Achieving macro- and micro-roughness on Ti alloy by etching without prior sandblasting: a surface characterization

S Szmukler-Moncler, C Blus, G Orrù

Oral Biotechnology Laboratory, Surgical Sciences Dpt, University of Cagliari, Italy

INTRODUCTION: Etching is currently the most popular method used to texture the surface of dental implants. Sandblasting prior to etching (SLA) is the only method to achieve a macro- and micro-surface texture with a S_a in the 1-2 μm range, a 'moderately rough' surface considered to be an optimized surface. However, SLA surfaces harbor remnant particles from the sandblasting process [l]. Some manufacturers consider the residual alumina particles as a foreign material worth getting rid of. Subsequently, they forgo an optimized moderately rough surface and stick to a 'minimally rough' micro-roughened surface displaying a Sa < 1 μm [l].

It has been recently claimed [2] that acid etching is typically not an appropriate treatment for α-β alloys because its biphasic nature leads to an enrichment of the Vanadium-rich β-phase on the surface.

The aim of the present paper is to show that it is feasible to achieve an optimized 'moderately rough' macro- and micro-textured surface on titanium alloy (Ti6Al4V) through etching only, without any prior sandblasting and to characterize the resulting surface.

METHODS: Implants made of Ti6Al4V were etched according to a proprietary recipe (Bioner, Sant Just Desvern, SP). The surface was characterized by optical non-contact profilometry SEM, XRD, AES profiling and H concentration measurement.

RESULTS: A macro- and micro-textured surface was obtained with a homogeneous texture of macro-pores in the 15-20 μm range (fig. 1), a S_a of 1.3 μm and a S_z of 11.2 μm. AES profile analysis showed no surface enrichment in either Vanadium or Aluminium. H concentration measured on 3 implants was found to be 79 ppm; no Titanium hydride was detected by XRD.

DISCUSSION & CONCLUSIONS: It is possible to achieve a macro- and micro-textured surface similar to the SLA surface without the need of any prior sandblasting. The treatment was reproducible even when applied to several other commercially available implants made of Titanium alloy. Contrary to what has been suggested, etching is suitable for the biphasic Ti6Al4V alloy. The reason why no hydride layer was identified at the implant surface is due to the presence of the body-centred cubic β phase that accommodates much more H than the close-packed hexagonal α phase does.

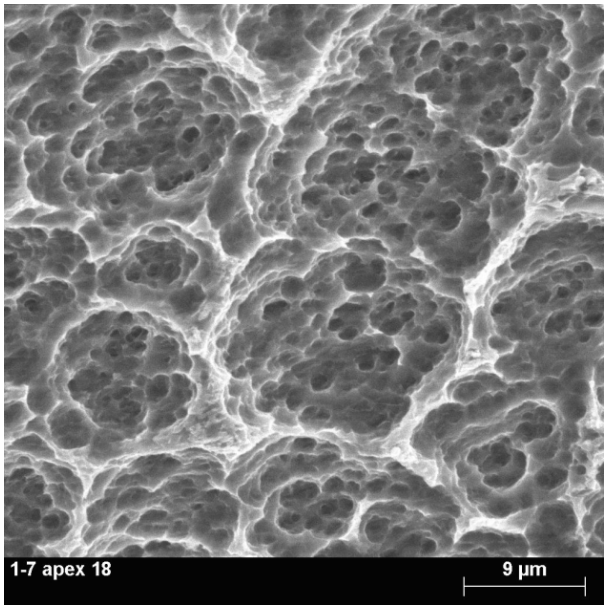

Fig. 1: SEM macrograph showing the macro- and micro-textured surface of the titanium alloy achieved with the proprietary etching recipe (mag x 2700).

ACKNOWLEDGEMENTS: BIONER SA is acknowledged for allowing publication of this research work.

Antibacterial coatings for medical applications, prepared by atmospheric pressure plasmas

S Spange, S Schmidt, A Pfuch, S Schimanski

INNOVENT e.V. Technologieentwicklung Jena, DE

INTRODUCTION: The presentation will give an overview of the preparation of layers for medical applications. The first part is concerned with an antibacterial layer system for additional modification of implants and wound dressings and their bactericidal and cytotoxic activity. The layer system was applied by using a novel atmospheric pressure plasma chemical vapour deposition (APCVD) technique on a variety of textile substrates, which are suitable as wound dressing materials. In the case of wound dressings an in vitro 3D skin model was used to investigate the cytotoxicity and skin tolerance. The second part focuses on plasma-chemical-oxidation (PCO®). With this technique it is possible to create customized oxide layers on titanium, magnesium or aluminium. For medical applications titanium-based alloys are primary used. A short look at two different coatings achieved with PCO® will be given: on the one hand a bioinert coating and secondly a bioactive coating. In-vivo results on these coatings on implanted intramedullary nails will be presented.

METHODS: With the APCVD the coating of different materials such as polymers, metals, glass or ceramics are possible in a wide range. The modifications with the coatings are from better corrosion resistance up to antibacterial properties, depending on the precursor used for the coating process. In most cases a silicon dioxide layer system with additional functionalization, with imbedded nanoparticles, is used for medical applications.

The PCO® produces ceramic-like coatings on anodically contacted substrate materials of aluminium, titanium and magnesium alloys at high bath voltages in aqueous electrolyte systems. The modification of the surface depends on the bath parameters and the electrolytes used during the process.

RESULTS: In Figure 1 two different coatings of textile material with zinc oxide and silver containing silicon dioxide layer for antibacterial properties are presented. Figure 2 shows two different PCO® coatings used in an animal model for better (bioactive) and no (bioinert) bone contact with a titanium implant.

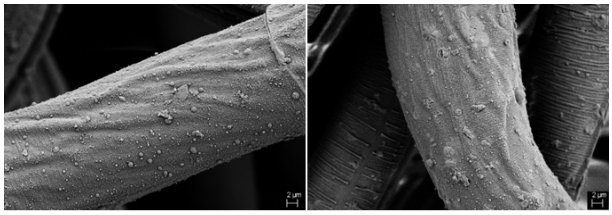

Fig. 1: SEM images of two APCVD modified PA6 textiles. One the left side a coating containing silver nanoparticles is presented. The right side shows an identical coating with zinc oxide nanoparticles, both for antibacterial use [1].

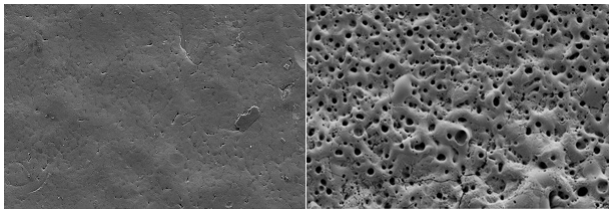

Fig. 2: SEM images of two PCO modified titanium alloys. The left side presents a bioinert coating and the right side a bioactive coating with tricalcium phosphate [2].

DISCUSSION & CONCLUSIONS: The methods of PCO® and APCVD are both suitable for medical applications and can be a good add-on for implant materials or other medical devices.

Spectracoat®: A new surface treatment technology to colour medical instruments, devices and implants

T-L Nguyen[1], J-C Puippe[1], S Estoppey[2]

[1] *Steiger Galvanotechnique SA, Innosurf department, Châtel-St-Denis, CH.*
[2] *Estoppey-Reber SA, Aegerten, CH*

INTRODUCTION: Steiger Galvanotechnique has developed a new product called « Spectracoat® » by combining Physical Vapor Deposition (PVD) and Electrochemical Treatments of a valve metal.

The material exhibits different crystallographic phases with their respective mechanical and optical properties. Independently from their phases, both display a chemical and biological inertness that makes the material biocompatible and corrosion resistant. Steiger Galvanotechnique demonstrates that the two phases can be achieved using different process types and parameters. A further oxide layer is formed in controlled conditions resulting in interferential colours.

Spectracoat® finds applications as a functional and decorative coating for the medical industry like identification and contact with human body.

METHODS: All depositions have been performed at the Innosurf department of Steiger Galvanotechnique using stainless steel or silicon wafer substrates as samples for characterization. The crystallographic structures of the coatings were determined by X-Ray diffraction (XRD) at the Swiss Federal Institute of Technology of Lausanne (EPFL, IPHYS). Optical micrographs, ellipsometry and nano-hardness have been measured at the University of Applied Sciences Western Switzerland (HES-SO HE Arc, IMA).

RESULTS: The collected XRD data of the as-deposited coatings are presented in Fig. 1. Characteristic peaks of the body-centered cubic phase α (110) and (220) appears respectively in the region of 38[°2θ] and 82[°2θ] while the hexagonal phase β (002) and (004) at 32[°2θ] and 69[°2θ].
The process type 1, Fig. 1a, that were performed by arc evaporation exhibits a predominantly α-phase. Under the influence of the process parameters during the direct magnetron sputtering, Fig. 1b, 1c, the growth of the layer yields preferentially to one form or another and in the case of 1d to a mix phase. As shown in Table 1, the β-phase is known to be harder but less ductile. Ellipsometric analysis demonstrates that oxide layers in the 60 nm range provide blue colour and 230 nm green colour.

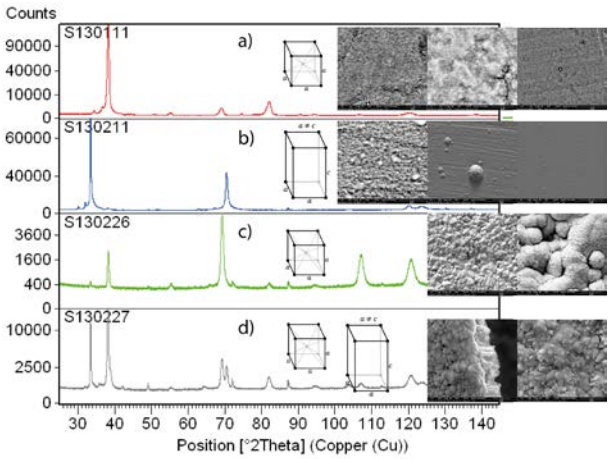

Fig. 1: XRD measurements (45 kV, 40 mA) a) α-bcc, process type 1 b) β-hexagonal, process type 2 c) α-bcc, process type 2 d) mix phases, bcc and hexagonal process type 2.

Table 1. Nano-hardness measurements.

	Hardness [HV]
α-bcc on stainless steel	500
α-bcc on silicon	450
β-hexagonal on stainless steel	1200
β-hexagonal on silicon	800

DISCUSSION & CONCLUSIONS: The study of the coating at Steiger Galvanotechnique has followed different steps: selection of the material depending on its hardness and density, characterization of the deposited metal and coloured oxide layer to finally end up with applicative tests in order to define the performance and limitations of the best crystallographic form to become Spectracoat®. To prove the potential of the product for medical purposes, additional cytotoxicologic study has been performed.

ACKNOWLEDGEMENTS: Kurt Shenk for the XRD, Catherine Csefalvay for the SEM and nano-hardness measurements and to all partners, customers and suppliers.

Novel titanium coatings on polymeric implants

S Ruch, A Salito

Orchid Orthopedics Switzerland GmbH, Dättwil, CH

INTRODUCTION: Polymeric implants are widely used in the medical device market. Polyether ether ketone (PEEK) is well accepted, especially in the field of spinal fusion implants [1]. Another important material is ultra-high molecular weight polyethylene (UHMW-PE) [2]. It is used for bearing material in knee, hip and shoulder arthroplasty. Major advantages of polymeric implants are their transparency to X-rays, elimination of artefacts in CT images and the bone preserving low stiffness. On the other hand, direct bone anchorage is not possible. One way how to overcome this drawback is by applying a porous titanium (Ti) coating onto polymeric substrate materials.

METHODS: Porous Ti coatings are applied onto PEEK and UHMW-PE by a combination of state of the art coating technologies. The coatings are characterized by their morphological properties. The mechanical stability of the substrate/coating systems was studied by intensive testing. For PEEK the conventional tests developed for metal coatings on metal can be applied (ASTM F1044, ASTM F1147). The nature of UHMW-PE does not allow to completely adhere to these standards. A wide range of tests (4-point bending tests, comparative tensile and shear studies and hip simulator testing) were performed instead.

For polymeric material the substrate micro-structure highly influences the material properties. The substrates were extensively examined to prove that the coating process does not detrimentally affect the material, especially for the temperature sensitive polyethylene. Differential scanning calorimetry (DSC) and infrared (IR) analysis were performed in this regard.

RESULTS: The morphological properties of both coatings correspond to conventional plasma sprayed Ti coatings applied on metal implants. Microscopic images are shown in Fig. 1. Mechanical testing reveal that the Ti coating on PEEK fulfils all standards developed for metal coatings on metal substrates. For the Ti coating on UHMW-PE no coating delamination up to a comparably high strain (6%) was observed and in dynamic testing no cracking of the coating at moderate maximum strain (0.75%) over 10^6 cycles was found. Tensile and shear testing showed clearly enhanced results for coated samples when compared with cemented specimens. In the hip simulator testing the coating demonstrated good primary stability, no spalling after removal (powerful knock-out) and low particle loss.

DSC and IR analysis showed equal results for melting point, crystallinity and oxidation rates for coated as well as reference polyethylene material.

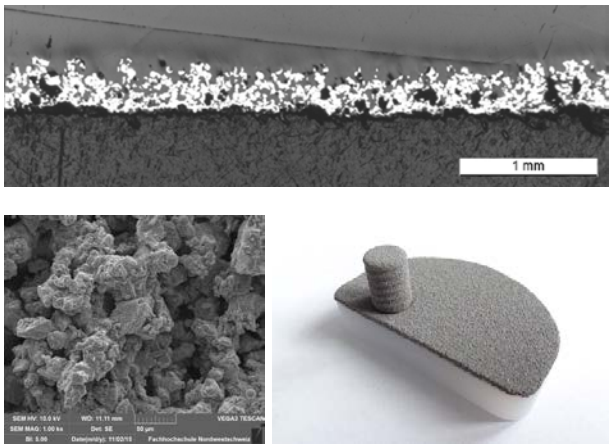

Fig. 1: Light microscope picture of Ti coating on UHMW-PE, SEM image of Ti coating on PEEK (1000x) and Ti coated UHMW-PE sample.

DISCUSSION & CONCLUSIONS: The PEEK coating has approval for FDA and is already applied on many customer implants.

Various testing on UHMW-PE demonstrate that the coating adhesion is more than adequate for the functionality. Comparative studies showed that coated systems are superior when compared to cemented systems currently applied. First customers started clinical studies and one year results are promising.

ACKNOWLEDGEMENTS: The authors like to thank L. Corté et al. from Mines-ParisTech as well as D. Baumgartner et al. from School of Engineering zhaw for the work they performed during cooperation.

Electron Beam for polymer material modification - let's get functional!

M Bielmann, E Callini, IR Bland

COMET Group AG, ebeam Technologies, Flamatt, CH

INTRODUCTION: Smart and functional surfaces are key to future medical implant technology. While we are normally driven by bulk mechanical properties in our selection of materials or compatibility with the physiological environment, smart surfaces or hybrid materials are tuned to ensure one without sacrificing the other.

TECHNOLOGY: Electron Beam (EB) technology is used in industrial processing for many decades – but remains obscure to most but the initiated. While the medical industry knows EB very well for toll sterilization of their products, the potentials in material modifications are generally not widely recognized. But EB has many interesting use-cases in materials modification of polymers relevant to the medical implant industry.

For example: Production of hydrogels and interface layers [1], thermo-responsive surfaces [2], shape memory polymers [3], Vitamin E grafting [4], hydrophilic grafts on hydrophobic polymers.

The market introduction of hermetically sealed EB engines to the market in 2012 dramatically opens up new usage patterns. The compactness of potential systems eliminates a former barrier for the technology: size. EB technology no longer is limited to high volume surface centres – EB can now be deployed inline in manufacturing processes onsite or even at small scale.

Figure 1 shows one specific variation of the technology as deployed for different application systems.

Fig. 1: Hermetically sealed EB engine consisting of Power supply and EB lamp.

DISCUSSION & CONCLUSIONS: While EB technology has been applied in industrial processes and service centers for decades, the technology has always been hampered by its size and cost. Sealed EB technology has the potential to change the fundamental paradigms – it allows the technology to be deployed in self-shielded, compact designs that potentially can be deployed in specialized companies or even hospitals.

Due to the size and cost benefits, many applications while successful on an academic scale have not been implemented can now be revisited for commercial viability. EB technology can sterilize surfaces in an instant at room temperature, modify substrates to give new functionality even at low volume and add value in many domains in medical technology.

EB technology is much more than a technique for sterilization – its main use case in industry is the modification of polymeric materials of commodity and large volume products. So far, it has presented a high entry barrier for adoption until today – while a new format of the technology might not seem a big leap forward, it is the ideal time to rethink the past and frame it in the present.

Multi-layer circuits with LCP and noble metals: Technology and characterization

CM Bee[1], A Kaiser[1], F Dupuis[2], R von Metzen[3], K Rueß[1], P Matej[1], C Herbort[1], B Holl[1], KH Fritz[2], G Bauböck[1]

[1] Cicor Advanced Microelectronics & Substrates (AMS), Ulm, DE. [2] Cicor Advanced Microelectronics & Substrates (AMS), Boudry, CH. [3] NMI Naturwissenschaftliches und Medizinisches Institut an der Universität Tübingen, Reutlingen, DE

INTRODUCTION: Electronic devices, especially for medical applications, often have high demands in regards to their overall size and flexibility. When the device is to be implanted into the human body, additional challenges of biocompatibility and biostability arise. These drastically limit the materials which can be used and exclude in many cases specific metals like, e.g., copper. This requirement commonly cannot be fulfilled with conventional circuits.

TECHNOLOGY: The presented technology reduces the involved materials to a very limited number. Thin Film technology offers the use of noble metals as conductive material with achievable feature sizes smaller than 10 µm (line/space). LCP (liquid crystalline polymer), a highly biocompatible polymer with low water uptake is used as flexible base and insulating material. Additionally, LCP can be laminated without the need of adhesives, enabling multi-layer circuits completely made out of biocompatible materials (see Figure 1).

Our contribution will describe the general aspects of this technology and discuss the process flow for the manufacturing of thin film based LCP multi-layer circuits.

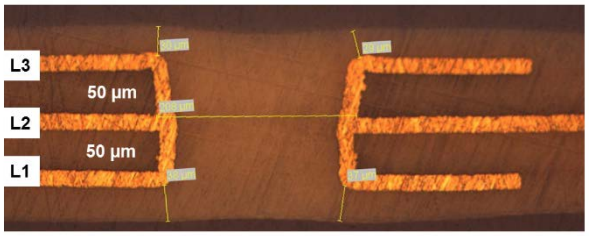

Fig. 1: Cross section of LCP multi-layer circuit.

CHARACTERISTICS: Samples were characterized regarding their stability in fluids (Figure 2). Therefore, test circuits were exposed to buffered saline solution (PBS) to simulated body conditions and harsh environments. In regular intervals, the complex impedance of the structure from 100 Hz to 200 kHz was measured to determine if any fluid has penetrated the LCP material.

Results show no changes in performance after >50 days, indicating a tight bond between the laminated layers. Nevertheless, this can only be seen as a first indication. Long-term testing needs to be undertaken, to confirm these promising first results.

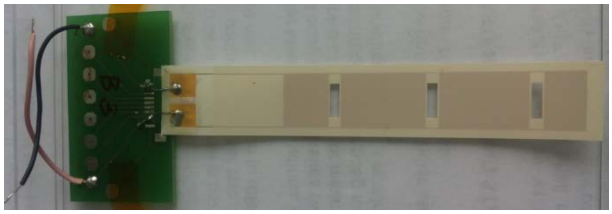

Fig. 2: LCP sample for stability characterization.

CONCLUSIONS: The presented technology for Thin Film flexible circuits enables the manufacturing of multi-layer systems, which are completely made out of highly biocompatible materials. Corresponding characterization results from stability examinations indicate a good performance in harsh environments, e.g. the human body.

This technology promises an excellent platform for the realization of medical devices, implants and new applications in the life science field.

EMG measuring and stimulation implant

M Voelker, A Nikas, A Holzberger, J Hauer

Fraunhofer Institute for Integrated Circuits IIS, Erlangen, DE

INTRODUCTION: The presented implant controls hand prostheses by EMG monitoring[1] and provides user feedback. The feedback signal is acquired by pressure sensors and applied to nerve stimulation. The development of a new generation of intuitively mind-controlled prostheses is an ongoing field of research. This approach improves the control interface towards the behavior of a real part of the body by two major strategies: i) Extracting a higher functional density by increasing the number as well as the selectivity of the recording electrodes. ii) Integrating a sensory feedback as a sensation to the patient providing a natural perception when touching or grasping objects with the artificial hand.

METHODS: The design and development of an implantable system has to include many different aspects. The limited space and low-power consumption requirements force to co-engineer the package, the printed circuit board (PCB), the interconnections, power supply and the application specific integrated circuits (ASIC).

The measurement and stimulation functions are integrated into two separate ASICs, which increase the flexibility in design, evaluation and re-use. The block diagram of the 8 channel EMG measurement ASIC is depicted in Fig. 1. The programmable gain between 50 V/V and 5000 V/V in combination with the high impedance inputs opens a wide range of medical sensing applications. The stimulation ASIC provides 4 independent, differential, high-voltage stimulation channels, which are able to supply up to 500 µA per channel. The stimulation ASIC integrates also supply voltage monitoring functions to enable closed-loop regulation of the inductive power supply.

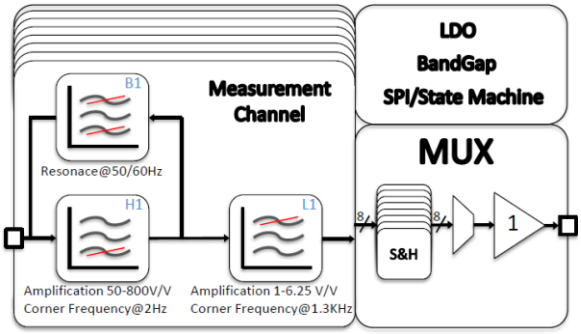

Fig. 1: EMG measurement IC (block diagram).

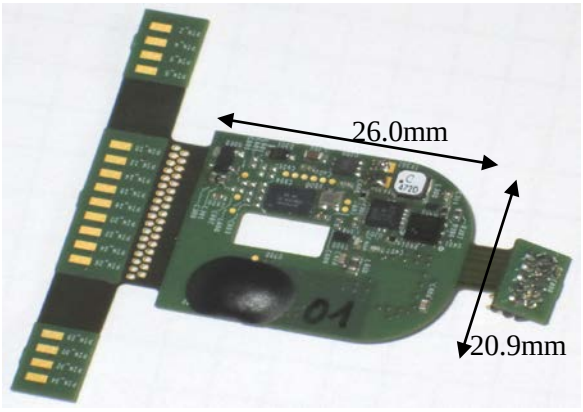

Fig. 2: PCB including ASIC and MCU (flex connections will be cut before housing).

The overall system control is implemented in a Cortex-M4 microcontroller (MCU). The selection of this MCU allows moving some signal processing into the implant and, this way, to minimize the required data transfer to the external prosthesis control. RF-data transmission using MICS conform radio transceiver as well as optical data transmission are under evaluation for this device. The development of different housing types using titan, ceramic and silicon is done in close cooperation.

RESULTS: The implant main board is shown in Fig. 2. The measurement system achieves an input referred noise level of only 1.7 μV_{RMS} across 1 kHz bandwidth. Both ASICs were tested as full functional. The evaluation of the whole system and the integration for electrical and in-vivo tests is currently under development.

ACKNOWLEDGEMENTS: This development is supported by the Fraunhofer Gesellschaft as the Fraunhofer Leitprojekt “Theranostische Implantate”.

Development of a highly integrated, multifunctional brain probe with extended functionality

D Schenk, C Steiner, C Röthlin

CARAG AG, Baar, CH

INTRODUCTION: Head injuries with involvement of the brain are among the most frequent causes of death, often young people are affected as a result of accidents [1].

Intracranial pressure (ICP) may rise due to swelling or a mass effect from a lesion, such as a haemorrhage, which leads, inside the closed skull, to a reduced cerebral perfusion pressure resulting in ischemia.

Today such patients will be monitored by intracranial pressure probes and, on the basis of the measured pressure, the cerebral perfusion will be concluded indirectly.

A direct measurement of the cerebral blood flow (CBF) will be only available by perfusion CT or MRI diagnostic. As CT and MRI are usually stationary devices, this will involve a time consuming and complex transport of a serious injured patient to the place of the medical imaging department.

METHODS: CARAG AG has developed a multifunctional brain probe for monitoring key parameters of brain function such as intracranial temperature, intracranial pressure and, as an innovation, the regional cerebral blood flow (rCBF) measured by an optical method, directly at patient's bedside. A cerebrospinal fluid (CSF) drainage as a means of reducing intracranial pressure is also integrated.

By the integration of a fibre optical near infrared spectroscopy probe, it is possible to calculate the regional cerebral blood flow by absorption measurements of an indicator dye. Light coupling is done by specifically designed optical components manufactured by micro injection moulding.

The measurement of the pressure is realised by a piezo resistive, silicon micro-machined sensor located in the tip of the probe.

The integration of a memory chip for storage of the individual calibration data of each probe allows the delivery of accurately calibrated probes.

The guidance of a drainage channel through the entire probe, from the drainage openings in the probe tip, passing the pressure sensor, the near infrared system and the temperature sensor requires an optimised use of the available cross section. This puts extremely high demands on miniaturisation**.**

RESULTS:

Fig. 1: Probe tip and middle piece.

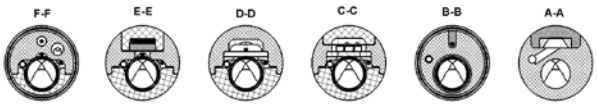

Fig. 2: Probe cross sections.

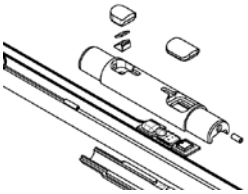

Fig. 3: Assembly middle piece.

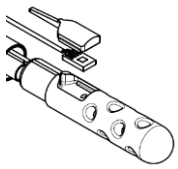

Fig. 4: Probe tip with pressure sensor.

DISCUSSION & CONCLUSIONS: An animal study with the Carag Brain Monitoring System (CBMS) consisting of probe, communicator and monitoring software indicates that the novel technique is safe, feasible, and accurate repeated measurements of absolute and dynamic changes of rCBF values. This technique also allows concomitant CSF drainage, with ICP and brain temperature monitoring. Future clinical investigation is scheduled to confirm the value of the CBMS technology in brain injured patients.

Implantable micro sensors for telemetric measurement of intraocular pressure at glaucoma patients

MG Ostermeier

Implandata Ophthalmic Products GmbH, Hannover, DE

INTRODUCTION: Accurate acquisition of intraocular pressure (IOP) data, particularly short-term and long-term fluctuations, plays an important role in the medical care of glaucoma patients. Non-invasive IOP measurement and self-tonometry with a telemetric IOP sensor can provide important data on the individual IOP profile. Implandata Ophthalmic Products GmbH (Implandata) has developed such a system, currently tested in clinical studies, expecting CE marking and market introduction in 2016.

METHODS: Implandata has established an implantable, permanent micro-sensor for telemetric measurement of intraocular pressure. The implant consists of a sensor chip with integrated capacitive pressure membranes, temperature sensor, AD converter, RF-front-end, E^{2}PROM and a gold structure bonded to the chip, which works as an antenna.

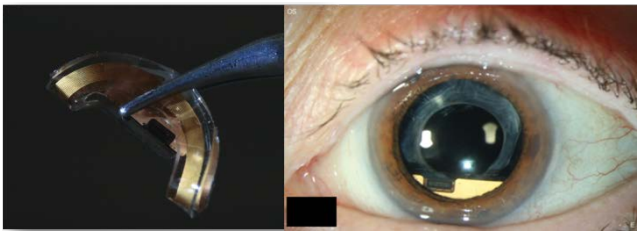

Fig. 1: Foldable implant (l) and implant in eye, behind the iris (r).

The sensor is hermetically sealed in medical grade silicon material, is passive and activated by applying a weak magnetic field via induction (RFID) provided from an external hand-held reader unit. Measured data is displayed and stored in the reader unit. Measurement can be initiated sporadically or continuously, as needed. A GSM module, which is connected to the reader unit, measured data is sent to a cloud based database, by which the eye doctor has access to, allowing remote patient care and tele-medical disease management. A patient smart-phone app delivers to the glaucoma patient the individual IOP information, combined with a medication reminder and alert function. The system provides direct measurement of IOP, measuring the absolute pressure in the eye, since the ambient pressure is measured at the same time by a pressure sensor, which is integrated in the reader unit. Thus, real IOP in mmHg can be delivered.

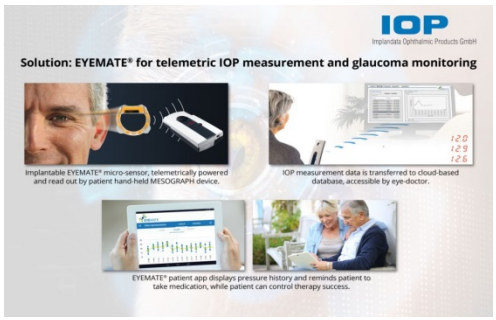

Fig. 2: Implandata EYEMATE system for telemetric measurement of IOP.

RESULTS: Pre-clinical and clinical testing of the implant demonstrates safety and functionality of the implant [1-4]. Up to date, 40 patients have been implanted with the sensor implant. Longest implant duration in a patient is now close to 7 years, accumulated implant stay exceeds 60 years without any device related adverse event and good functionality. Concordance of the implantable sensor measurements with Goldman applanation tonometry, shows a value of r^2 = 0,74. There were no sensor malfunctions and no need to explant the sensor so far. Anecdotal data demonstrate good utility in titrating glaucoma therapy and improving patient therapy adherence.

DISCUSSION & CONCLUSIONS: First in-human testing demonstrates functionality and safety of Implandata's telemetric IOP sensor. Personalized medication and therapy titration, as well improved patient adherence to therapy is shown anecdotally. Glaucoma experts believe that telemetric measurement of IOP will present vastly improved quantity and quality of IOP data, resulting in better and more efficient management of glaucoma, better disease outcome and improved quality of life for glaucoma patients.

Future Business Models

G von der Ropp

BMI Lab AG, St. Gallen, CH

INTRODUCTION: New products and services are not enough. Why do prominent firms, known for their innovative products, loose their competitive advantage and vanish from the business landscape?

They have lost their capabilities of marketing their former innovative strengths. The answer is simple and painful: these companies have failed to adapt their business models to the changing environment. Business model innovation will be the leading factor that determines the competiveness of your company.

On the other side, companies like IKEA, Apple or Airbnb successfully reinvented their industries by escaping the traditional industry logic and establishing innovative business models.

Business models describe how the magic of business works. There are four central dimensions: The target customer, the value proposition towards the customer, the value chain behind the creation and the revenue model that captures the value.

METHOD: The importance of business model innovation is evident. But how does one do this? Does it require you to have a Steve Jobs-type person in your organisation? Our research has shown that 90% of all business model innovations are recombinations of already existing pattern. Creating new business models is as much a systematic process as it is the fruit of genius.

The St. Gallen Business Model Navigator is a methodology that offers a systematic approach to develop and implement innovative business models. It encourages out-of-the-box-thinking and helps to overcome the dominant industry logic. Well-grounded in theory, it has proven its applicability in practical settings many times over, e.g. at Bosch or Swisscom.

Prof. Dr. Oliver Gassmann and Prof. Dr. Karolin Frankenberger, both from the University of St. Gallen, analysed more than 250 successful business model innovations. The analysis resulted in 55 common business model patterns, which can be used to create new business models.

The method consists of four phases, see figure 1:

1. Initiation – Analysing the ecosystem as well as trends and change drivers
2. Ideation – Creating business model ideas by applying the pattern cards
3. Integration – Detailing the business model and ensure consistency of all dimensions
4. Implementation – Iterating the business model concept until it is ready for market introduction.

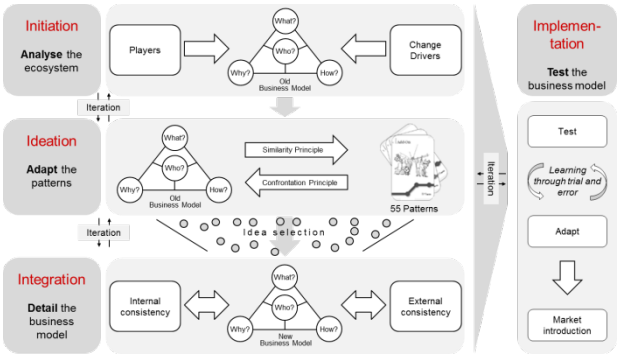

Fig. 1: The St. Gallen Business Model Navigator.

PRESENTATION: During a 30-minute presentation, von der Ropp will show the importance of business model innovation and introduce an effective approach to create future business models. Healthcare industry cases and other examples will illustrate this.

The BMI Lab is a spin-off from the Institute of Technology Management at the University of St. Gallen. We offer growth, differentiation and profitability based on business model innovation. We apply the St. Gallen Business Model Navigator in practical projects. Through action-based education we enable companies to build BMI capabilities. Through advisory we support the development and implementation of new business models.

Regulatory Constraints and Innovation: boon and bane?

HH Junker

TÜV SÜD Product Service GmbH, München, DE

INTRODUCTION: The Medical Device market is one of the highest regulated markets – since decades. Many countries in the world have implemented specific regulatory standards and rules that manufacturers of medical devices have to comply with. Such regulations vary, are similar or even equal. At the same time some countries do not have such standards and rules at all. However, in highly regulated countries with such standards and rules processes are implemented that slow down the process of market introduction of new devices. Are those standards and rules boon or bane?

DISCUSSION: Medical Devices are products that may save lives, make life liveable, must not have an effect on patients at all or even kill human beings - Medical Devices may impact the life of patients. Though, they are designed and produced under competitive market situations, they must not only be safe for the user, they also must achieve the performance as indicated by the manufacturer without putting unacceptable risks to the patients or having undesirable side effects. New medical diagnosis or therapeutic procedures involving Medical Devices need to proof that this new procedure, compared to existing procedures or alternative procedures, are having a benefit to the patient.

Long lasting regulatory approval processes slow down the time to market leading to the fact that patients cannot be diagnosed or treated with the newest innovative medical devices.

Effective regulatory standards and processes may ensure uniform safety levels and uniform performance levels for the benefit of both - the manufacturer and the user/patient.

Missing regulatory standards and processes may shorten the time to market bringing new products much faster to the users and patients.

Boon or Bane?

- Regulatory requirements are set by several and different individuals and experts
- Regulatory requirements are reflecting state of standard, sometimes state-of-the-art
- Regulatory requirements provide design inputs to manufacturers without a need for individual investigations
- Compliance to regulatory requirements helps manufacturers in case of vigilance/incident cases
- Regulatory requirements need to be internationalized as much as possible
- Regulatory requirements are not automatically regulatory constraints against innovation
- Regulatory requirements in case of innovations (or: state-of-the-art) need special attention
- Regulatory requirements shall reduce risks to the patients:

  Patients need special care.

n!ce – the restorative dental ceramic of the future

A Burg, A Kounga, D Buschmann, C Appert

Institut Straumann AG, Basel, CH

INTRODUCTION: For all-ceramic dental restorations oxide ceramics and glass-ceramics are the most prominent inorganic materials used for the prosthetic region. While oxide ceramics are certainly mechanically very stable, dental restorations made thereof still do underperform in terms of esthetics. Moreover, their mechanical properties make them unfavorable for chairside made restorations. However, glass-ceramics, in their turn, exhibit very pleasing esthetics and mimic natural teeth better in both mechanical and optical properties thus rendering them the material of choice for restorations in the anterior region of the mouth.

N!CE GLASS-CERAMIC: Straumann has developed a novel lithium disilicate strengthened lithium aluminosilicate glass-ceramic material [1] (Table 1) which enables a CADCAM fabrication of high performance dental restorations. Furthermore, the restorations can be milled chairside from blocks (Figure 1) and placed in just one session at the dentist. The material presented here is available in two translucency levels and in six colors allowing for a large variety of individual restorations.

Table 1. The n!ce chemical composition corresponds to a lithium disilicate strengthened lithium aluminosilicate glass-ceramic materia [1].

Elements	Weight (%)
SiO_2	64 – 70
Li_2O	10.5 – 12.5
Al_2O_3	10.5 – 11.5
K_2O	0 – 3
Na_2O	1 – 3
P_2O_5	3 – 8
ZrO_2	0 – 0.5
CaO	1 – 2
Coloring oxides	0 – 9

USP (Unique Selling Point): Whereas competitors' materials are typically milled in a partially crystallized stage and require an additional time consuming firing step, the Straumann material can be milled as-received, polished and then placed in the patient's mouth. No additional firing step is required thus shortening the workflow considerably. Straumann's material is the first dental ceramic that, after milling and polishing without additional heat treatment, exhibits excellent esthetics and superior mechanical properties (Table 2).

Fig. 1: n!ce blocks are intended for use in chairside CADCAM workflows for dental restorations.

Table 2. n!ce exhibits superior physical properties without an additional firing step.

Flexural strength (3-point bending)	≥ 350 MPa
Fracture toughness (SEVNB)	≥ 1.5 MPa√m
Chemical solubility	≤ 50 µg / cm^2
CTE (100 – 500 °C)	7.1 ± 0.5 10^{-6} K^{-1}
Glass transition temp. (Tg)	590 ± 20 °C

Development of patient-specific orbital floor implants made of shape memory alloys

C Rotsch[1], R Grunert[1], J Lichtenstein[2], M Wagner[3], H Essig[3], S Posern[4], F Pabst[4], S Hanus[5], V Reichmann[5], WG Drossel[1]

[1] Fraunhofer Institute for Machine Tools and Forming Technology IWU. DE. [2] University Hospital Schleswig Holstein, DE. [3] University Hospital Zuerich, CH. [4] Hospital Dresden-Friedrichstadt, DE.

[5] Textile Research Institute Thuringia-Vogtland, DE

INTRODUCTION: Fractures of the orbit may be occurring by blunt trauma to the eye, for example, in traffic, work and sports accidents. The treatment of orbital floor defects is often done surgically by use of implants from rigid materials such as titanium, which are inserted in the eye socket through an open approach on the lower eyelid [1]. The implants should support the defect bone, keep the eyeball in place and allow the attachment of new tissue cells. The implants can be produced individually by the manufacturer or metal meshes can be adapted by the surgeon during the surgical intervention. The new approach is to implant an artificial orbital floor into the body in compressed form over relatively small approaches. Arriving at the fracture position, it develops self-reliantly in the previously memorized shape.

METHODS: The pseudo elasticity of NiTi has the peculiarity that it can withstand large mechanical deformations - comparing to other metals - of up to 8% without being plastically deformed. In combination with the good biocompatibility [2] the material can be can be used to develop flexible, yet stable implants.

Two possible approaches were investigated in this project. In the first approach the implant is made of customized and structured NiTi metal sheets. The second approach provides a textile structure with integrated shape memory wires. The bases for the patient-specific geometry for the implant geometry are CT datas of eye sockets. A surface model or three-dimensional model of the implant can be created with commercial software tools. The derived three-dimensional shape of the model is projected onto a two-dimensional plane to receive the required outline. The geometry can be cut out of the metal sheet or can be embroidered on a textile carrier. To realize a 3D geometry the sheets or textiles must undergo a shape setting. A special forming tool and a heat treatment are necessary. The geometry of the forming tool is based on the CT data and it is manufactured by rapid prototyping technology (e.g. laser beam melting) or by CNC machining for the patient.

RESULTS: First prototypes of the patient specific implants made of NiTi were developed. The mechanical behaviour and the difference between planned and achieved geometries were examined. In first tests with an anatomical model and human cadavers, which were done by the clinical partners, the artificial orbital floor were implanted into the body in compressed form over relatively small approaches. Arriving at the fracture position, it develops self-reliantly in the previously memorized shape. In future, the perioperative trauma can be reduced by the smaller approaches.

DISCUSSION & CONCLUSIONS: A process chain for the technical implementation of a patient-specific orbital floor implant was developed. The advantages of NiTi material and the possibilities of rapid prototyping technologies were combined.

Fig. 1: Images of the first implant trials, left. implant inside the surgical instrument, right: final shape of the implant [3]

ACKNOWLEDGEMENTS: We thank the BMBF for funding the project FORMPLANT (13GW0017). We also thank the project partners Medical School Hannover, EC Coating GmbH, Julius Boos jr. GmbH & Co. KG, Alphaform Glaho GmbH and PTZ-Prototypenzentrum GmbH.

Industrialization of complex medical devices in high labor cost countries

M Dubey

CPAutomation SA, Villaz-St-Pierre, CH

INTRODUCTION: The Swiss medical industry develops and produces complex medical devices in Switzerland. In order to stay competitive (especially in a high labor cost country like Switzerland), production needs to be continuously optimized. Thanks to cutting edge technologies and high level of innovation, the Swiss machine builder industry can contribute to their success in Switzerland. Medtronic and CPAutomation SA collaborate successfully since many years to optimize the production of high value added complex medical devices in Switzerland. Thanks to this collaboration, Medtronic produces thousands of high quality and cost effective medical devices in their Tolochenaz plant.
CPAutomation SA supplies turnkey systems based on standard configurations and platforms. Its customers have the benefit of a large range of competencies in the fields of micro assembly, micromanipulation, laser machining and intelligent aesthetic inspection.

CHALLENGES: The medical industry requires high quality automated equipment that offers high reliability, and must be flexible so that it can be implemented in lean manufacturing production lines. They also require robust solutions providing minimal down time. The equipment configuration and operation must be easy to use and ergonomic for all operators. Operators are required since their main function is quality control. In addition, the global competition is quite large so that costs and delivery time must be optimized. In order to achieve these goals, Medtronic decided to lower its level of automation [1] below the "great divide" (level 2 or 3).

Table 1. The five levels of automation.

		Load Machine	Machine Cycle	Unload Machine	Transfer Part
Level	1	Manual	Manual	Manual	Manual
	2	Manual	Auto	Manual	Manual
	3	Manual	Auto	Auto	Manual
		The "great divide"			
	4	Auto	Auto	Auto	Manual
	5	Auto	Auto	Auto	Auto

RESULTS: The market feedback is that fully automated, multi-process equipment induces high costs and very low flexibility which in this global fast changing environment are no longer required. The market is moving toward single process, semi-automated machines which show much higher flexibility with low capital investment costs (Fig. 1).

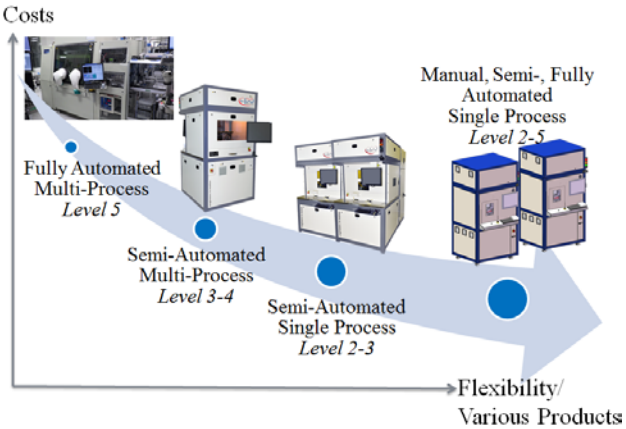

Fig. 1: Cost of manufacturing equipment in function of flexibility and level of automation.

DISCUSSION & CONCLUSIONS: To achieve level 2 and 3 of automation, CPAutomation has standardized their automated cells (Fig. 2) which bring the following advantages to the customers: simplified concept and quotation, shorter delivery times, higher flexibility, improvement of the serviceability (non-complex cell), optimized cost and limiting of risk.

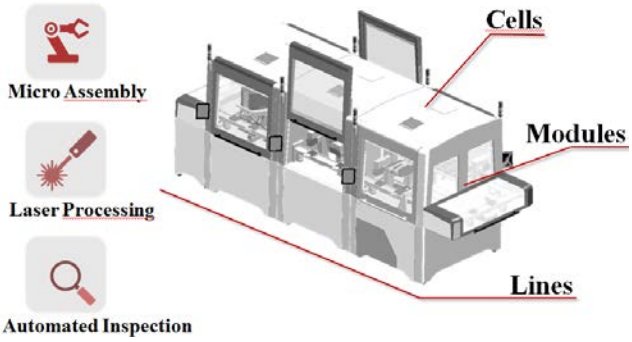

Fig. 2: The CPAutomation SA standardized automated platform concept.

ACKNOWLEDGEMENTS: the authors wish to thank Mr. Dominique Piguet from Medtronic for fruitful discussions.

483 response: common pitfalls and how to avoid them

D Drago[1], N Singer [1,2]

[1] *School of Medicine and Health Sciences, George Washington University, Washington, DC, USA.*
[2] *Compliance Alliance, Arlington, VA, USA*

INTRODUCTION: The Food and Drug Administration (FDA) conducts inspections of medical device manufacturers to check compliance with regulatory requirements [1]. When a company fails to comply, the FDA can respond with enforcement tools. They include, but are not limited to, inspectional observations (FDA 483), warning letters, and recalls. Recent years have seen an increase in 483s, and subsequent warning letters, issued by FDA [2]. When companies receive a 483, they are permitted to respond in writing. If FDA receives the response within 15 business days, FDA officials will take the company's corrective action into consideration when determining whether or not to issue a warning letter [3]. Additionally, if the agency is planning on issuing a warning letter, the letter will acknowledge the company's response and comment on the adequacy of the company's corrective actions [4]. Many companies may find that they are not ready to respond effectively within 15 days. The time-pressure, and the potential consequences, may represent significant challenges. These include the possibility of the company being subject to negative publicity, and having to allocate more resources to functions that develop and implement corrective actions.

METHODS: The authors undertook a review of existing literature and conducted open ended semi-structured interviews with experts. The goal of the interview process was to explore, through different perspectives, gaps of knowledge, perceived challenges, areas of opportunity, and current best practices. The group of interviewees comprises former and current FDA officials and regulatory and quality staff in medical device companies.

RESULTS: Analysis of the data yielded six potential common pitfalls in responding to FDA 483s: (1) failing to understand the basis for each observation, and the underlying facts supporting them; (2) failing to address broader issues implicated by the observations, i.e. failing to apply a 'systemic' approach; (3) including new issues in the response that were not addressed by FDA in the 483; (4) failing to include a narrative that accompanies completed actions; (5) failing to draft a response that is clear, concise, easy to understand, and contains evidence of the company's corrective actions; (6) failing to run a consistency/quality check of the whole package prior to submission.

DISCUSSION & CONCLUSIONS: The data collected revealed that some companies unknowingly increase the potential of not responding adequately to a FDA 483. Based on the analysis of the data, the authors suggest some strategies. They can help companies to better control/prevent key aspects of the process, and overcome what appear to be common pitfalls in responding to inspectional observations.

ACKNOWLEDGEMENTS: The authors thank all professionals who took the time to assist in the collection of the data.

Challenges and consequences for industry based on the revision of ISO 10993-1, -17 and -18

A Poth

Eurofins BioPharma Product Testing, Planegg, DE

INTRODUCTION: The important standards for biological evaluation and risk analysis are explained in three parts. ISO 10993-1 provides the frame-work and describes the general principles of the biological evaluation, ISO 10993-18 provides information on the qualitative and quantitative characteristics and finally ISO 10993-17 gives guidance on the derivation of the allowable limits for the leachable components of the medical devices. All the three major standards are going to be revised.

METHODS: For ISO 10993-1 "Evaluation and testing within a risk management process" it was discussed to change the flow-chart for the systematic approach for the biological evaluation of medical devices with the focus on the chemical characterisation of the medical devices. As a consequence Annex A 1 "Evaluation tests for consideration" of ISO 10993-1 needs to be revised by adding a new column including chemical characterisation as a test parameter. It was further discussed to include additional test parameters for certain device categories and additional toxicological endpoints for evaluation based on the US-FDA modified matrix as outlined in the US-FDA draft document ISO International Standard ISO 10993, "Biological evaluation of medical devices Part 1: Evaluation and Testing" (2013). By including additional requirements it was discussed that chemical characterisation and cytotoxicity testing will be mandatory and all other toxicological endpoints will be evaluated on a case-by-case basis within a toxicological risk assessment. A major revision of ISO 10993-17 on allowable limits for leachable substances is in works. The experts of TC 194 are discussing risk assessment approaches to use the concept of Threshold of Toxicological Concern (TTC), a concept which is already established and accepted for genotoxic pharmaceutic impurities. If it can be shown that an impurity is below the TTC, then it is assumed that the level of the chemical substance is of no significant risk and no further evaluation is required with regard to that impurity. TTC allows definition of threshold values for substances below which there is insufficient material to cause a toxicological hazard and no further evaluation is required. The concept may also be applied more generally to unidentified contaminants. The inclusion of TTC in Part 17 would be a significant advance which will allow avoidance of unnecessary animal testing if materials characterisation can demonstrate leachables are below the TTC. This concept is planned to be implemented as an Annex in ISO 10993-17.

A major revision will be made on ISO 10993-18 including the technical and scientific experience made during the last 10 years since its publication. Within the experts it was discussed expanding on the choice of extraction types (exaggerated versus simulated-use extraction) and to better define the experimental requirements for investigating extractables and leachables. It was further discussed on how to best describe the stepwise chemical characterization process and the revisions needed to the associated flowchart. The revision will include a specific subclause on analytical methods, including the topic of qualification and validation. The experts of the working group also discussed approaches to setting analytical evaluation thresholds (AETs), recognizing that this will have to be developed in alignment with thresholds of toxicological concern (TTCs).

DISCUSSION & CONCLUSIONS: Based on the proposed revisions it can be foreseen that in future the chemical characterization will be a key parameter in the assessment of the biological and toxicological evaluation of medical devices. It can also been foreseen that the proposed step-wise chemical characterization will be of more complexity especially for high risk devices, including more complex analytical methods for structure elucidation of unknown chemical substances released but also the evaluation of release kinetics of chemical compounds from medical devices. Another focus will be the toxicological evaluation of the medical devices based on the outcome of the chemical characterization.

Adaptive clinical study design – shorten your time to market

M Weber

Integrated Scientific Services, ISS AG, Biel, CH

INTRODUCTION: Device development is an iterative process and study designs may be refined or improved as device development progresses. Clinical performance outcomes, user feedback, adverse events or difficulties in deploying or delivering a device can lead to changes to the device during a clinical study. Manufacturers may anticipate iterations of the materials of construction based on clinical data generated during the early feasibility study. Clinical studies are considered as clinical research on human beings and need approval from ethics and competent authorities. Any change in these approvals are time and effort consuming steps.

The FDA has released recently a draft guidance for Industry and Food and Drug Administration Staff on Adaptive Designs for Medical Device Clinical Studies [1]. Together with the rules issued by the FDA for recognition of clinical data generated outside the US, European manufacturers may improve their time to market.

Advantages and limits of the adaptive design for medical device clinical studies will be discussed.

METHODS: According to FDA an adaptive design for a medical device clinical study is defined as a clinical trial design that allows for prospectively planned modifications based on accumulating study data without undermining the trial's integrity and validity [1]. In an adaptive design, interim data analysis is used to assess initial trial assumptions. If the assumptions were incorrect, pre-planned adaptations are implemented to adjust sample size or stop early for efficacy or futility without undermining trial validity or integrity. Sponsors can also accelerate time to submission by implementing a seamless adaptive design, which combines the feasibility and pivotal studies into one trial [2].

DISCUSSION & CONCLUSIONS: While the primary goal is scientific discovery, clinical trials must also fulfil multiple regulatory, clinical, and ethical requirements [3]. Medical Devices are often developed in different phases starting with a feasibility trial followed by pivotal investigations. Each phase is evaluated independently and no adaptation of outcomes and patients is possible. Learnings need to be incorporated into independent clinical trials with extending the development time. Unplanned modifications during feasibility studies may frequently occur and without a proper preplanning the integrity and validity of a scientifically valid study is not given.

Randomised clinical trials (RCT) are the gold standard in obtaining clinical evidence. For medical devices RCT designs are not always feasible and adaptive clinical designs may be a valuable alternative.

Adaptive trial designs can be used for many study design adaptations like dropping a treatment arm, changing the randomization ratio, modify the inclusion/exclusion criteria, changing the hypothesis or endpoint and also seamless transition of study phase, and others, the medical device design is more challenging to change.

Adaptations of the device or the endpoint should be avoided in the pivotal phase of the trials. In case of seamless studies where the feasibility investigation smoothly transitions to a pivotal study no significant changes to the device are possible.

According to FDA, adaptive designs may enable more timely device development decision-making and therefore, more efficient investment in resources in a clinical study. From an ethical standpoint, adaptive designs may optimize the treatment of subjects enrolled in the study and safeguard their welfare from ineffective or unsafe treatments and interventions at the earliest possible stage [1].

How to meet FDA's criteria for reprocessed medical devices

N Revellin

NAMSA, Chasse-sur-Rhône, FR

INTRODUCTION: Reusable medical devices are devices that hospitals can reprocess and reuse on multiple patients. Due to high complexity in design and increasing difficulty to reprocess, FDA has published a guidance outlining general considerations for the design and safety of all reusable medical devices as well as what is important to include in the Instruction for use (IFU) for users to follow. 510(k) submissions should include validated reprocessing methods and instructions.

METHODS: FDA Guidance lists six criteria that should be addressed in the instruction of use.

RESULTS:

Criterion 1: Appropriate reprocessing instructions should be developed according to the intended use of the medical device and soiling and contamination should reflect clinical use.

Criterion 2: Adequate sterilization or disinfection will depend on the thoroughness of cleaning. IFU should therefore clearly state how to achieve thorough cleaning.

Criterion 3: Depending on the Spaulding Classification [1] and the intended use of the device, either sterilization or disinfection (high, intermediate, or low level) should be recommended.

Criterion 4: Technically feasible instructions including legally marketed accessories should be developed (see Table 1).

Criterion 5: Users should precisely understand how to implement safely and effectively the entire reprocessing procedure, such as the need of special accessories, the instruction for point-of-use processing, the disassembly and reassembly instruction, the cleaning method and the cleaning agent, the rinsing step, and the visual inspection.

Criterion 6: Reprocessing instructions should be understandable, clear, in a sequential order, and detailed.

Table 1. Examples of Sterilization Cyles Used in the USA.

Sterilizer	Temperature and Exposure Time	Minimum Drying Time
Gravity-displacement	132°C-15 minutes	15-30 minutes
Dynamic-Air-Removal	132°C-4 minutes	20-30 minutes

DISCUSSION & CONCLUSIONS: Mastering the FDA's Guidance is the first step in getting new, reusable device into the US marketplace.

Innovation – a precious diva

J Bernhard, K Limacher, A Mellmann

CARAG AG, Baar, CH

INTRODUCTION: Attending international medical conferences, it catches the eye that innovative new medical devices are often not yet available on the US market. Even US based companies choose to launch their new products in Europe and other markets before they introduce them in their home market. Regulatory complexity may be one of the reasons. But also in the EU, the desire for safety continuously increases, and results in exacerbated regulatory requirements. The time and money consuming process of bringing an innovation to the market is outlined on the basis of a novel heart implant.

METHODS: The engineers at CARAG AG have specialized in the development of cutting edge medical devices. One example is the Carag Bioresorbable Septal Occluder CBSO, the world's first septal occluder with resorbable framework.

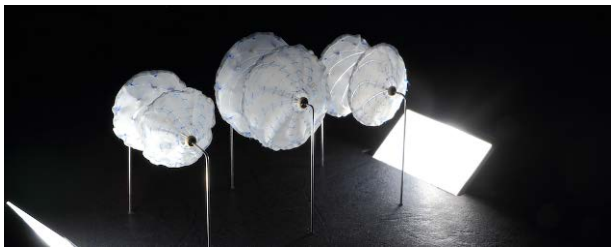

Fig. 1: CBSO, three sizes for different defects.

In a first stage, an occluder design suited for the use of bioresorbable materials had to be developed. In a second stage, a bioresorbable material with sufficient mechanical stability and suitable degradation characteristics had to be engineered. Because of the importance of the device behavior in-situ (i.e. the septum of a beating heart) over the entire degradation period, the design and materials had to be validated in an animal model. Accelerated testing in the laboratory was not sufficient.

In a third stage after design freeze, functional and biocompatibility testing, risk evaluation and control, production setup, labelling, usability, clinical evaluation and many other tests had to be performed, both internally and by specialized subcontractors. This resulted in numerous reports.

In a fourth stage, the entire documentation had to be filed for a first-in-human (FIH) clinical investigation. Because of the different national requirements for clinical investigations even within Europe, decision was made to limit the study to one country/one legislation – Germany.

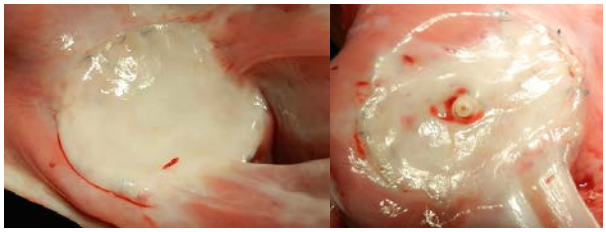

Fig. 2: Macroscopic views (right and left atrial disc) of an endothelialized CBSO, 3 months after implantation in swine.

In a fifth stage, the data of the FIH clinical investigation is integrated, assessed and commented in the clinical evaluation. The full documentation is thoroughly reviewed by our notified body. The examination of the design, together with an extensive in-house audit of the quality management system, will finally lead to the EC certificates required for the marketing of a class III medical device in the European single market.

RESULTS: The development of the CBSO from first concepts to design freeze (stages I & II) took about five years of committed work, turning the device into a CE marked class III medical device (stages III-V) took another five years. The entire development was a double-digit million Swiss francs investment.

DISCUSSION & CONCLUSIONS: A septal occluder with a bioresorbable framework is a clinical desire. Aside from the technological challenges of such an innovative endeavor, the regulatory hurdles contribute considerably to the time to market and the associated costs. This will be reflected not only in the pricing of medical devices, but also bears the risk that the early availability of novel devices on the European market will be affected, since companies choose to investigate and launch new products elsewhere.
A critical discussion of value of innovation versus desire for safety is needed.

ACKNOWLEDGEMENTS: Thanks to Dr. Björn Söderberg and PD Dr. Matthias Sigler for their support during the animal experiments, and to Prof. Dr. Horst Sievert for his patronage during the clinical investigation and beyond.

Three-dimensional prosthesis planning based on conventional x-ray radiographs

S Schumann[1,2], J Stifter[1], T Schwägli[1], G Zheng[2]

[1] *Medivation AG, Brugg, CH.*

[2] *Institute for Surgical Technology and Biomechanics (ISTB), University of Bern, CH*

INTRODUCTION: The current state of the art in prosthesis planning relies on a single planar X-ray radiograph. For many orthopaedic interventions a true three-dimensional (3D) planning would be important. Even though 3D imaging technologies such as computed tomography (CT) would be suitable, the extra costs, exposure of radiation and additional expenditure of time can normally not be justified. In order to overcome the current limitations in prosthesis planning, we are introducing a new solution, which enables 3D prosthesis planning with only two radiographs.

METHODS: In comparison to CT, conventional X-ray imaging is rather inexpensive, exposes patients to less radiation and is readily available. But conventional radiographs only provide two-dimensional (2D) views of the anatomy and thus lack of full 3D information. By correlating the information of radiographs from different views, a patient-specific model of the particular anatomy can be reconstructed and further used to perform a 3D planning of the prosthesis components.
For the planning of knee replacements, two radiographs of the leg need to be acquired in standard views (anterior-posterior and lateral). During X-ray acquisition, a special appliance is wrapped around the patient's knee to immobilize the joint and to calibrate the radiographs [1] (Fig. 1, left). The radiographic images are further analyzed to detect specific anatomical features [2].

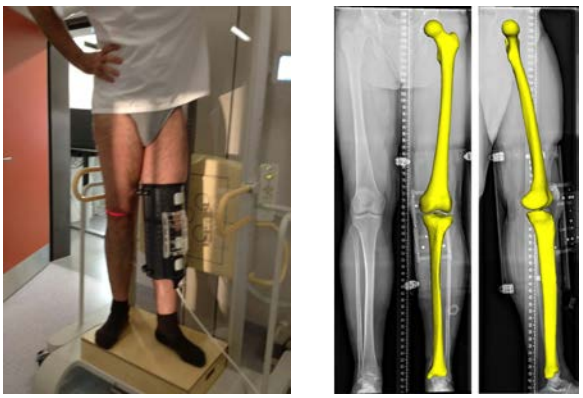

Fig. 1: Left: Acquisition of radiograph in lateral view. Right: Patient-specific 3D model reconstructed from two radiographs.

These features together with a statistical shape model are applied in a non-rigid optimization scheme to reconstruct a patient-specific model of the leg [3] (Fig. 1, right).
In an ethically approved pilot study, this new technology was evaluated in 25 patients undergoing total knee arthroplasty (TKA). Preoperatively, CT and X-ray images were acquired of the concerned leg. The CT images were segmented and 3D surface models of the femur and tibia were extracted. These models further served as ground truth. The X-ray images were used to compute patient-specific models according the described pipeline. For both model types (CT and reconstructed), specific anatomical parameters were measured and compared to each other.

RESULTS: As shown in Tab. 1, five parameters, mostly relevant for the preoperative planning of TKAs and osteotomies were analysed.

Table 1. Average angular deviations between reconstructed and CT models.

	Avg. angular deviation
angle between anatomical & mechanical axis	0.29°
femoral antetorsion	2.09°
neck-shaft angle	0.58°
tibial torsion	2.12°
tibial slope	0.96°

DISCUSSION & CONCLUSIONS: The conducted pilot study has shown the feasibility of our new solution for 3D prosthesis planning from two radiographs.

ACKNOWLEDGEMENTS: This work has been supported by the Commission for Technology and Innovation (CTI), Project No. 18193.1 PFLS-LS.

dokspot.com – digital instructions for medical devices

C Derché, H Strobel

dokspot GmbH, Zürich, CH

INTRODUCTION: Every day, medical device manufacturers ship products including printed instruction booklets with redundant languages around the world. These booklets not only have a financial cost, they also may not be readily available when needed and they are a burden on our environment.

dokspot is a solution: a novel internet based service that digitally links products and instructions. With this dokspot aims at transforming the way medical device manufacturers handle instructions and communicate them to their customers. dokspot is a fully compliant and trustworthy solution.

By using dokspot, companies can provide their customers with digital product information at the right time, for the right product, and in the right language. dokspot establishes the direct link between the medical device and the information needed for its safe and secure application.

METHOD: Figure 1 illustrates the concept of the dokspot solution. Medical device manufacturers (left side) upload their instructions to dokspot (top). Healthcare professionals (right side, these are the medical device users and customers of the medical device manufacturer), can conveniently and directly access this information on dokspot anytime and anywhere without searching. dokspot links device and instructions directly and unambiguously. The physical product is shipped to the healthcare institution (bottom) without instructions on paper. This significantly simplifies processes and operations for the manufacturer and reduces hospital waste.

dokspot meets the requirements of EU[1)] and FDA[2)] regulations, enabling businesses to go digital after assessing device related regulations and risk.

RESULTS: Medical device manufacturers benefit from digital instructions through lower cost and increased process efficiency. An overview of the improvements is presented in Table 1.

Improvement	**Outcome**
Time to market	4-6 weeks faster / instruction language
Direct cost, e.g. print	minimum 50% lower
Entering new markets	4-6 weeks faster / instruction language
CO_2 Emissions	app. 8 kg CO_2 saved / 1 kg instr.

Table 1: *Improvements and outcomes through adaption of dokspot.*

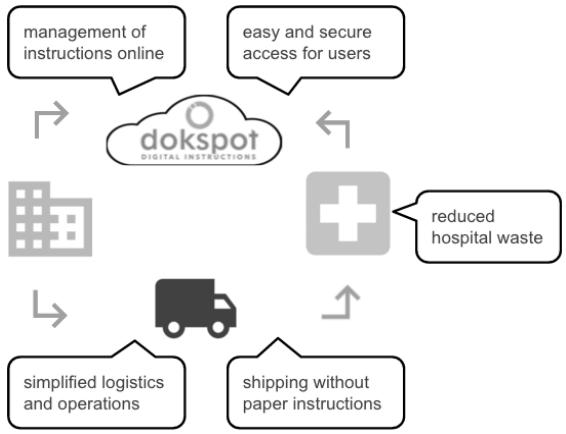

Fig. 1: *dokspot (www.dokspot.com) enables medical device manufactures to link devices with digital instructions and other information related to safe and effective product use.*

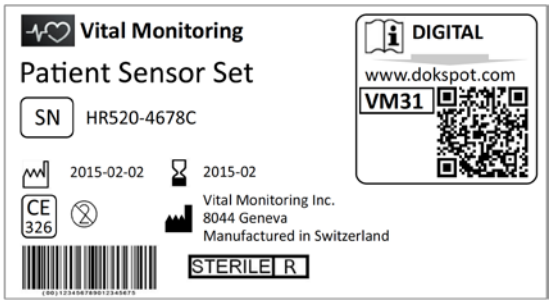

Fig. 2: *Medical devices are labelled with a unique dokspot code. Using this code, device users can access instruction direct and unambiguous in less than 10 seconds.*

DISCUSSION & CONCLUSIONS: The dokspot solution reduces complexity of manufacturing processes and increases operational speed. By adapting the dokspot solution, manufacturers can increase profit and reduce time to market without upfront investments. Assessment of compliance with regulations and risk is a prerequisite to use digital instructions for medical devices.

Alteration of electrostatic potential of the titanium implant surface by antibacterial copper deposits

Yu Dekhtyar[1], M Selutina[1], C Jung[2]

[1] Riga Technical University, Latvia. [2] KKS Ultraschall AG, Steinen, CH

INTRODUCTION: The extent of implant associated infections is strongly related to the properties of the implant surface such as surface roughness, hydrophobicity and electrostatic charges [1]. Different strategies are proposed for surface modification to prevent implant associated infections. These strategies may be roughly classified as: (i) preventing bacteria adhesion and (ii) killing bacteria by antibacterial agents. We have shown that copper as antibacterial agent can be deposited onto the oxide layer of titanium implants. The release of copper from the surface induces an antibacterial effect [2]. In the present study we demonstrate that the copper deposits on the implant surface alters the electrostatic potential of the titanium oxide surface which might play a role for the antibacterial effect.

METHODS: Discs of cpTi grade 4 (Ø12 mm, 2 mm) were anodized and copper-deposited by the Spark-Assisted Anodizing method using proprietary electrolyte and process parameters (KKS TioCel^{TM}) [3]. The absolute concentration of copper lies between 5 and 200 ng/mm^2 [4]. Copper dot surface density was determined using scanning electron microscopy (Phenom ProX). The surface electrical potential was identified as the electron work function (φ) measured by ultraviolet photoelectron emission detection with the use of a hand-made spectrometer [5]. The photoelectron work function is directly proportional to the surface electrical potential ($\varphi = -e \cdot \phi$; e and ϕ being the electron charge and the electrostatic potential at the surface layer that emits the electrons, respectively).

RESULTS: Copper deposits are homogeneously distributed over the disc surface (Fig. 1). The work function φ of the anodized titanium surface decreases with increasing copper concentration (Fig. 2).

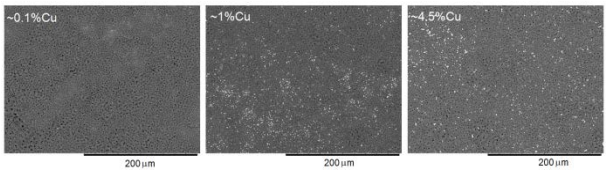

Fig. 1: Scanning electron microscope images of titanium discs with copper deposits (white dots).

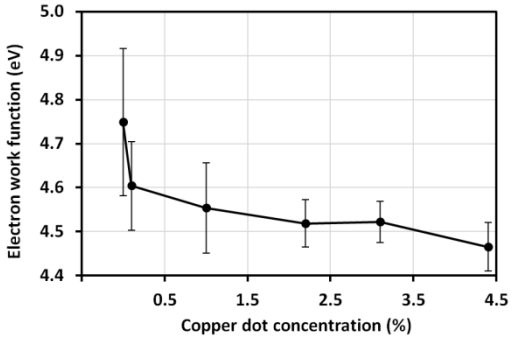

Fig. 2: Electron work function in dependence of the copper dot surface concentration given in %.

DISCUSSION & CONCLUSIONS: The electron work function φ is a measure for the minimum energy required to extract an electron from the surface of a solid material. The decrease of the value of φ means a decrease of the negative surface potential, indicating that the potential is shifted to positive values. This suggests that adhesion of bacteria may slightly be favoured with increasing copper surface concentration because the outer membrane of most bacteria reveals a negative surface potential [1]. The enforced adhered bacteria are however directly exposed to the released copper ions which kill the bacteria. Such synergistic effect might play a positive role for the antibacterial function. The synergistic effect might also be hold *in vivo* where body fluid proteins interact first before bacteria adhere on the implant surface.

ACKNOWLEDGEMENTS: The research was supported by the COST Action TD1305 "Improved protection of medical devices against infection" and by the Latvian Council of Sciences grant 491/2012.

Hard coatings: a smooth ceramic on a metal implant

D Dumitriu La Grange[1], N Goebbels[2], A Santana[2], R Heuberger[3], T Imwinkelried[3], L Eschbach[3], A Karimi[1]

[1] Institute of Physics, Swiss Federal Institute of Technology (EPFL), Lausanne, CH.
[2] IHI Ionbond AG, Olten, CH. [3] RMS Foundation, Bettlach, CH

HIGHLIGHTS:

- Structural and tribological behavior of arc-deposited Nb-Ti-N coatings was investigated.
- Cathodic arc deposition of Nb-Ti-N coatings from compound TiNb cathodes is accompanied by the formation of metallic macroparticles rich in niobium.
- Niobium rich droplets embedded throughout the coatings thickness were detected using microscopy techniques.
- The metallic niobium inclusions are related with a poor cohesion of the coatings. Debris from Nb-Ti-N coatings act as third-body wear particles in pin-on-discs tests against UHMWPE surface.

INTRODUCTION: Ternary niobium-titanium-nitrides were investigated as a potential coating for metallic femoral heads or femoral condyles in hard-on-soft orthopaedic implants, in order to reduce the ion release of the metallic substrate and to reduce wear.

METHODS: $Nb_{1-x}Ti_xN$ coatings with x = 0.6-1 were deposited by cathodic arc using TiNb compound cathodes. The microstructure and properties of the coatings such as hardness, elastic modulus, adhesion, resistance to wear and the wear of the ultra-high-molecular-weight polyethylene (UHMWPE) counter surfaces were characterized using XRD, TEM/STEM, EDS, nanoindentation and pin-on-disc friction and wear tests.

RESULTS & DISCUSSION: The niobium-titanium-nitride coatings deposited from TiNb cathodes have a multilayered structure associated with a periodical oscillation in niobium and titanium composition. Throughout the coating, macroparticles consisting of a Nb rich core and a nitridated titanium porous shell were evidenced by STEM and EDS. Increasing the nitrogen pressure during deposition reduced the amount of metallic Nb droplets. The presence of niobium in the coatings slightly increased the hardness (H) and Young's modulus (E) values, but did not affect the H/E ratio. In adhesion tests the metallic niobium rich droplets were deformed at the contact between the diamond stylus and the coating, as shown by SEM images.

The underlying mechanisms of wear were investigated. Both friction coefficients and wear of UHMWPE pins sliding on niobium-titanium-nitride coatings were comparable to the ones on titanium-nitride. The coatings were affected by wear as well (in the range of 0.4-0.7 μm / million pin-on-disc cycles), as profile measurements and XRD data revealed.

The performance of the coatings in terms of wear is sensitive to their composition, microstructure and textural orientation, as well as the presence of defects, such as inclusions of voids and macrodroplets.

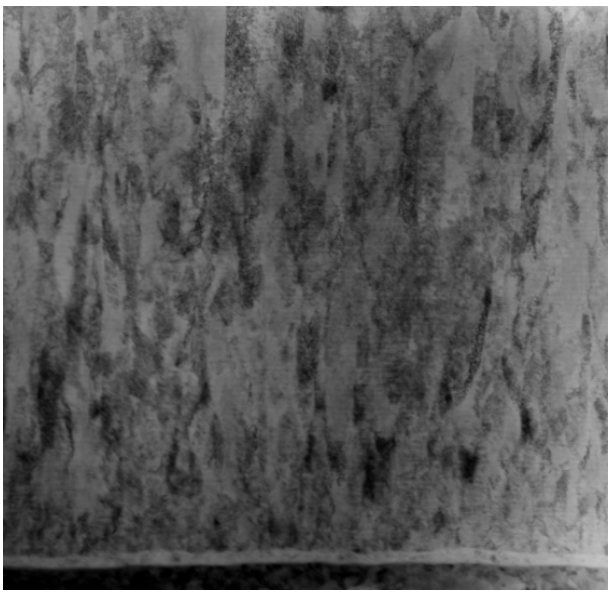

Fig. 1: TEM cross-section of a Nb-Ti-N coating, showing dense columnar growth and a multi-layered structure.

OUTLOOK: Advanced deposition techniques, such as HiPIMS, will introduce the new generation of droplet free coatings for biomedical implants. Tuning the microstructure of the coatings towards an increased toughness will increase their durability beyond the current performance.

Preliminary microstructural investigation of Mg cubes produced by SLM

F Wohlfender[1,2], S Saxer[1], B Wiese[3], J Rüegg[1], A Dietschy[1], R Schumacher[1], M de Wild[1]

[1] *University of Applied Sciences Northwestern Switzerland, School of Life Sciences, Muttenz, CH.*
[2] *University of Basel, Swiss Nano Institute, Basel, CH.*
[3] *Helmholtz-Zentrum Geesthacht, Zentrum für Material- und Küstenforschung GmbH, DE*

INTRODUCTION: The ability to fabricate customized and resorbable metallic implants provides significant improvements in osteosynthesis. We try to combine the benefits of resorbable magnesium alloys with the versatility of the selective laser melting (SLM) process [1]. Preliminary metallographic investigations, SEM and XPS measurements of the starting raw material (spherical Mg powder, d_{50}-value 57 µm) and of the created objects indicate that a surface oxide layer limits the fusion of the powder during the SLM process.

METHODS: 3D Mg objects (Fig. 2a) were built in a SLM Realizer 100 machine (MCP Realizer, Germany). A 100 W continuous wave Ytterbium-fibre laser with a wavelength between 1068 and 1095 nm is used to melt the magnesium powder on a Mg substrate. The chemical surface composition of the Mg powder (AZ91, SFM, Switzerland) was analysed by XPS (PHI 5600, Physical Electronics, USA). For depth profiling, the surface of the embedded powder was repeatedly argon sputtered (600 s, 3 kV, 1.6 µA, $2 \cdot 10^{-8}$ torr) and analysed by XPS.
To reveal the microstructure, polished samples were etched with a 4% Nital solution for 1 min. Comparative images of the polished Mg structures before and after etching were taken with an SEM (TM-3030Plus, Hitachi, Japan). The porosity of the samples was visualized and optically quantified by light microscopy (BX61, Olympus, Japan).

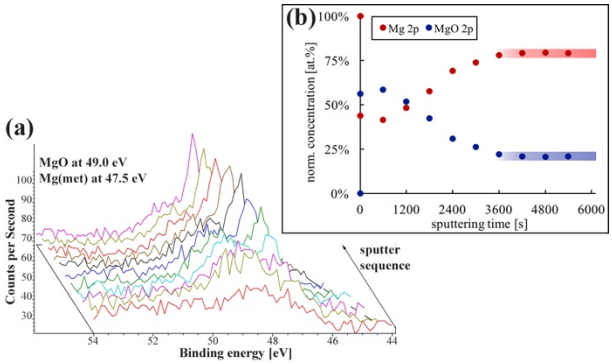

Fig. 1: XPS depth profiling. (a) Stacked Mg 2p spectra of Mg powder during Ar sputtering and (b) depth profiles of the metallic Mg and the MgOxide peaks.

RESULTS: The Mg2p and MgO2p peaks of the powder saturate after 3600 s sputter time (see Fig. 1a and 1b). With the sputter rate of 0.43 pm/s, the thickness of the surface oxide layer was determined as 1.5 nm.
Fabrication of Mg cubes by SLM was successfully achieved within a wide range of process parameters. Although the cubes show a solid appearance (Fig. 2a), a significant inner porosity was found after metallographic preparation (Fig. 2b). Polished and etched cross sections exhibit shell-like structures with inner skeletons (Fig. 2c).

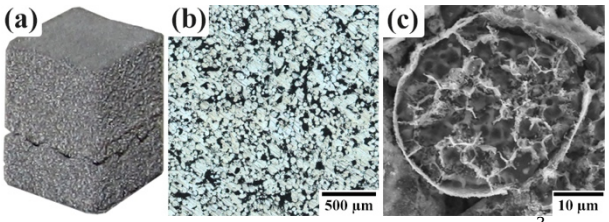

Fig. 2: Mg SLM samples. (a) Photo of (5 mm)^3-cube with subjacent support structure, (b) light microscopy picture of the cross section, (c) after Nital etching, residual shells from the oxide layer were discovered in SEM analysis.

DISCUSSION & CONCLUSIONS: The measured thickness of the Mg oxide layer is in line with literature [2,3]. Melting of the powder particles' oxide layer is found to be a major challenge in the SLM-treatment of Mg [4]. The high porosity of the investigated 3D-structures may correlate with limited fusion of the powder caused by the particles' oxide layer. The shell-like etching residues are supposed to consist of the MgO layer, while the skeletal structures are assigned to the intermetallic phase $Mg_{17}Al_{12}$.

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Glass laser welding – the smart way for hermetic implant and in-body sensor encapsulation

B Scheidegger, N Vogel

GlencaTec AG, Niederwangen, CH

INTRODUCTION: In 2014 GlencaTec AG spun-off from mb-microtec a well-established company in the development and production of micro-components. GlencaTec provides specialized laser micro welding services in a patented room temperature method for advanced hermetic glass encapsulation with significant application for electronic medical implants, stimulators and in-body sensors. Its microfabrication solutions improve manufacturing processes and provide an excellent alternative for microscale sealing of especially glass but also a variety of materials enabling a new category of micro-product portfolios. Alternative manufacturing process are fusion or anodic bonding with the disadvantage of high process temperatures or extraneous materials like titanium (disadvantage of electrical shielding), ceramic (disadvantage of process costs, limitation for miniaturisation and hermetic sealing) or plastic (disadvantage of missing long term hermeticity).

TECHNOLOGY & MATERIAL: GlencaTec's process ensures an implant's high hermeticity and, preserves the integrity of embedded elements by protecting them from moisture. GlencaTec's room temperature glass welding technology can successfully be performed with no additive material which helps to avoid biocompatibility issues. The welding is done at the material interface so that the surface or transparent top layer is undamaged during the process. Hermetically welded wall thickness can go down to 0.02 mm, see Fig. 1.

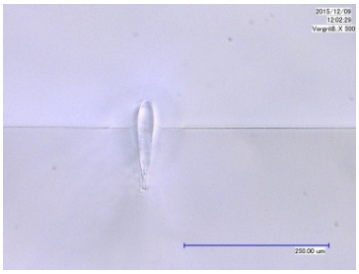

Fig. 1: Images of a laser welding seam (planar glass encapsulation process).

The benefits of glass include durability, electrical resistance, high melting point, chemical inertness, transparency and capacity for optical transmission in visible, ultra-violet and near-infrared light, making it a highly desirable cost effective material in several industries. Due to the low attenuation coefficient of glass a prominent advantage for implants is superior transmission of RF signals for reading or powering.

Cylindrical Glass Encapsulation (CGE)

A CGE implant typically consists of one single tubular glass component. The dimensions of today's CGE implants make them more and more injectable, with sizes as small as D: 1 mm, L: 10 mm with wall thicknesses of just 0.1–0.6 mm, see Fig. 3.

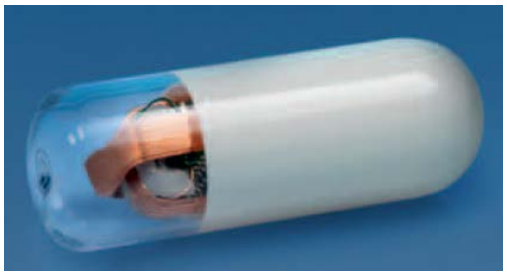

Fig. 2: Images of a Cylindrical Glass Encapsulation for diagnosis of the digestive system (Motilis Medica, D: 8.25mm; L: 25 mm).

Planar Glass Encapsulation (PGE)

A planar glass encapsulated implant is flat. The PGE process provides for high feature lead (feedthroughs) density in extremely small implants and high hermeticity. Feedthroughs are integrated in the bottom or/and cover glass shell of the encapsulation package. Dimensions of the PGE can be as small as H: 3 mm, L: 3 mm with a wall thickness from 0.3 mm to 1.5 mm, see Fig. 3.

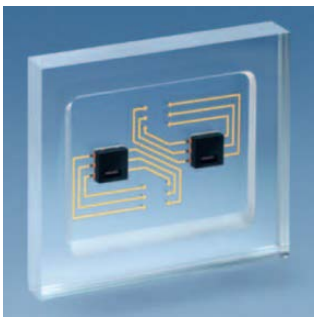

Fig. 3: Example of a Planar Glass Encapsulation (GlencaTec with humidity sensors, *L: 26 mm; H: 23mm; T: 5.1mm).*