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Mechanical characterization of anti-infectious, anti-allergic, and bioactive coatings on orthopedic implant surfaces

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Abstract In total joint replacement much effort has been made to reduce implant loosening. We investigated different implant coatings (copper integrated titanium dioxide (TiO_2–Cu), titanium nitride (TiN), plasma polymerized allylamine (PPAAm), and calcium phosphate (CaP)) regarding the adhesion strength and wear resistance. Standardized scratch and adhesive tests were applied. Abrasive wear was measured with artificial bone and bone cement using a special testing machine. All tested coatings have higher bonding strengths than the 22 N/mm^2 required for medical implant surface coatings by ASTM standard 4711-F. Using bone cement, wear testing revealed higher wear rates in most cases. Polished surfaces reduce the amount of wear, whereas rough surfaces highly increase the wear rate due to three-body wear, especially ceramic surfaces. In general, the application of bone cement in conjunction with modified implant surfaces can lead to an increase in wear rate.

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Introduction

Aseptic implant loosening, mainly caused by particle wear ("wear disease") [1, 2] is the most common reason for total hip and knee revision surgery today. Approximately 75% of implant revisions are due to aseptic loosening [3] which can also be induced by stress shielding. According to Malchau et al. [3] 6% of all total hip replacement revisions are caused by implant infections which is the second most frequent reason for endoprostheses failure. Besides the surgical treatment associated risks that patients have to take, early and late infections also have a high economic impact. In the US alone the economic damage and the associated treatment expenses caused by implant infections are approximately 1.82 billion US dollars every year [4]. Other reasons for decreased implant longevity are allergic reactions to the implant material [5, 6], poor primary or secondary implant stability [7, 8], osseous fractures, implant material failure [3], or dislocations of the artificial joint [9].

In total joint replacement much effort has already been put into the reduction of the risk of aseptic implant loosening, so that early and late implant infections have moved into the focus of research. Since the variety of possible implant materials is highly limited due to the high mechanical and biocompatible [10, 11] requirements, the main emphasis is on implant surface coatings. Surface coatings are already successfully applied on implant surfaces to increase bone on-growth and abrasive wear resistance [12] or reduce the release of allergenic ions [6].

There are different approaches to reduce the risk of implant infections. Gristina et al. [13] proposed the principle of the "race for the surface" where it is believed that the first cells to be able to proliferate on the implant surface will succeed in colonizing and suppressing other competitors. Hence, surface coatings are designed to either act as anti-infectious or

promote fast bone on-growth. A different method to obtaining an anti-infectious coating is an anti-adhesive coating, but the use is limited to temporary implants since proliferation of both bone cells and bacteria is inhibited.

Anti-infectious surfaces can be achieved by diverse approaches. Gollwitzer et al. [14] integrated antibiotics in a biodegradable PDLLA (poly D,L-lactid) surface coating and showed a considerable reduction in colony forming units (cfu) of bacteria. Growing antibiotics resistance of bacteria in hospitals make this type of prevention contradictable. A more promising coating approach is the integration of metal ions such as silver (Ag^{+}) [15, 16] or copper (Cu^{2+}) ions [17] at concentration levels toxic to bacteria but tolerable by the surrounding tissue. Investigations using zinc (Zn) have also shown anti-microbial effects [18]. Bio-active coatings, such as calcium–phosphate [19], are designed to promote cell on-growth by specifically altering the surface topology. Increasing the surface area or using materials that improve cell adhesion result in a faster proliferation of bone cells on implant surfaces. In case of sensitivity against implant materials like nickel, cobalt, or chromium anti-allergic implant surfaces are used in total knee replacement.

Although the biological aspects of implant surface coatings are of great significance, the mechanical properties also play a key role for the functionality and successful clinical use of coated implants. In particular the bonding strength, to the metallic substrate, and the abrasive wear resistance of the coating have to be assured during application in order to prevent early implant loosening. The aim of this experimental study was to analyze the adhesive strength and wear resistance of different new anti-infectious and bio-active surface coatings in comparison to commonly used implant surface modifications.

Materials and methods

Implant surface modifications

For the tests medical-grade titanium alloy (Ti6Al4V) samples were coated with titanium-dioxide with integrated copper ions (TiO_2–Cu) [20, 21], plasma polymerized allylamine (PPAAm) [22], calcium phosphate (Bonit®) [23], and titanium nitride (TiN) [24]. Details of the tested coatings are given in Table 1.

The TiO_2–Cu coating is considered to be an anti-infectious coating because of its release of copper ions at concentrations which are toxic to bacteria but non-toxic to bone cells [25]. PPAAm and Bonit® are bio-active coatings which function in different ways. Allylamin in PPAAm coatings immobilizes amino groups on the surface of the Ti6Al4V test samples and changes the initial weak negative zeta potential [26] to a positive zeta potential [22] which increases initial cell adhesion due to the pericellular, negatively charged hyaluronan (HA) matrix cell coat [22, 27–30]. Calcium phosphate (CaP) coatings achieve their bio-active characteristics by enlarging the surface area and increasing the wettability which results in good blood supply of the areas to be colonized by new bone cells. Titanium nitride (TiN) coatings are not anti-infectious or bio-active surface modifications, but they are anti-allergic, increase the wear resistance [31], and are commonly applied on orthopedic implants (e.g., in total knee replacement) representing a reference coating.

Additionally, corundum blasted ($R_a = 2.07$ µm) Ti6Al4V samples with and without TiN coating as well as polished Ti6Al4V specimens ($R_a = 0.01$ µm) were used for comparison of rough and polished coated surfaces, respectively.

Table 1 Properties of the anti-infectious, bioactive, and wear resistant surface coatings used for the investigations

Coating	TiO_2–Cu	PPAAm	CaP	TiN
Preparation process	Sol–gel dip coating	Microwave exited, pulsed, low pressure gas discharge Plasma	Electro-chemical deposition	Physical vapor deposition (PVD)
Chemical composition	Ti, O, Cu^{2+}	C, N, O	Ca^{2+}, PO_4^{3-}	Ti, N
Surface roughness[a] R_a/R_z (µm)	1.37/9.59	0.92/6.88	2.96/15.67	0.07/0.68
Thickness[b] (µm)	5–10	0.05–0.1	20–30	4–12
Nano-hardness[c] (GPa)	7.5	2.7	n/a	17.4

n/a not available

[a] Measured using a Hommel Tester T8000 (Hommel-Etamic, Schwenningen, Germany)

[b] According to coating manufacturers data

[c] Measured using CETR universal tester UNMT-1 (Schaefer Technology, Langen, Germany) except PPAAm coating, measurement by Physical Electronics, Ismaning, Germany

Adhesive bonding strength

The adhesive bonding strength of surface coatings to the implant substrate was determined using qualitative and quantitative methods, as described by Fritsche et al. [32]. The scratch test represents a qualitative method according to the ISO standard 20502 [33] by means of analyzing and comparing different surface coatings. In the presented tests a Rockwell C diamond was used to scratch the surface of coated Ti6Al4V test sheets (dimension: 150 × 30 × 1 mm) at different contact loads whilst the test sheets were moved horizontally at a constant velocity of 100 mm/min. The loads were applied increasingly in steps of 5 N every second using a universal testing machine (Z050 (KAF-TC, 2.5 kN), Zwick/Roell, Ulm, Germany) [32]. The maximum applied force was 75 N. The arising scratches were analyzed by light microscopy at 100× magnification. Cracks, delamination, or coating perforation represent the critical loads L_{c1}, L_{c2}, and L_{c3}, respectively [33].

A method to quantify the adhesive bonding strength is the standard adhesive test according to DIN EN 582 [34]. For each test two cylindrical test samples made of Ti6Al4V, 50 mm long and 25 mm in diameter, were taken, one coated and the other corundum blasted. After cleaning with acetone (Labscan, Gliwice, Poland) the surfaces were attached together using a special adhesive glue (Klebbi, Sulzer Metco Europe GmbH, Hattersheim, Germany) providing an adhesive strength of approximately 75 N/mm^2. After curing and hardening under pressure (0.25 N/mm^2) in a furnace at 180 °C for 50 min, the specimens were cooled down to room temperature. Using a universal testing machine (Z050, Zwick/Roell, Ulm, Germany) the force needed to tear the test samples apart was recorded and the adhesive strength σ_{adh} was calculated using formula (1). Additionally, a corundum blasted Ti6Al4V surface was tested as reference.

$$\sigma_{adh} = \frac{F}{A} \ (F = \text{measured force}, A = \text{face surface area}). \quad (1)$$

Abrasive wear resistance

Abrasive wear tests were carried out in a special testing device [35, 36] modified by Fritsche et al. [32]. Cylindrical Ti6Al4V test samples (coated, corundum blasted, or polished) with a diameter of 12 mm were used. Cyclic relative motions (1.5 × 10^6 cycles), with an amplitude of 500 µm at 5 Hz under a constant contact pressure of approximately 2 MPa, were applied at the interface between the surface of the test samples and both artificial bone (PU Foam, 30 pcf, SAWBONES, Malmö, Sweden) and bone cement (Palacos®, Heraeus Kulzer GmbH, Hanau, Germany). The experiments were repeated three times using new test samples. The generated wear was collected in a container and measured gravimetrically. Scanning electron microscope (SEM) micrographs and energy dispersive X-ray (EDX) analysis of the exposed implant surfaces concluded the investigations.

Calculations and statistical methods

All data were stored and analyzed using the SPSS statistical package 15.0 (SPSS Inc. Chicago, Illinois, USA). Descriptive statistics were computed for continuous and categorical variables [37]. The statistics computed included mean and standard deviations of continuous variables, frequencies, and relative frequencies of categorical factors. Comparisons within the groups were achieved using the Post Hoc test (LSD). All p values resulted from two-sided statistical tests and values of $p < 0.05$ were considered to be statistically significant.

Results

Adhesive bonding strength

Considering load case L_{c3} [32] significant differences between the surface coatings were determined in the scratch tests. The highest value for L_{c3} was obtained for the TiN coating which amounted to 75 N followed by the TiO_2–Cu coating where surface perforation was detected at a load of 65 N. Both PPAAm and CaP coatings revealed coating perforation at 5 N. Figure 1 shows the scratches made for each surface exemplarily.

The results for the standard adhesive tests are displayed in Fig. 2. The non-coated, corundum blasted surface (cb-Ti6Al4V) served as a reference for the adhesive strength of the special adhesive glue which averaged 76 N/mm^2. The highest adhesiveness was measured for the TiO_2–Cu coating with an average bonding strength of 90 N/mm^2. For the PPAAm and TiN coatings an average of 80 and 75 N/mm^2 was measured, respectively. The lowest adhesive bonding strength was assessed for the biodegradable CaP coating averaging 32 N/mm^2.

Abrasive wear resistance

In the wear tests the generated amount of total wear debris varied widely depending on the surface coating and the friction counterparts (Fig. 3).

Using artificial bone the polished (p-Ti6Al4V) and corundum blasted titanium alloy (cb-Ti6Al4V) samples produced an average wear amount of 2.2 and 6.3 mg per 1 million cycles (mg/MioCycl), respectively, but without statistical

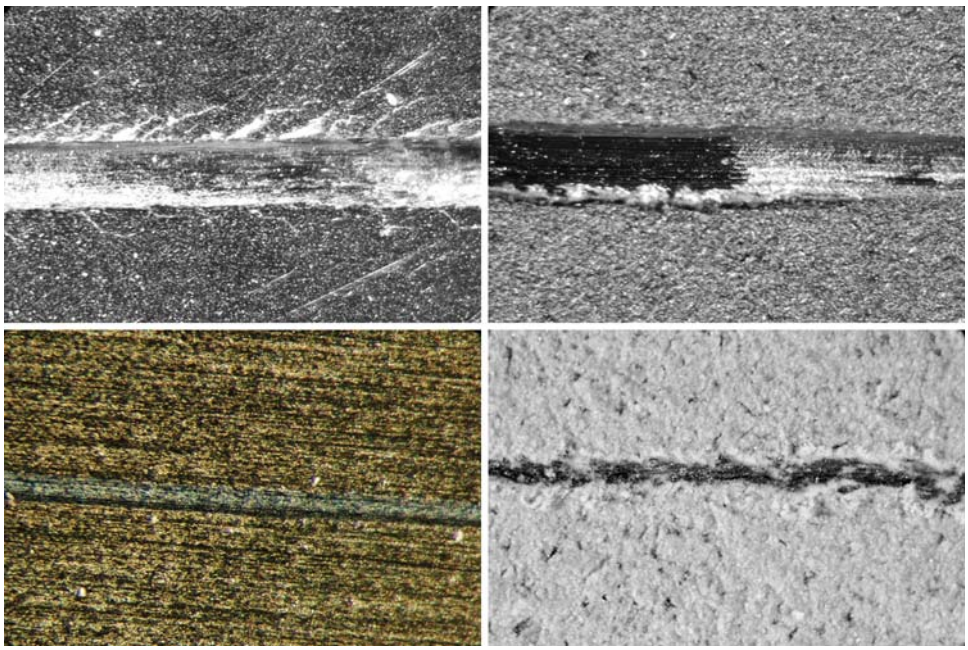

Fig. 1 Scratch test L_{c3} results of TiN at 75 N (*top left*), TiO_2–Cu at 65 N (*top right*), PPAAm at 5 N (*bottom left*), and CaP at 5 N (*bottom right*)

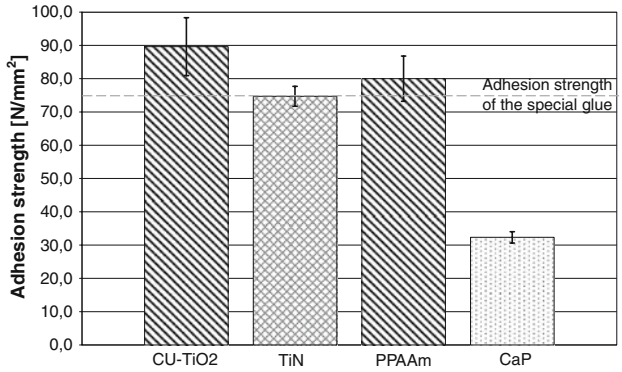

Fig. 2 Results of the standard adhesive bonding strength test

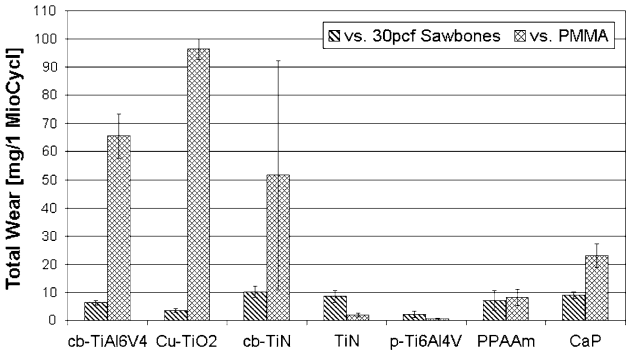

Fig. 3 Results of the wear tests using artificial bone (30 pcf Sawbones) and Palacos® bone cement (PMMA)

significance ($p = 0.120$). Both surface modifications served as references for polished and rough implant surfaces. The PPAAm, TiN, and CaP coatings produced 7.1, 8.6, and 9.0 mg, whereas the TiN coating on a corundum blasted Ti6Al4V surface (cb-TiN) generated the highest wear output averaging 10.1 mg when tested with artificial bone which is significantly higher than the wear measured for the TiO_2–Cu coating ($p = 0.001$) and the p-Ti6Al4V surface ($p = 0.001$). The least wear rate was generated using the TiO_2–Cu coating which averaged 1.4 mg. This is significantly different to the PPAAm, CaP, TiN, and cb-TiN coatings ($p < 0.009$).

With the use of bone cement (PMMA) as friction counterpart an increase in generated wear debris was observed in most cases. Only the polished p-Ti6Al4V and TiN samples produced less wear debris with PMMA than with artificial bone, i.e. for the p-Ti6Al4V surface 0.6 mg and for TiN coating 1.9 mg wear were measured. This difference in wear amount has no statistical significance ($p = 0.873$), but compared to all other surface modifications, with the exception of the PPAAm and CaP coating ($p > 0.575$ and $p > 0{,}143$), the wear rate is significantly reduced ($p < 0.003$). PPAAm, CaP, corundum blasted cb-TiN, and corundum blasted cb-Ti6Al4V generated an average of 8.2, 23.1, 51.6, and 65.6 mg wear debris, respectively. The highest amount of wear debris, with a statistically significant difference to all other tested surface modifications, with the exception of cb-Ti6Al4V ($p = 0.550$), was measured for the TiO_2–Cu (Fig. 3) in conjunction with bone cement averaging 96.4 mg ($p < 0.008$).

SEM micrographs and EDX-analysis showed that the TiO_2–Cu and the polished TiN coatings resisted the abrasive wear testing and did not delaminate or wear away. No wear scratches were observed on the TiO_2–Cu coating for any of the tests (Fig. 4), whereas the TiN coating showed light wear signs in SEM after abrasion (Fig. 5). Signs of wear could also be detected for the cb-Ti6Al4V and the

Fig. 4 TiO_2–Cu surface coating before (*left*) and after wear testing using artificial bone (*middle*) and PMMA (*right*)

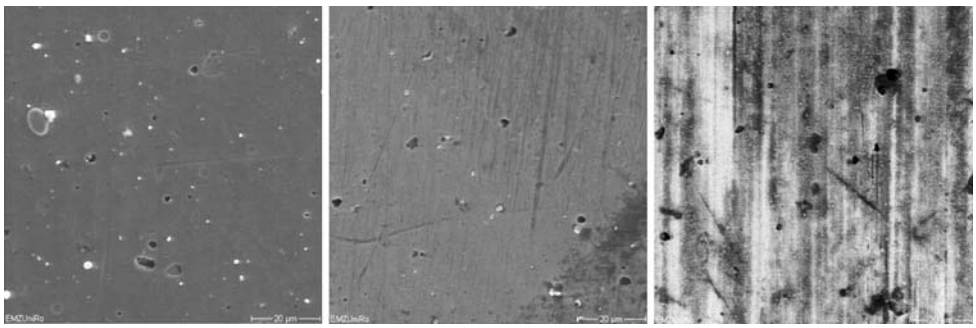

Fig. 5 TiN coated surface before (*left*) and after wear testing using artificial bone (*middle*) and PMMA (*right*)

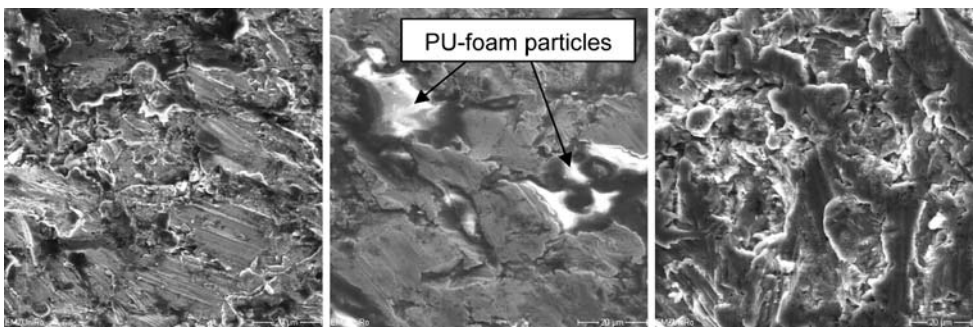

Fig. 6 cb-Ti6Al4V (corundum blasted) surface before (*left*) and after wear testing using artificial bone (*middle*) and PMMA (*right*)

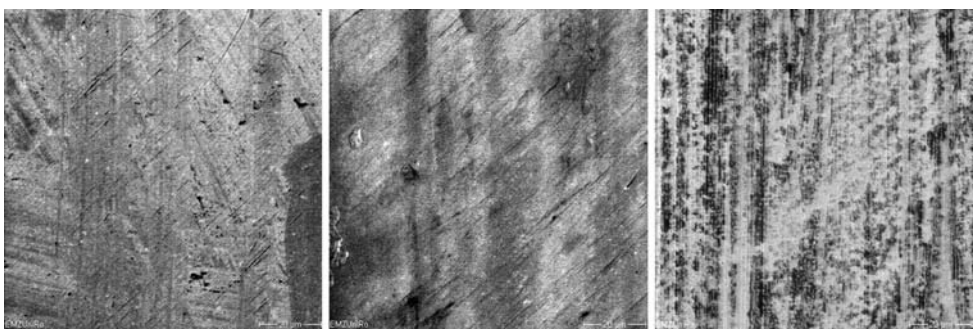

Fig. 7 p-Ti6Al4V (polished) surface before (*left*) and after wear testing using artificial bone (*middle*) and PMMA (*right*)

p-Ti6Al4V surface modifications (Figs. 6, 7). The corundum blasted TiN coating partially showed signs of total abrasion in some areas of the test sample. The CaP coating, however, was abraded so that only the metallic substrate was subjected to wear after 1.5 million cycles (see Fig. 8). The exact moment of delamination was not determined. The analysis of the PPAAm coating is difficult, since it is a very thin coating. Therefore, complete abrasion could not be clarified by SEM and EDX analysis since traces of the coating were detected (Fig. 9).

Discussion

Bioactive and anti-infectious implant surfaces have to meet the requirements of promoting bone on-growth and at the

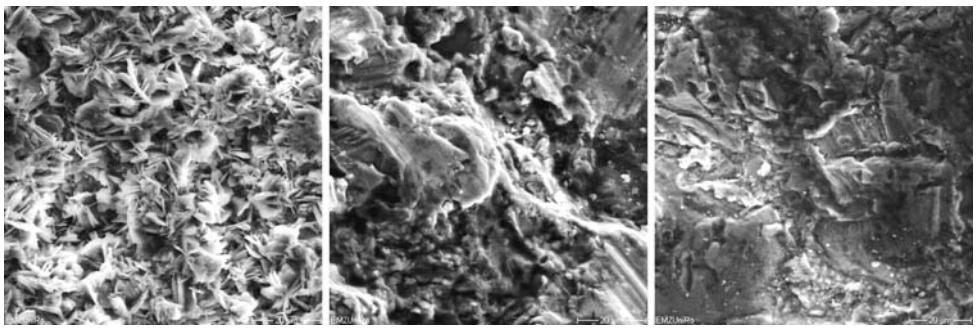

Fig. 8 CaP surface coating before (*left*) and after wear testing using artificial bone (*middle*) and PMMA (*right*)

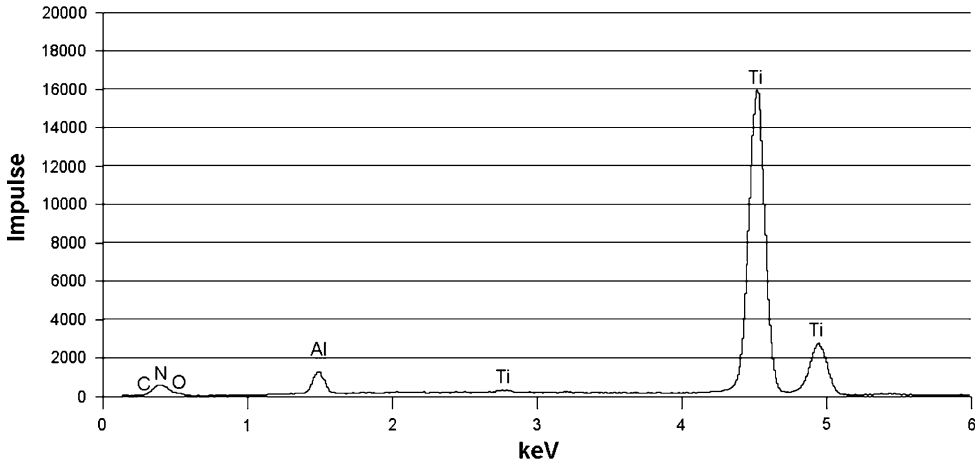

Fig. 9 EDX analysis of the PPAAM coating after wear testing

same time preventing bacterial infections. Long term functionalization of the implant surface has to be guaranteed in situ. Bonding strength and abrasive wear resistance of implant surface coatings are very important properties regarding clinical application. Anti-allergic implant coatings require maximum wear resistance for their use in articulating surfaces. To minimize the risk of future aseptic implant loosening, delamination of the coating during implantation must be avoided, as well as the production of abrasive wear particles due to micro motions in the body. In order to investigate these properties a number of tests were preformed in this study.

The scratch test is a qualitative method and showed great differences between the surface coatings considering load case L_{c3} [32]. The recorded loads for the ceramic coatings such as the TiO_2–Cu and TiN surface coatings are higher than those found in the literature [38, 39]. Chipping or delamination did not occur in our tests which could be explained by the ductility of both the Ti6Al4V substrate and the TiO_2–Cu and TiN coatings. Cracks (L_{c1}) were only observed for the TiN coating. For measurements of very thin coatings (thickness $\leq$ 0.1 μm) such as the PPAAm or the CaP coatings the test setup is not precise enough, since the minimum force that can be applied in our test setup is too high. Investigations using a micro scratch test setup will help to characterize the coatings further.

Using the standard adhesive test the adhesion bonding strength can be measured directly. With the exception of the CaP coating, in all cases the adhesion strength averaged 75 N/mm^2 or more, which is approximately the adhesiveness of the special adhesive glue. Since no coating delamination was observed, the coating bonding strength is presumably higher. All tested coatings have higher bonding strengths than the 22 N/mm^2 required for medical implant surface coatings by ASTM standard 4711-F [40].

The abrasive wear tests simulated a worst case scenario of implant loosening, i.e., under dry conditions. In situ micro motions are small, especially after osseous integration of the implant, and body fluids would lubricate the friction counter parts, resulting in reduced wear particle release. Using artificial bone the wear rates are moderate and the specimen's topology seems to have a small impact on the wear rate. No specific increase or decrease in wear rate, comparing rough and polished surfaces, was observed whilst testing with PU-foam. However, using PMMA bone cement containing zirconium dioxide (ZrO_2) particles, wear rates depend highly on the surface properties, i.e., surface roughness and hardness. Abraded radiopaque ZrO_2 particles

from the bone cement, supplemented for X-ray monitoring, promote three-body wear which can result in high wear rates. Polished surfaces reduce the generated amount of wear significantly, whereas rough surfaces highly increase the wear rate and caused three-body wear, in particular using the ceramic surfaces TiN and TiO_2–Cu. For the latter, not only the three-body wear but also the remaining micro-topography contributes to an increase in wear rate.

First results of the chemical analysis of the wear debris using the PMMA by means of atomic absorption spectrometry (AAS, ZEEnit 650 Analytik Jena, Jena, Germany) [41] show that more Ti-particles were generated with the non-coated rough surface of the titanium alloy (39.2 mg/L) compared to all coated samples. Considering these coated surfaces, the most Ti-particles were detected for the CaP coating (26.0 mg/L), suggesting that the coating resisted abrasion initially, but after a short time the substrate (Ti6Al4V) was completely subjected to wear as determined by the EDX analysis. The small amount of Ti-particles found for the TiN coating (3.1 mg/L), however, is not from the substrate but from the TiN coating itself, since SEM and EDX analysis did not determine coating delamination. The measurements show that the debris contained only small amounts of TiN wear particles. EDX analysis of the TiO_2–Cu coating also revealed no complete abrasion of the coating. Therefore, the determined Ti-particles (18.1 mg/L) in the chemical wear composition derived from the TiO_2–Cu coating. PPAAM could not be investigated, since not enough wear could be retrieved from the investigations.

Even though the tested bio-active surface modifications are not used with bone cement in normal situations, there are clinical circumstances that make the use of bone cement inevitable, e.g., partial cementing of cement-less implants. Hence, it is important to know that an increase in the amount of wear generated is possible with the application of bone cement. The complete abrasion of the CaP coating was expected. Since it is a non-permanent coating, which is meant to be degraded in the human body within a few weeks, its bonding strength to the substrate is relatively weak. Degradation and bone on-growth should have taken place by the time complete abrasion of the implant coating occurred.

In subsequent investigations, we are using micro-scratch and tribology tests for further characterization of the PPAAm and CaP coatings. We are determining the specific amount of surface particles released from the coated surfaces by atomic absorption spectrometry (AAS) [41]. Further, microbiological investigations of the presented new bioactive and anti-infectious surface coatings [21], cell adhesion assessment [42] and animal studies will complete the preclinical analysis.

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