced by nitrogen. Additionally, high nitrogen content is also responsible for the increased strength and improved corrosion resistance.

High-nitrogen stainless steels, in addition to high strength, also show high work-hardening rates [45, 46] and good high-temperature mechanical properties as compared with conventional steels. The strengthening mechanisms of nitrogen alloying are attributed to: (i) interaction/pinning between dislocations and interstitial nitrogen atoms because of the electrostatic attraction [47] and (ii) formation of dislocation-nitrogen complexes that may drag the dislocations [48]. Large lattice distortion associated with interstitial nitrogen also strengthens steels [47]. Short-range ordering involving substitutional and interstitial elements (like Cr-N) may contribute to the strengthening of N-containing stainless steels [49].

With the increasing popularity of research on high-nitrogen stainless steels, many recent studies focused on the effects of nitrogen on the fatigue properties of steels. Addition of nitrogen to austenitic stainless steels changes the stacking fault energy and hence affects the dislocations structure and fatigue behavior. Planar dislocation arrangement due to nitrogen alloying is thought to be one of the reasons for the enhanced fatigue properties [50, 51]. Maeng and Kim [52] recently compared the dislocation structure at the fatigue crack tips of 316L and 316LN stainless steels. They concluded that the nitrogen would prevent dislocations from crossing slips in the plastic zone around crack tips, and thus fatigue crack growth would be retarded in 316LN. Therefore, nitrogen alloying is believed to be beneficial to the fatigue resistance of stainless steels [51, 53, 54], reducing the tendency for dislocation cross slips and favoring the planar dislocation slips, thereby promoting the slip reversibility and giving rise to the earlier cyclic softening [51, 54].

The metallic implants which replace the failed hard tissues, such as artificial joints, bone plates and dental implants, are conventionally used under severe cyclic loading conditions. Therefore, the high-nitrogen nickel-free stainless steels, which typically exhibit high strength, ductility and toughness, are the perfect candidates for the structural material of these implants. Maruyama et al compared the fatigue behavior in air and in the simulated body fluid for two high-nitrogen nickel-free stainless steels made, respectively, by nitrogen absorption (Fe-23Cr-1N) and pressure electroslag remelting (P-ESR) processes (Fe-24Cr-2Mo-1N) [55].

![Figure 2. Development of biocompatible nitrogen-containing austenitic stainless steels (reproduced with permission from [21] © 1996 The Iron and Steel Institute of Japan).](image-url)
result revealed no difference between the S-N (stress-number of cycles to failure) curves in air and in simulated body fluid for both steels. The fatigue strength at $10^7$ cycles for Fe-24Cr-2Mo-1N was 320 MPa, higher than 245 MPa for Fe-23Cr-1N.

With increasing use of high-nitrogen stainless steels, the effect of nitrogen on the corrosion behavior of steels has been intensively studied. The beneficial role of nitrogen is clearly identified on the localized corrosion phenomena, e.g. pitting corrosion and crevice corrosion. This net effect of nitrogen, in conjunction with chromium and molybdenum, can exceed corrosion and crevice corrosion. This net effect of nitrogen, identified on the localized corrosion phenomena, e.g. pitting effect of nitrogen on the corrosion behavior of steels has been Fe-23Cr-1N.

Table 1. Chemical compositions of stainless steels for surgical implants in ASTM, wt% [26, 27, 67–71].

| Steels   | C  | Cr  | Ni  | Mn  | Mo  | Cu  | Si  | N   | Others |
|----------|----|-----|-----|-----|-----|-----|-----|-----|--------|
| F138,139 | ≤ 0.03 | 17–19 | 13.0–15.0 | ≤ 2.0 | 2.25–3.0 | ≤ 0.5 | ≤ 0.75 | ≤ 0.1 | – |
| F745     | ≤ 0.06 | 16.5–19.0 | 11.0–14.5 | ≤ 2.0 | 2.0–3.0 | ≤ 0.5 | ≤ 1.0 | ≤ 0.2 | – |
| F1314    | ≤ 0.03 | 20.5–23.5 | 11.5–13.5 | 4.0–6.0 | 2.0–3.0 | 1.5–3.0 | ≤ 0.75 | 0.2–0.8 | V: Nb: 0.1–0.3 |
| F1586    | ≤ 0.08 | 19.5–22.0 | 9.0–11.0 | 2.0–4.25 | 2.0–3.0 | ≤ 0.25 | ≤ 0.75 | 0.25–0.5 | Nb: 0.25–0.8 |
| F2229    | ≤ 0.08 | 19.0–23.0 | ≤ 0.05 | 21.0–24.0 | 0.5–1.5 | ≤ 0.25 | ≤ 0.75 | 0.85–1.1 | – |
| F2581    | 0.15–0.25 | 16.5–18.0 | ≤ 0.05 | 9.5–12.5 | 2.7–3.7 | ≤ 0.25 | 0.2–0.6 | 0.45–0.55 | – |

3.2. Development of high-nitrogen nickel-free austenitic stainless steels for medical applications

As nitrogen is an austenitic phase forming element, it is used to develop low-nickel or nickel-free austenitic stainless steels. Nitrogen has been taken as an alloying element in many industrial stainless steels to replace and save the expensive nickel. This type of nitrogen-containing austenitic stainless steels possesses excellent combination of strength, toughness, good corrosion and wear resistance, and it is expected to eliminate nickel allergy in medical applications.

The currently used stainless steels for medical and surgical purposes, such as 316L, still contain 13–16 wt% Ni [25–27]. Because of the potential hazards of Ni, some nitrogen-containing low-Ni or Ni-free austenitic stainless steels have been gradually developed over the last years, and this progress for surgical stainless steel can be seen in table 1 [67–71]. With the development of new surgical stainless steels and the modification of ASTM medical standard, the nickel content is decreasing and nitrogen content is increasing, up to 1.1% in F2229 stainless steel, i.e. Biodur 108 alloy developed by Carpenter Technology Corporation of USA. Biodur 108 has been widely used in processing of medical devices or instruments [72, 73].

Generally, the steels with nitrogen content that can be achieved with the conventional melting technique is defined as the high-nitrogen steels, including the ferritic steels with nitrogen over 0.08% and the austenitic steels with over 0.4% of nitrogen. Currently, high-nitrogen steels are usually produced by pressured electroslag remelting, counter-pressure casting, plasma arc melting and powder metallurgy [74–76]. In the development and production of high-nitrogen nickel-free stainless steels, Mn is also added to further enhance the nitrogen content; Mn is also a nickel substituting alloy element. Therefore the properties and related mechanisms of Fe–Cr–Mn–N and Fe–Cr–Mn–Mo–N types of nickel-free stainless steels are studied and applied in different industrial fields.

In 1995, at the fourth international conference on high-nitrogen steels (HNS95), Uggeowitzer et al from Switzerland introduced the development and the properties of a new austenitic stainless steel [22], which contained 15–18% chromium, 3–6% molybdenum, 10–12% manganese and about 0.9% nitrogen. Besides being nickel-free, the steel was further characterized by excellent corrosion resistance, absence of ferromagnetism and outstanding
mechanical properties. These properties are beneficial for medical applications. At the same conference, Menzel et al from Germany proposed using high-nitrogen Ni-free austenitic stainless steels for medical applications [21]. They analyzed the feasibility and application of a new biocompatible high-nitrogen nickel-free stainless steel, Fe-18Cr-18Mn-2Mo-1N, and suggested to develop a Fe-15Cr-(10-15) Mn-4Mo-0.9N stainless steel by reducing the Mn and Cr contents and increasing the Mo content. Then, numerous studies have focused on the properties, especially corrosion and wear in body fluid, and on in vitro and in vivo biocompatibility of different Fe–Cr–Mn–Mo–N nickel-free stainless steels.

In 1999, Uggowitzer and Thomann studied wear-corrosion behavior of biocompatible austenitic stainless steels in Hank’s solution, distilled water and NaCl solution [77], and compared the newly developed P558 alloy (Fe-17Cr-10Mn-3Mo-0.49N-0.2C) with 316L and Rex734 (Fe-21Cr-9Ni-3Mn-2Mo-0.41N) stainless steels. P558 alloy showed an outstanding mechanical properties and excellent corrosion resistance; it was more resistant against the dry wear, wear–corrosion and crevice corrosion than Rex734, and its pitting corrosion resistance was equal to that of Rex734.

Also in 1999, Carpenter Technology Corporation reported a new high-nitrogen nickel-free austenitic stainless steel (Bioud®108 alloy), Fe-23Mn-23Cr-1Mo-0.9N [78–80], which can be considered as an alternative to the two common austenitic stainless steels, BioDur Type 316L alloy (ASTM F138) and BioDur 734 alloy (ASTM F1586); BioDur 108 was listed in ASTM standard in 2002 (ASTM F2229). This alloy exhibits significantly higher strength, in both annealed and cold worked conditions, than any of the conventional nickel-containing stainless steels used in medical fields.

A typical yield strength of BioDur 108 alloy is approximately 606 MPa (88 ksi) in the annealed condition. In comparison, typical yield strength of BioDur 316L is approximately 241 MPa (35 ksi). The nitrogen-strengthened BioDur 734 and Fe-22Cr-13Ni-5Mn steels, with more nitrogen than BioDur 316L but less than BioDur 108 alloy, typically exhibit approximately 448 MPa (65 ksi) of yield strength in the annealed condition. The high nitrogen content in BioDur 108 alloy enhances the effect of cold working and further increases the strength level [72, 73]. Figure 3 shows the yield strength of BioDur alloys achieved with different amount of cold working.

It was demonstrated that the corrosion resistance of BioDur 108 alloy is essentially equivalent to that of BioDur 734 alloy and BioDur 22Cr-13Ni-5Mn alloy, and is significantly greater than that of the widely used BioDur 316L alloy [72]. Finally, biocompatibility of BioDur 108 alloy is favorable in every respect, qualifying the alloy as a candidate material for biomedical implant and instrument applications [72].

Kraft et al from Germany studied the Bioud 108 alloy implant in vivo in striated muscle microcirculation [81]. They associated reduction of the nickel content in stainless steel with a considerably lower inflammatory response to the skeletal muscle microvascular system, compared with the regular 316L steel. Preliminary biological and mechanical studies of the novel nickel-free stainless steel approved it as a feasible alternative to the conventional stainless steels.

Mölder and Fischer et al from Germany studied the mechanical, chemical and tribological properties of a nickel-free austenitic steel, X13CrMnMoN18-14-3 (brand name P2000) [82], and assayed its biocompatibility by osteoblastic MC3T3-E1 cells [83]. This nickel-free austenitic steel showed extremely high strength, high ductility and superior corrosion resistance, and the cells growing directly on this steel were indistinguishable from the control cell cultured plastic material with respect to morphology and growth parameters during the cells test. However, regarding the biocompatibility, further studies are needed to understand the influence of cellular functions.

Montanaro et al from Italy have investigated in vitro the mutagenicity and genotoxicity of a new nickel-free stainless steel (Fe-17Cr-10Mn-3Mo-N), namely P558, in comparison to the AISI 316L [84, 85]. The result of the cytogenetic effect and Ames test proved that P558 alloy is devoid of genotoxicity and mutagenicity, and suggested that this nickel-free stainless steel represents a better alternative to other conventional medical stainless steels.

Fini et al studied effects of P558 in vitro on primary osteoblasts and in vivo after bone implantation into the sheep tibia, with comparison to ISO 5832-9 stainless steel and Ti6Al4V [86, 87]. The in vitro results demonstrated that the effect of P558 on osteoblast viability, pro-collagen I, transforming growth factor β-1 and tumor necrosis factor did not significantly differ from those exerted by Ti6Al4V and controls. Furthermore, P558 enhanced osteoblast differentiation, as confirmed by alkaline phosphatase activity and osteocalcin levels, and reduced interleukin-6 production. At 26 weeks, the bone-to-implant contact was higher for P558 than for stainless steel (28%, P < 0.005) and Ti6Al4V (4%, P < 0.05), and was higher for Ti6Al4V than for stainless steel (22%, P < 0.005). The results demonstrated that P558 has good biocompatibility and is a promising implant material. The biocompatibility of P558 was probably due to the absence of Ni-related...
Figure 4. Histological sections of Ni-free P558 (left), ISO 5832-9 SSi (middle) and Ti6Al4 V (right), 26 weeks after surgical implantation into sheep tibial diaphysis. The higher magnification clearly reveals direct bone apposition to the material surface. The bone tissue near the implant surface is of high quality, and resembles the compact bone (basic fuchsine and light green ×4) (reproduced with permission from [86] © 2003 Elsevier Ltd).

Figure 5. Microscopic images of the cells cultured on the disks of 316L, Fe–Cr–Mo and Fe–Cr–Mo–N stainless steels sterilized by UV-irradiation (reproduced with permission from ref. [94] © 2004 Elsevier Ltd).

negative effects on cells and tissues. Fini et al also evaluated comparably the soft tissue response to P558, ISO 5832-9 stainless steel and Ti6Al4 V [88]. Four and 12 weeks after surgery, the histomorphometric measurements of implants with surrounding tissue revealed a stronger inflammatory response, in terms of capsule thickness, surrounding ISO 5832-9 stainless steel implants (with 9.8% Ni content) both in rat subcutis and in rabbit muscle, independent of shape and site of implantation. However, a progressive decrease in capsule thickness could be seen around P558 (with < 0.02% Ni content) and Ti6Al4 V implants, respectively. Fini et al concluded that this nickel-free stainless steel would be a good substitute biomaterial for conventional 316L and Ti6Al4 V in orthopedic field.

Most of coronary stents are made of a Cr–Ni–Mo stainless steel (AISI 316L) due to its excellent combined properties, but this steel is a potential allergen. Most other materials, like cobalt-based L605 or tantalum alloys, are relatively expensive and are rarely used. The newly developed high-nitrogen nickel-free austenitic stainless steel (Fe–Cr–Mn–Mo–N) may offer an alternative material for such specific application. Weiss et al [89] investigated comparably the simulation for fatigue deformation and microstructure characterization of stents with equal design, produced from 316L and from high-nitrogen nickel-free stainless steel (DIN EN 1.4452, similar to ASTM F2229-02). They concluded that this high-nitrogen nickel-free stainless steel stents can be suitable for clinical use, but further study is still needed. Their results gave a more comprehensive understanding of the influence of the stents material on the structure–property relationship under monotonic and cyclic deformations, as a basis for ongoing development of new materials for stents optimization.

Although manganese is widely used as a substitute for nickel in high-nitrogen nickel-free stainless steel, its addition may hinder production of fine steel foils and wires. To get around this problem, Niinomi et al [90] and Kuroda et al [91] have devised a new, ingenious way to
produce the nickel-free austenitic stainless steel wires. They used a Fe-24Cr-2Mo ferritic stainless steel as the starting material. After shaping the raw material into wires, the wires were heated in nitrogen atmosphere, thereby realizing austenitization. Nickel-free austenitic stainless steel products and small precision devices can be easily obtained through this process. Since wires and thin plates are commonly produced in steel-making industry, the effect of nitrogen adsorption on austenitic stainless steel wires and plates has been recently studied by Tsuchiyama et al [92] and Kuroda et al [93]. Yamamoto et al conducted the cytotoxicity tests on Fe–Cr–Mo, Fe–Cr–Mo–N and 316L stainless steels in both static and dynamic conditions to evaluate the biocompatibility of Fe–Cr–Mo–N, a high-nitrogen nickel-free austenitic stainless steel manufactured by nitrogen adsorption [94, 95]. Fe–Cr–Mo–N steel showed higher cell growth than 316L in static and dynamic conditions, as shown in figure 5, i.e. Fe–Cr–Mo–N steel has better cytocompatibility than 316L—a clear advantage for its application in medical fields.

High-nitrogen nickel-free stainless steels with lower toxicity to human body constitute the next generation of stainless steels for surgical implant applications. The currently used metallic implants still suffer from the problem that their elastic modulus is different from that of the bones [96]. However, mechanical properties of the porous metals can be adjusted to match those of replaced bones by changing the porosity and pore sizes. The pores on metals can also permit good attachment of tissues to the surface of biocompatible metals, allowing the tissue to enter the metal. Alvarez et al from Japan studied the lotus-type porous Fe-25Cr, Fe-23Cr-2Mo and AISI 446 stainless steels that were fabricated by continuous zone melting technique in pressurized hydrogen and helium gas [98–101]. The porosity of the samples varied in the range 44–48% and the mean pore sizes (145–374 µm) were in the desired range for medical applications. The fabricated lotus-type porous nickel-free stainless steel was nitridized at high temperature, up to a nitrogen concentration of 1.0%, which was sufficient for the steel to maintain almost single-phase austenitic structure at room temperature. The combination of very low magnetic susceptibility, light weight, mechanical properties close to the human cortical bones, together with good enough corrosion resistance of high-nitrogen nickel-free stainless steel, makes this lotus-type porous Fe–Cr–N alloys very attractive for bone implant applications.

Alvarez et al also investigated the bone response to the lotus-type porous nickel-free stainless steel implants using Sprague–Dawley rats [102]. The histological examination showed that the bone grew into the pores (sizes between 70–650 µm) with apparent direct contact to the implant surface. At 12 weeks, new bone covered almost the entire available pore space and there was a scarce thin fibrous band on the surface of the implant. Maximum compressive shear strength of 24 MPa was obtained at 12 weeks, which was substantially higher than the typical shear strength achieved by porous coated materials. These results clearly indicate that the lotus-type porous structure could allow bone cells and tissues to penetrate the implant throughout superficial porous spaces, which could result in an efficient biological fixation responsible for the mechanical stability at the implantation site. Therefore the lotus-type porous nickel-free stainless steel may be a potential biomaterial in some special clinical applications.

In China, studies on melting, microstructure and properties of high nitrogen nickel-free stainless steels

| Steels                  | Cold deformation (%) | $\delta_{0.2}$ (MPa) | $\delta_{0.5}$ (MPa) | $\delta_{5}$ (%) | $\psi$ (%) | Hv10 |
|-------------------------|----------------------|----------------------|----------------------|------------------|------------|------|
| 316L                    | 0                    | 225                  | 555                  | 64               | 72         | 146  |
| BIOSSN4 (N: 0.46%)      | 0                    | 559                  | 938                  | 54               | 64         | 244  |
|                         | 10                   | 887                  | 1018                 | 39               | 62         | –    |
|                         | 20                   | 1044                 | 1101                 | 31               | 59         | –    |
|                         | 30                   | 1183                 | 1238                 | 24               | 54         | –    |
|                         | 40                   | 1352                 | 1394                 | 13               | 51         | –    |
|                         | 50                   | 1446                 | 1502                 | 8                | 48         | –    |
| BIOSSN4 (N: 0.62%)      | 0                    | 537                  | 884                  | 52               | 71         | 262  |
|                         | 10                   | 857                  | 1008                 | 36               | 73         | 316  |
|                         | 20                   | 1041                 | 1105                 | 30               | 70         | 350  |
|                         | 30                   | 1175                 | 1215                 | 24               | 68         | 380  |

Figure 6. S–N curves from axial tensile/tensile fatigue of BIOSSN4 and 316L steels at ambient conditions and in 0.9% NaCl solution at 37 °C (reproduced with permission from [110] © 2006 Metallurgical Industry Press).
Table 3. Abrasions of BIOSSN4 and 316L steels to 304 stainless steel [110].

| Samples  | Load (g) | Abrasion medium       | Abrasion distance meters | Relative wear value | Original hardness Hv 500 | Hardness after abrasion Hv 500 |
|----------|----------|------------------------|--------------------------|---------------------|--------------------------|-------------------------------|
| 316L     | 900      | In air                 | 560                      | 1.78                | 164                      | 370                           |
| BIOSSN4  | 900      | In air                 | 560                      | 2.49                | 252                      | 440                           |
| 316L     | 900      | 37°C, 0.9% NaCl solution | 560                      | 1.20                | 164                      | 292                           |
| BIOSSN4  | 900      | 37°C, 0.9% NaCl solution | 560                      | 7.67                | 252                      | 400                           |

Figure 7. Blood platelets on BIOSSN4 and 316L steels dipped in fresh human blood plasma for 25 minutes. (a) BIOSSN4, (b) 316L and (c) size distribution of blood platelets (reproduced with permission from [109] © 2005 Elsevier Ltd).

have been extensively conducted at the Institute of Metal Research CAS, Northeastern University, Yanshan University, China Iron and Steel Research Institute and other institutions [103–107]. Yang and co-workers from Institute of Metal Research, CAS, developed a new high-nitrogen nickel-free austenitic stainless steel (BIOSSN4) for medical application [108–112], with nominal composition of Fe-18Cr-15Mn-2Mo-(0.45–0.7)N. BIOSSN4 steel has excellent combination of strength and toughness, sufficient corrosion fatigue strength, good wear resistance, better corrosion resistance, favorable biocompatibility and good processability, compared with the conventional 316L stainless steel. Table 2 lists the mechanical properties of BIOSSN4 steel in comparison to 316L. It can be seen that both yield strength and ultimate strength of BIOSSN4 steel are much higher than those of 316L steel, 2–3 times higher in strength and close in plasticity, and the strength of BIOSSN4 steel was increased with increase of the cold deformation. Beyond 30% cold deformation, the ultimate strength of BIOSSN4 was increased about 50% and its yield strength was more than doubled.

The fatigue behavior and erosion resistance of BIOSSN4 steel, compared with 316L stainless steel, at ambient conditions and in 37°C 0.9% NaCl solution were also studied [110]. Compared to 316L, the high-nitrogen BIOSSN4 steel showed higher fatigue strength, as demonstrated in figure 6, and better wear resistance, as summarized in table 3.

The newly developed high-nitrogen nickel-free BIOSSN4 stainless steel has passed the standard
biocompatibility evaluation by the Medical and Biological Products Inspection Institute of China, including cytotoxicity, hemolytic, acute toxicity, sensitization, genotoxicity and other necessary tests for the implants [109]. Additionally, Yang and co-workers also studied in vitro the blood platelets adhesion on surfaces of BIOSSN4 in comparison to 316L stainless steel [108, 109]. BIOSSN4 steel showed better platelets adhesion resistance compared with 316L stainless steel after dipping in fresh human blood plasma for 25 min and 3 h, as shown in figures 7 and 8, respectively [109]. Fewer human blood platelets clung to the BIOSSN4 samples than to the 316L samples, and the platelets on BIOSSN4 showed weaker agglomeration and distortion, indicating that BIOSSN4 should possess better anti-platelet adhesion performance than the widely used 316L stainless steel. The above result further suggests that the high-nitrogen nickel-free stainless steels possess better blood compatibility, representing a prospective application potential for coronary stents.

Yang and co-workers also studied the clotting kinetics of blood on BIOSSN4 steel in comparison to 316L stainless steel (see figure 9) [111]. The initial clotting time of BIOSSN4 was about 44.6 min, and that of 316L steel was obviously shorter (about 38.6 min), indicating that the high-nitrogen nickel-free stainless steel should have better thrombin resistance than 316L stainless steel.

Figure 8. Blood platelets on BIOSSN4 and 316L steels dipped in fresh human blood plasma for 3 hours, (a) BIOSSN4, (b) 316L and (c) size distribution of blood platelets (reproduced with permission from [109] © 2005 Elsevier Ltd).

Figure 9. Kinetics of blood clotting on nickel-free stainless steel and 316L stainless steel (reproduced with permission from [111] © 2007 Scientific.net).
In the past decade, several high-nitrogen nickel-free austenitic stainless steels have been developed for medical application, as can be seen in table 4, mainly focusing on Fe–Cr–N, Fe–Cr–Mo–N and Fe–Cr–Mn–Mo–N systems. Nickel-free stainless steels generally show excellent mechanical properties (see table 5), and even in the annealed condition (soft state), their strength is much higher than that of the conventional stainless steels used for implants, e.g., 316L, whereas their elongation is comparable. As the strength of stainless steels can be increased by cold deformation, nickel-free stainless steels also exhibit a stronger potential for work hardening than the conventional stainless steels (figure 3). This will open up new possibilities for higher strength implants or for reduction of implant sizes where limited anatomical space is often an issue, for instance, microvascular stents with finer meshes. Although the evaluation of nickel-free stainless steels with regard to surgical implants is yet incomplete, these steels demonstrate satisfactory biocompatibility and might be used in medical fields in the near future. Recently, BioDur 108 stainless steel has become available on the market.

### 4. Conclusions

The adverse effects of nickel ions release in human body have prompted the development of high-nitrogen nickel-free austenitic stainless steels for medical applications. In such steels, nitrogen not only replaces nickel for austenitic structure stability but also significantly improves steels properties. By combining the benefits of stable austenitic structure, high strength and good plasticity, better corrosion and wear resistance, and superior biocompatibility compared to the currently used 316L stainless steel, the newly developed high-nitrogen nickel-free stainless steel will be a reliable substitute to the conventional medical stainless steels. The potential applications of these novel steels include implantation materials, orthopedic and orthodontic devices, as well as decorations and jewelry items.

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### References

[1] Brown B H, Smallwood R H, Barber D C, Lawford P V and Hose D R (eds) 1999 *Medical Physics and Biomedical Engineering* 1st edn (London: Taylor and Francis) p 120
[2] Kamachimudali U, Sridhar T and Raj B 2003 *Sadhana* 28 601
[3] Guapapa I 2002 *Mater. Charact.* 49 73
[4] Trainsel M, Maguer D, Hildebrand H and Iost A 1990 *Clin. Mater.* 5 309
[5] Walczak J, Shahgaldi F and Heatley F 1998 *Biomaterials* 19 229
[6] Staffolani N, Damiani F, Lillii C, Guerra M, Staffolani N, Belcastro S and Locci P 1999 *J. Dent.* 27 449
[7] Pulido M and Parrish A 2003 *Mutat. Res.* 533 227
[8] Herting G, Wallinder I and Leygraf C 2008 *J. Environ. Monit.* 10 1092
[9] Takazawa K, Miyagawa H and Hariya A 2003 *Japan. Soc. Artif. Organs* 6 71
[10] Eliades T, Pratsinis H, Kletsa D, Eliades G and Makou M 2004 *Am. J. Orthod. Dentofacial Orthop.* 125 24
[11] Rae T 1981 *J. Bone Joint Surg.* B 63 435
[12] Ruff C and Belisio D 2006 *J. Am. Acad. Dermatol.* 55 32
[13] Beddoes J and Bucci K 1999 *J. Mater. Sci.: Mater. Med.* 10 389
[14] Coogan T P, Latta D M, Snow E T and Costa M 1989 *CRC Crit. Rev. Toxicol.* 19 341
[15] Vahter M, Berglund M, Akesson A and Liden C 2002 *Environ. Res.* 88 145
[16] Bal W, Kozowski H and Kasprzak K 2000 *J. Inorg. Biochem.* 79 213
[17] Denkhaus E and Salnikow A K 2002 *Crit. Rev. Oncol./Hematol.* 42 35
[18] Ries M et al 2003 *Am. Heart J.* 145 737
[19] Wataha J et al 2001 *J. Biomed. Mater. Res.* 58 537
[20] Klein C L, Nieder P, Wagner M, Köhler H, Bittingerr F, Kirkpatrick C J and Lewis J C 1994 *J. Pathophysiol.* 5 798
[21] Menzel J, Kirschner W and Stein G 1996 *ISIJ Int.* 36 893
[22] Uggowitzer P, Magdowski R and Speidel M 1996 
ISIJ Int. 36 901

[23] Lu S H (ed) 1995 Stainless Steel (Atomic Energy Press)

[24] Lo K, Shek C and Lai J 2009 Mater. Sci. Eng. R 65 39

[25] ISO 5832-1:2007(E) Implants for Surgery-Metallic Materials-Part 1: Wrought Stainless Steel

[26] ASTM F 138-03 Standard Specification for Wrought 18Chromium-14Nickel-2.5Molybdenum Stainless Steel Bar and Wire for Surgical Implants (UNS S31673)

[27] ASTM F 139-03 Standard Specification for Wrought 18Chromium-14Nickel-2.5Molybdenum Stainless Steel Sheet and Strip for Surgical Implants (UNS S31673)

[28] Speidel M O and Uggowitzer P J (eds) 1998 Materials in Medicine: Biocompatible Nickel-Free Stainless Steels to Avoid Nickel Allergy (vdf Hochschulverlag AG an der ETH Zürich) p 191

[29] Nat. Res. Council 1975 Medical and Biological Effects of Environmental Pollutants, Nickel (Washington, DC: Committee on Medical and Biological Effects of Environmental Pollutants, National Academy Sciences)

[30] International Agency for Research on Cancer 1990 IARC monographs on the evaluation of carcinogenic risks to humans Chromium, Nickel and Welding (Lyon: IARC) p 49

[31] European Parliament and Council Directive 94/27/EC of June 30 1994 Off. J. Eur. Commun. Nr L. 188/1, 22.794

[32] Balamurugan A, Rajeswari S, Balosier G, Rebelo A and Ferreira J 2008 Mater. Corros. 59 855

[33] Hanawa T 2004 Mater. Sci. Eng. C 24 745

[34] Foussereau J and Laugier P 1966 Trans. St. Johns Hosp. Derm. Soc. 52 220

[35] Halpin D S 1975 J. Bone Joint Surg. Br. 57 451

[36] Rooker G D and Wilkinson J D 1980 J. Bone Joint Surg. Br. 62 502

[37] Beyhien C et al 1998 Eur. Heart J. 19 (suppl) 1947

[38] Williams D F 1987 J. Mater. Sci. 22 3421

[39] Koster R, Bieuf D, Kiehn M, Sommerauer M, Kahler J, Baldus S, Meinerz T and Hamm C W 2000 Lancet 356 1895

[40] Bergman M, Bergman B and Soremark R 1980 J. Oral Rehabil. 7 325

[41] Pereira M C, Pereira M L and Sousa J P 1998 J. Biomed. Mater. Res. 40 40

[42] Iyengar G V and Iyengar V 1994 Determination of Trace Elements ed Alfaasi Z B (New York: VCH Publishers) p 543

[43] Poehler O E M 1983 Degradation of Metallic Orthopedic Implants, Biomaterials in Reconstructive Surgery (St. Louis, MO: C V Mosby Company) p 158

[44] Black J 1981 Systemic Distribution and Excretion, in: Biomedical Engineering and Instrumentation (New York: Marcel Dekker) p 180

[45] Muller P, Solenthaler C, Uggowitzer P and Speidel M O 1993 Mater. Sci. Eng. A 164 164

[46] Kubota S, Xia Y and Tomota Y 1998 ISIJ Int. 38 474

[47] Balachandran G (ed) 2004 High Nitrogen Steels and Stainless Steels—Manufacturing Properties and Application (UK: Alpha Science International, Pangbourne)

[48] Owen W, Stein G and Witulski H (eds) 1990 Proc. Conf. High Nitrogen Steels 90 (Aachen, Germany, October, Stahleisen, Düsseldorf) p 42

[49] Saller G, Spirakel-Hahn K, Scheu C and Clemens H 2006 Mater. Sci. Eng. A 427 246

[50] Kim D, Chang J and Ryu W 2008 Int. J. Press. Vessels Piping 85 378

[51] Vogt J 2001 J. Mater. Process. Technol. 117 364

[52] Maeng W and Kim M 2000 J. Nucl. Mater. 282 32

[53] Vogt J, Font J, Reynard C, Robert G and Dhers J 2001 Metall. Trans. A 22 2385

[54] Massel K, Vogt J and Font J 2002 ISIJ Int. 42 310

[55] Maruyama N, Sanbe M, Katada Y and Kanazawa K 2009 Mater. Trans. 50 2615

[56] Gavriliuk V G and Berns H 1999 High Nitrogen Steels: Structure, Properties, Manufacture, Applications (Berlin: Springer) p 190

[57] Baba H, Kodama T and Katada Y 2002 Corros. Sci. 44 2393

[58] Olefjord I and Wergrelius L 1996 Corros. Sci. 38 1203

[59] Palit G C, Kain V and Gidayar H S 1993 Corrosion 49 977

[60] Baba H and Katada Y 2006 Corros. Sci. 48 2510

[61] Lu Y, Bandy R, Clayton C and Newman R 1983 J. Electrochem. Soc. 130 1774

[62] Olefjord I, Brox B and Jevelstam U 1985 J. Electrochem. Soc. 132 2854

[63] Gavriliuk V 1996 ISIJ Int. 36 738

[64] Milititsky M, Matlock D, Regully A, Dewispelaere N, Penning J and Hanninen H 2008 Mater. Sci. Eng. A 496 189

[65] Iolto R J, Hanninen H E and Ulakko K M 1996 ISIJ Int. 36 837

[66] Ustinovshikov Y, Ruts A, Bannykh O, Blinov V and Kostina M 1999 Mater. Sci. Eng. A 261 82

[67] ASTM F 745-07 Standard Specification for 18 Chromium-12.5 Nickel-2.5 Molybdenum Stainless Steel for Cast and Solution-Annealed Surgical Implant Applications

[68] ASTM F 1314-07 Standard Specification for Wrought Nitrogen Strengthened 22 Chromium-13 Nickel-5 Manganese-2.5 Molybdenum Stainless Steel Alloy Bar and Wire for Surgical Implants (UNS S29108)

[69] ASTM F 1586-02 Standard Specification for Wrought Nitrogen Strengthened 21 Chromium-10 Nickel-3 Manganese-2.5 Molybdenum Stainless Steel Alloy Bar for Surgical Implants (UNS S31675)

[70] ASTM F 2229-02 Standard Specification for Wrought, Nitrogen Strengthened 23 Manganese-21 Chromium-1 Molybdenum Low-nickel Stainless Steel Alloy Bar and Wire for Surgical Implants (UNS S29108)

[71] ASTM F 2581-07 Standard Specification for Wrought Nitrogen Strengthened 11 Manganese-17 Chromium-3 Molybdenum Low-Nickels Stainless Steel Alloy Bar and Wire for Surgical Implants (UNS S29225)

[72] Walter M 2006 Adv. Mater. Process. 4 84

[73] Raposo H 2009 Adv. Mater. Process. 9 23

[74] Berns H 1995 Z. Metallkd. 86 156

[75] Balachandran G, Bhatia M, Ballal N and Krishna R 2000 ISIJ Int. 40 478

[76] Tao Y and Gammal T 1999 Steel Res. 70, 135

[77] Thomann U and Uggowitzer P 2000 Wear 239 48

[78] Biodur* 108 alloy (nickel-free high-nitrogen austenitic stainless steel alloy) 1999 Alloy Digest 8 SS-757

[79] Gebeau R and Brown R 2001 TMS Annual Meeting: Struct. Biomater. 21st Century p 157

[80] Gebeau R and Brown R 2001 Adv. Mater. Process. 159 46

[81] Kraft C, Burian B, Perlick L, Wimmer M, Wallny T, Schmitt O and Diederich O 2001 J. Biomed. Mater. Res. 57 404

[82] Koch S, Büscher R, Blümchen T, Braun H, Rüinemann C, Schuster D and Fischer W 2002 Materialwiss. Werkst. 33 705

[83] Mölders M, Fischer A and Wiemann M 2002 Materialwiss. Werkst. 33 775

[84] Montanaro L, Cerrellati M, Campoccia D and Arciola C 2006 J. Mater. Sci.: Mater. Med. 17 267

[85] Montanaro L, Cerrellati M, Campoccia D, Prati C, Breschi L and Arciola C R 2005 Int. J. Artif. Organs 28 58

[86] Fini M et al 2003 Biomaterials 24 4929

[87] Fini M et al 2004 J. Biomed. Mater. Res. B: Appl. Biomater. 71B 30

[88] Tschon M, Fini M, Giavaresi G, Borsari V, Lenger H, Beraner J, Chiesa R, Cigada A, Chiusoli L and Giardino R 2005 Int. J. Artif. Organs 28 1003
[89] Weiss S, Meissner A and Fischer A 2009 J. Mech. Behav. Biomed. Mater. 2 210
[90] Niinomi M, Hanawa T and Narushima T 2005 JOM 57 18
[91] Kuroda D, Hanawa T, Hibaru T, Kuroda S, Kobayashi M and Kobayashi T 2003 Mater. Trans. 44 3414
[92] Tsuchiyama T, Fukumaru T, Egashira M and Takaki S 2004 ISIJ Int. 44 1121
[93] Kuroda D, Hanawa T and Hibaru T 2003 Mater. Trans. 44 1363
[94] Yamamoto A, Kohyama Y, Kuroda D and Hanawa T 2004 Mater. Sci. Eng. C 24 737
[95] Kuroda D, Hanawa T and Asami K 2003 Mater. Trans. 44 2664
[96] Bobyn J, Mortimer E, Glassman A, Engh C, Miller J and Brooks C 1992 Clin. Orthop. Relat. Res. 274 79
[97] Robertson D, Pierre L and Chahal R 1976 J. Biomed. Mater. Res. 10 335
[98] Alvarez K, Hyun S and Nakajima H 2007 Adv. Mater. Res. 15–17 756
[99] Alvarez K, Hyun S, Tsuchiya H, Fujimoto S and Nakajima H 2008 Corros. Sci. 50 183
[100] Alvarez K, Hyun S, Fujimoto S and Nakajima H 2008 J. Mater. Sci.: Mater. Med. 19 3385
[101] Alvarez K, Sato K, Hyun S and Nakajima H 2008 Mater. Sci. Eng. C 28 44
[102] Alvarez K, Hyun S, Nakano T, Umakoshi Y and Nakajima H 2009 Mater. Sci. Eng. C 29 1182
[103] Li H et al 2007 J. Iron Steel Res. Int. 14 63
[104] Fu R, Zheng Y and Ren Y 2001 J. Mater. Eng. Perform. 10 456
[105] Fu R, Zhao P, Wang C, Qiu L and Zheng Y 2004 Trans. Mater. Heat Treat. 25 417
[106] Dong H, Lang Y, Rong F and Su J 2009 High Nitrogen Steels Conf. Proc., HNS2009 p 21
[107] Lang Y, Zhou Y, Rong F, Chen H, Weng Y, Su J and Dong H 2009 High Nitrogen Steels Conf. Proc., HNS2009 p 195
[108] Ren Y, Yang K, Zhang B, Wang Y and Liang Y 2004 J. Mater. Sci. Technol. 20 571
[109] Ren Y, Yang K and Zhang B 2005 Mater. Lett. 59 1785
[110] Ren Y, Yang K, Zhang B and Shan Y 2006 Proc. Int. Conf. on High Nitrogen Steels 2006 (Beijing: Metallurgical Industry Press) p 185
[111] Ren Y, Yang H, Yang K and Zhang B 2007 Key Eng. Mater. 342–343 605
[112] Ren Y, Wan P, Liu F, Yang K and Zhang B 2009 High Nitrogen Steels Conf. Proc., HNS2009 p 208