Modifying titanium implant surfaces with antibacterial copper: Is this feasible?

C. Jung[1], M. de Wild[2]

[1] KKS Ultraschall AG, Medical Surface Center, Steinen, CH, [2] University of Applied Sciences Northwestern Switzerland, School of Life Sciences, Muttenz, CH

INTRODUCTION: Implant associated infection is a burden for patients. It may appear not only directly after surgery but also after a long post-surgery period in some cases. Furnishing implant surfaces with infection inhibiting properties would therefore be a very welcomed approach. Here, we introduce the approach for modifying the surface of titanium implants with antibacterial copper. Based on the results of a number of studies [1-6], it is concluded that copper-modifying anodized implant surfaces is a feasible approach and has the potential for industrial up-scaling.

METHODS: Discs of cpTi grade 4 (∅ 12 or 14 mm, 2 mm thick) were anodized and Cu-modified using the spark-assisted anodizing method run in a combined anodizing/deposition process using proprietary electrolyte and proprietary process parameters (KKS TioCel^{TM}) [1,2] (Figure 1).

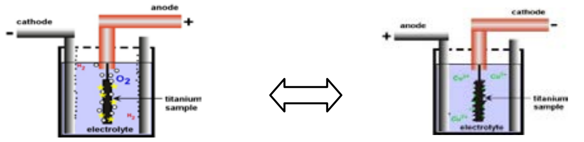

***Fig. 1**: Sketch of the electrochemical method for combined titanium anodizing (left) and copper depositing/doping process (right).*

RESULTS: The anodized discs show a rough fine-porous outermost layer and an underlying conversion layer (Figure 2 left). The R_a-value of the outermost layer is ca. 0.6 µm. Using appropriate electrochemical process parameters, Cu can be deposited onto and/or into the titanium oxide layer as detected by XPS depth profile analysis using Ar^+ sputtering [3] (Figure 2 right).

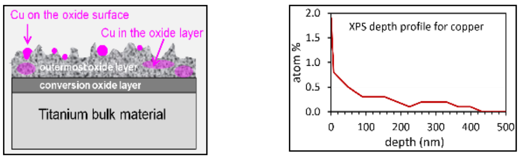

***Fig. 2**: Sketch of the anodized titanium with Cu onto and into the outermost layer (left) and Cu XPS-depth profile (right).*

The copper deposits on the surface have a size of few nanometers up to 2 µm (Figure 3) and are ablation tests and wear analyses in synthetic bone show a limited loss of copper (< 24%) [4].

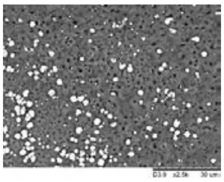

***Fig. 3**: SEM image of a copper modified titanium surface (Hitachi TM3000, backscattered mode, x2500); white spots are copper deposits.*

Studies on the Cu release into simulated body fluid demonstrate that the kinetics follow known release profiles with an initial burst phase followed by a slow phase. After 290 days, all surface copper is released into calcium-free SBF [5]. The viability of human primary gingival fibroblasts (HFIB-G), of immortalized gingival keratinocytes (IHGK) and of an osteosarcoma cell line (SaOs-2) on copper-modified discs was tested [6]. The cells presented slightly different resistance against Cu (fibroblasts < osteoblasts < keratinocytes) with a mean Cu amount of 13 µg/disc (43 ng/mm^2; 4.3 µg/(ml reaction volume)) for i.e. 50% cell viability (IC_{50}). This value is in the range of the lethal Cu concentration for *Staph. aureus* (~5 µg/ml [2]) indicating a good antibacterial effect with an acceptable cell viability of 50%.

DISCUSSION & CONCLUSIONS: The physicochemical and biological data obtained so far do strongly indicate that modifying the surface with copper is a feasible approach to give titanium implants an antibacterial property. The electrochemical technique is related to practice applications and has the potential to scale-up.

REFERENCES: [1]C. Jung (2010) *eCM*, **19** (Suppl 2):4. [2]C. Jung, N. Ryter, J. Köser, W. Hoffmann, L. Straumann, N. Balimann, F. Meier, M. de Wild, F. Schlottig, I. Martin, U. Pieles (2012) *eCM*, **23** (Suppl 1):16. [3]C. Jung, L. Straumann, A. Kessler, U. Pieles, M. de Wild (2014) BioNanoMat 15 (S1). [4]L. Straumann, A. Kessler, U. Pieles, M. de Wild, C. Jung (2014) *eCM*, **28** (Suppl 6):21. [5]A. Kessler, L. Straumann, U. Pieles, M. de Wild, C. Jung (2014) *eCM*, **27** (Suppl 2):24. [6]C. Jung, S. Mathes, E. Bono, C. Walker, A. Kessler, L. Straumann, M. de Wild, E.B. de Haller (2015) *eCM*, **29** (Suppl 2):24.