## ANTIBACTERIAL POTENTIAL of Zn- and Cu- SUBSTITUTED HYDROXYAPATITE COATINGS DEPOSITED by RF-MAGNETRON SPUTTERING: STRUCTURE and PROPERTIES<sup>1</sup>

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A tremendous number of traumatic cases associated with the bone fractures fostered the market need for implants that can provide immobilization of bone fragments using minimally invasive surgical access and quicker recovery of the patient. In order to address this problem, we introduced newly developed intramedullary implants. Those implants already proved their effectiveness in cases where fixation of a proximal bone fracture of tubular bones is needed. On the other hand, the problem of postoperative infections still the main challenge for modern health care. In case of severe post-implantation infection revision surgery is usually needed as the treatment with antibiotics does not provide the desired outcome. Therefore, our approach to this challenge lies in the surface modification of intramedullary implants by an RF magnetron deposition of antibacterial calcium phosphate (CaP) based coatings with the addition of Zn or Cu. The ions of Zn and Cu are known to have an antibacterial effect and their application is extensively researched in the biomedical engineering field.

We aim to develop novel bioactive and antibacterial coatings with enhanced osseointegration properties consisted of CaP+Zn and CaP+Cu based materials on Ti-6Al-4V and Ti-6Al-7Nb alloys of medical applications. We aim for improvement of the immunocompatibility of the novel implants as well as their antibacterial properties. And finally, we are working towards a translation from model samples to coated implant prototypes for validation of the improved osseointegration, antimicrobial activity, and immunocompatibility in order to demonstrate the proof-of-concept of the developed surfaces.

The targets for sputtering were sintered from hydroxyapatite with the addition of Zn and Cu ions that is substituting Ca in the cation lattice prepared by mechanochemical synthesis. A vacuum installation, with a planar magnetron operated at 13.56 MHz, was utilized for the CaP+Zn and CaP+Cu deposition. The thickness of the deposited films was measured by Calotest. For the coating's characterization methods such as an X-ray diffraction, scanning electron microscopy (SEM) and atomic force microscopy (AFM) were used. For biological assessment of developed coatings in vitro cytotoxicity test with MG-63 and C2C12 cell lines was used. Antimicrobial testing was performed with E.Coli using a disk diffusion assay.

The estimated thickness of the deposited coatings was in the range of ~1.0  $\mu$ m for both CaP+Zn and CaP+Cu. An SEM revealed that both types of coatings remain dense, homogeneous without any inclusions and discontinuities. According to AFM, the deposited coatings alter the implants' roughness insignificantly and mostly repeats the shape of an original surface. However, it is possible to detect globular-like surface features of the deposited coatings revealed to be quasi-amorphous according to an XRD data. This is beneficial for the coatings stability on the implant that is undergoing mechanical stress during implantation. Moreover, amorphous coatings will be dissolved more quickly releasing antibacterial ions and ensuring the antibacterial effect. Deposited coatings showed the absence of toxic effect in vitro and noticeable antibacterial effect.

In our study, we addressed the problem of antibacterial surfaces for implants and specifically for intramedullary fixator developed by us. We were able to functionalize the surface of an implant with bioactive (Ca and P releasing) antibacterial coatings and performed preliminary study in which we discussed its properties and effectiveness in vitro.

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