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Post-operative Effects on Silver Coated Tumor Endoprosthesis and Biofilm Prophylaxis Systems

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Abstract. Despite the high state of the art in limp replacement and the reconstructive tumor surgery, failures cannot be excluded. Investigations on post-operative effects on explanted silver coated modules of MUTARS® prostheses have disclosed changes in the silver surface. Both, the silver coatings and the perioperative lavage with antiseptics reduce efficiently the risks of infections.

INTRODUCTION

Based on years of experiences in the reconstructive tumor surgery, the Clinic and Policlinic of Orthopeadics of the Westphalian Wilhelms University and the company Implantcast GmbH, Buxtehude, Germany, developed the prosthesis system "Modular Universal Tumor and Revision System" (MUTARS®). The modularity and the different dimensions of the components enable to adjust individually the prostheses to the patients. More than 12,000 MUTARS® prostheses and arthroplasties of the adjacent joints have been implanted successfully.

Despite the high state of the art in the limp salvage of bone tumors by endoprosthesis improved by selected materials and design, neither perioperative infections nor mechanical failures or septic and aseptic loosening cannot be totally excluded [1-3]. Henderson et al [4] has classified five types of failures in endoprosthetic reconstruction:

- soft-tissue failure (type I) caused by tendon rupture or wound dehiscence,
- aseptic loosening (type II) because of biomechanical defects,
- structural failure (type III) caused by fatigue of the material, stress cracking by biocorrosion and weight and force overloading
- infections (type IV) indicated by post-operative microbial proliferation resulting in inflammation, septic loosening and microbial systemic distribution,
- recurrence and progression tumor (type V).

Soft-tissue failures are functional deficiencies of the soft-tissue attachments to the implant. Disruptions or insufficiencies in periarticular ligamentous and tendinous rearrangements effectuate instabilities and incorporation failures. Palumbo et al [5] estimated the soft-tissue defects to 12 % of all failures, and their absolute incidence to 2.9 %. Obviously, aseptic loosening is the most common case of mechanical failure accounted to 25 % by Jeys et al and Unwin et al. [6, 7]. Whereas the modular endoprosthetic design has been improved continuously, the structural failures are indicated to about 17 % of cases [5]. Therefore, improvements in metallurgy, design, and processing are continuously under progress. Perioperative infections are known risk factors in endoprosthesic surgery ranging from 20 to 30 % [3, 8]. Generally, extended operative procedures increase the risk of infections. In addition to the

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systemic prophylaxis adjuvant perioperative irrigations with antiseptics reduces microbial contaminations. Coatings of elemental silver on the endoprosthetic modules have been successfully applied [3, 9]. Silver nanoparticles provide large antimicrobial properties, but their cytotoxic and genotoxic potentials are under discussion [10]. Limb preservation surgery is mainly executed for primary bone tumors. According Palumbo et al [5] the tumor recurrence and progression amount about 17 % of endoprosthetic implantation failures. Suppression of sarcoma progression is possible applying adjuvant chemotherapies in order to reduce the risk of amputation [11].

The MUTARS® system offers the functional replacement in cases of osseous defects. For the joint replacements, there are available constrained rotational knee components, constrained hinge joint for the elbow joint and inverse components for the shoulder joint. The intramodullary stems consist of $TiAl_6V_4$ for cementless fixation, or of CoCrMo alloy for cementation. The cementless stem is endowed with a microporous surface, or can be furnished with a hydroxyl apatite coating. Providing the correct implant length in each individual case, variable extension modules are used for the bone defect reconstruction. The silver coating (MUTARS® Silver) as anti-infective prophylaxis against perioperative infections is CE certified and clinically established [3]. The head of the hip joint consists of UHMWPE (ultra-high molecular weight poly ethylene), or alternatively of a vitamin E modified crosslinked poly ethylene or ceramics. The modular proximal tibia is endowed with an UHMWPE inlay. The lock for the knee joint is manufactured from the high performance polymer PEEK (poly etherether ketene) and has been clinically approved.

Titanium nitrite coatings (TiN) on polished CoCrMo joint components are offered for the prevention against allergic reactions, and to reduces wear as well. A woven attachment tube of poly ethylene terephthalate (PET) is designed for both, the refixation of tendons and the soft tissue in order to achieve post-operative tissue integration. The fixation with non-degradable suture material prevents against luxation [12].

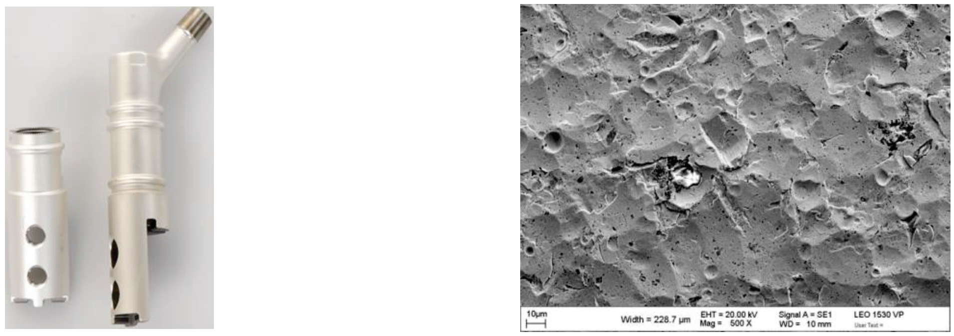
METHODS

MUTARS® modular tumor endoprosthesis explanted after different wear periods were investigated on the material properties using optical microscopy, SEM (scanning electron microscopy) and EDX (energy dispersive X-ray spectroscopy). The research was focused on biofilms, as well as on superficial effects caused by the biologic environment. Additionally, the suitability of different antiseptic lavage agents for silver coated tumor endoprosthetic implants were tested.

RESULTS

Changes on the Silver Coated Modules

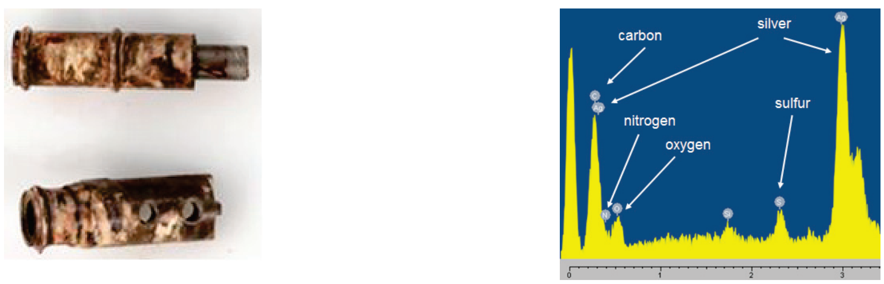
Surfaces of the silver coated modules of the tumor endoprosthesis were investigated before implantation and after explantation. The modules are supplied with a silver layer of 10-15 µm on a core of TiAl6V4 which is furnished with gold coating of 0.2 µm. The pieces are sand blasted providing a clean and uniform texture. Figure 1 shows both, two examples of the endoprosthesis modules (a) and a SEM micrograph of the silver surface of such kind of unused implants. The effect of sand blasting (Fig. 1b) to the galvanically deposited silver is marked by a micro-texturing according the diameters of alumosilicate particles of about 20 µm. The surface is uniformly closed. The few artifacts of the biocompatible blast particles captured in the surface do not cause any adverse implantation effects such as increased immune response, inflammation or wound healing deceleration.



(a) (b)

FIGURE 1. Examples of unused modules of a MUTARS® tumor endoprosthesis (a), the SEM micrograph of the blasted silver surface visualizes the texture of the coating before implantation (b) (executed by *ZEISS Leo 1530 VP*)

The strong adherent yellow to black colored layers were analyzed using EDX spectroscopy (Fig. 2b). Besides the signals for silver significant amounts of carbon, nitrogen and sulfur are recognizable. A small signal for silicon indicates remaining artifacts of the blasting material which were stable fixed in the silver coating during the whole wearing period.



(a) (b)

FIGURE 2. Examples of explanted modules of a MUTARS® tumor endoprostheses (a) after about 3 years wearing period, the EDX spectrum of the silver surface (b) indicates the deposit of nitrogen and sulfur containing species (executed by *ZEISS Leo 1530 VP*)

The contact and the interaction of the silver surface with soft tissue and interstitial liquid cause the adhesion of proteins. Spreading and denaturation takes place [13]. Enzymes, ROS (*reactive oxygen species*), catalytic effects of silver, and Ag^+ ions induce the degradation of proteins by cleavage such as α, β-elimination followed by forming adherent chelate complexes. The interaction with cysteine sequences and with protein disulfide bridges generate sulfur and nitrogen containing surface compounds (Fig. 3a, b) which degrade subsequently to the black colored, insoluble Ag_2S.

(a) (b)

FIGURE 3. Possible interactions of the silver surface with the HS function of cysteine sequences of proteins (a) and the disulfide bridges of cystine segments (b)

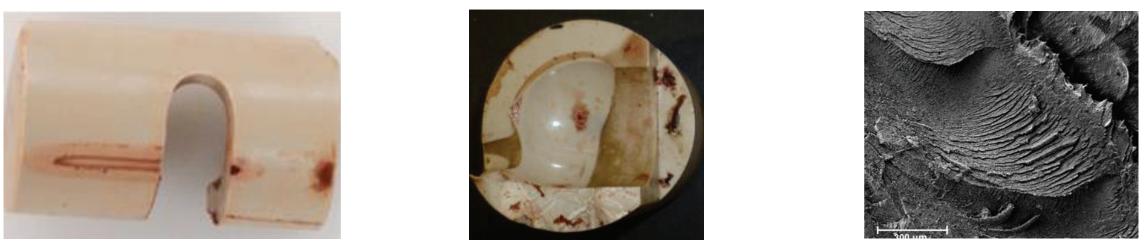
The yellow to black colored surfaces layers consist of mixtures of Ag_2S, Ag_2O and further compounds which are strongly fixed. Local or systemic toxic effects or any activation of the immune system have not been indicated, and the antiseptic activity of silver is not restricted during the critical early postoperative phase.

Structural failures

UHMWPE is commonly used in joint replacement as low friction arthroplasty coupled with metal bearings. UHMWPE provides a high rate of satisfaction, outcome and survivorship in both total hip replacement and total knee replacement. Major disadvantage is the generation of wear debris from polyethylene which can lead to particles induced osteolysis, and aseptic loosening as well. Highly cross-linked poly ethylene has been developed (XLPE) in order to improve the wear resistance [14]. The mostly applied gamma-sterilization generates small amounts of radical fragments within the PE matrix which reduce the mechanical performance and support the oxidative decomposition. The modification of XLPE with vitamin E as radical scavenger and antioxidant provides the synergetic effect to upgrade to mechanical properties of the PE furnished joints [15]. With respect to the general properties of PE and the large mechanical load, the hip and tibia inlays play an important role in the longtime implant stability.

PEEK provides obviously a larger resistance against irradiated. Tests at high levels of gamma radiation (3 times higher doses than for normal sterilization) have shown that the physical or chemical properties do not change, except the molecular weight distribution becomes slightly smaller [16].

According the high biocompatibility and the outstanding mechanical properties PEEK has been well approved as tibia joint lock. The cases of lock ruptures are estimated to about 1 %. Figure 4 shows an explanted unimpaired PEEK-lock (Fig. 4a) in comparison to a broken lock (Fig. 4b, c).



(a) (b) (c)

FIGURE 4. Explanted unimpaired PEEK lock of a knee joint (a), one part of the broken lock (b) and a SEM micrograph of the fracture plane (c)

The revision of the knee endoprosthesis was indicated by strongly constrained motion abilities of the female patient (56 years old). The SEM micrographs (Fig.4 c as typical example) showed scalelike tearoff edges. Additional microscopic pictures of the fracture plane made recognizable ball like areas and further texture inhomogenities. Therefore, a manufacturing defect such as insufficient mixing in the extrusion process has been considered.

Prophylaxis against Perioperative Infection

More than 20 explanted tumor endoprosthesis were investigated on biofilms. Neither the metallic components nor the PEEK lock devices were microbial contaminated. Only in one case, the UHMWPE inlay of the knee joint was colonized by *Staphylococcus epidermidis* (Fig. 5).

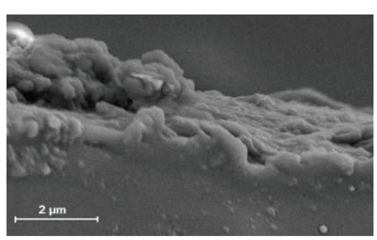


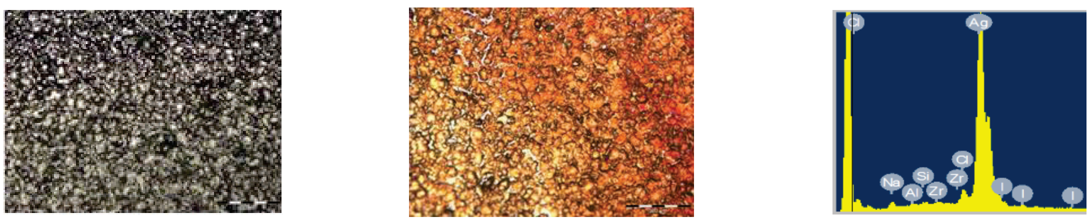
FIGURE 5. Biofilm of *Staphylococcus epidermidis* on an explanted UHMWPE inlay of a knee implant (*ZEISS Leo 1530 VP*)

It should be emphasized that the PET attachment tubes were also free of any adherent biofilms. The low number of microbial contamination may be caused by both, the antibacterial silver coating on the endoprothetic modules and the carefully executed perioperative lavage of wound and implant with antiseptics.

Perioperative prophylaxis against microbial contaminations are commonly executed with antiseptics such as Betaisodona® (povidon iodide complex in saline), Lavasept®, Prontosan® (poly hexamethylene biguanide), hydrogen peroxide or formaldehyde. After the treatment of silver coated endoprosthetic modules with Betaisodona® the surface changes the surface color to red as shown in Fig. 6.

Due to the oxidation potential of adherent iodine, the use of iodine containing lavages such as Betaisodona® should be avoided. Reactions with proteins take place forming undefined biomacromolecules which cover the silver surface and decrease the antimicrobial efficacy.

Test series with hydrogen peroxide and formaldehyde did not effectuate any changes in the silver surface. These antiseptics are approved in the clinical practice of joint replacements. Lavesept® and Prontosan® are useful alternatives without risks to change the material properties.



(a) (b) (c)

FIGURE 6. Pictures of the unused silver surface (a) and the Betaisodona® treated silver surface (b). Especially the signals for surface iodine indicate the reaction with silver, and the existence of strongly adsorbed iodine and chlorine (c)

Summary

The limp salvage of bone tumors using endoprosthesis such as MUTARS® prostheses and arthroplasties provides a high state of the art. Failures in the materials performance, loosening, perioperative infections or recurrence cannot be excluded, and that stimulates continuously progresses in the design, material properties and surgical techniques. Silver coated modules of tumor endprosthesis contribute significantly in the reduction of surgery associated infections. The surface color of silver changes to yellow or black during the wearing period caused by reactions with proteins and reactive oxygen radicals. Toxic or other adverse effects of that dark layers are unknown. Poly ethylene as low friction material for joints faces several mechanical problems, and the stability against oxidation is insufficient. Highly cross-linked XLPE and vitamin E modified PE provide increased wear and oxidative resistance. PEEK as high performance polymer has been widely approved in arthroplasty. Nevertheless, failures are possible such as demonstrated by a joint lock rupture. Quality defects in manufacturing cannot be excluded.

Biofilms or fragments of them could not find on the metallic components of the explanted tumor endoprosthesis. Both, the antimicrobial silver coating and the perioperative antiseptic lavage with hydrogen peroxide or formaldehyde are obviously appropriate measures to minimize infections associated post-operative failures.

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