European Society for Bioresorbable Implants

BOOK OF ABSTRACTS

1st ESBI CONFERENCE 2022

18th – 20th of May 2022

DPU Krems

AUSTRIA

DANUBE PRIVATE UNIVERSITY
Fakultät Medizin/Zahnmedizin

European Society for Bioresorbable Implants

1st Annual ESBI Conference in 2022

18TH – 20TH OF MAY 2022 DPU KREMS, STEINER LANDSTRASSE 124, KREMS - AUSTRIA

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Europäische Union Investitionen in Wachstum & Beschäftigung. Österreich.

The European Society for Bioresorbable Implants – ESBI and the DPU Krems

invite you to the conference:

→ RECENT DEVELOPMENTS IN BIORESORBABLE IMPLANTS ←

Date	Wednesday 18th of May
Location	DPU Krems, Steiner Landstrasse 124, 3500 Krems
Programme	Arrival, Registration
18:30 hrs	Get together at Loibnerhof, Wachau
Date	Thursday 19th of May
Location	DPU Krems, Steiner Landstrasse 124, 3500 Krems
Programme	
08:30-08:45	C. Kleber/ E. Kny/A.W. Hassel: Welcome and introductory remarks
08:45-09:15	S. Virtanen: Biodegradable metals: Challenges for understanding and controlling the corrosion behavior in biological environments
09:15-09:45	W. Knoll: Responsive Polymer Brushes on Graphene Field-Effect Transistors as Novel Platform for Ion Detection
09:45-10:15	Coffee break
10:15-10:45	I. Milosev: Metals in orthopedic applications: joint collaboration between surgeons and engineers
10:45-11:15	D. Galusek: Bioactive glasses and glass-biopolymer composites doped with therapeutic ions
11:15-11:45	G. Mitov: Bioresorbable shell bending with 3D-printed templates in vertical alveolar ridge augmentation
11:45-13:00	Lunch-Break

13:00-13:30 T. Doll: Bioresorbable Materials in Active Implantable Medical Devices

13:30-14:00 A. W. Hassel: A Novel Approach for Tailor-Made Implant Materials

14:00-14:30 E. Kny: Improvement of biodegradable implants by functional coatings

14:30-15:00 H. Kitzinger: The clinicians view: requirements for bioresorbable fixation devices for musculosceletal injuries

15:00-15:30 Coffee-Break

15:30-16:00 J. Čapek: Zn-based biodegradable alloys – their prospects in implantology

16:00-16:30 M. Pacheco: Inside the corrosion and encrustation trend of biodegradable Mg alloys: towards the development of a biodegradable metallic ureteral stent

16:30-17:00 M. Werner: Bioabsorbable Scaffolds in Vascular Medicine

17:00-17:30 B. Domingues: Biodegrable and electrically responsive polymer hydrogel as a drug delivery system to manage ureteral stent-associated pain

17:30-18:00 C. von See: Challenges in 3D-printing of bone substitutes

18:00-18:15 Closing remarks

19:00 Social event: Visit of a wine tavern in Krems

→ RECENT DEVELOPMENTS IN BIORESORBABLE IMPLANTS ←

May 19, 2022
DPU Danube Private University
Steiner Landstrasse 124, 3500 Krems

S. Virtanen

Department of Material Science and Engineering, Friedrich-Alexander University, Erlangen, D

"Biodegradable metals: Challenges for understanding and controlling the corrosion behavior in biological environments"

Low-corrosion resistant metals, such as Mg, Fe, and Zn, have been in the focus of intensive research activities in view of their potential use in biodegradable implants. Biodegradable implants are of interest for applications, where the presence of the implant in the body is only desired for the time of healing (temporary implantation). A major part of the investigations has been carried out on Mg and its alloys, less work has been dedicated to Fe- or Zn-based materials. In all cases, the general challenge is to tailor the materials and surfaces to achieve the desired and controlled corrosion rate for the targeted applications. For Mg alloys, specific concerns arise from possibly strong hydrogen gas evolution and accompanied alkalization of the electrolyte during Mg dissolution. A further challenge is to elucidate the influence of the complex biological environment on the corrosion mechanisms of these materials. For successful applications, detailed knowledge on the corrosion rate and mode in the biomedical application is required. Implant corrosion has been studied *in vitro* in different types of simulated body solutions. Drastically different behaviours can be found for biodegradable metals when changing the type of physiological solution used as an electrolyte; in many cases the complexicity of the media makes it challenging to attribute the specific corrosion behaviour observed to a single parameter in the electrolyte. The presentation discusses some critical factors influencing the observed corrosion rates, such as presence of proteins or living cells in the electrolyte. The degradation rate in the biological environment should be adjusted for the specific application, to match the healing behaviour of the surrounding tissue. For the control of corrosion, research has targeted development of new alloys as well as coatings and surface modification. The presentation will summarize some coating approaches based on biodegradable synthetic or natural biopolymers. Finally, recent developments for experimental techniques to monitor corrosion rates will be briefly introduced.

W. Knoll

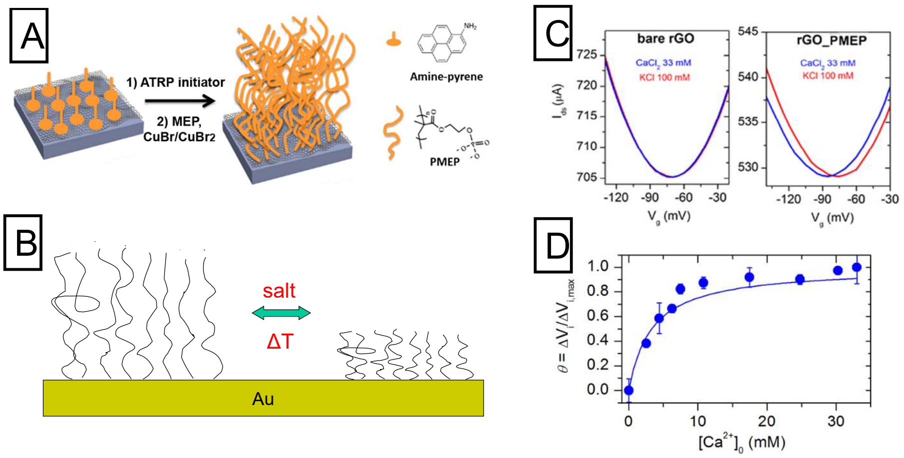
Austrian Institute of Technology and DPU Krems, A

"Responsive Polymer Brushes on Graphene Field-Effect Transistors as Novel Platform for Ion Detection"

Polyelectrolytes are charged macromolecules that interact - either as free coils in solution or when grafted to a solid surface as so-called brushes - with ions from their aqueous environment. Their configurations in 3D thus depend on the pH, the ionic strength, or the chemical nature, and the valency of the co-and counterions of the surrounding solution.

While polymer scientists focused their research primarily on the impact of ionic conditions on structural polymer properties one can reverse the perspective and use the (known) response of polyelectrolytes as a monitor to quantify changes in the ionic milieu.

In this lecture, I will briefly review some of the most prominent effects that ions can exert on polyelectrolytes and then introduce a novel platform to monitor ion concentrations, i.e., polyelectrolyte brushes grafted to either the gate electrode or directly to the channel of a field-effect transistor. Any ion-induced reorganization of the polyelectrolyte brush is associated with the redistribution of the charges of the system polymer/ionic milieu and can be sensitively monitored by recording the induced changes of the source-drain current through the device.



I. Milosev

Jožef Stefan Institute, Jamova and Valdoltra Orthopaedic Hospital, Slovenia

"Metals in orthopedic applications: joint collaboration between surgeons and engineers"

Increasing life expectancy and a more active and quality lifestyle in old age is the cause of the constant increase in diseases of the joints, which ultimately lead to surgery. The diseased joint is replaced with an implanted prosthesis, the functionality of the joint is restored, and thus the pain caused by the disease, usually arthritis, is reduced. In the last ten years alone, the number of operations on implanted hip and knee prostheses has increased several times, and that number is projected to increase. In such conditions, it is necessary to develop materials and designs of artificial joints with a longer lifespan in situ and enable the patient a more active and painless lifestyle.

Materials used to make various orthopaedic prostheses include metal, polymer and ceramic materials. Each of these materials must meet stringent requirements for use in the biological environment. Metallic materials must primarily have high corrosion resistance, and wear resistance is also extremely important for artificial joints. In orthopaedics, we use three metal alloys: titanium-based alloys, cobalt-based alloys and stainless steel. The lecture will present some basic considerations of materials properties and examples from clinical practice, which we perform in collaboration with orthopaedic surgeons. Changes in the material after the action in the body include various types of corrosion and wear of the material. The consequences of these processes are reflected locally and systemically in the human body.

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D. Galusek,
Aldo R.
Boccaccini

Institute of Biomaterials, Friedrich-Alexander University Erlangen-Nuremberg, Germany
Centre for functional and surface functionalized glass, Alexander Dubček University of Trenčín, Slovakia,
Joint Glass Centre of the IIC SAS, TnUAD and FChFT STU, Trenčín, Slovakia

"Bioactive glasses and glass-biopolymer composites doped with therapeutic ions"

Biologically active ions are used for doping bioactive glasses to enhance their therapeutic effect and to introduce additional functionalities. Extensive studies have been carried out showing the potential of such doped bioactive glasses, with the therapeutic ions promoting bone growth, wound healing, angiogenesis, or having a strong antibacterial effect. By their physical nature, bioactive glasses are commonly used as implants and agents for the regeneration of hard tissues, especially bones. Its incorporation into suitable biopolymers, such as chitosan, polylactic acid, etc., offers additional opportunities for soft tissue (skin, cartilage) treatment and regeneration.

This contribution gives an overview of the results of the collaboration of two institutes – the Centre for functional and surface functionalized glass in Trencin, Slovakia, and the Institute of Biomaterials at the Friedrich-Alexander University of the Erlangen-Nuremberg, Germany in the frame of their joint doctoral programme in the field of biomaterials. Various bioactive glasses (silicate, borosilicate, borate) were prepared both by conventional melt quenching or by sol-gel methods, in various forms, ranging from solid bulk glasses to mesoporous glass nanoparticles with ordered and disordered pore structures and doped by various biologically active ions, such as Zn, Cu, Ga, B and Ce. Depending on the nature of the dopant, the glasses were characterized *in vitro* from the point of view of their bioactivity, cytocompatibility with various cell lines, and antibacterial activity against both Gram positive and Gram negative bacteria. Selected compositions were incorporated into various biopolymers, and glass-polymer fiber composites with potential applications in wound healing were prepared by electrospinning.

Acknowledgment
The research presented in this presentation was carried out by members of the collaborating groups (in alphabetical order) Si Chen, Fatih Kurtuldu, Liliana Liverani, Martin Michálek, Nurshen Mutlu, Zuzana Neščáková, Susanta Sengupta, and Kai Zheng.
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G. Mitov

DPU Krems, A

"Bioresorbable shell bending with 3D-printed templates in vertical alveolar ridge augmentation"

Objectives. Alveolar ridge and vertical augmentations are challenging procedures in dental implantology. Shell techniques combined with autologous bone substitute materials are well documented. We applied 3D imaging and CAD techniques to plan an augmentation and create an individualized bending form for the adjustment of a resorbable biopolymer membrane made of polylactide.

Method. We present two cases with a vertical alveolar ridge defect in the maxilla. The cone beam computed tomography data were processed, and the desired augmentation volume was planned using a 3D. STL data were used to print a bending form. A bioresorbable KLS Martin 0.2-mm poly-D, L-lactic acid membrane was bended accordingly and placed into the defect via a tunnel approach in both cases and fixed using osteosynthesis screws. A mesh graft of autologous bone chips and hydroxylapatite material was augmented beneath the shell.

Results. The operative procedure was fast and without peri- or postoperative complications or complaints. A correct fitting of the material in the location and bone quality type II at the time of implant placement resulted in good primary stability.

Conclusions. A custom-made 3-D form for bending confectioned biomaterial pieces is an appropriate method for individualized adjustment in shell techniques. The advantages over direct printing of the biomaterial shell and products on the market, include cost-efficiency and avoidance of regulatory issues.

T. Doll, M. Nguyen, K. Formeny, V. Scheper, N. Verhaert, P. Wagner

Hannover Medical School MHH - BioMaterial Engineering Cluster of Excellence Hearing 4 All & Katolieke Univesiteit Leuven

"Bioresorbable Materials in Active Implantable Medical Devices"

Active Implantable Medical Devices (AIMD) are, by definition, delivering energy inside the human body and thus are high risk, class III of medical devices. In numbers of implantations, pace makers are leading in the market, however, due to their high power consumption, they come with batteries and thus need to be replaced in ten years intervals with several clinically unresolved drawbacks like abandoned electrodes that cannot be explanted. Cochlear implants (CIs) and retina implants, are, in number of electrodes, by far more complex and advanced, have undergone higher levels of miniaturization and cope with inductive powering by external sources. Hence, they can stay in place lifelong. As, in the case of cochlear implants, implantation is provided as early as in the age of six months for deaf babies, the guaranteed lifetime should be 100 years.
You may be wondering, how this conference contribution will contribute to the discussions on biodegradability? I comes into play when we want to address several phases in this log period: The functionality of existing AIMD can be improved or extended using the advantages of biodegradable materials. One focus of our research is the application of biodegradable materials in CIs. In those, the functionality can be extended from a stimulation device towards a temporary measurement unit using the available implant for inflammation detection. Emerging and future applications can also be further improved with biomaterials. This talk will provide you with ideas to sketch your individual roadmaps and future collaborations within and spreading out from ESBI, by giving examples for such implants, starting with sensory devices, active movement, drug delivery devices or a flexibility management for eased CI insertion. Also a wide range of other topics like deep brain stimulation, chronic pain management (e.g. migraine), spinal cord injuries or sphincter implants could be approached using biodegradable materials.

A.W. Hassel*
D.Recktenwald,
C. Mardare
A.I. Mardare

TIM, JKU Linz and DPU Krems, A

"A Novel Approach for Tailor-Made Implant Materials "

In a first instance bioresorbable implants must do their job as e.g. blood vessel supporting device. This is still best achieved using metallic implants. Matching contradictory requirements of the application is as usual achieved using alloys rather than pure metals. This way the properties like mechanical strength, toughness, hardness, elastic modulus, non-poisonousness, and corrosion stability may be all optimized simultaneously if a multi principal element alloy is used. Biodegradability in the end means some kind of destruction and removal of the implant. This can be achieved from a corroding alloy in which the constituting and thus released metals are non-toxic. They should possess a sufficient solubility but also sufficient chemical stability. Looking at the periodic system of the element, one should exclude noble gases, toxic elements, noble metals and also the very reactive alkali metals or valve metals. After this restriction has narrowed down quite a bit. Some elements however such as Fe, Zn, Mg are still good candidates. Other metals like the less frequently used lanthanoides e.g. Dy may still contribute. The development of an alloy is still a long way to go. In an attempt to accelerate such material development, we have developed the CALMAR system for the preparation of combinatorial material libraries. This way it is possible to generate some 10.000 different alloys on a single 4" wafer. Its investigation is then realised using scanning droplet cell microscopy with coupled down-stream analytics by means of ICP-OES and ICP-MS. Amongst others Zn-Mg-Dy alloys have been studied and the results will be presented to illustrate the advantages of the chosen approach.

E. Kny,
C. Kleber,
F. Pfaffeneder-Mantai

DPU Krems, A

"Improvement of biodegradable implants by functional coatings"

Biodegradable metal implants are based on either Mg, Zn or Fe, respectively their alloys. Alloying is used to modify the mechanical properties of the implants for their intended specific clinical application. Biodegradable metals have been and are used for cardiovascular stents, for orthopedic bone fixation and mechanical stabilization. The degradation and dissolution of Mg and Zn systems occurs usually too fast in the body and must be retarded and modified by either alloying and/ or by application of ceramic and polymer layers on top of the implant. A dissolution happening too fast is endangering the unwanted prematurely loosening of the mechanical stabilization effect, can cause the evolution of gaseous hydrogen in the case of Mg, large changes of the pH of bodily fluids and generates too much of metallic ions which cannot consumed by the body without clinical side effects. Implants based on Fe dissolve usually not fast enough and their dissolution has to be speeded up by alloying and by changes in the implant preparation process. The presentation is summarizing the state of the art in the application of coatings on biodegradable metal implants and is giving an outlook on further needed and anticipated developments.

H. Kitzinger,
S. Salminger

DPU Krems,
A

“The clinicians view: requirements for bioresorbable fixation devices for musculosceletal injuries ”

Bioresorbable implants can provide support, deliver drugs and degrade away after service, offering a promising alternative to common metal implants for patients. As bioresorbable screws are already used on a daily base in trauma care other devices, such as plates, are still not used in general. Among the known and well reported problems related to biodegradable implants are complications due to delayed or incomplete degradation process which can cause an inflammatory response interfering the recovery of the injured site. Moreover, mechanical strength of biodegradable implants needs to be improved. But besides those general qualities bioresorbable implants should not only have the same usability as metal implant systems during surgical procedures but should offer even more benefits than metal implants in order to become the new golden standard. Those desirable properties are summarized from a clinician´s perspective and illustrated with clinical case studies.

J. Čapek,
J. Pinc

FZU - Institute of Physics of the Czech Academy of Sciences, CZ

"Zn-based biodegradable alloys – their prospects in implantology "

Zn-based metallic materials have been introduced as potential biodegradable materials ten years ago. Since then, many Zn-based alloys or even composites have been prepared and investigated. In contrast to other metals considered as biodegradable materials (magnesium and iron), zinc and its alloys possess a more suitable corrosion behavior for implantology. Some studies even claim that zinc possesses ideal corrosion rates for cardiovascular stents. On the other hand, pure zinc reaches very low strength and ductility, especially in the as-cast state. To achieve a reasonable mechanical performance, suitable alloying and thermomechanical treatment of the Zn-based materials have to be performed. Another demerit of the Zn-based alloys is their low temperature stability and creep resistance. Also the biological response, for example osteoconductivity, of the Zn-based materials could be enhanced. Those issues could be overcome by designing new alloys, processing routes or surface treatments.

M. Pacheco et al.

I3Bs - Research Institute on Biomaterials, Biodegradables and Biomimetics of University of Minho PRT

"Inside the corrosion and encrustation trend of biodegradable Mg alloys: towards the development of a biodegradable metallic ureteral stent"

The utilization of biodegradable materials for ureteral stents is one of the most recent and appealing research topics in endourology[1,2]. Biodegradable polymers have been the most explored for this aim, but biodegradable metals have been gaining popularity as a promissory strategy as well, due to some particularities such as slower degradation rate and expected high radial force of a biodegradable metallic ureteral stent, compared with a biodegradable polymeric one. However, investigations on biodegradable metal's performance in ureteral stent's environment are scarce. Hence, it is of utmost importance to characterize the behaviour of biodegradable metals in ureteral stent's context and provide useful information for the progress of ureteral stents quality. In the present work, five Mg alloys were selected and studied in urinary tract conditions, regarding the corrosion pattern and encrustation propensity, for further investigations on biodegradable metals for urological applications

The analysis of the corrosion layer formed on the metal's surface is associated with compounds usually found on encrusted urinary catheters and stents, which is not a desirable characteristic in this context[3,4]. Besides, non-homogeneous degradation is a problem that must be addressed. Indeed, by optimizing the producing parameters of the metals, an ongoing work, we intend to improve the metal's characteristics in terms of encrustation and homogeneous degradation. The unwanted characteristics of biodegradable metals pointed out in this work will permit a more directed approach in further works, getting us closer to the main aim: the development of a biodegradable ureteral stent.

Acknowledgements:

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M. Werner

DPU Krems, A

“Bioabsorbable Scaffolds in Vascular Medicine ”

Atherosclerosis is the main cause of arterial obstructions and causes a number of diseases including coronary artery disease and myocardial infarction, cerebral infarction and peripheral artery disease. Revascularization of these obstruction can prevent occurrence of these diseases or positively influence the course of the disease.

The implantation of metallic stents has become a standard procedure to improve the outcome after revascularization of arteries. However, the permanent presence of a metallic stent in the arteries is associated with a number of potential disadvantages. Especially the peripheral arteries represent a harsh environment for metallic stents, since mechanical forces like bending, torsion or compression occur during normal activities.

Thus, the use of a bioresorbable stents (BRS), which stabilizes the vessel for a defined period after implantation but is then resorbed, is a compelling concept. Several trials have investigated a number of different BRS. They are either based on polymers like polylactic acid or magnesium alloys.

The current clinical evidence on safety and efficacy of these devices will be summarized in this presentation. BRS have a potential to improve patient outcomes in vascular medicine, however many questions remain open and the development as an efficient therapeutic approach is still in an early stage.

B. Domingues, E. Lima, A.A. Barros, R.L. Reis

I3Bs - Research Institute on Biomaterials, Biodegradables and Biomimetics of University of Minho, PRT

Biodegradable and electrically responsive polymer hydrogel as a drug delivery system to manage ureteral stent-associated pain"

The increasing interest in personalized pharmacotherapy has prompted the development of novel and sophisticated stimuli-responsive drug delivery systems. The use of an external trigger, such as an electrical field, enables spatial-, temporal-, and dosage-controlled release of drugs, allowing local concentrations to produce the required therapeutic effects.[1] Electrically responsive drug delivery systems represent an attractive alternative to treat ureteral stent-associated pain, a well-known and frequent side effect of stent placement.[2] A hybrid approach incorporating a conducting polymer, such as polyaniline, within a polymeric scaffold made of a natural polymer, such as gelatin, may present advantages for drug delivery application, including electrochemical activity, excellent biocompatibility, and tissue-like mechanical properties.[3] Here, we show a biodegradable electroactive hydrogel, synthesized by *in situ* crosslinking of gelatin-graft-polyaniline by genipin, at body temperature. These hydrogels were loaded with lidocaine, a local anesthetic, whose intravesical and intraureteral administrations have been proven to be safe.[4] Test tube inversion method and rheology measurements were performed to characterize those hydrogels properly. The biocompatibility of hydrogels was confirmed by carrying out appropriate tests, following ISO10993-5, and using L929 mouse fibroblast (ATCC NCTC clone 929) and G/G mouse uroepithelial (DSMZ ACC 224). Tests were performed with liquid extracts of material and with the material itself. The conductivity of the hydrogels in the swollen state was verified, and it was confirmed that conductivity varies proportionally with the amount of polyaniline present on the hydrogel. The degradability was accessed by allowing hydrogels to stay in artificial urine (ASTM F1828), in a dynamic *in vitro* system. We proved that the developed hydrogel system is capable of programmed drug delivery, in response to electrical stimuli, in artificial urine, at body temperature. Loaded with an anesthetic with local action, as lidocaine, these biodegradable electroactive hydrogels may represent a novel suitable strategy for efficient ureteral stent-pain management.

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C. von See

DPU Krems, A

Challenges in 3D-printing of bone substitutes

3D-printing and additive manufacturing enables to design and manufacture delicate structures and geometries. Especially when compared to molden techniques or casting as well as milling, internal structures of geometrical bodies is individual feasible. In combination with the 3D radiological data availability prior to bone augmentation the combination of 3D-printing and individualization of bone substitutes is self-evident. But still there is not such a 3D-printed bone substitute augmentation material on the market. This is due to the specific linker materials necessary for 3D-printing. Thus, a closer look on additive manufacturing technical solutions on the market in the combination with resorbable bone substitute materials will be given.

NOTES

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