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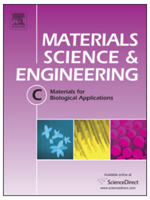

Hierarchical periodic micro/nano-structures on nitinol and their influence on oriented endothelialization and anti-thrombosis

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ABSTRACT

The applications of hierarchical micro/nano-structures, which possess properties of two-scale roughness, have been studied in various fields. In this study, hierarchical periodic micro/nano-structures were fabricated on nitinol, an equiatomic Ni–Ti alloy, using a femtosecond laser for the surface modification of intravascular stents. By controlling the laser fluence, two types of surfaces were developed: periodic nano- and micro/nano-structures. Evaluation of water contact angles indicated that the nano-surface was hydrophilic and the micro/nano-surface was hydrophobic. Endothelial cells aligned along the nano-structures on both surfaces, whereas platelets failed to adhere to the micro/nano-surface. Decorrelation between the responses of the two cell types and the results of water contact angle analysis were a result of the pinning effect. This is the first study to show the applicability of hierarchical periodic micro/nano-structures for surface modification of nitinol.

1. Introduction

Several types of metal stents, made from such materials as stainless steel, Co–Cr alloy, and Ni–Ti alloy, have been used in clinical applications for interventional therapy of vessel occlusion. Stainless steel and Co–Cr alloy are often used for their corrosion resistance with passive films, whereas the equiatomic Ni–Ti alloy, nitinol, has been utilized as a self-expanding stent because of its properties of shape memory and superelasticity [1–3]. To minimize complications of restenosis in stent implantation, surface modifications for the bare metals have been developed. A representative example is drug-eluting stents, which inhibit the proliferation of smooth muscle cells in arterial media and suppress restenosis. Another complication encountered during stent implantation is late thrombosis as a result of retardation of endothelialization on stent surfaces due to coated polymers, drugs or unknown matter. Thus, the development of surface modifications that can accelerate endothelialization on stent surfaces is highly desirable [4].

It is known that periodic micro- and nano-structures on a material surface contribute specific properties. The applications of micro- and nano-patterning on surfaces have focused on biomaterials, such as dental implants and stents [5–7]. Hierarchical micro/nano-structures possess properties of roughness at two-scale roughness, and applications for such structures have been developed in a variety of fields, including biotechnology [8,9]. Organisms with hierarchical micro/nano-structures exhibit more complex properties, such as the regulation of adhesion and detachment of geckos' footpads or the hydrophobicity and planing effect of lotus leaves [10,11]. Although material surfaces have been created by mimicking these designs, feasible designs and the substrates on which they can be fabricated are limited.

Femtosecond laser irradiation can produce periodic nanostructures on metals and semiconductors [12,13]. The periodic structures self-form at the laser focusing spot and are formed perpendicular to the laser electric field polarization vector [12]. Their period can be controlled by the output of the laser. Although the mechanism of the structure formation by the laser irradiation remains unclear, nanoplasma and/or surface instability generated by the femtosecond laser would be involved in the formation [13–15]. We previously reported that the periodic nanostructures formed on titanium dioxide films by femtosecond laser irradiation regulated cell alignment along the structures [16].

In this study, the nitinol surface was modified using the femtosecond laser technique. Hierarchical periodic arrays with nano- and/or micro-structures were obtained on the nitinol substrate depending on the laser fluence, which is the irradiation energy per unit area. The surface properties were investigated, as were the effects of the structures on the interaction between the surfaces and endothelial cells or platelets.

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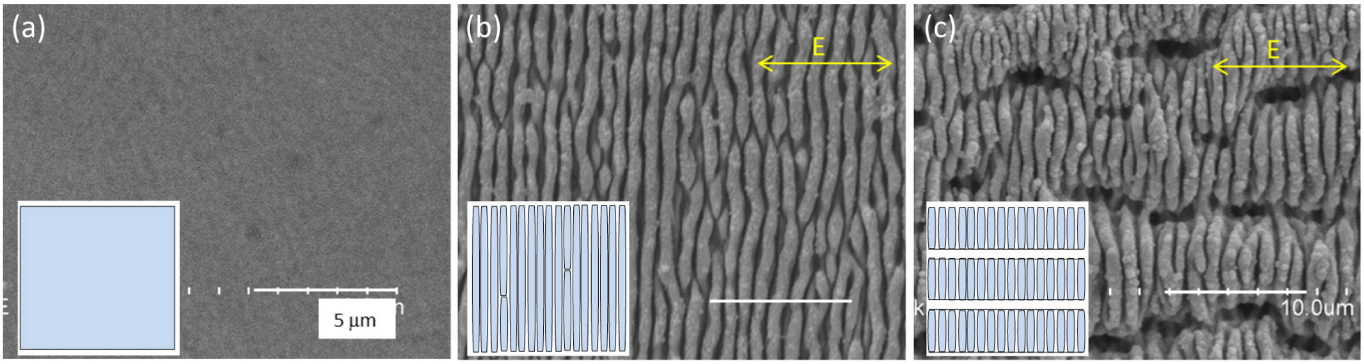

Fig. 1. SEM images of nitinol with and without femtosecond laser irradiation and the schema of their designed pattern. (a) As-polished, (b) nano-, and (c) micro/nano-surface. Scale bars, 100 μm.

2. Materials and methods

2.1. Sample preparation

Nitinol discs (ϕ6 mm × 2 mm) were cut from a rod and successively ground using 320# and 600# waterproof abrasive paper (creating the as-polished surface). The samples were then ultrasonically cleaned in acetone, ethanol and distilled water. Next, the discs were irradiated with a femtosecond Ti:sapphire laser, at two laser fluences, 0.2 and 0.8 J cm^{-2} in air. The experimental setup was performed as described in detail in our previous study [16]. The wavelength, pulse duration, and repetition rate of the femtosecond laser were 775 nm, 150 fs, and 1 kHz, respectively. The average laser scanning speed and hatching distance were 1 mm/s and 15 μm, respectively.

2.2. Surface morphology

The surface morphologies of the prepared specimens were observed using scanning electron microscopy (SEM, Hitachi S-3400NX, Tokyo, Japan) at 10 kV. The surface roughness values of the specimens were investigated using atomic force microscopy (AFM, SPM-9700, Shimadzu, Kyoto, Japan). Each sample was imaged with a 30 μm × 30 μm piezoscanner and a silicon nitride cantilever (Olympus, Tokyo, Japan) operated in the contact mode.

2.3. Contact angle measurements

Contact angle measurements were performed using the sessile drop method at room temperature with a commercial contact angle meter (Kyowa Interface Measurement and Analysis System, Tokyo, Japan) [17]. A 1.0 μl droplet of distilled water was dropped from the tip of a microliter syringe. Three samples from each group were used for the measurements.

2.4. X-ray photoelectron spectroscopy (XPS)

XPS was performed using an electron spectrometer (JPS-9010MC, JEOL, Tokyo, Japan) with a Mg Kα line (1253.6 eV). The binding energies were calibrated using the energy of the C 1s peak of contaminant carbon, i.e., 285.0 eV. The take-off angle of the photoelectron was 90° from the surface of the alloy. To estimate the photoelectron peak intensities, the background was subtracted from the measured spectrum according to Shirley's method [18].

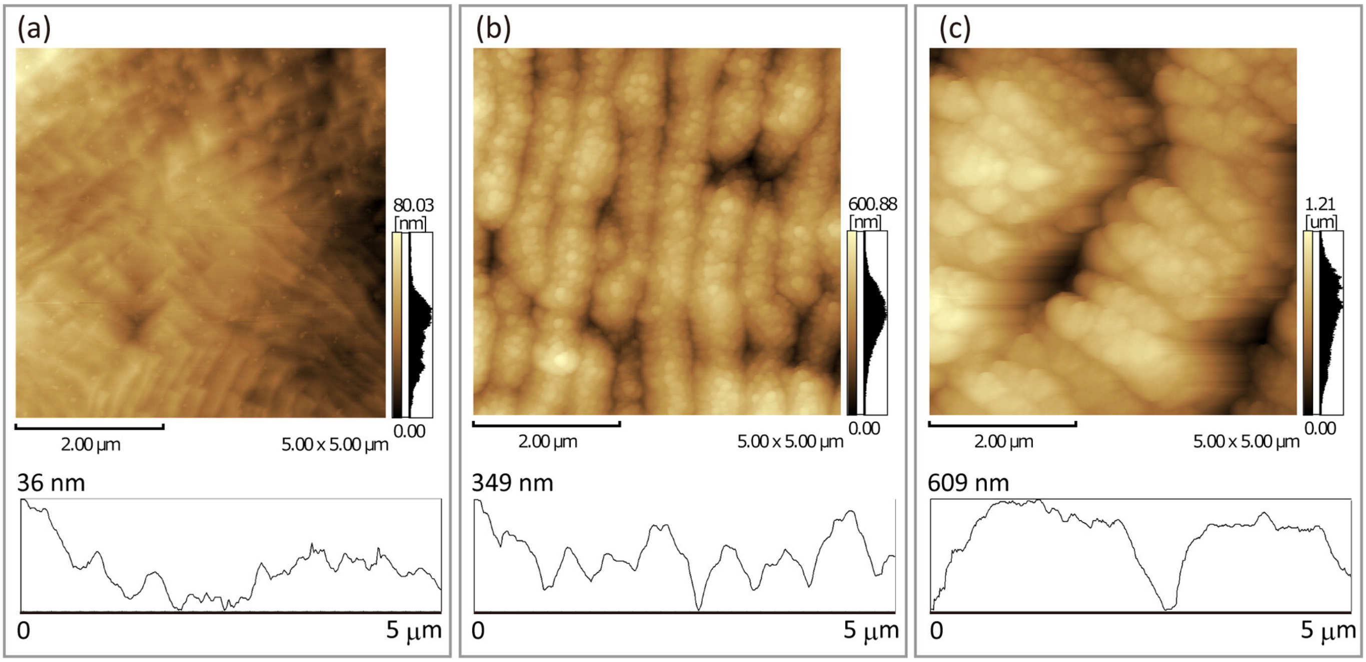

Fig. 2. AFM images and section analysis of the (a) as-polished, (b) nano-, and (c) micro/nano-surfaces. All profiles were measured within a 5 μm × 5 μm AFM scan area.