

Antimicrobial Surface Finishing for Medical Implants by means of Metal Plasma Immersion Ion Implantation and Deposition

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Introduction

Medical implants are widely used in surgery and dentistry, i.e. for total joint replacement or dental implants. Although regenerative medicine is highly sophisticated, an implant remains a foreign material in the human body and therefore its surface properties should meet certain criteria. First and foremost the implanted material has to be biocompatible. In particular no adverse reaction should be provoked and a fast integration into the functionality of the respective tissue has to be guaranteed. Additionally, implants should exhibit an antimicrobial effect to minimize the implant-associated risk of infection. This is still a huge problem in clinical practice since the microorganisms can cause severe infections in combination with tissue necrosis in the worst case. The microorganisms can persist against antibiotics and the body's immune system. Hence, revision surgery is required in most cases.

Titanium implant surfaces should ideally be designed to promote the attachment of target tissue cells. At the same time, they should prevent bacterial adhesion, achievable through specific modification strategies. In the last ten years different methods for coating, doping or alloying titanium with antimicrobial effective metals were in the center of fundamental and industrial research. From these metals, copper has some advantages as an antimicrobial surface finish, since it combines good antimicrobial properties with a certain bio-tolerance with regard to eukaryotic cells [1]. Furthermore, copper is a micronutrient and is not accumulated inside the human body.

In this contribution, we present results of antimicrobial titanium surfaces generated by the insertion of copper. The surface was prepared via copper implantation and deposition into the subsurface and on the titanium surface by means of plasma ion immersion implantation and deposition (Cu-PIII&D), a combined method to dope the subsurface and to coat the metallic implant material in one single step. Compared to conventional coatings a considerably stronger bonded coating can be realized by the PIII&D technique. Depending on the sample mounting and the process parameters, the absolute amount of copper on and in the surface and therefore the copper release from the surface can be adjusted respectively.

Materials and Methods

Substrates: The plasma treatments, physicochemical surface analysis as well as biological investigations were accomplished with 11 mm diameter polished titanium samples, with a roughness of about $R_a=20$ nm and of so called "chemically pure" (cp) quality, supplied by DOT (Rostock, Germany).

Experimental setup: The setup is described in detail in Polak et al. [2]. Plasma Immersion Ion Implantation & deposition (PIII&D) was performed using a RF excited background plasma which was generated with two coplanar, disc-shaped copper electrodes of 12 cm diameter arranged with a distance of 16 cm. The power was disposed by an 13.56 MHz RF generator (PFG 600 RF, Hüttinger Elektronik, Freiburg, Germany) connected through a matching network (PFM 1500A, Hüttinger Elektronik, Freiburg, Germany) to both electrodes. To get quite homogeneous ion density distribution above the PIII&D electrode, both RF electrodes were operated with the same voltage without phase displacement. Vaporized water was used as process gas at a pressure of 5×10^{-3} mbar. A 6 cm diameter sample carrier was placed between the RF two electrodes. The sample carrier made of copper is shown in **Fig. 1**. The titanium samples were placed on copper cones to create a distance between the sample holder and the titanium discs. A pulsed voltage was applied to the the sample carrier and to the probes via a high voltage feed through connected to a pulse amplifier (RUP 3-15A, GBS-Elektronik, Großkrummannsdorf, Germany). The pulse amplifier was operated at 5 kV with up to 48 mA and a repetition rate of up to 100 Hz. The pulse generation was controlled by a waveform generator (DG535, Stanford Research Systems, Sunnyvale, CA, USA) which delivers square pulses to the pulse amplifier. With a RF power of 20 W up ion flux densities to the sample of up to 0.5 mA/cm^2 could be obtained. This results in a sample temperature of up to 600 °C.

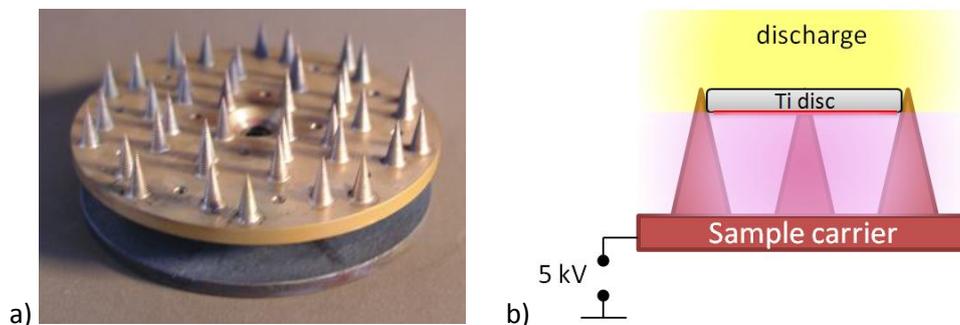


Fig. 1: a) Photo of the copper sample carrier. b) Schematic illustration of the sample positioning. The surface to modify was the bottom of the titanium discs (indicated in red).

Analysis: The surface of the modified titanium discs was analysed using X-ray Photoelectron Spectroscopy (Axis Ultra, Kratos, Manchester, UK) with subsequent Ar sputtering as iterative method to obtain depth profiles. Elemental quantification was done with CasaXPS (V2.3.15, Casa Software Ltd, Teignmouth, UK).

The release of copper from the modified samples was measured using Atom Absorption Spectroscopy (AAS) with implemented electro-thermal atomisation unit (ZEEnit 650, Analytik Jena AG, Jena, Germany). The samples were incubated in 700 μl solution consisting of Dulbeccos Modified Eagle Serum (DMEM), 10% fetal calf serum and 1% Gentamicin at 37 °C for different periods. Afterwards, 20 μl of this copper enriched solution was atomized inside the atomisation unit and its absorption was determined. To get absolute values the system was calibrated with solutions of well defined copper concentration.

Results and Discussion

The mounting of the titanium discs on this special sample holder led to some interesting phenomena. Besides the typical copper implantation and deposition of the upper side of the samples copper significant amounts of copper were found on the side facing the sample holder as well. Since the mounting cones and the samples are electrically conductive the voltage pulses propagate from the sample carrier over the cones to the discs. Hence, in the range of the plasma frequency of the ions, there is a zero electrical field between the discs and the sample carrier. Every ion generated in this

region will not be accelerated, neither to the discs nor to the sample carrier. The ions implanted in the bottom of the discs are therefore only ions from the immersion plasma accelerated towards the sample carrier, backscattered from the sample carrier. Furthermore, there is a highly dense copper vapour between the sample carrier and the titanium discs with particle energies in the range of some eV. This results in copper condensation with additional implantation of positive oxygen and hydrogen ions from the water vapour used as background gas. Since the distance between the discs and the sample carrier can be adjusted towards the mean free path of the ions, this method allows metal-PIII&D with high densities in a comparable high pressure regime of 10^{-2} mbar without additional metal sources like magnetrons or arc discharges.

The aim of the present work was to use this technique to enhance titanium discs with an antimicrobial finish. The key features of metal releasing modifications is the released concentration per time and the long time release. Therefore, the amount of metal – here copper – in or on the substrate has to be adjusted. Furthermore, the compactness and the chemical structure affect the long time release.

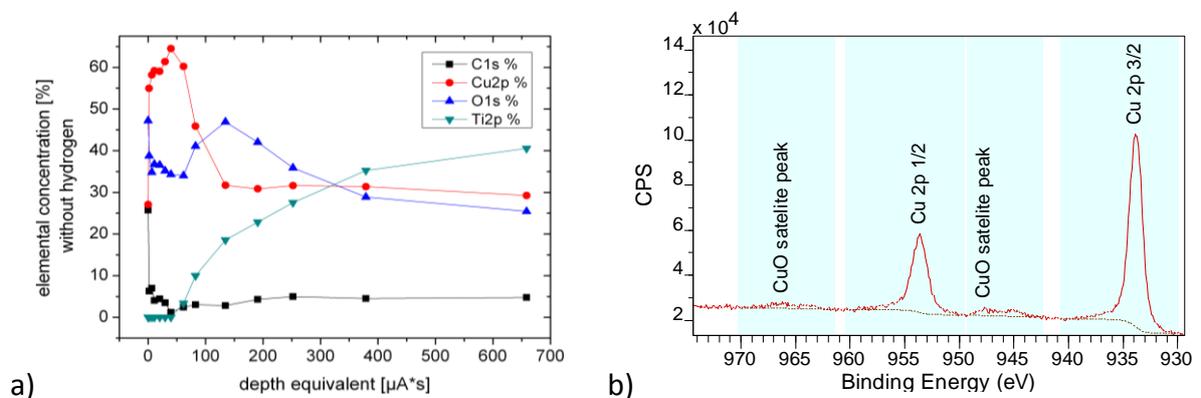


Fig. 2: a) Depth profile of the modified bottom of titanium discs measured with XPS. Hydrogen is not detectable. The depth equivalent is a multiplication of Ar-ion-current towards the surface multiplied with the sputtering time. Process parameters: $1 \cdot 10^{-2}$ mbar, 48 mA ion current, $6 \cdot 10^{18}$ ions \cdot cm $^{-2}$, 30 s process duration. b) Copper peak measured with XPS. Only small oxide satellite peaks appear. Hence, metallic copper is implanted in the discs and/or coated on the discs.

A typical depth profile of the modified surface after 30 s plasma treatment is presented in **Fig. 2a**. The profiles measured for different process times (up to 10 min) show similar profiles. On the surface, a small layer with contaminations like hydrocarbons was found. Subjacent, there a deposited copper layer with about 60% copper and 40% oxygen incorporation was detected. However, the copper was mostly in the metallic state and only small amounts of copper oxide could be detected (see **Fig. 2b**). The thickness of this copper layer was strongly dependant on the process time. After 120 s plasma treatment the layer thickness was found to be about 3-fold. Under the copper layer the amount of titanium from the bulk material increased. Furthermore, an oxygen aggregation was detected. The oxygen is assumed as a combination of titanium oxide layer and implanted oxygen due to the backscattering process. Again, only small amount of Copper oxide and mostly copper in the metallic state were detected. Surprisingly, while the concentration of oxygen continuously decreased for higher depth the amount of copper remained nearly unchanged at about 30%. The interpretation of this effect is part of our future investigations.

Another possibility to control the amount of copper in and on the surface is to vary the ion current towards the sample carrier by increasing the on/off ratio of the PIII&D voltage pulses. This results in an increased amount of sputtered particles from the sample carrier and therefore a higher density of copper in the gas phase. To investigate the antibacterial effect of the so modified titanium discs the copper release from the surface was measured after different periods of time. The results are shown in **Fig. 3**. A surface modified with an ion current of 0.5 mA corresponding to about $7 \cdot 10^{16}$ ions \cdot cm $^{-2}$ showed a comparatively low copper release in the range of some μmol/l. For 5 mA ion current

corresponding to about $7 \cdot 10^{17}$ ion \cdot cm $^{-2}$ the release in between the first 24 h reached the needed value of 0.5 mmol/l. It is well known that this value is sufficient to get a good antimicrobial effect. However, after 48 h no copper is left on and/or in the surface [3]. To improve the antimicrobial efficacy and the long term release, the ion current was further increased. This caused saturation for the maximum releasable copper at about 3.2 mmol/l. We assume, that this is the upper limit for copper release in DMEM bounded by the diffusion of copper from the bulk to the liquid. But the higher ion current influenced also the long term release. For an ion current of 48 mA corresponding to $6 \cdot 10^{18}$ ions \cdot cm $^{-2}$ even after 7 days of incubation in DMEM about 1 mmol/l copper was still released. Hence, with this method it is possible to adjust the release of copper per time and also the release of copper over the time.

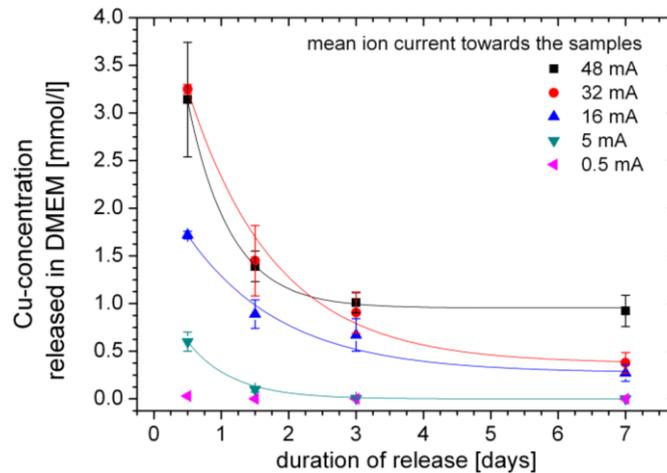


Fig. 3: Copper concentration released in Dulbeccos Modified Eagle Medium (DMEM) after different periods of time.

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