Mutual relationship between implants and bone surface

Point of view of an orthopaedic surgeon

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INTRODUCTION: The relationship between bone and implant depends on many factors. Implants are defined by the material, the micro- and the macrostructure of the surface, the size and the rigidity. Composed implant may be produced as such (e.g. Femoral component of a hip prosthesis covered with hydroxyapatite) or may be produced in the operation theatre (e.g. femoral component cemented with methylmetacrylate). The properties of the bone differ in the bone density, the elasticity, the vascularity, and the transmission of forces. Defining the interrelation of bone and implant we have to consider whether bone is surrounding the implant, whether there is force transmission from bone to implant, or whether the implant is just adjacent to the bone without transmitting forces to it. The topic of this article is to analyse the relationship between implant and bone under different conditions.

ANALYSIS OF DEFINED COMBINATIONS:

a) Non cemented cup in the acetabulum: The implant is usually impacted in the premoulded acetabulum. The force transmission can be at its natural place, craniomedial, in the center of the cup. Using a flattened so called pressfit cup, at least immediately after implantation force transmission happens at the periphery of the cup. Frequently the acetabular components are but partially integrated due to the elastic behaviour of the acetabulum, closing at weight bearing, opening at discharge.

b) Rigid ceramic block in either rigid or elastic bony environment: An important prerequisite for direct osseous integration of an implant is the adaptation of the elasticity of the bone to the implant and vice versa. The complete bony integration of a rigid ceramic block is easy in the epi/metaphyseal area, but it fails in the diaphyseal area, if it is not protected by a rigid type of osteosynthesis as e.g. a medial plate instead of a lateral one (Fig 1).

c) Cementing an implant in the medullary cavity of a diaphyseal bone: Filling the gap between a femoral component and the proximal femur with polymethylmetacylate cement allows

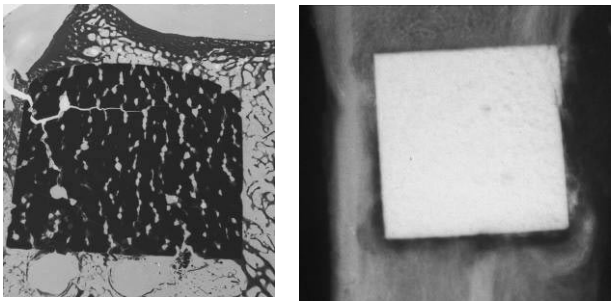

Fig. 1: A rigid hydroxyapatit block placed in a tibial head(left) and in the diaphysis of a femur (right) of a dog, protected by a plate. After 3 month integration in the rigid epi/metaphysisis is complete, but only partial in the elastic diaphysis.

immediate stable fixation of an implant, but in some models of femoral prosthesis loosening happens already after a few years. This was observed, when one changed e.g. the metal of the straight stem (ME Müller) from a CoNiCrMo alloy to a Ti6Al7Nb alloy. The rigid stem out of the first alloy protects the cement, which is sensitive to fatigue, from degradation. This is not the case with the more elastic titanium alloy.

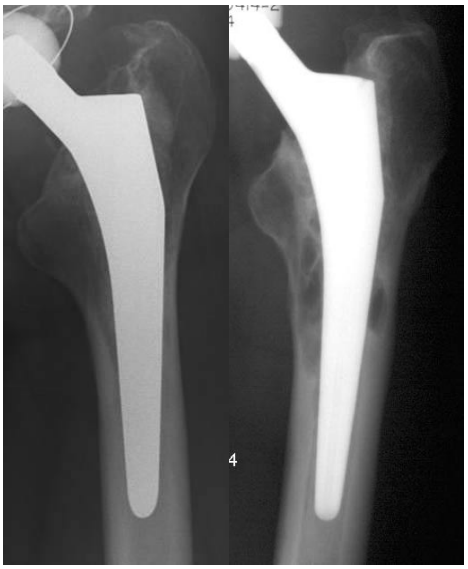

Fig. 2: perfectly integrated CoCr stem after 20 y (left) versus a loose Ti stem of the same size after 4 ½ years (right).

Multiple additional examples are presented in order to show that any implant has to be adapted to its place of use and function.

Bioresorbable Metals for Implant Application

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INTRODUCTION: In the last decade, two material classes have been the focus of bio-degradable applications: polymers and metals. Of the two, metallic materials show the greater mechanical strength, and degradation products provoke fewer inflammatory reactions. Iron and magnesium alloys are possible candidates for use in cardiovascular intervention and osteosynthesis. Whereas iron corrosion is very slow, magnesium alloys have appropriate corrosion rates in physiological media. Magnesium also shows a Young's modulus similar to that of bone (E = 3–20 GPa), which makes it particularly interesting for osteosynthesis applications.

As early as the 1930s, feasibility studies showed the good resorbability and high biocompatibility level of magnesium bone-fixation implants. Recently, various *in-vitro* and *in-vivo* tests clearly confirmed these findings and extensive investigations and developments on biodegradable Mg-alloys started worldwide. As for Fe-based alloys, preliminary *in-vivo* studies have already shown their potential for degradable medical applications: stents made of pure iron implanted into porcine aorta did not induce any local or systemic toxicity. However, because of the very low degradation rate of pure iron in physiological media, such implants are considered to reveal reactions similar to those found in permanent applications. Consequently, alloy modifications are required aiming at increased degradation rate, and improved physical and mechanical properties.

Mg-ALLOY RESEARCH AT LMPT: In our work we aim at optimizing the property profile of Mg alloys – amongst other things by various alloy development approaches of which we present two aspects here. In the first part we focus on alloy design considerations for achieving crystalline Mg alloys suitable for both, coronary stent applications and osteosynthesis. In the second part we present amorphous Mg alloys as a, in this context, new class of biomaterials that exhibit very interesting characteristics for temporary bone implants. Caused by its hexagonal crystal structure and the associated limited number of independent deformation modes the ductility of Mg-alloys is rather limited. Ultrafine-grained Mg-alloys, however, have been shown to offer improved deformation potential. In this study we report on successfully executed design strategies that result in significant grain-size reduction down to few micrometers, by applying conventional processing routes.

Metallic glasses exhibit strengths and elastic limits that are significantly higher than those observed for their crystalline counterparts – at very limited plasticity. From an electrochemical point of view and particularly with respect to implant applications, metallic glasses generally offer two advantages over crystalline metals: they usually exhibit a homogeneous single-phase structure without the occurrence of intergranular corrosion, and they are capable of solving much higher amounts of alloying elements which inhibits galvanic corrosion. Overall these factors enable homogeneous degradation processes and allow modifying the corrosion resistance of magnesium by much less restricted addition of nobler elements.

Fe-ALLOY RESEARCH AT LMPT: Here the influence of specific alloying elements on the electrochemical modification of the Fe matrix and the controlled formation of noble intermetallic phases is of high interest. Manganese and palladium have been shown to be suitable alloying additions for this design strategy: Mn lowers the standard electrode potential, while Pd forms noble (Fe, Mn)Pd intermetallics acting as cathodic sites. We discuss the efficiency and the potential of the design approach, and evaluate the resulting characteristics of the new alloys. The newly developed Fe-Mn-Pd alloys reveal a degradation resistance that is at least one order of magnitude lower than observed for pure iron. Additionally, the mechanical performance is shown to be adjustable not only by the choice of alloying elements but also by heat treatment procedures.

REFERENCES:

A.C. Hänzi, I. Gerber, M. Schinhammer, J.F. Löffler, P.J. Uggowitzer, (2010) *Acta Biomat.* doi:10.1016/j.actbio.2009.10.008;

B. Zberg, P.J. Uggowitzer, J.F. Löffler (2009) *Nature Materials* **8**, 887 – 891.

M. Schinhammer, A.C. Hänzi, J.F. Löffler, P J. Uggowitzer (2010) *Acta Biomat.* doi:10.1016/j.actbio.2009.07.039.

Passivity and corrosion of metals

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INTRODUCTION: The corrosion of metals is controlled by thermodynamics and kinetics. While in certain environments many metals will corrode due to the thermodynamic laws, the corrosion is limited to very low values due to a kinetic barrier: the passive film. The understanding of the passive film, its formation and breakdown is therefore essential to understand the performance of the alloys.

PASSIVITY: Stainless steels, iron alloys having at least 12% chromium, and titanium are well known for their corrosion resistance due to the formation of a passive film. Without a passive film iron alloys would corrode in many environments, including body fluids of all kinds.

Only by adding various alloying elements stainless steels form spontaneously a very thin passive film on the surface, which is composed of iron and chromium oxides and hydroxides. The models established so far show that the passive film is of an electronic nature with defects incorporated in the film. The electronic nature of the passive film and the defects allow the transport of electrons and ions through the film. In consequence, even with a passive film present on the surface, a very slow dissolution will take place. This can be seen in the potential vs. current plot of a stainless steel (Fig 1).

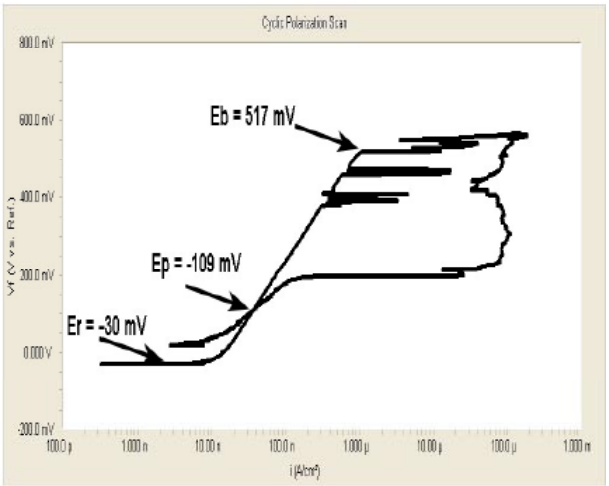

Fig. 1: Potential current plot for stainless steel 1.4404 in solutions acc. ASTM F2129-06 [1].

Close to E_r the transition from active to passive takes place, this is followed by the passive state. But, already in the passive state current fluctuations can be seen which are related to metastable localized breakdowns of the passive film due to chlorides present in the environment [2]. These localized attacks can be identified in the scanning electron microscope as attacks on the metal.

At E_b the stable pitting of the alloy is reached. This state is maintained in the reverse scan until E_p is reached where the active repassivates again. The passive film has changed its constitution depending on the applied potential. In the course of these processes, ions are released from the base metal through the film or from the film.

While the passive film on stainless steels is composed of oxides and hydroxides, the film on titanium and its alloys is formed of oxides. These oxides are more stable than the hydroxides on the stainless steels. Over a wide potential range the current does not increase, which indicates the stability of the film on titanium. But, even titanium alloys will slowly release ions to the environment.

CORROSION TESTING: Beside proprietary corrosion testing standards for medical implants, mainly the ASTM F2129 standard is used to asses the corrosion properties of metals. In addition to these electrochemical tests the heavy metal ion release has to be determined. Electrochemical tests, rest potential E_r measurements, wear tests and ion leaching tests will give the information necessary to qualify metals for implants.

REFERENCES: [1] S. Rosenbloom et al. (2007) *An assessment of ASTM F 2129 electrochemical testing of small medical implants*, Paper 07674, Corrosion 2007, NACE [2] R. Morach (1994) *Zur Entstehung lokaler Korrosionsangriffe auf passiven Metallen*, Diss10677, ETH Zürich

Surface properties of titanium implants treated by spark-assisted anodizing

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INTRODUCTION: The low density, good mechanical stability and biocompatibility make titanium to an ideal implant material. However, biocompatibility does not mean that the surface is inert versus biological responses. In addition, interaction of the titanium surface with other solid materials when used in multi-component implants may induce interfacial destruction and failure. Therefore surface treatment is a requirement for many applications. We have established a surface treatment technology based on the phenomenon of the dielectric breakdown with spark appearance at the titanium implant, which we call "Spark-Assisted Anodizing (SAA)".

METHODS: Samples of cp Ti gr. 2, 4 and Ti6Al4V were mechanically pre-treated, cleaned in an ultrasonic bath with an alkaline cleaner, rinsed with de-ionized water and dried at 100°C. Samples were contacted at the anode, introduced into an electrochemical cell filled with an alkaline electrolyte of proprietary composition and anodized under galvanostatic conditions. Surface topography was analyzed using the FRT MicroProof® device. Layer thickness was determined by XPS depth profile analysis (PHI Quantum 2000 XPS spectrometer, Ar^+ sputtering). Initial friction coefficients were measured with the CSM "ball-on-disc" tribometer using a steel 100Cr6 ball. X-ray diffraction analysis was performed using the diffractometer MRD-XL (PANalytical, Cu target).

RESULTS: During the electrochemical process O_2 evolution at the anode is induced followed by the appearance of sparking due to dielectric breakdown. The voltage for oxygen and sparking appearance depend on the composition of the electrolyte. The anodized samples show a porous outermost layer and an underlying conversion layer. The outermost layer can be removed by sand blasting. The grey-brownish conversion layer reveals a R_a value of 0.3-0.4 µm and shows a concentration gradient for the elements from the outer-surface over *ca.* 3 µm to the basic titanium material (Figure 1). The initial friction coefficient is generally lower by 30-40 % compared to the untreated or colour-anodized samples. The outermost porous layer consists of amorphous precipitated material from the electrolyte and titanium with embedded anatase and rutile TiO_2 crystals. The conversion layer is amorphous with few rutile crystals. The SAA treated samples passed successfully the biocompatibility tests according to ISO 10993/parts 3, 4, 5, 10.

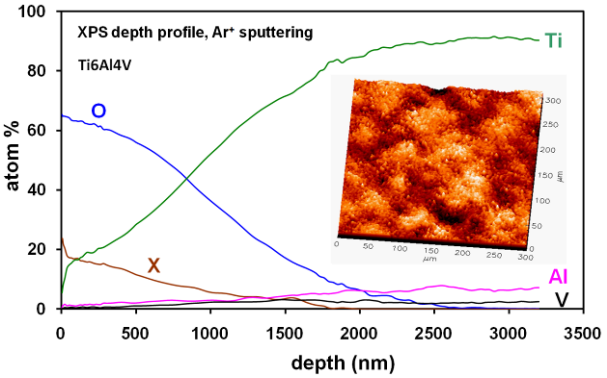

Fig. 1: Atom % of the elements as function of the depth obtained from XPS measurements on a Ti6Al4V sample. "X" indicates an element from the electrolyte deposited into the layer. The inset shows the typical surface topography of the conversion layer obtained by the SAA process after removal of the outermost porous layer

DISCUSSION & CONCLUSIONS: Dielectric breakdown in an electrolyte accompanied with sparking has been observed already in 1880 [1] and later for a number of valve metals by several scientists [2]. Because of the interplay between the solid state of the metal and the liquid state of the electrolyte, the gas state of oxygen and the plasma state formed during the discharge event the mechanism of the anodizing process is very complex. The properties of the produced surface strongly depend on the electrochemical conditions. This process appears to be a good basis for the development of a surface finish of implants used for different applications [2]. The surface finish described above is marketed by KKS Ultraschall AG as TioDark™.

REFERENCES: [1] N.P. Sluginov (1880) *J Russian Phys and Chem Soc* **12**:193. [2] E. Matykina, A. Arabell, P. Skeldon, G.E. Thompson (2009) *Acta Biomaterialia* **5:** 1356–1366.

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Investigating the porosity of 3D printed calcium phosphate scaffolds

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INTRODUCTION: Ceramic scaffolds are widely used for bone augmentation in regenerative medicine [1]. The performance of implant materials depends on its structure, morphology and in particular on its porosity. Additive manufacturing allows the production of bone-like structures with designed materials and morphologies [2]. The outer geometry and inner architecture of the structure is planned virtually and then physically realized in three dimensions.

METHODS: In this study the 3D Printer Z-510 from Z-Corporation is used to create calcium phosphate scaffolds of variable designs by a binder-powder system. Cylinders of ø11mm, height h=11mm, and an orthogonal system of variable channel sizes (0.6-1mm) were created, see fig. 1a. The porosity of the green body was measured by two complementary methods: Mercury Intrusion Porosity (MIP, micromeritics AutoPore IV) and µ-computer tomography (µCT, SkyScan 1172, 100kV, 12.5µm voxel size). The morphology of the 3D printed scaffold was further analyzed by Scanning Electron Microscopy (SEM, Hitachi TM-1000, 15kV).

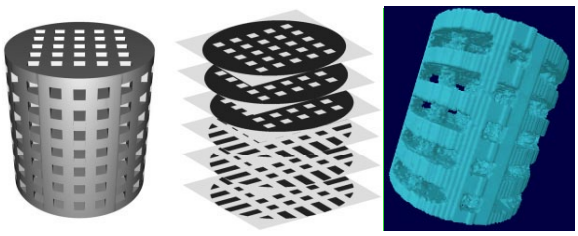

Fig. 1: a) CAD model and b) Three-dimensional reconstruction of the 3D printed scaffold as measured with µCT.

RESULTS: The µCT measurements reveal the structure with the designed pores (fig. 1b) and the corresponding porosity (table 1). The MIP measurements confirm the designed pores in the range of 450-1000µm; see fig. 2. However, the main part of the porosity is detected in the range between 5-50µm, independent on the design, even in the full cylinder without any intended inner structure (table 1). The pores are clearly visible in the SEM images, see inset fig. 2.

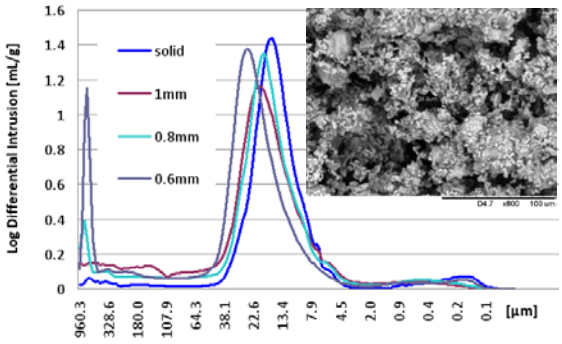

Fig. 2: Pore-size distribution measured with MIP. Inset: SEM image of the structure.

Table 1: Porosity measurements [%].

	CAD	µCT	MIP
solid	0.00	0.02	62.53
0.6mm	17.30	20.64	69.24
0.8mm	28.64	32.87	66.59
1mm	41.25	43.03	65.00

DISCUSSION & CONCLUSIONS: Two types of pores were detected in the scaffolds: The planned pores in the range of 600-1000µm and the material specific pores around 20µm. The intended pores are on the upper detection limit for the MIP method. The used µCT resolution is not high enough to resolve the inherent interparticular porosity, which arises from the powder-binder reaction. It remains interesting, however, to study the material specific porosity after sintering the structures and enhance the scaffolds strength.

REFERENCES:

[1] P.K. Yarlagadda, M. Chandrasekharan, J.Y. Shyan (2005), *Recent advances and current developments in tissue scaffolding. Biomed Mater Eng* **15**:159–77.

[2] A.C. Jones, C.H. Arns, D.W. Hutmacher, B.K. Milthorpe, A.P. Sheppard, M.A. Knackstedt (2009). *The correlation of pore morphology, interconnectivity and physical properties of 3D ceramic scaffolds with bone ingrowth. Biomaterials* **30**:1440-1451.

Laser Welding of Titanium

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INTRODUCTION: Refractory metals like tantalum and titanium have a high melting point and feature high corrosion resistance. Because of their partially good biocompatibility they are often used in medical device industry. The cheapest and most widespread refractory metal is titanium.
The technological obstacle of titanium welding is the high affinity for atmospheric gases at increased temperatures. That is why titanium is either welded by TIG or cw laser welding in a shielding gas box or by electron beam welding in a vacuum.

METHODS: Modern Nd:YAG laser sources have the facility to vary the release of energy inside of a pulse.
The basis of pulse forming is the internal control of the power output. The power of the output radiation is measured via an appropriate sensor and compared with the setpoint specified by the pulse shape. Systems in use today work at a frequency of 20 kHz, i.e. the output power is recorded at a time interval of only 50 µs, compared with the setpoint and adjusted accordingly.
The latest improvement to the method considers additional modulation of the pulse shape.

RESULTS: The microstructure development in the fusion zone depends on the solidification behaviour of the weld pool. *Fig. 1* depicts schematically the effect of pulse shape modulation on the weld pool temperature and solidification.

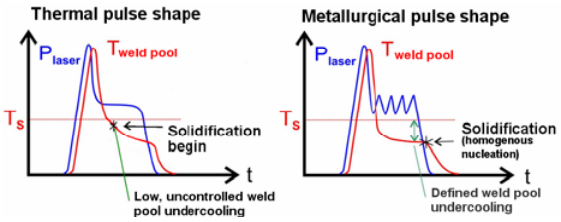

Fig. 1: Effect of pulse shape modulation on the weld pool temperature and solidification

The principles of solidification control the size and shape of the grains, segregation, and the distribution of inclusions and porosity. The solidification conditions during the welding of metallic materials are influenced essentially by the time-temperature regime. The laser beam welding distinguishes itself in comparison to the conventional fusion processes by high temperature gradients and high cooling rates. In the case of modulated pulse laser beam sources, it is possible to modify the time-temperature regime so that controlled nucleation can take place in a restricted time interval during the solidification. With a higher weld pool undercooling, the nucleation rate reaches a maximum so that a distinctively fine-grained structure originates. The pulse shape modulation of the heat source allows for a stabilization of the molten metal temperature and, additionally, defined weld pool undercooling takes place. At the end phase of the pulse, as compared to the thermal pulse shape, higher weld pool undercooling is used to increase the nucleation rate that leads to a "homogeneous" fine-grained structure. In the case of dissimilar alloys, the growth of intermetallic phases can be suppressed.
Due to the Nd:YAG laser beam pulse modulation, significant refinements of the solidification structure and a transition from columnar to equiaxed growth have been observed in titanium grade 1, austenitic stainless steels and aluminium 99.5%. In titanium grade 1, grain size refinement (about 30%) and in Cr-Ni austenitic stainless steel increased fraction (+8%) of finer grains have been reported.

DISCUSSION & CONCLUSIONS: A new, innovative laser beam welding process with a free scalable pulse shaping Nd:YAG laser was introduced. The laser involves a low energy input per unit length. Therefore, the laser-process-characteristic complex shielding gas apparatus (e.g. a long dragging nozzle) is not required any more. This new procedure thus provides a cost-effective way of welding refractory metal sheets [1-4].

REFERENCES:

[1] U. Zwicker (1974) *Titan und Titanlegierungen*, Heidelberg, Springer Verlag. [2] Merkblatt DVS 2713 (2003) *Schweißen von Titanwerkstoffen*, DVS-Verlag. [3] J. P. Bergmann (2003) *Beitrag zum Laserstrahlschweißen von Titanwerkstoffen*, Aachen, Shaker Verlag. [4] Titanium Information Group (1999) *Welding Titanium-A designers and users handbook.*

A Review: Understanding implantable grade PEEK's interface and interaction with cells

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BACKGROUND: The implant grade of the polymer polyetheretherketone (PEEK) has been extensively used in medical devices, such as spinal fusion cages, since its introduction in 1999. The PEEK biomaterial is a high performance and high purity thermoplastic. It is naturally radiolucent and allows clinicians to assess healing around an implant without imaging artefacts. In addition, PEEK has a reduced modulus to the traditionally used metals, which can benefit the surrounding bone by allowing transfer of mechanical stresses. The properties of PEEK are versatile and the material properties have been tailored in some instances for devices. For example, carbon-fibre (CF) additives have been used to enhance the material's mechanical strength and stiffness and tribological properties. Chopped CF-PEEK tensile strength can be raised from 100 to 230 MPa and the modulus increased from 3.5 to 18 GPa to make PEEK more similar to the properties of cortical bone.

As PEEK device applications have diversified into other applications such as Active Implantables, orthopaedic, craniomaxillofacial, dental and arthroscopy, the demands on the biomaterial have also changed. For example, recent publications[1,2] have verified the typical amount of bone to implant contact, showing a level of approximately 30% for PEEK. Whilst clearly sufficient for current PEEK device applications[3], in some new instances it may be preferable to increase this contact level if looking to use the biomaterial in new device applications requiring fixation to adjacent bone, such as hip cups or dental implants. Described are several methods of altering the properties of PEEK so as to benefit from its existing properties, whilst capitalising on additional ones.

PEEK compounds: PEEK can be compounded with materials such as Bioglass™, Tri-calcium phosphate and hydroxyapatite (HA) to alter mechanical properties in line with bone, but also confer additional surface bioactivity. Biological and mechanical properties of a PEEK:HA twin screw compounded material is reported (*Table 1*). Milled CF-PEEK compounds can lower the modulus over metals and reduce wear particle debris compared to ultrahigh molecular weight polyethylene, both which could benefit surrounding bone and immunological response.

Surface Modifications: PEEK can be covalently modified through wet chemistry, plasma modified to alter surface activity and hydrophilicity, or coated using other biocompatible materials such as HA or titanium.

Surface topography: Surface changes conferred by industrial processing methods such as injection moulding or machining, can have subtle influences on how bone cells and bacterial cells behave[4]. Osteoblasts differentiation can differ depending upon material type (unfilled vs CF-PEEK) and topography (*Figure 1*)[5].

Property	PEEK	30%HA PEEK
Impact (KJ/m2)	7.3	5.2
Flex Strength (MPa)	162.5	154.2
Flex Modulus (GPa)	4.0	5.6
Tensile Strength (MPa)	99.3	81.8
Strain at Break %	35.8	3.9

Table 1: Mechanical properties of twin screw compounded PEEK with 30%HA.

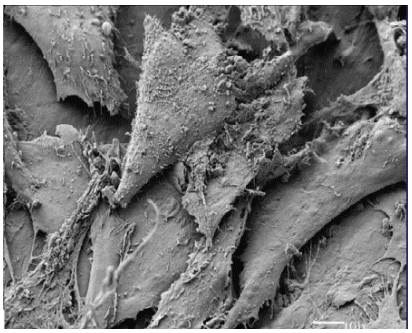

Figure 1:Human primary osteoblasts on PEEK.

REFERENCES: [1]C.M. Han, E.J. Lee, H.E. Kim, Y.H. Koh, K.N. Kim, Y. Ha and S.U. Kuh (2010) *Biomaterials* **31**:3465–3470. [2]F.P. Koch, D. Weng, S. Krämer, S. Biesterfeld, A. Jahn-Eimermacher and W. Wagner (2010) *Clin Oral Imp Res.* **21**:350–356. [3]C.C. Niu, J.C. Liao, W.J. Chen and L.H. Chen (2010) *J Spinal Disord Tech*, Jan 27. [4]E.T.J. Rochford, A.H.C. Poulsson, T.F. Moriarty and R.G. Richards (2010) *ORS* poster 2178. [5]K.B. Sagomonyants, M.L. Jarman-Smith, J.N. Devine, M.S. Aronow and G.A. Gronowicz (2008) *Biomaterials* **29**:1563-72.

Regulatory guidelines in the innovation process

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INTRODUCTION: The directive 93/42/EEC on medical devices was extended in September 2007 by the provisions of directive 2007/47/EC. The new directive has to be mandatory adopted on and after March 21st 2010 and implicates significant changes for manufacturers and notifies bodies.
The national implementation of the new directive in Switzerland is documented in the medical device enactment (MepV: SR 812.213). For manufacturers of medical devices there are possibly resulting certain consequences with respect to the conformity assessment of their products.

METHODS: By means of a document review the essential changes of the 93/42/EEC were analysed and evaluated under consideration of the regulations of the directive 2007/47/EC.

RESULTS: The most important points of the directive 2007/47/EC additionally regulating the medical device market are as follows:

- Software is defined an independent medical device, if it is intended to be used for diagnostic and/or therapeutic applications and if it is designated to guarantee a correct functioning of a medical device.
- The term „clinical data“ is now defined in a more comprehensive form.
- For a better differentiation of pharmaceuticals and medical devices, the applicable regulations are specified.
- The applicability of further guidelines (e.g. on personal protective equipment, machinery) is clarified.
- Inclusion of the technical documentation in the records to be audited.
- Surveillance of the sub-contractors.
- Changes in the classification of different medical devices.
- Extended storage obligation for documents on implantable medical devices (15 years).

DISCUSSION AND CONCLUSION: Manufacturers of medical devices should deal closely with these changes of the directive 93/42/EEC and the Swiss legislation on medical devices and should put into consideration the following aspects:

- Product classification
  Review of the classification of the own products acc. to the alterations in the annex IX of the MDD 93/42/EEC
- Development and review of clinical data
  A documented clinical assessment forms the condition to demonstrate the conformity with the essential requirements.
- Risk management
  Product and/or production changes, regulation changes give cause to seriously review the internal risk analysis and to adapt the risk assessment where applicable.
- Innovation process
  The strategic orientation of an innovation process has, besides the technological and the market development, to include the progress in the regulatory environment as well.

REFERENCES:

93/42/EEC	Council Directive of 14th Jun 1993 on medical devices.
2007/47/EG	Directive of the European Parliament of Sept 5th 2007
MepV	Medizinprodukteverordnung (SR 812.213 vom 1. April 2010).
ISO 13485	Medical Devices – Quality management systems – Requirements for regulatory purposes.
ISO/TR 14969	Quality management systems – Medical devices – Guidance on the application of ISO 13485.

Tileye – Inspection of Implant Surfaces

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INTRODUCTION: To meet the high standards on implant quality, 100% validation is a must. While dimensional checks can be automated to reduce costs, there exists no generic automated solution to detect non-dimensional defects on the surfaces or residues from production. Tileye fills this gap by building on recent advances in machine learning.

METHODS: There exist two basic strategies for the automation of visual inspection in the domain of flaw detection:

- *defect-oriented:* explicitly search for known defects as specified in a database
- *model-oriented:* find discrepancies between the inspection item and an existing model

The first approach is state-of-the-art and many readily available industrial software libraries offering mostly dimensional checks fall in that category. In the case of non-dimensional defects such as scratches or residues, in contrast, the model-oriented approach is the only viable option. However, depending on the visual complexity of the inspection item the construction of a precise model can become very difficult if not impossible.

The central idea behind the Tileye Inspection System is to circumvent this problem of model construction by providing an elaborate learning system imitating the human visual system, which is able to autonomously learn a precise model from a few good samples. Much like a human would be able to identify a defective item after thoroughly studying a couple of flawless examples, the system can identify any deviations between the learned model and the presented item and flag them as defects if they exceed a given threshold.

Given the sample images and a region of interest, the system extracts small tiles of 16x16 pixels for which it builds a high-dimensional statistical description. After an autonomous learning phase that involves the iterative adjustment of the object model, the system is able to reconstruct the most likely appearance of a tile. This reconstruction will not contain any features that were not present in the learning data, i.e. any types of defects. Thus, comparing each input tile to its reconstruction reveals any defects, such that they can be flagged by simple thresholding (Figure 1).

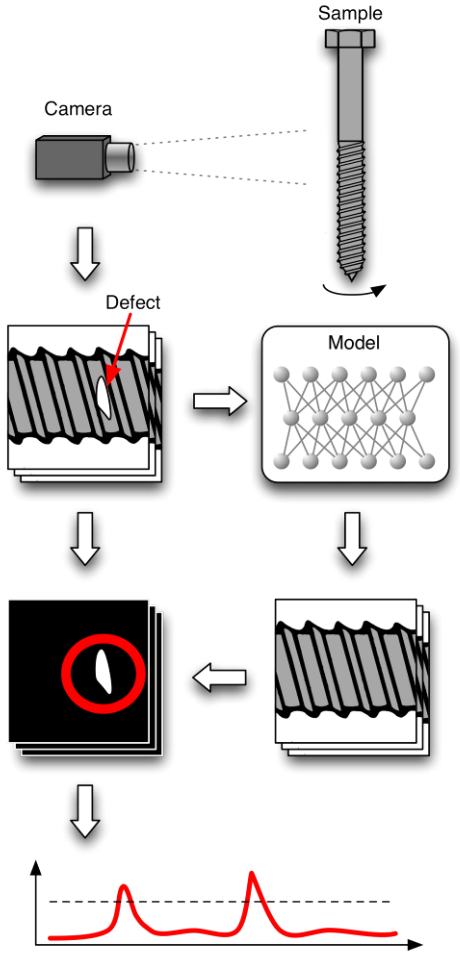

Fig. 1: The inspection procedure: comparing the incoming image with its reconstruction from a learned model reveals any defects.

CONCLUSION: Tileye is a new flexible vision system, which allows the inspection of complex implant surfaces based on a model autonomously learned from a few exclusively good samples. Since no a priori model of the implant is required, the inspection system not only reduces the effort and cost to implement automated quality inspection but also offers new possibilities and increased reliability.

ACKNOWLEDGEMENTS: This work was supported by the MCCS (Micro Center Central Switzerland).

High Resolution CT for 3D-Analysis of Biomedical Materials

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INTRODUCTION: High resolution computed tomography (micro CT) with industrial CT-scanners has become a powerful evaluation tool for a wide range of applications. Depending on sample size and material, resolutions down to one micrometer or even below can be achieved. This is much better than the resolution of common CT-scanners as used for medical diagnostics and makes these micro-tomography systems suitable for research on biomedical and other materials. Variations of the effective X-ray absorption coefficient related to the spatial distribution of the different materials within the specimen are imaged in three dimensions, visualising features such as material composition, bone density or porosity. The micro-CT data provides detailed information on tiny structures like porosity networks, replacing time consuming destructive preparations. Several biomedical applications will be briefly described including a comparison of X-ray tube based CT with synchrotron radiation based micro CT (SRμCT).

METHODS: The SRμCT measurements were carried out at the 2nd generation storage ring DORIS III at HASYLAB/DESY in Hamburg, Germany. The technical description of the CT apparatus and the beamline is given in the article of Brunke and references cited therein [1].

The X-ray tube based measurement were performed with the phoenix nanotom (GE Sensing & Inspection Technologies), a laboratory nanoCT system equipped with a 180kV/15W high power nanofocus (HPNF) tube which in the nanofocus mode provides an X-ray source size of down to <0.9 μm enabling the detection of < 0.5 μm size details. The pixel size of the 3-position virtual detector (i.e. 360 mm detector width) is 50 μm. Tube, detector and air bearing rotation unit are mounted on a granite structure to avoid the influence of vibrations or thermal expansion. For reconstruction of the volume data phoenix|x-ray uses a proprietary implementation based on Feldkamp's cone beam reconstruction algorithm. The reconstruction software contains several different modules for artefact reduction (e.g. beam hardening, ring artefacts, drift compensation) to optimise the results.

RESULTS: The direct comparison of the SRμCT and the CT results of three samples, a porous Al2O3 catalyst, sintered Ti6Al7Nb and part of a human vertebra, reveals that the phoenix nanotom to deliver excellent data quality which in many cases can even compete with SRμCT data. In total, the major advantages of the laboratory CT system are its large field of view, large scanning volume, high penetration power due to the 180kV tube, high scanning speed (scanned volume per time), ease of use and overall cost effectiveness. The synchrotron radiation CT, on the other hand, provides an excellent contrast resolution, precisely adjustable monochromatic radiation and therefore results free from beam hardening artefacts.

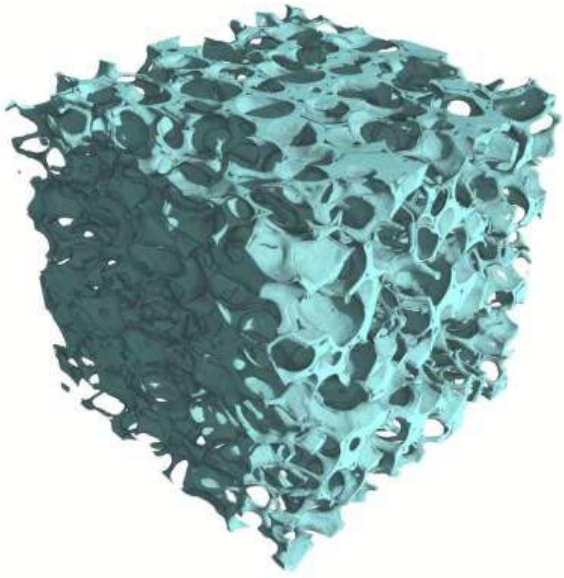

Fig. 1:3D-visualisation of the porosity network of a hydroxylapatite sample scanned with 5 μm voxel size.

High resolution CT systems have been further applied to implants like a cobalt-chrome hip cup and biomedical materials such as hydroxylapatite, see figure 1, with excellent results.

REFERENCES: [1] O. Brunke et al. (2008) *Proc of SPIE* **7078**: 70780U1-12.

Monitoring Elemental Release from Implants

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INTRODUCTION: The growing application of implants in dentistry, arthroplasty, etc., has led to the parallel development of techniques designed for use in monitoring the integrity of implants. One such technique is inductively coupled plasma-sector field mass spectrometry (ICP-SFMS), which is used to detect and quantify changes in elemental concentrations in body fluids [1] post operation. In this presentation examples of the application of ICP-SFMS to monitoring elemental release from implants will be given [2, 3], and the capabilities of the technique described.

METHODS: Serum was sampled using materials selected on the basis of minimizing trace element contamination of collected specimens [4]. Samples were prepared for analysis by diluting in de-ionized water (resistivity >18 MΩ), further purified by sub-boiling distillation in a more recent study [3], and acidified (0.2 M hydrochloric acid or 0.14 M nitric acid, depending on the elements of interest).

Analyses of serum samples were performed using an Element 2 ICP-SFMS instrument operated with a mass resolution of 4000 for the examples shown in Figures 1 and 2.

RESULTS: In the first study [2], Al, Ti and V concentrations (only V shown in Figure 1) were determined in serum samples collected during a 5 year follow-up of total hip arthroplasty (THA) comparing two cementing agents (Cemex and Palacos in Figure 1).

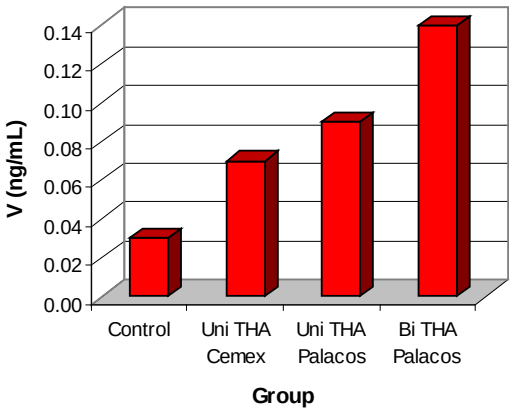

Fig. 1: Measured V concentrations in serum samples from controls and patients following unilateral (Uni) or bilateral (Bi) THA [2].

In a second study [3], post-operative levels of Ti were determined in patients with titanium alloy spinal instrumentation, as illustrated in Figure 2.

Table 1 provides selected limits of quantitation (LOQs) that can be achieved for the analysis of serum by ICP-SFMS.

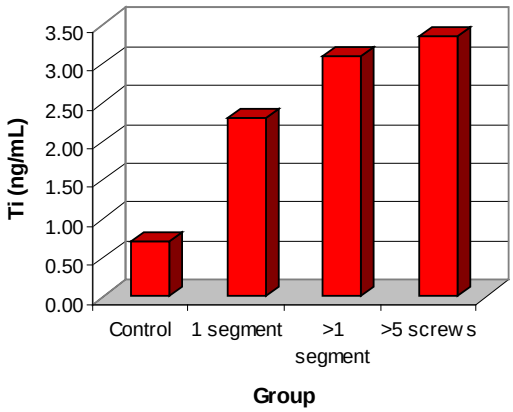

Fig. 2: Measured Ti concentrations in serum samples from controls and patients after instrumented spinal arthrodesis [3].

Table 1. LOQs for selected elements in serum and upper limits in the non-exposed population.

Element	LOQ (ng/mL)	Upper limit (ng/mL)
Al	2	6
Au	0.02	0.1
Co	0.03	0.2
Mo	0.04	0.9
Ni	0.1	0.6
Pt	0.004	0.005
Ti	0.3	0.3
V	0.09	0.1

DISCUSSION & CONCLUSIONS: In the two examples shown, ICP-SFMS could clearly recognize increases in metal ion levels in the serum post implantation. This is one indication of the onset of fixture failure.

REFERENCES: [1] I. Rodushkin et al. (2004) *Anal Bioanal Chem* **380**:247-257. [2] B. Nivbrant et al. (2001) *Acta Orthop Scand* **72**:572-584. [3] T.D. Richardson et al. (2008) *Spine* **33**:792-796. [4] I Rodushkin and F. Ödman (2001) *J Trace Elem Med Biol* **15**:40-45.

History of and State-of-the-Art in Total Knee Replacement

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INTRODUCTION: Today Total Knee Replacement (TKR) can be considered as a successful operation with regard to pain relief and functional improvement for the patient. Total knee prostheses are durable with 10- to 15-year implant survival rates of higher than 90% [1].

Nevertheless, some total knees might fail early after surgery. There are various reasons for TKR failures and quite often it is a combination of several factors. They have given us evidence for further improvements of implant designs, materials and surgical techniques.

HISTORY OF TKR: Towards the end of the 19th century it was Themistokles Gluck in Berlin who implanted a hinged knee joint made of ivory for the first time. These hinges provided good short-term pain relief but function and range of motion was highly limited. During the same period of time, some surgeons were trying to treat arthritis of the knee with a metal spacer, which was placed between the bones of the knee to eliminate the rubbing of irregular surfaces on each other. These implants, the McKeever (1957) and MacIntosh (1958, 1964), achieved some success but were not predictable, and many patients continued with significant symptoms.

Next, surgeons at Massachusetts General Hospital made prosthesis in the shape of the femoral half of the knee joint. This mold type arthroplasty helped in relieving symptoms but was not predictable nor were the results always lasting. These "primitive" replacements evolved from 1940 to 1965.

It was only in the later 1960's when a Canadian orthopaedist, Frank Gunston, from Sir John Charnley's Hip Center, developed a metal on polymer knee replacement secured to bone with a polymethylmethacrylate (PMMA) cement known only for dental applications at this time (1968). He actually transferred the “low-friction concept” established in Total Hip Replacement by J. Charnley to knee arthroplasty and developed the first unconstrained knee prosthesis system.

The introduction of prostheses components made of CoCrMo alloys articulating against polyethylene solved the problem of metallic wear of former concepts and led to a break through in knee arthroplasty.

STATE-OF-THE-ART IN TKR: Today’s designs and materials applied in TKR are based on the success of implant designs developed in the 1970ies. After this important period and until today the close cooperation between surgeons and engineers has led to today’s modern knee prostheses system. Their clinical success is basically based on the following main factors:

- better biomechanical understanding of knee function and kinematics [2]
- implant designs allowing enhanced and more natural kinematics [3]
- implant designs incorporating an adequate level of and indication specific constraints between femur and tibia component
- implant designs with an incorporated tolerance for a certain extent of implant component alignment or positioning errors
- enhanced mechanical and tribological properties of used materials and hence
- reduced polyethylene wear leading to a reduced risk for particle induced osteolysis or loosening of implant components
- improved instruments and surgical techniques
- well educated and experienced surgeons

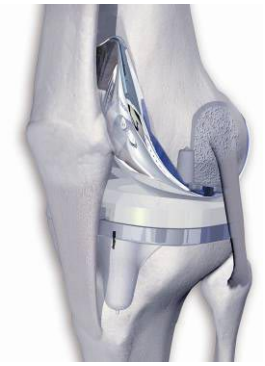

Fig. 1: Total Knee Replacement: Femur and tibia component made of casted CoCrMo Alloy (ISO 5832-4) with a UHMWPE inlay (ISO 5834-2) in-between.

REFERENCES: [1] Rasquinha VJ, Ranawat CS et al. (2006) *The press-fit condylar modular total knee system with a posterior cruciate-substituting design.* JBJS Am., May;88(5):1006-10.
[2] Pinskerova V, Freeman MA et al. (2004) *Does the femur roll-back with flexion?* J Bone Joint Surg Br. Aug. 86(6):925-31.[3] Victor J, Bellemans J (2006) *Physiologic kinematics as a concept for better flexion in TKA.* CORR 452:53-58.

Surfaces of metal-on-metal hip joints before, during and after tribological loading

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INTRODUCTION: The ongoing research and development in hip arthroplasty should lead to a longer lifetime of artificial hip joints. Possible improvements are attributed to enhanced surgical techniques, improved joint designs and materials, and are based on intensive interdisciplinary cooperation. Normally the clinical lifetime of artificial hip joints nowadays distinctly exceeds 10 years. Still problems may arise for several reasons. Thus it is important to understand the nature of sliding contacts in such a system. This contribution focuses on the comparison of surfaces of artificial metal-on-metal hip joints before, during and after wear in laboratory tests as well as after clinical application.

METHODS: For this contribution a large number of CoCrMo retrievals as well as samples of simulator tests have been investigated by SEM and TEM. Further details as to the chosen analysing methods can be found in [1-6]. In addition electrochemical testing acc. to [7, 8] was performed on three different surfaces: a simulator tested CoCrMo femoral head [9] (DePuy International, Leeds, United Kingdom) covered with denatured protein and wear particles generated during the wear test, a simulator tested CoCrMo femoral head that was treated with proteinase K, and a newly manufactured untested femoral head.

RESULTS & DISCUSSION: New Surface: The original surface after production reveals a 20 to 30 nm thick oxide passive film supported by nanocrystalline (nc) CoCrMo. While the first stems from passivation the latter is generated during grinding and polishing. Such surfaces are electrochemically passive and revealed a high polarization resistance.

Worn Surface: During running-in the thin nc-layer is worn away and the subsurface areas showed marked alterations of the microstructures. Directly at the surface nanocrystalline layers with a thickness of up to 400 nm are found. These layers are chemically modified not just by the known physi- or chemisorption or tribochemical reactions, which would generate a layer. They also stem from a process called mechanical-mixing, which introduces the interfacial and surrounding media (here denatured proteins of the pseudosynovia) into the surface material generating a nc metallo-organic composite, which allows for high shear rates in such contacts. Here no passive films have been found so far. At a distance larger than 400 nm below such surfaces one often finds nc-layers of the same grain size, but without denatured proteins. Analytical contact mechanical computer simulations revealed that in these areas a cyclic shear stress field prevails which might generate such micro- and nano-structures. Electrochemically the protein-containing mixed layer brings about a less noble surface. If one removes the metallo-organic composite the underlying nc-CoCrMo shows the best corrosion behaviour.

REFERENCES:

[1]Wimmer, M.A., et al. (2001) *Wear* **250**:129-139. [2]Wimmer, M.A., et al. (2003) *Wear* **255**:1007-1014. [3]Büscher, R. et al. (2005) *Wear* **259**: 887-897. [4]Jacobs, J.J., et al. (2009) *J. Am. Acad. Orthop. Surg*.**17(2)**: 69-76. [5]. Pourzal, R., et al. (2009) *Wear* **267(5-8)**: 689-694. [6]Wimmer, M.A. et al. (2009) J.Orth. Res. **28(3)** 436-443. [7]Munoz, A.I. et al. (2007) J. Electrochem. Soc. **154(10)**: . C562-C570. [8]Mathew, M.T., et al. (2009) Advances in Tribology. [9].Williams, S., et al. (2004) J. Biomed. Mater. Res. B Appl Biomater. **70(2)** 233-9.

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First Clinical Experience with Vitamin-Doped Cross-Linked Polyethylene

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INTRODUCTION: Highly cross-linked polyethylene (HXLPE) has been proven to reduce wear considerably, not only in hip simulator testing, but also in-vivo [1, 2]. There is, however, still some concern due to rising wear and oxidation in the long term [3]. The newest generation of cross-linked polyethylene is therefore protected against oxidation by a small amount of an antioxidant, vitamin E (alpha-tocopherol).

METHODS: The methods used to produce and test the vitamys® material, a HXLPE doped with 0.1% vitamin E, were reported in [4].

The RM-Pressfit vitamys® acetabular cup (Mathys Ltd Bettlach, Switzerland, figure 1) was first implanted in Sept. 2009. All implantations (N=298 up to March 2010) are documented in a prospective multi-centre clinical study involving 11 clinics in 5 countries (CH, DE, FR, NL and NZ).

Fig. 1: The RM-Pressfit vitamys® cup

RESULTS: In table 1, the mechanical properties of vitamys® are compared to conventional UHMWPE and a state-of-the-art HXLPE. The effect of manufacturing steps and in-vivo use on the oxidation resistance is shown in figure 2.

So far no major intra-operative complication related to the cup and no cup revision were reported.

Table 1: Comparison of mechanical properties

	UHMWPE [ISO 5834-2, Type 1]	HXLPE [2]	vitamys®
Yield strength	≥ 21 MPa	19 MPa	23 MPa
UT strength	≥ 35 MPa	30 MPa	37 MPa
Elongation at break	≥ 300%	210%	390%

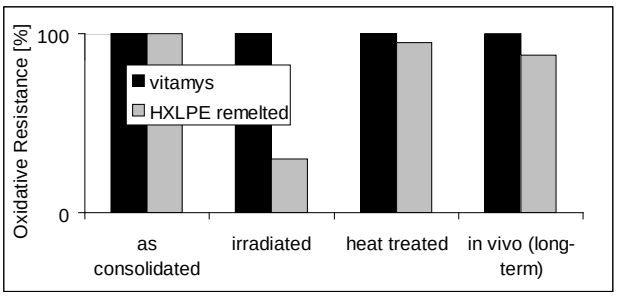

Fig. 2: Effect of production process and in-vivo use on oxidation resistance

DISCUSSION: 25 of the RM-Pressfit vitamys® cups (8.4%) were used with 28 mm heads, 57 (19.1%) with 32mm and 216 (72.5%) with 36 mm heads. It is interesting to note that the distribution of head sizes has changed significantly from the RM-Pressfit using standard UHMWPE (see figure 3). Surgeons aim to increase range-of-motion and thus decrease the luxation risk by employing bigger head sizes than previously possible.

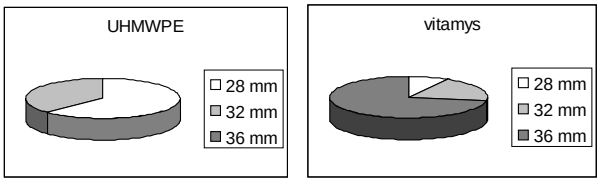

Fig. 3: Distribution of head sizes used in combination with standard PE (left) and vitamys®

In-vivo wear and migration will be followed up by RSA, EBRA and Martell studies and its results will be reported at a later stage.

CONCLUSIONS: The RM-Pressfit vitamys® possesses interesting features such as high elasticity (no stress-shielding), high ageing and wear resistance combined with clinically proven biological anchorage – making it suitable for young and active patients. Its first clinical experience is promising, but of course, much longer follow-up is needed.

REFERENCES: [1] E. Garcia-Rey et al (2008) *JBJS* **90-B**: 149-53. [2] M. Laurant et al (2008) *J of Arthroplasty* **23**:751-61. [3] P.E. Johanson et al (2010) *Annual Meeting AAOS* (New Orleans), paper 109. [4] R. Lerf, D. Zurbrügg, D. Delfosse (2010) *Biomaterials* **31**:3643-48

Retrospective Lifetime Estimation of Failed and Explanted DLC Coated Hip Joint Balls

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INTRODUCTION: In a clinical study the 8.5 year survivorship of DLC (diamond-like carbon) coated TiAlV femoral heads, articulating against polyethylene (PE) counterparts, was only 54%. The surfaces of explanted DLC-heads showed local coating delamination, as displayed in Figure 1, causing severe wear of the PE counterpart [1].

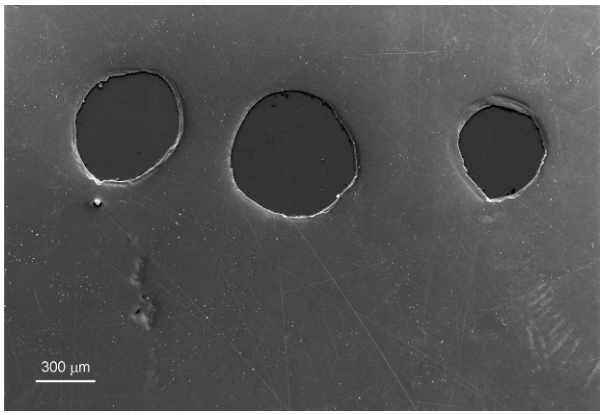

Fig. 1: Round spots of delaminated DLC coating from a femoral head articulating in-vivo against UHMWPE, as described in [1].

METHODS: A Rockwell indentation setup was used to induce the delamination of the DLC coatings. To expose this Rockwell indentation to conditions similar to in vivo, the explants were placed in phosphate buffered saline (PBS), or in Hyclone wear testing fluid (containing 30 g/l of proteins) at a constant temperature of 37 °C. For crack observation FIB cross sections have been cut on a FIB-Dual Beam instrument using a gallium ion beam. The coating composition was determined by XPS depth profiling.

RESULTS: The XPS depth profiles showed that the coating consists of an about 2.2 µm thick DLC coating, followed by several layers with an increase in the Si content. The last layer, bonding to the TiAlV, is an about 50-100 nm thick layer consisting mainly of silicon. By following a delamination crack under the DLC coating to its end by consecutive FIB cuts, we found an opening of about 50 nm, where the entire Si layer is missing. After making four Rockwell indentations into one of the explants, it was first submerged in PBS at 37°C for 228 days and thereafter the media was changed to Hyclone. The delamination of the coating was monitored by optical microscopy, as a function of days and is displayed in figure 2. In Hyclone, we obtained an average delamination speed of 170±15 µm/year.

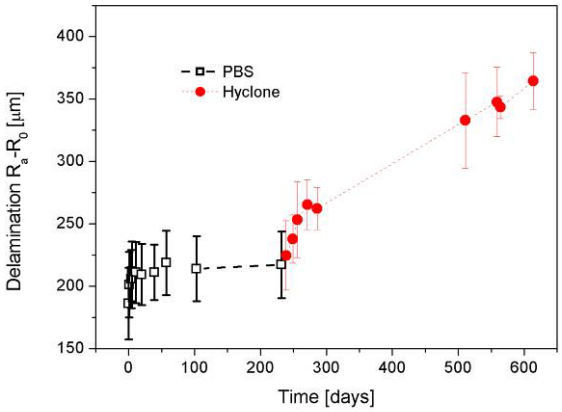

Fig. 2: Average delamination radius minus R_0 (Radius of the Rockwell indent) as a function of time submerged.

DISCUSSION & CONCLUSIONS: Investigation of failed DLC coated explants showed a crevice corrosion like attack of the Si-rich adhesion promoting interlayer. In our tests, crevice corrosion only occurred when submerged in Hyclone. Possibly, the presence of proteins in Hyclone supports the occlusion of the crevice and therefore the build up of crevice conditions. The measured delamination speed in Hyclone (figure 2) is within the range of the observed delamination spots after several years in-vivo (figure 1).

REFERENCES: [1] G Taeger, LE Podleska, B Schmidt, M Ziegler, D Nast-Kolb, Materialwiss Werkst 2003;34:1094-1100.

ACKNOWLEDGEMENTS: Financial support by the Swiss innovation promotion agency CTI and Synthes GmbH, Oberdorf, is gratefully acknowledged.

Large Metal-on-Metal Bearings – Current situation in 2010

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INTRODUCTION: Alternative bearing systems have been developed to minimize wear since aseptic loosening due to polyethylene wear is one major cause of hip replacement loosening.

SMALL DIAMETER METAL-ON-METAL BEARINGS: Small diameter (28 and 32 mm) metal-on-metal total hip prostheses were re-introduced in Europe in 1988 after an extensive in-vitro evaluation. To date, uncemented prostheses with a metal-on-metal bearing have demonstrated good clinical results with a follow-up of 10 years and more[1]. The analysis of the retrievals has confirmed the very low wear behaviour of these bearings with a steady-state linear wear of about 5 µm/year[2].

As metal-on-metal bearings are manufactured in cobalt chrome alloy, delayed hypersensitivity reactions were detected in a small number of patients.

LARGE DIAMETER METAL-ON-METAL BEARINGS: Based on these good results of small diameter metal-on-metal bearings, the size of these bearings was progressively augmented to give a more anatomical configuration. Larger bearings have distinct advantages both for joint stability and range of motion, minimizing therefore significantly the risk of dislocation.

As demonstrated by Dowson[3], the thickness of the synovial film in metal-on-metal bearings increases nearly parabolically, at a power of 2.19, with the head diameter, allowing these large metal-on-metal bearings to have a more favourable lubrication condition than smaller diameter metal-on-metal bearings. This better lubrication for large diameter metal-on-metal bearings was confirmed by exhaustive hip simulator tests done in different laboratories.

Based on the improved stability and tribology, large metal-on-metal bearings started to be an appealing concept, allowing the reintroduction on a large scale of hip resurfacing, especially in Great Britain and Australia.

RESULTS: The published results of large metal-on-metal bearings, especially resurfacing, are somewhat controversial. Results published by designing surgeons are excellent with 10-year survivorship in the range 96 – 98%. These excellent results are partially confirmed by independent studies and by national registries, which yield survivorship rates of 90 – 96%.

However, these independent studies point out new complications which seem to be specific to large diameter metal-on-metal bearings. These complications were described as effusion, cysts, necrosis or metallosis, milking fluid and pseudo-tumours. The incidence of these specific complications is highly variable and ranged from 0.1 to 8.0%. Extensive analysis of this phenomenon demonstrates that the following factors play a role:

- Positioning of the cup
  The incidence of these reactions is minimized by a good positioning of the cup (inclination: 40º ± 5º / anteversion: 20º ± 5º).
- Size of the bearing
  The incidence of these reactions is almost nil for cups larger than 50 mm.
- Gender
  Women are more prone to this complication than men.

The investigation of retrieved specimen for these specific complications demonstrates that these implants had an unexpected high amount of wear with an edge loading phenomenon in almost all cases. This excessive amount of wear may have triggered these complications, which could be described as toxic reactions[4].

CONCLUSIONS: These new specific complications associated with large diameter metal-on-metal bearings may be explained by an excessive amount of wear due to the loss of the lubrication film. The incidence of these complications can be reduced by a good positioning of the cup and by using head diameters larger than 50 mm.

REFERENCES: [1]C.P. Delaunay et al (2008) *CORR* **466**:340-346. [2]C.B. Rieker et al (2002) *Hip Int.* **12**:73-76. [3]D. Dowson et al (2004) *JoA* **19 - Suppl. 3**:124-130. [4]D.J. Langton et al (2010) *JBJS* **92B** 38-46.

Gentamicinpalmitate – A Novel Anti-Infective Coating of Implants

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INTRODUCTION: Implant-associated infections still represent a serious problem and an increasing risk in arthroplasty devastating for the patient and costly for any health care system. The implant as a foreign body is able to support periprosthetic infections as it can be colonised easily by bacteria and, in addition, serve as the retreat for germs which has the potential to cause a relapse. The use of self-adhesive antibiotic fatty acid complexes represents a new option for the anti-infective coating of such implants (Vogt et al., 2003).

METHODS: Gentamicinpalmitate was prepared according to Vogt et al (2003). Elution profiles were determined via fluorescent polarisation in the TDx (Figureott TDx system, Figureott Park, IL, USA). The determination of the antibacterial effectiveness was tested with the aid of proliferation assay (QualityLabs BT GmbH, Nuremberg / Germany) (Bechert et al., 2000). Scanning electron microscopy (SEM) of the coated and uncoated implants were conducted with the TM-1000 (Hitachi) (Hemoteq AG, Aachen / Germany). Biocompatibility tests were determined according to ISO 10993.

RESULTS: Solid gentamicinpalmitate is white to yellow in colour and was characterised as a fine crystalline, free flowing powder. The gentamicinpalmitate powder is based on gentamicin powder as described in the Ph. Eur. The gentamicinpalmitate powder was dissolved in an ethanol solution (20 %). This solution was utilised in a spray or dipping process for the coating of implants. Evenly thin coatings could be placed on the implants surfaces. The gentamicinpalmitate hereby proved to be a waxy solid matter, which easily adhered to the surfaces. Load content of approx. 50 µg to 250 µg of gentamicinbase per cm^2 surface were easily produced. The release behaviour of the gentamicin from surfaces coated with gentamicinpalmitate is consistently analogous with the elution of the gentamicin from well known gentamicin containing bone cements. All probes show a high initial release of the active ingredient within the first 24 to 48 hours, followed by a significantly reduced retarding elution phase in the subsequent days. All uncoated and/or active ingredient free test implants of references used in the in-vitro proliferation assay against *Staphylococcus epidermidis* DSM 18857 showed growth and accordingly could not inhibit the spreading of the test bacteria. In contrast to this, the antibacterial effect of all gentamicinpalmitate coated implants had a clearly detectable bactericidal effect in the test. In the proliferation assay the coated implants with approximately 250 µg gentamicinbase per cm^2 and samples with approximately 100 µg gentamicinbase per cm^2 showed no bacteria growth. In any case the gentamicinpalmitate showed a bactericidal effect against the deployed test germs and all biocompatibility tests fulfilled the ISO 10993.

DISCUSSION: Meta-studies with a large sample number in the United States of America show a sustainable reduction of infection risk with the usage of bone cements containing antibiotics (Parvizi et al., 2008). Gentamicinpalmitate as well as other antibiotic/antiseptic complexes with fatty acids have already been successfully tested *in-vitro* in vascular grafts, surgical sutures and dental titanium implants (Matl et al., 2008, Matl et al., 2009). It can be hypothesized that these *in-vitro* results are comparable to the well documented clinical findings of antibiotic loaded cemented arthroplasty, and can therefore potentially provide a significant contribution to the reduction of infection in the use of further medical implants.

REFERENCES: Bechert, T. et al. (2000) A new method for screening anti-infective biomaterials. *Nat Med*. 6 (9), pp.1053-1056; Kim, S. (2008) Changes in surgical loads and economic burden of hip and knee replacements in the US: 1997-2004. *Arthritis Rheum.* 59(4), pp.481-488; Matl, F.D. et al. (2008) New anti-infective coatings of medical implants. *Antimicrob Agents Chemother*. 52 (6), pp. 1957-1963; Matl, F.D. et al. (2009) New anti-infective coatings of surgical sutures based on a combination of antiseptics and fatty acids. *J Biomater Sci Polym Ed*. 20(10), pp.1439-1449.;Parvizi, J. et al. (2008) Efficacy of antibiotic-impregnated cement in total hip replacement. *Acta Orthop.* 79(3), pp.335-341; Vogt, S. et al. (2003) Porous implants with antibiotic coating, their preparation and use. *EP 1374923 B1*.

Aging of ZrO_2 - Al_2O_3 Dispersion Ceramics – Is it a Subject Matter of Discussions at all?

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INTRODUCTION: Alumina and zirconia ceramics have established themselves in joint endoprosthetics for more than two decades. The use of dispersion ceramics made of the two-component system Al_2O_3-ZrO_2 is a possibility to further improve the mechanical properties. ZTA ceramics (zirconia toughened alumina) and ATZ ceramics (alumina toughened zirconia) play a decisive role. These dispersion ceramics excel by outstanding strength and extremely good wear behaviour.
The present study investigates the aging kinetics of ATZ ceramics under hydrothermal conditions (Low Temperature Degradation – LTD) and tests the influence on strength. 3Y-TZP was used as reference.

METHODS: Discs with a diameter of 20 mm and a thickness of 2 mm of the materials ATZ (80 wt% 3Y-TZP, 20 wt% Al_2O_3) and 3Y-TZP were prepared. After sintering and hot isostatic pressing the plates were aged under hydrothermal conditions in the autoclave at temperatures ranging from 70°C to 134°C over periods of time of up to 5,000 hours.
After aging, the monoclinic phase content was determined as measure of the degradation of the material using XRD and Rietveld refinement. The isothermal transformation curves (ITC) were drawn up for the different aging conditions. The saturation limit of transformation was determined based on the transformation curves. The activation energy for phase transformation was calculated by using *lnK*-factor and Arrhenius plot [1].
An examination of the depth of the monoclinic surface layer using the scanning electron microscope was performed on selected test specimens after creation of cross sections. For evaluating correlation with the local monoclinic content, the surface of specimens aged to the saturation limit was removed by means of focussed ion beam treatment in steps of 3 µm and the monoclinic content was determined [2].
Biaxial bending strength according to ISO 6474 was determined for untreated and for aged plates of a thickness of 2 mm (ATZ) and 0.3 mm (ATZ / 3Y-TZP).

RESULTS: The determined saturation limit for ATZ ceramics amounted to 58 wt% monoclinic ZrO_2. Activation energy for phase transformation tetragonal → monoclinic for ATZ was determined with 96.5 ± 4 kJ/mol. When comparing the isothermal transformation curves at 134°C / 2 bars for 3Y-TZP and ATZ, it turned out that the aging of the ATZ ceramics only starts after aging periods increased by the factor of 8.
The penetration depth of the monoclinic phase is found in the cross section of the aged specimen (Fig. 1).

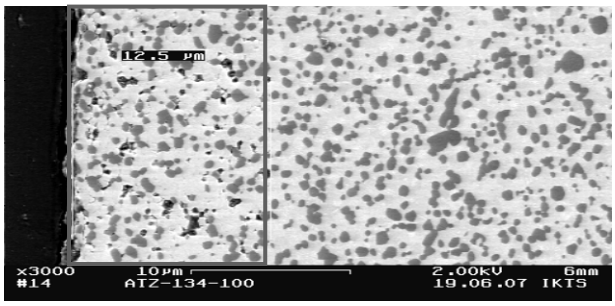

Fig. 1: FESEM of cross section area of aged ATZ

This correlates very well with the results of the XRD phase analysis performed on the specimens treated by ion beam. A constant decrease in the monoclinic phase portion from 56% to 2% over a range of 14 µm is found here.
The biaxial strength of the aged ATZ plates of a thickness of 2 mm increases by 17% compared to the initial state. A drop in strength occurs for the thin plates of a thickness of 0.3 mm after aging. This amounts to 15% for ATZ and to 35% for 3Y-TZP. The formation of micro cracks and disintegration of structure during phase transformation has a stronger effect on the thin plates than on the plates of a thickness of 2 mm. A compressive strain of the surface occurs during the aging process in this case.

DISCUSSION & CONCLUSIONS: By using dispersion ceramics, tendency to LTD is strongly decreased compared to 3Y-TZP. So LTD is not a point at issue for dispersion ceramics used in endoprosthetics. This offers new choices for artificial joints, dispersion ceramics will have a high potential for applications in endoprosthetics.

REFERENCES: [1] J. Schneider et. al. *Low Temperature Aging Behaviour of Alumina-Toughened Zirconia;* J. Am. Ceram. Soc. 91 [11]; (2008) 3613-3618. [2] S. Begand et al. *Surface Properties after Ageing of Dispersion Ceramic and its Influence on Strength;* Key Engineering Materials Vols. 396-398 (2009) 157-160.

Surface Finishes up to Rz 0.2 µm on Medical Implants

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INTRODUCTION: Extremely smooth and a high gloss finish – these are the surface finish requirements for medical implants. To achieve these finishing goals reliably and economically, more and more medical implant manufacturers are utilizing the drag finishing technology.

METHODS: Increasing life expectation and the practice of extreme sports are leading to increased wear of bones and joints. The last resort to overcome these problems is the implantation of an artificial joint. The use of such implants, such as artificial knees, hips, elbows, ankles, etc., has been growing rapidly all over the world. To meet their growing demand, medical implant manufacturers are expanding their capacity for products made from titanium and other high-alloy metals, and they are looking for solutions for economic and high-quality production of these precision castings. A major focus lies on the surface treatment of these components. To prevent contamination, their surface must be extremely smooth. Compared to robotic grinding and buffing, Rösler drag finishing systems offer many advantages. They allow the grinding/polishing of 24 parts, distributed over four workstations at a time. With drag finishing, the parts never touch each other. Another big advantage of the drag finishing technology is that the parts are completely ground/polished, irrespective of their shape. Several implant manufacturers are already using the Rösler drag finishing technology for their products.

RESULTS: Drag Finishing reduces the Rz from 18 µm to 0,2 µm. The surface reading on implants prior to drag finishing is usually Rz = 18 µm. The implants are mounted to parts-specific parts fixtures, which are in turn mounted to the four rotary workstations of the drag finisher. The parts are then "dragged" through a bowl filled with grinding or polishing media. RPM and rotational direction of the independent workstation drives can be adjusted. To achieve the required surface finishes, the operating angle of the workstations can also be adjusted. Usually the finishing of implants requires multiple steps. Each process is documented and stored in the system PLC. The first two steps are generally pre-grinding with ceramic media, followed by a fine grinding step with plastic media. The subsequent high gloss polishing is done in specially prepared dry polish media. The four workstations are equipped with quick connect couplings for easy mounting and dismounting of the work piece fixtures. The specially developed fine grinding plastic media provides surfaces finishes of down to 0.2 µm!

Fig. 1: The surface of medical implants must be extremely smooth and show a high polish. Such finishes can be achieved with the drag finishing technology in an economical manner.

Fig. 2: Drag Finishing allows the surface finishing of parts without the parts touching each other. The drag finishing process produces excellent surface finishes irrespective of the shape of the parts.

ACKNOWLEDGEMENTS: The text is based on experiences by Rösler Oberflächentechnik GmbH, Mr. Rüdiger Böhm.

Packaging of sterile medical devices – an overview for manufacturers

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INTRODUCTION: When medical products that are to be inserted into the body and left there, either temporarily or permanently (→*Implants)*, or are intended for single-use only (e.g. surgical instruments) are introduced into the market, this represents a tough challenge for the cleaning concept, the packaging system, the sterilisation process and process security. If the relevant processes are not followed or mastered, a latent hazard develops for patients and/or the surgical staff. The worst case scenario: insertion of a contaminated product→primary source of infection→systemic sepsis→death of patient. In addition to the human tragedy, this type of incident also presents a risk to the existence of any manufacturer involved with the product, and must be avoided at all times. The medical technology sector is increasingly being serviced by new manufacturers who do not yet have much experience of dealing with sterile products. The presentation presents essential information regarding to the design, realisation and implementation of sterile packaging concepts.

METHODS: The paper provides an introduction into matters of importance to manufacturers of medical products, such as the responsibilities, complexity and risks involved in sterile projects. It also explains normative and technical requirements for sterile packaging, presents typical packaging concepts, along with their advantages and disadvantages, introduces conventional sterilisation processes, provides a list of the required facilities and equipment, and demonstrates the use of packaging services (→*contract packers*), responsibilities, processes, approximate project durations and costs.

RESULTS: Packaging concepts for sterile medical products place heavy demands on the manufacturer or distributor and include many critical processes. The effects of time constraints, the consequences of decisions made in the past and the complexity involved in the interaction between many participating locations are frequently underestimated. The responsibility for fulfilment of the requirements for sterile products rests with manufacturers/distributors, who can either develop and operate the infrastructure necessary for packaging/sterilisation themselves or contract the task out to a packaging services provider. If required, this service provider will develop/manufacture the optimum packaging system, determine a suitable cleaning process, pack the products in a low-particle, low-microbe atmosphere within a clean room of the required ISO Class, finish the products off with labels, boxes and user information, and provide extensive support during registration of the product and validation of the packaging. Final sterilisation is usually contracted out by the packaging service provider to a specialist, certified sub-contractor.

Fig. 1: Appropriate equipment is mandatory in order to minimize particle and microbe load.

DISCUSSION & CONCLUSIONS: The time required to carry out a sterile project is often underestimated in the first instance. Realistic planning, inclusion of the subject of packaging at an early stage of the development project and collaboration with qualified partners are certainly to be recommended. Because the regulatory systems are complex and the necessary infrastructure is cost-intensive, and because a clean room should be reasonably well-used for efficiency reasons, collaborative ventures with a packaging service provider are particularly sensible for smaller businesses and when companies are entering the medical technology sector for the first time. However, larger manufacturers can benefit too, and the division of the packaging task between several service providers can significantly increase the level of strategic security to guard against disastrous production stoppages (→*second sourcing*).

Radiation sterilisation / Radiation crosslinking for implants

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INTRODUCTION: Radiation sterilisation is a standard method for terminal sterilisation of medical implants. The different technologies and their optimal use are explained. Also is described, how crosslinking of UHMWPE for implant use is performed on an industrial scale.

METHODS:

Radiation sterilisation can be performed by the following methods:

1. Treatment with Gamma radiation

The treatment can be performed on entire pallets on well defined loading patterns in order to assure a dose range within the requested limits. Release criteria are the dwell time, normalized to source strength and routine dosimetry performed typically on each pallet at a reference position.

2. Treatment with Electron Beam

Product has to be de-palletized for a sterilisation of entire products including packaging. Mostly a treatment with 10 MeV electrons is performed, in order to have sufficient penetration. Single or double side treatment is possible. The useful penetration depth for single side treatment is around 3.7 cm at density 1, for double side treatment around 7-8 cm.

3. Treatment with X- Rays

The treatment with X- Rays is new in the market but may gain wide acceptance in the future. No radioactive source is required. Advantages are the possibly better penetration in the material and the faster throughput. As with Gamma, entire pallets can be processed. Material degradation may be lower compared to gamma treatment due to homogeneity/ speed of the process.

Radiation crosslinking of UHMWPE is mostly performed by 10 MeV Electron beam. Depending on the specification, preheating of the materials and/or tempering after the irradiation may be applicable. Practical aspects such as the useful penetration depth and product configuration are considered.

Some processes with Gamma treatment are also used, whereby here some specific restrictions for the homogenous treatment within the requested dose range may be required, such as reducing the amount of material in the direction of the radiation. No experience for X-ray cross-linking of UHMWPE so far exists.

RESULTS: All radiation sterilisation methods are defined in the ISO 11137: 2006[1] standard. Process validation requires a minimum of 3 dosemapping runs with minimal and maximal density/ configuration

Responsibilities of the manufacturer of the implants and the contract service provider are defined in a quality agreement (QA): The contractor provides qualification of the equipment and assures the correct dose application in the entire product. The manufacturer specifies the minimal and maximal dose to be applied and is responsible for the final release of the goods. Also the microbiological validation (mostly according to VDmax method) and the testing of materials at maximal dose are under the responsibility of the manufacturer.

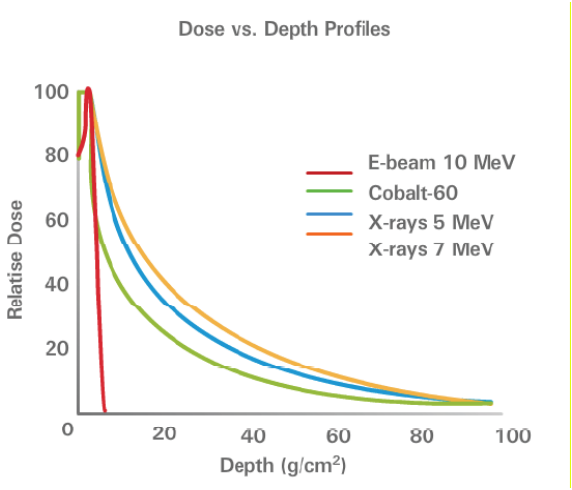

Fig. 1: Penetration of the different types of radiation into materials

DISCUSSION & CONCLUSIONS:

Radiation sterilisation and crosslinking of UHMWPE are highly specialised processes. Investment in industrial facilities is generally in excess of CHF 15 Mio. Therefore it makes often sense to subcontract such services with a specialised service provider.

REFERENCES: [1] ISO 11137/: 2006 Sterilization of health care products -- Radiation --.

FAILURE MECHANISMS OF DLC COATED JOINT REPLACEMENTS

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INTRODUCTION: Diamond Like Carbon (DLC) is a very promising coating material to improve biomechanical properties of articulating implants due to its extreme hardness, chemical inertness, wear resistance and biocompatibility [1]. Although in several instances, DLC - coated implants were tested with particular regard to film delamination under different conditions, many implanted medical devices like joint replacements have failed due to coating delamination after a few years. Slow delamination, in the order of a few µm/year, is very difficult to detect but can lead to a complete failure of the coating after a sufficient time in vivo. To give a reliable adhesion lifetime prediction for DLC coated implants, a thorough estimation of all potential failure mechanisms is of particular importance. Beside mechanical failure, other delayed interface crack growth mechanisms also have to be considered, especially hydrogen embrittlement, galvanic, crevice, and pitting corrosion as well as stress corrosion cracking (SCC).

METHODS: Ball-on-socket implants made from CoCrMo were coated with DLC using a Plasma Activated Chemical Vapour Deposition (PACVD) method with acetylene (C_2H_2) as process gas. These implants were tested in a joint simulator setup [2] running in synovial testing fluid (Thermo Scientific Hyclone®). Beside these test implants, also 2 series of explants retrieved after 2 and 8 years in vivo which failed due to coating delamination, were investigated to analyze the failure mechanism. Different analytical (FIB; XRD; EDX) and imaging methods (SEM; TEM) were used to determine and understand the main causes of failure.

RESULTS: Beside mechanical failure, which can easily be detected in simulator tests, different corrosion processes at the interface between the DLC coating and the substrate are most reasonable for film delamination (see figure 1). Here, the coating delamination is controlled by SCC and crevice corrosion (CC) mechanisms since they show strong dependence on stress and environment. We present new methods to determine three pertinent failure mechanisms, in detail stress corrosion cracking, crevice corrosion (CC) and mechanical failure of coated implants, especially in respect to long term delamination. In the case of SCC it will be shown that SCC may occur in a few nanometer thin reactively formed interface layer. Under certain conditions also crevice corrosion occurs.

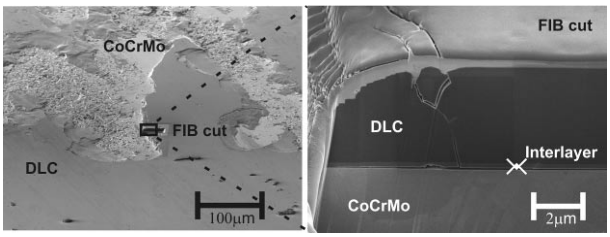

Fig. 1: SEM picture of a local defect on a DLC coated implant (left) and enlarged FIB transversal cut showing the interface crack (right).

DISCUSSION & CONCLUSIONS: Important failure mainly occurred due to CC of the adhesion promoting interlayer or due to a reactively formed interface material susceptible to SCC, where slow crack propagation occurs in corrosive media such as body fluid. We found testing in saline solutions to be insufficient, as proteins play an important role, especially as they may provide CC-conditions. Simulator testing shows that mechanical failure is mainly caused by third body wear involving wear particles.

REFERENCES: [1] R. Hauert (2008), in *Tribology of Diamond-Like Carbon Films: Fundamentals and Applications* (eds. C. Donnet and A. Erdemir) Springer, p. 494. [2] G. Thorwarth, C.V. Falub, U. Müller, B. Weisse, C. Voisard, M. Tobler, R. Hauert (2009), Acta Biomat. (Article in Press DOI: 10.1016/ j.actbio. 2009.12.019).

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Advanced Heat Treatment Methods for High Performance Surgical Tools

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INTRODUCTION: Advanced heat treatment methods for high performance surgical tools use the possibility to enhance surface hardness and corrosion resistance of hardenable stainless steels by thermochemical processes. In a specific process know as solution nitriding a high nitrogen case with dissolved nitrogen is formed at process temperatures beyond 1000°C [1].Solution nitriding has the advantage that surface properties of near net shaped products can be improved with only minor changes of the core properties. While the beneficial effect of nitrogen on corrosion resistance has been known for more than 20 years [2], there are no guidelines available for the selection of an optimal alloy and heat treatment combination.

METHOD: Solution nitrided stainless steels with German industrial standard 1.4016, 1.4021, 1.4057 are benchmarked with 1.4112 and 1.4108. The latter is a high nitrogen steel containing 0.4 wt.-% nitrogen and 0.3 wt.-% carbon. As a guideline for alloy and heat treatment selection it is assumed that selected alloys for solution nitriding can dissolve further nitrogen to an amount, such that wt.-%C + %wt.-%N = 0.7. The effect of enhanced nitrogen on surface hardness is similar to carbon and can be estimated using empirical hardness - carbon content relations. The effect of nitrogen on corrosion resistance can be qualitatively predicted using the pitting resistance equivalent:

PRE = %Cr + 3.3%Mo + 16%N.

The expected balance between hardness and corrosion resistance of standard heat treated and solution nitrided products are represented in figure 1. Such a representation may serve as a guideline for the selection of suitable alloy and heat treatment combinations provided that the suggested trend is confirmed. Two different hardening parameters were examined:

Type A: 1020°C (Type A*: 1020°C / 0.2 bar N_2)

Type B: 1100°C / 1 bar N_2 + 1020°C / 0.2 bar N_2

Type A* & B heat treatments were deep frozen at minus 80°C before tempering. Every sample was tempered at 180°C.

Pitting corrosion potentials on polished samples were determined by measuring current-density curves with an EC-pen in 1M NaCl solution at 22°C and a process speed of 2 mV/s.

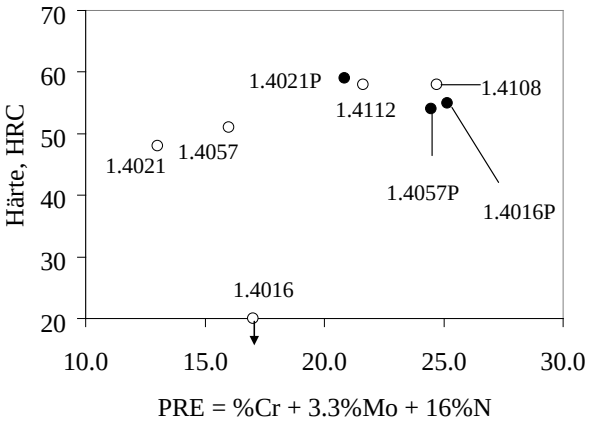

Fig. 1: Hardness - PRE relations for standard vacuum treatments (open symbols) and solution nitriding treatments (closed symbols) assuming wt.-%C + wt.-%N = 0.7. The strong increase in hardness for 1.4016 results from a transformation of a superferritic into a martensitic hardenable structure.

RESULTS & DISCUSSIONS: Results listed in table 1 suggest that resistance to pitting corrosion can be improved by solution nitriding.

Table 1. Measured pitting corrosion potentials

	Type A	Type B
1.4123 (A*)	250	not meas.
1.4016	-150	180
1.4021	100	200
1.4057	100-200	300

However, technically optimal solution nitriding parameters are not the same for all alloys. For example the result shown for 1.4016 is below its potential.

The guideline shown in figure 1 can be extended by incorporating further alloys like 1.4104 and 1.4122.

REFERENCES: [1] M. Gavriljuk & H. Berns (1999) *High Nitrogen Steels*, Springer, p. 215ff. [2] J. Truman (1987), U.K. Corrosion 87, Inst. Of Corr. Sci. and Tech., Brighton, p.111.

Fast and effective – CRYOCLEAN® snow and dry ice blasting for surface cleaning

M. Maurer[1] & M. Blanke[2]

[1]*PanGas AG, Dagmersellen*

INTRODUCTION: With CO_2-snow-cleaning all impurities can be removed in a single treatment step. The "dry" procedure is particularly suitable for inter-/cleaning (drying, degreasing, micro-deburring) of plastic, metall and ceramic parts in the complete production process.

METHODS: The cleaning, intercleaning and deburring of surfaces with CO_2-procedure between the working steps established itself in the market more and more. The procedure enables a cleaning free of residues and this in manual or in fully automated mechanical processes. The advantages of the CO_2-cleaning technologies are well used by celebrated Swiss companies in the precision-mechanics, medical and watch-and-clock industry. CO_2-cleaning is used for metal, engineering-plastic and ceramic components. The demands are always the same. The parts must be rationally freed of guts oils, emulsions, edge shavings, fingerprints and other pollutions to allow a proper and save next production step. These demands can be fulfilled by the CO_2-cleaning technologies of PanGas AG / Linde AG (CRYOCLEAN®Snow) which are integrated in manual and automated processes. In advance of the integration of these technologies extended attempts take place with the customer and/or with technology lab of PanGas AG.

RESULTS: Today numerous manufacturers are using carbon dioxide as an environment-friendly cleaning medium - instead of water/solvent based cleaners. Because CO_2-snow-cleaning leaves not only clean, but also dry surfaces, most energy-intensive and costly water treatment and drying-processes can be avoided. CO_2 - for medical and also industrial applications - is obtained from by-products of chemical processes, namely from the waste products of ammonia, alcohol and fertilizer production. The CO_2 will be „caught“, cleaned (purities have to fit customer demands), compressed in several steps and finally condensed. This liquified CO_2 will be stored under pressure. It will be filled under pressure into cylinders and bundles or it can be delivered to a tank at the customer site. Our customers decided on the application of the CO_2-technology not least because of the low investment costs but also of the low running costs. The complete cleaning device consists only of a compact constructed treatment station and it is essentially less expenses-intense than other methods for example PowerWash- or US-arrangements. CO_2-cleaning devices can also be adapted easily in existing manufacturing processes because they use very compact designs.

Fig. 1: CRYOCLEAN® snow pretreatment of a plastic part prior to a painting process.

REFERENCES: [1]M. Maurer, PanGas AG, *Trockene, automatisierte Zwischenreinigung in der Produktion*, Dagmersellen, 2008 [2]M. Blanke, Linde Gas AG, *CO_2-Schneestrahlen - Sauber und trocken in einem Arbeitsschritt*, Unterschleissheim, 2009.

ACKNOWLEDGEMENTS: This template was modified with kind permission from M. Curcic + M. Blanke, Linde Gas AG.

Biological safety testing on implant devices

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INTRODUCTION: The biological evaluation of an implant device is an essential step in the process of certification. Therefore, any potential risk for the use of the device in humans should be investigated thoroughly.

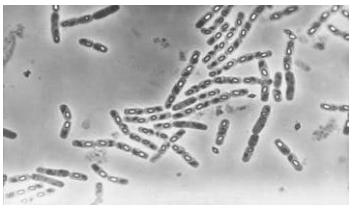
COMPENDIUM: The preferential aim of ISO 10993-1, re-issued in October 2009, and now titled 'Evaluation and testing within a risk management process', is the protection of humans from biological risks arising from the use of an implant device. This includes risks from the biological compatibility of the device itself as well as from any microbiological contamination from the manufacturing process.

If the materials have a demonstrably safe history of use in a specified role and physical form that is equivalent to the new device, literature data can be sufficient for proving the biocompatibility. But it can also be appropriate to perform in vivo studies for the detection of different local and systemic adverse effects of a new implant device. Within these studies additional potential risks of the newly developed implant device can be detected. ISO 10993-1 specifies the suitable choices of in vivo studies. The objective of implantation studies is to characterize the impact and development of the tissue response after implantation of a medical device. This includes the final integration or resorption and degradation of the respective material.

As the tissue configuration in the vicinity of an implant changes with time, ISO 10993-6 recommends to perform studies for short term as well as for long-term implantation periods. The respective periods for each implantation device shall be determined by the intended clinical exposure. Long-term studies are defined as studies exceeding 12-18 weeks. For these studies it is advisable to use larger species than rodents.

At BSL BIOSERVICE, biocompatibility studies for multiple kinds of implants, such as orthopaedic implants, osteoinductive materials, drug delivery systems, tissue engineering products or cardiovascular implants can be performed. Generally these studies have defined endpoints such as irritation, sensitisation, systemic toxicity or genetic toxicity. For some specific clinical uses additional studies for functional implantation can be necessary to determine the functionality and biocompatibility of the device under biological conditions. Possible endpoints could be the ingrowth behaviour of tissue into an implant or the mechanical resistance at the intended implantation location. For the examination of e.g. fracture repairs, long bone defect repairs, cortical, cranial, trabecullar or maxillofacial defects as well as for the examination of orthopaedic prosthetic infection, the intraosseous implantation is the most suitable way to test.

Regarding the microbiological safety, it is mandatory to control the hygienic status of manufacturing, to validate the steps of the production process and to control the product. The estimation of the bio burden is the basic test within the whole concept and is the basis for the success of the sterilization procedure. The sterilization process must be validated. Within the performance qualification microbiological tests often are necessary e.g. using bio indicators.



For products with an antimicrobial efficacy, e.g. silver coated surfaces; a panel of tests is available to examine the antimicrobial effect.

SUMMARY: Evaluation of biological safety is mandatory for each implant device. It is necessary to create individual testing strategies for proving the biocompatibility as well as microbiological safety. These strategies need to be uniquely tailored considering the nature of the material as well as the intended clinical use of the device.

Synthetic Nanomaterials between Innovation and Uncertainty

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INTRODUCTION: Nanostructured surfaces or surface modifications are well established, e.g. dental implants with acid-etched Titanium surfaces or, in orthopaedics, femoral components coated with solution-precipitated hydroxyapatite. As long as nanoscaled structures consist of established materials and are well fixed to a surface or immobilised in a matrix, they are feasible and controllable. However, complexity dramatically increases for other intended applications, such as:

- free nanoparticles, either to target degenerative diseases locally or resulting from wear or degradation processes of coated or reinforced matrices
- nanofibres or nanorods to reinforce structural composites and wear-resistant implant components or for scaffolds to engineer calcified and soft tissues [1].

How can this situation be handled with regard to safety and possible risks of synthetic nanomaterials?

APPROACH: Swiss and European authorities concluded that present legislation covers synthetic nanomaterials although they are not specifically mentioned. Thus, as for any other chemical substance, responsibility for safe handling of synthetic nanomaterials rests with industry. However, standardised scientific and methodological prerequisites, such as testing procedures, hardly exist, i.e. the risk involved with production and application of synthetic nanomaterials often cannot be quantified. This creates considerable uncertainty and may keep investors and businesses from exploiting the enormous potential of nanotechnology.
Even when risk cannot be quantified, the so-called precautionary principle still takes effect. This legal principle obliges decision-makers to anticipate harm before it occurs and to take appropriate cautionary measures. To help to systematise this evaluation the Swiss Federal Offices of Public Health and for the Environment developed the Precautionary Matrix for Synthetic Nanomaterials [2].

PRECAUTIONARY MATRIX: Like a checklist, the Precautionary Matrix allows to evaluate synthetic nanomaterials (including processes and applications) in a traceable manner, following these steps:

1. Make an inventory of materials which should be tested for nano-relevance and precautionary need.
2. Check the nano-relevance of each material.
3. Structure (process) steps for all nano-relevant materials, each of which can be covered separately by the Matrix.
4. Find the position of nano-relevant (process) steps in the value chain and decide applicability.
5. Fill in general information in the Matrix. Define the responsible contact person in your company.
6. Fill in the technical part of the Matrix, according to the parameters.
7. Determine sources of information.
8. Obtain information using the relevant questions from the Matrix.
9. Delimit the relevant sources of risk and determine the classification.
10. Clarify any need for action. If appropriate, initiate measures.

RESULTS: Outcomes of an evaluation using the Precautionary Matrix are:

- classification of precautionary need
- detection of knowledge gaps
- targeted detection und depiction of risk potentials for workers, consumers and the environment
- needs of action.

CONCLUSIONS: The Precautionary Matrix for Synthetic Nanomaterials allows a traceable, consistent and structured approach to nanosafety for materials, processes and applications if a regular risk analysis is not feasible. However, for first use, the assistance of a specialist is advisable.

REFERENCES: [1] Streicher RM, Schmidt M, Fiorito S, Nanostructures and Nanosurfaces for Artificial Orthopedic Implants, Nanomedicine 2 (2007) 861-874. [2] Höck J, Epprecht T, Hofmann H et al: Guidelines on the Precautionary Matrix for Synthetic Nanomaterials. Federal Office of Public Health and Federal Office for the Environment, Berne 2010, Version 2.