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Chapter 3

FABRICATION AND SURFACE MODIFICATION OF POROUS NICKEL-TITANIUM SHAPE MEMORY ALLOY FOR BONE GRAFTS

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ABSTRACT

Equiatomic porous nickel-titanium shape memory alloys (NiTi SMAs) are becoming one of the most promising biomaterials for bone grafts because of their unique advantages over currently used biomaterials. For example, they have good mechanical properties and lower Young's modulus relative to dense NiTi, Ti, and Ti-based alloys. Porous NiTi SMAs are relatively easy to machine compared to porous ceramics such as hydroxyapatite and calcium phosphate that tend to exhibit brittle failure. The porous structure with interconnecting open pores can also allow tissue in-growth and favors bone osseointegration. In addition, porous NiTi alloys possess good shape memory effect (SME) and superelasticity (SE) similar to dense NiTi alloys. In order to optimize porous NiTi SMAs used in bone grafts, current research focuses on the fabrication methods and surface modification techniques to obtain adjustable bone-like structures with good mechanical properties and excellent superelasticity as well as a bioactive passivation layer on the entire exposed surface to block nickel leaching and enhance the surface biological activity. This chapter describes the recent progress in the fabrication process and surface modification methods of porous NiTi SMAs and discusses subsequent effects of these processes and techniques on the materials properties from the perspective of bone grafts applications.

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ABBREVIATIONS AND SYMBOLS

SMAs  Shape memory alloys
SME  Shape memory effect
SE  Superelasticity
PM  Powder metallurgy
EPS  Elemental powder sintering
CS  Combustion synthesis
SHS  Self-propagating high temperature synthesis
SPS  Spark plasma sintering
CF-  HIP Capsule-free hot isostatic pressing
MIM  Metal injection molding
PIII  Plasma immersion ion implantation
EIS  Electrochemical impedance spectroscopy
SBF  Simulated body fluids
PBS  Phosphate buffered saline
CVD/PVD  Chemical/physical vapor deposition
XRD  X-ray diffraction
SEM  Scanning electron microscopy
XPS  X-ray photoelectron spectroscopy
OM  Optical microscopy
ICPMS  Inductively-coupled plasma mass
HA  Hydroxyapatite
EDS  Energy-dispersive spectroscopy
TF-XRD  Thin Film X-ray diffraction
MP  Mechanically polishing
SCE  Saturated calomel electrode
HBSS  Hanks’ balanced salt solution
MPS  Mean pore size

1. INTRODUCTION

1.1. Necessity of Artificial Bone Implants

Bones in the skeletal system provide the supporting structure for the body. Bone is a structural composite composed of collagen fibers with hydroxyapatite nano-crystals precipitated along the collagen fibrils [1]. Bone also contains other constituents such as mucopolysaccharides, blood vessels, and bone cells. The low elastic modulus collagen fibers are aligned in bones along the main stress directions. The high elastic modulus hydroxyapatite minerals constitute approximately 70% of the dry bone mass and contribute significantly to the bone stiffness. Bone can remodel and adapt itself to the applied mechanical environment, which is generally known as Wolff’s law [2]. However, bone will fracture under excessive loading or impact (schematically shown in Figure 1).
There are many types of bone fractures depending on the crack size, orientation, morphology, and location [3]. Ettinger, et al. have revealed that easy vertebral bone fractures in many postmenopausal women are due to osteoporosis [4]. Therefore, there is a necessity to replace bone substance that has been lost. The lost bone can be replaced by endogenous or exogenous bone tissues, but they are still not satisfactory. The use of an endogenous bone substance involves additional surgery [5]. In addition, the endogenous bone is available only in limited quantities [6]. The major disadvantage of exogenous bone implants is that they may be rejected by the human body and diseases may be transmitted together with these implants [6]. Furthermore, the clinical performance of exogenous bone is considerably inferior to fresh endogenous graft materials [5]. Therefore, there is a big potential market for artificial bone implants. According to the report of MedMarket Diligence [7], the worldwide market for orthopedic biomaterials such as allografts, synthetic bone substitutes, bone growth factors, polymers, ceramics, etc. is growing steadily due to a concurrent evolution of surgical procedures, the emergence of innovative products and a dynamic and growing patient population. The current orthopedic biomaterials market worldwide has an annual revenue of $5 billion with annual percentage increases in double digits and will reach $10 billion by 2011 (Figure 2). Although the orthopedic biomaterials sector is expanding, it is expected that the volume of materials required will never exceed tens of tons, compared to thousands of tons in other developing engineering markets [8].

1.2. Types, Structures and Properties of Bone

It is very important to know the types, structures, as well as physical, chemical, and mechanical properties of the bone tissues because they provide quantitative parameters necessary for the fabrication and design of artificial bone replacement implants. There are different types of bone in the human body, for example, long or short bone, regular or irregular bones, and compact or cancellous bones according to different standards [9].
Figure 2. Growth of orthopedic biomaterials market segments (2006-2011) [7].

Figure 3. Schematic of osseous (bone) tissue [9].

Figure 3 depicts the structure of a typical bone structure. It is very difficult to generalize the bone structure because most bones have an elaborate construction. A “typical” bone is made up of an outer shell of dense compact bone enclosing a core of porous cellular, cancellous, or trabecular bone [10]. Human bone is mainly composed of collagen (20 wt. %), hydroxyapatite mineral (69 wt. %), and water (9 wt. %) [11]. In addition, other organic materials such as proteins, polysaccharides, and lipids are also present in small quantities [12]. Collagen, which can be considered as the matrix, is in the form of small microfibers. It is difficult to observe distinct collagen fibers because of its net-like appearance [12]. The
diameter of the collagen microfibers varies from 100 to 2000 nm. Hydroxyapatite (HA) mineral provides stiffness to the bone. The HA crystals present in the form of plates or needles are about 40–60 nm long, 20 nm wide, and 1.5–5 nm thick [11-13], and the mineral phase present in the bone is not a discrete aggregation of the HA crystals, but rather is made of a continuous phase which is evidenced by a very good strength of the bone after complete removal of the organic phase [11].

The hierarchical levels of the structural organization in a human compact bone are illustrated in Figure 4. The mineral-containing fibers are arranged into lamellar sheets (3–7 mm thick). 4 to 20 lamella arranged in concentric rings around the Harversian canal form an osteon [11]. The cross sections of the compact bone showing cylindrical osteons with blood vessels running along Harversian canals (in the center of each osteon) are shown in Figure 5(A). The metabolic substances can be transported by the intercommunicating systems of canaliculi, lacunae, and Volkman’s canals, which are connected with the marrow cavity [11]. The various interconnecting systems are filled with body fluids and their volume can be as high as 19% [11].

![Hierarchical structures in a human long bone](image)

Figure 4. Hierarchical structures in a human long bone [8, 11].

The cellular structure of cancellous bone is shown in Figures 5(B), (C) and (D) [14]. It is known that cancellous bone is made up of an interconnected network of rods or plates. A network of rods produces low density, open cells whereas one of the plates gives high density, virtually closed cells. The relative density of cancellous bone varies from 0.05 to 0.7 (technically, any bone with a relative density less than 0.7 is classified as “cancellous”) [14].
Figure 5. Images showing the structure of bones. (A) Optical micrograph of transverse cross section showing the microstructure of compact lamellar bone—human femora; (B) SEM image of a specimen taken from the femoral head, showing a low density, open-cell, rod-like structure of cancellous bone; (C) SEM image of a specimen from the femoral head, showing a higher-density, roughly prismatic cell structure of cancellous bone; (D) SEM image of a specimen from the femoral condyle, of intermediate density, showing a stress-oriented, parallel plate structure of cancellous bone with rods normal to the plates [13, 14].

Figure 6. Stress-strain curve for human compact bone [11].
As shown in Figure 6, the stress-strain curves of compact bones exhibit a linear elastic region, followed by a flat plastic region at about 0.8% strain at lower strain rates. It can be found that bone exhibits a tough behavior at low strain rates but fractures more like a brittle material at high strain rates [11, 15]. The slope of the stress-strain curve, i.e., the elastic modulus of the bone, increases with increasing mineral content [12, 13]. At low strain rates, bone exhibits excellent toughness mostly due to its hierarchical structure (shown in Figure 4), which stops cracks after little propagation [12]. The properties of compact human bones are listed in Table 1.

Table 1. Mechanical properties of compact human bones [8]

<table>
<thead>
<tr>
<th>Property</th>
<th>Test direction related to bone axis</th>
<th>Parallel</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tensile strength (MPa)</td>
<td></td>
<td>124–174</td>
<td>49</td>
</tr>
<tr>
<td>Compressive strength (MPa)</td>
<td></td>
<td>170–193</td>
<td>133</td>
</tr>
<tr>
<td>Bending strength (MPa)</td>
<td></td>
<td>160⁴</td>
<td></td>
</tr>
<tr>
<td>Shear strength (MPa)</td>
<td></td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Young’s modulus (GPa)</td>
<td></td>
<td>17.0–18.9</td>
<td>11.5</td>
</tr>
<tr>
<td>Work of fracture (J/m⁴)</td>
<td></td>
<td>20–27 (random)</td>
<td>98 (high strain rate)</td>
</tr>
<tr>
<td>Kₘ (MPa·m¹/₂)</td>
<td></td>
<td>2–12²</td>
<td>0.007</td>
</tr>
<tr>
<td>Ultimate tensile strain</td>
<td></td>
<td>0.014–0.031</td>
<td>0.002</td>
</tr>
<tr>
<td>Ultimate compressive strain</td>
<td></td>
<td>0.0185–0.026</td>
<td>0.004</td>
</tr>
<tr>
<td>Yield tensile strain</td>
<td></td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>Yield compressive strain</td>
<td></td>
<td>0.010</td>
<td>0.011</td>
</tr>
</tbody>
</table>

Figure 7. Compressive stress-strain curves for several relative densities of wet cancellous bone [19]
The compressive stress-strain curve of cancellous bone is shown in Figure 7. The curves exhibit three regimes of behavior, namely the linear-elasticity, plastic collapse-plateau, and densification areas. The small strain and linear-elastic response of low-density of the near-isotropic cancellous bone originate from the elastic bending of the cell walls [16-18]. The linear-elastic regime ends when the cells begin to collapse. Progressive compressive collapse gives the long, horizontal plateau of the stress-strain curve which continues until opposing cell walls meet and touch, causing the stress to rise steeply [19]. The main mechanical properties of a cancellous human bone are shown in Table 2.

Table 2. Solid cell-wall properties for a cancellous human bone [18]

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young’s modulus</td>
<td>12GPa</td>
</tr>
<tr>
<td>Compressive strength</td>
<td>136MPa</td>
</tr>
<tr>
<td>Tensile strength</td>
<td>105MPa</td>
</tr>
</tbody>
</table>

1.3. Niti Shape Memory Alloys (Smas) in Bone/Hard Tissue Replacement

In recent years, rapid development of biomaterials such as biopolymers [2], bioceramics [20], composites materials [2], and hybrid materials [8] may falsely give us an impression that there is no longer any future for metals and alloys as biomaterials due to their intrinsic shortcomings such as corrosion, wear resistance, tissue response and systemic biocompatibility. However, in the past three decades, research and innovations in materials engineering have led to considerable improvement in metal and alloy properties as well as new types of products for a wide area of medical applications. Some medical applications of biomaterials are shown in Table 3 [21, 22].

Table 3. Examples of biomaterials and their applications [21, 22]

<table>
<thead>
<tr>
<th>Material</th>
<th>Principal applications</th>
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<tr>
<td>Metals and alloys</td>
<td></td>
</tr>
<tr>
<td>316L stainless steel</td>
<td>Fracture fixation, stents, surgical instruments</td>
</tr>
<tr>
<td>CP-Ti, Ti-Al-V, Ti-Al-Nb, Ti-13Nb-13Zr, Ti-Mo-Zr-Fe</td>
<td>Bone and joint replacement, fracture fixation, dental implants, pacemaker encapsulation</td>
</tr>
<tr>
<td>Co-Cr-Mo, Cr-Ni-Cr-Mo</td>
<td>Bone and joint replacement, dental implants, dental restorations, heart valves</td>
</tr>
<tr>
<td>Ni-Ti</td>
<td>Bone plates, stents, orthodontic wires</td>
</tr>
<tr>
<td>Gold alloys</td>
<td>Dental restorations</td>
</tr>
<tr>
<td>Silver products</td>
<td>Antibacterial agents</td>
</tr>
<tr>
<td>Platinum and Pt-Ir</td>
<td>Electrodes</td>
</tr>
<tr>
<td>Hg-Ag-Sn amalgam</td>
<td>Dental restorations</td>
</tr>
</tbody>
</table>
Among these biomaterials, near-equiaxial NiTi shape memory alloys have recently led to rather spectacular medical applications and achieved the largest commercial success [23-26]. The combination of good biocompatibility, good strength, and ductility with specific functional properties such as the shape memory effect (SME) and superelasticity (SE) has made it a unique biomaterial. In NiTi SMAs, SME is based on the temperature-induced transformation whereas SE is based on the stress-induced transformation [26]. In particular, the SE of NiTi SMAs results in a unique combination of high strength, high stiffness, and high pliability, and very few other materials or technology can offer such unique combinations. The important mechanical properties of NiTi SMAs are listed in Table 4. At present, NiTi SMAs are used in orthodontic arch wires [27], dental root implants [28], stents [29], orthopedic implants [30], and some medical instruments/tools [31]. However, their high Young’s modulus causes mismatch with human bones, thereby hampering wider applications in bone implants. Therefore, it is necessary to decrease the Young’s modulus of this alloy but not impair its good mechanical properties, unique SME and SE.

**Table 4. Mechanical properties of NiTi SMAs [22]**

<table>
<thead>
<tr>
<th>Property</th>
<th>Young’s Modulus</th>
<th>Fatigue strength N=106</th>
<th>Ultimate tensile strength</th>
<th>Transformation temperatures</th>
<th>Maximum recovery stress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>80GPa</td>
<td>350MPa</td>
<td>700-1100(annealed)</td>
<td>-100-1000°C</td>
<td>600-900MPa</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1300-2000(not annealed)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A low stiffness close to that of the natural bone can provide better load transfer whereby stimulation of new bone formation is released and high stiffness results in bone resorption. Therefore, in recent years, porous NiTi shape memory alloys are becoming one of the most promising biomaterials. Besides a lower Young’s modulus and good mechanical properties, the porous structure with interconnected open pores is suitable for tissue ingrowth and transport of nutrition [32, 33]. In addition, this structure favors the fixation of bone implants [33-35]. Simske, Rhalmi and Assad et al. [34-38] have disclosed that this porous NiTi SMA has no apparent toxicity to cells and tissues. Therefore, various fabrication processes have been developed to produce porous NiTi SMAs products as discussed in Section 2.

### 2. Fabrication Methods

It can be found from the Ni-Ti phase diagram in Figure 8 [39] that equiatomic NiTi SMAs have a high melting point of about 1310 °C. Only powder metallurgical methods are thus suitable for the fabrication of porous NiTi SMAs.
All the PM processes are based on the following reactions [40].

\[
\text{Ni} + \text{Ti} \rightarrow \text{NiTi} + 67 \text{ kJ/mol} \quad (1) \quad \text{Ni} + \text{Ti} \rightarrow \text{Ti}_2\text{Ni} + 83 \text{ kJ/mol} \quad (2)
\]

\[
\text{Ni} + \text{Ti} \rightarrow \text{Ni}_3\text{Ti} + 140 \text{ kJ/mol} \quad (3)
\]

The reported PM processes can be described as followings.

2.1. Elemental Powder Sintering (EPS)

Traditional elemental powder sintering (EPS) in an argon atmosphere is one of the simplest methods. The process involves the use near-equiaxial elemental nickel and titanium as raw materials. The fully mixed powders are compressed at different cold pressures and the compacts are finally sintered under vacuum or argon atmosphere at higher temperatures for various time durations. The sintering temperature and sintering time influence the phase composition, pore size, and mechanical properties. The reported maximum porosity achieved by this method is below 45 vol%. However, the porous NiTi produced by EPS does not possess large recovery strain [40, 41]. In addition, the pore size cannot be controlled precisely, and the sintered products have more secondary phases which impair the SE and mechanical properties of these porous SMAs. The typical morphologies are displayed in Figure 9.
2.2. Combustion Synthesis (CS)

Combustion synthesis (CS) is often used to fabricate porous NiTi SMAs in the early stage due to its simplicity. In the CS method, the fully blended Ni and Ti powders with near equiatomic ratio are pressed into cylindrical pellets under different pressures and then put into a tube furnace under a protective gas preheated to various temperatures, and finally ignited. In comparison with EPS, the porosity of porous NiTi SMAs by CS increases in the range of 50-70 vol% and the size of most pores ranges from 200–600 μm. The typical images of porous NiTi SMAs produced by CS are shown in Figure 10.

The shortcoming of this process is that the compressive strength of the porous NiTi alloy produced by CS is low due to the irregular pore shape and distribution [43, 44]. The compressive behavior is described by the stress-strain curve in Figure 11.
2.3. Self-Propagating High Temperature Synthesis (SHS)

Self-propagating high-temperature synthesis (SHS) is often used to synthesize ceramics and some intermetallics [45-49] including NiTi intermetallic compounds. In comparison with conventional processes such as EPS and CS, the SHS method provides advantages with respect to time, energy savings, and easier processing, and the porosity and pore shape can be controlled easily. This method is similar to CS. The difference is that the exothermic reactions (1), (2) and (3) carried out along the green bar. Using this method, anisotropic pore structures can be easily achieved and it can be attributed to the convective flow of liquid and argon during combustion. Li et.al. used this method to synthesize porous NiTi SMAs with larger porosity and linear channels [50]. The typical micrographs of porous NiTi SMAs are depicted in Figure 12.

Figure 12. Typical micrographs of porous NiTi produced by SHS [50]. (a) Optical image; (b) SEM image.
Kim's results show that porous NiTi alloys made by SHS are brittle and the tensile strength is as low as 15-25 MPa [51]. This is possibly ascribed to the high porosity and formation of unidirectional porous channels. A recent report [52] reveals that a proper post-sintering heat treatment can induce the formation of a single NiTi phase which possesses better SE. The compressive behavior of porous NiTi SMAs produced by this method is illustrated by the stress-strain curve in Figure 13.

![Figure 13. Compressive stress-strain curve of porous NiTi SMAs produced by SHS [52].](image)

2.4. Spark Plasma Sintering (SPS)

Spark plasma sintering (SPS) is one of the spark plasma systems (SPS) [53]. Spark plasma system includes spark plasma sintering (SPS), spark plasma consolidation (SPC), spark plasma joining (SPJ), spark plasma growth (SPG) and spark plasma reaction (SPR) [54]. The spark plasma system is widely used for sintering of metals and ceramics, consolidation of polymers, joining of metals, crystal growth, and chemical reactions. SPS which is based on the idea of using the plasma on electric discharge machine to sinter metals and ceramics is proposed in the early 1960s by Inoue et al. [55, 56]. SPS is mainly characterized by the spark plasma created by a pulsed direct current during heat treatment of the powders in a graphite die. The high-energy plasma is generated between the gap of two electrodes in the electric discharge machine [54]. The reported porosity of porous NiTi SMAs prepared by SPS is lower than 30 vol% and their typical microstructure is exhibited in Figure 14.
Figure 14. Microstructure of porous NiTi specimens: (a) 25% porosity; (b) 13% porosity [57].

Zhao et al. sinter porous NiTi alloys of two different porosities by spark plasma sintering (SPS) [57]. Their results show that the porous NiTi with 13% porosity has higher compressive strength and excellent SE similar to dense NiTi alloys. The 25% porosity sample exhibits lower compressive strength. The compressive stress-strain curve is shown in Figure 15.

Figure 15. Compressive stress–strain curve of porous NiTi SMAs produced by SPS tested at room temperature [57].

2.5. Hot isostatic Pressing (HIP)

The traditional HIP process has unique characteristics such as consolidation of powders such as near-net-shape capability, ability to partially melt the compact without destroying the shape, and economical post-HIP heat treatment. The HIPing process can be illustrated by Figure 16.
Lagoudas et al. have prepared porous NiTi from mixed Ni and Ti powders filled with argon gas by hot isostatic pressing (HIP) [59]. However, the compressive strength is still low and it is possibly due to the irregular pore shape and pore distribution in the porous NiTi. Greiner et al. have fabricated porous NiTi alloys by mixing pre-alloyed martensitic NiTi powders and small amount of elemental Ni powders. The mixture is HIPed under an argon atmosphere [60] and they obtain porous NiTi by long time creep expansion at high vacuum and high temperature. As shown in Figure 17, these porous products show excellent SE and higher compressive strength.

Figure 16. Schematic diagram of traditional HIP process [58].

Figure 17. Compressive stress–strain curves for aged porous NiTi prepared by HIP with 0%, 5.6%, 11% and 16% porosity [60].
Unfortunately, the porosity of the porous NiTi prepared by this method is lower than 20% although the sintered porous NiTi has been creep expanded for 100 hrs. Besides, the long expansion time and high temperature heat treatment are not economically attractive. In addition, the size of most pores obtained by this process is only 10-50 μm (shown in Figure 18), which is still much smaller than the 50-500 μm pore size suitable for bone ingrowth and tissue integration [61].

Figure 18. (a) SEM micrographs of 18.8% porous NiTi prepared by HIP; (b) high magnification detail of (a) [60].

2.6. Capsule-Free Hot Isostatic Pressing (CF-HIP)

Capsule-free hot isostatic pressing (CF-HIP) is quite different from traditional HIP. It generally induces the porous structure of sintered materials. CF-HIP is often used to improve the mechanical properties of ceramic materials while retaining adequate porosity [62, 63]. The typical schematic diagram of a CF-HIP apparatus is displayed in Figure 19. Using this method, Yuan et al. have fabricated porous NiTi SMAs with a porosity of 40% with pore size ranging from 50 to 200 μm [64]. Although the porous materials have good mechanical properties, it is relatively difficult to adjust the pore size, distribution, and porosity by CF-HIP. Our research group has fabricated porous NiTi SMAs with adjustable porous structure and good mechanical properties using CF-HIP with NH₄HCO₃ as the space holder, as shown in Figure 20 [65].

Figure 19. The schematic diagram of CF-HIP unit.
2.7. PM Processes with Space Holders

One of the most promising methods to produce adjustable porous NiTi SMAs is by sintering of compacted or extruded powder mixtures during PM processing that contains removable space-holder materials such as ammonium acid carbonate (NH$_4$HCO$_3$) with CF-HIP [65], NaF with HIP [66], NaCl with HIP [67] or with metal injection molding (MIM) [68], and TiH with EPS [42]. Some reports indicate that 25-80% porosity can be achieved in titanium by this method [69, 70].

3. Surface Modification

Nickel is a main component of NiTi. In order to realize SE, near-equiatomic NiTi SMAs are often used. More widespread applications of NiTi SMAs are limited by the toxicity and hypersensitivity caused by nickel ions released from alloys with a nickel concentration of
about 50 at% [71-73]. The corrosion resistance of NiTi and toxicity of the by-products released from corroded surfaces have been reported [74, 75]. A surface barrier layer such as titanium oxide, titanium nitride, or titanium carbide has been shown to improve the wear resistance, corrosion resistance and biocompatibility of dense NiTi shape memory alloys (SMAs) [76-80]. Compared to conventional dense NiTi, the complex surface morphology and large surface areas of porous NiTi pose a more serious issue with regard to Ni release. Furthermore, the complex surface morphology and large surface area of the porous structure make the surface very difficult to be modified by line-of-sight techniques such as laser gas nitriding [81], ion beam modification [82], and arc discharge ion plating [83]. The demand for the proper surface modification techniques is thus more stringent. Considering the complex surface morphologies, the following modification techniques have been developed to treat the exposed surface of porous NiTi SMAs.

3.1. Oxidation

Heat treatment (Atmospheric oxidation) is one of the common methods to produce a layer of protective titanium oxide on the surface of NiTi to avoid the allergic and toxic effects stemming from the released nickel ions [84-87]. The samples are often put into an unsealed furnace and treated at various temperatures for different duration. Firstov et al. have calculated the equilibrium phase diagram of Ni50Ti50-O under the assumption that oxygen is insoluble in the compounds NiTi and Ni3Ti and that nickel is similarly insoluble in the oxides of titanium (shown in Figure 21) [87].

Chu and Wu have proposed that surface oxidation of equiatomic NiTi at higher temperature of 550 to 1000°C proceeds in four stages as illustrated in Figure 22 [85]. In the early stage of oxidation, Ti is oxidized first to form oxides while Ni remains unchanged due to the higher affinity of Ti with oxygen than that between Ni and oxygen. In the second stage, the rutile crystal grows resulting in the formation of a local Ni-rich zone beneath this layer. As oxidation proceeds, titanium atoms diffuse outward while oxygen atoms diffuse inward. The diffusivity of Ti in rutile is faster than that of oxygen [88], whereas Ni appears to follow a Kirkendall effect for its inter-diffusion with Ti. This results in an outward growth of rutile and an inward growth of Ni-rich phases, such as Ni (Ti), inducing the formation of a mixed layer of TiO2 and Ni (Ti) beneath the outer layer. The formation of large voids beneath the surface layer is partly ascribed to the different growth rates of rutile crystals in the vertical and lateral directions. As the oxidation time increases, outward movement of Ti atoms gives rise to the formation of a Ni-rich phase TiNi3 and Ti-depleted layer.

Based on these oxidation theories of dense NiTi and the non-line-of-sight nature of atmospheric oxidation, we have reported the characteristics of porous NiTi after oxidation in air [89]. The phase components and surface layer structure after high temperature oxidation are in good agreement with the results acquired from dense materials [85], as shown in Figure 23. However, lower temperature oxidation induces some differences. It can be observed from the XPS results (Figure 24) that the intermediate transition layer is composed of TiO2, TiO, Ti2O3 and NiTi. In view of nickel release and cyto-compatibility, the oxidation temperature should not be higher than 450 °C because the nickel concentration significantly increases when the oxidation temperature exceeds 450°C (shown in Figure 25).
Figure 21. Calculated equilibrium phase diagram of NiTi–O [87].

Figure 22. Schematic diagram of oxidation scale formation of equiatomic NiTi alloy [85].
The unexpected result is possibly due to the lamellar structure of the surface layer with a thicker porous intermediate mixture including nickel-rich Ni$_3$Ti, NiTi and rutile as well as larger voids when the temperature is higher than 450°C [85]. Therefore, nickel can diffuse more easily from the porous NiTi when the solution penetrates into the porous intermediate and nickel-rich layer in the immersion tests. In addition, the oxidized surface at a temperature higher than 450°C does not favor osteoblast attachment and proliferation. This topic will be discussed in more details in Section 4.

Figure 23. XRD patterns acquired from porous NiTi SMA after oxidation at different temperatures: (a) Unoxidized, (b) 300oC, (c) 400oC, (d) 450oC, (e) 550oC, (f) 600oC, and (g) 800oC [89].

Figure 24. XPS analysis acquired from the wall of an internal pore of porous NiTi oxidized at 450oC. (a) small area XPS depth profile, (b) the deconvoluted Ti2p spectrum [89].
3.2. Oxygen Plasma Immersion Ion Implantation

A plasma which can be regarded as the fourth state of matter is composed of highly excited atomic, molecular, ionic, and radical species. It is typically obtained when gases are excited into energetic states by radio frequency (RF), microwave, or electrons from a hot filament discharge [90]. Plasma immersion ion implantation (PIII) which excels as a non-line-of-sight technique has been demonstrated on components with irregular geometries [80, 91-93]. In addition, a good theoretical understanding of PIII into complex-shaped samples such as mechanical gears and ball bearings has been developed and simulation software is available to determine ion trajectories and ion fluence distributions on different types of surfaces [94-97]. Furthermore, PIII has been successfully utilized to improve the surface mechanical and biological properties of dense NiTi SMAs [98-100]. The schematic drawing of the PIII instrument used in our work is shown in Figure 26. We have successfully treated porous NiTi SMAs using oxygen PIII using parameters listed in Table 5 [101, 102]. As shown in Figure 27, the small area XPS depth profiles reveal that Ti exists only as TiO₂ on the surface of the O-PIII sample whereas three chemical states of Ti can be observed on the surface of the untreated sample, namely, Ti⁰ (NiTi), Ti²⁺ (TiO) and Ti⁴⁺ (TiO₂). It also implies that O-PIII is an effective technique to treat most of the exposed surface of porous NiTi SMAs with complex topographies. Moreover, O-PIII results in the formation of a gradient surface layer composed of outermost TiO₂, intermediate transition layer with components of TiO₂, Ti₂O₃, TiO, and a trace amount of NiTi, and NiTi substrate.
Figure 26. Schematic drawing of the PIII facility at City University of Hong Kong.

Table 5. Oxygen plasma immersion ion implantation (O-PIII) parameters [102]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF Power</td>
<td>1000 W</td>
</tr>
<tr>
<td>Sample Voltage</td>
<td>40 kV</td>
</tr>
<tr>
<td>Pulse Width</td>
<td>50 μs</td>
</tr>
<tr>
<td>Frequency</td>
<td>200 Hz</td>
</tr>
<tr>
<td>Pulse Duration</td>
<td>120 min</td>
</tr>
<tr>
<td>Base Pressure</td>
<td>$1 \times 10^{-5}$ Torr</td>
</tr>
<tr>
<td>$O_2$ Working Pressure</td>
<td>$6.0 \times 10^{-4}$ Torr</td>
</tr>
</tbody>
</table>

The inductively-coupled mass spectrometry (ICPMS) results unequivocally indicate that O-PIII can suppress the leaching of Ni ions from the porous samples [101,102]. This is superior to other techniques which may have difficulty dealing with non-planar surfaces. In our work [102], the untreated (mechanically polished) sample shows higher nickel release, probably due to the thinner oxide layer on the surface. Another important factor is that the pores cannot be oxidized during mechanical polishing, whereas these pores are more effectively implanted during PIII. For pores with sizes from 50μm to 400μm, they are sufficiently big that the plasma can penetrate inside and so the sidewalls can be adequately implanted, as PIII has been shown to implant the sidewalls of sub-micrometer trench structures in integrated circuits having aspect ratios exceeding 30 [103]. However, we are not implying that all the sidewalls of the pores are always adequately implanted during PIII as small and
deep pores are still difficult to be implanted. Nonetheless, our immersion tests reveal the unambiguous improvement offered by O-PIII.

Figure 27. XPS spectra of Ti2p and Ni2p acquired from the untreated and O-PIII porous NiTi samples. The solid line (black color) indicates the experimental spectra and the dash dot line (green color) indicates the fitted spectra: (a) Ti2p from O-PIII sample; (b) Ti2p from untreated sample; (c) Ni2p from O-PIII sample; (d) Ni2p from untreated sample. [102]

3.3. Chemical Treatment

Chemical treatments have been reported to be effective in modifying the surface of Ti and Ti-based alloys to favor the formation of bioactive apatite on the surface in simulated body fluids (SBF) and prevent nickel ions from leaching from the dense NiTi SMAs [104-107]. It is believed that this method is suitable for the modification of the complex surface of porous NiTi due to its non-line-of-sight nature which is better than that in plasma immersion ion implantation (PIII) and air oxidation [89, 102, 108]. In the chemical treatment, different chemical solutions such as hydrogen peroxide solution ($\text{H}_2\text{O}_2$), $\text{H}_2\text{SO}_4$, and $\text{NH}_4\text{O}_3$ are often used to pre-treat titanium metal to form a layer of titania film followed by alkaline treatment [109-111]. However, these reports focus on the enhancement of surface bioactivity of dense materials, and few studies have been carried out on porous NiTi SMAs. A recent investigation
by Jiang and Rong [112] reveals that HNO₃ solution and subsequent NaOH treatment can enhance the formation of hydroxyapatite (HA) on the surface of porous NiTi immersed in SBF. It also depresses nickel leaching and they ascribe the superior behavior to the formation of TiO₂ and NaTiO₃. We have achieved good results using a hydrogen peroxide solution in conjunction with subsequent sodium hydroxide treatment of porous NiTi SMAs [113-115].

After treatment in 10M NaOH solution with H₂O₂ preoxidation, a layer of spiculate structure is formed on the surface of porous NiTi SMA, as shown in Figure 28(a). After 5 days of immersion in SBF at 37°C, some precipitates are found on the surface with discontinuous distribution, Figure 28(b). The quantity and size of these precipitates increase as the immersion time increases. After immersion in SBF at 37°C for 15 days, the surface is almost completely covered by a layer of precipitates, as shown in Figure 28(c). The higher magnification image reveals that there are small pores and cracks on the precipitates. Figure 28(d) discloses that the apatite particles may nucleate and grow gradually at different regions. These particles merge with each other while growing as the immersion time increases. The pores and cracks are also formed simultaneously.

Figure 28. Morphologies of the porous NiTi treated by 30% H₂O₂ aqueous at 80oC for 4hrs and subsequent 10M NaOH aqueous treatment at 60oC for 24 hours: (a) without immersion; (b) after immersion in SBF for 5 days; (c) after immersion in SBF for 15 days; (d) higher magnification of (c). [113]
Figure 29. TF-XRD pattern of H2O2 and subsequent NaOH solution treated sample [113].

Figure 29 shows the TF-XRD pattern of porous NiTi alloys modified by H2O2 solution pre-oxidation and subsequent NaOH solution treatment. The XRD pattern reveals that the surface layer on the porous NiTi alloys is composed of predominantly Na2TiO3 and TiO2 after H2O2 and NaOH modification. The NiTi phase and minor Ti2Ni phase signal should come from the substrate. After immersion in SBF at 37ºC for 15 days, the EDS results in Figure 30 suggest the formation of precipitates composed of calcium and phosphorus on the modified porous sample, as shown in Figure 28 (c). Na and O peaks are also detected and they probably originate from Na2TiO3 and TiO2 below the precipitates. The Ti and Ni signals come from the substrate.

Figure 30. EDS profile of the porous NiTi alloy modified by H2O2 solution and subsequent NaOH solution after immersed in SBF for 15 days [113]
Figure 31 shows the TF-XRD pattern of chemically treated porous NiTi soaked in SBF for 15 days at 37°C. It can be observed that the precipitate layer is dominantly composed of apatite. Minor amounts of TiO$_2$ and Na$_2$TiO$_3$ exist in the surface layer, stemming from the chemical reaction during chemical modification [112] as confirmed by the TF-XRD pattern in Figure 29.

It can be found from Figure 32(a) that after treatment in H$_2$O$_2$ and subsequently NaOH, the surface layer on the porous NiTi alloy is about 800 nm thick and exhibits a graded structure. Figure 32(b) shows the high resolution XPS spectra of Ti2p of this porous sample. It is obvious that from the surface to the substrate, Ti2p3/2 exhibits three different binding energies of 458.3eV, 459.1eV and 454.5eV, corresponding to the surface layer, intermediate transition layer and substrate, respectively. According to the reported binding energies of Ti2p3/2 in different compounds [116], Ti2p in the surface layer should exist in TiO$_2$$^2$$. In the middle layer, Ti2p exists as TiO$_2$, Ti$_2$O$_3$, TiO and TiO$_2$$. It can be inferred that the outermost layer is composed of Na$_2$TiO$_3$ and the next transition layer is made up of Na$_2$TiO$_3$, TiO$_2$ Ti$_2$O$_3$ and TiO. As the depth increases, the quantities of TiO$_2$ and TiO$_2$$^2$ diminish while the amount of metal Ti (NiTi) increases. When analyzing the depth profile curves shown in Figure 32(a), it is evident that the surface layer on the chemically modified porous NiTi alloy is composed of mainly Na$_2$TiO$_3$ and the middle layer comprises TiO$_2$ and Na$_2$TiO$_3$ with trace amounts of NiTi, Ti$_2$O$_3$ and TiO. The quantities of TiO$_2$ and Na$_2$TiO$_3$ gradually decrease near the substrate. NiTi is predominant while TiO$_2$ and Na$_2$TiO$_3$ become less in concentration when the depth is over 800 nm.

Figure 31. TF-XRD pattern of the porous NiTi alloy modified by H$_2$O$_2$ solution and subsequent NaOH solution after immersed in SBF for 15 days. [113]
Figure 32. XPS analysis the porous NiTi samples modified by H2O2 solution and subsequent NaOH solution. (a) depth profile, (b) high resolution XPS narrow spectra of Ti2p. [113].

Our recent research reveals that long time alkali solution treatment can induce the formation of hierarchically nanostructured titanates on three-dimensional microporous Ti-based alloys [117].
3.4. Physical vapor Deposition (PVD)

PVD is fundamentally a vaporization coating technique, involving transfer of materials on an atomic level. It is an alternative process to electroplating. The raw materials/precursors used for deposition start out in a solid form. PVD processes are performed under a vacuum environment and generally include four steps, namely evaporation, transportation, reaction, and deposition. The schematic diagram of this process is shown in Figure 33 [118]. During the first stage, a target consisting of the material to be deposited is bombarded by a high energy source such as a beam of electrons or ions. The atoms are vaporized from the surface of the target. The second process is the movement of vaporized atoms from the target to the substrate. In some cases, we want to get coatings composed of metal oxides, nitrides, carbides and other such materials. In these cases, the target will consist of the metal. The atoms of metal will react with the selected gas during the transportation stage. The last stage is the formation of coatings on the substrate surface. In some cases, the reactions between the target materials and reactive gases may also take place at the substrate surface simultaneously during deposition.

![Figure 33. Schematic diagram of the PVD process [118].](image)

This technique is different from the aforementioned three techniques due to its line-of-sight nature. Not many research groups have treated porous NiTi using this technique. Lemaire et al. have reported that TiN and TiO\(_2\) coatings can be deposited on porous NiTi SMAs by PVD [119]. They claim that the coatings cover the entire exposed surface area, even in the center of 8 × 17 mm\(^2\) samples with 210 ± 110 μm pores. Nickel ion release decreases relative to an untreated sample by factors of 10 and 14 for TiN and TiO\(_2\) coatings, respectively. On a whole, the porous NiTi SMAs treated by PVD show higher nickel release compared to other surface modification techniques. The natural disadvantage of PVD for the treatment of porous NiTi with complex surface morphologies is its line-of-sight nature meaning that it is extremely difficult to coat workpieces with complex 3D topographies.

There are many other line-of-sight techniques such as chemical vapor deposition (CVD) and laser treatment. However, these processes are not suitable for the surface modification of porous NiTi with complex three-dimensional topographies.
Table 6. Nickel release concentrations of various porous NiTi products immersed in SBF

<table>
<thead>
<tr>
<th>PM processes</th>
<th>Porosity (vol%)</th>
<th>Pore size (µm)</th>
<th>Surface modification methods</th>
<th>Ni release concentrations (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF-HIP</td>
<td>40</td>
<td>50-200</td>
<td>Oxygen-PIII</td>
<td>0.06–0.18 (untreated)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.01–0.05 (treated)</td>
</tr>
<tr>
<td>CF-HIP with Ar expansion</td>
<td>42</td>
<td>50-400</td>
<td>Oxygen-PIII</td>
<td>7–28 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.2–0.3 (untreated)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.05–0.08 (treated)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>70 days</td>
</tr>
<tr>
<td>CF-HIP with space holder + homogenization</td>
<td>48</td>
<td>50-500</td>
<td>Atmospheric oxidation at 450 °C</td>
<td>0.45 (untreated)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.2 (treated)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6 days</td>
</tr>
<tr>
<td>CF-HIP with space holder</td>
<td>56</td>
<td>50-800</td>
<td>Chemical treatment</td>
<td>0.54 (untreated)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.39 (30% H$_2$O$_2$, 80°C, 4 hrs)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.35 (10M NaOH, 60°C, 24 hrs)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.30 (30% H$_2$O$_2$, 80°C, 4 hrs plus 10M NaOH 60°C 24 hrs)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15 days</td>
</tr>
<tr>
<td>SHS + homogenization</td>
<td>65</td>
<td>100-320</td>
<td>TiN and TiO$_2$–PVD coating; SBF soaking</td>
<td>0.66–0.85 ppm (not homogenized)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.17–0.30 ppm (untreated)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.04–0.09 ppm (TiN)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.06–0.07 ppm (TiO$_2$)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.05–0.07 ppm (SBF pre-soak)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.03–0.04 ppm (TiN + SBF pre-soak)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.06–0.07 ppm (TiO$_2$ + SBF pre-soak)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1–16 days</td>
</tr>
<tr>
<td>SHS</td>
<td>61</td>
<td>200-600</td>
<td>HNO$_3$/NaOH with HA coating</td>
<td>6.7 ppm (untreated)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>0.48 ppm (treated)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>50 days</td>
</tr>
</tbody>
</table>

4. **In Vitro and In Vivo Studies**

Since synthetic materials often integrate poorly with host tissues and result in infection or other adverse body response [120-122], porous NiTi SMAss should be fabricated by different
processes and modified by different techniques and a large number of in vitro and in vivo tests must be conducted before clinical applications.

4.1. In vitro tests

4.1.1. In Vitro Nickel Release Test

According to the Bansiddhi et al.'s survey [123] and our group's immersion test results, the nickel concentrations released from porous NiTi SMAs are summarized in Table 6. Earlier research indicates that the cell growth rate of cultured fibroblasts is depressed and the cell morphology also changes when the cobalt or nickel concentrations are higher than 15 ppm [124, 125]. Shih et al.'s result further confirm that for rat aortic smooth muscle cell, its growth inhibition becomes significant when the nickel concentration exceeds 9 ppm and the corrosion products also alter the cell morphology, induce cell necrosis, and decrease cell numbers [126]. As shown in Table 6, the short-term immersion tests indicate that released nickel concentrations from all the porous NiTi SMAs are much lower than 9 ppm, even for the untreated porous products with most pose size in the range of 200-600 μm and higher porosity of above 60 vol%. It is obvious that the surface layer formed by different modification techniques can significantly suppress the nickel leaching in short term tests. These surface layers generally exhibit a graded structure and are composed of titanium dioxide, titanium nitride, sodium titanate, or composites of these materials. It is noted that the released nickel concentration is different from porous NiTi prepared by different methods and various modification techniques possibly due to the different porous structure and various surface layer structure and compositions. In addition, deposition of HA on the surface is also favorable when nickel release is depressed.

4.1.2. In Vitro Corrosion Test

The corrosion performance of NiTi is closely related to nickel ion release. Some reports show the failure of corroded NiTi stents and grafts retrieved from patients after 5 to 43 months [127]. In comparison with dense NiTi SMAs, the complex surface morphology and larger surface area of porous NiTi make porous NiTi more susceptible to corrosion in the biological environment in which corrosion accelerates nickel ion leaching from the nickel-rich substance. In simulated body fluids (SBF), the corrosion behavior of porous NiTi alloys is directly related to the porous structure such as porosity, pore size, pore shape, and pore distribution. In addition, the surface roughness, crevices, complex geometry, internal angles, restriction of the flow of solution species, and residual stress may also influence the corrosion rate [127-131]. Other materials characteristics such as thickness, phase composition, and structure that are modified by different surface treatment techniques also substantially affect the corrosion behavior of the materials [76, 80, 132].

Electrochemical techniques such as potentiodynamic polarization measurements and electrochemical impedance spectroscopy (EIS) are commonly employed to monitor the corrosion and electrochemical behaviors of NiTi SMA. In general, a standard three-electrode apparatus is usually placed in a glass cell immersed in a 37°C water bath filled with different electrolyte solution such as SBF, Hank's solution and physiological solution. The working electrodes are the porous NiTi alloys. The counter electrodes usually consist of two graphite rods mounted diametrically opposite to each other, and all the potentials are expressed with
reference to a standard calomel electrode (SCE) connected to the working electrode through a Luggin probe. Li et al.'s research reveals that porous NiTi has a much lower value of potential breakdown than dense NiTi SMAs either in a 0.9% NaCl solution or in Hank's solution, as shown in Figure 34 [133]. This is possibly caused by the large exposed surface area and complex morphology. These results are confirmed by other groups. Table 7 summarizes the corrosion results using the potentiodynamic polarization method [134]. The corrosion resistance of porous NiTi SMAs depends on the conditions. It can be found from Table 7 that the porous NiTi has higher corrosion resistance in Hank's solution and the porous NiTi from traditional powder sintering has lower corrosion resistance. In addition, the porous NiTi with pores filled has higher potential breakdown value than that without filling.

Figure 34. Polarization curves of porous and solid NiTi SMAs in solution of (a) 0.9% NaCl, and (b) Hank's; curve 1: Solid NiTi SMA; curve 2: porous NiTi SMA with pores filled by resin; curve 3: porous NiTi SMA without filling [133]

<table>
<thead>
<tr>
<th>NiTi material</th>
<th>Test medium</th>
<th>$E_{corr}$ (mV)</th>
<th>$i_{corr}$ ($10^{-6}$ A cm$^{-2}$)</th>
<th>$E_{haut}$ (mV)</th>
<th>Conditions</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Porous</td>
<td>0.9% NaCl</td>
<td>-300</td>
<td>60</td>
<td></td>
<td>Powder sintering</td>
<td>[134]</td>
</tr>
<tr>
<td>Solid</td>
<td>-400</td>
<td>1200</td>
<td></td>
<td></td>
<td>Polished disc</td>
<td></td>
</tr>
<tr>
<td>Porous</td>
<td>0.9% NaCl</td>
<td>-300</td>
<td>101 to 131</td>
<td></td>
<td>SHS, pore size $&gt;100 \mu m$ pore unfilled</td>
<td>[133]</td>
</tr>
<tr>
<td>Porous</td>
<td>0.9% NaCl</td>
<td>-300</td>
<td>228 to 262</td>
<td></td>
<td>SHS, pore size $&gt;100 \mu m$ pore filled</td>
<td>[133]</td>
</tr>
<tr>
<td>Solid</td>
<td>0.9% NaCl</td>
<td>-300</td>
<td>562 to 592</td>
<td></td>
<td>SHS, pore size $&gt;100 \mu m$ pore unfilled</td>
<td>[133]</td>
</tr>
<tr>
<td>Porous</td>
<td>Hank's</td>
<td>-300</td>
<td>122 to 152</td>
<td></td>
<td>SHS, pore size $&gt;100 \mu m$ pore filled</td>
<td>[133]</td>
</tr>
<tr>
<td>Solid</td>
<td>Hank's</td>
<td>-300</td>
<td>634 to 662</td>
<td></td>
<td>SHS, pore size $&gt;100 \mu m$ pore filled</td>
<td>[133]</td>
</tr>
<tr>
<td>Porous</td>
<td>Hanks'</td>
<td>-277/-281</td>
<td>173/16</td>
<td></td>
<td>SHS, pore size 100 $\mu m$ before/after surface treatment CR $= 0.02$ to 0.76 mm/year</td>
<td>[134]</td>
</tr>
<tr>
<td>Porous</td>
<td>Hanks'</td>
<td>-286/-153</td>
<td>136/15</td>
<td></td>
<td>Electroplated disc CR $= 7.85 \times 10^{-5}$ mm/year</td>
<td>[134]</td>
</tr>
<tr>
<td>Porous</td>
<td>HBSS</td>
<td>-638 $\pm$ 99</td>
<td>0.5 $\pm$ 0.7</td>
<td>270 $\pm$ 70</td>
<td>SHS, 230 $\pm$ 130 mm and a porosity of 65 $\pm$ 10%</td>
<td>[134]</td>
</tr>
<tr>
<td>Solid</td>
<td>Hank's</td>
<td>-457</td>
<td>0.009</td>
<td>888</td>
<td>Electropolished disc CR $= 7.85 \times 10^{-5}$ mm/year</td>
<td>[134]</td>
</tr>
</tbody>
</table>

Our recent research shows that EIS is also an effective technique to study the electrochemical behavior and stability of the surface layers on the exposed areas of porous NiTi SMAs fabricated by different surface modification techniques in SBF [135]. The results show that non-line-of-sight techniques such as PIII and chemical treatment are useful surface
modification techniques to produce protective films on the surface of porous NiTi alloys and that the surface films produced by different modification techniques significantly influence the electrochemical behavior of porous NiTi electrodes.

4.1.3. In Vitro Cell Culture Test

*In vitro* cell culture tests have been carried out on various NiTi foams before and after surface modifications. Porous NiTi SMAs fabricated by both SHS and CF-HIP exhibit good cytocompatibility, even without any surface modification. As shown in Figure 35(a), for example, peripheral blood leukocytes can immediately attach to the surface of porous NiTi produced by SHS and exhibit rapid viability within 24 h [38]. Our short-term *in vitro* test (8 days) shows that osteoblasts can attach and proliferate well on almost the entire exposed surface, even the inside of the exposed pores of porous NiTi produced by CF-HIP (shown in Figure 35(b)). Porous NiTi samples made by other processes (e.g. MIM with space holder) also show strong proliferation and attachment of cultured cells [68]. Our cell culture tests show that mice osteoblast cells can attach and grow successfully on the modified surface of CF-HIP fabricated porous NiTi using either 450°C low temperature oxidation, O-PIII, or chemical process (shown in Figures 35(c), 35(d) and 35(e), respectively). However, the released nickel concentrations significantly influence how well osteoblast cells adhere and proliferate on the porous NiTi surfaces. As shown in Figure 34(f), the 600 °C oxidized surface does not favor attachment of osteoblasts because immersion tests show that higher temperature oxidation induces higher nickel concentration. Figure 25 confirms that a nickel concentration of 10 ppm released from the 600 °C oxidized porous NiTi. Our results are in agreement with the findings of Gu et al. [136]. In their study, no cell attachment can be observed on the porous NiTi surfaces containing unreacted, elemental Ni left from an incomplete SHS process, while fast proliferation and differentiation are found after surface treatment.
4.1.4. In Vivo Tests

In vivo study of porous NiTi implanted in animals is a critical step before the biometal can be clinically implanted into patients. Kim et al. show no apparent adverse reactions on or around the implant area in proximal tibia of rabbit after 6 weeks, and the in-grown bone has similar properties to the surrounding bone [51]. Other groups have also indicated that porous NiTi shows excellent bone implant contact and a high level of bone ingrowth in rabbits and rats without signs of loosening [137-138]. Our recent in vivo tests in rabbit’s tibia for 105 days show that bone tissues can contact and grow well on the entire surface and bone tissues grow smoothly into the inside of the interconnected internal pores [117]. Our work also shows that a high porosity (48%) does not exhibit obvious superiority for bone contact and ingrowth compared with low porosity (42%). Kuja et al. have implanted 3 types of porous NiTi into rats for 30 weeks, and their results reveal that a porosity of 66.1% (MPS 259±30 μm) shows the best bone–implant contact (51%). However, a porosity of 46.6% (MPS 505±136μm) with bone–implant contact of 39% is not significantly inferior in this respect and shows significantly lower incidents of fibrosis within the porous implant. A Porosity of 59.2% (MPS
272±17μm) leads to lower bone–implant contact values [137]. It indicates that the porosity of implants is not the only predominant factor influencing bone ingrowth. The condition of bone ingrowth is possibly determined by the combination of porosity, pore size, shape and some other factors. More work should be carried out to investigate the action mechanism between bone tissues and porous NiTi scaffolds in the future.

5. IMPLANT APPLICATIONS

In 1997, Biorthex commenced the development of a porous nickel-titanium alloy, Actipore™, to address the challenge of host bone to implant fixation [139]. The Canadian company has developed three porous NiTi products derived from its Actipore™ technology. Two of them are advanced interbody fusion device indicated for lumbar fusion: the Actipore™ PLF system and the Actipore™ PLFx system, and the third Actipore™ ACF system is indicated for cervical fusion. The photos of these products are shown in Figures 36(a), (b) and (c), respectively. The new porous nitinol product via anterior approach is also been developed (Figure 36(d)). Actually, many research groups including our group in Hong Kong have been developing various porous NiTi implants and applying these products clinically to repair bone tissues in different parts of different animals such as cranial bone of rabbits [34], distal femoral metaphysis of the rats [137], two noncontiguous intervertebral lumbar sites in sheep [37], distal part of femur/tibia of rabbits under weight-bearing [117], as shown in Figures 36(e), (f), (g) and (h), respectively. These clinical implantations in animals have yielded satisfactory results. That is, porous NiTi SMAs are suitable for bone tissue ingrowth and repair of various injured bones. However, few long-term clinical results have been reported, and the nickel-release behavior in animals after long-term implantation as well as subsequent effects on tissues has not been systematically investigated. The effects of the pore shape, size, and surface morphologies on bone tissue growth are also not known in details. The mechanism between surface layers produced by different surface modification techniques and bone tissues in clinical implantation is also not well understood. Therefore, more work must be done before these new porous NiTi SMAs scaffolds have more widespread clinical uses.

6. CONCLUSION

Since Itin et al. reported the excellent properties and promising applications in orthopedic fields in 1994 [33], porous NiTi SMAs have attracted the attention of a large number of biomaterials researchers. Many groups have achieved great progress in fabrication, surface modification, and biocompatibility research of porous NiTi SMAs. Besides discussing the research work of our group in this field, the present chapter systematically reviews the progress of this biometal, mainly focusing on the fabrication techniques and modern surface modification processes used in this area as well as the subsequent effects of these products and modification process on the in vitro and in vivo biological behavior of porous NiTi SMAs.
Fabrication and Surface Modification of Porous Ni-Ti Shape Memory Alloys...

Figure 36. Porous NiTi implant products. (a) PLF and (b) PLFx for lumbar interbody devices fusion devices, (c) ACF implant for anterior cervical interbody fusion devices, and (d) Actipore™ Vertebral Body Replacement System [139], (e) porous nitinol implants to repair cranial bone of New Zealand White rabbits for 12 weeks, Ingrown bone (B) is readily distinguished from porosities (P) and the nitinol (N) material. [34], (f) porous nitinol implanted in the distal femoral metaphysis of the rats for 30 weeks (b=bone, i=implant, f=fibrosis, bm=bone marrow) [137], (g) implanted at two noncontiguous intervertebral lumbar sites in sheep for 12 months. Metal (M), cartilaginous tissue (C), osteoid (O), bone tissue (B), and fibrous tissue (F). Stevenel’s blue and Van Gieson’s picro-fuchsin staining [37], (h) bone tissues can also grow into the exposed internal pores for 105 days (black indicating porous NiTi scaffold, and pink indicating bone tissues) [117].

The PM method is the main fabrication technique. EPS, CS, SHS, HIP, MIM, CF-HIP and PM processes with space holders have been developed for fabrication of the porous NiTi SMAs, and these methods are based on the exothermic reactions between nickel and titanium powders. Several surface modification techniques have been employed to produce bioactive protective layers on the surface of the porous alloy, and these techniques are proven to be effective in suppressing nickel release and improving the biocompatibility of this alloy. Among these techniques, PIII, chemical treatment, and low temperature atmospheric oxidation are the most effective processes due to their non-line-of-sight nature. They are suitable for the surface modification of products with complex morphologies. Both short-term in vitro cell culture and in vivo animal implantation tests confirm that the porous NiTi SMAs are biocompatible and have no obvious toxicity. Although some products have been developed and implanted in various animals, the mechanisms between this porous implant and bone tissues, such as effects of the porous structure, surface layer, and interface on bone tissue growth, are not well understood. More work must be done in this area as the market demand for bone implants increases in the near future.

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