Surface modified NiTi smart biomaterials: Surface engineering and biological compatibility

Mir Saman Safavi, Aydin Bordbar-Khiabani[2], Frank C. Walsh[3], Masoud Mozafari[4,5], Jafar Khalil-Allafi[1,*]

[1] Research Center for Advanced Materials, Faculty of Materials Engineering, Sahand University of Technology, Tabriz, Iran, P.O. Box: 513351996.

[2] Department of Chemical and Metallurgical Engineering, School of Chemical Engineering, Aalto University, 02150 Espoo, Finland.

[3] Electrochemical Engineering Laboratory & National Centre for Advanced Tribology, Faculty of Engineering and the Environment, University of Southampton, Southampton, SO17 1BJ, UK.

[4] Tissue Engineering and Regenerative Medicine Department, Faculty of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran, Iran.

[5] Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital, University of Toronto, Toronto, Canada.

[*]Corresponding author: Jafar Khalil-Allafi, Email: allafi@sut.ac.ir

Abstract

NiTi metallic biomaterials have a broad spectrum of clinical applications from heart stents to orthopedic implants. In recent years, the use of NiTi smart biomaterials has received growing attention due to their striking features, including a low elastic modulus, favorable corrosion protection, shape memory behavior and acceptable biocompatibility. However, the leaching of Ni ions from the surface of NiTi, the need for decreased elastic modulus and the desire for improved biological properties, including better material-cell interactions, biomineralization, and antibacterial activity, have provided the driving force for a wide variety of surface-modification techniques to address these problems before using NiTi *in vivo*. Depending on the target application, both dry and wet coating techniques have been employed to deposit biocompatible and bioactive layers over NiTi smart biomaterials. The influence of such coatings on the biological characteristics of the NiTi, including cell attachment, viability, proliferation, differentiation, and bone-forming ability, is illustrated. R & D activities have proved fruitful but much work needs to be done before clinical use of coated-NiTi. **Keywords:** Biocompatibility; NiTi; Smart biomaterials; Surface modification.

Abbreviations

CaP	Calcium phosphate
CCK-8	Cell counting kit-8
CPED	Cathodic plasma electrolytic deposition
DMEM	Dulbecco's modified Eagle medium
EPD	Electrophoretic deposition
GO	Graphene oxide
HAp	Hydroxyapatite
HDTMS	Hexadecyltrimethoxysilane
hMSCs	Human bone marrow mesenchymal stem cells
HUVEC	Human umbilical vein endothelial cells
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
MWCNTs	Multi-walled carbon nanotubes
PBS	Phosphate buffered saline
PDA	Polydopamine induced biomimetic mineralization
PHDC	Poly (2-hydroxyethyl methacrylate-co-2-(dimethylamino) ethyl methacrylate-co-7-hydroxy-4-methylcoumarin methacrylate)
PZC	Point of zero charge
SBF	Simulated body fluid
TiO_2	Titanium dioxide

1. Introduction

In the healthcare industry, increasing life expectancy together with the high demand for surgical instruments and bio-implants, have rendered smart biomaterials increasingly important [1-4]. Nearly equiatomic nickel-titanium (NiTi, also called Nitinol) alloys belong to a class of advanced materials known as smart or shape-memory alloys. These materials also possess superelasticity, resulting from a reversible solid-state phase transformation between parent (austenite) and product (martensite) phases. They have a similar elastic modulus to natural bone, a compressive strength

higher than natural bone and an excellent corrosion resistance in physiological solutions, motivating research in their use as biomedical implants. Biomedical engineering applications considered have included orthodontic implants, cardiovascular stents, artificial heart valves, orthopedic staples and guidewire as well as several surgical and dental instruments [5-13].

Ideally, biomaterials are nontoxic, non-allergenic and non-carcinogenic. A biomaterial can manifest toxicity when it releases soluble chemical species. The high nickel content in NiTi alloys is the major concern in its biological compatibility for long-term clinical applications. Due to severe inflammatory reactions inside the body caused by Ni-rich implants, the amount of Ni released from NiTi implants can pose allergic diseases, such as "nickel dermatitis" and "asthma" in which skin and respiratory cells are involved, respectively. The amount of Ni ions released depends on the type of body fluid or tissue in contact with the implant [14-18]. It has been shown that the amount of Ni release from solid NiTi implants is about two orders of magnitude lower than that from porous ones [19].

NiTi surfaces are normally covered by TiO_2 with traces of nickel oxides. Generally, leaching of Ni ions is prevented by a dense, protective TiO_2 layer which provides good corrosion resistance and biocompatibility. The stability of the TiO_2 layer and the rate of metal ion transfer through it are crucial factors controlling the dissolution rate of nickel [20]. In order to prepare homogeneous, uniform, defect-free, and thick TiO_2 layers on NiTi implants, various surface modification techniques have been proposed, including ion implantation, oxidation, heat treatment and surface coatings. In addition to reducing the release of nickel ions, specific metallic ions and phases have been incorporated into TiO_2 layers or deposited directly on the surface of NiTi biomaterials to enhance osteoconductivity, antimicrobial, antibacterial, anti-friction and corrosion protection properties. The surface topography also significantly affects the interaction of NiTi implants with

bone tissue cells by affecting surface wettability [21-23]. Although earlier reviews on surface modification of NiTi biomaterials have been published [24], many further detailed studies have been conducted in recent years. This review presents recent advances in NiTi surface modifications and their biological characteristics over the past 5 years.

2. *In vitro* biocompatibility

A biocompatible implanted material should be in harmony with surrounding cells and tissues so that it should not cause any inverse local or systemic host responses [25]. When discussing *in vitro* biocompatibility in this paper, emphasis is placed on cell attachment, viability, spreading, differentiation, and proliferation. In general, NiTi shows acceptable biocompatibility; however, some obstacles, including Ni ion leach out, limits its potential spacious biomedical applications [5]. Both organic and inorganic coating types have been applied using a broad variety of the surface modification techniques to bypass this challenge. While there are few reports dealing with the application of organic materials, such as GO [26] and chitosan [27], to coat NiTi, a numerous number of attempts have been made to improve the *in vitro* biocompatibility of NiTi by the deposition of inorganic coatings, such as CaP family [28], ZrO_2 [29], and Al_2O_3 [30]. Recently, the synergistic combination of organic/inorganic coating materials in the form of either single layer (composite coating) or multilayer systems have garnered great attention [22, 31]. The latter strategy allows the possibility of employing different coating approaches to obtain the desired outcome [22]. There are other low-cost strategies, such as anodizing, hydrothermal, and Fenton oxidation, which precipitate an oxide-containing layer on the NiTi. The oxide layer formed is mainly composed of Ti oxides due to their lower formation enthalpy, i.e., more favorable thermodynamic conditions [27, 32, 33]. This layer is proven to improve *in vitro* biocompatibility.

For instance, it is reported that the nanotubular morphology of the formed oxide layer over the NiTi after anodizing is responsible for enhanced cell viability after 7 days of incubation with HUVEC [27].

Overall, the *in vitro* biocompatibility of the biomaterials depends on surface chemistry, roughness, wettability, and charge. In the case of NiTi, the concentration of the released Ni ions can noticeably affect this property. While the concertation of the released Ni ion determines the number of viable cells upon the immersion period, surface roughness and wettability affect the cell adhesion. The overwhelming majority of the surface modification attempts have resulted in an improved biocompatibility of NiTi, where there are a higher number of the living cells on the coated-NiTi with much more elongated and extended morphology [27, 33, 34].

Ni ions can be leached out from the surface of implanted NiTi due to the corrosive nature of physiological body fluids, which often contain Cl^- ions and oxygen species, leading to pitting corrosion. It is to be noted that the atomic ratio of the Ni to Ti is a key parameter in determining the concentration of the released Ni. NiTi containing a high Ni content with a large surface area, shows different Ni release mechanism, via chemical dissolution [33, 35]. Metal ions can be released due to friction between the joints. The released Ni has been shown to be directly incorporated into the living cells, changing their functions [36]. The cell activity is inversely related to released Ni content, where a significantly higher cell number can exist over the protected NiTi with lower Ni release [35]. The formation of a dense layer over the NiTi can act as a protective barrier against the Ni leaching. Simply put, the more the coating is corrosion resistant, the lower Ni is leached out [37]. It is possible to minimize the concentration of the released Ni by controlling the operating parameters and increasing the number of the deposited layers [36, 38, 39]. As a novel strategy, the surface of NiTi can be modified by heat treatment under a He and H_2 atmosphere.

The concentration of Ni released is reduced by surface modification and there is higher concentration of Ni within the HUVEC when using He atmosphere, highlighting the importance of the operating process [36]. The application of a layered system, in which there is no Ni near the outer layer is a feasible approach to decrease the concentration of the leached Ni [22, 38]. For instance, the concentration of Ni ions released from NiTi decreases by 90 and 93% with the deposition of HAp and (nitride layer/HAp/ciprofloxacin) three-layered system, respectively [22]. McNamara et al. [20] have reported that the application of a magnetron sputtered tantalum oxide film over NiTi limits the Ti migrating out, leading to a Ta/Ti interlayer, which can act as a hurdle against Ni releasing from the implant. Apart from the chemical composition of the deposited layer, the type of deposition technique changes the amount of the released Ni. Unlike the methods in which the NiTi serves as an anode, e.g., plasma electrolytic approaches, Ni was not incorporated in the growing film when employing cathodic routes, such as CPED [37].

The application of the biocompatible coatings over the NiTi may change the morphology of the attached cells, where a higher number of filopodia and lamellipodia are present all over the surface the coated-NiTi when incubation with eukaryotic cells [39]. As mentioned earlier, surface roughness and wettability are two important factors in realizing the improved cell attachment. The higher the surface roughness and hydrophilicity, the higher the cell adhesion is obtained. The achievement of high cell adhesion depends on the final application of the surface treated-NiTi. While orthopedic applications are in dire need of higher cell attachment, the biomaterial enabling lower cell adhesion are suitable for cardiovascular applications since it diminishes the risk of blood coagulation [34]. The application of post-treatments, including hydrothermal approach, is highly recommended to enhance the wettability of the coated-NiTi, when the deposited coating resulted in increased contact angle value. It is illustrated that the contact angle value of the NiTi increases

from ≈146 º to ≈152 º with the application of the bioinert Al_2O_3 film, followed by a drastic drop to ≈3º with post-hydrothermal treatment, fulfilling the high cell adhesion needed for orthopedic applications [30]. Fig. 1 shows the influence of the surface-modification on the morphology of HUVECs after 1 day of culture. The enhanced cell adhesion after alkali treatment is attributed to the increased surface roughness. Moreover, the applied HDTMS coating promotes cell spreading [34].

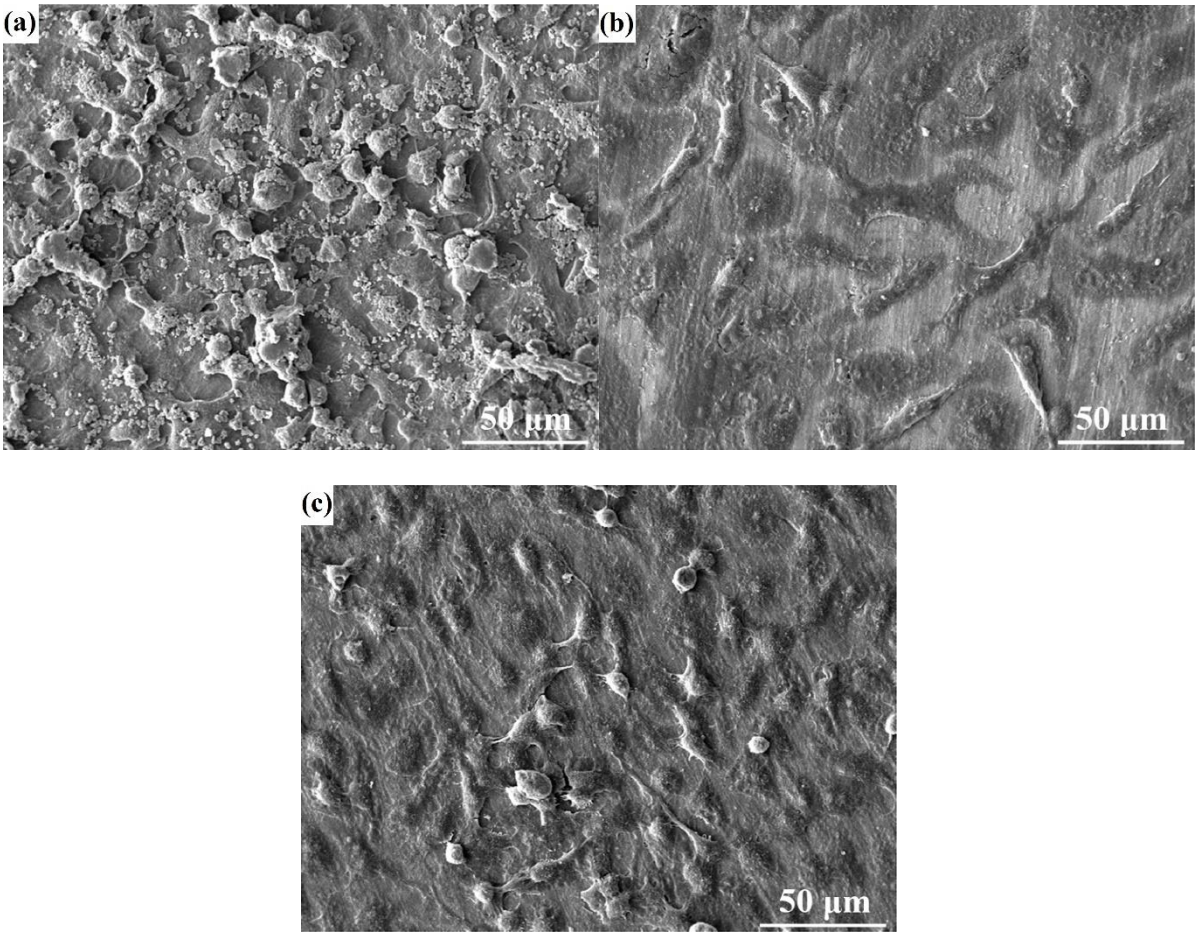

Fig. 1. The influence of surface-modification on the morphology of HUVECs after 1 day of culture: (a) NiTi, (b) alkali-treated NiTi at 120 ºC, and (c) HDTMS-coated NiTi [34].

Cell proliferation and differentiation depend greatly on the surface morphology, structure and chemical composition of the deposited layer [30, 33]. Although Ni leaching has not as high

importance as the aforementioned factors, its influence should also be taken into consideration [22, 28]. The porous morphology of the film positively contributes to cell proliferation [30]. Besides, the scale-like structure of the deposited layer promotes the cell attachment [28]. It is well-established that the CaP family coatings, in particular HAp, facilitate the mentioned functions [30]. The coatings with poor corrosion resistance cannot support cell proliferation for prolonged time due to the destructive influence of the increased concentration of the Ni ions [22]. Table 1 summarizes the surface roughness, contact angle, released Ni ion concentration, and the optical density values of the surface-modified NiTi biomaterials.

Table 1. Surface roughness, contact angle, released Ni ion concentration, and the optical density values of the surface-modified NiTi biomaterials.

Coating type	**Deposition technique**	**Surface roughness *vs.* bare NiTi (%)**	**% Decrease in Ni ion release *vs.* bare NiTi; test medium**	**% Contact angle *vs.* bare NiTi () & test medium**	**Incubated cell type**	**& increase in O.D value *vs.* bare NiTi ; measurement technique**	**Ref.**
PHDC	EPD	---	25; SBF	27 & not reported	NIH-3T3 cells	48; MTT	[35]
HDTMS	Hydrothermal pre-treatment followed by HDTMS functionalization	74 (increase)	---	35 (decrease with hydrothermal), 19 (increase with HDTMS) & distilled water	HUVECs	7; CCK-8	[34]
Ca doping ZrO_2	CPED	---	86; Hank's solution	---	osteoblast-like cells	13; MTT	[29]
Al_2O_3/HAp	CPED/PDA induced biomimetic mineralization	---	96; SBF	4 (increase with Al_2O_3), 98 (decrease with hydrothermal) & not reported	hMSCs	55; CCK-8	[30]
Nitride layer/HAp/Cip	Nitrogen plasma immersion ion implantation/sol-gel/sol-gel	85 (decrease)	92; SBF	---	MC3T3-E1 cells	15; MTT	[22]
Graphene oxide	Electrodeposition	---	90; SBF	---	MC3T3-E1 cells	29; CCK-8	[39]
DCPD	Electrodeposition	2566 (increase)	90; SBF	---	MC3T3-E1 cells	22; CCK-8	[28]

3. *In vitro* bioactivity

In simple terms, osseointegration is the process of fusion between the living bone and synthetic implant. When osseointegration occurs appropriately, the implanted material can only be detached from the bone through fracture. The surface of the material is the site for initial functional and structural connection with the bone. The ability of the biomaterial to form apatite, which serves as a bridge to link the bone to the implant, commonly defined as bioactivity. A poor osseointegration may result in the generation of fibrous tissues, leading to a failure in implantation. The higher volume of the formed apatite and similarity of its chemical composition to the stoichiometric HAp, guarantees the enhanced bioactivity [29, 40].

In general, the bone-forming ability of a biomaterial depends on a variety of the factors, including surface chemistry, roughness, and design. There are several solutions, such as SBF, DMEM, PBS, Hank's solution, developed to provide a prediction if the biomaterial is bioactive *in vivo*. Depending on the nature of the used medium and composition of the biomaterial, the studied biomaterial can either undergo biomineralization or biodegradation. While during the former, the formation of apatite increases the mass, the latter phenomenon causes mass loss. It is to be noted that the SBF is the most commonly used medium to study the *in vitro* bioactivity of the biomaterials. The SBF medium contains calcium and phosphate-containing salts, which are essential for generation of apatite [29, 41].

All in all, NiTi suffers from an appropriate *in vitro* bioactivity, where there is a few, or in some cases, no apatite forms over its surface upon immersion in SBF [29]. The application of suitable layers, including CaP family, GO, ZrO_2, and TiO_2, can profoundly address this challenge. Among

the deposited layers, pure HAp and particle reinforced-HAp coatings provide fascinating *in vitro* bioactivity [29, 37, 40-42]. Doping HAp with biocompatible elements and compounds, such as silicon and titanium, can give rise to their biomineralization behavior [31, 43]. The HAp-coated NiTi can supply Ca^{2+} ions when they are immersed into the SBF. On the other hand, the hydroxyl ions that adsorbed on the surface of the coating can be exchanged with the Ca^{2+} and H^{+} ions that are present on the surface of the coating, leading to an increased pH. Accumulation of hydroxyl ions on the surface is of prime necessity for apatite nucleation. The release of Ca^{2+} ions from the surface of the coating makes the surface negatively-charged, which leads to the accumulation of the Ca^{2+} ions at the coating/solution interface. These ions can react with existing phosphate ions in SBF to form apatite. There is a continuous competition between the amount of the dissolved coating material and the formed apatite during the immersion period [44]. The mechanism governing the increased bioactivity with the incorporation of the reinforcing agents, e.g., Ti, is related to a change in the value of PZC due to the formation of some oxide and intermetallic compounds. The higher the difference between the PZC of coating and SBF, the higher is the absorption rate of the Ca, phosphate and hydroxyl ions is [31]. Moreover, the included nano-scaled reinforcing phases, including MWCNTs, provide larger effective surface area for the nucleation of the apatite. Also, if the embedded reinforcements lead to a more hydrophilic surface, a higher amount of Ca, phosphate and hydroxyl ions can be adsorbed on the coating, leading to an improved biomineralization [31]. . It is worth mentioning that the formed apatite over the coated-NiTi is usually Ca-deficient HAp since the existing Na^{+}, K^{+}, and Mg^{2+} ions in SBF can replace Ca^{2+} in the HAp crystal lattice [29].

Another feasible approach to improve the in vitro bioactivity of the NiTi is the application of pre-treatments, such as mechanical polishing, acid-etching/immersion in alkali solution, and heat

treatment. These treatments can affect both volume fraction and chemical composition of the formed apatite on the bare NiTi and HAp-coated NiTi [41]. It is found that a higher content of apatite particles with Ca/P molar ratio close to 1.67 can be formed on the surface-modified NiTi compared to the bare one. The application of the bioactive coating not only changes the content and chemical composition of the formed apatite but also varies its morphology [31, 41, 43, 45]. The importance of processing parameters in realizing enhanced biomineralization is illustrated. It is reported that the GO layers obtained by electrodeposition at various times show different immersion behaviors, where the ones that precipitated at longer times may support enhanced biomineralization [39]. Coatings that are not fabricated under optimized conditions may undergo degradation upon long-time immersion in SBF due to the presence of surface defects [28].

4. Conclusions and future prospects

NiTi smart materials are metallic biomaterials, benefiting from a low elastic modulus, favorable corrosion resistance, and acceptable biocompatibility, and are considered as potential biomaterials for a variety of clinical applications. However, the leaching of Ni ions from the surface of NiTi, the need for decreased elastic modulus, and desire for improved biological properties, such as better material-cell interactions, biomineralization, and antibacterial activity, are remaining challenges which need to be addressed by the application of surface-modification strategies.

The bare NiTi provides suitable platform for various eukaryotic cells to attach to its surface, stay alive, growth, and proliferate; however, a better biological performance, in which a higher number of the living cells with more elongated morphology and higher proliferation can be obtained when its surface modifies with biocompatible coatings, in particular CaP family materials. The more

biocompatible chemical nature of these materials, decreased Ni ion release, and enhanced hydrophilicity of the surface with CaP deposition are three potential mechanisms governing such an enhancement. The importance of controlling operating factors and exploiting novel deposition strategies, such production of composite or layered coatings, in further improvement of these properties is stressed.

Unlike *in vitro* biocompatibility, bare NiTi shows poor *in vitro* bioactivity. It is essential to bypass such a challenge before employing NiTi *in vivo*. The application of surface-modification approaches is proven to be a key solution, where there are much more apatite grains with a composition close to the stoichiometric HAp can be formed over the coated-NiTi compared with bare one. Although multiple inorganic and organic coating materials have been developed to induce superior in vitro biomineralization, the best outcome is reported to be obtained when using HAp layers.

A recommended roadmap for future R&D works in this area includes the following targets:

- The application of novel surface engineering strategies, such as composite and layered coatings, exploiting biocompatible particles and elements.
- Optimizing the operating factors involved in the employed coating technology.
- The use of desirable pre-treatments and/or employing low-cost one-pot surface-modification techniques.

References

1. Safavi, M.S., et al., *RF-magnetron sputter deposited hydroxyapatite-based composite & multilayer coatings: A systematic review from mechanical, corrosion, and biological points of view.* Ceramics International, 2021. **47**(3): p. 3031-3053.

2. Safavi, M.S., et al., *Electrodeposited hydroxyapatite-based biocoatings: Recent progress and future challenges.* Coatings, 2021. **11**(1): p. 110.
3. Safavi, M.S., et al., *Progress in niobium oxide-containing coatings forbiomedical applications: A critical review.* ACS Omega, 2022. **7**(11): p. 9088-9107.
4. Mohandesnezhad, S., et al., *Enhanced bioactivity of 316L stainless steel with deposition of polypyrrole/hydroxyapatite layered hybrid coating: Orthopedic applications.* Surfaces and Interfaces, 2022. **28**: p. 101604.
5. Safavi, M.S., et al., *Additive Manufacturing: An opportunity for the fabrication of near-net-shape NiTi implants.* Journal of Manufacturing and Materials Processing, 2022. **6**(3): p. 65.
6. Khalil-Allafi, J., et al., *A survey on crystallization kinetic behavior of direct current magnetron sputter deposited NiTi thin films.* Physica B: Condensed Matter, 2021. **615**: p. 413086.
7. Wong, M. and H. Man, *Low-temperature fabrication of Ag-doped HA coating on NiTi.* Materials Letters, 2018. **229**: p. 229-231.
8. Sun, Y., et al., *The influence of substrate electropolishing on anodization behavior, corrosion resistance, cytocompatibility and antibacterial ability of NiTi alloy.* Materials Letters, 2020. **268**: p. 127631.
9. Dai, D., et al., *Graphene oxide nanocoating for enhanced corrosion resistance, wear resistance and antibacterial activity of nickel-titanium shape memory alloy.* Surface and Coatings Technology, 2022. **431**: p. 128012.
10. Yin, Y., et al., *One-step fabrication of Ag@ Polydopamine film modified NiTi alloy with strong antibacterial property and enhanced anticorrosion performance.* Surface and Coatings Technology, 2019. **380**: p. 125013.
11. Saugo, M., et al., *Immobilization of antibacterial metallic cations (Ga3+, Zn2+ and Co2+) in a polypyrrole coating formed on Nitinol.* Materials Science and Engineering: C, 2018. **86**: p. 62-69.
12. Dulski, M., et al., *Toward the development of an innovative implant: NiTi alloy functionalized by multifunctional β-TCP+ Ag/SiO_2 coatings.* ACS Applied Bio Materials, 2019. **2**(3): p. 987-998.
13. Pipattanachat, S., et al., *Biofilm inhibition and bactericidal activity of NiTi alloy coated with graphene oxide/silver nanoparticles via electrophoretic deposition.* Scientific Reports, 2021. **11**(1): p. 1-9.
14. Ohtsu, N., et al., *Surface characteristics, Ni ion release, and antibacterial efficacy of anodized NiTi alloy using HNO3 electrolyte of various concentrations.* Applied Surface Science, 2019. **492**: p. 785-791.
15. Weng, Z., et al., *Osteogenic activity, antibacterial ability, and Ni release of Mg-incorporated Ni-Ti-O nanopore coatings on NiTi alloy.* Applied Surface Science, 2019. **486**: p. 441-451.
16. Lee, C.-L., et al., *Electrochemical synthesis of a composite coating with antibacterial ability on NiTi alloy.* Progress in Organic Coatings, 2020. **146**: p. 105711.
17. Hang, R., et al., *Length-dependent corrosion behavior, Ni^{2+} release, cytocompatibility, and antibacterial ability of Ni-Ti-O nanopores anodically grown on biomedical NiTi alloy.* Materials Science and Engineering: C, 2018. **89**: p. 1-7.
18. Meng, L., et al., *Polymeric nanoparticles-based multi-functional coatings on NiTi alloy with nickel ion release control, cytocompatibility, and antibacterial performance.* New Journal of Chemistry, 2019. **43**(3): p. 1551-1561.
19. Mwangi, J.W., et al., *Nitinol manufacturing and micromachining: A review of processes and their suitability in processing medical-grade nitinol.* Journal of manufacturing processes, 2019. **38**: p. 355-369.
20. McNamara, K., et al., *Tantalum coating inhibits Ni-migration from titanium out-diffusion in NiTi shape memory biomedical alloy.* Applied Surface Science, 2021. **535**: p. 147621.

21. Hang, R., et al., *Self-assembled anodization of NiTi alloys for biomedical applications.* Applied Surface Science, 2020. **517**: p. 146118.
22. Shanaghi, A., et al., *Enhanced corrosion resistance, antibacterial properties, and biocompatibility by hierarchical hydroxyapatite/ciprofloxacin-calcium phosphate coating on nitrided NiTi alloy.* Materials Science and Engineering: C, 2021. **118**: p. 111524.
23. Zhang, J.-M., et al., *Antibacterial ability and cytocompatibility of Cu-incorporated Ni–Ti–O nanopores on NiTi alloy.* Rare Metals, 2019. **38**(6): p. 552-560.
24. Shabalovskaya, S., J. Anderegg, and J. Van Humbeeck, *Critical overview of Nitinol surfaces and their modifications for medical applications.* Acta Biomaterialia, 2008. **4**(3): p. 447-467.
25. Ghasemi-Mobarakeh, L., et al., *Key terminology in biomaterials and biocompatibility.* Current Opinion in Biomedical Engineering, 2019. **10**: p. 45-50.
26. Srimaneepong, V., et al., *Corrosion resistance of graphene oxide/silver coatings on Ni–Ti alloy and expression of IL-6 and IL-8 in human oral fibroblasts.* Scientific Reports, 2020. **10**(1): p. 1-12.
27. Mohammadi, F., et al., *Chitosan-heparin nanoparticle coating on anodized NiTi for improvement of blood compatibility and biocompatibility.* International journal of biological macromolecules, 2019. **127**: p. 159-168.
28. Guo, Y., et al., *The corrosion resistance, biocompatibility and biomineralization of the dicalcium phosphate dihydrate coating on the surface of the additively manufactured NiTi alloy.* Journal of Materials Research and Technology, 2022. **17**: p. 622-635.
29. Wang, H., et al., *Preparation of Ca doping ZrO2 coating on NiTi shape memory alloy by cathodic plasma electrolytic deposition and its structure, in-vitro bioactivity and biocompatibility analysis.* Surface and Coatings Technology, 2017. **325**: p. 136-144.
30. Wang, X., et al., *Enhanced corrosion resistance and bio-performance of Al_2O_3 coated NiTi alloy improved by polydopamine-induced hydroxyapatite mineralization.* Surface and Coatings Technology, 2019. **364**: p. 81-88.
31. Maleki-Ghaleh, H. and J. Khalil-Allafi, *Characterization, mechanical and in vitro biological behavior of hydroxyapatite-titanium-carbon nanotube composite coatings deposited on NiTi alloy by electrophoretic deposition.* Surface and Coatings Technology, 2019. **363**: p. 179-190.
32. Asghari, R., M. Safavi, and J. Khalil-Allafi, *A facile and cost-effective practical approach to develop clinical applications of NiTi: Fenton oxidation process.* Transactions of the IMF, 2020. **98**(5): p. 250-257.
33. Hang, R., et al., *Preparation, characterization, corrosion behavior and cytocompatibility of $NiTiO_3$ nanosheets hydrothermally synthesized on biomedical NiTi alloy.* Materials Science and Engineering: C, 2019. **97**: p. 715-722.
34. Rahimipour, S., et al., *Structure, wettability, corrosion and biocompatibility of nitinol treated by alkaline hydrothermal and hydrophobic functionalization for cardiovascular applications.* Applied Surface Science, 2020. **506**: p. 144657.
35. Meng, L., et al., *Colloidal particle based electrodeposition coatings on NiTi alloy: Reduced releasing of nickel ions and improved biocompatibility.* Materials Letters, 2018. **230**: p. 228-231.
36. Veverkova, J., et al., *Effect of Ni ion release on the cells in contact with NiTi alloys.* Environmental Science and Pollution Research, 2020. **27**(8): p. 7934-7942.
37. Wang, X., F. Liu, and Y. Song, *Enhanced corrosion resistance and in vitro bioactivity of NiTi alloys modified with hydroxyapatite-containing Al2O3 coatings.* Surface and Coatings Technology, 2018. **344**: p. 288-294.
38. Ren, Y., et al., *Microstructure, mechanical properties and biocompatibility of laser metal deposited Ti–23Nb coatings on a NiTi substrate.* Materials Science and Engineering: A, 2022: p. 143402.
39. Guo, Y., et al., *Corrosion resistance and biocompatibility of graphene oxide coating on the surface of the additively manufactured NiTi alloy.* Progress in Organic Coatings, 2022. **164**: p. 106722.

40. Tohidi, P.M.S., et al., *Pulsed electrodeposition of compact, corrosion resistant, and bioactive HAp coatings by application of optimized magnetic field.* Materials Chemistry and Physics, 2020. **254**: p. 123511.
41. Shokri, N., et al., *Enhanced corrosion protection of NiTi orthopedic implants by highly crystalline hydroxyapatite deposited by spin coating: The importance of pre-treatment.* Materials Chemistry and Physics, 2021. **259**: p. 124041.
42. Sattar, T., et al., *Improved in vitro bioactivity and electrochemical behavior of hydroxyapatite-coated NiTi shape memory alloy.* Journal of Materials Science, 2019. **54**(9): p. 7300-7306.
43. Khalili, V., et al., *Bioactivity and electrochemical behavior of hydroxyapatite-silicon-multi walled carbon nano-tubes composite coatings synthesized by EPD on NiTi alloys in simulated body fluid.* Materials Science and Engineering: C, 2017. **71**: p. 473-482.
44. Sabzi, M., S.M. Far, and S.M. Dezfuli, *Characterization of bioactivity behavior and corrosion responses of hydroxyapatite-ZnO nanostructured coating deposited on NiTi shape memory alloy.* Ceramics International, 2018. **44**(17): p. 21395-21405.
45. Dulski, M., et al., *Key properties of a bioactive Ag-SiO_2/TiO_2 coating on NiTi shape memory alloy as necessary at the development of a new class of biomedical materials.* International Journal of Molecular Sciences, 2021. **22**(2): p. 507.