[MEET THE EXPERT]
IMPLANTS

Materials - Surfaces - Manufacturing

22 - 23 April 2013

Congress Centre Kursaal Interlaken
CH-3800 Interlaken

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Conference Documentation

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General Information

How to get to the Congress Centre Kursaal Interlaken (CKI)

The Congress Centre Kursaal Interlaken is easily accessible by car and by train. For directions please visit http://www.congress-interlaken.ch/en/

Please use the north entrance at the Strandbadstrasse 44 (Riverside, see arrow). You can find the reception and registration desk immediately at this entrance.

Parking

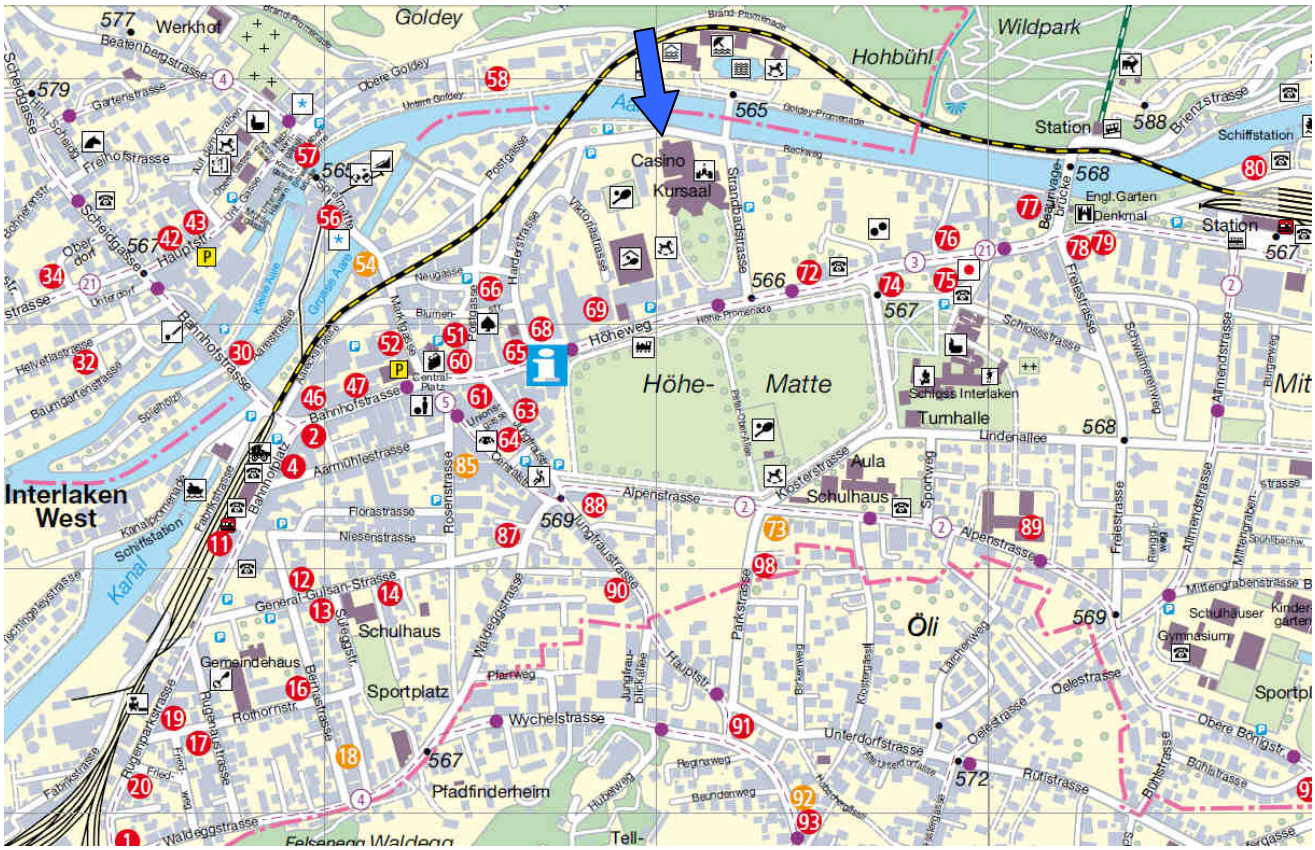
The parking lot of the Congress Centre Kursaal can be used. Congress-Tickets for CHF 6.00 per day are available at the information of the CKI.

Wardrobe

An unattended cloakroom is next to the reception of CKI in the basement (no liability).

Site map / Hotel accomodation

A number of hotels are within walking distance from the Congress Centre Kursaal Interlaken. For the location of the hotels please see the following site map.



Hotels:

68 Hotel Metropole

78 Hotel Carlton-Europe

Aperitif

The Aperitif in the poster and exhibition area (Monday 17:10 – 18:30 h) is kindly supported by the municipality of Interlaken.

Dinner

The Conference Dinner must be booked at the registration. It will be held on Monday 22nd April **19:00 h** at the **Hotel Metropole**. The Hotel Metropole is located close to the Congress Centre Kursaal on Höheweg 37.

Conference Secretariat

The conference secretariat is managed by Mrs Michelle Meyer.

Availability during the meeting: Tel +41 76 324 31 15

michelle.meyer@medical-cluster.ch

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Publication

All abstracts that qualify will be published online in a Supplement volume of the open access Journal eCells & Materials (eCM). www.ecmjournal.org
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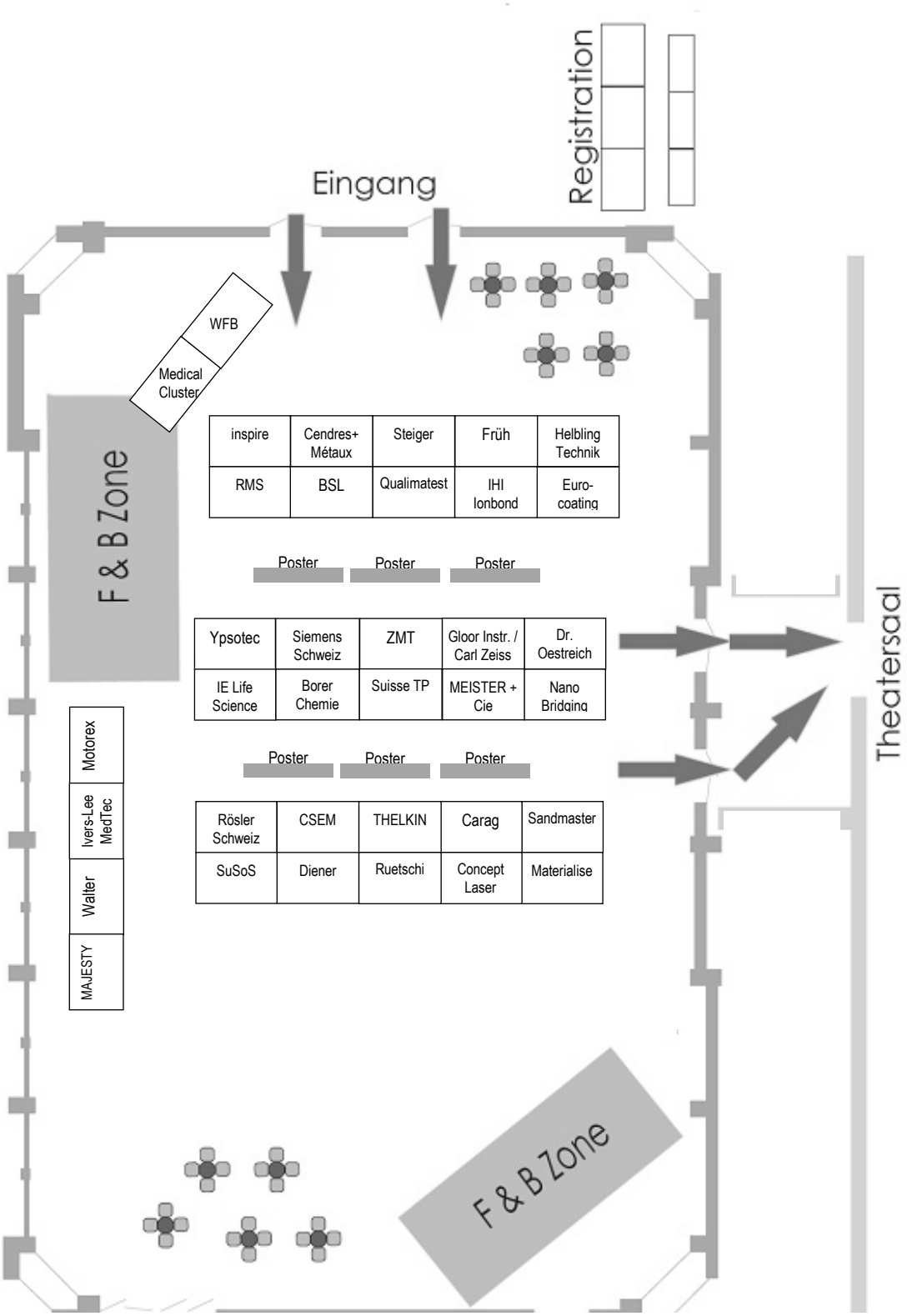
Exhibition Area



Meeting Program

Monday 22nd April 2013

From 09:30	Registration	
10:00 - 10:15	Welcome	
	Session 1 **Chair: Dr. Lukas Eschbach**	
10:15 - 11:00	Straumann's view of the dental market (industry partner) and the importance of Time to Market in a fast changing Industry (EN); Dr. Sandro Matter, Institut Straumann AG	
11:00 - 11:30	Keynote 1: Considerations on Patient Specific Implants (DE); Dr.-Ing. Jörn Seebeck, Zimmer GmbH	
11:30 - 12:00	Flash presentations exhibitors	
12:00 - 13:15	Lunch	
	Session 2 **Chair: PD Dr. Christiane Jung**	
13:15 - 13:45	Keynote 2: Biocompatible elastomers for 3D biomaterials by additive manufacturing (DE); Dr. Kirsten Borchers, Fraunhofer-Institute for Interfacial Engineering and Biotechnology IGB	
13:45 - 14:15	Keynote 3: Laser for the medical device industry – challenges in manufacturing and marking of medical implants (DE); Dr. Alexander Knitsch, TRUMPF Laser- und Systemtechnik GmbH	
14:15 - 14:45	Keynote 4: Electro-activation of passive implants – propositions from a technology perspective (DE); Dr. Urban Schnell, Helbling Technik Bern AG	
14:45 - 15:05	Flash presentations posters	
15:05 - 15:30	Break (Exhibition and Poster)	
	Session 3a: Passive implants **Chair: Prof. Dr. Michael de Wild**	**Session 3b: Electro-active implants** **Chair: Dr. Urban Schnell**
15:30 - 15:50	Development of a atrial septal occluder using an biodegradable framework (DE); Andreas Weishaupt, Carag AG	Implantable ceramic MEMS electrodes for cardiac pace makers (EN); Dr. Gurdial Blugan, Empa
15:50 - 16:10	Is the occurrence of periimplant osteosarcomas related to the use of cast stainless steel plates? (DE); Christoph Sprecher, AO Research Institute	Product engineering of active implants (DE); Daniel Thommen, Microdul AG
16:10 - 16:30	Development of a new glenoid implant (DE); Samuel Schenk, Mathys Ltd Bettlach	Glass encapsulation in intelligent embedded systems (EN); Frédéric Mauron, VALTRONIC
16:30 - 16:50	Antibiotic loaded plaster of Paris: Wear of artificial hip joints in the presence of gypsum particles (DE); Dr. sc. Roman Heuberger, RMS Foundation	PEEK casing for an active implant (EN); Dr. Thomas Degen, Sequana Medical AG
16:50 - 17:10	Employing biological and mechanical cues for bone regeneration (DE); Univ.-Prof. Dr.-Ing. Georg N. Duda, Charité - Universitätsmedizin Berlin	Evaluation of process capability of implant manufacturing (DE); Adrian Gammeter, Integrated Scientific Services, ISS AG
17:10 - 18:30	Exhibition / Poster / Aperitif	
From 19.00	Dinner at Hotel Metropole	

Meeting Program

Tuesday 23rd April 2013

	Session 4 **Chair: Prof. Dr. Michael de Wild**	
08:30 - 09:00	Keynote 5: Application of rapid prototyping in complex osteotomies of malunited bones (EN); Matthias Graf, Uniklinik Balgrist	
09:00 - 09:30	Keynote 6: Trends and developments of high-performance ceramics for implants (DE); Dr. Martin Zimmermann, Metoxit AG	
09:30 - 10:00	Keynote 7: Phase contrast and X-ray dark field imaging: New possibilities for non-destructive testing of materials and components (DE); Dr. Christian Kottler, CSEM	
10:00 - 10:30	Break (Exhibition and Poster)	
	Session 5a: Passive implants **Chair: PD Dr. Christiane Jung**	**Session 5b: Design, Quality, and RA** **Chair: Ralf Schindel**
10:30 - 10:50	Latest results in the development of a miniaturized hand held navigation system (DE); Dr. Bruno Knobel, Naviswiss AG	Breakthroughs in Patient matched medicine through advancements in 3d image analysis (EN); Sebastian De Boodt, Materialise
10:50 - 11:10	Colorimetry on implant surfaces for esthetically demanding applications (DE); Dr. Hans Schmotzer, SigmaRC GmbH	Patient specific implants for orthopedics – streamlining through smart software (DE); Jan Stifter, Medivation AG
11:10 - 11:30	CVD coating technology: a high temperature coating alternative for CoCr alloys (EN); Dr. Antonio Santana, IHI Ionbond AG	Application of computer tomography in industrial 3d measurements – Methods, application, precision (DE); Andreas Flechtmann, Werth Messtechnik GmbH
11:30 - 11:50	Silver as a lubricant additive in the implant manufacturing (DE); Dr. Bernhard Keller, MOTOREX AG	Approval of implants produced with Additive Manufacturing (EN); Oscar Hedin, Arcam AB
11:50 - 12:10	New opportunities for using tantalum for implants with Additive Manufacturing (EN); Ruben Wauthle, LayerWise NV	Regulatory Road for Combination Products (EN); PD Dr. Pierre Mainil-Varlet, Aginko
12:10 - 13:30	Lunch	
	Session 6 **Chair: Lukas Märklin**	
13:30 - 13:50	Fixation concept for a ceramic-metal back composite (DE); Dr. Martin Schmidt, Jossi Orthopedics AG	
13:50 - 14:10	Surface property modulation in high-precision cutting of materials for medical applications (EN); Armando Pereira, Agie Charmilles	
14:10 - 14:30	Dental ceramics: past, present, and future (EN); Dr. Simon Jegou, Nobel Biocare Services AG	
14:30 - 14:50	Contemporary dental implant systems: Clinical, biological and mechanical aspects (DE); Dr. med. dent. Urs Brodbeck, Zahnmedizin Zürich-Nord	
14:50 - 15:20	Keynote 8: Specificities of implant-associated infections (DE); Dr. Peter Wahl, Hôpital Cantonal Fribourg	
15:20	Conference end	

Biocompatible elastomers for 3D biomaterials by additive manufacturing

K. Borchers[2], C. Bierwisch[5], S. Engelhardt[7], C. Graf[4], E. Hoch[6], R. Jaeger[5], P. Kluger[2], H. Krüger[1], W. Meyer[1], E. Novosel[2], O. Refle[4], C. Schuh[2], N. Seiler[3], G. Tovar[2,6], M. Wegener[1], T. Ziegler[5]

Fraunhofer Institutes for [1]Functional Polymersystems IAP, [2]Interfacial Engineering and Biotechnology IGB, [3]Laser Technology ILT, [4]Manufacturing Engineering and Production IPA and [5]Mechanics of Materials IWM. [6]University of Stuttgart, DE. [7]Rheinisch-Westfälische Technische Hochschule Aachen RWTH, DE

INTRODUCTION: The future vision of implants comprises individually tailored prostheses and the generation of artificial tissue and organs generated from the patient's own cells. In order to develop artificial, biomimetic structures which perform as well as natural ones, we need fabrication processes that do not set any limits to the generation of shapes, and materials that allow for tailoring of their physical, chemical, and biological properties.

We introduce new biocompatible materials for the manufacturing of flexible structures by freeform fabrication.

METHODS: We develop printable and photo-crosslinkable material systems, either based on bio-polymers derived from the native extracellular matrix, e.g. gelatin or glycosaminoglycans, or fully synthetic resins [1-3]. We use (meth)acrylation of the precursor polymers to achieve photocrosslink-ability. Further chemical modifications and additives are applied in order to achieve inkjet-printable resin viscosities. Inkjet-printing combined with UV laser or two-photon-polymerization (TPP) in inert atmosphere is developed for 3D material structuring. Computational fluid dynamics are used to find optimal geometries for specific functions. Using bio-based materials inkjet-printing and 3D encapsulation of cell-laden bio-ink is performed.

RESULTS: The synthesis of polymers suitable for additive manufacturing processes was successful. Different types of non-degradable synthetic polymers were tailored to be non-cytotoxic and surface functionalization of the polymers with RGD peptide modified heparin-derivatives resulted in cell adhesion and proliferation to confluent monolayers. The material was crosslinked by UV laser and TPP and tubular systems were prepared e.g. with respect to future nutrient supply of large *in vitro* tissue constructs or blood vessel substitutes. The E-modulus of the crosslinked synthetic materials was adjustable. Modelling and computational fluid dynamics allowed for prediction of biomimetic bifurcations with optimized wall shear stress.

Fig. 1: Left: Computational evaluation of wall shear stress. Right: prototype of a branched tube, fabricated from newly developed cytocompatible elastomeric material by UV laser curing.

The new gelatin-based biomaterials constitute both, printable non-gelling precursor solutions and crosslinked hydrogels with tunable physico-chemical properties. Such bioinks were used for cell printing and 3D encapsulation of porcine chondrocytes.

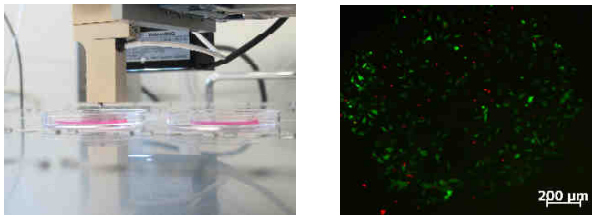


Fig. 2: Left: inkjet-printing of cell-laden gelatin-based bioink onto hydrogel substrates. Right: viable porcine chondrocytes after inkjet printing (green: live cells, red: dead cells).

DISCUSSION AND CONCLUSION: Our results constitute that so far individual tailoring of implants and generation of tissue substitutes by additive manufacturing remain sensitive hypotheses.

REFERENCES: [1] S. Engelhardt, E. Hoch et al., (2011) *Biofabrication* **3/2:**25-33. [2] W. Meyer (2012) *J Funct Biomater* **3:**257-268. [3] E. Hoch et al. (2012) *J Mater Sci Mater Med* **11:** 2607-2617.

ACKNOWLEDGEMENTS: To Fraunhofer Gesellschaft, EU (Artivasc 3D, 263416), Max Buchner Foundation.

Laser for the medical device industry – Challenges in manufacturing and marking of medical implants

A. Knitsch, B. Faisst

TRUMPF Laser- und Systemtechnik GmbH, Ditzingen, DE

INTRODUCTION: The medical device industry is ever challenging the manufacturing community for innovation, higher precision and miniaturization. In light of constantly changing shapes and sizes, along with lot sizes from a few hundred to tens of thousands and introduction of new materials, conventional manufacturing methods reach their limits. This is where the potential of today's industrial lasers raise to the occasion of providing a flexible yet cost effective manufacturing tool. In the field of medical implants where immaculate surfaces play a major role, laser welding with superior seam quality, laser cutting with excellent edges and laser annealing for product marking and traceability guarantee the desired biocompatibility.

LASER MARKING: Noncontact and low impact annealing with the laser is an established process produces colored oxide layers on the stainless steel or titanium surface. The surface quality remains fully intact; the color change is indelible and biocompatible like the base material. The laser works without the addition of dyes, acids or solvents, and can even be applied with great accuracy to areas that would have been impossible to reach with other methods. Within short marking time serial numbers, plain text or data matrix codes, logos and images can be created.

Medical instruments and implants are often produced from stainless steels with various alloys which contains at least 10.5% chromium to obtain sufficient corrosion resistance. This resistance is based on an enrichment of the chromium on the surface, which in turn allows the formation of an oxide layer. High temperature sterilization and aggressive, high alkaline cleaning methods can result in disturbances in the oxide layers of the stainless steel alloy. Susceptibility to corrosion and the risk of bleaching around the annealing increase as a result. An interdisciplinary task force has taken on this problem. One result was suitable laser parameters for permanent annealing without corrosive tendencies. In addition, passivation after the marking can significantly improve the Cr/Fe ratio, thereby drastically reducing susceptibility to corrosion.

LASER CUTTING: Where conventional cutting technologies reach their limits, the laser opens new possibilities. The advantages of laser cutting can be numerous in terms of efficiency, precision, speed, material variety and flexibility. Many times cutting applications are only possible with laser technology. For the fusion cutting process lasers with highest beam quality are developed to obtain both high cutting speed and excellent cut quality. A completely different approach is the sublimation cutting process with ultra-short pulse lasers. These lasers feature an unrivaled cutting quality without any heat influence on the processed material. Moreover the cutting process is independent of the material which enables e.g. polymer stent cutting.

LASER WELDING: The benefits of laser welding become clear in the manufacturing of surgical instruments: Quick tooling times and simple CAD transfer to the laser lead to reduced process times. Low heat input and precise welding reduce distortion to a minimum and only minimal, if any, reworking is necessary. These laser properties are also most important in welding of medical implants. For example the titanium housing of a pacemaker is hermetically closed by overlap spot welding. The melt-heat spreads from pulse to pulse across the housing, so that the sensitive electronics are not affected. The welding depth can be precisely adapted to the thickness of the titanium shells to prevent interior weld splatter. The resulting smooth and non-porous weld seam is biocompatible as the base material.

Electro-activation of passive implants – Propositions from a technology perspective

H. Bernhard, J.-N. Fehr, E. Gremion, N. Schneeberger, U. Schnell

Helbling Technik Bern AG, MedTech, Optics & Microtechnologies, Bern, CH

INTRODUCTION: In the past, the [MEET THE EXPERT] conference has been focused on materials, surfaces, and manufacturing aspects for passive implant applications, e.g., dental and orthopedic implants, artificial joint replacements, bone graft substitutes; passive implants having a broad academic research and industrial community in Switzerland.

METHODS: The keynote lecture shows examples of how today's passive implants can be electro-activated by convergence of passive and active technologies. The topic is introduced from Helbling's perspective as an engineering service provider of electro-active medical devices and implants [1].

RESULTS: A series of passive implants, which have been *electro-activated* with Helbling's support will be presented, among them an electronically controlled Gastric Band technology for telemetric obesity treatment, an electro-mechanic Hearing Implant (HI) substituting passive stapes prosthesis (Fig. 1) [2], and an AutoFocal Intraocular Lens (AF-IOL) combining liquid crystals, diffractive and refractive optics, photo detectors, microelectronic circuits, RF coils and rechargeable batteries to create smart optics (Fig. 2) [3].

Fig. 1: Implantable hearing aid DACS (direct acoustic cochlear stimulation) with external sound processor.

Then, we propose ideas where else electro-active functionality might be considered from an engineering perspective (without claiming medical significance).

Finally and for *proof of evidence*, further examples of electro-activated passive implants from other companies and research organizations will be referenced, e.g., a hip implant featuring a transponder platform to monitor the anchorage of an implant in the bone, intracorporeal energy harvesting for battery replacement of active implants, an intramedular leg lengthening device with a motorized nail, and transosseous ultrasonic stimulation and monitoring of bone healing into a telemedicine application.

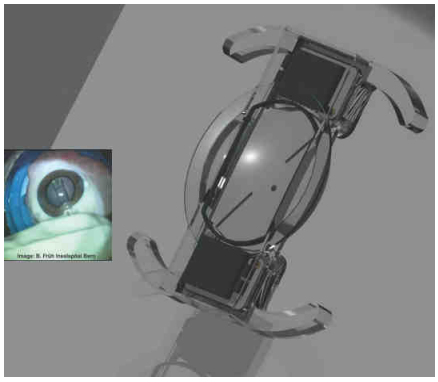


Fig. 2: Ophthalmic implant - AutoFocal Intraocular Lens (AF-IOL) designed to give patients a complete visual distance range.

DISCUSSION & CONCLUSIONS: The goal of the keynote lecture is to give the electro-active implant community a *voice* at the [MEET THE EXPERT] conference, to inspire the passive implant community, and to introduce the topical *Session 3b: Electro-active implants.*

REFERENCES: [1] www.helbling.ch, [2] R. Häusler, C. Stieger, H. Bernhard, M. Kompis (2008) *Audiol Neurotol* **13**:247-256. [3] J.S. Pepose (2011) *Advanced Ocular Care*, October 2011:48-54.

ACKNOWLEDGEMENTS: The authors gratefully thank the following persons for making their contributions available for the keynote lecture: Andreas Heinig (Fraunhofer Institute for Photonic Microsystems, Dresden), Magnus Jonsson (ARTORG Cardiovascular Engineering, Bern), Philip Procter (Medical Device Industry Consultant), Marc Ostermann (Zimmer GmbH, Winterthur), Marco Wieland (MyoPowers Medical Technologies SA).

Development of an atrial septal occluder using a biodegradable framework

A. Weishaupt[1], J. Bernhard[1], B. Söderberg[2]

[1] Carag AG, Baar, CH. [2] The Queen Silvia Children's Hospital, Göteborg, SE

INTRODUCTION: The Solysafe® Septal Occluder has been used for closure of atrial septal defects, including patent foramen ovale, with high closure rates, excellent tissue response and few major complications. Design, and over-the wire delivery technique provide the ability to retrieve and reposition [1]. It was voluntarily taken from the market due to isolated cases of irregularities with the metal framework. The development of a septal occluder based on the design of the established Solysafe® occluder but with a biodegradable framework presents significant new challenges compared to an occluder using a metal framework. This article outlines the challenges during development, production, sterilisation and implantation of such an occluder.

METHODS: The aim of the project was the replacement of the metal wires by a degradable material. Due to the mechanism of the device during implantation and deployment, the mechanical properties of the biodegradable material had to be equivalent or superior to those of the original material and eliminate the irregularities noted with the metal wire design. The degradable material has to keep the implant in position until it is ingrown completely. Different materials such as magnesium, degradable glass, and pure iron wires were tested without success because of the insufficient mechanical properties. First prototypes using a degradable polymer showed very promising results.

Based on the lower bending stiffness of the degradable polymers the diameter of the monofilaments had to be increased to reach the same behaviour the metal wires showed. Also, the filaments needed to be kept as thin as possible to allow the placement using a 12 F transseptal sheath.

The biodegradable material that is used for the framework degrades on the effect of hydrolysis [2] which causes a drop of inherent viscosity. Therefore, the biodegradable polymer is sensitive to water, moisture and high temperature. For this reason the monofilaments are stored under reduced pressure and the mounted implants are packaged and delivered in a sealed aluminium peel pouch filled with inert gas to prevent early degradation.

This moisture and temperature sensitivity impacts as well the process of sterilisation. Damage on the material that is caused by the sterilisation process has to be as low as possible. Thus, a major challenge was to minimize the impact on the material caused by sterilisation. Autoclaving is not possible as temperature and air humidity are too high and would destroy the material. Radiation also has a negative impact on the material since it causes an uncontrolled drop of inherent viscosity.[3] Ethylene oxide and H_2O_2-sterilisation are proper methods for sterilisation of the degradable polymer. For this device H_2O_2-sterilisation was chosen as the temperature and the effect on the material are the lowest.

The continuous movement of the beating heart and the removal of the residuals by the blood flow influence the biodegradation rate. These effects have to be taken into consideration for the determination of the biodegradation time.

RESULTS: An occluder with non degradable frame was transformed into an occluder with a biodegradable frame by critical adjustments on dimensions and design. The design allows a fast and easy placement followed by an immediate closure of an artificially created defect in an animal model.

DISCUSSION & CONCLUSIONS: A septal closure device that occludes and then 'goes away' has long been a desirable attribute of septal devices. Our results demonstrate that:

1. a biodegradable framework can be successfully incorporated in to an intracardiac device
2. the device can be safely, securely and consistently deployed in an ASD model
3. a fully biodegradable occluder seems feasible and development of such a device should be intensified

REFERENCES: [1] Söderberg B et al. "Septal defect closure using a device with biodegradable framework: chronic results in a swine model", accepted for presentation on EuroPCR 2013. [2] Williams D: "The Biocompatibiliy, Biological Safety and Clinical Applications of Purasorb® Resorbable Polymers", Independent Report for Purac Biomaterials, 2010. [3] Loo JSC et al.; Polymer Degradation and Stability 83 (2004) 259–265.

Is increased occurrence of peri-implanted osteosarcoma associated with cast stainless steel implants?

CM. Sprecher[1], RJ. Boudrieau[2], T. Suter[3], JH. Keating[2], RJ. McCarthy[2], S. Milz[1,4]

[1] AO Research Institute, Davos, CH. [2] Tufts University, North Grafton, USA.
[3] EMPA, Dübendorf, CH. [4] Ludwig-Maximilians University, München, DE.

INTRODUCTION: Peri-implant osteosarcoma (OS) occurrence was found in dogs treated with tibial leveling osteotomy (TPLO) and the Slocum® cast stainless steel TPLO plate [1-3]. Recently, it was assumed that the metallurgical inhomogeneity of the plate surface, or the corrosion resistance of the cast stainless steel material are related factors [1-2]. Therefore, the aim of the current study was to investigate the corrosion behavior of TPLO plate surfaces from animals with and without osteosarcoma. Special attention was paid to the influence of plastic surface deformation which is the result of contouring required for plate application to the bone.

METHODS: Eighteen retrieved Slocum® TPLO plates made of 316L cast stainless steel, 9 from dogs with (CwOS) and 9 from dogs without proximal tibial osteosarcoma (CnOS) were investigated. Three retrieved plates made of forged stainless steel (Synthes) from dogs without proximal tibial osteosarcoma (FnOS) were included as examples for a different manufacturing process. On all plates visual inspections with a stereomicroscope and local micro electrochemical corrosion measurements were performed in 1M NaCl on various local spots (d = 100 µm) and corrosion resistance factors (CRF) were calculated [4]. All measurements were performed on non-deformed and on plastic deformed surface areas.

RESULTS: The implant time in-situ was comparable for both cast groups (CwOS 59±19 months vs. CnOS 52±14 months) and was shorter for FnOS with 35±5 months. Microscopic inspections of all retrievals on the cast groups showed rough surfaces, residues of sharp edged material and signs of local corrosion attacks. Furthermore, local notches and more severe tool marks were found next to the contoured regions of the plate. On the forged plates only a few marks, but no residues or microscopic signs of corrosion could be distinguished. The CRF values determined on different local surface spots showed a wide variation for the cast plates and did not vary to that extent in forged plates (Figure 1). Consistently, the CRF values obtained from cast plates at non-deformed locations showed higher values compared to the CRF values from plastic deformed locations. Interestingly, this effect was not observed for the surfaces of forged plates.

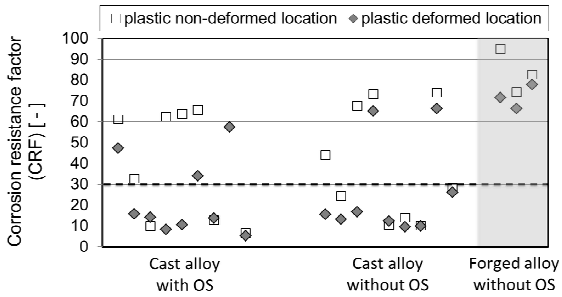


Fig. 1: The CRF values of 21 retrieved plates.

DISCUSSION & CONCLUSIONS: The micro electrochemical corrosion investigation showed no clear difference between local corrosion behaviors of the two groups of cast plates due to a large standard deviation. In comparison, the forged plates clearly exhibited higher corrosion resistance values throughout the various surface locations that were investigated. However, the overall number of measurements was smaller than for the cast plates. For plate adaptation to the bone shape the straight cast plates has to be bended in contrast to the anatomically pre-shaped forged plates. Our results clearly show that bending reduces the corrosion resistance of cast plates while forged plates are more unsusceptible to this alteration.
Currently, there is no clear causal connection between the surface properties of cast plates, the local CRF and the occurrence of peri-implant osteosarcoma. Nevertheless, the present results add to the speculation that osteosarcoma development might be related to local surface corrosion and the influence of that condition to neighboring bone cells.

REFERENCES: [1] R.J. Boudrieau, R.J. McCarthy, R.D. Sisson Jr. (2005) *J Am Vet Med Assoc* **227**:1613-7. [2] R.J. Boudrieau, R.J. McCarthy, C.M. Sprecher, et al (2006) **67**:1258-65. [3] W.M. Lackowski, Y.B. Vasilyeva, R.M. Crooks, et al (2007) *AJVR* **68**:908-16. [4] T. Suter and H. Böhni (2005) The Microcell Technique in *Analytical Methods in Corr. Science and Eng.* (eds. P. Marcus and F. Mansfeld) CRC Press, pp 649-696.

Development of a novel glenoid implant

S. Schenk[1], F. Dallmann[2], D. Delfosse[1]

[1] *Mathys Ltd., Bettlach, CH.* [2] *Mathys Orthopädie GmbH, Hermsdorf, DE*

INTRODUCTION: Today, the revision rate of total shoulder arthroplasty is still higher than for hip and knee arthroplasty. According to literature data, up to a third of the complications are linked to the glenoid component [1]. Cemented glenoid implants mostly fail because of wear of the bearing surface or because of cement failure. Uncemented metal-backed glenoids additionally show severe backside wear and screw- or tray breakage. To solve these problems a new glenoid implant has been developed, combining the new cross-linked, vitamin E stabilised vitamys® polyethylene for shoulder implants with the proven RM particle coating. This work introduces the concept of the new implant and summarizes the pre-clinical testing results.

METHODS: Wear behaviour of the new implant material was assessed using hip and shoulder simulators under different conditions. Furthermore push-out testing in PUR and bovine bone was used to test primary fixation, which is a prerequisite for osseointegration and long term fixation.

RESULTS: Shoulder simulator studies on vitamys® for shoulder implants showed wear reduction by a factor of three compared to standard UHMWPE (see figure 1).

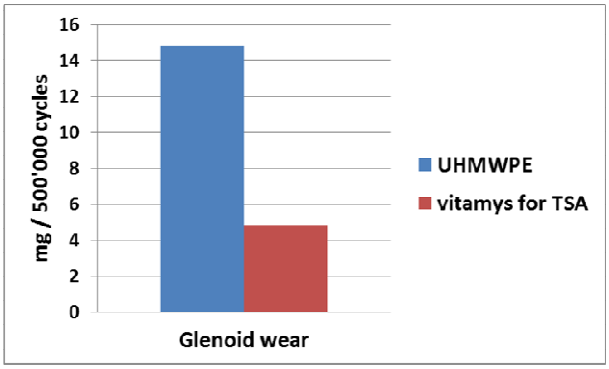


Fig. 1: Shoulder simulator wear rate of UHMWPE and vitamys® glenoids versus Al_2O_3 heads.

Hip simulator studies on vitamys® for hip implants showed no significant change in wear behaviour after artificial ageing, even after 60 days of ageing which corresponds to 40 years in-vivo [2]. The same behaviour is expected for vitamys® for shoulder implants as the amount of vitamin E is the same for both materials.

Push-out tests in PUR foam and bovine tibial trabecular bone showed that the dovel-like peg design can provide stable primary fixation. Push-out force in bovine bone was highly dependent on bone density and preparation method (see Fig. 2). In bovine bone with bone volume fractions similar to glenoid trabecular bone (20 – 30 %), push-out forces were between 250 and 730 N. Secondary stability will be attained due to osseointegration which is likely to start at the stable fixation pegs and move to the backside of the glenoid implant.

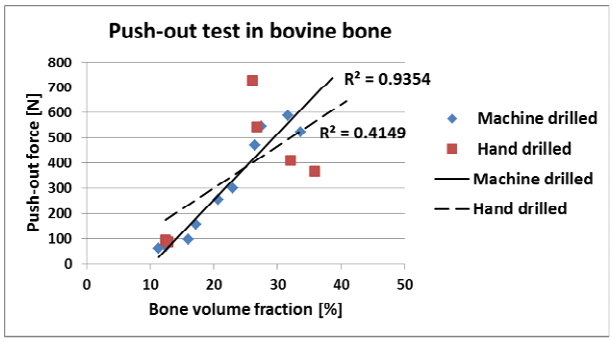


Fig. 2: Push-out forces of glenoid implants from primary fixation test in bovine bone blocks. Bone blocks prepared by hand or machine.

DISCUSSION & CONCLUSIONS: Combining the new vitamys® polyethylene for shoulder implants and the proven RM coating technology, the new glenoid implant was designed to reduce the amount of potential complications in total shoulder arthroplasty. Because the wear of the bearing surface is considerably lower and backside wear is eliminated, problems related to osteolysis might be avoided. Primary stability is provided by the fixation pegs and secondary stability is expected after osseointegration.

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ACKNOWLEDGEMENTS: Most of the experimental work was done by RMS Foundation, Bettlach (Switzerland).

Antibiotic loaded plaster of Paris: Wear of artificial hip joints in the presence of gypsum particles

R. Heuberger[1], J. Krieg[1], P. Wahl[2], E. Gautier[2]

[1] RMS Foundation, Bettlach, CH. [2] Department of Orthopaedic Surgery, HFR Freiburg, CH

INTRODUCTION: Prosthetic joint infections usually require an implant removal and a treatment with antibiotics. After recovery, a new joint is implanted. This two-stage-procedure is an enormous stress, especially for elderly patients. Alternatively, beads made of plaster of Paris (gypsum) loaded with antibiotics can be implanted at the infection site [1] without removing the prosthesis. There they are slowly dissolved and antibiotics are locally released to fight the bacteria [1]. There is however concern regarding 3rd-body-wear caused by small gypsum particles.

METHODS: Inlays made of ultra-high-molecular-weight polyethylene (UHMWPE) and cross-linked polyethylene (XLPE: vitamys®) against 28 mm CoCrMo heads and alumina pairings (36 mm, Bionit® 2, all n=3, from Mathys Ltd. Bettlach, CH) were tested using a hip simulator according to ISO 14242-1:2012 (Endolab, Germany).
10 g/L calcium sulphate hemihydrate (VWR, 1-100 µm particle size) was added to the standard test liquid, where the so called plaster of Paris forms the more stable dihydrate called gypsum.

RESULTS: In both cases, with and without gypsum particles in the test liquid, the wear of the inlays increased continuously (Fig. 1). In presence of the gypsum particles, the wear rates of the polymer inlays (red bars) were slightly higher than without gypsum (grey bars) (Fig. 2). The wear rates of the alumina inlays were 0.3±0.1 mg/mill. cycles both with and without gypsum. When no more gypsum was added to the metal-on-polymer articulations, the wear rates decreased (green bars). For the UHMWPE it was in the range of the reference samples while for the XLPE inlays it was still higher compared to the references.
All heads and inlays showed few scratches, but there was no obvious difference between the articulations with and without gypsum particles. On the polymer inlays, additionally some pitting was observed.

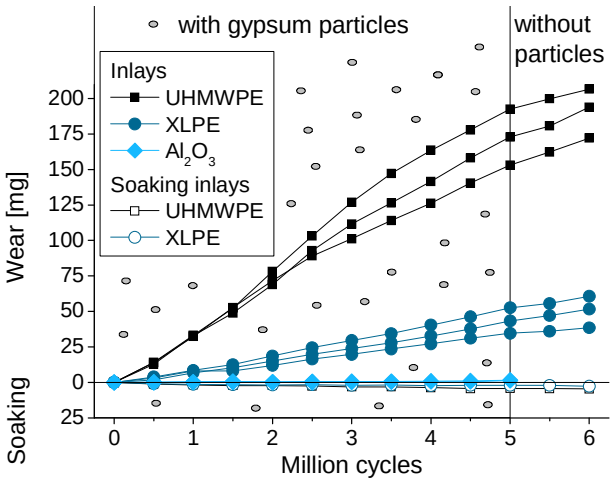

Fig. 1: Wear of the hip inlays in presence of gypsum particles in the test liquid. The polymer inlays were subsequently tested without gypsum particles.

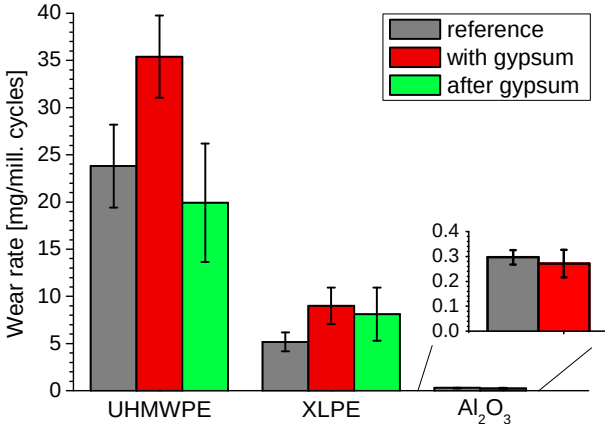

Fig. 2: Wear rate of the hip inlays. The reference inlays were tested at the RMS Foundation without gypsum particles.

DISCUSSION & CONCLUSIONS: Neither the alumina articulations nor the CoCrMo heads were affected by the gypsum particles since gypsum is a relatively soft material. Only the much softer polymers were worn 50-70 % more, but they recovered at least partially when no more particles were added. For ceramic-on-polymer articulations and mixed ceramics even less effects by the gypsum is expected, since these heads/materials are more scratch resistant.

Thus, if the infection is treated successfully with the antibiotic loaded plaster of Paris, this is a good alternative to the 2-stage-procedure in elderly patients.

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Employing biological and mechanical cues for bone regeneration

GN. Duda, A. Petersen, S. Checa, B. Wildemann

Julius Wolff Inst. & Center for Musculoskeletal Surgery, Charité - Universitätsmedizin Berlin, DE

ABSTRACT: Bone is one of the few tissues in the human body that has the capacity for scar less regeneration. Nevertheless, complication rates of up to 10-20 % are likely by means of delayed healing or non-unions [1].

Failed regeneration may be caused by biological deficits or mechanical demanding situations that impair endogenous cascades of healing. Approaches to locally deliver stimulatory factors to bone have been realized during the last decades. However, in most cases these concepts are not patient specific; they do not account for the deficits in the individual nor the specific trauma location. To be able to provide a platform for implant customization and to enable a "freedom of choice" for drug type, combinations thereof, and the applied amount, we developed intra-operatively applicable drug delivery systems (DDS). One example that is already available in the clinics is a poly(D,L-lactide) coated tibia nail (Expert Tibial Nail PROtect, DePuy Synthes) with incorporated antibiotics for a continuous release [2-5]. However, the drug itself and the location cannot be customized by such pre-coated approach. Thus intraoperative strategies are needed: Drug loaded patches that are glued to implant surfaces by rapid polymerization represent an additional strategy for implants customization (Fig. 1A) [6]. The gluing process does not impair the biological activity of the drugs within the patch, does not interfere with cellular activity or harm the mechanical stability after gluing to implant surfaces such as endoprosthetic devices.

But even if adequate local biological stimulation is available, mechanical conditions should support the healing cascade and not interfere with it. Surprisingly, a strong crosstalk between bone morphogenetic protein (BMP) signalling and mechanical tissue straining have been described (Fig. 1B). Mechanical conditions alter the effectivity of BMP proteins [7-9]. To include the mechano-sensitivity of healing in therapy concepts, a customized implant strategy has been developed to treat large bone defects. In this approach, rapid prototyping techniques are used to develop custom made scaffolds consisting of Ti beams, which meet at different angles, allowing tuning of their mechanical properties. Using computational algorithms, scaffolds were optimized to provide sufficient mechanical stimulus to tissue regeneration while avoiding implant fractures [10].

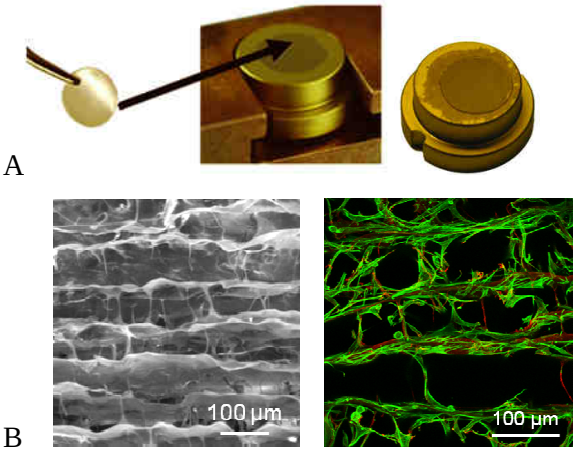

Fig. 1: Fast attachment of a drug loaded polyvinyl alcohol patch to an implant like metal surface by a cyanoacrylate adhesive (A); Soft biomaterial scaffold with specific pore architecture (Matricel GmbH) to investigate the relevance of mechanical signals on cell behaviour, e.g. BMP-signalling (left: SEM image of pore architecture, right: actin cytoskeleton showing cell organization inside pores) (B).

In summary, successful treatment strategies in bone regeneration shall address both, local and customized biological constrains and mecho-biological boundary conditions to foster healing. Such strategies require customization techniques, which are readily available and lead to personalized implant and treatment modalities. Approaches presented here exemplarily illustrate the power of solutions to treat the remaining shortcomings in delayed bone healing .

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Implantable ceramic MEMS electrodes for cardiac pace makers

G. Blugan

Empa, Swiss Federal Laboratories for Materials Science and Technology, Dübendorf, CH.

ABSTRACT: The conductive interface between the myocardial electrode and the tissue allows for transferring electron current from the pacemaker into the heart tissue. Unfortunately, state of the art metallic electrodes are known to produce inflammations leading to fibrosis. The fibrosis results in increased interface resistance over time, which may eventually require an early replacement of the battery and in extreme cases the electrode. Myocardial electrodes made by novel improved biocompatible materials like ceramics will therefore contribute to overcome these major drawbacks.

In this project the development of novel conductive ceramics are combined with advanced micro-moulding techniques to study novel 3D implantable electrodes for low power, long term pacemaker applications. Most ceramics are electrically insulating in nature. The challenge is to develop an electrically conductive ceramic which can be moulded using today's MEMS technologies. Polymer derived ceramics that exist as liquid precursors are a potential candidate material for shaping by micromoulding.

The first developed materials from PDCs with a modified microstructure for increased electric conductivity have been produced and are currently being evaluated by in-vitro biocompatibility tests, e.g. for cytotoxicity. We are currently investigating within a SNF funded project if these ceramic materials are similar in biocompatibility to zirconia and alumina ceramics.

A process validation approach to electronic medical implant engineering

D. Thommen, M. Herrmann

Microdul AG, Zurich, CH

INTRODUCTION: Typical active electronic implants require 50 or more manufacturing steps involving upward of 20 distinct processes. Each process needs to be thoroughly qualified and tightly controlled. Additionally, the security requirement, extremely high standards for medical electronics and perceived liabilities induce suppliers to insist on custom and highly specific process properties. In order to cope with the challenges of high process diversity, tight process control and cost versus a relatively low lifetime volume (compared to other industries), an efficient approach to process validation is essential.

THE CHALLENGE: In medical product engineering, production processes that cannot be verified require a documented validation demonstrating the process capability with respect to repeatability and reliability [1]. This represents a major effort during the product engineering phase. Thorough execution is crucial as even minor product changes and improvements require a disproportionate effort after the release of a medical implant module.

THE VALIDATION APPROACH: Validation is a three-pronged effort: Installation qualification (IQ) validates proper installation of the machinery. Operational qualification (OQ) validates the specific process step. Performance qualification (PQ), finally, validates the process application in the context of successive process steps executed by regular production personnel.

A process is influenced by the five parameters [2] shown in Figure 1. The sensitivity of the process to these parameters varies with the product types and the processes.

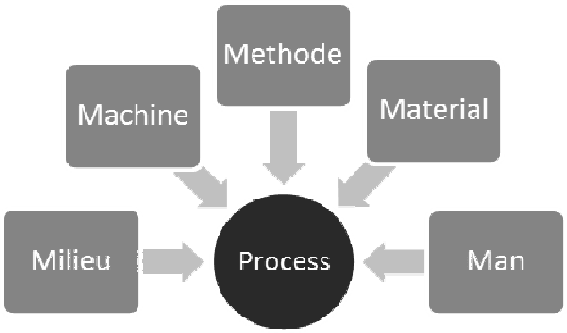

Fig. 1: Five parameters strongly influence process control.

The five process influence parameters can be linked to the three validation efforts: IQ covers machine and milieu, OQ covers method and PQ covers material and man.

A validation for one electronic medical implant represents a huge effort. Performing validations for a number of electronic medical implants needs a solid approach to keep the effort manageable.

The «secret» of such an approach relies on splitting the effort into the validation for the stable base and the validation for product specifics. Using the V-Model [3] illustrates how the split between base validation and product specifics can be accomplished (Figure 2): IQ lies at the bottom of the «V» and is independent of the specific product. PQ takes place at the top end of the «V». It typically requires three standard production runs with extended non-destructive and destructive process monitoring. It is clearly product specific and can be efficiently executed by following a standard test schedule. OQ is critical since it lies between the one time effort for IQ and the individual effort of PQ. Assuming that the basic OQ for the process already exists, good judgement must be applied to decide on the product specific effort that must be added for a solid OQ.

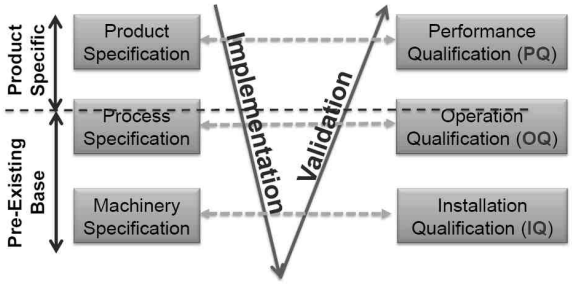

Fig. 2: V-Model for process validation.

CONCLUSIONS: The validation effort for multiple medical implants can be significantly reduced without sacrificing quality. The standardised approach judiciously adds product specific efforts to pre-existing base validations.

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Latest technologies of active implants

F. Mauron

Valtronic, Les Charbonnières, CH

ABSTRACT: Challenges of active implant developments are often their electronic autonomy, their size and tightness against body fluids and interfaces with excitatory tissue. Problems and recalls of active implants have frequently occurred because of power supply malfunctions, housing tightness issues and electrode/tissue incompatibilities particularly in long-term use.

Besides single use and rechargeable batteries, new power supply developments use energy supply by RF-transmission. Some future technologies are still in the concept stage such as energy harvesting and bio-fuel concepts.

Miniaturization is also very important. Wire-bonding with over molding is the state of the art approach. In some fancy applications, gold bump based ultrasonic Flip-Chip technology is already accessing the market. New methods of packaging of components are under consideration for future projects.

A major challenge has always been sealing and housing of active implants. Near titanium housing with ceramic feed-troughs and plastic-silicone housing with controlled humidity inside, the most innovative approach is a new technology of encapsulation providing superior biocompatibility and lifetime.

If connected to excitable tissue, active implants need electrodes classically made from Platinum. Some special applications require TiNi / IrOx Electrodes with surface enhancement. Future technologies may combine semiconductor properties with ionic currents.

In summary, the active implant field needs to overcome today's limitations that restrict applications and lead to severe side effects and recalls.

PEEK case for an active implant

T. Degen

Sequana Medical AG, Zürich, CH

ABSTRACT: The ALFApump is an implantable rechargeable pump designed to autonomously move ascites from the peritoneal cavity into the bladder indicated for patients with liver cirrhosis and certain types of cancer. The pump contains various sensors (pressure sensors, temperature sensors, movement sensors, Hall sensors and a humidity sensor) together with a motor, a PCB and various components.

To reduce costs and to allow for a fast development it was decided to use a PEEK casing. The main advantage of PEEK is cost and time (milling during development, molding for production). The disadvantage of this choice is the inherent non-hermiticity of PEEK.

This presentation would detail the additional measures taken because of non-hermeticity, additional discussion of choice of materials (motor, gears) and other experiences gained during the design and development of the device which received the CE mark in 2011. In addition the author will give a personal view on possible future trends and developments concerning active implants and choice of material.

Evaluation of process capability of implant manufacturing

UG. Hofer, A. Gammeter

Integrated Scientific Services ISS AG, Port, CH

INTRODUCTION: Many features of medical implants cannot be adequately described by the normal distribution. Consequently, capability indices based on parameter estimates assuming a normal distribution may be biased and not reflecting true process capability. Examples of features best described by distributions other than the normal include shape, surface quality, sphericity and angles, or position, coaxiality and concentricity.

METHODS: The calculation of capability indices (e.g., Cp and Cpk) is based on the location and dispersion of characteristic values with respect to a specified tolerance [1]. For example, Cp is expressed as the value of the specified tolerance divided by a measure of the length of the reference interval, usually 99,865% distribution quantile – 0,135% distribution quantile, which is equal to six standard deviations for a normal distribution.

Features where the deviation from a specified target value is expressed as an absolute value, i.e., ignoring the direction, are best described by fitting a truncated normal distribution [B1 in 2, 3] (*Figure 1*). Composite features are best described by fitting a Rayleigh distribution [B2 in 2].

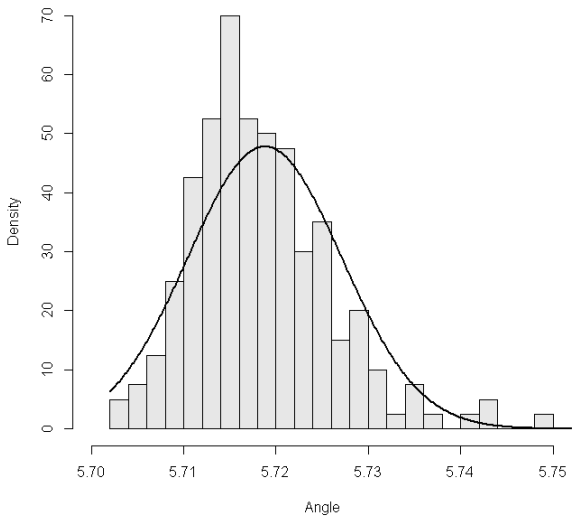

Fig. 1: Fit of a truncated normal distribution to a feature of an orthopedic implant (lot size = 200).

The estimation of the parameters for the aforementioned features directly from the sample rather than from the implied distribution has recently been challenged [3]. We used packages "mam" and "VGAM" of the R software [3] to fit truncated normal and Rayleigh distributions to selected implant characteristics and compared the resulting capability indices to those obtained with a normal distribution.

RESULTS: Table 1 shows the difference between Cpk value estimates for two implant characteristics (angle and position) based on no specific distribution, on the normal distribution and on a distribution suggested to best fit the selected character [2]. Cpk values ≥ 1.33 are acceptable according to the SOP of the manufacturer who supplied the data.

Table 1. Minimum process capability index Cpk estimated for two features of an orthopedic implant with no specific distribution implied and based on two different implied distributions.

	Angle	Position
No distribution implied	0.707	0.860
Normal	0.790	0.833
Truncated normal	1.246	-
Rayleigh	-	1.493

DISCUSSION & CONCLUSIONS: The capability of manufacturing processes of implants with shape, position and surface quality as key features should be estimated by using parameters from an appropriate distribution.

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ACKNOWLEDGEMENTS: The data set was kindly supplied by a manufacturer of orthopaedic implants.

Trends and developments of high-performance ceramics for implants

M. Zimmermann, S. Leyen, W. Rieger

METOXIT AG, Thayngen, CH

INTRODUCTION: Ceramic materials and especially oxide ceramics are well-known for their biocompatible properties. Beyond this aspect, these kinds of materials can also offer a lot of supplementary advantages when used as implants. Since several decades alumina is used as implant material for tribological pairings in Total Hip Arthroplasty. For dentistry, the use of zirconia as privileged material for the CAD/CAM applications is well recognized. More recently, composite ceramic material is also used as dental implant. METOXIT, as supplier for both the dental and orthopaedic community, has the potential to develop new ceramics which could potentially combine the advantages from both materials.

METHODS: A few years ago, METOXIT developed a new technology to obtain a ceramic coating onto ATZ Ziraldent® dental implants. This patented technology allows the production of a thin layer of porous ceramic structure for bony ingrowth, even onto complicated design such as screws. Figure 1 shows an enlarged view of this superficial porous microstructure. This successful technology called Zircapore® is documented up to 5 years in a prospective clinical survey.

The requests for a successful porous structure on orthopaedic implants are well described for metallic coatings, principally made of titanium alloy. Also, several ISO/ASTM standards are proposed to characterize the coating from a physical and mechanical point of view. The question is now: Can this Zircapore® technology be applied for a safe fixation of orthopaedic components?

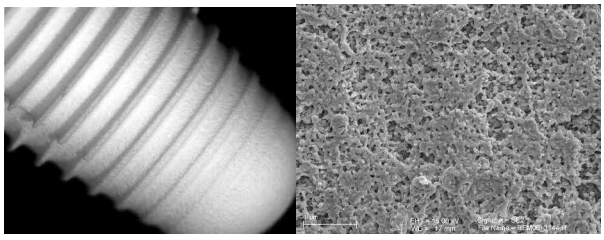

Fig. 1: Left: View of the tip of the dental implant. Right: Enlarged view of the coating showing the microscopic porous structure.

RESULTS: In collaboration with EMPA in the frame of a CTI project, a new superficial porous structure is developed for an application in resurfacing implants [1].

The osteoconductive potential of the Zircapore®–like structure has been analysed in-vitro using human bone cells. Cell adhesion is assessed by scanning electron microscopy (SEM), as shown in Figure 2.

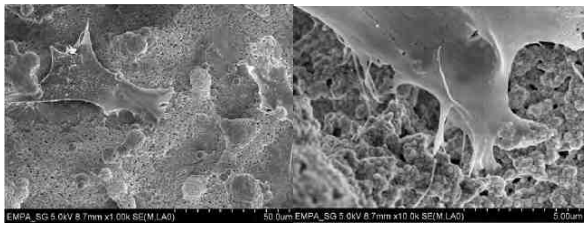

Fig. 2: SEM views (left 1k, right 10k magnification) of the cells adhered onto the Zircapore® surface.

Finite Element (FE) analyses are performed to characterise the push-in / push-out forces to impact a thin-walled resurfacing cup with various superficial structure in a pelvis model. The stress distribution within the cup and within the pelvis is analysed to investigate the influence of the cup design, see Figure 3.

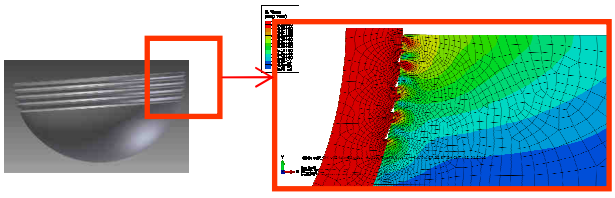

Fig. 3: Left: View of the cup implant. Right: Enlarged view showing the FE analysis with the stress distribution within the pelvis and the cup.

DISCUSSION & CONCLUSIONS: Oxide ceramics have optimal properties to be used as implants, e.g. for dental applications. For an application as full-ceramic, metal-free orthopaedic resurfacing implant, there is still multiple testing to be performed. However, at this stage, the manufacturing feasibility has been demonstrated.

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Phase contrast and X-ray dark field imaging: New possibilities for non-destructive testing of materials and components

C. Kottler[1], M. Krieger[1], V. Revol[1], R. Kaufmann[1], A. Konrad[2], A. Neels[1], A. Dommann[1]

[1] Centre Suisse d'Electronique et Microtechnique SA, Zürich, CH. [2] Konmed AG, Rotkreuz, CH.

ABSTRACT: Plastics and fibre composite materials have been attracting increasing attention as materials in engineering because of their outstanding thermo-mechanical properties. In particular in medical technology plastic engineering offers a wide range of opportunities. Specific advantages of plastics and composite materials are their robustness, biocompatibility and, in particular for implants, their X-ray transparency. For plastics engineering, however, not only new manufacturing processes but also appropriate non-destructive testing and characterization tools are required.

The presentation concentrates on a novel technique that has demonstrated great potential for non-destructive testing (NDT) and non-destructive evaluation (NDE). This method uses the Talbot-Lau grating interferometer principle [1]. It enables X-ray insights extended by two additional contrast mechanisms: X-ray Phase Contrast Imaging (XPCI) and Scatter Dark Field Imaging (SDFI) - two new imaging modalities that have been developed at CSEM for NDT applications [2-4]. Remarkably, a single measurement delivers also the conventional X-ray attenuation contrast image in other words it combines three contrast mechanisms simultaneously. In Fig. 1, the X-ray grating interferometer set-up at CSEM Zurich is shown.

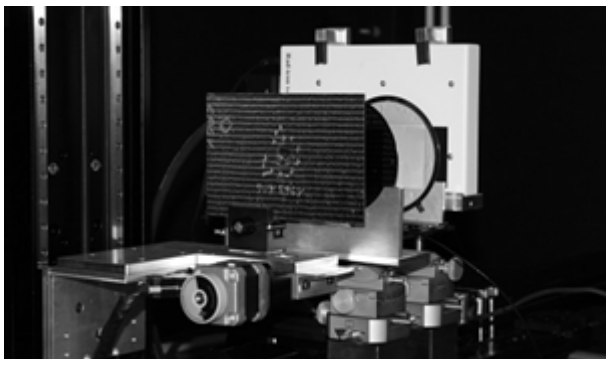

Fig. 1: A CFRP laminate is being imaged using the Talbot-Lau grating interferometer at CSEM Zürich.

The interferometer detects minor deflection and scattering that the X-ray beam encounters when penetrating the sample. These phenomena, though unobserved in conventional X-ray imaginging, are related to relevant material properties. On the one hand, this enables improved contrast in weakly absorbing materials, such as plastics or soft tissue, and, on the other hand, it offers spatial sensitivity to the materials micro-morphology, such as porosity. Moreover, the technique allows for single projection images as well as tomographic acquisition and computed reconstruction.

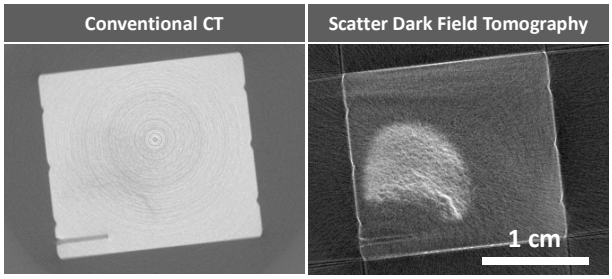

Fig. 2: Comparison of equivalent tomographic cross-sections of a PEEK specimen.

Due to its sensitivity to the microscopic structure, SDFI enables the detection of a variety of microscopic properties, such as fibre orientation in fibre-reinforced materials. In addition, also related defects such as cracks, delamination or fibre wrinkles can be detected. An example is shown in Fig. 2 where the tomographic cross-section of a fibre-reinforced PEEK specimen is shown: The comparison of the equivalent tomographic slices reveals a domain of enhanced porosity in the SDFI which remains undetectable in the conventional CT.

The presentation will illustrate various application opportunities and examples will be given for the superior detection of characteristics and defects. In addition, a benchmark with existing NDT methods is presented.

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Development of a miniaturized hand-held navigation system for medical applications: recent results

B. Knobel[1], C. Findeisen[2], G. Imboden[1]

[1] Naviswiss AG, Laufen, CH, [2] IFE Industrielle Forschung und Entwicklung GmbH, Laufen, CH.

INTRODUCTION: A novel approach of an optical navigation and measurement system for computer-assisted surgery (CAS) is presented. The main features of the miniaturized hand-held system include clip-on abilities to a handle, instruments or a tool, an integrated optical surface scanner, and miniaturized tags attachable to the patient.

METHODS: State-of-the-art optical navigation systems for supporting CAS incorporate more than 20 years of experience. Nevertheless, there are many limitations like line-of-sight problems, clumsy optical locators, a substantial number of the required instrumentations and its logistics, time consuming registration procedures, or related complex workflows with the CAS.

The novel approach reduces or avoids many of those limitations do to a miniaturized hand-held system (Fig. 1). The system includes a stereo camera and at least one patterned tag (Fig. 1, insert). The tags are attachable to the patient. The identifications, the positions and the orientations of the tags are measured (6-dof, degrees of freedom). A clip-on mechanism permits attaching the camera to a handle, an instruments or a tool. An integrated optical surface scanner measures the surface topology of implants or body parts (Fig. 2). Presently, the prototype is wired for power and data processing. The measuring volume depends on the used optics design. For the system as shown in Fig. 1 the designed field view is about 60° and the measuring distance ranges from about 180 mm to 350 mm.

RESULTS: The position and angular accuracies (RMS) of the prototype is smaller than 50 μm and smaller than 0.5° within the measuring volume, respectively.

The miniaturized hand-held system has the potential for more economic workflows of the CAS, for quality management of the surgical procedure, for its usage for orthopaedics surgery, for new workflows for surgery of soft tissue like the liver using modified tags, or for new workflows for its usage in the field of laparoscopy.

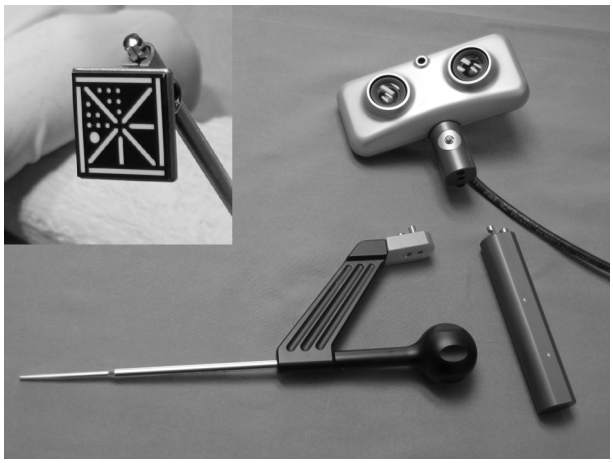

Fig. 1: The prototype of a miniaturized hand-held system includes stereo cameras with a typical working distance of 250 mm, an integrated laser surface scanner, a clip-on adapter for a handle or an instrument, and tags for 6-dof measurements that are attached to the patient. (insert): a 15 mm x 15 mm tag.

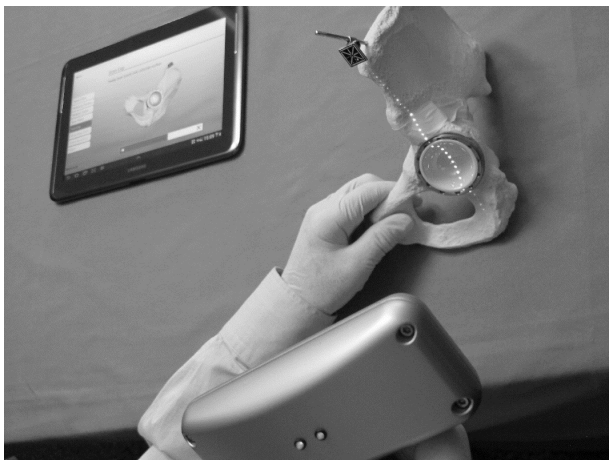

Fig. 2: The laser scanner of the system measures the surface of a hip joint prosthesis inserted into a pelvis model.

DISCUSSION & CONCLUSIONS: The novel approach of the miniaturized optical navigation and measurement system is widely accepted by surgeons and has the potential for more economic or new CAS workflows especially towards soft tissue surgery.

Colorimetry on implant surfaces for esthetically demanding applications

H. Schmotzer[1], S. Stübinger[2,], D. Velten[3]

[1] SigmaRC GmbH, Cham, CH. [2] Musculoskeletal Research Unit (MSRU) and Competence Center for Applied Biotechnology and Molecular Medicine (CABMM)Vetsuisse Faculty, University Zurich CH. [3] Hochschule Offenburg, Fakultät für Maschinenbau und Verfahrenstechnik, DE

INTRODUCTION: The surface colour of implants is rarely the focus of attention. However, in certain aesthetically demanding applications, e.g. fracture plates for hand surgery or dental implants and abutments the surface colour does become important. In patients with thin soft tissues or after bone resorption, the dark grey colour of metals, in particular titanium, results in a dark shadow leading to unsatisfactory aesthetic results. Different solutions have been proposed and are in clinical use. It was the goal of this study to compare the different surfaces and their effect on the colour of thin soft tissue.

METHODS: 12mm cpTi or ZrO_2 discs were used in this study. The discs were surface treated according to standard commercial processes to represent surfaces currently in clinical use. The surfaces were as follows: (1) turned, (2) polished, (3) sandblasted and acid etched, (4) pink anodisation, (5) TiNbN coated (golden) (6) ZrO_2. Additionally, an experimental surface for Ti was included (7). For colour measurements (CIELAB) a commercially available camera was used (color-guide, BYK-Gardner, Germany). First, measurements were taken on the surfaces after undergoing a commercial cleaning (5 discs per surface). After that, the surfaces were covered by thin gingival sheets (0.5-1.0 mm) [1] obtained from fresh pig jaws and the colour measurements repeated. Each specimen was tested on every surface (total 8 specimens). The colour of the jaws prior to resection of the tissue specimen was determined as reference.

RESULTS: The results are illustrated in Figures 1 and 2.

DISCUSSION & CONCLUSIONS: The colour values measured correlated generally very well with the optical impression. The results demonstrate clear differences between the surfaces. However, the colour value of the surface in the dry state did not always translate into a lighter or darker colour when covered with tissue; e.g. (3).

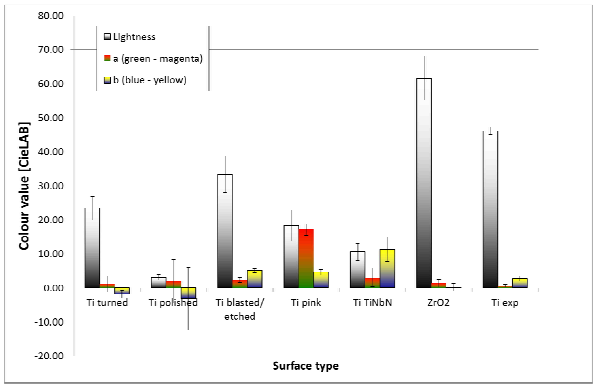

Fig. 1: CIELAB values of experimental surfaces as received.

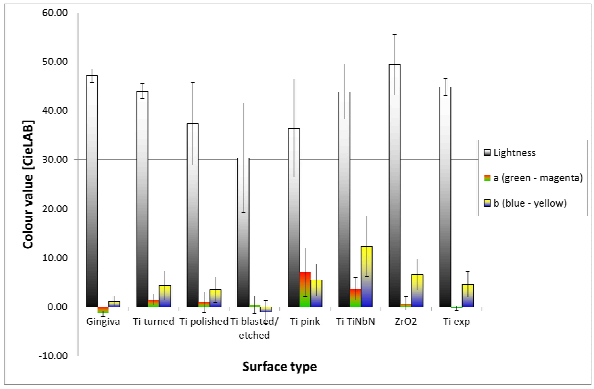

Fig. 2: CIELAB values of experimental surfaces after coverage with gingival sheets in comparison to native gingiva.

As seen clinically, ZrO_2 appeared lighter than the natural tissue. The pink (5) and golden (6) surfaces shifted the visible tissue colour towards the respective colour spectrum (magenta (5), yellow (6)). Further the anodised surface (5) appeared rather dark both when dry and when covered by tissue.

Our data suggest that colour measurements for aesthetically demanding implants surfaces should be conducted simulating the clinical conditions through appropriate in-vivo modelling.

REFERENCES: [1] R.E. Jung (2007) *Int J Periodontics Restorative Dent* **27(3):** 251-257.

ACKNOWLEDGEMENTS: We would like to thank IGS, CH, for providing the colour camera and Metoxit, CH for the ZrO_2 samples.

CVD coating technology: A coating alternative for CoCr alloys

H. Strakov[1], A. Santana[1]

[1] *IHI Ionbond AG, Olten, CH*

INTRODUCTION: One solution to avoid the CoCr particles released from the implants due to wear and corrosion is to coat a metal joint with a more wear resistant low corrosion ceramic coating. This has been proposed as for example titanium and zirconium nitride coatings on medical implants. But for the material systems such as CoCr, the problem with ion release from the substrate causing long term problems such as inflammation and aseptic loosening requires mostly dense multilayer films with higher fracture toughness. Ionbond has been pioneer of PVD multilayer coatings applied on knee systems. The relatively soft CoCr substrates theoretically require a thick hard coating in order to avoid as much as possible the egg-shell effect. Physical Vapour Deposition (PVD) coatings, evidenced to be good technology for multilayer coatings however layer interfaces would, theoretically, require higher coating deposition temperature to avoid as much as possible coherency stresses between the coating layers.

METHODS: CoCr alloys can be coated by using Chemical Vapour Deposition (CVD) technology at temperatures higher than 800°C. At such temperatures the CVD coating applied on implants with complex geometries exhibit, in all its 3D shape, rather uniform coating thickness distribution which guarantee a good ion release blockage. For the articulating surfaces the density of CVD multilayer coatings showed advantage in mechanical and wear behavior. Such advantage is due to the CVD's higher coating thickness combined with a dual or multi dual layer deposited at high temperature leading to virtually no risk for delamination whether if in between the substrate or in between layers.

RESULTS: Femoral components are compared in terms of implantation feedback and simulator results.

The coatings used for comparison are:

- CVD bilayer (top layer ceramic Al_2O_3)
- PVD multilayer - AS coating from Aesculap, with top layer made of a ZrN compound),
- PVD-Medthin™ 01 TiN

The coatings associated with their technologies are compared through their structure, thickness distribution, roughness and adhesion.

Fig. 1: left: PVD-Medthin™ 01 TiN. TiN is FDA approved since 2002 and sold in USA, Europe, Australia and emergent markets, etc; middle: PVD multilayer Ionbond-Aesculap AS coating 510K approved, on sale in USA, Europe and other countries; right: CVD dual and multilayers coatings by Ionbond.

DISCUSSION & CONCLUSIONS: The CVD bilayer (TiCN +Al_2O_3) coating with its higher thickness and better thickness distribution on 3D geometry consists in a good alternative coating when compared with the PVD deposition coatings. The CVD coating is limited for application in CoCrMo since TAV alloys become brittle during coating process attributed to the high reactivity of the reaction gases with the TAV. The Ionbond CVD bilayer (TiCN +Al_2O_3) coating evidences interesting properties compared to other ceramics in the market such as Oxinium (ZrO_2) because:

- CVD preserves the fracture toughness of the CoCrMo substrate as CVD is not a diffusion process but a coating (adding material) process.
- CVD has a superior hardness on the top layer(> 20 GPa)

Regarding the PVD coatings the feedback from the market after over one decade of implantations is excellent and suggests an increase in volume of coatings on implants.

ACKNOWLEDGEMENTS: We would like to thank for the collaboration in the characterization:

a. DePuy Orthopaedics, Warsaw, IN – USA

b. Institut de Physique de la Matière Condensée (ICMP)- École polytechnique fédérale de Lausanne-CH.

Silver as a lubricant additive for implant manufacturing

BM. Keller [1], MA. Gehri [1], S. Maric [2], H. Fisch [2]

[1] preenTec AG, Marly, CH. [2] Motorex AG, Langenthal, CH

INTRODUCTION: Implants are manufactured from a broad variety of metals e.g. titanium alloys. During the manufacturing process, metalworking fluids, so-called lubricants, are used. Today, lubricants are highly complex systems which also contain human incompatible compounds. Water based lubricants are preserved with biocides. Without proper conservation, lubricants are infected by micro-organisms within a short time. This leads to increased production costs, and potentially endangers the health of employees. Unfortunately, the use of biocides also poses problems. Employees who come into direct contact with biocides, either by inhalation of aerosols or through skin contact at their working place, may experience adverse health effects. The use of biocides results in potential endotoxin release that triggers pro-inflammatory reactions and fever.
Here we demonstrate the potential of stabilizing metalworking fluids with silver components, for use in the metalworking industry.

METHODS: Through the oligodynamic effect, silver shows antibacterial and antifungal properties, even at low ppm concentrations. In the past, the incorporation of silver compounds into lubricants was limited due to the reactivity of silver e.g. oxidation and unselective reactions with sulphur containing molecules. This led to reduced long term activity of the silver and reduced stability of the lubricant.
Encapsulating silver compounds into an organic matrix makes it possible to incorporate them, with good stability, into lubricants [1]. The particle size must be within the submicron scale: small enough to avoid clogging filter systems and big enough to avoid any atypical size effects characteristic of nanoparticles.
The biological evaluation of medical devices is an essential step in their development. Therefore any potential risk of the devices in humans should be investigated thoroughly. Medical devices meant for use in the human body have to be tested for haemocompatibility and pyrogenic activity, since any contamination can induce pro-inflammatory reactions [2]. Residues of biocide products are known to be potential pyrogenic contaminants. Therefore the absence of biocides in the implant production chain is preferable.

RESULTS: Encapsulating silver compounds into organic matrices and then incorporating these into lubricants, results in a technically and biologically stable, nontoxic, biocompatible metalworking fluid. By varying the silver concentration into the lower ppm range, the neutralizing effect can be shifted towards a biostatic state, i.e. the working fluid bacteria fall into a so called “dormant state”. The bacterial activity, as determined by gene probes and fluorescence measurements, was far below 10% of normal state bacterial activity [3].

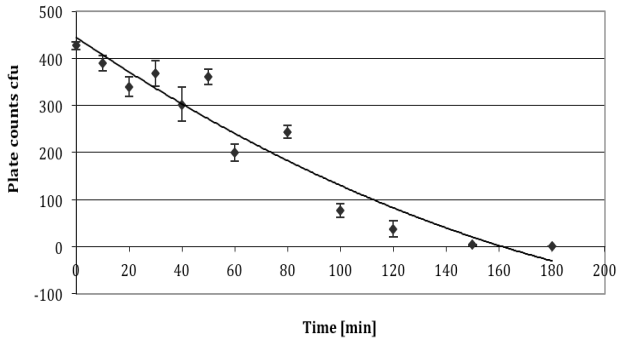

Fig. 1: 100ml of a PMC fluid was infected with Pseudomonas putida to reach a total concentration of 10^6 bacteria per ml. The flask was shaken with 140 rpm at room temperature. In the first hour, 1 ml (in triplicate) was taken diluted and plated in Petri dishes. The Petri dishes were incubated for 48 hours at room temperature and the cell forming units were counted afterwards. After 180 min. all the bacteria were neutralized.

DISCUSSION & CONCLUSIONS: MOTOREX AG Langenthal has recently developed silver containing lubricants, which are available under the trade name of PMC "precious metal catalyst". This new technology keeps the lubricant bio-stable without the use of common biocides. Moreover, these lubricants are non-toxic and therefore very useful for applications in the medical sector.

REFERENCES: [1] M. A. Gehri, B. M. Keller, P. Regenass (2008) Patent EP1938690A1: *Sterilisierung und Konservierung von Fluiden.* [2] M.B. Gobet, M.V. Sefton (2004) *Biomaterials* **25**: 5681-5703, [3] B.M. Keller, Publication in progress.

New opportunities for using tantalum for implants with Additive Manufacturing

R. Wauthle[1,2], J.-P. Kruth[2], ML. Montero[3] L. Thijs[3], J. Van Humbeeck[3]

[1] LayerWise NV, Heverlee, BE. [2] KU Leuven, Department of Mechanical Engineering, Leuven, BE.
[3] KU Leuven, Department of Metallurgy and Materials Engineering, Leuven, BE

INTRODUCTION: Tantalum is generally known as a dense, ductile, very hard material and its high resistance to corrosion of acids. Besides a highly biocompatible material, tantalum also has a very good apposition to human bone. Bone tends to grow very close to the tantalum surface, making tantalum a perfect material for bone implants. However, due to the high density, high melting point, high cost and difficulty to machine it using conventional machining, the use of tantalum for implants is currently limited to surface coatings and coated carbon porous structures. Selective Laser Melting (SLM) is an Additive Manufacturing technology which uses a focused laser beam to subsequently melt thin layers of metal powder to create functional full dense metal parts. AM allows for almost complete freedom of design and efficient material consumption. Given the unique properties of tantalum as a material combined with the advantages of AM to overcome current issues in using tantalum, this could open up a lot of new opportunities for the use of tantalum for medical implants.

METHODS: All parts were manufactured using the Selective Laser Melting technology. In order to characterize the solid properties of tantalum processed with SLM, test samples with almost full density were tested at the test facilities of KU Leuven Department of Metallurgy and Materials Engineering.

RESULTS: Figure 1 illustrates the nearly full (99.6 ± 1 %) achieved density with a cross section view using Light Optical Microscopy (LOM) and a top view indicating the melt tracks under secondary electron microscopy (SEM).

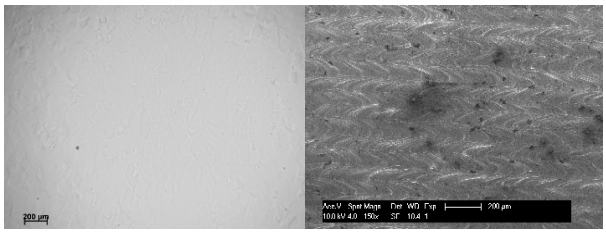

Fig. 1: LOM of a cross section view (left) and SEM of a top surface (right).

Table 1 summarizes the mechanical properties of SLM processed test samples and compares it to the properties required by ISO 13782 'Unalloyed Tantalum for Surgical Applications'.

Table 1: Comparison of mechanical properties of Ta required by ISO 13782 and processed by SLM.

	ISO 13782	**SLM Ta**
Tensile strength [MPa]	170-520	513-540
Yield strength [MPa]	140-345	463±9
Elongation [%]	2-30	29±1
Young's modulus [GPa]	n.a.	168±8
Hardness [HV]	n.a.	207±2

DISCUSSION & CONCLUSIONS: From the results presented above it can be stated that the mechanical properties of tantalum parts processed using Selective Laser Melting achieve the requirements of ISO 13782. Furthermore, processing conditions and their influence on the compression yield strength have been investigated[1]. SLM therefore seems to be a novel method to manufacture tantalum implants. In a next step, porous tantalum scaffolds are being investigated. SLM allows manufacturing complex porous structures which enforces bone ingrowth and prevents stress shielding [2]. In this continued research the static and dynamic mechanical properties of a defined lattice structure will be evaluated under compression. Also, the *in vitro* and *in vivo* behaviour of the SLM tantalum scaffolds will be investigated.

REFERENCES: [1] L. Thijs et al. (2013) *Strong morphological and crystallographic texture and resulting yield strength anisotropy in Selective Laser Melted tantalum* (in review) [2] J. Van der Stok et al. (2012) Selective Laser Melting-Produced Porous Titanium Scaffolds Regenerate Bone in Critical Size Cortical Bone Defects, *J Orthop Res* **31(5):** 792-799.

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Breakthroughs in patient matched medicine through advancements in 3D image analysis

S. De Boodt[1], C. Bichlmeier[2], L. Vigneron[1]

[1] Materialise NV, Leuven, BE. [2] Materialise GmbH, Gilching, DE

INTRODUCTION: Today, with the increasing use of 3D medical imaging (e.g. CT or MRI), it is possible to analyse in detail 3D patient anatomy to extract personalized features and measurements for designing patient matched devices, but also to quantify trends and population specific shape information for standard implant design.

METHODS: In order to create a patient matched implant or surgical instrument, a medical image based workflow is performed (Fig. 1). Starting from a CT or MRI scan of the patient, a group of voxels that belongs to the anatomy of interest is selected in a process called segmentation. From the segmented anatomy an accurate 3D triangulated surface model is created. On this anatomical model, complex 3D measurements or a virtual surgery can be performed. Based on this analysis and planning, a patient matching implant and/or surgical instrument is then designed. Finite element analysis (FEA) can be performed to simulate the loading conditions on the implant during the patient's daily activities and to optimize the design. Patient specific implants today are manufactured via milling or to an increasing extent via additive manufacturing (3D printing).

Medical image based engineering is also used to speed-up the design process of standard implants. When personalized measurements are analysed on a large number of patient cases, population analyses can be performed in order to extract trends and population-specific shape information. By using statistical shape modelling [1], it is possible to determine the average shape and the variation across the population (Fig. 2).

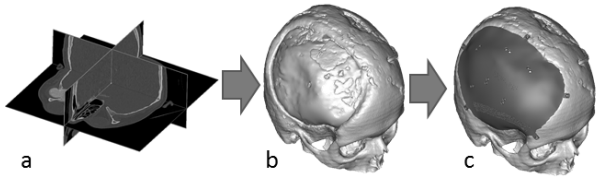

Fig. 1: Process of designing a patient specific implant. (a) Based on a 3D scan (CT/MRI) of the patient, (b) a 3D model of the defect is created and (c) a custom implant is designed.

RESULTS: Personalized analysis and surgical simulation allow for the design of custom implants that have shown to result in better surgical outcomes, and sometimes to be the only solution for extreme patient cases, such as for selected hip revision cases. A medical image based approach also allows for the design of patient-specific guides and is nowadays provided by the biggest implant companies, such as Biomet or Zimmer, for total knee replacement.

Image based population analysis have been used successfully to design standard implants that better fit the population. Using the average anatomy as the starting point, it is now possible to reduce the number of cadaver trails, thereby reducing R&D cost and reducing the time to market for a new device.

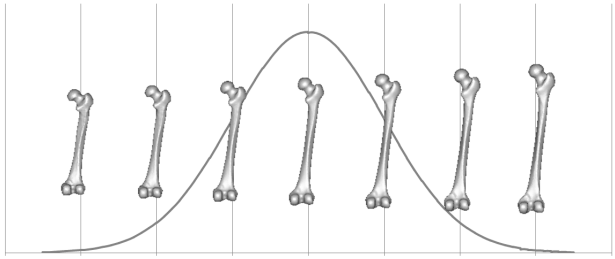

Fig. 2: Result of a population analysis performed on 40 Chinese femurs, showing the average femur shape (center) and the variation across the population.

DISCUSSION & CONCLUSIONS:

Advanced anatomical image processing, analysis, design and modelling software enables efficient production of high quality patient matched implants and surgical instruments.

In many cases, a standard implant still provides a sufficient solution. Advanced statistical modelling of medical image data makes it possible to faster and cheaper develop implants that better fit the population.

REFERENCES: [1] T.F. Cootes, C.J. Taylor, D.H. Cooper and J. Graham (1995) Comput Vis Image Underst **61**: 38-59.

Patient specific implants in orthopaedics – Efficient production with software

J. Stifter[1], A. Ringenbach[2]

[1] Medivation AG, Windisch, CH. [2] Institute for Medical and Analytical Technologies, University of Applied Sciences Northwestern Switzerland, Muttenz, CH

INTRODUCTION: Patient specific instruments and patient specific implants are used more frequently in Orthopedics. The advantage of patient specific technology is shorter operation time and reduced overall instruments use [1].

The process for the production of patient specific instruments or implants requires the precise segmentation of the obtained image data. This segmentation causes significant problems to orthopedic manufacturers when the amount of cases increases: It is a slow and human intense work and therefore not well scalable. Furthermore it is an error prone and quality wise not well controllable work.

Medivation in conjunction with the Institute of Medical and Analytical Technologies in Muttenz has developed an own software technology called Auto-3D to segment the image data mostly automated and with as least human interaction as possible. The aim of this study was to analyze the efficiency and precision of the newly developed segmentation tools.

METHODS: The software engine Auto-3D segments the CT data by first automatically initializing an anatomical shape based model. Then the software applies a fine-segmentation algorithm in defined regions.

Once this automatic process is finished, the software then guides the operator through a manual process of checking the automatic work in a step by step process. Segmentation errors can be manually corrected.

Then the software exports the surface models with accurate precision for further processing.

In this study we used 20 reference models that were manually segmented with a standard image processing software (Mimics, Materialise, Belgium) by an experienced operator. The output of the Auto-3D software was checked against these 20 reference models in terms of a) overall precision of the anatomical shape based model, b) automatic segmentation process, c) manual fine-adjustments. Furthermore, the time was compared between the segmentation of the reference model and the final result with the software engine.

RESULTS: Table 1 summarizes the time measurements. The mean time used to create the reference models was 38.0 minutes with manual segmentation (min 28...max 60) versus the mean time of 17.6 minutes (min 8...max 30) with the Auto-3D segmentation software which is highly significant ($p<0.001$).

Table 2 summarizes the difference between the reference models vs the different stages of the Auto-3D segmentation process. It can be seen, that after applying the automatic segmentation process, the precision (mean surface deviation) is already within 0.8mm.

Table 1. Time comparison between manual segmentation and the software Auto-3D.

	Conventional Software [minutes]	Auto-3D Engine [minutes]
Time	38.0	17.6
Min	28	8
Max	60	30

Table 2. Precision comparison between manual segmentation and the software Auto-3D. Stage 1 is the anatomic shape based model, stage 2 is after automatic segmentation and stage 3 is after manual fine-editing. All values in mm.

	Stage 1	Stage 2	Stage 3
Femur	1.5	0.8	0.25
Tibia	1.4	0.8	0.24

DISCUSSION & CONCLUSION: The Auto-3D software improves the time significantly. The precision reached was similar to manual editing. The overal process quality due to the standardized process was not measured in this study but is another obvious advantage of this approach.

The software is today in regular use and is recognized by more and more manufacturers.

REFERENCES: [1] JW Noble et al (2012) *The Value of Patient-Matched Instrumentation in Total Knee Arthroplasty,* Journal of Arthroplasty Vol. 27 No. 1 2012l.

Einsatz der Computertomografie in der industriellen 3D Messtechnik - Verfahren, Anwendung, Genauigkeit

D. Ferger, M. Heath, A. Flechtmann

Werth Messtechnik GmbH, Gießen, DE

KURZFASSUNG: Vor einigen Jahren wurde die Computertomografie als zusätzlicher Sensor in Koordinatenmessgeräte integriert. Dieser Vortrag zeigt auf, welche Möglichkeiten mit dieser relativ jungen Technologie bestehen um Bauteile vollständig und genau messtechnisch auszuwerten.

Am Beispiel eines medizintechnischen Kunststoff-Bauteiles wird die 3D-Komplett-Messung mit einem solchen CT-Koordinatenmessgerät vorgestellt. Darüber hinaus wird die CT-Auswertung eines medizinischen Stents vorgestellt.

Es werden Verfahren vorgestellt, wie z.B. die Rastertomografie und die Ausschnittstomografie, um Bauteile in noch höherer Auflösung darzustellen bzw., um kleinere Details zu erkennen, oder genauer zu messen.

Neben der dimensionellen Messung kann die Computertomografie auch zur Bauteilinspektion eingesetzt werden. Hier werden einige Anwendungsbeispiele aufgezeigt.

In zunehmendem Maß wird das Verfahren auch direkt zur Werkzeugkorrektur eingesetzt. Exemplarisch wird die Korrektur von Spritzgießwerkzeugen für LED Linsen erläutert.

Regulatory Road for Combination Products

P. Mainil-Varlet

Aginko, Marly, CH

ABSTRACT: The shifting borders among traditional drugs, biologics and medical devices are poised to produce safer and more effective combination products that offer new diagnostic and treatment options for patients. But such novel combination products pose numerous regulatory hurdles for sponsors, even when comprised of previously cleared components — devices, delivery systems, compounds or biologics. Combination products tend to be governed by different regulations based on their components: drug–device combinations may be subject to pharmaceutical law; device–drug combinations to device law; and diagnostic–drug combinations (also called companion diagnostics), very likely, new regulations.

Moreover, across the globe, such classifications are subject to different interpretations. A sponsor's first step for combination products is identifying the information a regulatory agency requires to determine the product's identity and assignment for review and clearance. Because global harmonization is still an unrealized goal, a combination product sponsor must have an excellent understanding of how the potential market is regulated and how obtaining a first market clearance might influence subsequent markets. A sponsor, therefore, might be well advised to seek the counsel of a qualified CRO early in the development process to obtain a detailed strategy for the proposed combination product's regulatory process, tailored by an assessment of the product and each applicable regulatory agency.

Regulatory approval of implants produced with Additive Manufacturing

O. Hedin

Arcam AB, Mölndal, SE

INTRODUCTION: Additive Manufacturing (AM) is already in full use for the production of CE-certified and FDA-cleared orthopaedic implants, with more than 30.000 EBM-manufactured acetabular cups with integrated trabecular structures for improved osseo-integration implanted to date.

This rapid development has caused a heightened interest for AM within the implant manufacturing industry in general, and subsequently an increased focus on how to obtain regulatory approval for implants produced with additive technologies.

In this paper we will discuss Arcam's experiences from how the implant manufacturers who have implemented AM in their production have gone about obtaining CE certification and FDA clearance for their EBM-manufactured orthopaedic and spinal implants.

BACKGROUND: Electron Beam Melting **(**EBM) technology manufactures parts by melting thin layers of metal powder. The energy source is an electron beam gun, and the process takes place in a vacuum chamber. The technology's additive, layer-based nature also enables the production of implants with the integrated trabecular structures that enhance the osseointegration.

For most implant applications AM is considered a special process – a process for which the product cannot be fully *verified* and consequently the process needs to be *validated*. Validating an AM-based manufacturing process requires extra vigilance on three levels.

Firstly, we need to understand the technical differences between additive and conventional manufacturing. Conventional manufacturing is based on removing material until the final part shape has been obtained. In AM material is added layer-by-layer to obtain the final shape which means that the material properties of the part are generated as the part is being built.

Secondly, AM technologies generically rely on a stable process for each layer. For EBM specifically, achieving a stable process means obtaining a thermal steady-state. As the heat balance depends on the cross-section of your part the parameters controlling the process may have to be adjusted to handle different geometries – they become geometry-dependent.

The third point of vigilance concerns the supply of raw material. With AM only the material that is actually needed to produce the implant is used. The remaining powder metal is recycled and reused. Hence, powder handling procedures must ensure rigorous quality control and full traceability of each part back to its source powder.

VALIDATION GUIDELINES: AM in general and the Arcam EBM process in particular (although widely used for production of implants and despite a large number of already certified medical devices) are still relatively new to most implant producers. To facilitate the validation process, Arcam has developed a validation template with Arcam's view on each aspect of FDA and ISO validation guidelines. Each of these guidelines is commented in detail and links are provided to relevant Arcam documentation, such as drawings, manuals, calibration reports and software documentation.

Fig. 1: EBM-manufactured acetabular cups.

RESULTS: In 2007, the two Italian orthopaedic OEMs Adler Ortho and Lima were awarded CE-certification for their acetabular cups featuring integrated porous structures. Under the trademarks of Fixa Ti-Por™ and DELTA TT™ these cups are now in volume production at Adler Ortho and Lima-Lto. In 2010 Exactech introduced the InteGrip™ cup and became the first U.S. manufacturer to offer FDA-cleared orthopaedic implants.

To date over 30.000 EBM-manufactured cups with integrated trabecular structures have been implanted, and approximately 2% of the global production of acetabular cups is now manufactured with EBM.

Fixation concept for a metalback/ceramic connection

M. Schmidt

Jossi Orthopedics Ltd, Islikon, CH

INTRODUCTION: "However, the metal-on-metal system generated adverse reactions in patients that are typical of all devices manufactured in this way." [1] This type of generalising statements is often communicated since two market leading orthopaedic companies recalled their metal-on-metal (MoM) hip resurfacing implants in 2008 and 2010. Instead of enquiring on the reasons for increased clinical failure, no distinction seems to be made between design and material, and MoM devices are generally dismissed. Nevertheless, the concept of hip resurfacing [2] is appreciated by surgeons and patients, thus creating a need for alternatives. From all accepted materials, only ceramic-on-ceramic (CoC) combinations are suited. Jossi Orthopedics' interest is to produce the titanium alloy metalback by its unique HybridManufacturing™ process, combining deep-drawing and precision machining.

EVALUATION: When looking for an alternative to MoM, a thorough evaluation is necessary to decide whether concept, material, design, or clinical handling led to failure of resurfacing devices. It turned out that both withdrawn products had design weaknesses, one acetabular component badly osseintegrating [3], the other MoM combination having too little clearance between head and cup, leading to increased friction and ultimately component loosening[4]. Since resurfacing needs large-diameter ball-heads and thin-walled acetabular cups, polyethylene is to be excluded for tribological reasons. Thus, only CoC is left to create the artificial joint components. Accepted combinations are Al-Al, ZTA-ZTA (zircona-toughened alumina) and ATZ-ATZ (alumina-toughened zirconia). On the acetabular side, the ceramic sliding surface is embedded in a titanium alloy metalback (Fig. 1) enabling cementless fixation and osseointegration, whereas a thin-walled ceramic ball-head is either cemented directly onto the femoral neck or a standard ball-head is fixed to a femoral stem.

RESULTS: Existing CoC resurfacing solutions are thoroughly protected by patents. The biggest obstacle therefore was not only to circumvent existing patents but to set an own IP protection. The crucial point was the connection between metalback and ceramic sliding surface. Having mastered this challenge, a setting instrument was developed, enabling a strong grip on the cup without interfering with the acetabular rim during impaction. Being solely a supplier to orthopaedic companies, i.e. without own branded products, the goal of Jossi Orthopedics always is to offer a complete solution to potential customers. The metalback/ceramic assembly then was presented to orthopaedic companies, however, in times of cost restrictions, it is rather preferred to buy a customised standard solution. Jossi's goal therefore is to collaborate with a ceramics producer.

Fig. 1: Metalback/ceramic assembly CeraGrip™, consisting of a thin-walled acetabular component (left), shown with femoral component for resurfacing (right). The ATZ ceramic components were provided by Metoxit, Thayngen, Switzerland.

DISCUSSION & CONCLUSIONS: Even being, as a supplier, only interested to produce a specific component, a complete solution should be targeted, and a strategic design feature should be IP protected. In the presented example, the crucial technological development is the connection between metal and ceramic, leading to an "invisible generic" solution. The titanium alloy metalback can be fully customised, e.g. by a proprietary porous coating, creating a distinct orthopaedic implant, however, with reduced time to market for the orthopaedic company.

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Surface property modulation in high-precision cutting of materials for medical applications

A. Pereira[1], R. Perez [1], R. Zaugg [2]

[1] *GF Agie Charmilles, Meyrin, CH.* [2] *Mikron Agie Charmilles AG, Nidau, CH*

INTRODUCTION: Current advances in conventional cutting and Electric Discharge Machining (EDM) technologies are now able to solve traditional problems limiting the manufacturing of medical implants or rendering it complex. These advancements are particularly in the material range and geometry, accuracy, surface adaptation and mechanical properties. Influences are expected on lifetime and tissue compatibility, namely related to intolerances from corrosion and toxic residues left by the machining process. Present and future technologies allow producing complex parts in shorter time due to the use of 5-axes devices and advanced tools, the integration of vision systems, and the application of strategies for modulating the surface finish.

METHODS: Various studies are reviewed which describe specific test parts prepared with GF Agie Charmilles Mikron HSM400U ProdMed and Cut 200 wire-EDM devices, integrating JauchSchmider rotary axes. Surface analyses were made with a Scanning Electron Microscope LEO and EDX Analyser and mechanical properties were measured with a CSM nano-hardness tester and a tribometer. Main materials under test were Cr-Co alloys, Ti-Al-V, Mg alloys, 316L stainless steels and Zirconia based ceramics. Specific test cuts were performed to adjust the main machining parameters for both high-speed milling and EDM processing for such materials.

RESULTS: High speed cutting processes allow outstanding processing of implants with accuracies within 2 μm, leading to surfaces polished down to 0.12 μm Ra and 0.4 μm Rz on Ti alloys. Thanks to adapted CAD-CAM strategies, the use of adapted tools and new machining control sensors, the optimisation of the efficiency in terms of wasted base material for the production of dental implants in Co-Cr alloys is achieved. Through "nesting" strategies, a percentage use of raw material of up to 93 % was achieved.

Novel EDM processing shows a leap in performance for the manufacturing of implants and medical devices through the implementation of supplementary rotary axes, on-machine vision systems and high frequency generators (above 10 MHz range pulses), enabling to modulate various surface roughness parameters independently. The use of alternative electrode materials eliminates the undesired Zn and Cu residues present at the surface and transferred to the part during the process [1]. Such elements can now be replaced by refractory metals (Ti or W) in order to produce surface modifications on the part which improve their resistance to corrosion and wear. The friction coefficient can be reduced by half with respect to standard processes. This provides a low cost method to eliminate intolerance risks by suppressing the chemical post-processing phases needed with the traditional EDM (figure 1).

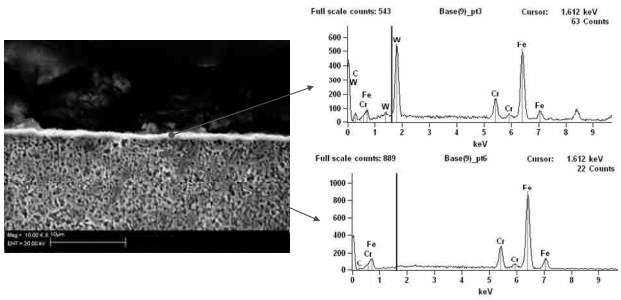

Fig. 1: Surface modification produced by a special EDM strategy introducing a C-W refractory alloy at the surface of steel and eliminating classical Zn and Cu contamination for medical implants.

DISCUSSION & CONCLUSIONS: Modern conventional and EDM technologies allow the processing of medical implants and devices with a greater flexibility. They are especially focused on achieving total biocompatibility and increased lifetime in different types of alloys and ceramics, and on reducing overall costs of the manufacturing process.

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Dental ceramics: past, present, and future?

S. Jegou[1]

[1] *Nobel Biocare Services AG, Kloten, CH*

Since the unraveling in the early 18th century of the centuries old secrets of the Chinese potters and the first utilization of porcelain for dentures by Duchateau in 1774 and for single crowns by Stockton in 1837 all-ceramic restorations have become today the golden standard in esthetic restorative dentistry. With the blooming of CAD/CAM manufacturing and digital treatments, patients can get new teeth in one single visit. With the help of intra-oral scanning, digital treatment planning, computer aided design and chair side milling of a large variety of dental materials, the whole treatment can be performed at the dental practice.

In this presentation, a historical review of the development of dental ceramics will be given up to today, with particular emphasis on the cornerstone ceramics and their clinical applications. Such materials encompass the feldspathic porcelains, the leucite and lithium disilicate glass-ceramics, the glass-infiltrated ceramics, and the oxide ceramics alumina, zirconia, and alumina toughened zirconia.

Finally recent developments will be presented and possible routes for future development will be proposed.

Fig. 1: Digital implant treatment planning with NobelClinician™ Software and IPad® app NobelClinician Communicator for patient communication.

Fig. 2: CAD design of a zirconia bridge in the NobelProcera™ Software.

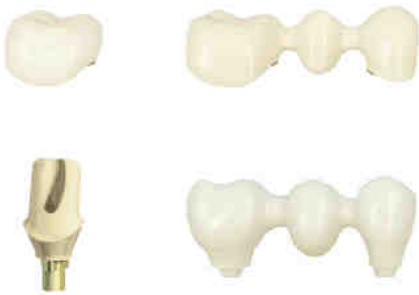

Fig. 3: Milled NobelProcera™ zirconia coping, bridge, abutment, and implant bridge (before veneering at the dental lab.)

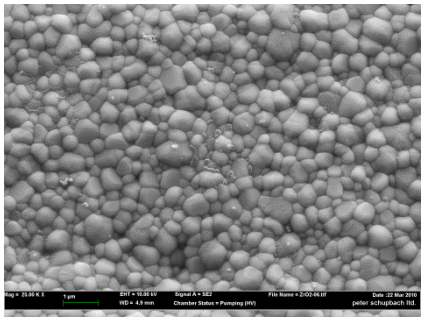

Fig. 4: SEM micrograph exhibiting the fine microstructure (scale bar = 1µm) of yttria-stabilized tetragonal zirconia polycrystalline (3Y-TZP).

Contemporary dental implant systems: Clinical, biological and mechanical aspects

U. Brodbeck

Zahnmedizin Zürich-Nord, Zurich, CH

ABSTRACT: Titanium has been established as the material of choice for endosseous implants resulting in a high degree of predictability. In recent decades, the clinical replacement of natural teeth by osseointegrated implants has represented one of the most significant advances in restorative dentistry. Since then, numerous studies of various clinical indications have documented high survival and success rates with respect to specific criteria [1]. Persisting osseointegration and restorations of good function have been key elements for the patient's subjective satisfaction, which is one criterion. One should never stop to have a critical and objective look even at successful concepts.

Many types of implants require trans-mucosal abutments to retain implant restorations. The implant-abutment-interface (IAI) comes more and more in the focus of the present research. Modern IAI can be divided into three groups: The internal conical, the flat-to-flat and the tube-in-tube IAI.

It is shown that this micro movement causes bacterial leakages, micro-pump effects in the sulcus and unintentional elastic deformations of the implant components. It is a clinical observation, that many IAI are not sealed and bacterial colonization is clearly visible in the implant and on the abutment screw after abutment removal. Unpublished data shows micro-particles as result of fretting in the IAI.

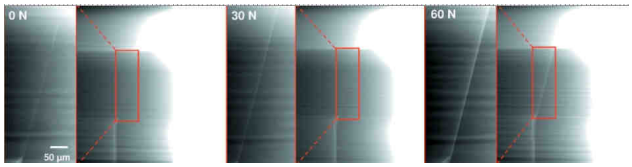

Fig. 1: Gap opening and micro movement of an abutment with short conical connection passive and under simulated load of 30 and 60 N [2].

The cortical bone-loss, loosening and fractures in IAI are discussed as consequences of micro-movements. The quality as well as the quantity of research is insufficient in relation to the immediate clinical effect of micro-movements on the IAI.

The data presented is indispensable in order to evaluate IAIs, to optimize them and to bring the results in correlation with the clinical results. The avoidance of abutment loosening, surface abrasion, fractures and the formation of bacterial colonies has not really been adequately considered in the construction of most IAIs.

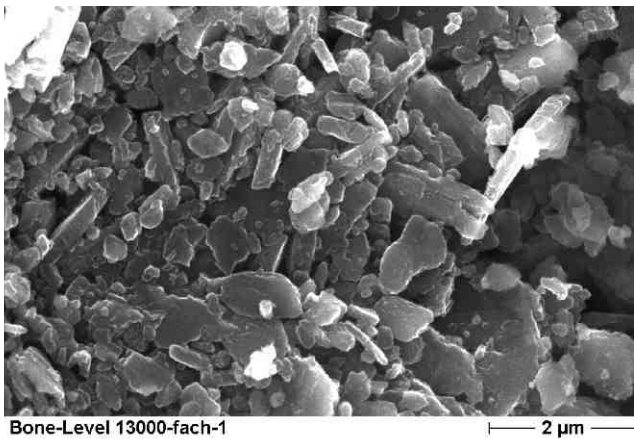

Fig. 2: Microparticles as a result of micro movement after 200'000 chewing cycles at the IAI [3].

Implant manufacturers should aim to reduce the micro-mobility by increasing the stability of the implant-abutment interface. Therefore, reducing the mobility of this connection by constructing physically tight connections with a high level of precision in the sub-micrometer range is considered to be an important precondition for microleakage prevention. With the current technology, micro-movements that are conditioned by chewing forces can only be avoided in IAIs if they have a conical self-locking effect.

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Specificities of implant-associated infections

P. Wahl

Hôpital Cantonal Fribourg, Fribourg, CH

ABSTRACT: The technological developments of the last decades allowed to offer implants in the treatment of an increasing array of medical conditions. In particular, modern orthopaedic surgery relies heavily on implants for the treatment of fractures or replacement of degenerated joints. Infection is identified more and more frequently as a cause of lack of fracture consolidation or loss of bony integration of prosthetic components, especially since the pathogenic role of low virulence bacteria has been recognized.

This presentation will give an overview of the key elements in the development of implant-associated infections and its treatment modalities. Particularly, formation of biofilm, importance of tissue integration, dysfunction of the immune system induced by the implant, limits of antibiotic treatment, and the clinical treatment guidelines will be discussed.

While the development of medical implants revolutionized the outcome of many diseases, their implantation also causes particular problems. Especially infections, which are difficult to treat, and can be debilitating for the patient or even induce a fatal outcome. As the particularities of implant-associated infections often make their diagnosis difficult, medical evidence regarding long-term outcomes and results of treatment of infections often is biased or has only limited comparability.

Poster Session

1 101 million cycle simulator wear characterization of diamond like carbon coated CoCrMo articulating implants
Dr. Dominik Jaeger, Empa, Laboratory for Nanoscale Materials Science

2 Smart NiTi constructs for 3D cell culture applications
Waldemar Hoffmann, Fachhochschule Nordwestschweiz

3 Effect of ultrasound on the electrochemical deposition of antibacterial copper particles at anodized titanium discs as model for titanium implants
PD Dr. Christiane Jung, KKS Ultraschall AG

4 Additive manufactured ceramic/ polymer scaffolds
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5 Macroporous titanium coatings for challenging substrates
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7 Simulierte Muskel- und Gelenkreaktionskräfte als Randbedingung für belastungsgerechtes Implantatdesign
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9 Biological safety testing on implant devices
Carolin Schmied, BSL BIOSERVICE Scientific Laboratories GmbH

10 Erfolgreiche Osseointegration von Titan-Implantaten: neueste Erkenntnisse über Biologische und biomechanische Voraussetzungen
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11 Bestimmung der technischen Sauberkeit von chirurgischen Implantaten und Instrumenten im Rasterelektronenmikroskop
Dr. Michael Hiltl, Carl Zeiss Microscopy GmbH

12 Data Analytics: progress without experimental design
Dr. Rodolphe Dewarrat, IMSD Sàrl

13 Advanced laser ablation for the surface microstructuring of cardiovascular implants
Dr. Jörn Lungershausen, University of Applied Sciences and Arts Northwestern Switzerland

101 million cycle simulator wear characterization of diamond like carbon coated CoCrMo articulating implants

K. Thorwarth[1], U. Müller[1], R. Figi[1], B. Weisse[1], G. Thorwarth[2], R. Hauert[1], D. Jaeger[1]
[1] *Empa, Swiss Federal Laboratories for Materials Science and Technology, Dübendorf, CH.*
[2] *DePuy Synthes, Dübendorf, CH*

INTRODUCTION: Diamond like carbon (DLC) coatings have been proven to be an excellent choice for wear reduction in many technical applications. However, for successful adaption to the MedTech field, layer performance, stability and adhesion in realistic physiological setups are very important and not consistently investigated [1]. Simulator testing as well as corrosion tests are of great importance to verify the long term stability of such a DLC coated articulating implant in the human body. Commonly one million cycles of simulator testing correspond to 1 year of articulation in the human body.

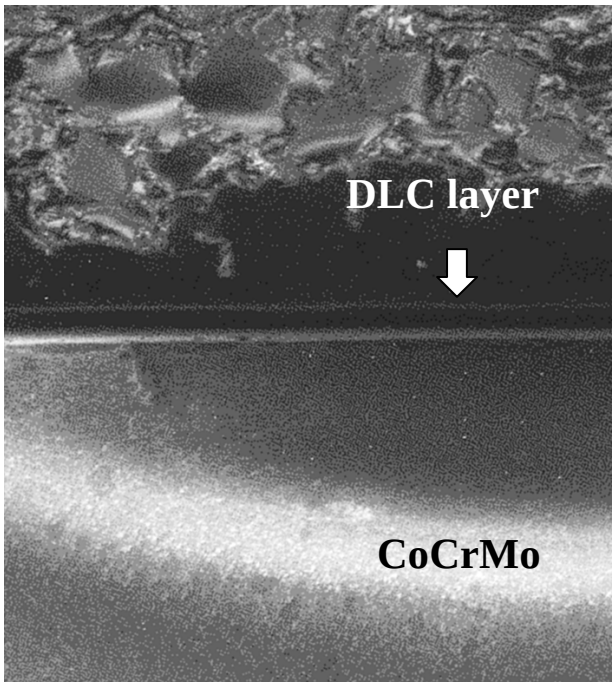

Fig. 1: Cross-section of a 4 μm thick DLC layer on a CoCrMo implant after 101 million cycles in a spinal disk simulator.

METHODS: Diamond like carbon coatings were deposited on CoCrMo biomedical implant alloy using a plasma-activated chemical vapor deposition (PACVD) process. As an adhesion promoting interlayer tantalum films were deposited using magnetron sputtering.

The implants were mounted in a spinal disk simulator where they undergone more than 101 million cycles. Within this time these implants were characterized by high wear resistance, low friction coefficients, high corrosion resistance and low defect growth. These results were obtained by means of optical microscopy, SEM/EDX, FIB cross section and profilometry. The coatings were further analysed using XRD and XPS.

RESULTS: It is shown that metal-on-metal (MoM) pairs perform well up to 5 million loading cycles, after which they start to generate wear volumes in excess of 20 times those of DLC-coated implants [2]. This is attributed to the slight roughening observed on unprotected metal surfaces as usually also observed in-vivo. The DLC on DLC inlay pairs show comparable low volume losses throughout the full testing cycle (up to 101 million cycles over a period of three years and two months).

DISCUSSION & CONCLUSIONS: To our knowledge this is the first time a simulator test of a DLC-coated articulating implant running for more than 100 million cycles (corresponding to over 100 years of articulation in-vivo) is presented.

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Smart NiTi constructs for 3D cell culture applications

W. Hoffmann[1,2], T. Bormann[1], F. Schlottig[3], M. Mertmann[4], I. Martin[2], D. Wendt[2], M. de Wild[1]

[1] Institute of Medicinal and Analytical Technology, University of Applied Sciences Northwestern Switzerland, Muttenz, CH. [2] Institute for Surgical Research and Hospital Management, University Hospital Basel, Basel, CH. [3] Thommen Medical AG, Waldenburg, CH. [4] Memry GmbH, Weil am Rhein, DE

INTRODUCTION: NiTi shape memory alloys have unique mechanical and physicochemical properties that are appealing for a wide variety of biomedical applications. Selective laser melting (SLM) is a versatile method to create porous scaffolds using computer aided design (CAD) [1]. With the ultimate goal of fabricating complex 3D NiTi implants for orthopaedic & dental applications, we validated the utilization of SLM-based NiTi constructs as scaffolds for Tissue Engineering applications. Targeting the beneficial properties, i.e. pseudoelasticity or the one- and two-way shape memory effect, NiTi scaffolds might be used as mechanically active implants stimulating the surrounding tissue and thereby assisting bone healing.

METHODS: We assessed the biocompatibility of NiTi scaffolds as well as the adhesion and proliferation of human bone marrow-derived mesenchymal stromal cells (hBMSC) and MG-63 osteosarcoma cells. The cells were cultured on rapid prototyped (RP) NiTi constructs both on two-dimensional disks and three-dimensional scaffolds. Cell adhesion on constructs was assessed both using SEM and confocal laser scanning microscopy (CLSM). Proliferation rates were assessed using the CyQUANT® Cell Proliferation Assay to determine cell numbers for several points in time.

RESULTS: Both cell types did not exhibit a cytotoxic effect cultured in extracts of NiTi constructs (data not shown). Following, MG-63 cells and hBMSC were seeded on 2D disks and 3D NiTi scaffolds revealing high colonization densities (Figure 1). Additionally, long-term cultures up to 21 days were performed in order to investigate hBMSC proliferation capacity cultured on NiTi constructs. hBMSC do proliferate on NiTi constructs with similar growth rates as on tissue culture plastic (TCP) (table 1) demonstrating that SLM-NiTi disks are permissive to cell proliferation. hBMSC indicate similar sprouting and cell adhesion behaviour as observed on TCP being the gold standard in vitro culture system. These findings indicate the high biocompatibility of NiTi constructs facilitating their further utilization as cell culture substrate.

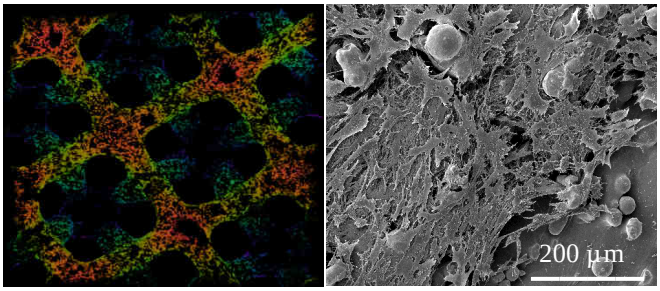

Fig. 1: Left: CLSM image of MG-63 cells cultured on a 3D NiTi scaffold (scale 3.4 mm x 3.4 mm). Right: SEM image of hBMSC cultured on 2D NiTi disk for 11 days.

Table 1. hBMSC growth rates [doublings/day].

NiTi 2D disk	TCP
0.170 ± 0.021	0.170 ± 0.033

DISCUSSION & CONCLUSIONS: The results demonstrate SLM-NiTi construct biocompatibility and underline their possible utilization as implant and/or scaffolding material exhibiting high colonization (adhesion and proliferation) capacities. Taking their unique shape memory properties into account, SLM-NiTi constructs could lead to personalized implants which allow for colonization and differentiation of host progenitors and at the same time might provide a unique platform to create active and thus *smart* implants.

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Effect of ultrasound on the electrochemical deposition of antibacterial copper particles on anodized titanium implant surfaces

L. Straumann[1], N. Balimann[1], F. Meier[1], M. de Wild[1], C. Jung[2],

[1] Fachhochschule Nordwestschweiz, School of Life Science, Muttenz, CH. [2] KKS Ultraschall AG, Medical Surface Center, Steinen, CH

INTRODUCTION: Bacterial infections taking place immediately or years after orthopaedic, trauma or dental surgeries cause serious problems for the patients. Implant surfaces exhibiting antibacterial properties preventing infections are therefore highly desired. We have recently established an electrochemical method to deposit the antimicrobial agent copper on the rough, fine-porous surface of spark anodized titanium samples. The antibacterial effect and the copper release rate were demonstrated [1]. Copper was deposited as clusters of different sizes, forms and surface distribution [1]. In this study we demonstrate how the surface distribution of the copper deposits can be affected by ultrasound applied during the electrochemical process.

METHODS: Mechanically pre-treated and ultrasonically cleaned discs of cp Ti (grade 4, ∅ 14 mm, 1.5 mm thick) were anodized according to the spark-assisted anodizing (SAA) method [2] to produce a rough, fine-porous surface. Copper was electrochemically deposited using proprietary electrolytes and process parameters. During the deposition process ultrasound was applied with a frequency either of 27 kHz or 80 kHz and a power of 350 W each. Deposition studies were performed for different copper concentrations in the electrolyte and different deposition times. The copper deposits were characterized by SEM/EDX.

RESULTS: In the absence of ultrasound, copper is deposited on the fine-porous oxide layer of the anodized samples as large clusters of nanometer-sized copper particles and with inhomogeneous surface distribution (Fig. 1 left). When ultrasound is applied, the copper deposits are much smaller (size of few nanometers) and homogeneously distributed over the sample surface (Fig. 1 middle). Compared to the experiments without ultrasound the amount of deposited copper is significantly increased for all deposition times when 27 kHz is applied (Fig. 2). However, for 80 kHz, less copper is deposited after longer deposition time (120 s) and the copper deposits are slightly larger than for 27 kHz (Fig. 1 right).

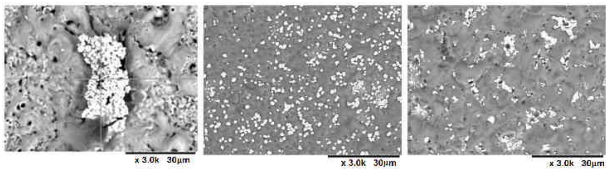

Fig. 1: SEM pictures of the surface of titanium discs (3000x magnification). Left: without ultrasound; middle: 27 kHz; right: 80 kHz. Copper appears as white spots.

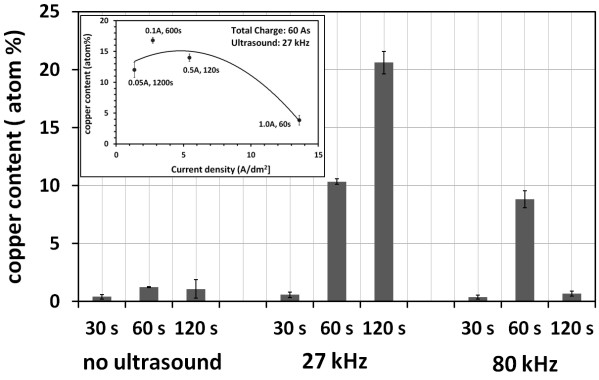

Fig. 2: Amount of copper deposited on the sample surface in the absence and presence of ultrasound and at three different deposition times.

DISCUSSION & CONCLUSIONS: Application of ultrasound during electro-chemical deposition of copper leads to a more homogeneous Cu allocation, to a frequency dependent deposit distribution and to an increased amount of deposited copper. It is suggested that the different size of the cavitation bubbles and acoustic streaming velocities for 27 kHz and 80 kHz may explain the different results [3].

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Additive manufactured ceramic/polymer scaffolds

S. Stevanovic[1], P. Chavanne[1], O. Braissant[2], U. Pieles[1] P. Gruner[3], R. Schumacher[1]

[1] FHNW - School of Life Sciences, Muttenz, CH. [2] LOB2 - Laboratory of Biomechanics & Biocalorimetry, University of Basel, CH. [3]Medicoat AG, Mägenwil, CH

INTRODUCTION: Tailor-made ceramic scaffolds in combination with the corresponding surface chemistry and biology is of great importance for successful implantation and guarantees a rapid osseointegration. This project investigates the fabrication of scaffolds with defined macro porosity by means of powder based 3D-printing. To reach mechanically stable structures, various post-processing methods like infiltration or thermal treatment have been applied.

METHODS: Two fabrication approaches were developed. On one hand cylindrical specimens (Ø 10 x 10 mm) were printed as a composite (hydroxyapatite/polymer). On the other hand printed hydroxyapatite (HA) specimens with open porosity were infiltrated with polymers after sintering. All structures were printed with acidic binder solution. Composites with HA as bulk material were blended either with 20 wt.-% or 30 wt.-% collagen, polycaprolactone (PCL) and chitosan. Specimens containing chitosan were post-hardened in acidic medium. Infiltration was performed with 4 wt.-% polyvinylalcohol (PVA), 3.6 wt.-% PCL and 10 wt.-% gelatine. The mechanical properties were determined by compressive strength (CS) measurements. Further analysis was performed by porosity measurement (Archimedes) and scanning electron microscope (SEM).

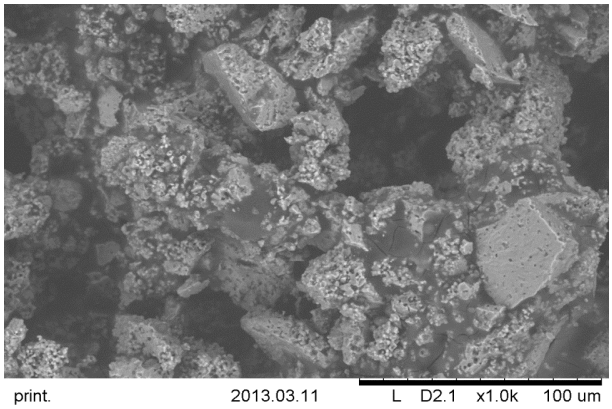

Fig. 1: SEM image of 3D-printed HA (bright, rough) / collagen (dark, smooth) composite.

RESULTS: Cylinders with chitosan showed the highest CS values among all other composites compared to printed and sintered HA cylinders.

Figure 1 illustrates the consistent distribution of a HA and polymer within the composite matrix. The porosity of all composite specimens decreased around 20 % compared to sintered HA samples.

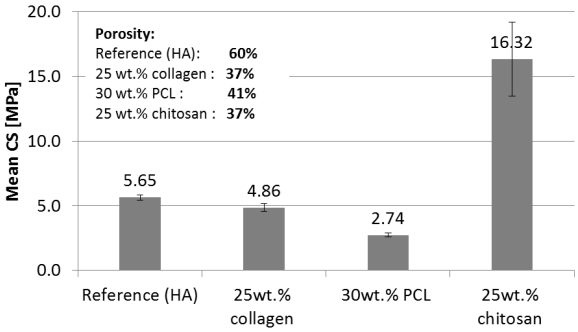

Fig. 2: Compressive strength and porosity of collagen, chitosan and PCL composite cylinders compared to a printed and sintered HA cylinder.

On the other hand, infiltration of the open porous specimens could increase the CS of an untreated specimen (CS 0.8 MPa, porosity: 90 %) up to 4.5x. The highest CS improvement of 3.7 MPa (porosity: 35 %) was achieved with gelatine infiltration. Compared to that PCL was found to be 0.9 MPa (porosity: 88 %) and PVA 1.0 MPa (porosity: 79 %).

DISCUSSION & CONCLUSIONS: In previous publications, CS of 3D-printed composites with other bio polymers are reported in a range of 0.5 - 5 MPa [1-2]. This emphasizes the potential of printed chitosan composites with their 16.3 MPa CS (Figure 2). In addition, the developed infiltration method led to a 4.5x higher compressive strength. However, the insolubility of chitosan, collagen and gelatine specimens needs to be further improved to ensure mechanical stability in body like environments.

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Macroporous titanium coating for challenging substrates

P. Robotti[1], G. Zappini[1], E. Preve[1], A. Drechsler[2], S. Stübinger[2,3], B. George[4]

[1] *Eurocoating spa, Trento, IT.* [2] *MSRU, Vetsuisse Faculty, University Zurich, CH.*
[3] *CABMM, University of Zurich, CH.* [4] *Surface Dynamics, Cincinnati, OH-USA*

INTRODUCTION: Macroporous metal structures obtained by thermal plasma spray (e.g. TiGrowth®) are becoming a reliable alternative strategy to reach a tough and time resistant bone fixation in metal joint replacement components [1]. Scope of this study is to highlight the possibility to extend the application of thermal sprayed titanium spongy surfaces to those non metal substrates that show limited osseointegrative potential [2].

MATERIALS & METHODS: By Modified Vacuum Plasma Spray (MVPS) a macroporous thick titanium coating (TiGrowth®) was applied either onto a Ti-6Al-4V or onto a polymeric substrate (PEEK Motis® Invibio, UK). MVPS is a lower temperature process than conventional VPS thus more respectful of the substrate properties [3].

The morphology of macroporous surfaces was characterized by Scanning Electron Microscopy (SEM). Porosity and thickness were measured through optical micrographic analysis. Mechanical tests were performed for evaluation of coating to substrate adhesion according to ASTM F 1147.

In n=6 sheep, 36 rods of PEEK Motis®, with and without TiGrowth® coating, were randomly implanted in the right and left wing of the pelvis. Animals were allocated to 2 and 12 weeks observation periods (each n=3). 12 samples of each surface were used for a pull out test. 6 samples were used for a histologic analysis.

RESULTS: Mechanical tests: Adhesion test results are summarized in Table 1.

Table 1. Adhesion Strength for TiGrowth® on Metal and TiGrowth® on PEEK substrate.

	Adhesion (MPa)	Std. Dev. (MPa)
TiGrowth® on Ti6Al4V, thickness @ 600 µm	47.9	5.6
TiGrowth® on PEEK, thickness @ 400 µm	43.8	2.4

Surface morphometric analysis: Micrographic sections showed titanium coatings with max thickness exceeding 900 µm on metals and 400 µm on PEEK. SEM analysis disclosed pore diameters distributed between 100 and 400 µm. The higher the thickness, the larger the pores obtained. Overall porosity was between 40 and 70 % with a continuity of interconnections.

In-vivo results: Pull out tests revealed a striking increase of the biomechanical implant-to-bone fixation from 2 to 12 weeks. (Figure 1).

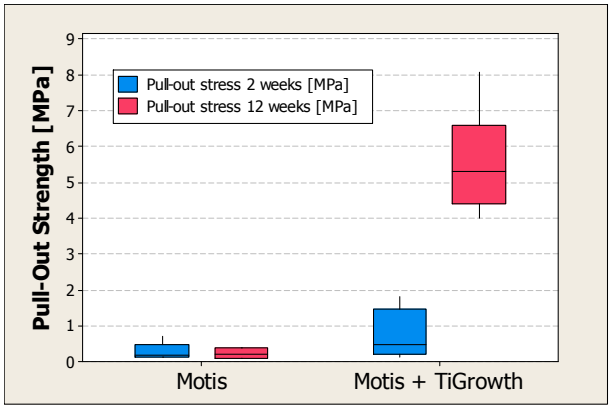

Fig. 1: Pull-out strength from sheep pelvis bone. Uncoated PEEK specimens vs TiGrowth® coated.

Preliminary histologic results confirmed an improved bone-to-implant contact for titanium coated PEEK vs uncoated PEEK.

CONCLUSIONS: Morphological analyses on TiGrowth® showed uncommon characteristics in terms of pores size, overall porosity and coating thickness for thermal sprayed coatings. Yet this had no major influence on coating adhesion to Ti6Al4V substrate, as required for orthopedic use. Adhesion was found adequate also for application on PEEK. In vivo results after 12 weeks clearly demonstrated significantly improved fixation values for titanium coated PEEK implants in contrast to uncoated PEEK specimens.

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Simulation of muscle and joint reaction forces as boundary conditions for implant design appropriate to the load

A. Nolte

CADFEM GmbH, Grafing b. Muenchen, DE

INTRODUCTION: The design of implants appropriate to load is difficult since in vivo load cases are not known in all details. Muscle and joint reaction forces are very difficult to measure. Application of simulation software to determine these is one answer to this question. Virtual testing of implants generates new knowledge about mechanical behaviour and the design can be improved based on that.

METHODS: A validated three dimensional musculoskeletal gait model [1] of the *AnyBody Modeling System* included in the *AnyBody Managed Model Repository Version 1.3.1* (AMMRV1.3.1) was used in this study. This model allows importing motion capture data as well as external forces measured by force plates in C3D format. The data was recorded at the Gaitlab of Orthopaedische Kinderklinik, Behandlungs-zentrum Aschau im Chiemgau. The female patient was 62 years old with normal weight and with a diagnosed cox arthrosis. For the musculoskeletal simulation the *AnyBody Modeling System* [2] version 5.0 including a polynomial muscle recruitment criterion of third order [3] has been used to calculate the muscle and joint reaction forces. In *AnyBody* the motion is divided in a discrete number of time steps defined by the user. For each step, muscles are recruited to gain mechanical equilibrium.

The results were applied to a finite element model in ANSYS 14 as boundary conditions. The model was meshed with tetrahedral elements. A rigid support fixed the femur at the condyles. Assuming an osseo-integrated implant allows using a bonded contact at bone-implant interface. A quasi-static analysis was performed for 10 time steps between heel strike and toe off.

RESULTS: Comparison of hip reaction forces of in vivo measurements [4] and simulation showed good correlation. The support reactions at the femur condyles determined with ANSYS correlated well with the knee reaction forces calculated by AnyBody. Maximum stress at the implant could be observed below the fatigue limit of approximately 600 MPa for medical titanium alloy Ti6Al4V.

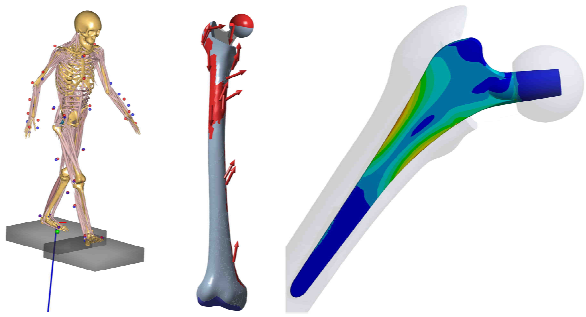

Fig. 1: From left to right: musculoskeletal gait model; finite element model with applied muscle and joint reaction forces; equivalent von Mises stress in the implant shaft.

DISCUSSION & CONCLUSIONS: Stress distribution in the implant is different if compared to simulated accreditation tests like ISO 7206 standard for hip implants and when only considering hip reaction forces. Contact conditions are unclear in vivo. Micro motion at the bone-implant interface could occur in reality. Much higher stress peaks are expected when higher load motions like running or stair climbing are investigated [4].

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Hemi-resurfacing implants of the shoulder: short term osseous integration

CM. Sprecher[1], V. Braunstein[1,2], D. Nehrbass[1], S. Milz[1,3], F. Gohlke[4], R. Hertel[5], M. Jäger[6], N. Südkamp[6], F. Schmidutz[1,7]

[1] AO Research Institute, Davos, CH. [2] Sportsclinic Munich, DE. [3] Department of Anatomy, University of Munich (LMU), DE. [4] Klinikum Bad Neustadt, DE [5] Lindenhofspital Bern, CH [6] Department of Orthopedic Surgery, University of Freiburg, DE [7] Department of Orthopedic Surgery, University of Munich (LMU), DE

INTRODUCTION: Hemi-resurfacing shoulder implants restore the joint function with less trauma and bone loss compared to total shoulder arthroplasty. Good clinical short- and mid-term results are reported in the current literature [1]. However, due to the radiopaque cup, only little is known about the bone remodeling processes under the implants.

The aim of this study was to evaluate two different shoulder resurfacing designs regarding their osseous integration at the implant interface and the bone stock under the implant.

METHODS: 10 uncemented hemi-resurfacing implants of the shoulder were retrieved from patients undergoing revision due to glenoidal erosion. 5 Epoca RH (Synthes, CH) and 5 Copeland (Biomet, USA) implants were analyzed.
The implants including the bone were embedded in polymethylmethacrylate and a section was taken through the centre of the implant with a diamond cutting saw. Sections were stained with Giemsa-Eosion and digitalized.

The relative bone density (BD [%]) under the resurfacing implant and the relative bone implant contact (BIC [%]) at the interface were analyzed using digital imaging software (KS400, Zeiss, D). The interface between implant and tissue was further evaluated by scanning electron microscopy (SEM) and the chemical composition of the materials was analyzed by energy dispersive x-ray analysis (EDX).

An unpaired t-test was used to compare the two implant designs and a $p<0.05$ determined significance.

RESULTS: Qualitative histological evaluation revealed an inhomogeneous bone distribution with a reduced bone stock under the implant shell. The quantitative evaluation of the BD confirmed the reduced bone stock (Fig.1, Tab.1). No significant difference was observed between the two implant designs ($p=0.43$).
Quantitative evaluation of the BIC showed a good ingrowth of the bone into both coatings (Fig. 1, Tab. 1). No significant difference was observed between the two implant designs ($p=0.88$). The interface analysis in the SEM confirmed the good bony ingrowths.

DISCUSSION & CONCLUSIONS: Regardless of the implant design, the cementless shoulder resurfacing implants showed a good bone implant contact at the interface. This suggests a sufficient initial stability with a good ingrowth of the bone into the implant surface and coatings. However, the bone stock under the implant shell appeared reduced in most implants. This is probably related to changes in the load transfer and an unloading of the bone, similar as seen in hip resurfacing arthroplasty [2].

Further studies are needed to confirm these observations and also to evaluate the load transfer of cementless shoulder resurfacing implants into the humeral head.

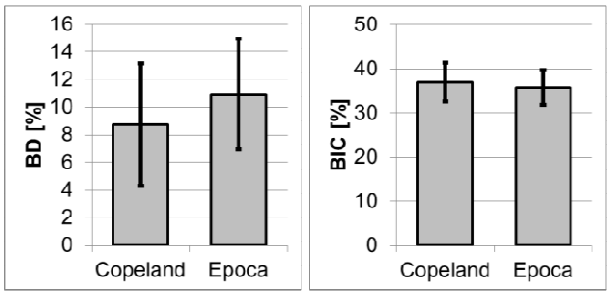

Fig. 1: Histomorphometric analysis of the Giemsa-Eosin sections from the Epoca RH and the Copeland: Bone density (left) and Bone Interface Contact (right).

Table 1: Quantitative evaluation results

	Bone density (BD [%])	Bone implant contact (BIC [%])
Epoca RH	10.9±4.0	35.8±7.2
Copeland	8.7±4.4	36.8±12.2

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BIOLOGICAL SAFETY TESTING ON IMPLANT DEVICES

C. Schmied, A. Friedrich

BSL BIOSERVICE Scientific Laboratories GmbH, Planegg, DE

INTRODUCTION: The biological evaluation of an implant device is an essential step in the progress 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, is the protection of humans from biological risks. This includes risks from the biological compatibility of the device and also micro-biological contamination.

For the assessment of the local effects after implantation, ISO 10993-6 has been established (currently under revision) including a new part for assessing the biological response of brain tissue to an implant.

At BSL BIOSERVICE studies for implants, such as orthopaedic implants, implants with contact to brain tissues, osteoinductive materials, drug delivery systems, tissue engineering products or cardiovascular implants are performed. Studies for functional implantation can be necessary to evaluate the functionality and biocompatibility under biological conditions in active mode. Possible endpoints could be the ingrowth behaviour of tissue into an implant, the mechanical resistance at the intended implantation location or the tissue reaction on electromagnetic radiation.

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.

A hygienic concept in the production of an implant prevents microbiological contamination. The hygienic concept includes a set of microbiological studies on the finished product as well as within the production process. Monitoring of the air, surfaces, and staff and of the water quality, knowledge of the microbial quality of the raw materials and additives are basical components. If a cleaning step is implemented in the manufacturing process, the efficacy must be proven e.g. by a combination of a test for cytotoxicity, of scanning electron microscopy (SEM) and x-ray photoelectron spectroscopy (XPS).

Fig. 1: Left: Orthopaedic implant. Right: Hygiene monitoring of surface by contact plates

The packaged product before sterilization is examined for the bioburden (= microbial load on the product). The bioburden is the basis for the success of the sterilization procedure, which must be validated. A study for endotoxins/pyrogens is necessary for devices with in-/direct contact to cardiovascular blood, cerebrospinal and lymphatic tissue and ophtalmological products.

Fig. 2: LAL-test for endotoxins

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 hygienic safety. These strategies need to be uniquely tailored considering the nature of the material as well as the intended clinical use of the device.

Bestimmung der Technischen Sauberkeit von chirurgischen Implantaten und Instrumenten im Rasterelektronenmikroskop

M. Hiltl

Carl Zeiss Microscopy GmbH, Oberkochen, DE

KURZFASSUNG: Das Rasterelektronenmikroskop (REM) wird bei der Überwachung der hohen Qualitätsanforderungen von medizinischen Komponenten, industriell hergestellten chirurgischen Instrumenten und Implantaten erfolgreich eingesetzt. Zunehmend steht die Überwachung der Technischen Sauberkeit dieser Produkte im Fokus. Üblicherweise werden die Oberflächen von Teilen in einer Wascheinrichtung mit einem flüssigem Medium gespült, die Flüssigkeit mit dem enthaltenen Restschmutz filtriert und gesammelt. Die Partikel bleiben auf einer Filtermembrane zurück und können mit einer Software im REM automatisiert analysiert werden. Das REM erlaubt die Bestimmung von morphologischen Informationen wie Größe und Form der Restschmutzpartikel mit großer Präzision. Erste Aussagen über Eigenschaften und Herkunft der Verunreinigung ist möglich. Die an das REM adaptierte und integrierte energiedispersive Mikrobereichsanalyse (EDX) ermöglicht eine qualitative und quantitative Bestimmung der chemischen Elementzusammensetzung partikulärer Materialien und die Einteilung in Materialklassen. Die etablierte Niedervakuumtechnologie erlaubt eine aufladungsfreie Untersuchung der zumeist nicht leitenden Filtermembrane und der darauf befindlichen Materialien. Es gilt festzustellen, welche Arten von Restschmutz vorhanden sind, aus welchem Material diese bestehen, ob die Partikel womöglich ein Problem im Einsatz verursachen können und was die mögliche Ursache bzw. die Quelle von störenden Partikeln ist. Um diese Fragen beantworten zu können müssen die Restschmutzpartikel direkt und jeder einzeln für sich analysiert werden.

Data Analytics: progress without experimental design

R. Dewarrat, A. Savoy

IMSD Gmbh, Montfaucon, CH

INTRODUCTION: Experimental design is an excellent tool to explore the properties of products and materials depending on various parameters. However, the number of distinct parameters or nonlinearities often turns most design plans to unrealistic schedules and need to be simplified and reduced, sometimes until a level where no more useful information can be expected.

However, daily production is, up to a certain extent, an experimental design: production temperatures and speeds have variations, suppliers change, etc. There is often a lot of information to extract from these small changes, as long as the data is collected and treated adequately: without interrupting the production cycle the so-called data analytics cycle [2] is running offline, applying statistical and data mining methods [1] to find out which parameters are critical, which combination of settings bring the best production quality, and finally to suggest which parameters are the most interesting to look at in a future design of experiment.

METHODS: There are quite some advantages of analysing in detail the production data prior to any expensive and time consuming design of experiment. One major advantage is that this analysis can take place without interrupting the production. The source of information is the data collected during the daily production processes and the analysis takes place offline and possibly includes external environmental data as humidity, temperature, working plans, etc.

The results of a data analytics cycle on daily production data are multiple. First it is easy then to rank the importance of all recorded parameters. This is important when considering increasing or reducing the amount of stored data as well as when needing to know which parameter has the highest influence on target Key Performance Indicators (KPIs) as costs, speed, quality or a combination of them.

Secondly the effects of these important parameters can be estimated and analysed either as a single effect or in combination with other parameters. Non-linear effects can be extracted as well using non-linear methods in the analysis as decision trees or neuronal networks [1].

Finally all kind of interactions and multidimensional effects can be discovered: it can well be, for example, that the quality of the production is, in average, the same on every production line but that there are differences when considering separately the quality depending on the various supplier as well.

From that point of the data analytics cycle many actions can be taken: it is possible to make a numerical model of the production based on the most important effects, it is possible to make recommendations about optimal or critical combinations [2].

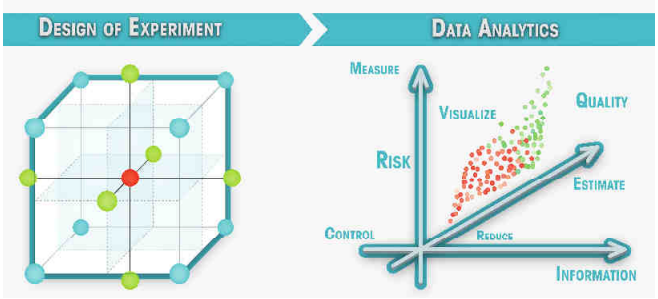

Fig. 1: Design of experiment and Data Analytics, two complementary approaches to explore parameter variations and optimize KPIs as costs, rate and quality.

DISCUSSION & CONCLUSIONS: Finally, when considering extending the production to settings that have not yet been used, the data analytics cycle will be an important source of information to define more precisely the design of experiment and to increase the chances of finding the optimal production point that is needed (Fig. 1).

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Advanced laser ablation for the surface microstructuring of cardiovascular implants

J. Lungershausen[1], A. Stumpp[1], A. Ferrari[2], D. Poulikakos[2], V. Kurtcuoglu[3]

[1] Institute of Product and Production Engineering, University of Applied Sciences and Arts Northwestern Switzerland. [2] Laboratory of Thermodynamics in Emerging Technologies, ETH Zurich, CH. [3] The Interface Group, Institute of Physiology, University of Zurich, CH.

INTRODUCTION: Cardiovascular diseases account for more than half of all deaths in the developed world. With our aging society, there is a growing demand for cardiovascular implants of all kinds, including heart valves, ventricular assist devices, stents, vascular grafts and pacemakers.

DEVELOPMENT NEEDS: One of the most pressing needs in implant design is the increase of device biocompatibility. This may be achieved by functionalization of the implant surface, for example by application of micro-scale surface textures. Today, the processing of micro-structured surfaces is mostly achieved via physicochemical technologies such as surface roughening, electrochemical polishing or etching, and micro-patterning via imprint lithography. While these methods are well suited for creating either surface topographies with random feature orientation or for application on flat substrates, they show serious limitations when used on three-dimensional surfaces.
In this study we aimed at developing a laser processing technology for the microstructuring of 3D implants and at defining an optimal surface design to improve healing of the endothelium after implant placement.

APPROACH AND RESULTS: In order to produce a high quality microstructured surface on a macroscopic 3D object, a novel laser structuring setup was established, which met the requirements regarding process stability (>24 hrs. of continuous laser structuring) and precision (one micron structure size or less). In contrast to a conventional laser-structuring process, which is usually performed using a 3D scanner (movement of the laser beam achieved by mirrors) in combination with an F-theta lens (for beam focussing), a four-axis control system to move the workpiece and a special aspherical lens was employed to concentrate the laser energy. This led to focussing diameters around one micrometre combined with an elongated region with almost constant beam intensity distribution along the optical axis. Thus, the ablation of material even in the sub-micrometre scale could be achieved (Figure 1).

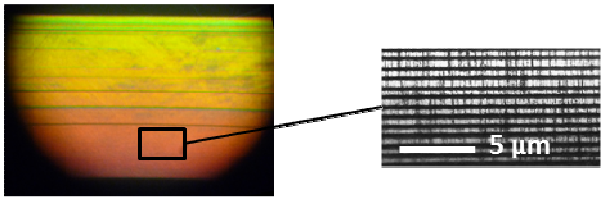

Fig. 1: Laser-ablated microgrooves in the sub-micrometre range on a curved surface acting as a diffraction grating with iridescent reflections.

To test the effect of micro-structures on endothelial wound healing, in vitro experiments were performed using a custom-made flow chamber that reproduces physiological flow conditions. It could be verified that substrates featuring a defined anisotropic topography with one micron parallel ridges (*Fig. 2*) improved the endothelial wound healing time by approx. 50 % compared to smooth, unstructured surfaces [1].

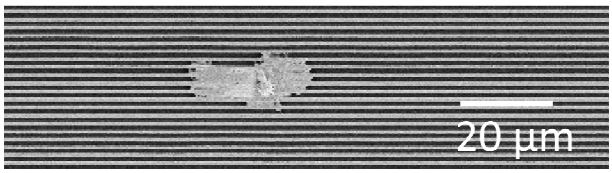

Fig. 2: Human Umbilical Vein Endothelial Cells (HUVEC) interacting with microstructured gratings: individual cell adhesion and spreading.

CONCLUSIONS: With the advanced laser ablation technique developed, it was possible to microstructure 3D surfaces in the micrometre and sub-micrometre range. Furthermore, it was shown that the laser processed prototypes meet the geometric requirements for improved endothelialisation. Currently, animal tests are on the way to validate the obtained results in vivo.

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Authors, Chairpersons, Organizer

Peter Biedermann
Medical Cluster
Wankdorffeldstrasse 102
3014 Bern
Switzerland
peter.biedermann@medical-cluster.ch

Dr. Gurdial Blugan
Empa
Überlandstrasse 129
8600 Dübendorf
Switzerland
gurdial.blugan@empa.ch

Dr. Kirsten Borchers
Fraunhofer IGB
Nobelstrasse 12
70569 Stuttgart
Germany
kirsten.borchers@igb.fraunhofer.de

Dr. med. dent. Urs Brodbeck
Zahnmedizin Zürich-Nord
Herzogenmühlestrasse 14
8051 Zürich
Switzerland
urs.brodbeck@zzn.ch

Sebastian De Boodt
Materialise
Technologielaan 15
3001 Leuven
Belgium
sebastian.deboodt@materialise.be

Prof. Dr. Michael de Wild
Fachhochschule Nordwestschweiz
Gründenstrasse 40
4132 Muttenz
Switzerland
michael.dewild@fhnw.ch

Dr. Thomas Degen
Sequana Medical AG
Technoparkstrasse 1
8005 Zürich
Switzerland
thomas.degen@sequanamedical.com

Dr. Rodolphe Dewarrat
IMSD Sàrl
Place du vingt-trois Juin 31
2362 Montfaucon
Switzerland
rodolphe.dewarrat@imsd.ch

Univ.-Prof. Dr.-Ing. Georg N. Duda
Charité - Universitätsmedizin Berlin
Augustenburger Platz 1
13353 Berlin
Germany
georg.duda@charite.de

Dr. Lukas Eschbach
RMS Foundation
Bischmattstrasse 12
2544 Bettlach
Switzerland
lukas.eschbach@rms-foundation.ch

Andreas Flechtmann
Werth Messtechnik GmbH
Siemensstrasse 19
35394 Giessen
Germany
andreas.flechtmann@werth.de

Adrian Gammeter
ISS AG
Allmendstrasse 11
2562 Port
Switzerland
adrian.gammeter@iss-ag.ch

Matthias Graf
Uniklinik Balgrist
Forchstrasse 340
8008 Zürich
Switzerland
matthias.graf@balgrist.ch

Oscar Hedin
Arcam AB
Krokslätts Fabriker 27A
43137 Mölndal
Sweden
oascar.hedin@arcam.com

Dr. sc. Roman Heuberger
RMS Foundation
Bischmattstrasse 12
2544 Bettlach
Switzerland
lukas.eschbach@rms-foundation.ch

Dr. Michael Hiltl
Carl Zeiss Microscopy GmbH
Carl Zeiss Strasse 22
73447 Oberkochen
Germany
michael.hiltl@zeiss.com

Waldemar Hoffmann
Fachhochschule Nordwestschweiz
Gründenstrasse 40
4132 Muttenz
Switzerland
waldemar.hoffmann@fhnw.ch

Dr. Dominik Jaeger
Empa
Überlandstrasse 129
8600 Zürich
Switzerland
dominik.jaeger@empa.ch

Dr. Simon Jegou
Nobel Biocare Services AG
Balz Zimmermann-Strasse 7
8302 Kloten
Switzerland
simon.jegou@nobelbiocare.com

PD Dr. habil. Christiane Jung
KKS Ultraschall AG
Frauholzring 29
6422 Steinen
Switzerland
cjung@kks-ultraschall.ch

Dr. Bernhard Keller
MOTOREX AG
Bern-Zürich-Strasse 31
4901 Langenthal
Switzerland
keller@preentec.ch

Dr. Alexander Knitsch
TRUMPF Laser- und Systemtechnik GmbH
Johann-Maus-Strasse 2
71254 Ditzingen
Germany
alexander.knitsch@de.trumpf.com

Dr. Bruno Knobel
Naviswiss AG
Ziegeleistrasse 52
4242 Laufen
Switzerland
knobel@naviswiss.eu

Dr. Christian Kottler
CSEM SA
Badenerstrasse 569
8048 Zürich
Switzerland
christian.kottler@csem.ch

Dr. Jörn Lungershausen
Fachhochschule Nordwestschweiz
Klosterzelgstrasse 2
5210 Windisch
Switzerland
joern.lungershausen@fhnw.ch

PD Dr. Pierre Mainil-Varlet
Aginko
Route de l'ancienne Papeterie
1723 Marly
Switzerland
pm@aginko.com

Lukas Märklin
Institut Straumann AG
Peter-Merian-Weg 12
4052 Basel
Switzerland
lukas.maerklin@straumann.com

Dr. Sandro Matter
Institut Straumann AG
Peter-Merian-Weg 12
4052 Basel
Switzerland
sandro.matter@straumann.com

Frédéric Mauron
VALTRONIC
Route de Bonport 2
1343 Les Charbonnières
Switzerland
fmauron@valtronic.com

Michelle Meyer
Medical Cluster
Wankdorffeldstrasse 102
3014 Bern
Switzerland
michelle.meyer@medical-cluster.ch

Alexander Nolte
CADFEM GmbH
Marktplatz 2
85567 Grafing
Germany
anolte@cadfem.de

Armando Pereira
Agie Charmilles
Rue du Pré-de-la-Fontaine 8
1217 Meyrin
Switzerland
armando.pereira@ch.gfac.com

Miroslaw Pienkowski
Trinon Titanium GmbH
Augartenstrasse 1
76137 Karlsruhe
Germany
mp@trinon.com

Pierfrancesco Robotti
EUROCOATING
Via al dos de la Roda, 60
38057 Pergine Valsugana
Italy
francescorobotti@eurocoating.it

Dr. Antonio Santana
IHI Ionbond AG
Industriestrasse 211
4600 Olten
Switzerland
antonio.santana@ionbond.com

Samuel Schenk
Mathys Ltd Bettlach
Robert Mathys Strasse 5
2544 Bettlach
Switzerland
samuel.schenk@mathysmedical.com

Ralf Schindel
inspire irpd AG
Lerchenfeldstrasse 5
9014 St. Gallen
Switzerland
schindel@ethz.inspire.ch

Dr. Martin Schmidt
Jossi Orthopedics AG
Alte Landstrasse 54
8546 Islikon
Switzerland
martin.schmidt@jossi-orthopedics.ch

Carolin Schmied
BSL BIOSERVICE Scientific Laboratories GmbH
Behringstrasse 6/8
82152 Planegg
Germany
cschmied@bioservice.com

Dr. Hans Schmotzer
SigmaRC GmbH
Alte Steinhauserstrasse 1
6330 Cham
Switzerland
hans.schmotzer@sigma-rc.com

Dr. Urban Schnell
Helbling Technik Bern AG
Stationsstrasse 12
3097 Liebefeld
Switzerland
urban.schnell@helbling.ch

Dr. Ing. Jörn Seebeck
Zimmer GmbH
Sulzer-Allee 8
8404 Winterthur
Switzerland
joern.seebeck@zimmer.com

Christoph Sprecher
AO Research Institute
Clavadelerstrasse 8
7270 Davos
Switzerland
christoph.sprecher@aofoundation.org

Sabrina Stevanovic
Fachhochschule Nordwestschweiz
Gründenstrasse 40
4132 Muttenz
Switzerland
sabrina.stevanovic@fhnw.ch

Jan Stifter
Medivation AG
Dorfstrasse 69
5210 Windisch
Switzerland
jan.stifter@medivation.ch

Daniel Thommen
Microdul AG
Grubenstrasse 9
8045 Zürich
Switzerland
daniel.thommen@microdul.com

Dr. Peter Wahl
Hôpital Cantonal Fribourg
1708 Fribourg
Switzerland
peter.wahl@h-fr.ch

Ruben Wauthle
LayerWise NV
Kapeldreef 60
3001 Heverlee
Belgium
ruben.wauthle@layerwise.com

Andreas Weishaupt
Carag AG
Bahnhofstrasse 9
6340 Baar
Switzerland
andreas.weishaupt@carag.com

Dr. Margit Widmann
SQMT
Gasse 20
4524 Günsberg
Switzerland
widmannm@hotmail.com

Dr. Martin Zimmermann
Metoxit AG
Emdwiesenstrasse 6
8240 Thayngen
Switzerland
martin.zimmermann@metoxit.com

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