

Titanium nitride-based coatings on implantable medical devices

I. Gotman* and E.Y. Gutmanas

Department of Materials Science and Engineering, Technion, Israel Institute of Technology, Haifa, 32000 Israel

Physical and chemical surface properties play an important role in the performance and clinical success of implantable devices. Once a prosthetic device is implanted, its surface becomes a site of various biochemical reactions and bacterial adhesion, as well micromotion and gross sliding. All these events can contribute to a less than optimal host response and eventually lead to the prosthesis failure. Creation of a surface coating is an attractive approach to alter the interaction of the implant with its surroundings since it allows modification of surface characteristics without changing the bulk material properties. Titanium nitride hard coatings have a long history of clinical use, especially on bearing surfaces of joint replacements. Moreover, there is an accumulating body of evidence suggesting that titanium nitride-based thin layers applied to non-articulating surfaces of various orthopaedic and blood-contacting implants result in improved clinical outcomes. Beyond the biological and functional requirements, a durable coating must strongly adhere to the device, i.e. be mechanically and chemically compatible with the substrate. The coating method (deposition vs. diffusion) has an important role to play in the adhesion of titanium nitride films.

This paper is an overview of the current state-of-the-art of titanium nitride-based coatings on medical implants, methods of their deposition, *in vitro* properties, *in vivo* behavior and clinical performance.

Keywords: titanium nitride (TiN), physical vapor deposition (PVD), diffusion coating, powder immersion reaction assisted coating (PIRAC), adhesion, artificial joints, wear simulation tests, titanium nitride oxide (TiNOX), blood-contacting properties, stents

1. Introduction

When implanted in the human body, medical devices come in contact with a complex and highly dynamic environment of mechanical stresses and aggressive biological fluids. The performance of these implantable devices, therefore, depends upon both bulk and surface properties of biomaterials they are made of. The bulk properties determine the mechanical behavior of the implant whereas the surface characteristics control the interactions that take place between the implant and the components of the body (biocompatibility). In many cases, the right balance between these two sets of properties is difficult to achieve and the surface characteristics of a biomaterial chosen for its favorable bulk properties are less than ideal for the intended application within the human body. Metals, primarily medical grade stainless steel, cobalt-chromium-molybdenum alloys and titanium and its alloys, are biomaterials of choice for load-bearing medical devices due to their excellent bulk properties—high strength, toughness and ease of process-

ing. All these metals, however, are prone to corrosion and wear in physiological solutions to various extents. These less than optimal surface characteristics often lead to adverse host reactions, lack of integration and eventual failure of both orthopaedic and blood-contacting implantable devices. One of the approaches to improving the surface characteristics of metallic implants without compromising their bulk properties is the deposition of a biocompatible, wear resistant, corrosion resistant coating.

Titanium nitride (TiN) hard coatings have been used extensively to improve the hardness, friction and corrosion resistance of surfaces in tool drilling, cutting, etc. This is also the hard coating with the longest (around 25 years) history of clinical use. Already in 1988, a patent was granted for a method of applying a thin layer of TiN onto orthopaedic implants [1]. Hip, knee and ankle joint replacements whose articulating surfaces are coated with TiN or TiN-based (TiNbN) layers are commercially available from several companies in Europe, North America and Asia (Fig. 1).

The rationale behind using titanium nitride as a wear resistant coating in joint arthroplasty is its high hardness (HV 2400–2800), high scratch resistance, low friction coefficient and good wettability by synovial fluids. TiN is physiologically inert, non-toxic and not carcinogenic, and

* Corresponding author

Irena Gotman, e-mail: gotman@technion.ac.il



Fig. 1. Examples of commercially available titanium nitride-coated joint replacements: TiNbN-coated CoCoMo alloy total hip replacement (Van Straten Medical) (a); TiN-coated Ti alloy articulating unit of total hip replacement (Endotec) (b); TiN-coated total knee replacement (CELLUMED) (c); TiNbN-coated CoCoMo alloy ACCIS hip resurfacing device (Van Straten Medical) (d).

its use in implantable devices is approved by FDA [2]. The golden colored TiN coatings can be deposited on stainless steel, CoCr or titanium alloy components. Both the medical grade stainless steel (316 and 316L) and CoCr alloys contain Cr and a certain amount of Ni ions that, when released in the body fluids, are known to cause allergic reactions. Coating CoCr articulating surfaces with TiN has been reported to reduce the release of these metal ions into the body fluids [3, 4]. Titanium alloys (e.g. Ti6Al4V) are currently used in implant surgery because of their excellent corrosion resistance/biocompatibility and because of their low elastic modulus preventing the stress shielding of peri-prosthetic bone. However, the use of titanium alloys in sliding and bearing applications is curtailed by their poor tribological performance under abrasive and adhesive wear [5]. Applying a thin TiN surface layer to articulating joint replacement components made of Ti alloys may provide them with the required high wear resistance. Such TiN-coated Ti alloy parts can be offered as substitutes to the traditional CoCr components in both knee and hip systems, e.g., for metal-sensitive patients.

Coatings adhesion is one of the most critical aspects of any coating-substrate system and a key indicator of the long

term performance of the coated component [6]. Coatings with weak adhesion can delaminate from the substrate as a result of internal residual stresses developed during processing and/or as a result of stresses and strains experienced during clinical use. This is particularly important in tribological applications such as artificial joints, where coating detachment from articulating surfaces can lead to an aggravated wear situation. Not only that the underlying (softer) substrate becomes exposed; partial delamination of the coating also leads to surface roughening which increases the wear rate of the counterpart material. In addition, hard coating flakes can work as abrasive particles on the surfaces in tribological contact [7]. The adhesion of ceramic coatings on metal alloys depends on the film properties (thickness, microhardness) and substrate characteristics (material, surface quality, hardness), as well as on the structure and properties of the interfacial zone. The latter is the strong function of the coating method used. Numerous methods currently exist to create ceramic films on the surface of a metal [8]. The concept of physical or chemical vapor deposition (PVD or CVD) methods is to deposit a ceramic coating onto the metal surface, Fig. 2a. Due to the sharp change of properties at the ceramic–metal interface, these externally

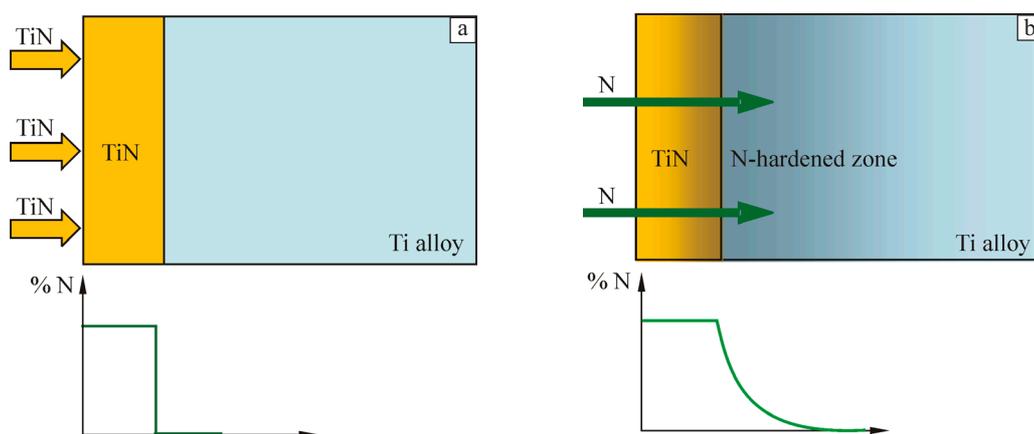


Fig. 2. Schematics of externally applied (PVD, CVD) (a) and diffusional (b) titanium nitride coatings on Ti alloy substrate with typical nitrogen depth profiles. Note an abrupt change of nitrogen concentration in (a) vs gradual change of nitrogen concentration in (b) at the ceramic–metal interface.

applied coatings carry a potential for adhesive failure and have not been quite reliable under load or during articulation. Another, a much less industrially exploited class of ceramic coatings are surface films created by reactive diffusion of a non-metallic element (e.g., nitrogen) into the surface, Fig. 2b. In contrast to externally applied PVD/CVD layers, such diffusional coatings are characterized by a gradual change of properties at the ceramic–metal interface which has a beneficial effect on coating adhesion and durability. One disadvantage of this approach is that the process is limited by diffusion and very long processing times may be needed to grow coatings sufficiently thick to provide artificial joints with long lasting wear resistance.

Along with the documented wear studies and clinical tests of hard TiN coatings as bearing surfaces of joint replacements, there is an accumulating body of evidence suggesting that titanium nitride-based thin layers applied to non-articulating surfaces of various orthopaedic and blood-contacting implants result in improved clinical outcomes. In the present paper, the processing methods and microstructure of titanium nitride-based coatings, as well as their *in vitro* properties, *in vivo* behavior and clinical performance are reviewed.

2. Titanium nitride coatings by physical vapor deposition (PVD)

2.1. PVD techniques of TiN deposition

Commercial TiN-based coatings on stainless steel, CoCr and Ti alloy implants are applied by physical vapor deposition. Physical vapor deposition is a generic term for a large family of vacuum deposition techniques where a solid source (target) is converted into vapor by physical means [9, 10]. The coating process consists of three main steps: (i) evaporation—removal of material from the target; (ii) transportation of the plasma constituents to the substrate; and (iii)

condensation of the coating on the substrate. The source material for producing TiN coating is pure titanium, and nitrogen gas is introduced during the evaporation process. Nitrogen reacts with the ionized titanium vapor to form a TiN compound that is then deposited on the substrate as a thin film.

The quality of generated plasma material depends on the method of producing metal vapor, the main technologies being arc evaporation (AE), electron beam (E-beam) evaporation and sputtering. The positively charged plasma constituents travel to the negatively charged substrate in straight lines; thus, only areas exposed to the plasma are coated making physical vapor deposition a “line-of-sight” process.

In physical vapor deposition by evaporation, the conversion into vapor phase is achieved by applying thermal energy to the source material [11]. In electron-beam evaporation (EB-PVD), a focused high kinetic energy electron beam is used to melt the source material in a crucible and to evaporate into partially ionized gaseous phase. Coatings produced by electron-beam evaporation are smooth, dense and defect free. The coating thickness, however, is limited to the volume of the crucible, and film adhesion is poor.

In cathodic arc physical vapor deposition, titanium (or another metal) is vaporized from a solid target (cathode) by means of an electric arc. The extremely high temperature at the small (a few micrometers) cathode spot leads to the local melting, evaporation and ionization of the source material. Magnetic fields are used to rapidly move the arc (and the cathode spot) over the entire surface of the target, so that the total surface is eroded over time. Due to the high kinetic energy of the depositing species (much greater than in other physical vapor deposition processes), a several nanometer thick intermixed layer of the substrate and coating can be formed which improves coating adhesion while minimizing residual stresses. The main drawback of this

technique is the emission of micrometer-sized liquid droplets of the target material from the arc spot. These particles can be trapped in the growing film and extend through the coating thus strongly deteriorating its physical and mechanical properties.

Sputtering is one of the most versatile physical vapor deposition processes available for various metallic and ceramic (carbide and nitride) thin film preparation [12]. In the basic sputtering process, a target (or cathode) plate is bombarded by energetic ions (typically ionized inert gas such as argon) generated in a glow discharge plasma, situated in front of the target. The bombardment process causes the removal, i.e. “sputtering”, of target atoms, which may then condense on a substrate as a thin film [11]. Using a magnetic field to trap secondary electron emission near the surface of the target (magnetron sputtering) results in a denser plasma on the target surface which leads to higher sputtering and, correspondingly, higher deposition rates. Sputtered films are typically denser and have a better adhesion to the substrate than evaporated films, however they have higher compressive stresses and a higher (compared to deposition via evaporation) level of impurities that can be introduced into the growing film due to the use of heavy sputtering atoms.

Regardless of technology used, all the PVD coatings are grown by adding a new material to the surface and do not involve the substrate material constituents. Moreover, physical vapor deposition processes are typically carried out at low substrate temperatures (180–500 °C) which allows for coating deposition without detrimentally affecting bulk properties. On the other hand, only physical (rather than chemical) bond is created between the coating and the substrate often leading to weak coating adhesion.

2.2. Adhesion of PVD TiN coatings

Under many tribological situations, hard coating/soft substrate systems rarely fail due to conventional wear but rather by fracture of the coating (cohesive failure) or debonding of the coating from the substrate (adhesive failure) [13]. From the practical point of view, the adhesion of a coating to the substrate is a function not only of fundamental adhesion (i.e. chemical bonds across the interface) but also of many other factors such as coating thickness and mechanical properties, residual stresses (arising from the fabrication process) and mechanical properties of the substrate. As the low temperature physical vapor deposition process does not generally involve diffusion phenomena and chemical reactions at the coating–substrate interface, the adhesion between the substrate and the hard layer is weak. Technically, the bonding strength of PVD coatings can be improved, to some extent, by removing contaminations from the substrate surface prior to layer deposition. This, however, requires elaborate and high-cost cleaning operations.

Coating detachment in areas where the coated surface is exposed to mechanical wear is the dominant failure mode of PVD TiN coatings. High residual stresses associated with ceramic PVD films on metal substrates [14] could be one of the reasons of TiN layer failure. Tensile stress in the coating causes through-thickness microcracking while compressive stress tends to promote microcrack propagation along the interface. It has been shown by a scratch test that 1.2–1.7 μm thick TiN coatings applied on Ti alloy substrates by arc ion plating (AIP) are prone to localized adhesive failure [15]. In addition, the wear behavior of TiN layer, both in abrasion and adhesion, is strongly deteriorated by the presence of coating defects such as pinholes and embedded microparticles [16, 17]. These defects are typically formed due to deposition of droplets during the coating process and their subsequent removal or leveling-off by post-coating polishing.

Under the synergistic action of corrosion and wear, both pinholes and prior mechanical damage (caused for example by third body abrasion *in vivo*) make TiN coated implant surfaces more vulnerable to subsequent corrosion. In these defects, galvanic corrosion between the relatively passive coating and the relatively active small exposed substrate surface can lead to blistering and localized loss of the TiN coating [15, 17]. Accelerated corrosion of the underlying substrate at microdefects present in PVD TiN coating was observed for both Ti alloy and CoCr substrates [15, 18]. The process of the localized TiN layer loss is assumed to be further promoted by the relaxation of residual stress in the coating.

The less than optimal wear performance of PVD TiN-coated articulating implants is also attributed to the low hardness of the substrate immediately beneath the hard nitride thin film and the sharp transition of hardness and elastic modulus across the PVD coating/substrate interface [19]. The sudden change of properties is due to the fact that little or no diffusion across the film/substrate interface and, subsequently, no subsurface strengthening take place at the low temperature of the physical vapor deposition process. When load is applied to the hard TiN physical vapor deposition film on a relatively soft metallic substrate, plastic deformation is always initiated in the substrate material at the coating/substrate interface. The yielding substrate is unable to support the coating while the hard TiN film is unable to accommodate the deformation, so the coating fractures just like the shell of a boiled egg and triggers catastrophic third-body wear [20]. This typically occurs under point contact loading caused by debris particles between the articulating surfaces, or contact with hard components like the rim of the metal shell of the cup, or in the area of point-and-line contact in total knee arthroplasty. The “eggshell-effect” is more pronounced for the softer substrates, e.g. Ti alloy. The failure of EB-PVD TiN films (Tecvac Ltd, Cambridge) on Ti6Al4V substrates after cyclic loading tests [5] demon-

strates the need to provide substrates with enhanced load-supporting characteristics.

2.3. PVD TiN layers as wear-resistant coatings on joint replacements

Joint arthroplasty is a highly successful and cost effective surgical procedure for the treatment of osteoarthritis or inflammatory arthritis of the hip and knee. Over the past decade, indications for joint replacement procedures traditionally offered to older adult population, have expanded into younger and more active patients. This resulted in demands for a greater service life of artificial joints with the target life-expectancy longer than the patient who receives the prosthesis.

One limitation for the longevity of joint replacements is related to the wear of their articulating components. The phagocytosis of wear debris particles by macrophages is believed to lead to periprosthetic bone resorption (osteolysis) and subsequent implant fixation failure. Such ‘aseptic loosening’ of the prosthesis may necessitate a revision (reoperation), which is the definitive measure of clinical failure of a joint arthroplasty.

Different material combinations are used as joint bearings for hip and knee arthroplasty but the ideal bearing couple is yet to be developed. Both metal-on-metal (CoCrMo-on-CoCrMo) and ceramic-on-ceramic (alumina-on-alumina) combinations have extremely low wear rates, significantly lower than the most commonly used bearing couple consisting of CoCrMo alloy articulating against ultra-high molecular weight polyethylene (UHMWPE). Although ceramic-on-ceramic bearings generate less debris, squeaking continues to be an issue, as well as concerns for brittle fracture of these components [21–24]. Metal-on-metal articulations have greatly reduced the volumetric wear rate of hip prostheses; however, because of nanosized metal wear particles, the absolute number of wear particles has greatly increased. This is believed to lead to increased blood levels of metal ions, and ultimately to an increased prevalence of metal allergy [25].

Creating a titanium nitride surface layer on a metallic substrate would provide the desired combination of the high fracture toughness of metals with the inertness and excellent wear performance of ceramics.

Determining if hard coatings are effective in reducing the wear of joint replacements requires the use of reliable wear testing techniques. Joint simulators are the standard tools for evaluation of wear resistance. Joint simulators are designed to reproduce the physiological kinematics and physical forces acting on the joint during movement, however they are still limited in their ability to simulate the lubrication conditions, the loads, and the motions that occur over a broad range of daily activities. Moreover, tribology and wear mechanisms are different for different joints, so results obtained on a hip simulator are not always relevant for a knee (or other joint) replacement. Thus, in or-

der to properly assess the potential of a hard coating to reduce *in vivo* wear rates, simulator tests should be conducted under a variety of conditions.

A limited number of hip or knee simulator comparisons of TiN-coated materials to traditional CoCr alloy or other coating options can be found in literature, and their results are rather contradictory. First hip simulator studies of titanium nitride coatings running against ultra-high molecular weight polyethylene were conducted by Pappas et al. back in 1990’s [26, 27]. The coatings were applied on wrought Ti6Al4V alloy by a proprietary physical vapor deposition process, and the tests were conducted in distilled water. The results of the first, 10 million cycle study [26] showed that under the same testing conditions, the wear of UHMWPE articulating against TiN-coated 32 mm femoral heads was 3 times lower than for the CoCr alloy heads of the same diameter. In the second study [27], 47 mm diameter femoral hip resurfacing cups with a polished 8 μm thick TiN coating were run against UHMWPE inserts for 48 million cycles. The wear of the TiN coating was $<2 \mu\text{m}$, and no delamination was observed. Minor wear, scratching and burnishing of the TiN surface were visible to the naked eye after 35 million cycles. Since no reference CoCr femoral cups were used in this 48 million cycle test, the wear of ultra-high molecular weight polyethylene was compared to the results for the CoCr heads from the previous, 10 million cycle study, and was found to be significantly lower. Due to the different geometry of the femoral components, however (47 mm diameter TiN-coated Ti6Al4V cups versus 32 mm diameter CoCr heads), the validity of such a comparison is questionable.

Another hip simulator study [28] compared, among others, the wear performance of TiN coatings on 28 mm diameter CoCr femoral heads articulating against UHMWPE acetabular cups. Approximately 10 μm thick TiN layers were deposited by AEPVD. Simulation studies were run for up to five million cycles in 25 % (v/v) bovine serum. Wear loss of polyethylene was determined volumetrically. TiN-coated heads produced polyethylene wear two times higher than the control uncoated heads. Although the authors observed no coating failure, a strong increase and a large scatter R_q of the total height of the surface roughness profile (from $0.490 \pm 0.240 \mu\text{m}$ before testing to $2.063 \pm 5.077 \mu\text{m}$ after testing) strongly suggests that localized loss of the TiN coating has occurred. At the same time, no roughening of the uncoated CoCr heads was observed after five million cycles which might explain the lower UHMWPE wear associated with these heads compared to the TiN-coated heads.

The same authors observed cohesive failure of a similar $\sim 10 \mu\text{m}$ thick arc evaporation AEPVD deposited TiN coating on a 28 mm CoCr femoral head after two million cycles wear simulation against an uncoated CoCr insert [29]. The wear of the TiN-coated heads was lower than the uncoated heads, but it caused relatively high wear of the cor-

responding CoCr inserts. It was hypothesized that Ti droplets remaining on the as-deposited TiN coating surface might have been an initial originator of cohesive failure.

In a different study [4], the same authors tested AEPVD TiN coated 28 mm diameter CoCr femoral heads articulating against similar coated CoCr inserts in 25 % (v/v) bovine serum. Wear loss was determined gravimetrically and converted into volume loss. Both TiN-coated heads and TiN-coated inserts demonstrated much lower wear compared to the traditional metal-on-metal prostheses. By the end of the two million cycles period, the overall wear of the coated couples was ~20-fold lower than for the uncoated ones. The concentrations of Co, Cr and Mo ions from the TiN-coated combination were at least 20-fold lower. At the same time, some localized damage to the TiN coating was seen on the coated heads even after the relatively short period of two million cycles corresponding to no more than two years *in vivo*. It may be hypothesized that larger areas of coating delamination and correspondingly higher wear would be observed if the test was continued for a longer time period.

Oñate et al. [30] tested the wear behavior of TiN coating in a simplified knee wear testing machine where the contact between femoral condyles and tibial plates is approximated by a ball-on-plate geometrical contact. A 3–4 μm thick TiN layer was produced by a proprietary ion plating physical vapor deposition process. 32-mm-diameter TiN-coated and uncoated CoCr femoral heads were subjected to a combined rolling-sliding motion against UHMWPE plates. The tests were run in distilled water as the lubricant for up to five million cycles. Wear evaluation of ultra-high molecular weight polyethylene plates was carried out by weight loss measurements. High wear loss occurred in the case of PVD TiN coated CoCr wearing against ultra-high molecular weight polyethylene. After five million cycles, TiN coating induced a UHMWPE wear five times higher than the control (uncoated) material. When the worn surfaces of the TiN coated balls were observed, small areas of approximately 70 μm without a coating were detected. These areas corresponded to hard phases of the CoCr microstructure in which the coating had not nucleated or adhered properly. According to the authors, detachment of the coating particles from these areas was responsible for the presence of scratches and the high weight loss of the UHMWPE plates.

In [31] CoCr femoral components coated with titanium niobium nitride (TiNbN) via physical vapor deposition were tested in a knee simulator against UHMWPE tibial inserts. The test was run at 1 Hz in a standard walking cycle at a temperature of 37 °C using 30 % fetal calf serum and 0.8 % sodium azide as a lubricant. In the course of five million cycles experiment, the bare CoCr component experienced a much more pronounced roughening than the TiNbN-coated ones. However, the asymmetrical distribution of surface roughness in TiNbN-coated specimens may be in-

dicative of coating detachment. According to the authors, the TiNbN layer was intact to the naked eye at the end of five million cycles however no microscopic examinations were performed. Coating CoCr femoral components with TiNbN produced no obvious improvement in UHMWPE wear as measured gravimetrically and by surface profiling. The authors, therefore, conclude that despite the lack of benefit in terms of polyethylene wear TiNbN-coated implant may be an option for patients with metal ion allergies.

Weisenburger et al. [32, 33] tested metal-on metal total hip resurfacing specimens with 44 mm diameter PVD TiN-coated and uncoated CoCr femoral heads, acetabular liners, and acetabular shells on a hip simulator. The specimens were mounted anatomically and were lubricated with bovine serum diluted with deionized water to have 20 g/l protein concentration at 37 °C. The specimens were subjected to the loading and rotations of the walking cycle at 1 Hz. Over five million cycles (Mc), the uncoated heads displayed a wear rate of 1.84 ± 0.18 mg/Mc while the coated femoral heads wore at 4.37 ± 2.01 mg/Mc. Wear results were similar in the case of the uncoated and coated metal acetabular liners (1.35 ± 0.11 mg/Mc and 4.16 ± 2.06 mg/Mc, respectively). However, all three TiN coated specimens displayed a loss of coating on both the head and liner in the articulating region, Fig. 3. Extreme “run-in” wear was found on one TiN coated specimen. The higher wear observed on the coated specimens was likely due to the removal of the coating, and the coating particles causing third body wear (evidenced by higher level of scratching on coated components). According to the authors, the eventual loss of the TiN coating on all three coated specimens is of concern, as this coating is marketed commercially in some parts of the world.

The same authors reported the results of extended testing of TiNbN-coated 65 mm femoral components on a force-control knee simulator against conventional UHMWPE tibial inserts [34]. Over eight million cycles, UHMWPE tibial inserts paired with TiN-coated femoral components wore at ~ 11.2 mg/Mc while the control insert wore at ~ 9.0 mg/Mc. Similarly to the above hip simulator test, all TiNbN-coated components clearly showed loss of coating in the articulating region which increased in size as the tests progressed. Third body wear from the coating removal debris (evidenced by scratches) must have caused the higher polyethylene wear observed with the coated specimens. The authors suggested that the coating process had to be altered to create a more durable coating able to withstand many years of articulation within the body.

Bell and Fisher [35] performed wear simulation comparison of a total ankle replacement (TAR) whose talar and tibial components are CoCr alloy (Mobility, DePuy International) with the Buechel Pappas (BP) total ankle replacement whose metallic components are made of PVD TiN-coated titanium alloy. It is important to mention that TiN-coated BP prosthesis is one of the few total ankle replace-

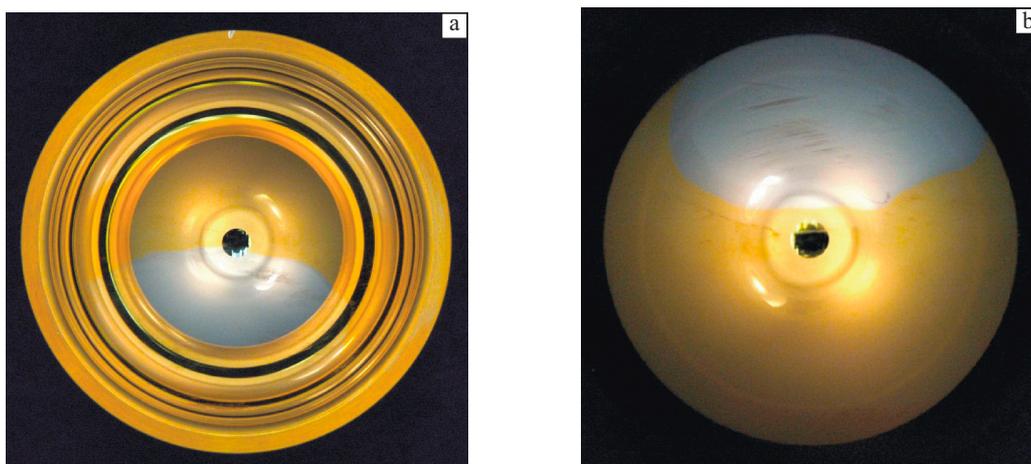


Fig. 3. TiNbN-PVD-coated femoral head (a) and acetabular liner (b) showing clear areas of coating removal following a 5 million cycle simulation test [33].

ment designs with a good clinical history. The simulator tests were run in 25 % (v/v) bovine serum for six million cycles. No statistically significant difference was observed between UHMWPE wear bearing against TiN-coated titanium alloys and uncoated CoCr alloy.

The results of different wear simulation tests with PVD TiN-coated joint prostheses are summarized in Table 1. Despite some inconsistency in findings, the results of laboratory simulation testing point at the problematic aspect of PVD TiN coating adhesion.

Although *in vitro* wear simulation tests reviewed do, to some extent, approximate *in vivo* conditions, they cannot completely replace animal testing because of their inability to reflect the true complexity of biological and mechanical processes around joint replacements. Unfortunately, practically no animal studies evaluating the performance of TiN-coated bearing surfaces have been reported in literature. One of the possible reasons could be the lack of an accepted animal model of the human hip and knee [36–38].

Scarce literature information is available concerning the clinical performance of surface modified wear resistant joint replacements in general and of titanium nitrided-coated implants in particular. Several studies of titanium nitride coated components have reported good clinical outcomes, but they do not describe the condition of the articulating surfaces in any detail [39–42]. In [43], the aseptic loosening of the femoral component in patients with cemented total hip replacement was more common (but not significantly different) with titanium nitride-coated titanium modular heads than with cobalt chrome modular heads. The comparison, however, was complicated by issues involving the bone cement and cementing technique.

Examination of a 32-mm-diameter PVD TiN-coated modular Ti6Al4V head of a hip prosthesis retrieved post-mortem one year after the arthroplasty surgery showed that wear debris can originate from a TiN-coated femoral head

as delaminated surface asperities and manifest as adhesive wear on the articular surface [44]. In [45], four cemented prostheses having Ti6Al4V alloy femoral stems and modular TiN-coated femoral heads articulating on UHMWPE counterfaces were harvested at revision from four patients 18 to 96 months after hip arthroplasty. TiN fretting and coating breakthrough occurred in two of the four examined components. The visible scratching of the other two components suggested that third body abrasion of the coating was taking place prior to implant failure. The authors concluded that TiN coated titanium alloy femoral heads were inadequate in the task of resisting *in vivo* third body wear and their use should not be advocated. It is worth mentioning, however, that the reported performance of physical vapor deposition TiN coatings may be partially due to the inadequate coating quality (non-uniformity, voids, titanium droplets) that can possibly be improved by polishing and a more stringent control and/or modification of the deposition process. Still, the reported failures of the coated joint replacements question the adhesive and cohesive durability of PVD TiN coatings.

3. Diffusional titanium nitride layers

Problems with weak adhesion and detachment of externally deposited PVD layers have led to the development of surface nitriding treatments that modify the surfaces to an increased depth [46, 47]. One such method is nitrogen-ion implantation that uses a highly energetic beam of ions that bombard a metallic titanium surface and become incorporated into it to increase hardness and to reduce friction [48]. Unfortunately, the depth of modification in ion implantation is very small (0.1–0.2 micrometers at typical energies of 50–100 keV) and cannot provide any significant improvement in wear behavior or load support from the substrate [49–51]. Much larger depths of modification can be

Table 1. A summary of literature reports on wear simulation tests of physical vapor deposition TiN-coated articulating components of joint replacements.

Articulating couple	Lubricant / test duration	Result	Reference
Hip simulator			
PVD-TiN-coated Ti6Al4V against UHMWPE	Distilled water 10 million cycles	Lower UHMWPE wear with TiN-coated Ti6Al4V than with CoCr alloy	[26]
PVD-TiN-coated Ti6Al4V against UHMWPE	Distilled water 48 million cycles	Lower UHMWPE wear with 47-mm TiN-coated Ti6Al4V femoral cups than with 32-mm CoCr femoral heads (see [149])	[27]
PVD-TiN-coated CoCr against UHMWPE	25 v/v bovine serum 5 million cycles	Higher UHMWPE wear with TiN-coated than with uncoated CoCr alloy Roughening of TiN coated head-TiN layer detachment?	[28]
PVD-TiN-coated CoCr against CoCr	25 v/v bovine serum 2 million cycles	Higher wear with TiN-coated than with uncoated CoCr alloy Cohesive failure of TiN layer	[29]
PVD-TiN-coated CoCr against PVD-TiN-coated CoCr	25 v/v bovine serum 2 million cycles	Lower wear for TiN-coated than for uncoated metal-on-metal couple Localized damage to TiN coating	[4]
PVD-TiN-coated CoCr against PVD-TiN-coated CoCr	Bovine serum 5 million cycles	Higher wear for TiN-coated than for uncoated metal-on-metal couple Loss of TiN coating	[32, 33]
Knee simulator			
PVD-TiN-coated Co-Cr against UHMWPE	Distilled water 5 million cycles	Higher UHMWPE wear with TiN-coated than with uncoated CoCr alloy Some detachment of TiN layer	[30]
PVD-TiNbN-coated CoCr against UHMWPE	Bovine serum 5 million cycles	Higher UHMWPE wear with TiNbN-coated than with uncoated CoCr alloy Loss of TiN coating	[34]
PVD-TiNbN-coated CoCr against UHMWPE	30% fetal calf serum + 0.8% sodium azide 5 million cycles	Similar UHMWPE wear with TiNbN-coated and uncoated CoCr alloy TiNbN layer intact to the naked eye Asymmetrical distribution of surface roughness in TiNbN-coated specimens- TiNbN layer detachment	[31]
Ankle simulator			
PVD-TiN-coated CoCr against UHMWPE	25 v/v bovine serum 6 million cycles	Similar UHMWPE wear with TiN-coated and uncoated CoCr alloy	[35]

achieved by nitrogen-diffusion-hardening methods. Nitrogen is diffused into the substrate at elevated temperatures, reacts with the metal and forms metal nitrides to impart hardness on the surface up to a certain depth. In contrast to physical vapor deposition, substrate material constituents are actively involved in the modified layer formation. Depending on the nitriding temperature and time, a several

micrometer thick compound layer consisting of two distinct titanium nitrides (TiN and Ti₂N) is obtained. This is followed by a several tens of micrometers thick diffusion zone—solid solution of nitrogen in titanium, α -Ti(N) [52–57]. Unlike the case of physical vapor deposition, the compound (nitride) layer that grows from the bulk material is supported by the hardened diffusion zone providing a gra-

dual hardness change across the subsurface layer. At relatively low temperatures (≤ 700 °C), no (or extremely thin) titanium nitride layer is formed on the surface and the increase in hardness is attributed to diffusion hardening [58].

3.1. Commercial nitriding methods

For successful diffusion treatment, nitrogen has to be in the atomic or ionic state. There are several commercial nitriding methods, the difference lying in nitrogen supply. In salt bath nitriding, the source of nitrogen is molten salt; in gas nitriding, nascent nitrogen is produced by dissociation of ammonia, and in plasma nitriding (ion nitriding), molecular nitrogen is split into ions in an electromagnetic field [59, 60]. Plasma nitriding is the preferred nitriding route for titanium alloys as it faster than traditional gas nitriding and provides close control of microstructure allowing nitriding with or without compound layer (TiN–Ti₂N) formation. Compared to the gas and salt bath nitriding, plasma nitriding is more environmentally friendly (does not use salts or ammonia that may be harmful to the workers) and results in less surface roughening. Plasma nitriding has several important drawbacks including limited temperature control, inhomogeneous plasma distribution and expensive equipment.

3.2. Powder immersion reaction assisted coating nitriding

Powder immersion reaction assisted coating (PIRAC) nitriding [61–64] has been proposed as an attractive alternative to conventional nitriding techniques. In PIRAC, Ti alloy parts to be coated are annealed at 700–900 °C in sealed chromium steel containers, Fig. 4. Chromium in the steel is a strong oxide-forming element and it reacts with atmospheric oxygen at the annealing temperature. The formation of Cr₂O₃ prevents oxygen from penetrating through the container walls, so that a very low partial O₂-pressure ($\leq 10^{-5}$ Pa) is maintained inside the container without application of any vacuum pumps. Nitrogen pressure inside

the container is built-up by inward diffusion of atmospheric nitrogen through the container walls which is made possible due to the low nitride-forming capability of the steel constituents (including Cr). Powders of thermodynamically unstable nitrides (e.g., Cr₂N or Mo₂N) can be used as an additional nitrogen source. These compounds will decompose in the container creating a certain partial pressure of nitrogen not exceeding, however, the equilibrium pressure of the corresponding nitride formation at a given temperature, e.g., ~ 135 Pa for Cr₂N at 900 °C [65]. Nitrogen atoms, either diffused from the atmosphere or created due to nitride decomposition, will reactively diffuse into the titanium alloy substrate forming a nitrided surface layer. As powder immersion reaction assisted coating is not a line-of-sight process, PIRAC coatings uniformly conform to the substrate, even when the treated parts are porous or have complex shape and geometry. Examples of powder immersion reaction assisted coating TiN-coated implants are shown in Fig. 5.

The structure and composition of PIRAC nitrided titanium surfaces are similar to plasma nitrided surfaces: a several micrometers thick outer layer of the titanium nitride compounds (TiN/Ti₂N) is followed by a tens of micrometers thick zone of nitrogen-hardened metal (α -Ti(N)) (Fig. 6). The nitrogen content and, correspondingly, the hardness of the solid solution zone decreases gradually away from the surface (Fig. 7) thus eliminating an abrupt mismatch in properties between the hard nitride layer and the soft metallic substrate. This gradient Ti(N) layer in PIRAC coatings provides an optimal support for the hard ceramic (TiN) film and allows it to withstand scratching and severe bending without delamination and spallation (Fig. 8) [63]. An additional factor in the excellent adhesion of PIRAC TiN coatings on Ti alloys may be the low level of residual stresses compared to PVD TiN layers [63].

The rationale behind selecting bending test for evaluating the adhesion of a ceramic coating to a metal substrate is as follows. During bending, considerably higher stresses are developed in the TiN coating having a 4-fold larger elas-

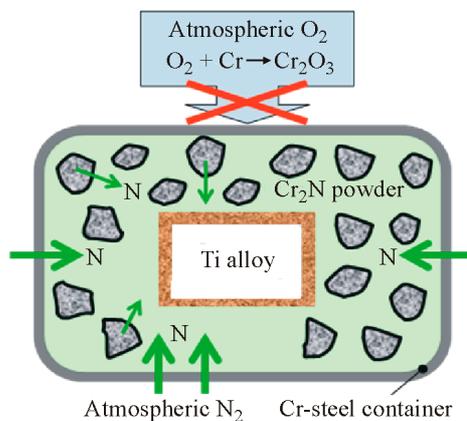


Fig. 4. A schematic of PIRAC nitriding process.

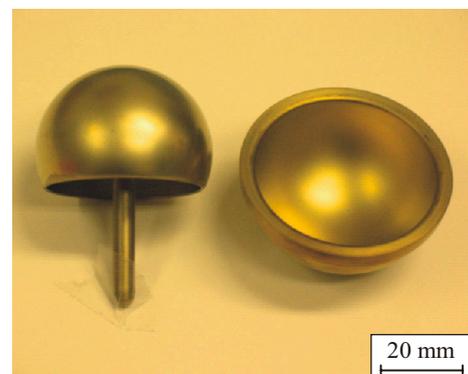


Fig. 5. PIRAC TiN-coated Ti6Al4V hip resurfacing implant.

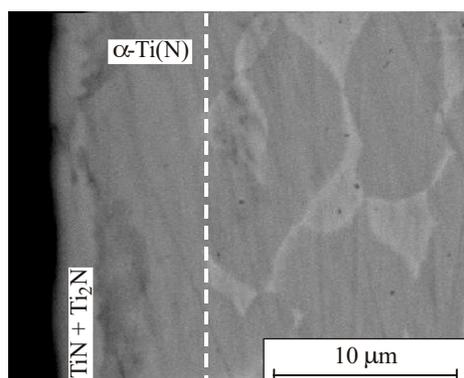


Fig. 6. SEM cross-section of Ti6Al4V alloy after PIRAC nitriding at 900 °C for 4 hours.

tic modulus than the Ti alloy substrate. While very thin coatings can deform elastically without delamination, thicker brittle coating films will either delaminate or crack (normally to the tensile strain direction) in the most highly strained area. If the adhesion is strong, cracking of the coating will occur before delamination. As the film thickness increases, however, the coating becomes stronger while the interfacial strength remains constant. This may lead to the failure mode transformation from coating cracking to coating delamination. By closely monitoring the load and the coating thickness at which the coating failure mode changes from fracture to interfacial delamination, the adhesion strength of the coating to the substrate can be evaluated.

One important consideration in PIRAC nitriding is the effect of the treatment temperature on the microstructure of Ti alloy substrate. As expected, nitriding Ti6Al4V components with the starting equiaxed α - β microstructure at temperatures not exceeding 950 °C (below β -transus) does not

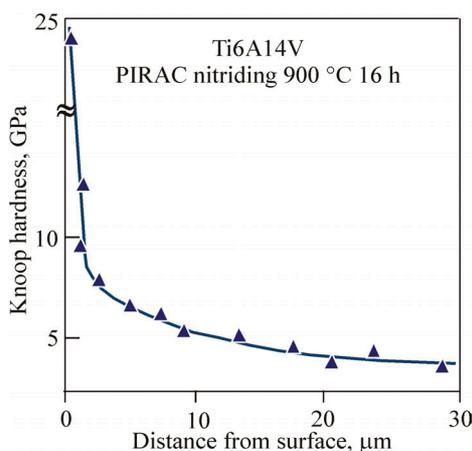


Fig. 7. Knoop microhardness profile of Ti6Al4V alloy PIRAC nitrided at 900 °C for 16 hours.

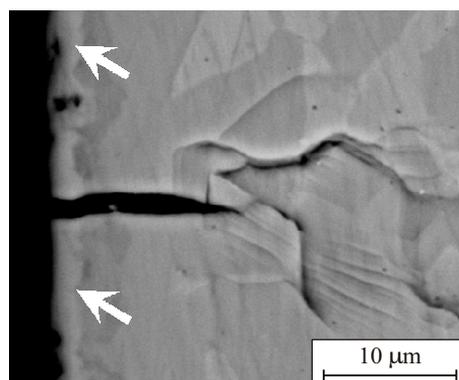


Fig. 8. SEM cross-sections of PIRAC-nitrided Ti6Al4V alloy specimen after three point bending test. Note the absence of delamination along the TiN-substrate interfaces (arrows).

lead to the formation of the undesirable lamellar $\alpha + \beta$ [61]. A certain coarsening of the microstructure takes place after longer exposures which may adversely affect the fatigue behavior of the nitrided component. To avoid coarsening, PIRAC nitriding can be performed at lower temperatures. It has been shown recently that PIRAC nitriding of Ti6Al4V at 700 °C for 48 h and at 800 °C for 4 h does not cause measurable microstructure coarsening and thus does not strongly deteriorate the fatigue strength of the alloy [66]. As for all diffusion controlled processes, however, PIRAC nitriding rate decreases exponentially with decreasing temperature and very thin coatings are obtained at low temperatures. Examples of PIRAC TiN coatings obtained after 8 and 48 hours exposure at 700 °C are shown in Fig. 9.

It can be seen that even at 48 h, the coating thickness including both the compound and solid solution layers does not exceed 3 micrometers. This is also confirmed by EDS depth profiles in Fig. 10. Similar nitrogen-diffusion zones were obtained after PIRAC coating treatments during 24 h at 750 °C or 8 h at 800 °C. The thickness of the TiN-Ti₂N compound layer increased with PIRAC temperature and time, however it did not exceed one micrometer even after 192 h at 700 °C and after 24 h at 750 and 800 °C. The relatively low surface microhardness values of Ti and Ti6Al4V alloy PIRAC nitrided at 700–800 °C (below 24–28 GPa typically reported for TiN), Fig. 11, confirm that the thickness of the hard ceramic surface layer is too small to completely mask the influence of the underlying substrate.

In order to obtain thicker diffusional TiN coatings, a combination of PIRAC nitriding and titanization treatments was employed [67]. In PIRAC titanization, a specimen is immersed into crushed Ti sponge admixed with 1–2 % metallic iodine and annealed in a sealed Cr-steel container (as in powder immersion reaction assisted coating nitriding). To prevent the penetration of atmospheric nitrogen, the container is placed in a similar container of a larger

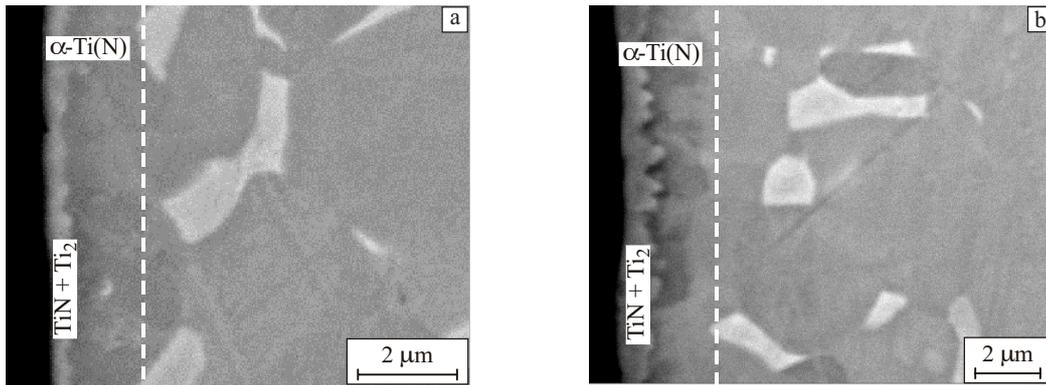


Fig. 9. SEM cross-sections of Ti6Al4V alloy after low temperature PIRAC nitriding: 700 °C, 8 h (a); 700 °C, 48 h (b).

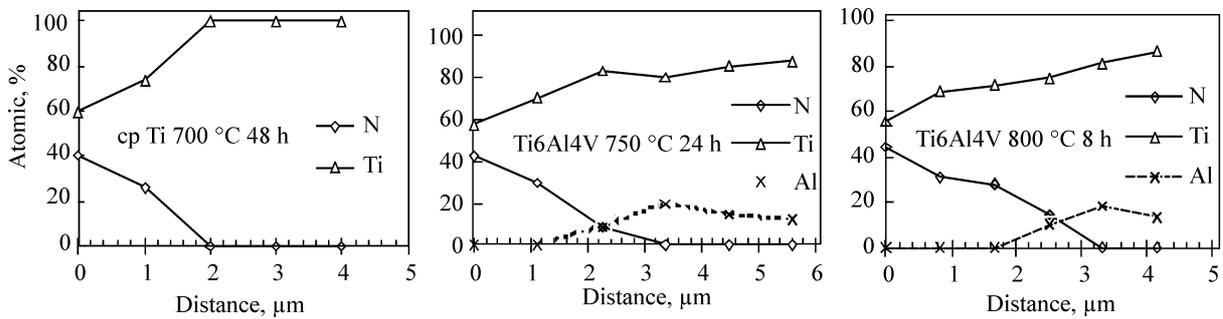


Fig. 10. EDS depth profiles of Ti6Al4V alloy substrates PIRAC nitrided at 700, 750 and 800 °C. Distance from the zero point to the topmost surface is ~1.5 μm.

diameter filled with fine Ti powder acting as a scavenger for N₂. During annealing, Ti sponge reacts with iodine to form a gaseous Ti iodide which transports Ti to the specimen surface. Reactive diffusion of Ti results in the formation of a Ti-enriched surface layer [68–70]. As shown in Fig. 12, PIRAC titanization of PIRAC prenitrided Ti6Al4V substrate results in the formation of a few micrometers thick near nitrogen-free Ti layer. During a subsequent PIRAC

nitriding treatment, the diffusion of nitrogen into the titanium layer proceeds not only from the gaseous environment in the reaction container but also from the underlying nitride layer. This leads to rapid transformation of titanium into titanium nitride. Figure 13 presents an example of EDS depth profile evolution of Ti6Al4V substrate following PIRAC prenitriding (stage 1), PIRAC titanization (stage 2) and PIRAC nitriding (stage 3). It can be seen that under conditions specified the three-stage PIRAC treatment re-

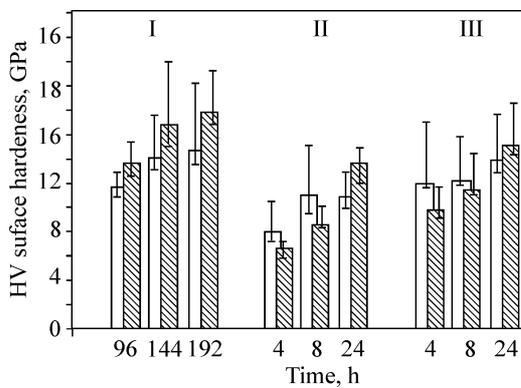


Fig. 11. Vickers microhardness of cp-Ti (white column) and Ti6Al4V (hatched column) alloy substrates PIRAC nitrided at 700 (I), 750 (II) and 800 °C (III).

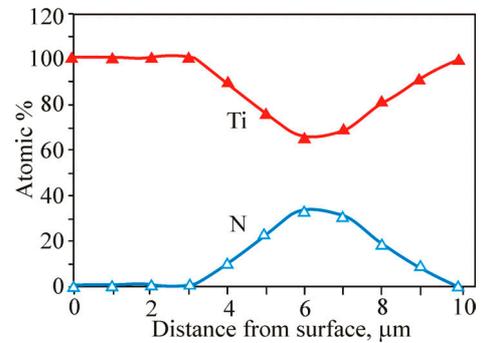


Fig. 12. EDS depth profile of a Ti6Al4V alloy substrate after PIRAC nitriding at 900 °C for 4 h followed by PIRAC titanization at 800 °C for 24 h.

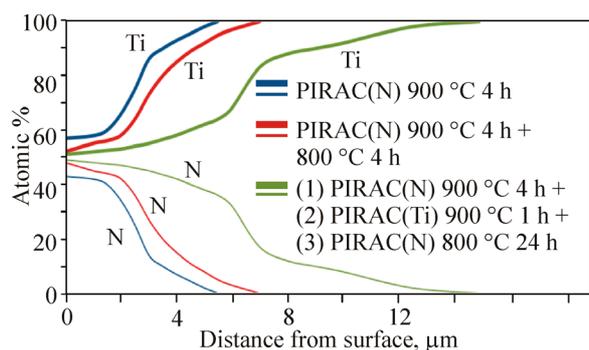


Fig. 13. EDS depth profiles of Ti6Al4V alloy substrates after PIRAC nitriding and combined nitriding-titanization PIRAC treatments.

sulted in the formation of a $\sim 6 \mu\text{m}$ thick compound ($\text{TiN} + \text{Ti}_2\text{N}$) surface layer—significantly thicker than the $\sim 2.5 \mu\text{m}$ layer obtained after single PIRAC nitriding. This result is also confirmed by the microhardness profiles in Fig. 14 showing that a much thicker hard surface layer is obtained following the three-stage nitriding-titanization-nitriding treatment. It should be mentioned that the total duration of the the three-stage PIRAC treatment in the presented case was 29 h, of which only 5 h were at 900°C and 24 h at the lower temperature of 800°C . According to estimations based on the kinetics of PIRAC nitriding of Ti6Al4V alloy [61], at least 45 h will be needed to obtain the same thickness in a single nitriding step at 900°C .

In vitro wear resistance of PIRAC nitrided Ti6Al4V alloy was tested in a hip simulator test [71]. 32 mm diameter PIRAC nitrided femoral heads (with a $2.0\text{--}2.5 \mu\text{m}$ thick titanium nitride layer) articulating against UHMWPE cups were tested in Ringer's solution at 37°C . After two million cycles in distilled water, PIRAC TiN–UHMWPE couples produced ~ 5 times less polyethylene wear than the control 316L steel–UHMWPE couples. Importantly, no signs of coating delamination were observed after four million cycles suggesting better adhesion than for PVD TiN layers.

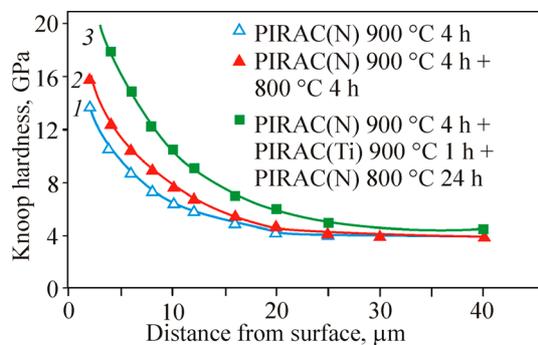


Fig. 14. Knoop microhardness profiles (25 g load) of Ti6Al4V alloy after PIRAC nitriding and combined PIRAC nitriding-titanization treatments.



Fig. 15. A computed tomography (CT) scan of a dog after unilateral total hip arthroplasty.

In an *in vivo* study by the authors of the present review [72], unilateral total hip arthroplasty was performed in 12 dogs, Fig. 15. The animals received total hip replacements with PIRAC TiN-coated Ti6Al4V femoral stems and heads (Fig. 16) articulating against UHMWPE acetabular cups. Hybrid implant fixation was used, with cemented acetabular cups and cementless press-fit femoral stems. Two dogs had postoperative complications and were lost to analysis. The other ten animals maintained normal gait pattern until sacrificed 2 to 3.5 years after surgery. In all dogs animals, clinical signs of aseptic loosening were observed during the follow-up period; in 7 dogs, no radiolucent signs of loosening were observed, either. Histological findings included a fairly small amount of metal/polyethylene debris and active osteoblastic (bone-building) activity around the



Fig. 16. PIRAC TiN-coated Ti6Al4V femoral components of the canine total hip replacement (produced in-house).



Fig. 17. An explanted PIRAC TiN-coated femoral head. Note the absence of any visible coating damage.

implants. Visual examination of the explanted TiN-coated femoral heads revealed no signs of coating loss by wear or spallation, Fig. 17. Similarly, no local coating detachment and only slight surface scratching was observed under scanning electron microscope, Fig. 18.

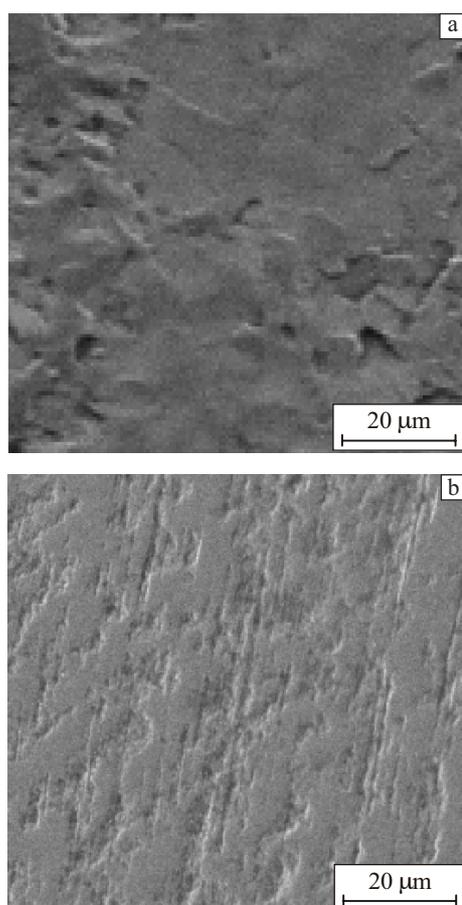


Fig. 18. SEM micrographs of PIRAC TiN-coated femoral heads: as coated (a); explanted 3.5 years post-op (b).

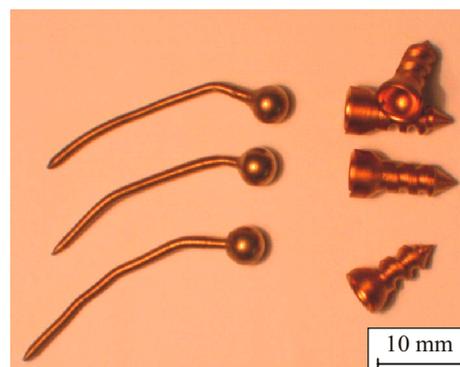


Fig. 19. PIRAC TiN-coated Ti6Al4V rat total hip replacement with metal-on-metal articulation (produced in-house).

In vivo performance of PIRAC TiN-coated metal-on-metal bearing couples was studied in a rat model of total hip replacement [73]. 316L stainless steel and TiN-coated Ti6Al4V ball-in-socket implants, Fig. 19, were implanted bilaterally in eight Wistar rats, Fig. 20. One week after surgery, the animals started to exercise on a treadmill for 2 h daily and were sacrificed 18 weeks post-op. Over the test period, the implanted hip replacements were subjected to the estimated 6–8 million stress cycles. Following explantation, pronounced surface roughening of steel articulating components was observed. In contrast to this, TiN-coated implants remained smooth and did not show any sign of ceramic layer delamination, Fig. 21.

The encouraging results of the two animal studies [72, 73] suggest that PIRAC nitrided Ti alloys can be a promising wear resistant material for articulating components of medical implants.

4. Duplex titanium nitride coatings

As discussed in the previous sections, diffusional TiN coatings produced by plasma or PIRAC nitriding of Ti alloys have excellent adhesion to the substrate, primarily due to the formation of the supporting layer of nitrogen-hard-



Fig. 20. X-ray of a rat after bilateral total hip arthroplasty.

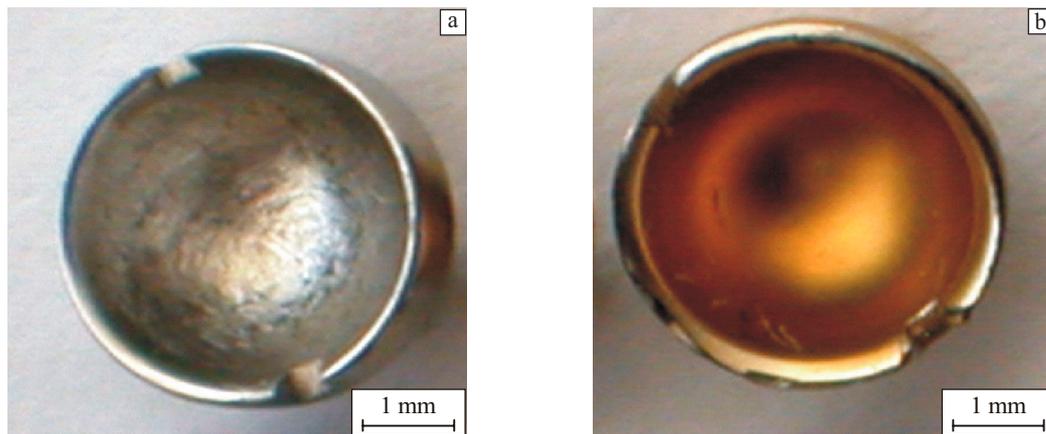


Fig. 21. Acetabular cups of the rats (total hip replacement) explanted 18 weeks post-op: stainless steel cup (a); PIRAC TiN-coated Ti6Al4V cup (b).

ened metal below the hard ceramic (TiN/Ti₂N) film. The growth of this ceramic film, however, is proportional to the square root of treatment time and is relatively slow. This is especially true regarding low-temperature processing regimes since the diffusion coefficient decreases exponentially with decreasing temperature. Thus, it is difficult to achieve thicknesses larger than ~5 micrometers within a reasonable time frame. Such relatively thin TiN layers could be insufficient to provide the bearing surfaces of joint replacements with long-lasting (tens of years) wear resistance. Physical and chemical vapor deposition (PVD and CVD) methods, on the other hand, with the typical deposition rates of several micrometers per hour, allow one to grow sufficiently thick TiN layers in a matter of a few hours. Under tribological conditions, however, these externally deposited coatings are prone to delamination and detachment due to weak adhesion and abrupt change of properties at the coating/substrate interface. To utilize the attractive properties of the two coating approaches while avoiding some of their drawbacks, “duplex” treatments which combine PVD (or CVD) coating with a diffusion treatment (nitriding) of the underlying surface have been proposed [74–77]. In this case, the nitrided layer with gradually decreasing hardness provides the required support to the hard PVD TiN coating. In [78, 79], plasma nitriding (PN) of Ti6Al4V and Ti5Al2.5Fe alloys was followed by plasma enhanced chemical vapor deposition (PCVD) of TiN layer. Compared to PCVD TiN layers on untreated substrates, the “duplex” coatings obtained exhibited stronger adhesion, as determined by scratch tests with continuously increasing load [78] and by indentation test [78, 79]. As a result, the wear resistance of PN–PCVD duplex treated Ti6Al4V alloy in pin-on-disc test against a steel ball was strongly improved [79]. In [80–83], ~3 μm thick plasma-assisted PVD (PAPVD) TiN coatings were deposited on bare Ti6Al4V alloy and on Ti6Al4V alloy diffusion-treated by plasma nitriding or combined oxida-

tion/nitriding. The adhesion of duplex diffusion/PVD TiN coatings to the metal substrate as measured by scratch testing was higher than of a non-duplex PVD layer. This was related to improvements in load-bearing capacity and chemical affinity between the coating and diffusion-treated surfaces. The highest critical loads were obtained for the specimens with the deepest hardened case obtained by the combined oxidation/nitriding treatment. The wear performance of such duplex diffusion/PVD TiN coated disks in reciprocating-sliding wear was significantly enhanced compared to the disks coated by physical vapor deposition only. The results presented in [82] show that the sequential plasma oxidation and nitriding diffusion pretreatment, in combination with a PVD TiN ceramic coating, can provide a significant reduction in surface impact wear when compared to either plasma diffusion treatments alone, or PVD TiN coatings deposited on non-pretreated Ti-alloy substrates. Rotating-bending fatigue tests carried out in [83] showed that the deposition of a hard PVD TiN layer alone was detrimental for fatigue endurance of Ti6Al4V alloy. In contrast to this, the use of the duplex diffusion/PVD coating treatment intended for the enhancement of wear resistance was capable of maintaining the intrinsically good fatigue properties of the metal alloy.

The adhesion of PVD TiN coating to titanium alloys can also be improved by PIRAC nitriding of the substrate prior to vapor deposition. Duplex TiN coatings of different thickness (from 9 to 15 μm) were grown on Ti6Al4V alloy by PIRAC nitriding at 800 °C for 4 h followed by 2 to 4 runs of plasma-assisted physical vapor deposition. The adhesion of the duplex coatings and the corresponding PIRAC-only and PAPVD-only films was assessed in three-point bending (as described in the previous section). All the specimens were loaded beyond the yield stress of the Ti alloy in order to cause some plastic deformation of the substrate. Under these conditions, delamination of all the PAPVD-

TiN films deposited on untreated Ti6Al4V was observed. In contrast, neither of the PIRAC or duplex PIRAC-PAPVD coatings delaminated from the substrate indicating a strongly improved adhesion. Figure 22 presents SEM micrographs (cross-sections) of the duplex-TiN and PAPVD-TiN coated specimens after bending. The detachment of the PAPVD-TiN film from the untreated substrate is clearly seen, Fig. 22a. In contrast to this, no visible delamination is present in the duplex coating, either along the PIRAC-PAPVD or along the PIRAC-Ti6Al4V interface, Fig. 22b. Instead, cracks normal to surface are formed in the brittle PAPVD-TiN film that propagate into the ductile substrate. This is despite the fact that the shown PAPVD-TiN film in the duplex coating is much thicker ($\sim 13 \mu\text{m}$ / 4 layers) than the PAPVD-TiN coating on the untreated substrate ($\sim 7 \mu\text{m}$ / 2 layers). These observations indicate that (i) the adhesion between the PAPVD-TiN coating and untreated Ti6Al4V substrate is weaker than the $7 \mu\text{m}$ thick TiN film, and that (ii) the interface between PAPVD-TiN and PIRAC-nitrided Ti6Al4V substrate in the duplex coating is stronger than the $13 \mu\text{m}$ thick TiN film. This not only confirms the beneficial effect of powder immersion reaction assisted coating prenitriding on the adhesion of PVD-TiN coatings but also provides a quantitative approach to evaluating the coating bonding strength.

5. Biocompatibility studies and non-wear related medical applications of TiN-based coatings

The biocompatibility of titanium nitride films, both externally deposited and diffusionally grown, was confirmed in a number of *in vitro* studies. When tested in human mesenchymal stem cell (hMSC) cultures, TiN-coated and uncoated Ti6Al4V alloy substrates (smooth, microrough (sand-blasted) and rough (plasma sprayed)) were shown to induce a comparable response in terms of both cell adhesion/proliferation and differentiation [84–86]. An enhanced bio-

logical response of of hMSC cells to titanium nitride was reported in [87], where a considerably larger number of cells adhered to reactively sputtered TiN coatings versus uncoated Ti6Al4V. In [88], osteoblast cells were cultured on smooth and porous-coated CoCrMo alloy discs, bare and coated with a 4 micrometers thick PVD TiN layer. For both surface topographies, osteoblasts showed similar differentiation and increased proliferation on TiN compared with CoCrMo surfaces. Good biocompatibility profile of TiN has also been demonstrated with other types of cells. When the growth of human umbilical vein endothelial cells (HUVEC) on different metallic substrates was studied, a significantly higher cell density was measured on sputtered TiN coatings compared to uncoated 316L stainless steel and NiTi alloy (Nitinol) [89]. It is worth noting that very similar cell behavior was observed on sputtered titanium oxide (TiO_2) surfaces. Several authors have emphasized that depending on the deposition method and processing parameters, titanium nitrided surfaces may have different stoichiometry, crystallinity and surface roughness, all of which can strongly affect cellular response [90, 91].

The few available *in vivo* studies (in the rat and rabbit models) have shown that bone healing around TiN-coated implants is similar (or slightly better) to bone response to uncoated titanium and Ti6Al4V implants] [92–95].

Another attractive feature of TiN coatings could be the inhibition of bacterial adhesion and proliferation, as demonstrated, for example in [85] for two different strains of *Streptococcus* on TiN-coated and uncoated plasma-sprayed titanium. Similarly to cellular response, microorganism colonization of a biomaterial is influenced not only by surface chemistry but also by surface roughness. It has been shown that the adhesion of *Candida albicans* to PVD TiN-coated titanium was significantly reduced compared to both plasma nitrided and untreated substrates [96]. The difference between the PVD coated and plasma nitrided surface was explained by the different composition (TiN versus pre-

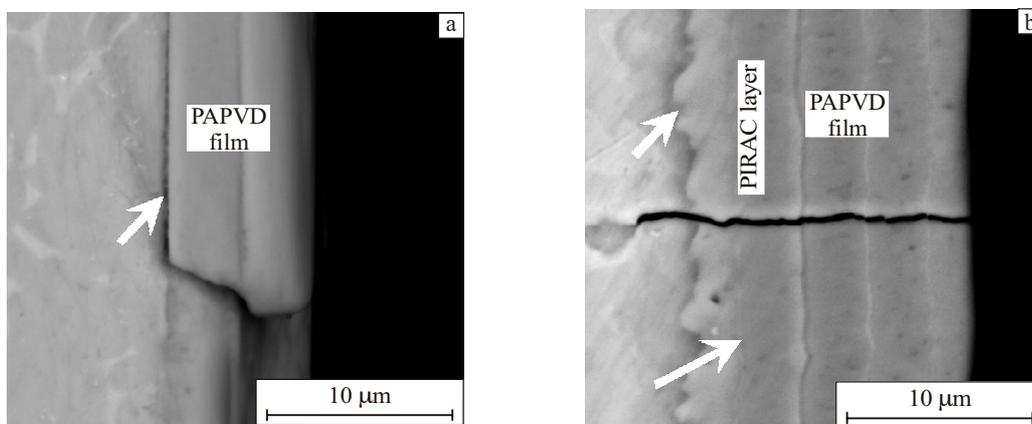


Fig. 22. SEM cross-sections of TiN-coated Ti6Al4V alloy after three point bending test: PVD-TiN coating on untreated substrate (a); duplex PIRAC-PAPVD coating (b). Note interface delamination (arrow) in a versus coating cracking and intact interfaces (arrows) in b.

dominantly Ti_2N phase, correspondingly) and by the significantly higher roughness of the latter surface. The higher susceptibility to bacterial adhesion of uncoated titanium substrate having a very low surface roughness (comparable to PVD-TiN) confirmed the effectiveness of titanium nitride coating as an antimicrobial modification. Reduced bacterial adhesion on TiN-coated versus uncoated titanium implants was also reported *in vivo*, after 24 h exposure in the oral cavity [97].

5.1. Titanium nitride oxide coating

Over the past decade, a derivative of titanium nitride—titanium nitride oxide (TiN_xO_y), known in the cardiologic community as TiNOX, has received considerable attention as a bioactive stent coating [98–110]. The proprietary TiNOX coating process is performed by plasma-enhanced vapor deposition of titanium in a prespecified gas mixture of nitrogen and oxygen. The titanium-nitride-oxide coating is deposited on all the surfaces of stainless steel stents, both inside and outside, Fig. 23. It is claimed that the coating adds strength to the stainless steel substrate making the use of thinner struts possible. Fatigue tests simulating 10 years of stent implantation with scanning electron microscope analysis have proven the integrity of the titanium-nitride-oxide coating. The coating was shown to remain intact after stent implantation without any signs of microfractures or damage from the most calcified lesions [100].

The need for such coatings stems from the high incidence of in-stent restenosis of bare-metal stents and an increased risk of life-threatening late thrombosis following the implantation of drug-eluting stents (DES). Titanium-nitride-oxide-coated stents are a new generation of biologically active stents (BAS). One such TiNOX stent, the Titan-2® bioactive stent (Hexacath, France) is approved for clinical use in Europe, Asia, and North, Central, and South America, with more than 5000 units already used worldwide [107].

A preclinical study of a titanium-nitride-oxide-coated stent in a porcine model back in 2005 demonstrated a 50% reduction of neointimal hyperplasia and a significant re-

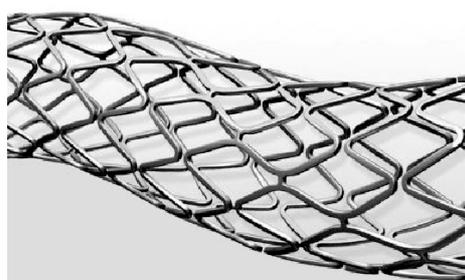


Fig. 23. Titanium-nitride-oxide coated stainless steel stent (TiNOX).

duction of platelet adhesion and fibrinogen binding as compared with an uncoated 316L stainless steel stent of identical design [97]. Since then, a substantial amount of data have accumulated supporting the favorable safety and efficacy profile of TiNOX-coated stents in a clinical setting [100, 104]. These stents have been shown superior to bare metal stents in reducing restenosis and major adverse cardiovascular events [99, 102]. Less consistent results were obtained when comparing the titanium-nitride-oxide-coated with drug-eluting stents. In [100, 103, 105], TiNOX-coated stents achieved better clinical outcomes as compared with paclitaxel-eluting stents at 3- and 5-year follow-up, both in unselected populations and in clinical scenarios of greater complexity (e.g. patients with acute myocardial infarction). In several other studies, a similar performance of TiNOX-coated stent and drug-eluting stents was reported in real-world population [104, 108] and in patients with multivessel coronary artery disease [107]. In a very recent report [106], titanium-nitride-oxide-coated stents were found inferior to everolimus-eluting stent in diabetic patients. The majority of papers describe TiNOX-coated stents as at least equivalent to DES in large patient populations. Meanwhile, TiNOX stents are free of cytotoxic drugs and polymer coatings which are associated with impaired re-endothelialization and do not need, therefore, prolonged dual antiplatelet treatment required with current drug eluting stents. This makes titanium-nitride-oxide-coated stents a safer and less-costly means of maintaining coronary patency [100], especially in patients unsuitable for long-term dual antiplatelet therapy.

Basing on the encouraging results with TiNOX stents, other properties of TiN_xO_y relevant for implantable devices have been tested. It has been shown, for example, that such coatings on roughened titanium substrates stimulate the proliferation of human primary osteoblasts (hOBs) *in vitro* without compromising their attachment and differentiation [111]. Similar results were reported in [112] whose authors concluded that TiN_xO_y coatings were highly biocompatible over a broad range of compositions.

Despite the reported good clinical outcomes of TiNOX stents, the mechanism leading to reduced neointimal hyperplasia around the titanium-nitride-oxide (TiN_xO_y) layer remains unclear. The most straightforward explanation provided is the superior biocompatibility of titanium and its compounds [107]. The biologically inert barrier TiN_xO_y mitigates the release of metal ions (nickel, chromium, cobalt) from the steel (or cobalt-chromium alloy) substrate thus minimizing inflammatory and hypersensitivity reactions leading to coronary restenosis. However, ion release characteristics of TiNOX stents have not been reported in literature. Moreover, there are no reasons to believe that the ternary titanium-nitride-oxide will act as a stronger barrier against ion release than the binary titanium oxide (TiO_2) or titanium nitride (TiN) compounds.

It is worth mentioning that the majority of papers dealing with TiNOX stents are written by clinicians, and at-

tempts to explain the mechanism of action of titanium-nitride-oxide and to relate it to the compound composition, microstructure and surface structure are scarce. The obvious lack of cooperation with chemists and materials scientists leads at times to inaccurate statements, such as the recurring reference to “nitric oxide (NO) particles on the titanium-nitride-oxide coating surface” [100, 110, 111]. Basing on the known restenosis-inhibiting effect of endothelium-derived nitric oxide and nitric oxide donor drugs [113–115], it has been stated by some authors that “the presence of nitric oxide (NO) particles on the stent surface might be beneficial with respect to intimal proliferation and platelet aggregation” [110]. It should be understood, however, that nitric oxide is a lipophilic gas and cannot exist as particles. Thus, there seems to be a confusion between the $\bullet\text{N}=\text{O}$ free radical and nitrogen chemically bound to oxygen (or oxygen bound to nitrogen) in the solid-state structure of titanium oxynitride, TiN_xO_y .

The beneficial effect of titanium-nitride-oxide coatings on cardiovascular stents has also been attributed to significantly reduced platelet adhesion and fibrinogen binding compared to bare stainless steel stents [100]. In [98], two different TiNOX coatings deposited by reactive physical vapor deposition with different oxygen-nitrogen ratio were studied. The coatings exhibited different *in vitro* behavior: the attenuation of fibrinogen binding and platelet adhesion was stronger for the coating with the lower (metallic) resistivity (presumably containing more nitrogen) than for the one with the higher (ceramic) resistivity (presumably with composition closer to TiO_2). Despite different *in vitro* results, however, the antiproliferative effect of the two coatings was similar while both revealed significantly less neointimal hyperplasia than stainless steel stents. In another paper [109], examination of blood compatibility of TiN_xO_y coatings as a function of composition (oxygen-to-nitrogen ratio) has shown that platelet adhesion and fibrinogen adsorption can be reduced by addition of nitrogen into the titanium oxide (TiO_2) layer. Both characteristics were at their highest for the nitrogen-free TiO_2 coating and all the tested TiN_xO_y coatings exhibited lower platelet adhesion and fibrinogen adsorption compared to TiO_2 , with no significant difference between $\text{TiN}_{0.3}\text{O}_{1.7}$, $\text{TiN}_{0.4}\text{O}_{1.6}$, $\text{TiN}_{0.7}\text{O}_{1.3}$ and pure TiN. This behavior was correlated with the lower hydrophobicity (smaller contact angle) of the nitrogen-containing layers. Such reasoning, however, does not explain the reduced platelet adhesion and fibrinogen binding to TiNOX coatings versus 316L stainless steel since both materials have comparable wetting characteristics [116]. On the other hand, if the attenuation of neointimal proliferation around TiN_xO_y -coated stents could be attributed to the inhibition of platelet adhesion and fibrinogen binding, stent coating with pure (oxygen-free) TiN should have the same antiproliferative effect. Such behavior of TiN-coated stents, however, has never been reported. It is clear from the above discussion that there still is a lack of understanding of the

relationship between the composition/microstructure of TiN_xO_y coatings, their *in vitro* properties and *in vivo* behavior. This is not surprising given the dearth of publications written by or in cooperation with materials scientists. One notable exception is the very recent paper by Banakh et al. [112]. In that paper, ~ 1.5 micrometer thick titanium oxynitride coatings with chemical compositions ranging from TiN to TiO_2 were deposited by varying the composition of the $\text{O}_2 + \text{N}_2$ reactive gas mixture during magnetron sputtering. The microstructure and composition of the TiN_xO_y coatings obtained were thoroughly studied employing X-ray diffraction, scanning electron microscopy with wavelength-dispersive X-ray spectroscopy and X-Ray photoelectron spectroscopy. It has been found that the coating microstructure changes with the oxygen ratio. Films with small and intermediate oxygen content ($\text{TiN}_{0.64}\text{O}_{0.35}$ and $\text{TiN}_{0.39}\text{O}_{0.87}$, respectively) were polycrystalline and had a crystal structure of TiN (FCC) with oxygen ions substituting for some nitrogen ions in the TiN lattice. The $\text{TiN}_{0.64}\text{O}_{0.35}$ film exhibited a well-developed columnar structure typical of sputtered TiN and had an average roughness in the 7 nm range. In the $\text{TiN}_{0.39}\text{O}_{0.87}$ films, the columns were less pronounced and the surface was smoother. Finally, the most oxygen-rich film ($\text{TiN}_{0.08}\text{O}_{1.92}$, essentially N-doped TiO_2) was amorphous and very smooth. All the coatings (including the TiO_2 -type film) had water contact angle around 72° – 73° , the only exception being the film with the lowest oxygen ratio ($\text{TiN}_{0.64}\text{O}_{0.35}$) having the much higher contact angle of 80° . These data are in contrast to those reported in [109] where the TiN and TiN_xO_y coatings exhibited a less hydrophobic behavior (smaller contact angle) than the pure TiO_2 . This only underscores the difficulty of relating the blood-contacting properties of TiNOX stents to their wetting behavior, which is a function not only of surface chemistry but also of surface contamination and roughness. Clearly, more cooperation between clinicians, biologists, chemists and materials scientists is needed to gain a deeper insight into the properties and biological behavior of titanium-nitride-oxide coatings.

6. Concluding remarks

Titanium nitride (TiN) is an attractive coating material for implantable devices due to its high hardness, non-toxicity and complete physiological inertness. PVD-TiN surface coatings technology is now relatively well-established within the orthopaedic industry. Despite promising laboratory test results, however, worrisome premature failure of such coatings on bearing surfaces of joint replacements has been observed in some wear simulation tests and on prostheses explanted from humans. Insufficient adhesion and inadequate load bearing capacity of the underlying softer metallic substrate are believed to be the major obstacles on the way to successful implementation of hard TiN coatings into clinical practice. These shortcomings of externally ap-

plied PVD TiN films can possibly be alleviated through the use of diffusional surface modification (e.g. plasma or PIRAC nitriding) capable of hardening the metallic substrate underlying the ceramic TiN layer. Even more attractive could be the application of duplex surface treatments involving primary substrate surface hardening (e.g. plasma or PIRAC nitriding) followed by the deposition of a thick TiN coating (e.g. by physical vapor deposition).

Along with the documented use of TiN coatings for enhancing the tribological performance of artificial joints, improved clinical outcomes are increasingly reported for non-articulating orthopaedic and blood-contacting implants coated with titanium nitride-based thin layers. Specifically, titanium nitride oxide (TiN_xO_y) coated stents (TiNOX) have been shown superior to bare metal stents and comparable to the state-of-the-art drug-eluting stents in reducing restenosis and major adverse cardiovascular events. However, the basis of such a beneficial effect of TiN_xO_y coatings remains largely unexplained, partially due to the dearth of investigations of the coatings composition, microstructure and surface properties, and their structure–properties relationship. More efficient collaboration between materials scientists, surface analysis experts and clinical researchers is anticipated to open new prospects for TiN-based coatings in medical device applications.

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