ARTICLE IN PRESS
SCT-21092; No of Pages 5
Surface & Coatings Technology xxx (2016) xxx–xxx
Contents lists available at ScienceDirect
Surface & Coatings Technology
journal homepage: www.elsevier.com/locate/surfcoat

Recent advances in anti-infection surfaces fabricated on biomedical implants by plasma-based technology

Ang Gao [a], Ruiqiang Hang [a,b], Paul K. Chu [a,*]

[a] Department of Physics and Materials Science, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, China
[b] Research Institute of Surface Engineering, Taiyuan University of Technology, Taiyuan 030024, China

ARTICLE INFO

Article history:
Received 5 January 2016
Revised 8 April 2016
Accepted in revised form 8 April 2016
Available online xxxx

Keywords:
Anti-infection surface
Plasma immersion ion implantation and deposition
Magnetron sputtering
Micro-galvanic couple
Schottky barrier

ABSTRACT

Infection is one of the major post-surgery complications in orthopedics and dentistry and plasma-based technology is effective in mitigating infection by introducing antibacterial agents into the biomedical implants. By selecting the proper elements and operating parameters in the plasma-based processes, anti-infection and osseo-integration can be accomplished simultaneously. In this mini-review, recent advance in the design and construction of anti-infection surfaces by plasma-based techniques is discussed with emphasis on plasma immersion ion implantation and deposition (PIII&D) and magnetron sputtering. The underlying mechanisms are discussed and a better understanding enables the design and fabrication of better anti-microbial surfaces.

1. Introduction

Implant-related infection is one of the most intractable complications in orthopedics and dentistry [1]. It commences with adhesion and colonization of pathogenic bacteria on the implant surface followed by the formation of biofilms which are highly resistant to antibiotics and the host immune system [2–6]. After biofilms are formed, it is difficult to treat thereby resulting in chronic suffering and even requiring removal of the dysfunctional implants in serious cases [7]. Surface treatment or deposition of coatings that incorporate bactericides is a direct and effective means to inhibit initial adhesion and kill bacteria to prevent post-surgery infection [8]. Compared to organic antibiotics, inorganic antibacterial agents such as silver (Ag), copper (Cu), and zinc (Zn), especially those with a nanoscale structure, possess advantages including good stability, broad-spectrum antibacterial properties, and low risk of occurrence of resistance [9,10]. In the case of Ag, although the antibacterial mechanism is still not completely understood, release of silver ions (Ag^{+}) that induce inactivation of bacterial proteins, condensation of DNA, and degradation of bacterial cell membranes appears to play a major role [11]. Since the host cells can be similarly impacted by these mechanisms, loading of these bactericides should be optimized to ensure minimal adverse effects and even promotion of host tissue integration simultaneously.

* Corresponding author.
E-mail address: paul.chu@cityu.edu.hk (P.K. Chu).

http://dx.doi.org/10.1016/j.surfcoat.2016.04.020
0257-8972/© 2016 Published by Elsevier B.V.

Plasma-based techniques are widely used to improve the surface properties of biomaterials [12]. From the perspective of anti-infection, plasma immersion ion implantation and deposition (PIII&D) is attractive because of the non-line-of-sight nature which bodes well for biomedical implants with a complex shape and it is easy to control the dopant concentration and depth [13]. Magnetron sputtering is also effective in incorporating antibacterial agents into the materials. By selecting the optimal processing parameters, both the antibacterial ability and biocompatibility can be improved. This mini-review aims at highlighting recent major advances in fabricating anti-microbial surfaces suitable for orthopedic and dental applications by plasma-based techniques. Attention is paid to the newly proposed antibacterial mechanisms based on the micro-galvanic couple and Schottky barrier.

2. Plasma immersion ion implantation and deposition

PIII&D, a versatile technique that can introduce a myriad of elements into the host materials, enables doping or synthesis of embedded nanoparticles in the near-surface of the substrate [14]. For example, as shown in Fig. 1b–d, after Ag is implanted into titanium by Ag PIII at an acceleration voltage of 30 kV for 0.5 h, 1 h, and 1.5 h, metallic Ag nanoparticles are homogeneously distributed on the surface [15]. As the implantation time is increased, the particles become larger (comparing Fig. 1c and d with Fig. 1b) and the Ag concentration goes up (Fig. 1e). During Ag PIII, when the local concentration exceeds the solubility limit, the system relaxes by nucleation leading to growth of Ag nanoparticles (NPs). On account of surface sputtering [16], some Ag NPs in the near

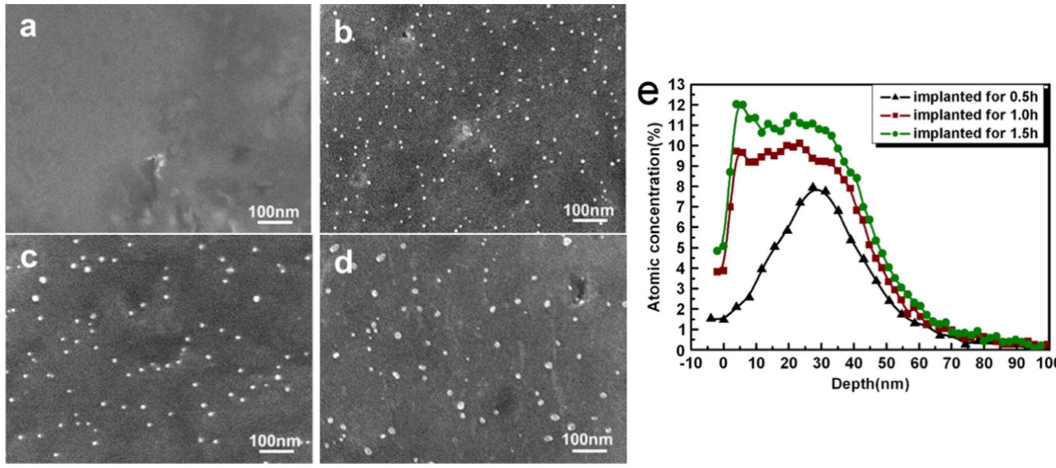

Fig. 1. SEM images of the titanium surfaces (a) before and (b–d) after Ag-PIII performed at the accelerating voltage of 30 kV for different durations: (b) 0.5 h; (c) 1.0 h; and (d) 1.5 h. The Ag NPs are dispersed on the surfaces and become larger when the implantation time is increased. (e) Silver depth profiles obtained from XPS after Ag-PIII for different durations [15].

surface are exposed. The Ag implanted surface has good antibacterial activity as it imposes bacteriostatic and bactericidal effects on both *Staphylococcus aureus* and *Escherichia coli* [17]. The anti-infection ability has also been verified *in vivo* by an implant-related infection model in rats [17,18].

The antibacterial mechanism of Ag NPs depends on the materials and environment. Besides the aforementioned release-killing ability, antibacterial mechanisms based on the micro-galvanic couple and Schottky barrier have recently been proposed when Ag is implanted into metallic and semiconductor substrates, respectively. By adjusting the ion implantation parameters, the ion concentration and depth distribution can be readily varied and consequently, the antibacterial ability can be controlled or optimized by careful manipulation of the implantation parameters.

2.1. Micro-galvanic couple

In corrosion science, a galvanic couple is established when two kinds of metals are in electrical contact with each other in a conducting corrosive environment. When Ag is implanted into a metallic substrate such as Ti to create Ag NPs, an antibacterial mechanism based on the galvanic couple is expected [15,17,18]. As shown in Fig. 2a, after the Ag implanted surface is immersed in a physiological liquid, a galvanic couple between each embedded metallic Ag NP and Ti matrix is triggered due to their different standard electrode potentials (−1.630 V for Ti and 0.7996 V for Ag). Owing to anodic protection rendered by the Ti matrix, only a small amount of Ag ions is released and hence, the direct antibacterial effects of Ag ions can be neglected. The Ti matrix serves as the anode and releases Ti ions (Ti^{n+}) by the anodic reaction $Ti \rightarrow Ti^{n+} + ne^-$. The generated electrons are transferred to the Ag NPs (red arrows) where they are captured by the electron acceptor according to the cathodic reduction reactions such as $2H^+ + 2e^- \rightarrow H_2$. Therefore, the protons (H^+) adjacent to the Ag NPs are continuously consumed and a proton depleted region is formed eventually. When bacteria approach the surface, the proton gradient in their intermembrane space will be disrupted. Since the proton gradient is requisite to maintaining the energy-dependent reactions in bacteria, its disruption eventually causes death of the bacteria. Hence, the antibacterial ability of the Ag PIII&D surface can be ascribed to the galvanic couple built between the embedded Ag NPs and metallic substrate.

Besides Ag, Zn [19] and Mg [20] have been implanted into Ti by PIII&D to take advantage of their antibacterial ability [9,21] as well as their capability to stimulate bone formation, since they are essential elements involved in many metabolic and cellular signaling pathways [22–24]. Although both *in vitro* and *in vivo* tests demonstrate the superior osteogenic activity, the bacteriostatic effects of individual Zn PIII or Mg PIII are not sufficient to prevent infection [19,20,25]. Therefore, dual-element PIII of Ag and Zn (Ag/Zn PIII) [26] or Ag and Mg (Ag/Mg PIII) [20,27] has been performed to enhance the antibacterial ability. In these situations, owing to the more negative standard electrode potentials, Zn and Mg replace the Ti matrix to be the anode forming the galvanic couples with the Ag NPs (Fig. 2b). Zn^{2+} and Mg^{2+} are then released because of galvanic corrosion after exposure to the physiological medium. As bacteria transport ions by energy-consuming processes, the presence of these ions in the microenvironment makes the living conditions of the bacteria harsher. Moreover, the Ag NPs serve as the cathode

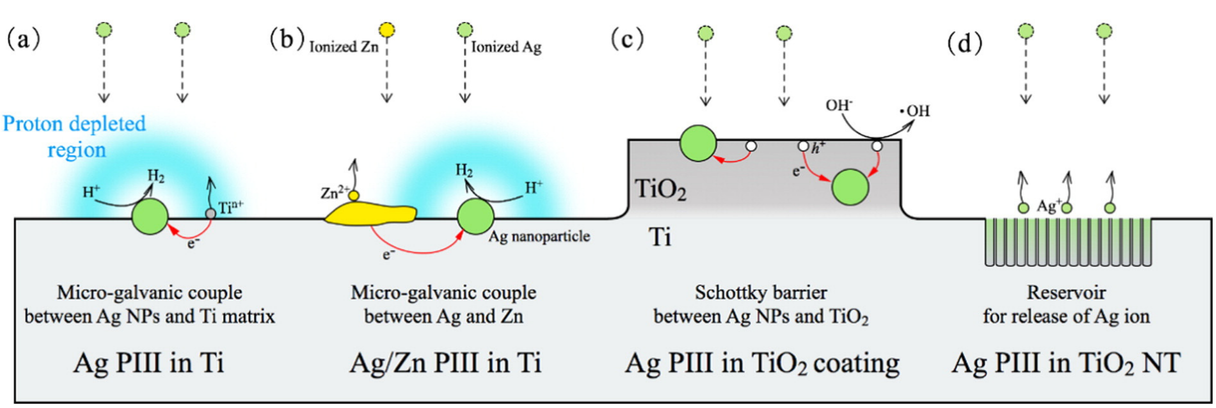

Fig. 2. Schematic illustration of the common strategies to prepare antibacterial surfaces suitable for orthopedic and dental applications by PIII&D.