Acta Biomaterialia 21 (2015) 20–34

Contents lists available at ScienceDirect

Acta Biomaterialia

journal homepage: www.elsevier.com/locate/actabiomat

Review

An overview of thin film nitinol endovascular devices

Shayan Mahdis [a], Chun Youngjae [a,b,*]

[a] Department of Industrial Engineering, University of Pittsburgh, Pittsburgh, PA 15261, USA
[b] Department of Bioengineering, University of Pittsburgh, Pittsburgh, PA 15261, USA

ARTICLE INFO

Article history:
Received 28 October 2014
Received in revised form 3 February 2015
Accepted 19 March 2015
Available online 31 March 2015

Keywords:
Thin film nitinol
Endovascular device
Sputtering deposition
Hemocompatibility
Stent graft

ABSTRACT

Thin film nitinol has unique mechanical properties (e.g., superelasticity), excellent biocompatibility, and ultra-smooth surface, as well as shape memory behavior. All these features along with its low-profile physical dimension (i.e., a few micrometers thick) make this material an ideal candidate in developing low-profile medical devices (e.g., endovascular devices). Thin film nitinol-based devices can be collapsed and inserted in remarkably smaller diameter catheters for a wide range of catheter-based procedures; therefore, it can be easily delivered through highly tortuous or narrow vascular system. A high-quality thin film nitinol can be fabricated by vacuum sputter deposition technique. Micromachining techniques were used to create micro patterns on the thin film nitinol to provide fenestrations for nutrition and oxygen transport and to increase the device's flexibility for the devices used as thin film nitinol covered stent. In addition, a new surface treatment method has been developed for improving the hemocompatibility of thin film nitinol when it is used as a graft material in endovascular devices. Both *in vitro* and *in vivo* test data demonstrated a superior hemocompatibility of the thin film nitinol when compared with commercially available endovascular graft materials such as ePTFE or Dacron polyester. Promising features like these have motivated the development of thin film nitinol as a novel biomaterial for creating endovascular devices such as stent grafts, neurovascular flow diverters, and heart valves. This review focuses on thin film nitinol fabrication processes, mechanical and biological properties of the material, as well as current and potential thin film nitinol medical applications.

1. Introduction

Nitinol, the acronym for Nickel Titanium Naval Ordinance, is an equiatomic nickel–titanium composition alloy that was first discovered in the 1960s during a study on space vehicle heat shields [1,2]. Since that initial discovery, two unique properties of nitinol (i.e., the shape memory and superelasticity) have been used in a wide range of medical applications, specifically endovascular devices such as stents, vena cava filters, and atrial septal defect closure devices [3–8]. The shape memory response of nitinol is defined as the recovery of the material's mechanical deformation when it is heated to above the transformation temperature (i.e., austenite phase) from a low temperature state (i.e., martensite phase) [8,9]. This shape memory behavior is beneficial in the catheter-based delivery devices, because the nitinol device can be easily collapsed into a small diameter catheter in its martensite phase and upon exposure to blood temperature, it deploys to its original shape (the austenite phase). Another unique feature of nitinol is the superelasticity that provides high resistance against plastic deformation during the device delivery in tortuous vasculature (i.e., kink resistance) and in the device placed in the artery or vein where cyclic hemodynamic loads occur (i.e., fatigue resistance). When mechanical loading is applied to superelastic nitinol (i.e., austenite phase), a reversible and elastic deformation with high strains is observed due to the stress-induced phase transformation or twinning. At the temperature above austenite transformation temperature, the phase transformation from austenite to martensite occurs under mechanical loading and the material can reversibly deform in a high strain (e.g. >10%). By removing the mechanical load, the phase transformation from martensite to austenite occurs and the material returns to the original shape without generating any plastic deformation [8]. This recoverable deformation is significantly greater than conventional metals such as surgical steel (e.g., >5%) [10].

Bulk nitinol has a long-track record of successful uses in many endovascular applications; however, nitinol-based devices are relatively bulky when used with synthetic graft materials such as expanded polytetrafluoroethylene (ePTFE) or Dacron polyester. In general, these devices could be used for treating vascular diseases in large diameter blood vessels such as abdominal aortic

* Corresponding author at: Department of Industrial Engineering, University of Pittsburgh, Pittsburgh, PA 15261, USA. Tel.: +1 412 624 1193; fax: +1 412 624 9831.
E-mail address: yjchun@pitt.edu (Y. Chun).

http://dx.doi.org/10.1016/j.actbio.2015.03.025
1742-7061/

aneurysms; however, it is difficult to deliver the synthetic polymer-covered nitinol devices in many trauma situations. For example, it is challenging to deliver the device into the calcified blood vessels (i.e., narrowed vasculature), the highly tortuous small vascular systems, and pediatric patient's blood vessels. Therefore, there is a significant need for the development of new biomaterials that are low-profile and hemocompatible, as well as deliverable to the desired disease locations with appropriate material properties such as elasticity, toughness, and fatigue resistance.

One novel material worth considering for developing a low-profile transcatheter device is the relatively new material, "thin film nitinol" [11]. While thin film is typically defined with the thickness ranging from nanometer scale to several micrometers, the thickness of thin film nitinol as materials in medical devices would be 3–12 μm depending on the type of applications. Because primary uses of thin film nitinol are graft for the stent, leaflet for the heart valve, or covered membrane in any low-profile endovascular device, the thickness should be at least 3 μm in order to prevent tearing issues during thin film microfabrication, prototype manufacturing, and device delivery. It should also be less than 12 μm to minimize any stress concentration issue that typically occurs in thicker films during the thin film microfabrication processes (i.e., creation of thin film nitinol and micro patterning). Therefore, the dimension of thin film nitinol is roughly an order of magnitude smaller than bulk nitinol used in stents (80–200 μm) or any synthetic fabric membranes (e.g., Dacron polyester or ePTFE with the thickness of 100–200 μm). The early fabrication processes used to produce thin film nitinol were mostly unsuccessful. Fabrication processes are vacuum evaporation [12], flash evaporation [13,14], ion beam sputtering [15], and laser ablation [16,17]. More recently, vacuum sputter deposition process for thin film nitinol was developed and was considered the preferred method, because of the precise controllability of the deposition process and the consistency of the quality of the films [18–20].

Since the high-quality thin film nitinol was successfully developed using a sputter deposition method, researchers have focused on developing practical thin film nitinol applications. Thin film nitinol could be easily compared with synthetic fabric membranes used in stent graft due to its dimension and use. While synthetic fabrics have been widely used in endovascular devices, these materials are relatively thick, which increase the total device size requiring larger catheter sizes. Therefore, devices manufactured with synthetic fabrics are typically used in big artery or vein such as thoracic or abdominal aortic vascular systems (up to 1 inch diameter), or sometimes used in peripheral arteries in lower extremity (i.e., >5–6 mm in diameter). However, thin film nitinol can be used in small caliber vascular system, including cerebral, carotid, coronary, renal arteries and veins, and so on. In addition, thin film nitinol exhibits superelastic property at body temperature, which improves the device apposition with vascular wall compared to any synthetic fabric that typically has wrinkles or permanent deformation. Vascular wall apposition is especially critical for the devices used in small and low blood flow vascular systems; therefore, thin film nitinol is a great candidate as a covering membrane for minimizing or preventing blood flow disruption and local thrombosis accumulation between the graft and vascular wall. Furthermore, it is possible to create uniform micro fenestrations on thin film nitinol with various sizes and shapes using micro fabrication techniques. With the micro fenestrations thin film enhances the surface functionality (i.e., oxygen and nutrition transport, as well as endothelial cell migration through the micro fenestrations) and device's flexibility. These beneficial features motivated scientists to study on various thin film nitinol based endovascular applications, such as a percutaneous heart valve, flow diversion device for treating intracranial aneurysms, stent grafts for treating both thoracic and abdominal aortic aneurysms, and a micro porous thin film nitinol covered stent for treating coronary or peripheral vascular diseases [21–25]. While thin film nitinol has several attractive features, there are a few challenges in developing endovascular devices with this material. The control of both compositional uniformity and thickness throughout the whole film on the substrate (e.g., 4 in. silicon wafer) is difficult; therefore, the films in the middle of the substrate are typically used for the device. Attachment of the film on structural backbone is also challenging, because the fabricated film is 2D planar metal sheet while the device requires 3D geometry. Several approaches that attempted to attach thin film nitinol on structural backbone include (1) microfabrication process with the deposition of sacrificial layer, (2) suturing the micro patterned film using ultra thin metallic wires, and (3) encapsulation of the thin film nitinol with the backbone using biocompatible polymer adhesives. While these all approaches demonstrated the feasibility and safety either *in vitro* laboratory or *in vivo* animal tests, more studies are needed for practical applications for human beings.

In this review, the development of thin film nitinol including manufacturing processes, mechanical and biological properties are explored with special attention to various medical applications in endovascular device arena. Current technologies to create thin film nitinol material are first reviewed, then, more fundamental aspects of thin film nitinol properties are discussed for designing and manufacturing specific applications in medicine, such as transcatheter-based vascular grafts or heart valves. In addition, various surface modification techniques are reviewed to compare their hemocompatibility improvement in thin film nitinol. Finally, current thin film nitinol medical applications are extensively reviewed describing target diseases, ideal material/device properties, design/manufacturing processes, and biocompatible attributes.

2. Creation of thin film nitinol

Sekiguchi et al. first produced thin film nitinol using a vacuum evaporation technique in 1983 [12]. Although vacuum evaporation is a simple method to create thin film nitinol with minimum contaminations, it was unsuccessful in producing a uniform thin film nitinol that contains shape memory effect. At the time of the process, the lower vapor pressure of nickel as compared to titanium resulted in a higher deposition rate of it; therefore, the molar fraction of nickel in the target dropped over time until the rate of titanium deposition surpassed that of the nickel. Consequently, the composition of thin film nitinol was not uniform, showing significant compositional variation of nickel and titanium throughout the thin film thickness. Nitinol alloy shows the shape memory behavior at near equiatomic composition of nitinol alloy and a slight deviation from this composition results in deteriorating of this property or a significant shift in transformation temperature due to the narrow range of intermetallic zone in the Ni–Ti phase diagram. Thus, compositional uniformity of nickel and titanium within thin film depth is an essential requirement for the thin film of nitinol in order to exhibit shape memory behavior and a specific phase transformation temperature regarding to the targeted application. To eliminate the lack of compositional control in the conventional vacuum evaporation method, Makino et al. suggested flash evaporation method [13,14]. This method significantly improved the control of the film alloy composition over the vacuum evaporation because of more accurate control of shutter opening time during deposition. The fabricated 6 μm thin film nitinol after being annealed at 500 °C exhibited (1) the shape memory effect at less than 60 °C and (2) superelasticity at more than 80 °C. While flash evaporation method demonstrated better results, there were still non-uniformity issues in alloy composition and structure (i.e., layered structure) due to the flash cycles.