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IMPLANTS

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Materials and Surface Technology for Implants

28/29 April 2021

Online Conference

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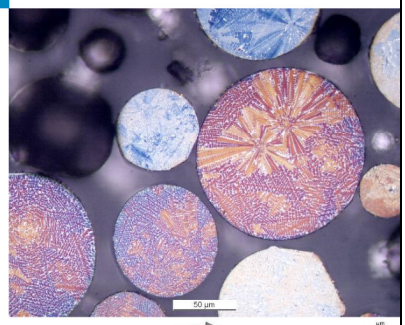

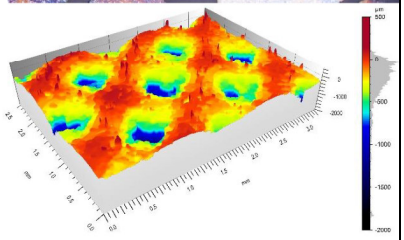

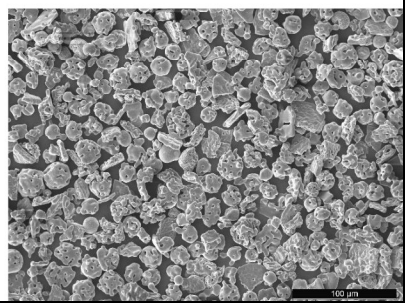

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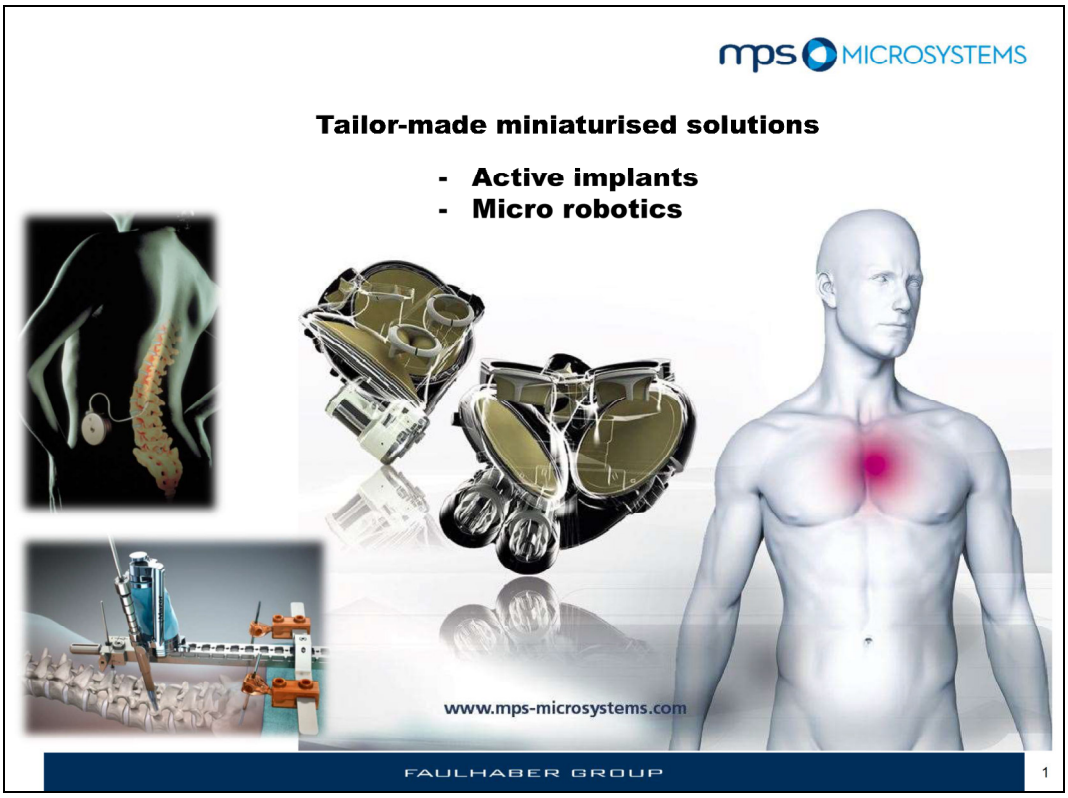

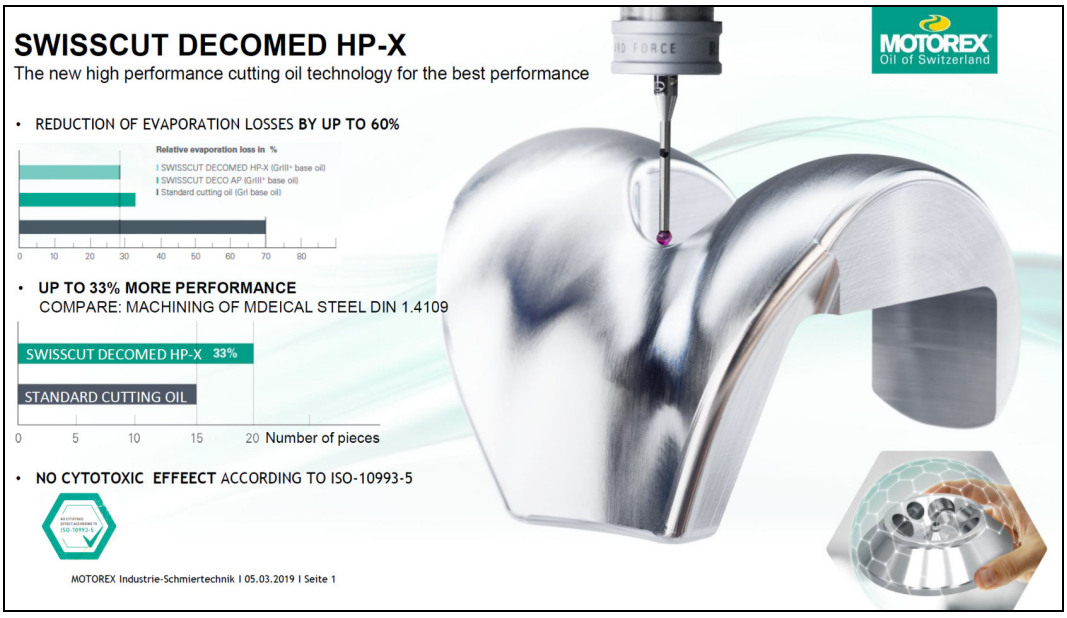

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Meeting Program Wednesday 28th April 2021

	08:00 *Welcome*
	08:15 – 08:45 Session 1: *Overview* Chairperson: Dr. Lukas Eschbach
08:15	Keynote 1: Dr. med. Daniel de Menezes, Spitalzentrum Biel/Bienne, Switzerland: *Improving efficiency and results of prosthetic joint surgery: Role of technology and materials from the perspective of a surgeon*
	08:45 – 09:45 *Poster and Exhibition (Breakout Session) / Virtual Coffee Break*
	09:45 – 11:30 Session 2: *Materials and Surfaces* Chairperson: Prof. Dr. Michael de Wild
09:45	Keynote 2: Beat Lechmann, DePuy Synthes, Zuchwil, Switzerland: *Trends related to materials, surfaces and technologies*
10:15	Prof. Dr. med. dent. Dr. rer. nat. Jens Fischer, University Center for Dental Medicine Basel, Switzerland: *What endosseous surface is appropriate for dental zirconia implants?*
10:35	Prof. Dr. Marta Monjo, University of Balearic Islands, Palma de Mallorca, Spain: *Multifuncional properties of Quercitrin coated porous Ti-6Al-4V implants for orthopaedic applications*
10:55	Dr. Dirk Hegemann, Empa, St. Gallen, Switzerland: *Rapid active, non-releasing antibacterial coatings based on Ag nano islets deposited on TiOx films*
11:15	Session discussion, Q&A roundup
	11:30 – 13:30 *Lunch Break / Virtual Meetings*
	13:30 – 15:40 Session 3: *Medical Device Regulation (MDR)* Chairperson: Francisco Faoro
13:30	Keynote 3: Shokoufeh Khodabandeh, Institut Straumann AG, Basel, Switzerland: *Medical Device Regulations – MedTech in EU beyond May 2020*
14:00	Dr. Marta Swierczynska, SFL Regulatory Affairs & Scientific Communication GmbH, Basel, Switzerland: *Challenges for implants under the new MDR*
14:20	Stefano Adami, Confinis AG, Sursee, Switzerland: *Additive Manufacturing of custom made and mass production of implants – Overview of regulatory and quality challenges posed by the MDR*
14:40	Dr. Ulrich Hofer, Integrated Scientific Services ISS AG, Biel, Switzerland: *Lean PMCF studies using real-world data*
15:00	Keynote 4: Dr. Richard Curno & Philippe Etter, Medidee Services SA, Lausanne, Switzerland: *Lessons learned from recalls*
15:30	Session discussion, Q&A roundup
	15:40 – 16:40 *Poster and Exhibition (Breakout Session)*

Meeting Program Thursday 29th April 2021

	08:00 *Welcome*
	08:00 – 09:30 Session 4: *Smart Devices & Analytics* Chairperson: Dr. Simon Berner
08:00	Keynote 5: Dr. Roman Dittmar, Institut Straumann AG, Basel, Switzerland: *Smart devices – Implants 4.0*
08:30	Ana Isabel Costa, Center of MicroElectroMechanical Systems, University of Minho, Guimarães, Portugal: *Highly porous Ti as bone substitute: triboelectrochemical characterization of highly porous Ti under fretting-corrosion conditions*
08:50	Dr. Olivia Kettner, Anton Paar GmbH, Graz, Austria: *Zeta potential of implant surfaces - correlation with hydrophilicity and porosity*
09:10	Session discussion, Q&A roundup
	09:30 – 10:30 *Poster and Exhibition (Breakout Session) / Virtual Coffee Break*
	10:30 – 12:30 Session 5: *Additive Manufacturing* Chairperson: Dr. Martin Stöckli
10:30	Keynote 6: Daniel Seiler, Hochschule für Life Sciences FHNW, Muttenz, Switzerland: *Trends in medical AM*
11:00	Jean-Jacques Fouchet, Z3DLAB SAS, Montmagny, France: *ZTi-Med®: a potential replacement for Titanium in medical*
11:20	Rashid Tikhilov, Vreden Russian Research Institute of traumatology and orthopedic, S-Petersburg, Russia: *The experience of using custom-made implants for gross acetabular defects*
11:40	Donatien Campion, 3D Medlab, Marignane, France: *4D Printing of expandable Spinal Cages: Development and applications*
12:00	Session discussion, Q&A roundup
	12:15 – 14:00 *Lunch Break/ Virtual Meetings*
	14:00 – 16:30 Session 6: *Cleaning* Chairperson: PD Dr. habil. Christiane Jung
14:00	Keynote 7: Peter Huonker, Früh Verpackungstechnik AG, Fehraltorf, Switzerland: *Industrial sterilization methods – an overview*
14:30	Lise Vanderkelen, Nelson Labs NV, Heverlee, Belgium: *Don´t forget to think about family grouping before doing reprocessing validations of medical devices and instruments!*
14:50	Elena Stübi, RMS Foundation, Bettlach, Switzerland: *Cleaning validation for instrument reprocessing: normative background and the test methods*
15:10	Dr. Sc. Marco Furlan, eCO2, Taverne, Switzerland: *A novel post-treatment process of medical and pharmaceutical material using scCO2*
15:30	Keynote 8: Ali Madani, AVICENNE, Paris, France: *Orthopedic market perspectives - Orthopedic contract manufacturing markets*
16:00	Session discussion, Q&A roundup
	16:15 *Meeting End*

What endosseous surface is appropriate for dental zirconia implants?

J. Fischer, N. Rohr

Department of Reconstructive Dentistry, University Center for Dental Medicine Basel, CH

INTRODUCTION: Dental implants are a valuable treatment option to replace missing teeth. Titanium is currently the material of choice. However, a general dispute on the biocompatibility of metals induced the development of metal-free options. Today, zirconia implants are rated a viable alternative to titanium implants in dentistry.

It is generally accepted that the surface roughness of the endosseous part of dental implants is a crucial parameter for osseointegration, meaning the direct structural and functional connection between living bone and surface of the load-bearing implant. The current dogma states that implants should exhibit a moderately rough surface of R_a = 1-2 µm to ensure a fast and long-term osseointegration [1].

However, data of a two-center clinical trial with a zirconia implant (ceramic.implant, Vita, Bad Säckingen, Germany) implies that a smooth surface may be as attractive to living bone as a rough surface because the bone level around the implants was equally distributed on the moderately rough endosseous and the smooth transmucosal part [2].

Aim of the study was to assess osteoblast and fibroblast behavior on smooth and moderately rough surfaces in comparison to biofilm formation.

METHODS: Cell culture experiments with osteoblasts (*MG-63*), fibroblasts (*HGF-1*) and a three-species biofilm (*S. sanguinis, F. nucleatum, P. gingivalis*) on zirconia specimens were performed. Zirconia discs (Ø 13 mm) with surface characteristics identical to those of the zirconia implant ceramic.implant (Vita) were used (R_a[rough surface] = 1.35±0.07 µm; R_a[smooth surface] = 0.10±0.00 µm).

Cell viability of both cell types was assessed. With osteoblasts cell spreading and gene expression of alkaline phosphatase, collagen type I, and osteocalcin were measured. Biofilm formation was quantified using safranin staining.

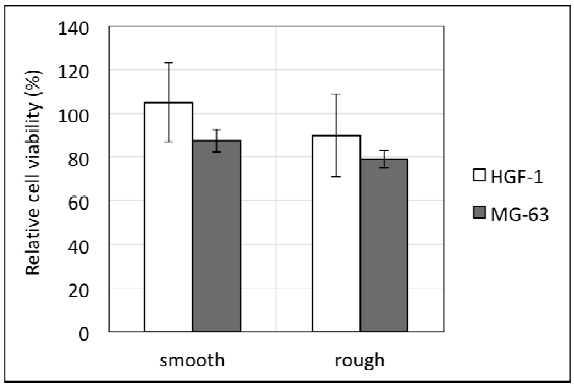

Fig. 1: Mean relative cell viability of fibroblasts and human osteoblasts after cultivation for 24 h.

RESULTS: Gene expression of osteoblasts was similar on moderately rough and smooth surfaces. Cell spreading of osteoblasts was significantly increased on the smooth surface by a factor of 1.65. Cell viability was significantly increased on smooth surfaces for osteoblasts and fibroblasts. (Fig. 1). Biofilm formation was significantly less on smooth compared to moderately rough surfaces.

DISCUSSION & CONCLUSIONS: Cell cultures revealed no benefit of the moderately rough over the smooth surface, suggesting that for zirconia a smooth surface might be at least as attractive to osteoblasts and fibroblasts and additionally reduces biofilm formation. In regard to production costs a smooth surface would be advantageous. However, the present results do not provide any information on how primary stability and time to osseointegration is affected by a smooth surface. Hence, a prospective controlled clinical trial with a smooth endosseous surface is of high interest.

REFERENCES

[1]Albrektsson T, Wennerberg A. On osseointegration in relation to implant surfaces. Clin Implant Dent Relat Res 2019;21:4-7.
[2]Rohr N, Balmer M, Jung RE, Kohal RJ, Spies BC, Hämmerle CHF, Fischer J. Influence of zirconia implant surface topography on first bone implant contact within a prospective cohort study. Clin Oral Impl Res, revised manuscript submitted.

Multifuncional Properties of Quercitrin Coated Porous Ti-6Al-4V Implants for Orthopaedic Applications

M.A. Llopis-Grimalt[1,2], A. Arbós[3], M. Gil-Mir[3], A. Mosur[4], P. Kulkarni[5], A. Salito[4], J.M. Ramis[1,2*] and M. Monjo[1,2*]

[1] *Group of Cell Therapy and Tissue Engineering, Research Institute on Health Sciences (IUNICS), University of the Balearic Islands,* [2]*Balearic Islands Health Research Institute (IdISBa) and* [3]*NuMat Medtech, S.L., Palma, ES.* [4]*Orchid Orthopedics, Baden-Dätwill, CH.* [5]*Orchid Orthopedics, Memphis, USA*

INTRODUCTION: One strategy to improve the outcome of orthopaedic implants is to use porous implants with the addition of a coating with an antibacterial biomolecule. In previous studies, a coating method by wet chemistry using the flavonoid quercitrin was developed [1]. We demonstrated that quercitrin coated surfaces were bioactive, presenting osteogenic, osteopromotive, antifibrotic and antibacterial properties [2, 3]. In this study we aimed to produce and test the biocompatibility and bioactivity of quercitrin coated porous Ti-6Al-4V implants on osteoblastic cells and S. epidermidis to demonstrate multifunctional properties of the coating.

METHODS: Porous Ti-6Al-4V implant were produced by 3D printing and further functionalized with quercitrin by wet chemistry. Implants were characterized in terms of porosity and mechanical testing, and the coating with quercitrin by fluorescence staining. Implant cytocompatibility and bioactivity was tested using MC3T3-E1 preosteoblasts by analyzing cytotoxicity, cell adhesion, osteocalcin production and alkaline phosphatase (ALP) activity under control and under bacterial challenging conditions using lipopolysaccharide (LPS). Finally, the antibacterial properties of the implants were studied using Staphylococcus epidermidis by measuring bacterial viability and adhesion.

RESULTS: Porous implants showed a pore size of about 500 µm and a porosity of 52 %. The coating was homogeneous over all the 3D surface and did not alter its mechanical properties of the Young modulus. Quercitrin coated implants showed higher cytocompatibility, cell adhesion and osteocalcin production compared to control implants. Moreover, higher ALP activity was observed for the quercitrin group under both, normal and bacterial challenging conditions. Finally, S. epidermidis live/dead ratio and adhesion after 4 hours of incubation was lower on quercitrin implants compared to the control.

DISCUSSION & CONCLUSIONS: Quercitrin functionalized porous Ti-6Al-4V implants present a great potential as an orthopaedic porous implant that decreases bacterial adhesion and viability while promoting bone cell growth and differentiation.

ACKNOWLEDGEMENTS: This work was supported by "Direcció General d'Innovació i Recerca del Govern de les Illes Balears" co-funded ERDF European Regional Development Fund, (Fondos FEDER) (PROCOE15/2017), the Ministerio de Educación Cultura y Deporte (contract to M.A. L.G; FPU15/03412) by the Instituto de Salud Carlos III, Ministerio de Economía y Competividad, co-funded by the ESF European Social Fund and the ERDF European Regional Development Fund (MS16/00124; IEDI-2017-00941).

REFERENCES: [1]Córdoba, A.; *et al.* Bioinspired Quercitrin Nanocoatings: A Fluorescence-Based Method for Their Surface Quantification, and Their Effect on Stem Cell Adhesion and Differentiation to the Osteoblastic Lineage. ACS Appl. Mater. Interfaces 2015, 7, 16857–16864. [2]Córdoba, A.; *et al.* Flavonoid-Modified Surfaces: Multifunctional Bioactive Biomaterials with Osteopromotive, Anti-Inflammatory, and Anti-Fibrotic Potential. Adv. Healthc. Mater. 2015, 4, 540–549. [3]Gomez-Florit, M.; *et al...* Quercitrin-nanocoated titanium surfaces favour gingival cells against oral bacteria. Sci. Rep. 2016, 6, 22444.

Rapid Active, Non-releasing Antibacterial Coatings Based on Ag Nano Islets Deposited on TiOx Films

D. Hegemann[1], Q. Ren[2], F. Zuber[2], F. Pan[2], B. Hanselmann[1], S. Gaiser[1], K. Maniura[2], K. Ruffieux[3]

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INTRODUCTION: Healthcare acquired infections (HAI) are a major burden for patients and healthcare costs. A large part of HAI is associated with percutaneous medical devices such as venous and urinary catheters as well as respiratory support devices [1]. To reduce HAI, critical devices are equipped with antibacterial properties, e.g. by addition of silver based on the antibacterial effect of Ag^+ ions.

To avoid possible issues related to metal release, photo-generated catalytically active oxygen vacancy sites in TiO_2 can also be considered as antibacterial surfaces. Most of all, stabilized O vacancies can be obtained by doping with a dissimilar metal generating electron-hole pairs with narrow band gaps [2]. Here, plasma technology is investigated to deposit Ag nano islets on TiOx films, making use of deposition conditions that directly generate O vacancies [3].

METHODS: For plasma deposition, a low pressure pilot-scale reactor was used allowing plasma cleaning/activation and magnetron sputtering from Ti and Ag targets in a one-step process. Thus, Ag nano islets with 4 nm average thickness have been deposited on TiOx films as catalytically active antibacterial surfaces as well as substoichiometric TiOx thin films and Ag 4 nm islands as references. Various substrate materials have been selected such as Si wafers and glass slides for characterization as well as medical grade thermoplastic polyurethane (TPU) and silicone materials as used for ureteral devices and catheters. All coatings showed excellent adhesion following an appropriate cleaning method.

Antibacterial efficacy was assessed with a modified method similar to ASTM E2180 but using a bacterial suspension instead of an agar slurry to detect volume activity over 10-60 min. Furthermore, an agar touch assay with 1, 10, and 30 min sample contact and diffusion assay with overnight incubation have been applied to observe contact killing and exclude leaching effects. *E. coli* DSMZ30083 and *S. aureus* MRSA were used as bacterial strains. Cytotoxicity of the plasma coatings was investigated according to ISO-norm 10993-5 showing no cytotoxic effects. Generation of reactive oxygen species (ROS) was detected using a fluorescent dye.

RESULTS: The non-releasing TiOx/Ag 4 nm plasma coatings and references have been investigated for ROS generation and related antibacterial activity (Figure 1) when stored in the dark, simulating implants or inserted catheters.

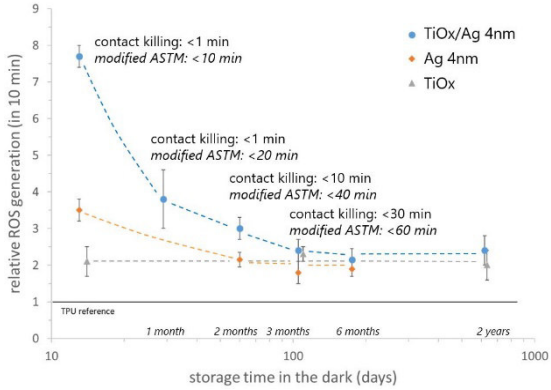

Fig. 1: ROS generation relative to uncoated TPU. For TiOx/Ag 4 nm coatings the time is indicated to show antibacterial activity yielding a reduction of more than 10^3 CFU ml^{-1}.

Initially high ROS generation enables rapid active surfaces by contact killing. Lowered ROS levels over time still yield a levelled antibacterial efficacy demonstrating stabilized O vacancies. The coatings can be reactivated by light exposure or plasma activation.

DISCUSSION & CONCLUSIONS: Plasma coating of Ag nano islets on TiOx yield non-releasing antibacterial surfaces suited for implants due to adjusted ROS generation.

ACKNOWLEDGEMENTS: Funding by Innosuisse, CH, is acknowledged (project no. 30078.1 IP-LS).

REFERENCES: [1]P.W. Stone et al. 2009 *Expert Rev. Pharmacoecon. Outcomes Res.* 9 417. [2]X. Pan et al. 2013 *Nanoscale* 5 3601. [3]M. Amberg et al. 2015 *Nanomed. Nanotechnol. Bio. Med.* 11 845.

European Medical Device Regulation (MDR 2017/745) – MedTech in EU beyond May 2021

S. Khodabandeh

Institut Straumann AG, Basel, CH

INTRODUCTION: The European Medical Device Regulation (MDR) will fully apply to the entire medical device industry as of 26th of May 2021. While this regulation aims at increasing safety, and transparency for the EU population, the impact on innovation and access to the state-of-the-art medical devices remains uncertain.
The new European Medical Device Regulation replaces the exiting Medical device directive which has been in place since 1993. The new regulation brings more restrictive requirements for sufficient clinical data, higher focus on active post-market surveillance, higher transparency via Eudamed database and higher scrutiny of the notified bodies among other changes.

DISCUSSION: High profile cases such as the P.I.P scandal, had led to a political pressure to make the regulation stricter to protect patients.

Disappearing notified bodies: In the EU, the surveillance of medical device manufacturers and approval of medical devices relies on a system of private notified bodies as opposed to a central or governmental function as seen in most other countries (e.g. FDA in US). Under MDR the scrutiny of these notified bodies has been increased significantly, leading to disappearance of some notified bodies. Despite the decline in the absolute number of the notified bodies, it should be noted that some of the gap will be complemented by the increase in size of the surviving ones. However, until full implementation of MDR in 2025, notified bodies will have to continue their surveillance activities under MDD in parallel to MDR, leading to a system overload in the next four years. This can cause delays in review processes, leading to delays in supply of medical devices in the EU.

Focus on Implants: Uncertainty about long-term effects of implants and implantable materials has translated to a much higher level of requirements for implantable medical devices. More specific and detailed requirements for sufficient clinical data and limitations in the use of equivalency with existing products on the market, may push manufactures to select other markets (e.g. USA) as their initial market prior to entering EU.

Catching up with technology: Medical devices cover a wide range of products and technologies that have developed greatly in the course of the past 20 years. Therefore, the introduction of MDR also allowed the commission to expand/include requirements to address the need for new generations of the devices including devices that contain nano materials and software. Due to high scientific uncertainty about the risks and benefits of nanomaterials, MDR requires such products to be assessed with highest scrutiny. As software becomes more and more integral part of our lives, MDR extends the requirements for devices that are or contain software. While previously most software would be self-declared, under MDR almost all software devices require notified body conformity assessment.

As a result, the increase in cost and efforts to bring new devices into the EU may cause a shift in the industry focus to; a) reduce risk by focusing on established technologies and minor modifications of legacy products, instead of investing in innovation or b) first enter other markets (e.g. USA) prior to entering EU. Either of those would reduce/delay access of EU patients to innovative medical devices but at the same time also protect EU patients from unknown long-term risks of such technologies.

REFERENCES: Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices.

Challenges for implants under the MDR

M. Swierczynska

SFL Regulatory Affairs & Scientific Communication GmbH, Basel, CH

INTRODUCTION: The application of the European Medical Device Regulation (MDR) impacts the development, CE-marking, and maintenance of implantable medical devices.

METHODS: The MDR places more emphasis on a life-cycle approach compared to the Medical Devices Directive. In addition to re-classifying some medical devices, it introduces new procedures within the conformity assessment process, provides more prescriptive guidance on the technical documentation, enhances supply chain oversight, and increases clinical data requirements. With the introduction of a new Unique Device Identification (UDI) System and implant cards, as well as establishing the Eudamed database, the MDR increases transparency and enhances the effectiveness of post-market surveillance. As a result of these increased requirements, to ensure MDR compliance, medical device manufacturers need to devote more resources to quality assurance, preparation of the device documentation, and, in certain situations, conducting clinical investigations to generate additional clinical data.

The MDR's risk-based classification depends largely on the intended purpose of the device as stated by the manufacturer. However, the classification of an entire device can be affected due to e.g., technological changes in the device components or the addition of new software-based functionalities. For instance, using nanomaterials to increase implant biocompatibility can influence device classification under the newly established Annex VIII Rule 19, which states that devices incorporating or consisting of nanomaterials should be classified based on the potential for internal exposure of the body to the nanomaterial.

Changes affecting device components can impact the conformity assessment pathway as well. New materials (e.g., substances, nanomaterials) for implants need to be compliant with the General Safety and Performance Requirements (GSPRs, MDR Annex I). The MDR introduces major changes to several GSPRs including the need for increased information on the chemical, physical and biological properties of the materials used in the device (GSPR 10), changes in the evaluation of the adsorption of substances (GSPR12.2), as well as specific requirements regarding nanomaterials (GSPR 10.6) and the information on materials for implants (GSPR 23.4u). The MDR also introduces a clinical evaluation consultation by an expert panel as a mandatory procedure during the conformity assessment process of Class III implantable devices.

CONCLUSIONS: Identification and implementation of changes mandated by the MDR require the involvement of almost all functions and a well-coordinated adaption of internal processes. Accordingly, manufacturers must subject their portfolio, documentation, and development process to a stringent gap analysis and implement a remediation plan to ensure timely MDR compliance and secure business continuity.

This presentation will provide details about MDR requirements and their implementation, putting emphasis on those requirements specific to implantable medical devices.

Additive Manufacturing of custom made and mass production of implants –Overview of regulatory and quality challenges posed by the MDR

S. Adami

confinis AG, Sursee, CH

INTRODUCTION: The Medical Device Regulation 2017/745 (MDR) changes the definition of custom-made devices by specifying that 'devices which are mass-produced by means of industrial manufacturing processes in accordance with the written prescriptions of an authorized person shall not be considered to be a custom-made'.
Since 3D printers are industrial manufacturing processes, this means that manufacturers need to identify specific criteria to define when a device is "mass-produced".
This work provides a proposed approach for defining a 3D printed custom-made device based on the current status of interpretation of the MDR.

DISCUSSION: Technological progress has allowed easier access and implementation of personalized medical devices. In the orthopedic industry it is now possible to produce implants and instruments that are individualized, for example, using additive manufacturing (3D printing) methods based on patient CT scans.
In parallel, the regulatory framework for custom made devices and in general for high-risk devices was found to be inadequate to prevent big scandals and the MDR was introduced with the aim of improving patient safety by increasing the regulatory requirements and the level of scrutiny.
In the case of custom made, the MDR introduced specific restrictions around devices that 'mass-produced by means of industrial manufacturing processes'. The MDCG 2021-03 0 clarifies that state-of-the-art industrial processes can be used to manufacture a custom made as soon as this is not mass-produced.
According to IMDRF 0 a mass-produced device is *based on standardized dimensions/designs*; is *not designed for a particular individual*; and is typically *produced in a continuous production run or homogenous batch*.
If the second criteria can be self-explanatory, the other two need more discussion.
A typical characteristic of a custom made is that it is not produced in batches, however companies typically produce more than one part to compensate for potential errors during production. Furthermore, it is a good practice to provide the surgeon with at least two devices to reduce potential risks during surgery (e.g. device falls on the floor). Moreover, in some instances, to treat particular cases, different devices are designed and produced to enable the surgeon to delay the choice of the best one at the time of surgery.
Companies need to establish specific criteria to define when a device is mass-produced, such as limit the number of a batch (e.g. to 5 pieces as proposed by FDA 0) and allow different designs or sizes to treat a specific case by including this requirement in the written prescription by the surgeon.
Custom made are in part based on standard designs, but they need specific characteristics that standard devices to not have. In such cases it is important to argue why the custom made is not a 'patient-matched medical device' or an 'adaptable medical device'.

CONCLUSIONS: Additive manufacturing techniques are not automatically qualifying a device as a custom made as these are nowadays used more and more also for standard production. Therefore, custom made manufacturers must identify appropriate criteria to define when a device is meeting the definition of custom made and rule out any doubts that these devices are mass-produced by means of industrial manufacturing processes.

REFERENCES: [1]MDGC 2021-3 - Questions and Answers on Custom-Made Devices - March 2021. [2]IMDRF/PMD WG/N49 FINAL: 2018 - Definitions for Personalized Medical Devices - October 2018. [3]FDA guidance - Custom Device Exemption – September 2014.

Lean PMCF studies using real-world data

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INTRODUCTION: Real-world data (RWD) are a possible source of clinical information manufacturers can use to meet Post-Market Clinical Follow-Up (PMCF) requirements under the MDR. Recognized advantages of RWD over clinical trials are a larger and more heterogenous patient population, broader range of end-users and the provision of long-term information about device performance and safety. However, RWD only come into their own if the underlying study designs adhere to the same scientific standards as clinical trials.

METHODS: RWD may be derived from electronic health records, surgery reports, registries, administrative claims data, collected from mobile devices or are patient-generated.
PMCF studies based on RWD should only use anonymized patient data and not interfere with a health care provider's (HCP) standard protocol for routine application of the device. Choice of an appropriate endpoint, e.g., a rate (failure, success, specific event) is crucial in that respect.
The selection of HCPs should be representative of the end-users of a device, e.g., not be restricted to high-volume surgeons or to clinicians involved in the product development.
Sample sizes must be statistically justified. This implies that manufacturers have an expectation regarding the real-world performance of their device, which is benchmarked against a reference value derived from the literature or from a competitor device.

STATE OF AFFAIRS: Regulators consider RWD a valid component of the clinical information used in regulatory decision-making, provided the data are acquired and analysed in line with scientific principles. RWD are as well part of the External Evidence (EE) used in clinical studies to reduce their length and bring new safe and effective technologies to market sooner. Whether HCPs can handle an increasing demand for supply of RWD remains to be seen. If the use of RWD is to be promoted, device manufacturers need more direct access to the sources of RWD, which is in conflict with current data protection regulations.

REFERENCES:

MDCG 2020-6. Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC. A guide for manufacturers and notified bodies, April 2020.

MDCG 2020-8. Post-market clinical follow-up (PMCF) Plan Template. A guide for manufacturers and notified bodies, April 2020.

FDA. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices. Guidance for Industry and Food and Drug Administration Staff, August 2017.

Medical Device Innovation Consortium (MDIC). External Evidence Methods (EEM) Framework. Draft, January 2021.

SMART Devices – Implants 4.0

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INTRODUCTION: This keynote lecture discusses the evolution of medical implants from mere inert "hardware" that primarily functions to bear mechanical loads to the future of sensing and measuring implants and implants as theranostic (therapy and diagnosis) devices. Goal is to highlight that the next generation of medical implants will incorporate sensor technology leading to new clinical workflows and business models and ample opportunities for collaboration between traditional device manufacturers, sensor technology and software / data management companies.

DEFINITION AND EXAMPLES OF SMART DEVICES: We provide a definition of SMART (Sensing Measuring and Advanced Reporting Technologies) devices including examples of some past and recent developments and a vision of how SMART devices may (continue to) enter and revolutionize traditional implantology. This is followed by a review on key trends and drivers creating (unmet) needs that may be addressed using SMART devices such as evidence based medicine, patient compliance and engagement and theranostics. Moreover, advances in both sensor technology and data processing / data management are highlighted that may allow unobtrusive continuous sensing combined with diverse technologies to reshape the clinical workflow for both acute and chronic disease management. We discuss examples of SMART devices applied both in orthopaedics and dentistry. Finally, we discuss the opportunities of strategic partnerships and open innovation to bring together traditional device manufacturers, sensor technology and software and data management companies in order to join forces and co-develop the implants of the future.

FUTURE TRENDS: Technical advances have supported the evolution of medical implants to SMART implants, i.e. from inert hardware towards preventative, predictive, personalised and participatory devices. The sensing technologies discussed in this keynote lecture and their future evolution will play a key role in realising the goal of unobtrusive continuous sensing for earlier diagnosis of diseases and improved monitoring of therapy success. Moreover, clinical workflows for both acute and chronic disease management will be reshaped due to the new "role" of SMART implants as (continuous) sensors of patient health and disease state. Finally, due to the interdisciplinary nature of SMART devices, ample opportunities exist for collaboration and open innovation. Most traditional device makers do not possess the required expertise on sensor technology and/or data processing / management. Vice versa, most software and sensor technology companies are not experts in medical implants and therefore joining forces and developing SMART devices together may be an attractive way forward to mitigate risks and benefit from the respective expertise of the development partners.

Highly porous Ti as bone substitute: triboelectrochemical characterization of highly porous Ti under fretting-corrosion conditions

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INTRODUCTION: Implants require long-term stability and rapid healing however, the existing Ti-based implant materials do not meet completely the current expectation. Lack of bioactivity, wear debris, and the biomechanical mismatch between the implant and the bone are still the major problems in the prostheses field and can cause aseptic loosening, fibrous encapsulation and osteolysis [1]. Macro-porosity in the Ti implant was presented as a beneficial way to reduce the biomechanical mismatch, in order to approach the value of Young's modulus of the implant to the one found in the bone [2]. It also allowed the possibility of ingrowth of new bone tissue inside of the pores [3]. The study of simultaneous wear and corrosion (tribocorrosion) is one of the most important aspects of the biomedical industry. There are micro-motions in the points of the implant fixation, leading to debris and ion release by fretting corrosion. This work aimed to investigate fretting corrosion behaviour of highly-porous Ti intended for orthopaedic applications.

METHODS: Highly-porous Ti samples (Ø = 12 mm) were processed by powder metallurgy with space holder technique. Characterization of the macro-porosity was performed. Fretting corrosion tests on highly-porous Ti, during 16 hours, were performed with a substantial range of loads. Electrochemical data was continuously monitored with a potentiostat connected to the fretting corrosion device where linear voltage displacement transducer sensors on the device were in charge of controlling a displacement of ± 40 µm sinusoidal displacement.

RESULTS: Concerning highly-porous Ti/Ti alloy contacts, several mechanical responses were obtained, from gross slip under low normal load until partial slip under high load. The threshold was highlighted.Friction (COF) decreased with increasing normal load. In addition, the same trend was assessed for dissipated energy, and that was not in accordance with dense/dense materials contacts behaviour. Despite the high amount of metal area exposed to the electrolyte (due to porosity), a decrease in the potential was observed, especially for the extreme loads, even if stick phenomenon was occurring.

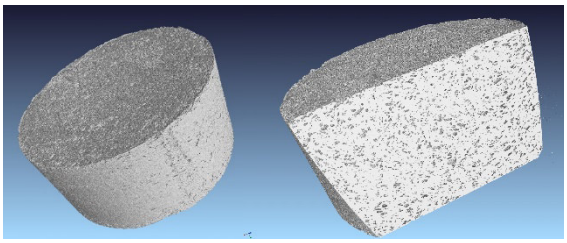

Fig. 1: Three-dimensional tomographic reconstructions of highly-porous Ti sample.

DISCUSSION & CONCLUSIONS: The surface morphology of the highly porous Ti was mostly preserved after 16 hours of fretting-corrosion solicitations. The benefits of porous titanium seem promising for replacing some metallic parts well used in dentistry and implants field.

REFERENCES: [1]Geetha *et al*., Prog. Mater. Sci. 54 (2009) 397–425. [2]Bansiddhi *et al.*, Woodhead Publishing Limited, 2014. [3]Alves *et al.*, J. Biomed. Mater. Res. Part B - Appl. Biomater. 107 (2019) 73–85.

ACKNOWLEDGEMENTS: This work was a result of the project Operation NORTE-08-5369-FSE-000051 supported by NORTE 2020, under the PORTUGAL 2020 Partnership Agreement, through the European Social Fund (ESF), and M-ERA-NET/0001/2015 project supported by FCT.

Zeta potential of implant surfaces – correlation with hydrophilicity and porosity

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INTRODUCTION: The zeta potential is driving the electrostatic interaction at the material-water interface. The attraction of proteins by an implant surface as a precursor for cell growth, or the repulsion of bacteria to prevent inflammation, may be predicted if knowing the zeta potential.

Surface functional groups, which introduce charge depending on their nature and the pH of the aqueous surroundings of an implant, are also determining the surface hydrophilicity. A correlation between the zeta potential and the water contact angle, which is commonly used to describe material hydrophilicity, seems feasible and is indeed observed for a series of alike materials.

Sample porosity contributes to the zeta potential analysis by means of ionic conductance, which is introduced by water (and water-borne ions) inside pores. The zeta potential indicates the effect of surface porosity even of thin-film coatings, which is otherwise difficult to assess.

Here we report on the assessment of the interfacial charge at titanium (oxide) surfaces and their interaction with proteins by the surface zeta potential. We attempt to derive qualitative information about surface hydrophilicity and sample porosity from the obtained zeta potential results.

METHODS: The zeta potential at the solid-water interface is calculated from the measurement of the streaming potential (SurPASS, Anton Paar, Austria). The principle of the streaming potential is based on the flow of a test solution through a capillary channel created between material surfaces.

Disks (15 mm diameter) of cp titanium were modified by a hydrothermal (HT) growth of anatase nanocrystals [1]. The zeta potential of cp Ti, HT-treated Ti, and Ti after UV exposure was determined using the adjustable gap cell for disks.

RESULTS: Fig. 1 shows the zeta potential of cp Ti and HT-treated Ti after UV exposure in the range between the physiological pH and the materials' isoelectric point. The effects of surface modification and UV activation are clearly visible. Adsorption of albumin (BSA), however, does not distinguish between these surfaces. Only the recording of adsorption kinetics (data not shown) reveals a slightly faster attraction of BSA towards the photochemically activated TiO_2 surface.

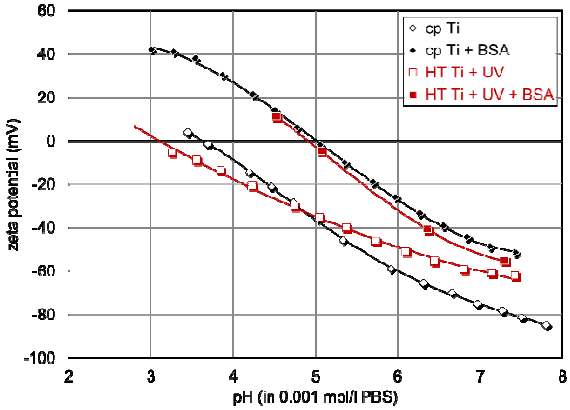

Fig. 1: pH dependence of zeta potential for cp Ti and HT- and UV-treated Ti before and after BSA adsorption.

DISCUSSION & CONCLUSIONS: The streaming potential method enables the analysis of the zeta potential directly at the surface of cp and modified titanium disks, which serve as a model substrate for the study of cell growth and proliferation. Although the net information of the zeta potential reveals only marginal differences between cp and HT-treated Ti, the detailed analysis reveals the transfer from an electrically conductive to a non-conductive surface upon HT growth of a thin-film coating of anatase, and an increase in surface hydrophilicity after UV activation of the TiO_2 top layer. The combination with protein adsorption (kinetics) studies using the zeta potential as an indicator for the increasing surface coverage of Ti and TiO_2 by BSA completes the characterization of the effectiveness of surface treatments.

REFERENCES: [1]Lorenzetti et al., Biomed. Mater. 10, 2015, 045012. [2]Espanol et al., ACS Appl. Mater. Interfaces 8, 2016, 908.

Trends in medical additive manufacturing

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INTRODUCTION: The Institute for Medical Engineering and Medical Informatics conducts research into diagnostics in living organisms and therapeutic systems. This work focuses on patient-specific solutions and on processing, analysing and communicating medical data. In cooperation with our partners, we address problems from the field of medicine and develop innovative solutions from the initial idea through to a functional model. Our fields of research are implant development, surgical support systems and medical computer sciences. [Ref https://www.fhnw.ch/im2]
The implant development research group has access to outstanding infrastructure and has expertise in developing [1] and testing [2] medical implants, particularly bone replacement materials. Its key competency is designing and producing complex components from polymers, ceramics, metals like titanium and shape-memory alloys [3] in small batches by means of additive manufacturing. Patient-specific implants (Fig. 1) as well as functional implant materials and surfaces [4], e.g. with antibacterial properties, are developed and studied.

SUMMARY: This presentation gives an overview on current trends in medical additive manufacturing and focuses on the different medical applications as well as industry opportunities, challenges and solutions. The latest trends in technology are discussed.

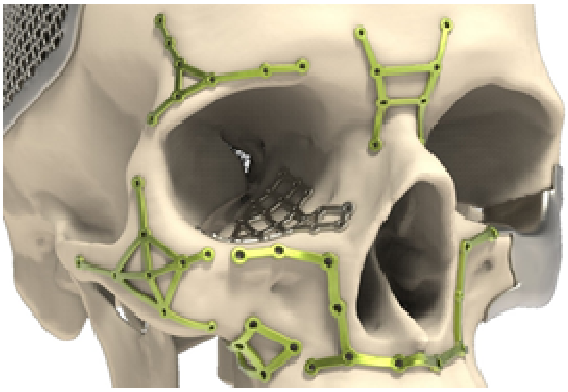

Fig. 1: Additive manufactured patient-specific titanium CMF implants. [Ref www.mimedis.ch]

REFERENCES: [1]S. Zimmermann, M. de Wild, *Density- and Angle-Dependent Stiffness of Titanium 3D Lattice Structures*, BioNanoMat 15 (S1), S35, (2014). [2]R. Schumacher, P. Lamprecht, S. Zimmermann, M. de Wild, A. Spiegel, *Comparison of SLM and conventionally produced implants using dynamic biomechanical loading*, RapidTech Erfurt, 2013. [3]Th. Bormann, et al., *Determination of strain fields in porous shape memory alloys using micro computed tomography*, Proc. of SPIE Vol. 7804 78041M-1-9 (2010). [4]M. de Wild, et al., *Surface Modification and In-vitro Investigation of Generatively Produced Implants*, Biomaterialien, 11, 157 (2010).

ZTi-Med®: a potential replacement for Titanium in medical − A dental implant application

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INTRODUCTION: With additive manufacturing (AM) becoming the new production foundry, it is also important to associate new brand of materials to respond to the needs of various industries. New Titanium enhanced powders like ZTi-Powder® have been introduced [1, 2]. ZTi-Powder® can have a role in orthopaedic implants like acetabulum for example.

Titanium alloys such as Ti64 is also widely used in the medical field in dental implants and medical devices manufacturing. However, many studies reported that unsatisfactory loads transfer from the implant devices and the relatively high elastic modulus of implant materials may lead to bone resorption. To overcome these issues, Z3DLAB developed a new dental implant design (DNA implant) and results showed that 84% of the implant's internal volume was colonized by bone cells. These results led to a published research paper in the Helion journal [3]. Also, Z3DLAB developed a new powder family called ZTi-Med® (Figure 1). These powders are called: ZTM35E, TZ10, TNZ14. These powders are characterized by their low elastic modulus (35 GPa compared to 100 GPa found in titanium alloys) and fatigue endurance. This paper shows the different ZTi-Med® materials along with their additive manufactured parts. As an application, a dental implant was manufactured using one of ZTi-Med® powders.

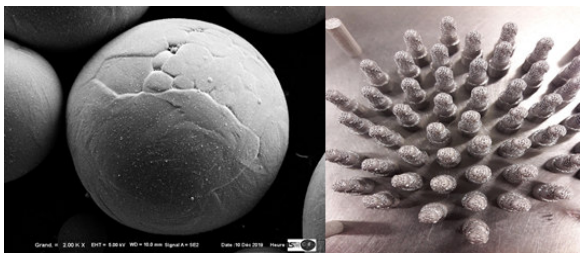

Fig. 1: ZTi-Med® Powder to dental implants, Nano-Zirconia coated on commercially pure Ti particles (left), final dental implant produced by SLM (right).

Table 1. Mechanical properties (ZTM35E)

Properties	Values
Young's Modulus (GPa)	35±3
Compressive Yield Strength (MPa)	624±27
Ultimate Compression Strength (Mpa)	1030±32
Ultimate Compression Strain (%)	58±2
Vickers Hardness (HV0,3)	258±11

DISCUSSION & CONCLUSIONS: In this paper, we show the work on powder preparation and additive manufacturing process that resulted in producing high density parts. The next step will be to investigate this material further using mechanical experiments to validate this low Young modulus and its consequences on stress shielding reduction.

ACKNOWLEDGEMENTS: This template was modified with kind permission from eCM conferences Open Access online periodical & eCM annual conferences.

REFERENCES: [1]Amine Hattal, Thierry Chauveau, Madjid Djemai, Jean-Jacques Fouchet, Brigitte Bacroix, Guy Dirras, *Effect of nano-yttria stabilized zirconia addition on the microstructure and mechanical properties of Ti6Al4V parts manufactured by selective laser melting,* Materials & Design 2019, 107909, Elsevier, doi.org/10.1016/j.matdes.2019.107909. [2]A. Hattal, T. Chauveau, M. Djemai, J.J. Fouchet, B. Bacroix, G. Dirras, *Data related to spectrum analyzes for phases identification, microstructure and mechanical properties of additive manufactured Ti6Al4V reinforced with nano Yttria stabilized zirconia,* Data in Brief, 2020, 29, 105249. [3]A-F. Obaton, J. Fain, M. Djemaï, D. Meinel, F. Léonar, E. Mahé, B. Lécuelle, J-J. Fouchet, G. Bruno, *In vivo XCT bone characterization of lattice structured implants fabricated by additive manufacturing,* Helion Volume 3, Issue 8, August 2017, e00374.

The experience of using custom-made implants for gross acetabular defects

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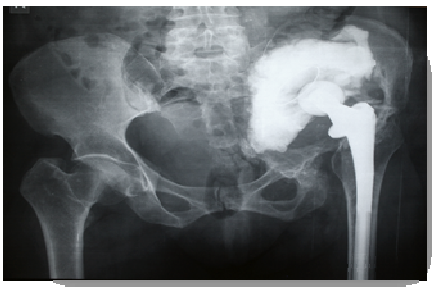
INTRODUCTION: The increasing availability of additive 3D technologies in medicine resulted in the use of individual designs, which minimize bone processing and optimize the fixation possibilities of revision implants. Individual 3D implants, as a rule, are used for the most complex acetabular defects, when the serial implants don't allow to get adequate fixation due to limited contact with host bone.

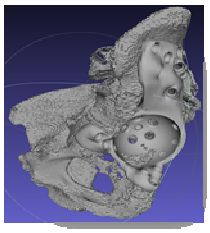
Purpose — to assess the mid-term results of the custom patient-specific implant for the treatment of severe bone loss in revision total hip arthroplasty.

METHODS: There were 115 acetabular revisions with custom acetabular implants performed from 2016 to 2019 in our hospital. There were 24 augments, 6 hemispherical cup, 2 bilobed cups, 62 triflanged cups and 9 flanged stemmed cups used.

RESULTS: Various patient-reported outcome measures showed in all cases a positive trend in pain, function and quality of life. Migration of the implant with a fracture of the flange was observed in one case (Fig 1).



a)



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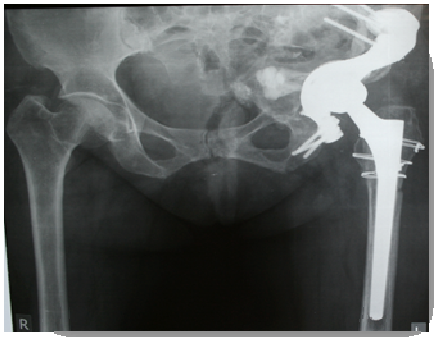

d)

Fig. 1: a) Rg before surgery with gross acetabular defects, b) and c) 3D implant, d) Rg after revision arthroplasty

DISCUSSION & CONCLUSIONS: The use of custom-made implants in the midterm follow-up period significantly improves function of the hip and the quality of life of patients. However, the questions of assessing the strength characteristics of both the developed implants themselves and the implant-bone contact zone remain open, including using finite element analysis, which from our point of view should be an integral stage of the modeling philosophy before printing. In addition, the use of specialized coatings in the area of contact with compromised bone should increase the long-term survival of the developed implants.

REFERENCES:

Kovalenko A.N., Tikhilov R.M., Shubnykov I.I., Bilyk S.S., Denisov A.O., Cherkasov M.A., Ibragimov K.I., *Minimum One-Year Outcomes after Revision Hip Arthroplasty with Custome-Made Implants: Function, Quality of Life and Patients Satisfaction.* Traumatology and Orthopedics of Russia. 2019; 25(1):21-31 (in Russian), https://doi.org/10.21823/2311-2905-2019-25-1-21-31.

4D Printing of Expandable Spinal Cages: Development and Applications

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INTRODUCTION: As the 3D Printing process is maturing, development is now focused on new materials for new applications. Some materials, such as shape memory alloys introduce an additional dimension that leads to a new nomenclature: 4D Printing. In the medical industry, shape memory alloys are typically used for stents and cardiovascular implants. However, shape memory alloys are difficult to process conventionally, and their shapes are limited [1]. Additive manufacturing processes such as laser powder bed fusion allow to overcome these limitations and offer the opportunity to produce new types of implants [2]. In this regard, expandable spinal cages were designed and developed for 4D Printing.

METHODS: Development of the expandable spinal cages was divided in two steps: Material development and design development.

Process development: From bibliography [3], several parameters sets were selected and adapted to a TruPrint1000 (Trumpf, Ditzingen, Germany). A design of experiment (DoE) was conducted, adapting parameters sets while increasing complexity in geometries: from weld seams to medical devices samples. Evaluation criteria thus evolved from visual inspection and ability to produce parts to density and mechanical properties of produced parts.

Design development: Additive manufacturing offers several design advantages, such as lattice structures, improving osseointegration, and design freedom. Moreover, expandable cages allow minimally invasive surgical approaches and a decrease in morbidity [4].

Design was done with CAD software Fusion 360 (Autodesk, USA), and focused on developing a structure that would exploit shape memory properties.

RESULTS: A low laser power, low speed parameter set was found to give the best quality for parts with high density (> 99 %). Surface state has a high influence on mechanical properties. Transformation temperatures are impacted by the thermal history; however, they are difficult to tailor with process parameters due to their connection to the structure and quality of the processed part. From a design point of view, 3D auxetic lattice structures were selected and used for their properties and responses to compression.

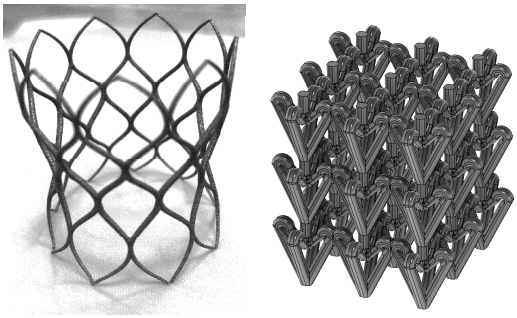

Fig. 1: 3D printed NiTinol aortic valve support (left), auxetic 3D lattice structure (right).

DISCUSSION & CONCLUSIONS: While shape memory alloys can be processed with additive manufacturing, the DoE highlighted some process limitations. Next development will be focused on chemical composition of the alloy, post-process steps, surface treatment and heat treatments, to ensure thermo-mechanical properties of the device, especially with a medical intended use. Design development will be pursued on expandable cages.

REFERENCES: [1]Lagoudas, D.C., Shape Memory Alloys, Springer, 2008, 435p. [2]Dadbakhsh, S., Speirs, M., Van Humbeeck, J., & Kruth, J. (2016), *Laser additive manufacturing of bulk and porous shape-memory NiTi alloys: From processes to potential biomedical applications,* MRS Bulletin, 41(10), 765-774. https://doi:10.1557/mrs.2016.209. [3]Dadbakhsh S., Speirs, M., Kruth J.P., (2014) *Effect of SLM Parameters on Transformation Temperatures of Shape Memory Nickel Titanium Parts: Effect of SLM Parameters on Transformation Temperatures of NiTi,* Advanced Engineering Materials, 16(9): 1140-1146. https://doi.org/10.1002/adem.201300558. [4]Hammad, A., Wirries, A., Ardeshiri, A. et al., *Open versus minimally invasive TLIF: literature review and meta-analysis,* J Orthop Surg Res **14,** 229 (2019). https://doi.org/10.1186/s13018-019-1266-y.

Industrial sterilization methods - an overview

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INTRODUCTION: Sterilisation is a method to reduce living microorganisms on dedicated objects. To reduce microorganisms there are basically two approaches: physical (e.g. irradiation, heat, filtration) and chemical (e.g. ethylene oxide) methods.

METHODS & RESULTS:

Irradiation method:
When focusing on irradiation methods, typically Gamma irradiation is the method of choice for industrial sterilization application. In the last years due to sourcing problem of Co^{60} and stronger regulation requirements, alternative methods are in focus. X-ray seems to be a promising alternative, as no waste is generated, no external source than electrical power is needed and the dose distribution within a pallet seems to be much more even than with a Gamma source. To evaluate the proper sterilisation method not only material properties are to be taken in consideration, but also a proper packaging configuration.
Industrial sterilisation methods are well defined in ISO norms, such as ISO 11137 for Gamma/e-beam/X-ray irradiation:
This norm is separated in 4 parts, which cover the following topics:
1. General requirements for the validation.
2. Dose establishment/monitoring of a proper method.
3. Dose mapping.
4. Dosimetry.

EO (ethylene oxide)
Beside irradiation method, EO treatment is a commonly used method for industrial sterilization. This method is regulated in ISO 11135. The agent is a gas, which inactivates together with humidity the microorganism. For the validation of this process physical (temperature, humidity, pressure) parameters, as well as microbial parameters must be taken in consideration and properly evaluated. Commonly used packaging component, which allows gas penetration but no microbial penetration is the Tyvek material.

DISCUSSION & CONCLUSIONS:

Irradiation method:
Advantage: Treatment at relatively low temperature; penetration of the whole pallet; parametric release possible; fast treatment method.
Disadvantage: Not all materials can be applied due to material property change (e.g. PE); in case of Gamma irradiation: high dependence on external Co^{60} source.

EO (ethylene oxide)
Advantage: Low cost gas; relatively low temperature application; usually no significant material property change.
Disadvantage: Long treatment time (de-gassing); microbial release (no parametric release); high security standard (EO is very well flammable).

REFERENCES:
ISO 11137: *Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices.*
ISO 11135: *Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices.*

Don´t forget to think about family grouping before doing reprocessing validations of medical devices and instruments!

L. Vanderkelen[1], K. Peymen[1] and A.N. Patel[2]

[1] Nelson Labs NV, Leuven, Belgium; [2] Nelson Laboratories LLC, Salt Lake City, USA

INTRODUCTION: Validating the cleaning and sterilization processes that occur at healthcare facilities is costly and orthopaedic and surgical implant device manufacturers could be spending a lot more time and money on testing by not considering family grouping when performing these validations. Validating cleaning and sterilization processes is an important and necessary step in ensuring patient safety and minimizing healthcare-acquired infections, corrective actions, and recalls. Family grouping or selecting a worst-case device (or devices) to perform these validations can be used by device manufacturers in many cases except when the device is very unique and specialized. These devices must be individually validated.

METHODS & RESULTS:

Cleaning Validation Family Grouping:

Performing a cleaning validation is a necessary step in order to evaluate the effectiveness of the cleaning process. To save time and money, manufacturers can choose to family group the devices for validation. There are three main approaches to evaluating whether family grouping is appropriate for the medical devices a manufacturer is validating—device use, material type, and device design.

Device Use: If the devices have similar use during surgical procedures, they can be grouped by their function, use, and degree of patient contact. Similarly configured devices or parts used for generally the same purpose and that contact comparable amounts of human tissue, blood, mucus, etc. may be grouped together for validation.

Material Type: If a group of devices are made out of the same metals and soft materials, they could qualify for family grouping. Devices are made from materials ranging from metal to ceramic to polymers, and sometimes, a mix of several materials. Each of these materials holds onto residue differently and, therefore, should be grouped accordingly.

Device design: Medical devices of similar size and challenge features may be grouped together as a family. The considerations that are employed in this type of grouping include the number of components, design challenges for cleaning and surface area.

In addition to considering the devices themselves, reprocessing instructions must be evaluated because only devices that go through the same reprocessing instructions can be divided into family groups.

Steam Sterilization Validation Family Grouping:

Family grouping for steam sterilization validations requires different considerations as compared to family grouping for cleaning. Additionally, whereas family grouping for cleaning validations will mostly consider worst-case devices, family grouping for steam sterilization may include the selection of a worst-case tray configuration (if appropriate). ISO/TS 17665-3:2014/(R) 2016 offers guidance to performing family grouping for steam sterilization validations by evaluating steam penetration resistance, device design, materials, weight as well as packaging.

Knowing the type of packaging is crucial for family groupings and packaging must be a part of the evaluation given that packaging sizes vary and influence volume-to-vent ratios.

DISCUSSION & CONCLUSIONS: Family grouping of medical devices or trays for cleaning or steam sterilization validations is very important. Validating every device or tray is not necessary, but also not preferred due to the cost and time of the validations. On the other hand, choosing worst-case devices and the rationale why other devices and trays would be adopted by these devices must be thoroughly justified and documented. The justifications must also be submitted to the FDA or the appropriate regulatory agency.

REFERENCES: ANSI/AAMI/ISO 17664:2017; AAMI TIR12:2020; FDA 2015/(R)2017. Guidance for Industry and FDA Staff –Processing/Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling; ISO/TS 17665-3:2014/(R) 2016.

Cleaning validation for instrument reprocessing: normative background and the test methods

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INTRODUCTION: Surgical instruments are often used during medical device implantation. Once used, the instruments have to be cleaned, disinfected and sterilized in a so-called reprocessing process. It is the responsibility of the companies selling the instruments to inform hospitals how to reprocess the instruments and to make sure that the reprocessing steps meet minimal requirements. The aim of this communication is to briefly review the normative background and the test methods available for cleaning validation of reusable medical devices.

METHODS: Reusable surgical instruments are the devices "*intended for surgical use in cutting, drilling, sawing, scratching, clamping, retracting, clipping or similar procedures, without a connection to an active device and which is intended by the manufacturer to be reused after appropriate procedures such as cleaning, disinfection and sterilization have been carried out*" [1]. According to the Medical Device Regulation (MDR) [1] that is in force since 25 May 2017, reusable surgical instruments are classified as class Ir medical devices ("r" stays for "reusable"). Usually, the conformity assessment of class I medical devices does not involve a notified body. However, for the class Ir medical devices, a notified body is involved in the aspects related to the reuse of the device, such as cleaning, disinfection, sterilization, etc.

RESULTS: Cleaning reusable surgical instruments can be considered one of the most difficult processes to monitor. ISO 17664:2017 [2] specifies that the manufacturers of reusable medical devices shall provide validated cleaning instructions with their products (at least one validated method). Unfortunately, existing standards, recommendations, and guidelines relevant for cleaning validations are inconsistent.

For example, ISO 15883-1:2006 [3] and ISO/TS 15883-5:2005 [4] are two of the key standards relevant to the cleaning validations of reusable surgical instruments. However, these standards do not provide well-described methods for demonstrating cleaning efficacy and clear acceptance limits for the protein contamination. Therefore, they must be taken elsewhere. Both standards are under revision currently.

Depending on the market where the reusable medical surgical instruments are sold, there are different acceptance limits for the residual protein contamination. For example, the FDA uses concentration-based values (certain amount of residues per surface), while the European approach is more amount and geometry based (absolute amount of residues per instrument).

In order to assess the cleaning performance, different protein marker detection methods exist: e.g. BCA assay, OPA-method, ninhydrin method, radionuclide method, etc. Each of these methods has advantages and disadvantages, and interferences are often observed. For example, the BCA assay is one of the most widespread assays used for cleaning validation of reusable surgical instruments. However, Fe cations and organic residues (especially lipids) from the production can interfere with this assay.

DISCUSSION & CONCLUSIONS: The manufacturers of reusable medical devices face a number of challenges due to the existing inconsistent standards, recommendations and guidelines. On the one hand, there are strict regulatory/legal requirements. On the other hand, there are many gaps in the current standards, recommendations, and guidelines regarding the implementation of cleaning validations and their methods.

REFERENCES: [1] Medical Device Regulation (MDR), Annex VIII, Chapter I. [2] ISO 17664:2017, *Processing of health care products – Information to be provided by the medical device manufacturer for the processing of medical devices*. [3] ISO 15883:2006, *Washer-disinfectors – Part 1: General requirements, terms and definitions and tests*. [4] ISO/TS 15883-5:2005, *Washer-disinfectors – Part 5: Test soils and methods for demonstrating cleaning efficacy.*

A novel post-treatment process of medical and pharmaceutical material using $scCO_2$

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eCO_2 SA, Taverne, CH

INTRODUCTION: Supercritical fluid-based extraction procedures, such as extraction of active compounds and removal of impurities, have been established as important processes since decades. The main advantages of using supercritical fluids resides in the tunable solvation properties based on temperature and pressure, moreover they also possess high diffusivity, low viscosity and absence of surface tension as there is no liquid to gas phase boundary.

METHODS: The use of supercritical carbon dioxide ($scCO_2$) in the post-treatment of medical and bio-material, such as implantable membranes, for final impurities removal or impregnation with active pharmaceutical ingredients (APIs), is becoming very important nowadays. There are several advantages in the use of $scCO_2$ as solvent such as low toxicity, negligible residuals as well as bacterial inactivation. Furthermore, the mild pressure and temperature (73 bar, 31 °C) needed to reach supercritical conditions allows to work with sensitive materials and products without damaging them. Moreover, classical extraction and impregnation methods based on alcohols and hydrocarbons compared to $scCO_2$ method show several drawbacks, such as low diffusion rate, long process time and high temperatures. Furthermore, in many cases hazardous solvents are used which imply increased efforts to remove the solvent or additional installation costs.

RESULTS: However, the implementation of a successful treatment process which can either be applied for impurities removal as well as for APIs impregnations is very challenging. Indeed, homogeneous conditions must be assured through the entire batch volume, in order to achieve the desirable product characteristics and robust reproducibility. The post-treatment process developed by eCO_2 is able to face all those challenges leading to cGMP compliant product purities and characteristics between the production batches.

The innovative nature of the process lies in the horizontally placed process chamber equipped with a special rotatable basket, depicted in Figure 1, which ensure homogeneous conditions throughout the entire process chamber volume. Furthermore, the basket design can be customized according to the material to be treated, thus maximizing the contact area with $scCO_2$. The rotation of the basket enhances mass transfer between $scCO_2$ and treated materials. Simultaneously, the absence of surface tension of the $scCO_2$ improves the penetration inside the material matrix, enhancing the diffusion and thus the mass transfer. These process features are essential for ensuring homogeneous conditions throughout the entire process, which is of paramount importance for the quality of the final product and thus for its reproducibility.

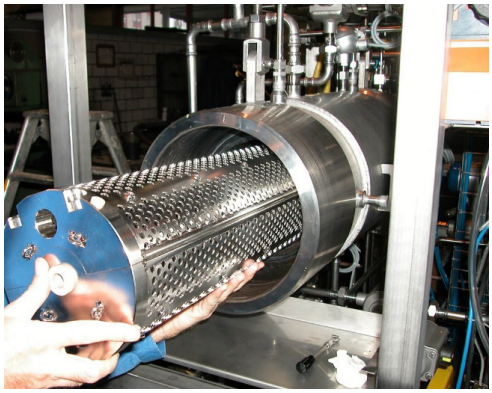

Fig. 1: Picture of the horizontally placed process chamber with the special rotatable basket.

DISCUSSION & CONCLUSIONS: The new proposed post-treatment process has been proved very promising as substitute of standard solvent-base processes. The tunability of the solvation properties by mild temperature and pressure conditions coupled with the rotation of the basket and the horizontal process chamber lead to homogeneous conditions. This involves, for the case of impurity removal treatments, a reduction by factor 10 of both process time and raw material expenses compared to the classical approaches. The homogeneous conditions, the even impurity removal or APIs impregnation and the batch-to-batch reproducibility make the proposed process compliant with the cGMP standards and, thus, can be applied in the pharmaceutical, medical, and food industries.

Poster Session

Posters can be accessed at www.rms-foundation.ch/en/meet

1	*Biodegradable magnesium implants: how to improve the surface properties?* Dr. Oksana Banakh, Haute Ecole Arc, La Chaux-de-Fonds, Switzerland
2	*Multilayer based on parylene and an oxide deposited by ALD for the packaging of medical devices* Prof. David Grange / Sophie Farine-Brunner, Haute Ecole Arc, La Chaux-de-Fonds, Switzerland
3	*MRI compatibility of additive manufactured auxetic NiTi parts* Felix Schuler, FHNW, Muttenz, Switzerland
4	*Protection of electronics for reprocessable surgical devices* Grégory Schaffner, Turck duotec SA, Delémont, Switzerland
5	*Cleaning processes in medical technology* Fabio Cordaro, Amsonic AG, Biel, Switzerland
6	*High-accurate form and roughness measurement of orthopedic implants using a new optical micro-coordinate measurement device* Robert Winkler, Alicona Imaging GmbH, Raaba/Graz, Austria
7	*Surface properties and fatigue resistance of AM-structures* Dr. sc. ETH Zürich Roman Heuberger, RMS Foundation, Bettlach, Switzerland
8	*Accelerated tests for lifetime prediction of interfaces and interlayers with respect to crevice and fatigue corrosion in body fluid* Dr. Roland Hauert, Empa, Dübendorf, Switzerland
9	*Implants surface modification: a reliable biomimetic approach* Dr. Agnese Carino, Medicoat AG, Mägenwil, Switzerland
10	*ICP-MS trace element analysis of calcium phosphate bone substitute materials according to USP 232/233 guidelines* Dr. Ronny Wirz, RMS Foundation, Bettlach, Switzerland
11	*Laser additive manufactured hemi-thoracic cage custom implant in Ti6Al4V* Pierfrancesco Robotti, Lincotek, Trento, Italy
12	*Protective pink coating for dental implant applications* Noora K. Manninen, Oerlikon Surface Solutions AG, Balzers, Liechtenstein
13	*Cleanliness of orthopaedic implants according to ISO 19227: differences and gaps compared to ISO 10993-18* Dr. Ronny Wirz, RMS Foundation, Bettlach, Switzerland
14	*Dry mechanical-electrochemical polishing of titanium* Sven Simeunovic, FHNW, Muttenz, Switzerland
15	*Adaptive density minimal surface structures for 3D printed medical implants* Niklaus Arn, Spherene AG, Zürich, Switzerland
16	*Process simulation software applied to the medical sector* Octavia Fleuchaus, TRANSVALOR S.A. Sophia Antipolis, France
17	*Post-treatment of wear protection layer* Felix Schuler, FHNW, Muttenz, Switzerland

Biodegradable Mg implants: how to improve the surface properties?

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INTRODUCTION: Due to their ability to resorb in the human body and to provide specific biological responses, Mg-based implants can be classified as bioactive and biodegradable materials. In the past decades, they were successfully used as cardiovascular and orthopedic implants. To provide mechanical integrity in the body over several months, the corrosion process must be precisely controlled. Plasma Electrolytic Oxidation (PEO) surface treatment has been proven an efficient method for corrosion protection of Mg alloys. We showed how PEO improves the corrosion resistance of AZ31. Different post-treatments improving biological properties of the Mg alloys can be considered in the fabrication chain of future resorbable implants.

METHODS: Polished AZ31 discs (30 mm diam.) were anodized by PEO using a CIRTEM® bipolar pulsed current source (f=100 Hz; J+= 30÷60 A/dm^2, J-= 0÷30 A/dm^2). The electrolyte contained 4 g/l NaOH and 6.3 g/l calcium glycerophosphate (pH=12.5). Treatment time was 5 min resulting in the anodized layer thickness of 15-20 µm. Two post-treatments were performed after PEO: 1) 50 nm-thick TiO_2 layer was deposited by Atomic Layer Deposition (ALD) and 2) a PLLA (poly-L-lactic acid) layer (10 µm-thick) was deposited by dip-coating. The surface and cross-section morphology were examined by Scanning Electron Microscopy (SEM) and optical microscopy. Corrosion tests were performed by potentiometry. Hydrogen gas evolution was measured by immersing the samples in HCl (0.25 M) solution. Biological assays with mouse fibroblast L929 cells were performed on the treated samples in order to assess their cytocompatibility. L929 cells were grown in contact with sample extracts, degraded during 24 and 72 hours in DMEM/F12 medium supplemented with 10 % FCS and 1 % PenStrep. WST-8 proliferation assays were used to assess cell viability in presence and absence of the coated sample extracts. Cell viability in absence of the sample was taken as 100 % viability.

RESULTS: The surface of anodized samples presents a morphology typical for PEO layers, showing a high percentage of open pores originating from arc discharges and gas emission through the growing PEO layer (Fig. 1, left). The potentiometry results show that PEO treatment enhanced the corrosion resistance by a factor of 300 (compared to non-treated AZ31). The emission of hydrogen gas, resulting from a reaction between Mg and HCl, was significantly retarded by PEO treatment. No hydrogen bubbles were observed during first 30 days of tests for PEO-treated samples, while 250 mL of gas was collected after 15 min of test with untreated AZ31 sample (same test conditions).

The results of biological tests indicated a poor cell viability for PEO-treated AZ31. The cell viability increased significantly (> 80%) after ALD post-treatment (Fig.1, right). PLLA coating resulted in a cell viability of 60% (compared to the reference).

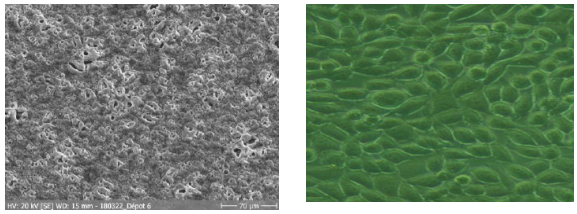

Fig. 1 (left): SEM image of the surface of PEO-treated AZ31; (right): optical microscopy image (200x) of L929 cells exposed during 24 h to the PEO-ALD sample.

DISCUSSION & CONCLUSIONS: PEO is a suitable surface treatment enhancing the corrosion resistance of Mg-based alloys. However, open pores in the PEO layer are problematic as they could initiate Mg ion release from the substrate in contact with a physiological medium, resulting in a pH increase in the surrounded area and poor biological response. Post-treatments (TiO_2 by ALD, dip-coating with PLLA) can further improve the corrosion resistance of the PEO-treated Mg alloys. They are necessary to obtain a favourable biological response in contact with viable cells.

Multilayer coating based on parylene-C and TiO_2 deposited by ALD for the packaging of medical devices

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INTRODUCTION: Implantable electronic devices intended to stay over long periods of time in the human body must be protected from the physiological environment by means of an encapsulation to avoid their failure during the use and achieve the highest longevity.
This encapsulation must be mechanically stable (to avoid damage due to, e.g. liquid infiltration that causes corrosion of the device), biocompatible, and have a high corrosion resistance. Our new multilayer coating showed promising results as a conformal packaging layer.

METHODS: This study aims to develop a thin encapsulation coating combining poly(chloro-p-xylylene) (commercial name parylene-C) layers with a thickness of 500 nm deposited by LPCVD, and 15 nm TiO_2 layers deposited by Atomic Layer Deposition (ALD) using tetrakis(dimethylamido)titanium ($Ti[N(CH_3)_2]_4$) and water as precursors with a process time of 8 hours maximum and a process temperature as low as possible.
The barrier performance of the layers has been tested by three different means: helium leak test, immersion of coated magnesium samples in Ringer's solution and immersion of coated Nd-Fe-B magnets in Ringer's solution.
The layers have been tested individually and combined by changing the order of the two layers and the number of alternation.

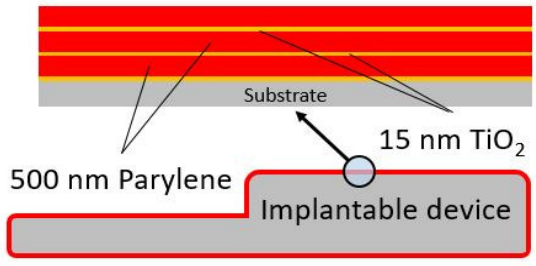

Fig. 1: Architecture of the multilayer coating composed of TiO_2 deposited by ALD and parylene-C deposited by LPCVD.

The optimized multilayer coating consists of 3 TiO_2 layers (15 nm-thick) alternating with 3 parylene-C layers (500 nm-thick) all deposited at a low temperature (50 °C) (Fig. 1). It exhibited a protection comparable to a 3 times thicker state of the art commercial barrier coating.

RESULTS: We noticed that parylene-C was damaged by an ALD process above 50 °C. Indeed, the permeability of a multilayer with TiO_2 deposited at 150 °C is higher than that of parylene alone or multilayer with TiO_2 deposited at 80 °C or 50 °C.
Moreover, barrier properties of TiO_2 deposited at 50 °C are as good as those of TiO_2 deposited at 80 °C or even at 150 °C (for the same layer thickness).
Finally, the optimized multilayer coating with a total thickness of 1.6 µm showed better or equivalent results in most of the tests than the commercial state of the art multilayer coating with a total thickness of 5 µm (Fig. 2).

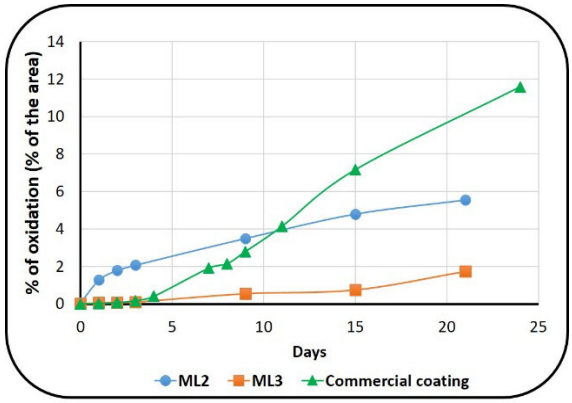

Fig. 2: Evolution of the oxidized area of coated Mg samples immersed in Ringer's solution : a multilayer made of 2 alternations (ML2), 3 alternations (ML3) and the commercial barrier coating.

DISCUSSION & CONCLUSIONS: The optimized multilayer coating showed excellent barrier properties with a thickness less than 2 µm. Nevertheless, progress has to be made in term of reproductively. Changing of reactor for every layer is detrimental. Therefore replacement of parylene-C by another material deposited by ALD is envisaged.

ACKNOWLEDGEMENTS: We would like to thank the HES-SO for its financial support in the frame of project "PolyPackAL".

MRI compatibility of additive manufactured auxetic NiTi parts

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INTRODUCTION: In the context of the SPIRITS project a 3D-printed design of an assistance robot for interventional surgery under Magnetic Resonance Imaging (MRI) is developed[1,2]. It is of the outmost importance that the manufactured components do not affect the image quality[3]. Artefacts in imaging could be caused on one hand by eddy currents due to the numerous loops of the auxetic structure (Fig. 1), and on the other hand by the nickel-containing shape memory alloy NiTi consisting of approx. 50 % Ni, which is ferromagnetic in its elementary form[3].

METHODS: Auxetic structures printed using selective laser melting (SLM) in medical degree pure titanium (strut thickness $s = 500$ µm) and a NiTi alloy ($s = \sim 600$ µm) were compared. Images were acquired with artefact susceptible TRUFI sequences at 3 T (Magnetom Skyra, Siemens Healthineers, Germany)

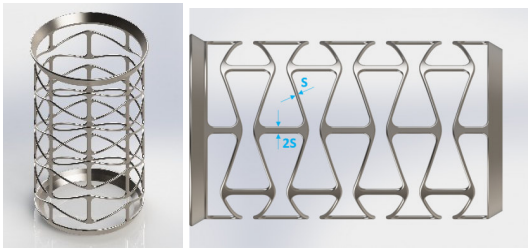

Fig. 1: CAD view of an auxetic structure (ø30 mm, h=50 mm).

RESULTS: All 3D-printed metallic structures could be mapped without any significant side effects such as heating, movement or intense disturbing image artefacts. It was found that NiTi structures lead to slightly larger artefacts than Ti (Fig. 2 and Fig. 3).

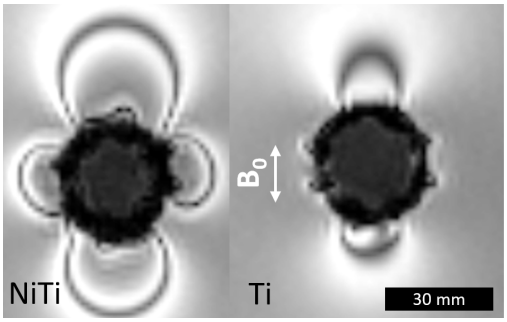

Fig. 2: MRI images of NiTi and Ti structures.

Furthermore, the signal inside both structures is significantly reduced by the induced eddy currents. The observed artefacts are primarily expressed radially in the direction of the main magnetic field B_0.

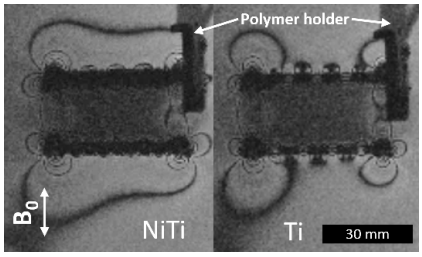

Fig. 3: MRI images of NiTi and Ti structures.

DISCUSSION & CONCLUSION: The observed imaging artefacts can be considered non-problematic due to the region of interest being in axial direction, outside of the auxetic structure. The reason for the major disturbances around the NiTi actuators could be the material difference but also the slightly thicker realization of the structures. Based on the observed behavior, no critical design flaw was identified.

REFERENCES: [1] W. Neumann, T.P. Pusch, M. Siegfarth, L.R. Schad, J.C. Stallkamp. *CT and MRI compatibility of flexible 3D-printed materials for soft actuators and robots used in image-guided interventions*. Med Phys. 2019;46(12):5488-5498. [2] A. Pfeil A, L. Barbé, B. Wach, A. Bruyas, F. Geiskopf, M. Nierenberger, *et al. A 3D-Printed Needle Driver Based on Auxetic Structure and Inchworm Kinematics*. ASME IDETC 2018; V05AT07A057. [3] A. Melzer, S. Michitsch, S. Konak, G. Schaefers, T. Bertsch. *Nitinol in magnetic resonance imaging*, Minim Invasive Ther Allied Technol. 2004;13(4):261-71.

ACKNOWLEDGEMENTS: The SPIRITS project is supported by the Region Grand Est, Land Baden-Württemberg, Land Rheinland-Pfalz, Cantons Baselstadt, Basellandschaft, Aargau, Swiss Confederation and by the program INTERREG Upper Rhine from the ERDF (European Regional Development Fund).

Protection of Electronics for Reprocessable Surgical Devices

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INTRODUCTION: Electronics destined to be placed in a reusable surgical device will likely have to go through reprocessing (commonly machine cleaning followed by steam sterilization) prior to a subsequent surgical procedure. Reprocessing is known to be very aggressive on electronics (even when protected) because of the temperature, pressure and chemicals involved. Protection of electronics through overmolding can be done by polymeric materials (despite their lower barrier effect properties compared with metals) as a result of the quasi absence of gaps, i.e. no microclimate inside of the housing. The risk of condensing of unwanted chemicals (mostly water after sterilization) is drastically reduced. Unlike the involved chemicals in gaseous phases that are relatively harmless for an overmolded electronic device, the chemicals in liquid phase (cleaning products, typically solutions of very strong bases, pH 11 and more) are chemically very aggressive and are to be reliably kept off of the electronics even after several reprocessing cycles. This article discusses this specific topic in the case of an overmolded electronic device.

METHODS: Overmolding allows to build a housing in one block and in one-step process around an electronic device. Except from the interface between the connection elements (typically fluor-polymer isolated conductors or golden pins) and the overmolding material, there aren't any potential ingress paths for a liquid. It is commonly known that interfaces are prone to ageing and to a delamination throughout the repeated reprocessing cycles.

In this study, we tested the sealing quality of an overmolded electronic device equipped with PTFE conductors. The PTFE conductors had been pre-treated in order to improve their adherence potential with the overmolding material. The testing method was to perform a dielectric test after an IP67 immersion in water at different ageing stages.

Ageing is performed in the air, inside a thermal shock chamber from 0 °C to 150 °C. The sterilization temperature range is typically from 20 °C to 135 °C. The extended temperature range for the ageing is meant to compensate for the higher thermal conduction coefficient of steam compared to air. Alternatively, another group of parts was aged inside of a tabletop sterilizer running in a loop. The sterilizer used for the test didn't completely cool down to room temperature at the end of each cycle, leading to a degraded test.

To test the sealing against the IP 67 standard, the samples have to be immersed for 30 minutes in water over-pressurized with 0.1 bar. The method for detecting potential water ingress into the housing is a dielectric test at 1500 volt performed in water. If the leakage current stays underneath the limit of 0.350 mA, the test is successful (see IEC 60947-1, §8.3.3.4)

RESULTS: Figure 1 shows the values of the dielectric test after an IP 67 immersion and after different ageing stages. The two different groups of parts tested (up to 556 sterilizations at 134 °C and aged up to 800 thermal shocks from 0 to 150 °C) are represented in black and grey. Both values are at least ten times below the acceptance criteria for this test. The outliner (part N°2) was defective from the beginning. After analysis, the root cause was a damaged conductor, outside of the overmolding area.

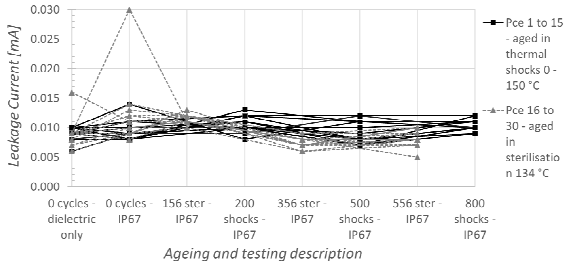

Fig. 1: Leakage current after an IP67 immersion in water and different ageing stages.

DISCUSSION & CONCLUSIONS: The results show a very low and stable leakage current, proving the sealing-performance between the PTFE and overmolding material interface in harsh environments. Additional tests also have been conducted in real environments (over a thousand machine cleanings plus steam sterilization cycles) without any failure of the electronic, which confirms the laboratory results. Similar work is currently in progress to study the performance of pre-treated gold pins in overmoldings.

Surface Properties and Fatigue Resistance of AM-Structures

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INTRODUCTION: Additive manufacturing (AM) is a promising technology that allows revolutionary possibilities such as "complexity for free". In contrast, the physical properties of these components are often neither known nor assessable. This entails new risks and challenges with regard to the quality and reliability of such products, especially for applications in medical technology.

METHODS: Simulating a 3D-structure for better bone attachment on an acetabular cup, a special grid structure made of the titanium alloy Ti6Al4V was deposited on bars made of the same alloy using laser metal deposition (1.9 mm high structure on 60 x 10 x 5 mm bar, produced at Fraunhofer Institute for Laser Technology ILT, Aachen, D). Surface properties of these structures were investigated using confocal microscopy and scanning electron microscopy (SEM). The fatigue resistance was subsequently investigated using a 4-point bending test (270 - 637 MPa, 10 Hz). Finally, a fracture analysis was performed on the tested samples.

RESULTS: The surface analysis showed small metallic droplets on the surface of the AM-structures. The roughness Ra of the structures ranged from 0.11 to 1.2 µm.
There was an early failure of the bars with the AM-structures in the 4-point bending test (< 300'000 cycles at 270 MPa vs. > 700'000 cycles at 600 MPa for Ti-bars w/o structure). The SEM-investigation showed multiple crack initiation within the AM-structure (Fig. 1 & 2).

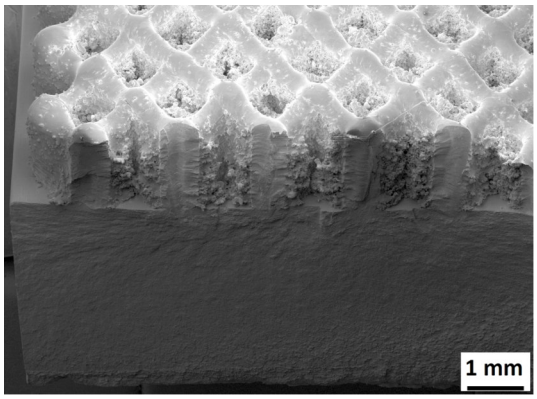

Fig. 1: SEM-image of the fracture surface. The AM-structure was deposited on a bar by laser metal deposition.

The metallographic examination of the broken samples showed additional secondary cracks that start at the interface (Fig. 3). The microstructure of the AM-structure and of the heat affected zone at the interface was dendritic, while the bar exhibited small grains. The AM-structures were harder than the bulk (389 ± 2 vs. 322 ± 10 $HV_{0.5}$). This was related to a higher oxygen content in the AM-structure.

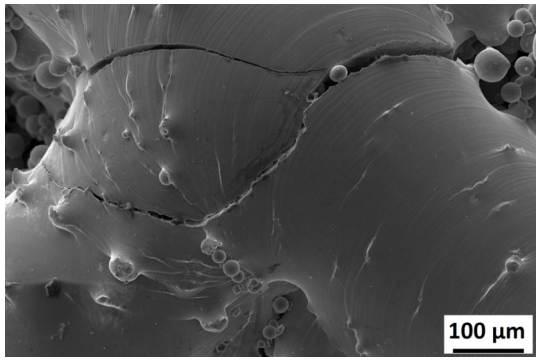

Fig. 2: SEM-image of the AM-structure with secondary cracks.

Fig. 3: Optical image of an etched cross-section to reveal the grain structure. The arrow points on a secondary crack at the interface.

DISCUSSION & CONCLUSIONS: The reason for the failure was the higher hardness due to a higher oxygen content of the AM-structures compared to the bulk material. Thus the upper part was more brittle than the bulk. This led to cracks in the AM-structure and at the interface, and finally to the early failure of the components due to the cyclic bending stress and notch sensitivity.
This example shows that application specific testing and analysis can be crucial for product failure prevention.

Accelerated tests for lifetime prediction of interfaces and interlayers with respect to crevice and fatigue corrosion in body fluid

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[2] *EPFL, Tribology and Interfacial Chemistry Group, Lausanne, CH*

INTRODUCTION: Coatings have an interface with the substrate where a few nanometer reactively formed material is generated with different properties compared to those of the coating or the substrate. Depending on the processing conditions, contaminations in the range of one atomic layer may be present, which can result in altered corrosion and fatigue behavior of this particular interfaces.

METHODS: To measure the chemical composition and reactivity of the nm-thick interface material, the coated sample was polished by an ion beam at an ultralow angle. Then, Auger Electron Spectroscopy (AES) measurements locally characterized the composition and microcapillary electro-chemical measurements determined the local reactivity [1]. Crevice corrosion, which is not accelerated in a physiological implant simulator, was accelerated in a dedicated crevice/confined space setup [2]. Corrosion fatigue testing of an interface in articulating simulator testing only lead to a good/bad result. By reciprocal sliding over a coating in media, an alternating load was generated at the interface. This test methodology did generate the Wöhler curve and the corresponding endurance limit of a particular interface [3].

RESULTS:

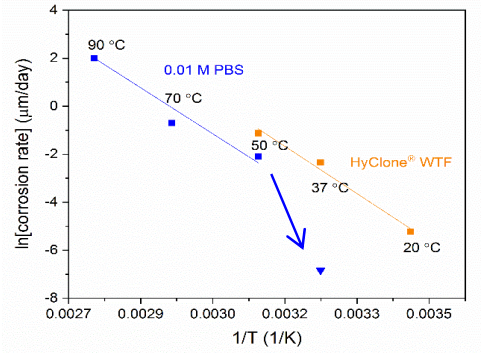

Fig.1: Arrhenius plot of Si in a crevice/confined space arrangement. Corrosion rate measured in the confined area at different temperatures, from [2].

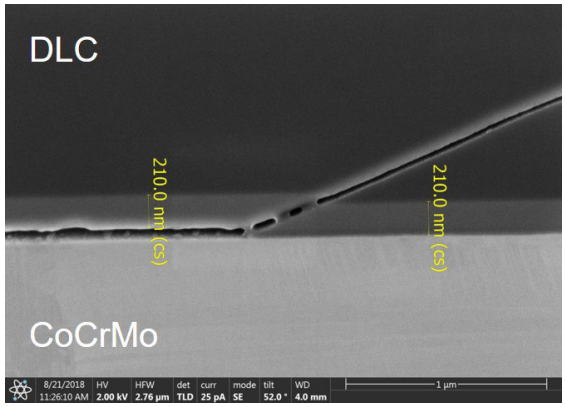

Fig. 2: FIB cross section of a growing crack in 4 µm DLC/Si-DLC (1.0 % O_2 contamination)/ CoCrMo after 13500 cycles in PBS. Plastic deformations of the Si-DLC are visible [3].

DISCUSSION & CONCLUSIONS: The temperature dependent corrosion rates yielded a linear Arrhenius relation, indicating a single rate limiting process step, with the activation energies (Ea) of 106 kJ/mol in 0.01 M PBS, and 109 kJ/mol in Hyclone®. The corrosion rate at 37 °C in PBS is lower than expected, leading to false lifetime expectations. This may be because conditions are not harsh enough, so passivation of Si is still effective and crevice conditions could not (yet) build up. Corrosion was most prevalent at the edge of the crevices, and pH indicators showed a pH increase, potentially due to oxygen reduction inducing OH^- release. Concerning corrosion fatigue at the interface, Wöhler curves for different interfaces are generated, showing the deteriorating influence of small interface contaminations. The induced plastic deformations are visible in figure 2, and result in a slowly ongoing local weakening of the material strengths.

REFERENCES: [1]E. Ilic et al., Surface & Coatings Technology, 375 (2019) 402-413. [2]E. Ilic, et al., Journal of the Electrochemical Society, 166 (2019) C125-C133. [3]A. Pardo, et al., Science and Technology of Advanced Materials, 20 (2019) 173-186.

Implants surface modification: a reliable biomimetic approach

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INTRODUCTION: Dental implants coated with bioactive ceramics are available on the market. Nevertheless, our cost-effective protocol for Ti surface modification aims to accelerate osseointegration and mitigate the temporary weakness in implant stability that occurs a few weeks after implantation. The implant surface is activated with a thin CaP layer using a wet biomimetic route [1].

METHODS: The here developed NanoCoat surface modification is applied to sandblasted and acid-etched surfaces, which are considered as the gold standard in the field. The NanoCoat protocol consists of a multi-step treatment, which generates a thin (~1 µm), chemically bonded nanoporous layer of Ti-based ceramics on the metal surface. Synthetic bone (calcium phosphate) is then grown on the surface in biomimetic conditions, according to an accelerated controlled method [1]. The deposition does not suffer from the line-of-sight issue, as well as does not mask the pristine microroughness.

RESULTS: In-vitro tests were comparatively conducted on ø14 mm Ti discs featuring different surface modification: machined, sandblasted and acid-etched (SLA), surface with grafting layer (GL) obtained by chemical and thermal treatments, and the final NanoCoat surface [1]. Biocompatibility was tested with human osteosarcoma MG63 cells. We investigated cytotoxicity and alkaline phosphatase activity for osteoblast differentiation. On the NanoCoat surface, MG63 cells proliferated at the same rate as on control (SLA) titanium surfaces and exhibited a healthy, spread morphology (Fig. 1). The alkaline phosphate activity (ALP) after two weeks, as an indicator of osteoblastic (bone-like) differentiation calibrated to protein content, was evaluated as well. The results demonstrate differences among the four surfaces (Fig. 2), whereby the NanoCoat surface features an osteoblastic differentiation with ALP activities twice as high as the gold-standard benchmark (i.e., SLA).

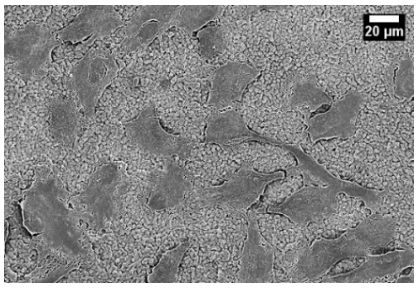

Fig. 1: MG63 cell spreading and proliferation on a substrate with NanoCoat surface.

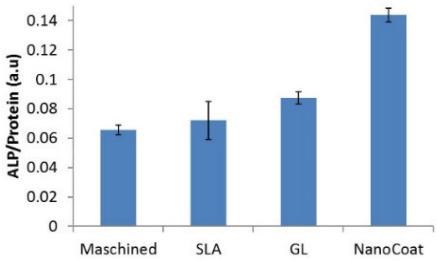

Fig. 2: Comparative ALP assay carried out on four different substrates. The error bars correspond to ±SD.

DISCUSSION & CONCLUSIONS: The experimental results combined with the observed process stability show the ability of the NanoCoat technology as a potential surface treatment for dental implants. The bioactive surface modification, applied as a showcase on dental screws, can further be used on any Ti-based permanent implant, such as craniomaxillofacial, spinal, and orthopaedic implants.

ACKNOWLEDGEMENTS: We thank the Swiss Nanoscience Institute and Medicoat AG for the financial support, and Hager & Meisinger for supplying the implants.

REFERENCES: [1]A. Carino, *et al.* (2018) *Formation and transformation of calcium phosphate phases under biologically relevant conditions: Experiments and modelling*, Acta Biomaterialia **74**: 478.

ICP-MS trace element analysis of calcium phosphate bone substitute materials according to USP 232/233 guidelines

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INTRODUCTION: Bone substitute materials made of β-tricalcium phosphate and hydroxyapatite must fulfil the requirements of ISO 13175-3:2012. One fundamental change that will occur once the revised version of this standard has been approved is that the impurity limits set by the standard are not concentration-based anymore (e.g. maximum 50 ppm heavy metals), but release-based (maximum tolerable daily exposure). This is a paradigm shift in the way the biocompatibility of a bone graft substitute is assessed, but is in line with recent changes introduced for the biological assessment of medical devices (e.g. ISO 10993). The revised ISO 13175-3 standard will request to determine the impurity levels of β-tricalcium phosphate and hydroxyapatite according to the United State Pharmacopeia (USP) chapters USP 232 (product-specific risk analysis) and USP 233 (test validation). The two USP chapters were written based on the recommendations of the *International Council for Harmonization (ICH Q3D)* and therefore are not only decisive for the USA, but also for other authorities, in particular the European. Standards as ASTM and ISO start to refer to the new USP guidelines as well. RMS Foundation has faced a number of new challenges during this method validation using ICP-MS since the element threshold concentrations drop significantly when more implant material biodegrades in a shorter amount of time (consequence of the product specific risk analysis).

METHODS: Inductive coupled plasma mass spectrometry (ICP-MS) is an extremely sensitive technique that allows simultaneous quantification of all target heavy metal elements in calcium phosphates (CaPs) down to trace levels in the µg/L or sub-µg/L range. Target elements according to USP 232 are: Cd, Pb, As, Hg, Co, V, Ni, Tl, Au, Pd, Ir, Os, Rh, Ru, Se, Ag, Pt, Li, Sb, Ba, Mo, Cu, Sn, and Cr.

RESULTS: According to USP 233, quantification of heavy metals has to be proven by showing an accuracy between 70 – 150 % at the target concentration of the corresponding heavy metal element. Within this validation study, it could be shown that this requirement could be met (Fig. 1). The corresponding target concentrations based on the performed risk analysis for CaP bone substitute materials had a range as low as 0.08 µg/L for Cd up to 60.00 µg/L for Mo.

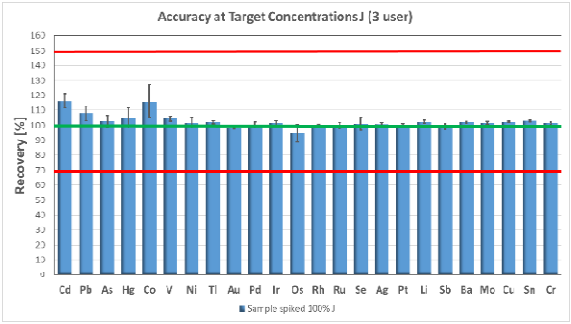

Fig. 1: Recovery rate of the 24 target elements at the target concentrations achieved at the RMS laboratory.

DISCUSSION & CONCLUSIONS: The resulting LODs were at least 3 times lower (LOD for Co: 0.066 µg/L) than the respective threshold limit (Co: 0.2 µg/L). The least sensitive analyte was copper with a validated LOD of 0.179 µg/L.

In conclusion, the method meets the requirements of USP 232 and USP 233 when testing the elemental impurities present in calcium phosphate products according to a risk assessment assuming 2.875 g of CaPs dissolved in the body per day.

REFERENCES:

USP <232> Elemental Impurities – Limits, in: United States Pharmacop. Natl. Formul. (USP 38-NF 33), United States Pharmacopeia Convention, 2012: pp. 245-248.

USP <233> Elemental Impurities – Procedures, in: Second Suppl. to United States Pharmacop. Natl. Formul. (USP 38-NF 33), United States Pharmacopeia Convention, 2012: pp. 243-244.

Laser Additive Manufactured hemi-thoracic cage custom implant in Ti6Al4V

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INTRODUCTION: Artificial hemi-thoracic cage reconstruction is a challenging task because of the geometrical complexity, the large dimension of the whole part and the necessary elasticity of the component subjected to cycling deformation to accommodate the chest expansion during the breathing. Additive Layer Manufacturing (ALM) was the preferred choice to fabricate the part. The patient specific shape can be replicated feeding an Additive Manufacturing (AM) equipment with a 3D model obtained through CT-scan images segmentation.
Design for Additive Manufacturing (DFAM), specific 3D printing process selection and set up, post processing and geometrical controls are all key engineering capability for successfully deliver such a complex implantable component.

MATERIALS & METHODS: The 3D model of the component was obtained through DICOM and segmentation at the Biomedical Engineering Department, Canary Islands Institute of Technology.
In the DFAM stage Materialise E-stage Software was used. The component was made of Ti6Al4V alloy. 3D printing was attempted using a Concept Laser M2 or, in alternative, an EOS M290 ALM equipment.
Two different types of recoaters were tested: soft (silicon wiper) on the M2 equipment and medium (carbon comb) on the M290 equipment.
Post processing applied: Heat treatment in vacuum over the beta-transus temperature, band saw detachment, manual supports removal and deburring, surface smoothing by glass beads blasting.
The geometrical conformity between nominal and actual shape was assessed using a fully-integrated laser scanner. The non-contact measurement method acquires a cloud of points to map the surface of the component.

RESULTS & DISCUSSION: The Software helped to define the best support strategy able to minimize the time for AM, suggesting the support dimensions and the part orientation during building (Fig. 1). Moreover, it helped in minimizing the necking connections between the supports and the part in order to decrease the finishing work. These design choices are in trade off with the opposite necessity to increase the supports and connections dimensions to hold the part in the desired position during the building, nevertheless the local thermal stresses.
The two recoaters tested exhibited different friction forces against the component during the powder spreading. The run with the medium type recoater failed because it caused breaks in the supports. The part swelled and the recoater impinged leading to job crash. By opposite the soft recoater was successful, enabling the part manufacturing along with the use of light supports structures and connections thus minimizing the following post processing steps.
Based on the equipment set up and parameters used, the print of the hemi-thoracic cage implant was successfully completed with the M2 machine. This process reached also a native smoother surface finishing.
After AM, the thermal treatment was essential to guarantee the conformity of the mechanical performances and the microstructure with the ASTM F3001, the norm applicable for the implantable grade Ti6Al4V ELI through ALM.
After glass bead blasting, the Ra detected on the solid surface of the part was < 3 μm.
The Laser scanner was a suitable tool enabling fast and precise dimensional quality control for such a complex custom implant.

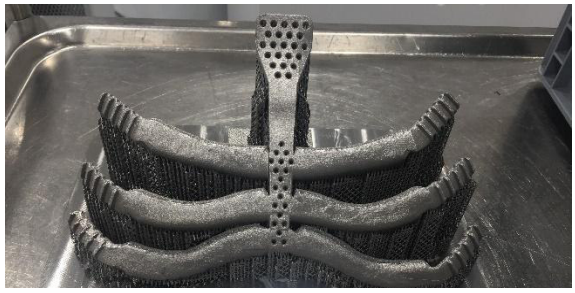

Fig. 1: ALM Hemi-Thoracic cage in Ti6Al4V.

ACKNOWLEDGEMENTS: This work is part of FAMAC Research Project, partially funded by Provincia Autonoma di Trento, Italy.

Protective pink coating for dental implant applications

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INTRODUCTION: Physical vapor deposited (PVD) coatings are widely used in the dental market for aesthetic reasons. The most common materials in this given application are TiN coatings and diamond-like carbon (DLC) coatings due to their aesthetic properties combined with biocompatibility and their wear resistance. Currently new challenges are imposed by the market, especially regarding the aesthetic properties of dental implants, therefore the main goal is to achieve colours similar to gingiva (gum), skin and teeth. In this context, TiCN based coatings are regarded as a promising coating material due to their inherent pink colour.

METHODS: TiCN coatings with a pink colour have been produced by (Scalable Pulsed Power Plasma) S3p technology. The coatings are characterised in terms of structure by X-ray diffraction (XRD) and chemical composition by electron dispersive spectroscopy (EDS) and elastic recoil detection analysis (ERDA). The coatings topography is also analysed in comparison to arc coatings by scanning electron microscopy (SEM) and profilometry. The colour stability in corrosive environments is also reported, for which the coatings were immersed in 25 wt.-% NaCl solution for 34 days. The substrate materials were made of Ti6Al4V alloy and SS316L. The saline solution was refreshed every 7 days, and the colour was measured by spectrophotometry in order to determine the CIE L*a*b* colour parameters. The variation of colour of as-deposited coating and coating immersed in saline solution is determined by the calculation of ΔE parameter. The samples were also visually inspected by optical light microscopy in order to evaluate the presence of corrosion.

RESULTS: BALIMED TICANA consists of a multilayer coating featuring 3 layers of TiCN with gradual increase in carbon content, ranging from 3 at.-% up to 10 at.-%, as determined by EDS and ERDA. The chemical composition and texture in the top layer provide the characteristic pink colour. The coating consists of a fcc-TiCN structure, as determined in XRD analysis. The use of S3p technology provides a clear advantage over arc evaporation technology since the number of droplets and particles is largely reduced. The coating shows a stable colour (ΔE=0.7) after 34 days of immersion in solution with 25 wt.-% NaCl without any sign of localized corrosion.

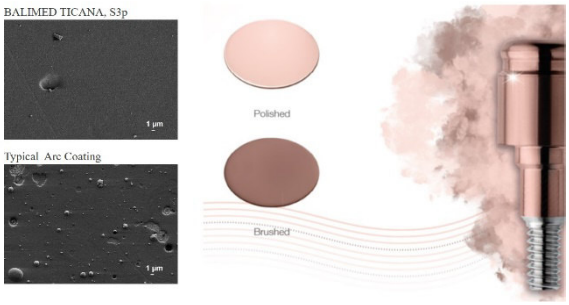

Fig. 1: Scanning electron microscopy (SEM) top view micrographs with comparison of S3p BALIMED TICANA and typical arc coating. Picture of colour achieved with BALIMED TICANA on dental abutment.

DISCUSSION & CONCLUSIONS: BALIMED TICANA is a multilayer TiCN-based coating with pink colour, obtained via introducing a carbon content of 3 at.-% to 10 at.-%. The coating is deposited by S3p technology, providing highly smooth surface combined with high level of hardness.

REFERENCES

[1]Kurapov Denis, Krassnitzer Siegfried, TiCN having reduced growth defects by means of HiPIMS, EP 3445890 B1, European Patent, 21 April 2017. [2]Krassnitzer Siegfried, Kurapov Denis, High-power pulse coating method, US10392694B2, USA Patent, 27 August 2019. [3]BALIMED TICANA, Oerlikon Balzers, Accessed in March 2021, Available Online: https://www.oerlikon.com/balzers/se/en/portfolio/balzers-surface-solutions/pvd-and-pacvd-based-coatings/balimed/balimed-ticana

Cleanliness of Orthopaedic Implants According to ISO 19227: Differences and Gaps Compared to ISO 10993-18

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INTRODUCTION: The evaluation of the cleanliness and biological safety of an orthopaedic implant is a central part of the conformity assessment procedure for market approval. There are two documents describing the cleanliness: ISO 19227 coming from the cleaning processes development and validation and ISO 10993-18 describing the chemical characterisation of medical device materials for the biological evaluation.
In this work, we have taken a closer look at the differences and gaps with regard to the evaluation of the cleanliness of implants.

METHODS: The two standards were compared in terms of their recommendations to test implant cleanliness. Differences and gaps were reported.

RESULTS & DISCUSSION: An important difference is that ISO 19227 focusses on extractable contaminants, while in ISO 10993-18 the investigations can start with the characterization of bulk and surface properties, including leachable and extractable contaminants.
Both standards mention the importance of a risk assessment based on the analysis of the contaminants. However, a limit value of 0.5 mg/implant of total hydrocarbon and organic carbon (THC & TOC) is mentioned in ISO 19227. Although it is mentioned, that this value "can serve as a starting point for acceptance levels", this does not make sense from a toxicological evaluation point of view and could give manufacturers a false sense of security if they follow this example. For example, the threshold of toxicological concern (TTC) for carcinogenic substances, which could be released from a long-term contacting medical device (> 10 years), is 1.5 µg/day (according to ISO/TS 21726). Therefore, limit values have to be determined in a case by case risk assessment, depending on the implant type, site of implantation and exposure or based on the historical clinical performance of the device.
This brings us to the next topic that is missing in ISO 19227, the analytical evaluation threshold (AET) concept. The AET is the concentration threshold below which extractables or leachables identification is not required. Thus, the chosen analytical method requires a quantification limit that is lower than the AET. This is often not the case with THC and TOC, if used as stand-alone methods.

CONCLUSIONS: ISO 19227 is very helpful in the development and validation of a cleaning process. The proposed analytical methods TOC and THC can be potentially useful for process control of an established cleaning process. However, the list of possible test methods is not sufficiently comprehensive. Focusing on specific examples of test methods and giving suggestions on how to derive an acceptance criterion could give a false sense of security.
A general acceptance limit of 0.5 mg/implant is not appropriate, as the size, complexity, manufacturing and cleaning process of implants are diverse. Thus, limit values have to be determined in a toxicological risk assessment and are usually supplemented by the requirement that the device is visually clean.
Therefore, we suggest that the chemical characterisation of orthopaedic implants should be performed according to ISO 10993-18. Surface contamination is then considered and evaluated as part of the chemical characterisation. If necessary according to the risk mitigation plan, even small amounts of contamination should be identified and quantified. If the toxicological assessment shows that the surface contamination is problematic, the cleaning process must be improved in accordance to ISO 19227.

REFERENCES: ISO 19227:2018-03*: Implants for surgery - Cleanliness of orthopedic implants – General Requirements*. ISO 10993-18:2020-01: *Biological evaluation of medical devices – Part 18: Chemical characterization of medical device materials within a risk management process.* ISO/TS 21726:2019-02: *Biological evaluation of medical devices - Application of the threshold of toxicological concern (TTC) for assessing biocompatibility of medical device constituents.*

Dry mechanical-electrochemical polishing of titanium

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INTRODUCTION: The post-processing of metallic implants has been given more attention with the continuing rise of additively manufactured (AM) implants. In response to the growing demand, novel automated methods for electropolishing [1] have entered the market in recent years. One such method is the electro-polishing process known as *DLyte*, used e.g. for 316L stainless steel [2]. The aim of this study is to assess the post-processing quality of this process on AM cranial titanium plates. Foremost, the influence of process times on the roughness was investigated using conventionally produced rods made of titanium.

METHODS: *Manufacturing of the samples*: Conventionally produced titanium grade 5 rods (Bibus Metals AG) served for roughness tests. Each rod contained four sections where the surface has been roughened, rough machined, fine machined or mechanically polished. AM cranial titanium plates were manufactured by Selective Laser Melting (SLM) using a SLM Solutions 250^{HL} system (SLM Solutions, Lübeck, Germany). The powder used for this process was titanium grade 2 (Realizer GmbH, Borchen, Germany). *Post-processing:* Each manufactured sample was dry polished using the DLyte H10 (DLyte, Barcelona, Spain) in combination with DLyte TI MIX as the electrolyte. The samples were mounted to metallic specimen holder acting as the anode. The samples were then inserted into the polymeric electrolyte and polished for 90 min in total with 15 min processing intervals between analysis. The voltage during the polishing was fixed to 35 V with the polarity as a cyclic factor.

RESULTS & DISCUSSION: The roughness R_a was lowered significantly throughout all four surface sections of the Ti rods as seen in fig. 1. The R_a value of the fine machined titanium surface was reduced from 0.43 µm to 0.09 µm within 90 min processing time. The polished and rough machined surfaces exposed a similar smoothing trend whereas the roughened surface reduced more linearly from R_a 1.17 µm to R_a 0.77 µm within 90 min treatment.

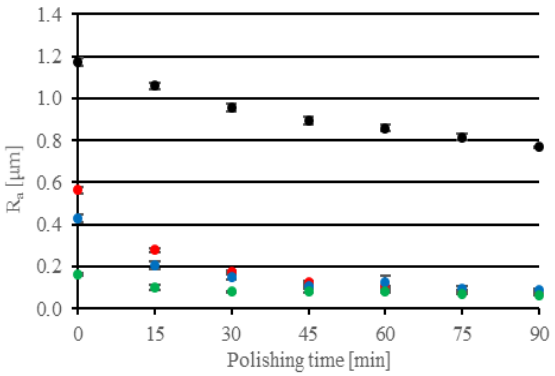

*Fig. 1: Decrease of R_a as a function of the polishing time of the roughened (**black**), rough machined (red), fine machined (blue) and mechanically polished (green) surface.*

The AM cranial plates showed a significantly improved surface quality as seen in fig. 2. With the DLyte post-treatment the surface has become overall smoother, shiny and with less cavities.

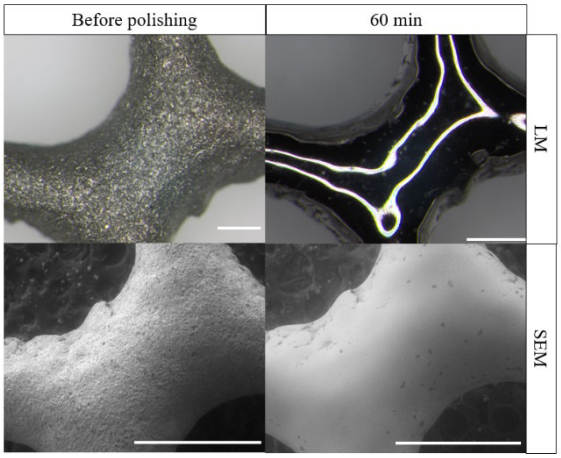

Fig. 2: LM and SEM images of a sandblasted AM titanium strut before polishing (left column) and 60 min polishing time (right column) (scale 1 mm).

CONCLUSIONS: The DLyte technology improved the surface quality of the tested titanium rods especially in cases where the samples had a low R_a value beforehand. The DLyte process has shown great potential in the post-processing of AM titanium implants.

REFERENCES: [1]D. Landolt, et al., Electrochimica Acta 48, 3185-3201 (2003). [2]Y. Bai, et al., Materials and Design 193 (2020), 108840.

Adaptive Density Minimal Surfaces for 3D-printed Implants

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INTRODUCTION: While an increasing range of possibilities for 3D-printed medical implants is implied by the latest 3D design and engineering methods, they are far from unlocking the full potential offered by this new production route, failing to address main requirements on the internal structure of implants, whilst maintaining structural stability: easy access for cleaning, maximum surface area for osseointegration or internal coatings with slowly degrading substances, open-porous structures allowing high fluid-flow for fast vascularization and bone growth. Also, the impact of suboptimal design on the additive manufacturing of titanium implants limits their competitiveness toward traditionally produced implants: tedious removal of support structures, thus non-controllable surface texture and residues from mechanical removal, and shape sacrifices to avoid closed powder pockets.
Additive manufacturing offers new possibilities for a *change of minds* in the design of medical implants thanks to the (relative) freedom of shape and the *complexity for free* ruleset, thus paving the way for implants where all of the afore-mentioned requirements are addressed.

METHODS: To this purpose we developed a freely configurable 3D-structure with an *Adaptive Density Minimal Surface* geometry (ADMS), which is able to computationally emulate both the plate- and rod-type geometry of trabecular bone (Fig. 1), as well as the near-solid cortical bone. ADMS structures feature open channels through the entire implant, maximized inner surfaces and allow for support-free printing and easy cleaning [1].

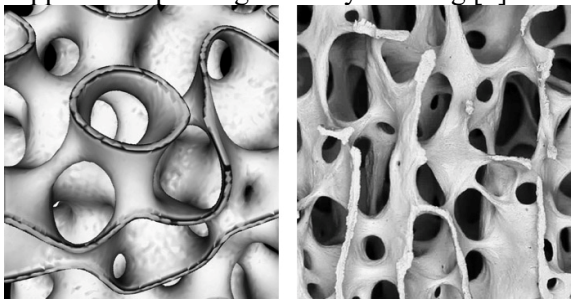

Fig. 1: ADMS geometry (left) vs. trabecular bone structure.

RESULTS: Locally configurable ADMS parameters include load case, thickness, channel diameter and porosity or structural density. As *minimal surfaces*, ADMS exhibit a smooth curvature distribution and are thus exceptionally stable using the minimal amount of material [1].

A variety of ADMS samples with different gradients applied on structural density and surface thickness have been designed. On both top and bottom, solid endplates have been added for a defined load application during mechanical testing.

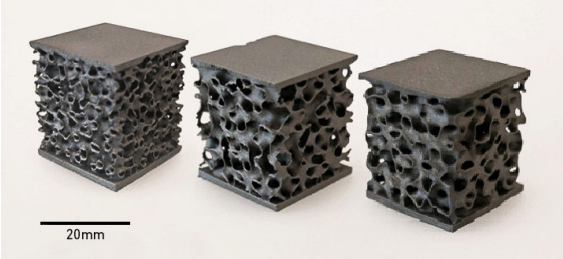

Fig. 2: Support-free 3D-printed titanium samples with different generation parameters.

The designed ADMS-samples have been 3D-printed by Selective Laser Melting (SLM) on a SLM Solutions 250^{HL} system (SLM Solutions, Lübeck, Germany) out of titanium grade II powder with a d_{50}-value of 40 µm (Fig. 2).
We were able to show that all proposed ADMS sample structures can be successfully manufactured by SLM without build supports.

DISCUSSION & CONCLUSIONS: It was shown that scaffolds based on ADMS microarchitectures can be successfully produced out of titanium by SLM. In particular, support structures are not necessary, which is of great advantage during production and post-treatment.

ACKNOWLEDGEMENTS: This study was supported by Innosuisse: grant 43760.1 IP-LS.

REFERENCES: [1] Patents PCT/IB2019/ 054076, PCT/EP2020/063727.

Post-treatment of wear protection layer

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[2] *ANAXAM, PARK INNOVAARE: deliveryLAB, Villigen, Switzerland.*

INTRODUCTION: The aim of the proprietary plasma-sprayed wear protective layer is to extend the life of titanium surfaces which are subject to abrasion wear. The rather limited wear-resistance of titanium parts could be compensated by a hard ceramic plasma-sprayed coating, in particular on sliding surfaces[1]. Therefore, a novel multi-component Al_2O_3/TiO_2 powder mixture as starting material is injected in the plasma flame, where the particles melt. On the flight to the sandblasted implant surface, the droplets start to cool down before they impact the substrate with high kinetic energy. There they immediately solidify under high cooling rates forming the multi-component surface coating. This thermal quenching is the reason for the formation of not fully ceramized, non-stoichiometric, partially electrically conductive, oxygen-deficient, crystalline phases and for the appearance of pores and micro cracks[2]. We identified under what conditions these phases form and how they can be subsequently transformed.

METHODS: Vickers HV1 hardness (Zwick-Roell, Germany), SEM (TM3030, Hitachi) and XRD measurements (Bruker Phaser D2 diffractometer, in Bragg-Brentano geometry) were done on polished, anodized and heat-treated single and mixed Al_2O_3/TiO_2 coatings, see fig. 1. High-resolution Synchrotron X-ray micro-computed tomographic SXRμCT measurement were performed with 1 mm^2 cut strips from post-treated samples to inspect the coating and the interface between the coating and the Ti grade 5-substrate.

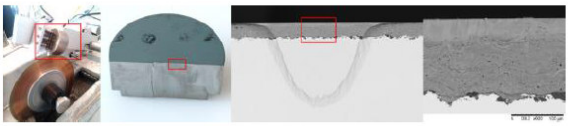

Fig. 1: Cross-section preparation with diamond saw and ion-milling for SEM investigations.

RESULTS: While anodization showed only little effect, the hardness significantly increased after thermal oxidation (fig. 2a). Crystallographic analysis showed a clear change in the phase composition. Oxidation of non-stoichiometric phases and reduction of high temperature phases was observed in the thermally treated samples (fig. 2b). XRD indicates that thermal treatment induces transformation into rutile. This also explains the increase in hardness after post-treatment.

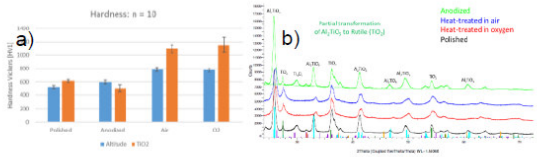

Fig. 2: a) HV1- and b) XRD-measurement after different post-treatments.

With SXRμCT several features were found at the interface and in the coating (fig. 3): 1) A rippled interface, having a coating-substrate interlayer with thickness ~40 μm, 2) an agglomeration of pores near the interface, 3) smaller pores in the coating, 4) different grey levels inside coatings due to different intensity measured. The variation in intensity in distinct volumes can be caused by different phases present inside the coatings.

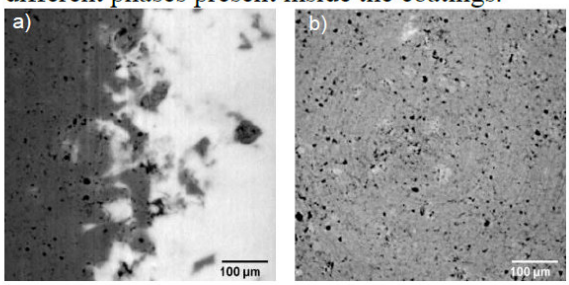

Fig. 3: a) Reconstructed SXRμCT images of the substrate-Al_2O_3 coating interface. b) Reconstructed cross-section through the Al_2O_3 coating.

DISCUSSION & CONCLUSION: Appropriate heat treatments seem to have a positive influence on the multi-component Al_2O_3/TiO_2 wear protection layer in terms of mechanical, structural, crystallographic and tribological properties.

REFERENCES: [1] N. Vogt, K. Wozniak, A. Salito, M. de Wild, Biocompatible wear-resistant VPS coatings, Current Directions in Biomedical Engineering 2(1): 31–34 (2016). [2] A. Richter, et al. Emergence and impact of Al_2TiO_5 in Al_2O_3-TiO_2 APS coatings. IOP Conf. Ser.: Mater. Sci. Eng. 480 012007 (2019).

ACKNOWLEDGEMENTS: We would like to thank the Swiss Nano Sciences Institute SNI and Nanoargovia for their support of the project.

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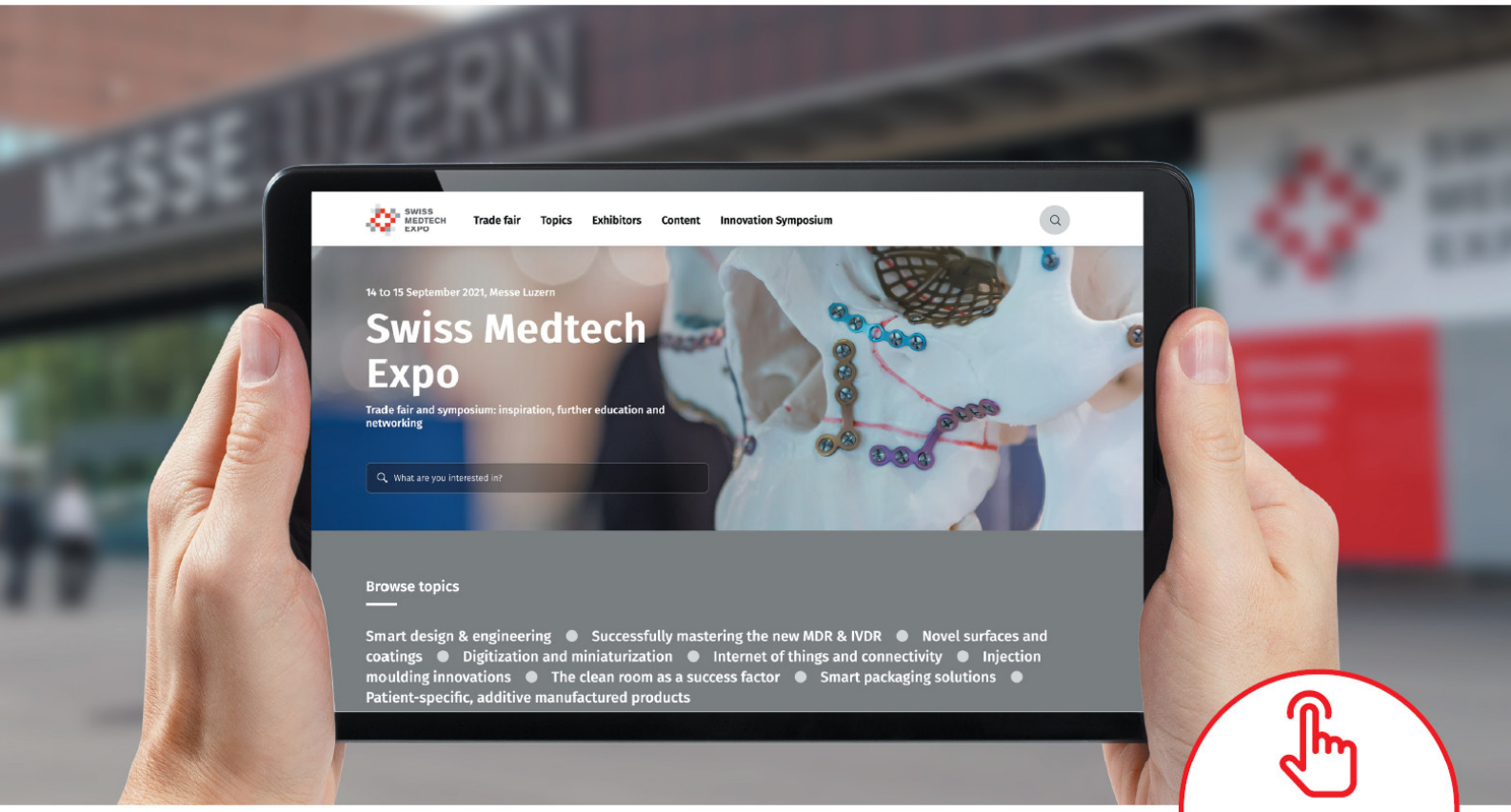
Notes

SWISS MEDTECH EXPO will take place



OVERVIEW, OFFERS AND REGISTRATION

Be part of the Swiss Medtech Expo

With your registration you receive complete planning security: Swiss Medtech Expo 2021 will definitely take place – as a trade fair in Lucerne or as a digital event. You will benefit from a fully developed concept, which Messe Luzern has already successfully implemented at other trade fairs.

HEALTH TECH CLUSTER SWITZERLAND

SWISS MEDTECH

MESSELUZERN