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# Oral presentations

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**ORAL PRESENTATIONS**

## Oral Session - Blood Pump Development, O1-O6

### O1
### MINIATURIZATION AND OPTIMIZATION OF A VENTRICULAR ASSIST DEVICE

*Hallier S[1], Torner B[1], Wisniewski A[2], Müller J[2], Peter N[2], Wurm F[1]*
[1]Institute of Turbomachines, University of Rostock, Rostock, Germany; [2]Berlin Heart GmbH, Berlin, Germany

**Introduction:** Objective of the paper is to describe the challenges of miniaturization of a pump for use as Ventricular Assist Device (VAD) and adequate solutions.
**Material and methods:** A pump design was analyzed by involving design concept of a turbomachinery system considering separately defined requirements of a VAD. The turbomachinery design methods were adopted and extended to the special needs of a VAD. The targets of the design were miniaturized dimensions, high reliability, high efficiency, low acoustic radiation and, with highest priority, limited blood damage. The optimization was done by numerical simulations of the flow field and the rotordynamics. For the flow field simulation different numerical models were used. Part of the optimization was a comparison of RANS-methods and LES regarding their potential to reproduce zones with high blood damage.
The bond graph methodology was used to perform rotordynamic analysis. For assessment of blood damage an existing method was extended in order to analyze the local blood damage in the flow field. The used methods and the validation are explained in detail in the paper.
**Results:** The result of the optimization is a pump with dimensions that allow the use as a VAD and implantation by minimal invasive methods. The numerically analyzed blood damage is lower compared to published results. A validation of the numerical results regarding blood damage is in progress.
**Discussion:** The paper shows the successful design and optimization process of a VAD with the target of a miniaturization by keeping low blood damage properties of the VAD.

### O2
### DESIGN CHANGES OF THE VENTRICULAR ASSIST DEVICE SPUTNIK

*Selishchev S, Telyshev D*
Biomedical systems, National Research University of Electronic Technology, Moscow, Russian Federation

**Introduction:** Our research team focused on axial flow VADs since 2009. During our researches the Sputnik LVAD was designed and registered in Russia in the year 2012. Since the year 2013 the twenty implantations of the Sputnik LVAD were done in Russia. The development of the second generation of the Sputnik VAD was started in the year 2014. The main goal of the research is decreasing the pump size and power consumption without increasing the risk of hemolysis and thrombosis.
**Material and methods:** Sputnik LVAD was modified within the scope of studies. Diffuser design was redefined, thus, allowing removing taper expansion of rotor bundle and decreasing the overall pump weight-size parameters. Change in the rotor suspension scheme is different design of the outlet: rotor tightens via 2 magnets with their poles directed towards. Therefore, magnets repel and permanent surface contact is formed.
**Results:** The length of the implantable pump was reduced from 81 mm to 70 mm and the maximum diameter was decreased from 34 mm to 29 mm. Elimination of the taper expansion, new geometry of the diffuser and the rotor design changes allowed to reduce device energy consumption by 15%. Impeller diameter was changed from 15.6 mm to 13.8 mm, pump weight was reduced from 246 g to 205 g.
**Discussion:** The existing world trend towards reducing of VAD weight-size parameters offer new opportunities to increase the number of patients who initially could not be treated with VAD implantation due to a chest volume deficiency, especially in the pediatric cardio surgery.

### O3
### CURRENT AND SPEED RESPONSE OF THE HVAD IN SINGLE AND DUAL STATOR CONFIGURATION

*Maw M[1], Aigner P[2], Schima H[3], Moscato F[1]*
[1]Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Vienna, Austria; [2]Ludwig-Boltzmann-Cluster for Cardiovascular Research, Vienna, Austria; [3]Department of Cardiac Surgery, Medical University of Vienna, Vienna, Austria

**Introduction:** The housing that encases the HeartWare HVAD impeller contains two stators, situated at the top and bottom of the housing. For detailed investigation of the pump dynamics and the influence on flow estimation, a detailed knowledge of the interaction between the two stators is desirable. Therefore a setup was established, which allowed the characterization of the HVAD operation in single and dual stator configuration.
**Material and methods:** The temperature-controlled mock-loop setup consisted of a positive displacement pump, an air trapped reservoir and a controllable pinch valve. This facilitated modulation of inlet and outlet pressure. Water/glycerol mixtures constituted the working fluids. Static and dynamic measurements were conducted. During dynamic measurements the displacement pump produced a sinusoidal 0.5-20 Hz pressure head sweep.
**Results:** The static and dynamic responses of the single and dual stator configurations were identified at working points between 0-12 L/min and 0-200 mmHg. In both the static and the dynamic tests, motor current uptake was up to 5% and 20% higher for bottom and top single stator mode respectively, compared to dual stator mode. Current peak dynamic response was shifted from 4.9 ± 0.2 Hz in dual stator configuration to 3.0 ± 0.2 Hz in single stator configuration. Current and speed showed resonant behaviour at lowest and highest speeds, which are, however, outside of the clinically used range.
**Discussion:** The characterization of the current and speed response of the HVAD could be performed over a wide frequency range. In combination with effective filtering, it can be used to further optimize a highly-responsive flow estimator for different regular and extreme working conditions.

### O4
### INVESTIGATION OF THE PERMANENT MAGNETIC BEARINGS FOR RELIGA HEART ROT CENTRIFUGAL BLOOD PUMP

*Altyntsev I, Kurtyka P, Darłak M, Kustosz R*
Artificial Heart Laboratory, Zbigniew Religa Foundation for Cardiac Surgery Development, Zabrze, Poland

**Introduction:** The aim of this study was to improve the construction of the permanent magnetic bearings (PMB) for the impeller suspension system used in the centrifugal blood pump ReligaHeart-ROT (RH-ROT).
**Material and methods:** The investigation consisted of two phases, for defining forces generated by PMB acting on the impeller. Numerical calculations were conducted to verify efficiency of variable PMB construction. The magnets dimensions and positions were subjected to varying. The experimental analyses were performed on specially build test stand, utilizing radial and axial force sensors. The results obtained from both phases were compared, to verify measurement errors and improve analyses accuracy. All measurements were performed at the maximal impeller eccentricity of 0.2 mm. The impeller axial movement in the pump housing was analysed in the range of ±0.15 mm from nominal position, defined by the RH-ROT construction. The main guideline for analyses was to maximize stabilizing radial forces, while maintaining minimal the axial one.
**Results:** The force characteristics were obtained, as the result of performed analyses. The investigation of diverse magnet configurations allowed to developed magnetic system construction, increasing radial force and maintaining axial force values at suitable level. The initial radial forces maximum equalled 0.8N for the bottom, and 0.3N for the top magnetic bearing. New magnetic system increased radial forces to 2.1N for the bottom, and to 1.56N for the top magnetic bearing, respectively.
**Discussion:** The results obtained during analyses allowed to improve the PMB used in RH-ROT, which provide the stable suspension of the impeller.
**Acknowledgement:** Projects no. PBS1/A5/20/2012 and RH-ROT/266798/STRATEGMED-II supported by NCBiR.

**O5**

### BENCHMARK OF CENTRIFUGAL IMPELLER DESIGNS USING COMPUTATIONAL FLUID DYNAMICS: CLINICAL VAD VS. INDUSTRIAL PUMP

*Boës S[1], Wiegmann L[2], Ochsner G[1], de Zélicourt D[2], Meboldt M[1], Kurtcuoglu V[2,3], Schmid Daners M[1]*

[1]Product Development Group Zurich, Department of Mechanical and Process Engineering, ETH Zurich, Zurich, Switzerland; [2]The Interface Group, Institute of Physiology, University of Zurich, Zurich, Switzerland; [3]Zurich Center for Integrative Human Physiology, University of Zurich, Zurich, Switzerland

**Introduction:** The design of ventricular assist device (VAD) impellers is dominated by the geometric constraints of bearing and actuation system, as well as by the requirement of low hemolysis and thrombogenicity. Centrifugal pumps in larger dimensions used e.g. for pumping water, oil or gas have been built and optimized for decades, mainly aiming to improve the pump's hydraulic performance and efficiency. In our work we aimed to create a comprehensive performance benchmark for impellers used in VADs that includes parameters of hydraulic performance, efficiency, shear stress and flow disturbances, to allow a quantitative comparison of industrial-type and clinical VAD impellers.
**Material and methods:** We used established quantitative guidelines (JF Gülich, Centrifugal Pumps, Springer, 2014) for industrial pump design to construct a miniaturized impeller in the dimensions matching an implantable VAD. We simulated the transient flow fields using computational fluid dynamics, included Lagrangian particle tracking to follow erythrocytes and compared the flow patterns and cell paths to those observed in an established impeller design (HVAD, HeartWare Inc., Framingham, MA, USA).
**Results:** The benchmark demonstrates that the impeller designed according to industrial guidelines outperforms the HVAD in terms of hydraulic performance and efficiency. It also elucidates geometric optima with respect to number of blades, thickness of blades and gap size between rotor and housing.
**Discussion:** The benchmark allows for identification of pump features with the potential for optimization of the impeller design compared to existing VAD impellers. It demonstrates that performance benchmarks should be considered as tools for the design and optimization of VAD impellers.

**O6**

### TIME RESOLVED 3D-VELOCITY MEASUREMENTS IN A SCALED UP HEARTMATE II BLOOD PUMP MODEL

*Schuele C, Menzen C, Affeld K, Kertzscher U*

Biofluid Mechanics Laboratory, Charité - Universitaetsmedizin Berlin, Berlin, Germany

**Introduction:** For the prediction of the hemocompatibility of rotary blood pumps numerical blood damage models are used. Theses models require the assessment of the flow field inside the pump. The latter usually is obtained through numerical flow simulations (CFD). Theses simulations are rarely experimentally validated. Especially the turbulence inside a blood pump is not validated. Objective of this work is to present an experimental method to asses especially the time scales of turbulent motion. Therefore time resolved measurements of 3D velocity fields inside an exemplary rotary blood pump - HeartMate II – have been performed and are compared to corresponding simulations
**Material and methods:** Stereoscopic particle imaging velocity (Stereo-PIV) was applied to the flow field of an enlarged model of a HeartMate II pump with transparent casing. Images were acquired at a frequency of 8 kHz. A water-glycerol mixture with a viscosity of 3.5 mPas was used as blood replacement fluid. The pump was run at operating conditions corresponding to 9000, 10000, and 10600 rpm at volume flows between 4.5 and 5 L/min.
**Results:** 3D time resolved velocity fields were successfully measured and turbulent structures of different scales were identified. Spatial length scales of turbulence were directly calculated and all nine components of the Reynolds shear stress tensor could be evaluated in a 2D plane.
**Discussion:** Good agreement between mean velocities of the measurement and the Reynolds averaged Navier-Stokes (RANS) simulations could be shown, although some differences in the averaged fluctuating velocities were found.

## Oral Session - Vascular Access and New Perspectives, O7-O12

**O7**

### COMPUTER SIMULATION OF THE ARTERIOVENOUS FISTULA MATURATION

*Jodko D, Obidowski D, Reorowicz P, Jozwik K*

Institute of Turbomachinery, Lodz University of Technology, Lodz, Poland

**Introduction:** The arteriovenous fistula is a widely accepted vascular access for haemodialysis. The fistula is a surgically created connection between patient's artery and vein. Once this connection is made, a maturation process begins and lasts for a few weeks. This process is still not well understood. The aim of this paper is to show an innovative approach to modelling of the vein deformation during the maturation process in a-v fistulas.
**Material and methods:** In the first step of the maturation, the process was considered to be a mechanical response of the vein wall exposed to an increased blood pressure, and Fluid Structure Interaction techniques were used to simulate this stage. In the second step, a further extension of venous lumen as a biological process, in which a progressive decrease in the WSS is observed, was modelled. This approach is based on the shell theory equations, to which a novel model of a hyperelastic biological material is introduced. The proposed model assumes a certain relationship between the material constant factor and the area-averaged WSS, which is a function of the flow.
**Results:** Dilation of the vein was modelled as a two-step complex biomechanical process. The obtained results concerning the final diameter of veins are compared with averaged diameters obtained in a group of patients.
**Discussion:** This is probably the first attempt to model a deformation of the cephalic vein during the fistula maturation. The project was supported mainly by the National Science Centre in Poland (2014/13/N/ST8/04031) and partially by the Fund for Young Scientists from the LUT.

**O8**

### INFLUENCE OF THE ARTERIAL NEEDLE DIRECTION ON ACCESS FLOW MEASUREMENT

*Lopot F, Vermirovska J, Svara F, Polakovic V*

Department of Medicine, General University Hospital, Praha, Czech Republic

**Introduction:** Access flow (QVA) evaluation from recirculation at inverted needles is the preferred method in haemodialysis (HD) vascular access surveillance. The measurement procedure is well defined except for the direction of the arterial needle used during the measurement. We investigated influence of needle direction, either along the access flow (antegrade – AG) or against it (retrograde – RG) on the QVA.
**Material and methods:** QVA was measured by ultrasonic dilution in 25 patients during two consecutive HDs with the arterial needle in AG- in the first and RG-position in the second HD. The measurement was done at two extracorporeal blood flows (QB = 200 and 300 ml/min). QVA values obtained at corresponding QBs during both HDs were compared and ΔQVA (%) evaluated.
**Results:** Measurement with the arterial needle in AG position gave steadily higher QVA values than in RG position. The ΔQVA ranged from 5 up to 50% and was always more pronounced at QB = 300 compared to QB = 200 ml/min, presumably because of stronger breaking effect of higher blood flow being returned against the access flow. There was no significant systematic difference in QVA with the arterial needle in AG position for QB = 200 and 300 ml/min. Measurements are going on both in native fistulas and synthetic grafts to asses possible effect of access vessel elasticity in QVA suppression with RG needle position and to quantify the effect of QB.
**Discussion:** Direction of the arterial needle (AG/ RG) significantly affects QVA value, which calls for inclusion of the AG position among the measurement conditions.

**O9**

**CLINICAL USE OF AVF.SIM SYSTEM FOR SURGICAL PLANNING OF ARTERIOVENOUS FISTULA FOR HEMODIALYSIS**

*Bozzetto M[1], Rota S[2], Vigo V[3], Casucci F[3], Lomonte C[3], Morale W[4], Senatore M[5], Tazza L[6], Lodi M[7], Remuzzi G[2], Remuzzi A[1]*

[1]Bioengineering Department, IRCSS - Istituto di Ricerche Farmacologiche Mario Negri, Bergamo, Italy; [2]Unit of Nephrology and Dialysis, ASST Papa Giovanni XXIII, Bergamo, Italy; [3]Unit of Nephrology and Dialysis, Ente Ecclesiastico Ospedale F. Miulli, Acquaviva delle Fonti (BA), Fonti, Italy; [4]Unit of Nephrology and Dialysis, A.O. Cannizzaro, Catania, Italy; [5]Unit of Nephrology and Dialysis, Ospedale Annunziata, Cosenza, Italy; [6]Department of Urology and Nephrology, Catholic University, Rome, Italy; [7]Unit of Nephrology and Dialysis, Ospedale Santo Spirito, Pescara, Italy

**Introduction:** Arteriovenous fistula (AVF) is the best vascular access (VA) for hemodialysis, but its creation remains challenging. We previously developed and validated in a controlled clinical study a patient-specific computational model to predict blood flow volume (BFV) in AVF for different surgical configurations on the basis of demographic and clinical data, as well as preoperative ultrasound measurements. In the present research we aimed at investigating power of prediction and usability of the computational model in routine clinical setting.
**Material and methods:** We developed a web-based system (AVF.SIM) that integrates the computational model in a single procedure, including data collection and transfer, simulation management and data storage. An observational usability test was conducted to compare predicted vs. measured BFV and evaluate acceptance of the system in clinical routine. This test involved six Italian nephrology units for a six-month period.
**Results:** Out of the 74 patients selected, complete data from 60 patients were included in the final dataset. Predicted brachial artery BFV showed a good correlation with measured values (in average 787 ± 306 vs. 751 ± 267 mL/min, R = 0.81, p<0.001). For distal AVFs the mean difference (±SD) between predicted vs. measured BFV was -2.0 ± 20.9%, with 50% of predicted values in the range of 86-121% of measured BFV. Feedbacks provided by clinicians suggested that AVF.SIM is easy to use and well accepted in clinical routine, with limited additional workload.
**Discussion:** Clinical use of AVF.SIM system could help perform more efficient AVF planning, allowing individualization of VA care and improving surgical outcome.

**O10**

**HEALTH RELATED QUALITY OF LIFE IN HEMODIALYSIS PATIENTS WITH DIFFERENT NUMBER OF PREVIOUS ARTERIO-VENOUS FISTULA THROMBOSIS**

*Gelev S, Gerasimovska V, Dejanov P, Selim G, Dzekova P, Trajceska L, Sikole A*
Department of Nephrology, University Clinic, Skopje, The Former Yugoslav Republic of Macedonia

**Introduction:** The aim of this study was to evaluate whether presence of the arterio-venous fistula thrombosis (AVFth) may have an impact on health related quality of live (HRQoL) in our hemodialysis (HD) patients.
**Material and methods:** In cross-sectional study we examined 98 patients (56 male, mean age 53.6 ± 12.8 years, HD duration 120 ± 69.3 months). The patients were stratified according to the number of previous AVFth in three groups. We compared physical component summary (PCS) and mental component summary (MCS) scores (derived from SF-36 questionnaire) among the groups of patients.
**Results:** Patients (n = 39) without previous AVFth (group 1) had higher (p = 0.02) PCS as well as higher (p = 0.01) MCS score in comparison with patients (n = 45) with 1-2 previous AVFth (group 2) and patients (n = 14) with 3 and more AVFth (group 3). We did not found differences in both PCS and MCS scores among the group 2 and group 3 of the patients. Multivariate adjusted logistic regression analysis showed that the OR for the lower PCS and MCS scores increased significantly [OR = 1.02, CI (1.01-1.04), p = 0.024 for the group with 1-2 AVFth; OR = 1.06, CI (1.02-1.11), p = 0.038 for the group with 3 and more AVFth] in HD patients with the previous AVFth.
**Discussion:** HD patients with previous AVFth had lower HRQoL scores. AVFth presence is significantly associated with lower PCS and MCS scores.

**O11**

**CHANGING PERSPECTIVES IN EXTRACORPOREAL TREATMENTS – FROM PASSIVE MACHINE MONITORING TO ACTIVE PHYSIOLOGIC PATIENT DATA**

*Kleinekofort W*
Department of Engineering, RheinMain University of Applied Sciences, Wiesbaden, Germany

**Introduction:** Current machines for extracorporeal treatments have to deliver long alarm-free therapy periods, which are necessary to deliver a maximum of effective treatment during limited therapy time. Therefore it is crucial that the pressure alarm algorithms, which are integrated into haemodialysis machines, are robust and tolerant to random signal changes. However, a reduction in sensitivity is always a risk for the patient.
**Material and methods:** Effects of high ultrafiltration pulses (4 l/h for 5 min) on extracorporeal pressures, blood flow and relative blood volume are analysed during haemodialysis treatments with a FMC 4008 haemodialysis device. The pressure variations, which are induced by local flow and viscosity changes of the blood, are monitored and analysed using feed-back algorithms.
**Results:** Blood viscosity and blood flow in the venous part of the extracorporeal circuit are constantly varying with changes in ultrafiltration; therefore the flow resistance varies during dialysis. This has direct effects on the extracorporeal pressure signal. At the start of ultrafiltration the venous pressure drops within a minute by 30 mmHg and relaxes to a lower level after viscosity increase. At the end of ultrafiltration the venous pressure strongly increases above the former pressure and then relaxes to a new pressure level.
**Discussion:** It is well known that a low sensitivity threshold of pressure sensors in haemodialysis machines is a risk for the patient. However, the low sensitivity is mainly the answer to unnecessary pressure alarms during therapy, which come from physiologic changes. New adaptive feed-back algorithms will help to combine both maximum patient security and additional physiologic information.

**O12**

**CHALLENGE TO THE NEXT STAGE OF ARTIFICIAL KIDNEY**

*Matsuda K[1], Moriguchi T[1], Yamane T[2], Kokubo K[3], Yamamoto K[4]*

[1]Emergency and Critical Care Medicine, University of Yamanashi School of Medicine, Yamanashi, Japan; [2]Mechanical Engineering, School of Engineering, Kobe University, Kobe, Japan; [3]Medical Engineering and Technology, Kitasato University School of Allied Health Sciences, Kanagawa, Japan; [4]Medical Engineering, Kawasaki University of Medical Welfare, Kurashiki, Japan

**Introduction:** We had three challenges for the next stage of artificial kidney. At first, we made a new tiny hemofilter (size 68 × 98 × 18 mm, membrane area 0.3 $m^2$) with very fine hollow fibers (φ100 μm) for downsizing and fouling-free. Secondly, we made a small centrifugal blood pump (impeller dia: φ34 mm) for a simple and easy blood purification. Thirdly, we made a portable hemofiltration system (size 300 × 160 × 95 mm) with the tiny hemofilter and the small centrifugal blood pump. In this study, the three challenges were examined with a goat.
**Material and methods:** A double lumen vascular access catheter (10.8 Fr, BloodMax HC, Nipro®, Japan) was placed into the carotid vein of a healthy 30 kg goat under general anesthesia. After awakening, the portable hemofiltration system was put on the back of the goat. The blood flow rate was set at 80-100 mL/min with 3000 rpm. The filtration flow rate was set at 180 mL/hr using a conventional infusion pump (FP-N11, Nipro®, Japan). The heparin infusion rate was set at 1500-2000 unit/hr to maintain the activated clotting time between 180 and 250 sec.
**Results:** Continuous hemofiltration with the portable hemofiltration system could be performed for 6 days and 10 hrs without the change of a tiny hemofilter and the small centrifugal blood pump.
**Discussion:** We can conclude that the portable hemofiltration system is useful for the long-term continuous hemofiltration in a disaster area or a developing country of hemodialysis. In future, the system may be applied to a wearable or implantable artificial kidney.

## Oral Session - Biomaterials Synthesis and Characterization, O13-O18

### O13
### DIAMOND-LIKE-CARBON COATING FOR EXTENDED POLYTETRAFLUOROEHYLENE: POTENTIAL FOR EXPANSINO OF APPLICATION TO THE MEDICAL FIELD

*Fujii Y[1], Oozawa S[1], Osaka D[1], Nakatani T[2], Uchida H[3], Sano S[1]*
[1]Cardiovascular Surgery, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama, Japan; [2]Research Institute of Technology, Okayama University of Science, Okayama, Japan; [3]Department of Chronic Kidney Disease and Cardiovascular Disease, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama, Japan

**Introduction:** Diamond-like-carbon (DLC) is a coating material, which has potential for medical applications because of its possible high biocompatibility. However, DLC had been a coated over metals only, and not over soft fabrics such as polytetrafluoroethylene, dacron, and polyester. Recently, we developed a new technology to prepare DLC coatings for soft fabrics, and in this study, we tried to apply it to extended polytetrafluoroethylene (ePTFE).
**Material and methods:** DLC was coated over the surface of an ePTFE sheet by using a magnetron spattering system. The presence of DLC coating was confirmed with Raman spectrography. The stress-strain correlation was determined by performing the tensile test (80% stretched-out), and the condition of the surface of DLC coated ePTFE was observed by scanning electron microscopy (SEM). Inflammatory response was studied by implanting the DLC-coated ePTFE in the subcutaneous tissue of rats.
**Results:** Raman spectrography confirmed the existence of DLC coating on the surface of ePTFE with the observed typical waveform. The DLC coating (20-nm-thick) had no cracks and showed close adherence to ePTFE after the tensile test. The number of abnormal cells between the ePTFE sheet and fibrous tissue after implantation was significantly smaller in the case of DLC-coated ePTFE than in the case of DLC uncoated ePTFE.
**Discussion:** DLC was successfully coated on the surface of ePTFE, and it is durable and showed no cracks after 80% stretching. The inflammatory response of DLC-coated ePTFE is clearly different from that of uncoated ePTFE, and it indicates that DLC attenuates inflammatory response.

### O14
### CARDIOVASCULAR SCAFFOLDS FABRICATED FROM BLOOD PROTEIN SOLUTIONS VIA ELECTROSPINNING

*Mueller M[1], Dreyer L[1], Repanas A[1], Krolitzki B[1], Knigge S[1], Wang I[2], Pfeiffer D[2], Glasmacher B[1]*
[1]Institute for Multiphase Processes, Leibniz Universität Hannover, Hannover, Germany; [2]Institute for Cell Biology, Histology and Embryology, Medical University Graz, Graz, Austria

**Introduction:** Polymeric scaffolds offer many advantages for generating functional tissue. However, synthetic materials often lead to undesirable immune reactions. This study aims to use blood proteins in the fabrication of scaffolds for cardiovascular applications. Fabrication, long-term stability, and influence on cell proliferation will be investigated.
**Material and methods:** Platelet rich plasma (PRP) was prepared from whole porcine blood by centrifugation and processed to platelet lysate (PL). Influence of protein solutions on cell viability of fibroblasts was analyzed using MTT assay. Blends of polyethylene glycol (PEO, MW 400 K) and PL were electrospun, and subsequent glutaraldehyde cross-linking was examined. Samples were incubated in PBS (m/v ratio 50 mg/1.5 ml) for 28 d and then analyzed with regard to weight loss and protein release.
**Results:** By centrifugation platelet concentration was successfully raised by 720%. Ultrasound treatment caused the highest decrease in number of platelets (92%). The addition of 10% PL to fibroblast cell culture medium resulted in a 62% increase in cell number compared to control (10% FBS). Solutions of 3.7 m% PEO and 7.5 m% PL led to homogeneous scaffold morphology (fiber diameter 150 nm) and could be spun in a tubular shape. Cross-linked samples showed a weight loss of 43% after 28 days, while untreated samples lost 96% of their weight after 3 days. Here, protein concentration increased with weight loss.
**Discussion:** The results prove the feasibility of fabricating patient specific scaffolds via electrospinning of blood protein/PEO blends. The promising effect on cell viability will be verified by future experiments with endothelial cells.
**Acknowledgement:** REBIRTH(EXC 62/1).

### O15
### REDUCING WATER TRANSMISSION OF DYNAMICALLY LOADED POLYURETHANE BY MULTILAYER BARRIER COATINGS APPLIED BY PLASMA-ENHANCED CHEMICAL VAPOR DEPOSITION (PECVD)

*Lierath C*
Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, RWTH Aachen University, Aachen, Germany

**Introduction:** In this study, multilayer barrier coatings were applied on polyurethane membranes to generate a barrier coating against water transmission (WT), which may also resist elongations of up to 10%. Single barrier coatings, e.g. with silicon oxide, lead to little reduction of WT due to its low resistance against elongation.
**Material and methods:** On polyurethane samples, multilayer coatings consisting of inorganic $SiO_x$ and organic $SiO_xC_yH_z$ layers were applied by PECVD. Water Vapor Transmission Rate (WVTR) was measured for unloaded flatsheet samples to compare the barrier properties in dependence of layer thickness, amount of dyads and order of layer material. The samples were uniaxially loaded up to 7% and analyzed by Laser-Scanning-Microscopy in order to compare the cracking behavior of the various coatings. Coatings with promising results were applied on preformed polyurethane membranes and tested in a durability tester over 3 weeks to determine the WT under a dynamic load of up to 10% elongation. All measurements were compared to those of untreated samples/membranes.
**Results:** By using multilayer coatings, WT was reduced by up to 16% compared to untreated membranes/samples. WVTR was reduced by up to 71%. Furthermore, using a higher amount of dyads lead to a higher reduction of WVTR. A higher resistance of multilayer coatings against elongation was measured compared to single layers and could be further improved by varying coating parameters.
**Discussion:** In summary, WVTR as well as WT through polyurethane could be reduced by using multilayer coatings and, simultaneously, the resistance against elongation could be improved.

### O16
### LIFETIME PREDICTION FOR THE DESIGN OF A NEW POLYMERIC HEART VALVE PROSTHESIS

*Serrani M[1], Brubert J[1], Stasiak J[1], De Gaetano F[2], Costantino M[2], Moggridge G[1]*
[1]Department of Chemical Engineering and Biotechnology, University of Cambridge, Cambridge, UK; [2]Department of Chemistry, Materials and Chemical Engineering, Politecnico di Milano, Milano, Italy

**Introduction:** In the development of a clinically viable polymeric heart valve prosthesis (PHV), the achievement of an adequate device lifetime remains one of the main challenges to solve. Our group has recently developed a new bio-inspired PHV made of a styrenic block copolymer. The aim of this work is to implement a modelling tool which, combined with experimental data on the polymer fatigue properties, will allow to predict the device lifetime in order to optimise the valve design.
**Material and methods:** A finite element model of the polymeric valve was developed. The block copolymer mechanical behaviour was described by an anisotropic hyperelastic constitutive law; the material parameters were estimated by uniaxial tensile tests. A MATLAB routine was implemented to define the material orientation within the valve leaflets, based on experimental data of the material microstructure. Physiological pressure and boundary conditions were applied to simulate the valve closing. In parallel, crack propagation tests were performed on polymeric samples to find the relationship between number of cycles to failure and Strain Energy Density (SED) for the material.
**Results:** The simulations allowed to calculate the maximum SED in the valve for different designs and working conditions. These results, combined with the experimental data obtained by the crack propagation tests, allowed to predict for each design the valve lifetime under the specified load.
**Discussion:** The computational tool we have developed allowed to optimise the PHV design in terms of durability. This method can be also applied to predict the lifetime of different polymeric devices subjected to cyclic loads.

**O17**

### CLOSER LOOK INTO EXPERIMENTAL SET-UPS OF THE HIGHLY COMPLEX MAGNESIUM DEGRADATION

*Knigge S, Evertz F, Glasmacher B*
Institute for Multiphase Processes, Leibniz Universität Hannover, Hannover, Germany

**Introduction:** Magnesium is a high potential material for degradable osteosynthesis and cardiovascular implants. So far, numerous studies are focused on characterizing the degradation by in vitro testing aiming to predict in vivo degradation. But the lack of standardization leads to a high variation of experimental conditions so that comparison of data is hampered. Furthermore, little attention is given to different phases of degradation. This leads to inadequate prediction of in vivo degradation.
**Material and methods:** We developed an experimental guideline for immersion tests concerning choice of testing fluid and testing duration. Three different phases of degradation represented by significantly diverting degradation rates proof that test duration is playing a major role. Cylindrical magnesium samples were tested in SBF, PBS and porcine blood plasma for 44 days. Degradation was monitored by measuring the magnesium concentration in the test fluid.
**Results:** Results confirm that the degradation stability is highly dependent on the test fluid and test duration. PBS and blood plasma lead to a steady degradation within the first two days while SBF shows high variation until the seventh day of observation. Whereas for a extended testing duration (>30 days) a decreasing degradation rate was measured in all fluids which results from a significant reduction of surface area due to degradation.
**Discussion:** The fast initial degradation and the deceleration at a later time bias the degradation rate which is relevant for prediction. Therefore, a reliable prediction of in vivo degradation and the data comparison can only be reached with within the stable phase of degradation.
**Acknowledgement:** Thanks to SFB599.

**O18**

### IN VIVO BIOCOMATIBILITY STUDY OF AN INNOVATIVE ELASTOMER FOR LONG TERM IMPLANTS APPLICATION

*Zawidlak-Węgrzyńska B[1], Ścigała P[2], Janiczak K[1], Gawlikowski M[1], Cieśla P[1], Kustosz R[1], Gonsior M[1], El Fray M[3], Piegat A[3]*
[1]Artificial Heart Laboratory, Zbigniew Religa Foundation for Cardiac Surgery Development, Zabrze, Poland; [2]Emergency and Specialty Animal Medical Center, Piekary Slaskie, Poland; [3]Polymer Institute, Biomaterials and Microbiology Technologies Department, West Pomerania University of Technology, Szczecin, Poland

**Introduction:** The aim of the study was to evaluate the tissue reaction after implantation of the new elastomeric biomaterial, consisting of the poly(terephthalate ethylene) (PET) and dimerized parts of fatty acids (DLA) - (PET/DLA) modified by D-glucitol.
**Material and methods:** The implantation examinations were carried out according to the ISO-10993-6. Fifty New Zealand white rabbits, both sexes, weighing 3000-3500 g, were used. The implants (flat samples of 10 mm diameter and 1 mm thickness) were aseptically inserted in the both dorsal muscle, as the negative control Bionate-II-90A and Bionate-II-55D (DSM) were used. The observation was performed at 4 and 12 weeks after implantation. The biomaterial sample fixed tissue were histologically analyzed. Chemical study of explanted polymers was carried out using Fourier transform infrared spectroscopy (FTIR) and gel permeation chromatography (GPC).
**Results:** The implant micro-section evaluation showed that, the investigated material implanted for 4 and 12 weeks caused no response-mild fibrosis. There was no muscle degeneration, nor necrosis, nor any other significant change observed. FTIR spectra and GCP (molecular weight distributions) showed no measurable differences for implanted and non-implanted material.
**Discussion:** PET/DLA polymer implanted in dorsal rabbit muscle did not induce any adverse tissue reactions. Chemical analysis indicated that, the material was not affected during in vivo implantation. The complete biocompatibility evaluation should be performed in order to confirm PET/DLA properties necessary for long term medical implant devices.
**Acknowledgement:** This work has been supported by the Polish National Centre for Research and Development – project no. PBS1/A5/2/2012.

## Oral Session - Tissue Engineering. Bone and Cartilage, O19-O24

**O19**

### 2D TRANSPORT MODEL OF rPBBs FOR BONE TE PREDICTS THAT RADIAL FLUX UNIFORMITY CONTROLS $O_2$ DISTRIBUTION IN CELL ACTIVITY-DEPENDENT FASHION

*Donato D[1], Falvo D'Urso Labate G[2], Debbaut C[1], Segers P[1], Catapano G[2]*
[1]IbiTech-BioMMeda, Ghent University, Ghent, Belgium; [2]Department of Environmental and Chemical Engineering, University of Calabria, Rende, Cosenza, Italy

**Introduction:** Radial perfusion of annular porous scaffolds seeded with osteogenic cells in radial packed-bed bioreactors (rPBBs) may help realize large engineered bone constructs. Uniform oxygen distribution in constructs enables control of cell proliferation and differentiation but is effected by the interplay of medium perfusion and cell activity. In this work, the effect of medium radial flux distribution on dissolved oxygen pericellular spatial distribution in constructs cultured in rPBBs was studied for increasing cell activity with a 2D transport model.
**Material and methods:** Steady momentum and dissolved oxygen transport in the three compartments of axisymmetric rPBBs was described with a 2D model in terms of Navier-Stokes, Darcy-Brinkman, and convection-diffusion-reaction equations, for Michaelian oxygen cell consumption. Cells were assumed uniformly distributed in construct. Dimensionless model equations were solved under conditions typical of bone TE to predict the effect of the dimensionless groups on oxygen spatial distribution in construct. Radial flux uniformity was ensured with suitable bioreactor design along a radial flux uniformity criterion reported earlier.
**Results:** Axial oxygen concentration distribution was consistently uniform in construct with axially uniform radial perfusion fluxes. Non-uniform radial fluxes induce increasingly non-uniform oxygen distribution as cell metabolic activity increases with formation of hypoxic/anoxic areas. Increasing medium flow rates improve axial uniformity of oxygen distribution at any cell metabolic activity.
**Discussion:** Medium radial flux distribution significantly influences oxygen concentration spatial distribution in constructs cultured in rPBBs. Increasing medium perfusion flow rates help match increasing cell activity and avoid hypoxic/anoxic culture anywhere in construct as tissue matures.
**Acknowledgment:** Study co-funded by MIUR (PRIN 2010/MIND).

**O20**

### TIME EVOLUTION OF OXYGEN CONCENTRATION PROFILES AS CELLS GROW AND DIFFERENTIATE IN rPBBs FOR BONE TE FROM A 3D TRANSIENT TRANSPORT MODEL

*Falvo D'Urso Labate G[1], Torchia F[1], Debbaut C[2], Segers P[2], Catapano G[1]*
[1]Department of Environmental and Chemical Engineering, University of Calabria, Rende, Cosenza, Italy; [2]IbiTech - BioMMeda, Ghent University, Ghent, Belgium

**Introduction:** Perfusion of osteogenic cells seeded in porous hollow constructs in radial packed-bed bioreactors (rPBBs) must provide an even oxygen supply to cells for uniform tissue maturation, as in natural long bones. Cell density influences local construct permeability and pericellular oxygen level. A transient 3D transport/reaction model including cell proliferation and differentiation was used to study the interplay of mass transport and cell seeding, as a means to adjust operating conditions to cells needs in rPBBs with axial inlet and lateral outlet port.
**Material and methods:** Flow transport in rPBBs was described with Navier-Stokes (hollow cavity and peripheral annulus) and Darcy-Brinkman (construct) equations. Diffusion/advection equations were used for oxygen transport. Cell oxygen consumption and proliferation were described with Michaelis-Menten and two-substrates Monod kinetics with death term. Cell growth was assumed to uniformly decrease size of interconnected pores, changing construct porosity and permeability. Conservation equations were solved numerically for geometries and operation typical of bone TE.
**Results:** At axially uniform cell seeding, uniform radial fluxes ensure even cell proliferation, whereas non-uniform radial fluxes cause initial non-uniform cell proliferation, but cell growth eventually equalizes the radial fluxes. Operation

of slender constructs at low feed flow rates in which cells are seeded non-uniformly causes uneven cell proliferation, also with uniform radial fluxes. At axially non-uniform cell seeding, non-uniform radial fluxes along rPBB length cause non-uniform cell proliferation hindering uniform tissue maturation.
**Discussion:** Model predictions stress the importance of optimizing cell seeding to promote uniform bone tissue maturation in vitro in rPBBs.
**Acknowledgment:** Study co-funded by MIUR (Project PRIN 2010/MIND).

**O21**
**OSTEOGENIC DIFFERENTIATION OF RAT BONE MARROW STROMAL CELLS ENCAPSULATED INTO PHOTOCROSSLINKED COLLAGEN-LIKE POLYPEPTIDE HYDROGELS**
*Nurlidar F, Yamane K, Kobayashi M, Terada K, Ando T, Tanihara M*
Materials Science, Nara Institute of Science and Technology, Nara, Japan

**Introduction:** Cells cultured in three-dimensional (3D) scaffolds can behave like cells in their native microenvironment. Therefore, 3D scaffold is very important to guide cell differentiation for tissue regeneration purpose. A key challenge in this field is to develop 3D scaffolds that are cytocompatible, can mimic cell microenvironment and support cell differentiation. Collagen-like polypeptide, poly(Pro-Hyp-Gly), is promising to fabricate 3D scaffolds due to its similar features with native collagen and biocompatibility. It also doesn't contain pathogenic substances. In this work, we investigated rat bone marrow stromal cell (rBMSC) behavior and their osteogenic differentiation when encapsulated in 3D scaffolds of poly(Pro-Hyp-Gly).
**Material and methods:** We simultaneously encapsulated rBMSCs into poly(Pro-Hyp-Gly) hydrogel by photocrosslinking of methacrylated poly(Pro-Hyp-Gly) under visible light in the presence of eosin Y, triethanolamine and 1-vinyl-2-pyrrolidinone. Viability of the encapsulated cells and their osteogenic differentiation were investigated to demonstrate cytocompatibility of poly(Pro-Hyp-Gly) hydrogel as a 3D scaffold for cell encapsulation.
**Results:** Simultaneous cell encapsulation results in homogeneous distribution of the encapsulated cells within the 3D scaffolds. Cells in the 3D scaffolds incubated in 20% FCS/α-MEM remained viable during 7 days of incubation. They were able to form aggregate and bone nodules when incubated with osteogenic medium. Scanning electron microscope (SEM), Alizarin red S and von Kossa staining showed that calcium was deposited in the 3D scaffold suggesting that rBMSCs in the scaffold have differentiated into osteoblasts.
**Discussion:** These results showed that poly(Pro-Hyp-Gly) hydrogel can serve as cytocompatible 3D microenvironment for osteogenic differentiation of rBMSCs.

**O22**
**BONE TISSUE ENGINEERING WITH POLYCAPROLACTONE/ HYDROXYAPATITE BIOMIMETIC SCAFFOLDS**
*Garcia Garcia A[1], Schlatter G[2], Anne H[2], Egles C[1], Bedou F[3], Legallais C[1]*
[1]BMBI UMR 7338, Université de Technologie de Compiègne, Compiègne, France; [2]UMR 7515 ICEPEES, Université de Strasbourg, Strasbourg, France; [3]UMR 7337 Laboratoire Roberval, Université de Technologie de Compiègne, Compiègne, France

**Introduction:** Preparation of nanofibrous scaffolds mimicking the native structure of tissues is one of the major challenges of tissue engineering. Cells interaction, structure and mechanical solicitations should also be reproduced to achieve tissue reconstruction. Here, we propose to elaborate 3D Honeycomb-like scaffolds made of electrospun poly(ε-caprolactone) (PCL) nanofibers and electrosprayed hydroxyapatite (HA) microparticles that mimics the native tissue. The differentiation of C3H10T1.2 embryonic murine cells into osteoblastes will be monitored.
**Material and methods:** The scaffold was made by the alternative deposition of electrospun PCL (Mw = 80 $kg.mol^{-1}$) layers and electrosprayed HA (nanopowder with d ≤200 nm) layers over a microstructured collector, forming the honeycomb-like structure. C3H10T1.2 embryonic murine cells were cultured over the electrospun scaffold for 96 h. Cell colonization, viability, infiltration, morphology and differentiation were evaluated.
**Results:** Our scaffold showed good biocompatibility after 5 days of culture. In addition cell adherence and homogeneous cells distribution within the scaffold is significantly enhanced. Cells covered the entire scaffold surface inside and outside the honeycomb cavities. Moreover, combined qualitative ALP activity stain and the increase of osteocalcin expression, showed a differentiation through bone tissue.
**Discussion:** We demonstrated an effective control over the morphology and topography of the engineered scaffold. Cells C3H10T1.2 which have been proved as cells with capacity of differentiation over adipocytes, osteoblasts and tenocytes, have been oriented for a bone tissue phenotype proving that our topography has a direct influence on cell behavior.

**O23**
**MACROPOROUS PLA CONSTRUCT SUPPORTING THE OSTEOINDUCTIVE POROUS CHITOSAN-HYDROXYAPATITE HYDROGEL FOR BONE TISSUE ENGINEERING**
*Rogina A[1], Pribolšan L[2], Gómez-Estrada L[3], Gallego Ferrer G[4], Marijanović I[2], Ivanković M[1], Ivanković H[1]*
[1]Faculty of Chemical Engineering and Technology, University of Zagreb, Zagreb, Croatia; [2]Faculty of Science, University of Zagreb, Zagreb, Croatia; [3]Ikasia Technologies SL, Burjassot, Valencia, Spain; [4]Center for Biomaterials and Tissue Engineering (CBIT), Universitat Politècnica de València, Valencia, Spain

**Introduction:** Chitosan-hydroxyapatite based composites have proved to exhibit great biocompatibility, minimal foreign body reaction and good wettability, although biomechanical properties cannot meet applications in vivo. To overcome the mechanical drawback, additional synthetic polymers such as PLA is used. The aim of this research is to produce a three-component system with suitable microstructure, bioactivity and mechanical properties for bone tissue repair.
**Material and methods:** Material's preparation is divided in steps: 1) 3D printing of PLA; 2) *in situ* synthesis of chitosan-hydroxyapatite (CHT-HA) suspension; 3) impregnation of PLA scaffold with CHT-HA suspension, and freeze-gelation of PLA/CHT-HA scaffold. The scaffold's composition and microstructure were investigated by FTIR spectroscopy, X-ray and DSC analysis and SEM imaging. Osteogenic properties were evaluated by in vitro cell culture of hMSCs during 21 days using q-PCR.
**Results:** The X-ray and FTIR identification has confirmed successful *in situ* formation of hydroxyapatite within chitosan matrix of PLA/CHT-HA scaffold. Freeze-gelation has provided porous structure of CHT-HA within PLA scaffold with good pore interconnectivity, confirmed by SEM imaging. The proliferation of hMSCs cultured on PLA/CHT-HA scaffold during 7 and 14 days indicates favourable microenvironment. Quantitative analysis of gene expression measured at 21 day of culture confirmed better osteogenic properties of PLA/CHT-HA scaffold indicating hydroxyapatite influence in osteogenesis stimulation.
**Discussion:** The combination of 3D printing and freeze-gelation has provided production of highly porous scaffold suitable for cell proliferation. *In situ* precipitation of calcium phosphate as bioactive component is suitable for preparation of more bioresorbable hydroxyapatite. Positive osteogenic signal of PLA/CHT-HA scaffold highlights the potential use in bone reconstruction.

**O24**
**BIODEGRADABLE MICROSPHERES FOR ARTICULAR CARTILAGE REGENERATION**
*Sancho-Tello M[1], Milián L[1], Zurriaga J[2], Forriol F[3], Martín de Llano J[1], Mínguez M[4], Carda C[1]*
[1]Departamento Patología, Universidad de Valencia; INCLIVA, Instituto Investigación Sanitaria Hospital Clínico Universitario de Valencia, Valencia, Spain; [2]Servicio Traumatología, Hospital Clínico Universitario de Valencia, Valencia, Spain; [3]Servicio Traumatología, Hospital Clínico Universitario de Valencia; ERESA, Valencia, Spain; [4]Servicio Traumatología, Hospital Clínico Universitario de Valencia; INCLIVA, Instituto Investigación Sanitaria Hospital Clínico Universitario de Valencia, Valencia, Spain

**Introduction:** The study of biodegradable microspheres as mechanical support for articular cartilage regeneration "in vivo", by histological evaluation of the neotissue formed after microspheres implantation in articular cartilage lesions.
**Material and methods:** New Zealand rabbits underwent a surgery with drilling of 3 mm lesion in the femoral condyle, allowing bleeding from subchondral bone. Defects were filled with microspheres made of polylactic acid (PLLA) or PLLA and Chitosan (50/50, PLLA+QT); control group received

no filling. Lesions were covered by a PLLA membrane in all groups. Three months after surgery, animals were sacrificed and samples were obtained and processed for histological study using standard techniques.
**Results:** A good restitution of the chondral surface was macroscopically observed in all groups, with a whitish appearance and eventual irregular surface. Microscopic study revealed that microspheres induced the presence of a neotissue similar to articular hyaline cartilage, but with immature appearance, that was thicker in PLLA group and with persistence of biomaterial particles underneath the neocartilage, whereas it was thinner in PLLA+CHT group, where no biomaterial was observed. Neotissue in control group had a fibrous appearance.
**Discussion:** Microspheres provide invading mesenchymal cells from subchondral bone, a three-dimensional environment favorable in order to induce their differentiation to the chondral phenotype, with the synthesis of a chondral matrix and thus achieving articular cartilage regeneration.
**Acknowledgement:** Biomaterials were generated at the Center of Biomaterials and Tissue Engineering, Universitat Politecnica de Valencia, Spain. This study was supported by Spanish Ministerio de Economía y Competitividad (project MAT2013-46467-C4-4-R) and Valoritza i Transfereix INCLIVA project (Valencia, Spain).

## Oral Session - Blood Trauma in VADs, O25-O30

### O25
### CHARACTERIZATION OF BLOOD DAMAGE UNDER DYNAMIC AND STATIC CONDITIONS USING MULTIPLE HEMOLYSIS MARKERS

*Wiegmann L[1], de Zélicourt D[1], Speer O[2], Kurtcuoglu V[3]*
[1]The Interface Group, Institute of Physiology, University of Zurich, Zurich, Switzerland; [2]Erythrocyte Laboratory, University Children's Hospital Zurich, Zurich, Switzerland; [3]The Interface Group, Institute of Physiology and Zurich Center for Integrative Human Physiology, University of Zurich, Zurich, Switzerland

**Introduction:** Hemolysis is an important risk factor in patients with artificial organs and a constant concern in the design process. Yet, beyond the general agreement on the detrimental impact of elevated shear stresses, the exact influence of fluid forces on single cell integrity and hemolysis remains poorly understood. In this parametric experimental study, we systematically characterized the hemolytic impact of pressure and shear stresses in the ranges relevant for artificial devices and standard blood handling procedures.
**Material and methods:** We simulated the transient flow fields inside a ventricular assist device and used Lagrangian particle tracking to probe possible erythrocyte paths and typical stress histories. Based on this, we designed a pressure chamber and a set of PDMS microchannels to independently characterize the effect of static and dynamic parameters. Attention was paid to the background damage induced by preparatory procedures. Endpoint measures include free hemoglobin, osmotic resistance and membrane phosphatidylserine exposure.
**Results:** We reproduced characteristic stress histories with magnitudes of up to 400 Pa and gradients of 1-5 Pa/µm in channels that allow for single cell characterization (10 × 10 µm). Pressure drop across the channels was in the range of bars. We investigated its effect through independent parametric variations. We further observed that even standard clinical and experimental procedures, such as centrifuging and pipetting, induce measurable hemolysis.
**Discussion:** While micro-fabricated arrays (including the proposed experimental setup) have clear potential for the characterization of hemolysis at single cell level, our results also emphasize the need to carefully consider all experimental steps and imposed forces, which we have characterized here in detail.

### O26
### THE INFLUENCE OF OPERATING CONDITIONS ON THE FLOW FIELD IN A ROTARY BLOOD PUMP

*Thamsen B, Gaebler J, Affeld K, Kertzscher U*
Biofluid Mechanics Laboratory, Charité - Universitaetsmedizin Berlin, Berlin, Germany

**Introduction:** Current rotary blood pumps (RBPs) are designed for a specific operating point. However, RBPs interact with the cardiovascular system leading to varying operating conditions during the cardiac cycle. Consequently, lower flow rates frequently occur which are suspected to promote thrombosis. Aim of this study was to examine the flow field in the HeartWare HVAD at different operating points using computational fluid dynamics.
**Material and methods:** Based on dimensions from an explanted pump, a geometric model of the HVAD was generated. Blood was modeled as Newtonian fluid and the flow field was simulated solving Reynolds-averaged Navier-Stokes equations with a sliding mesh approach and a k-ω shear stress transport turbulence model for a nominal and a low flow condition (5 L/min and 2 L/min). General flow structures as well as shear stress distributions were analyzed and compared.
**Results:** The overall flow characteristics were very similar for both flow condition: a flow separation occurred in all impeller channels on the suction side of the blade. A flow separation at the volute tongue was seen at 2 L/min. The surface area of the rotor and housing with low wall shear stresses (<5 Pa) was three times larger for the lower flow rate (515 vs. 173 mm²).
**Discussion:** Although overall flow structures were very similar in the nominal and low flow condition, in the latter case a flow separation zone was identified at the volute tongue and low wall shear stresses occur in larger areas of the blood contacting surface. Consequently, the low flow condition might be more susceptible for thrombosis.

### O27
### ABILITIES OF ULTRASONIC METHODS APPLICATION TO MICRO-EMBOLUS DETECTION IN MECHANICAL HEART SUPPORTING SYSTEMS

*Gawlikowski M[1], Lewandowski M[2], Jaworek M[1]*
[1]Artificial Heart Laboratory, Zbigniew Religa Foundation for Cardiac Surgery Development, Zabrze, Poland; [2]Institute of Fundamental Technological Research PAS, Warsaw, Poland

**Introduction:** Thromboembolism still has been one of the most fundamental problem in mechanical circulatory support (MCS). Theoretical study showed, that micro-clots founded in blood may be detected by ultrasonic echo analysis. Goal of study was to investigate character of ultrasonic echo reflected on blood in order to find large objects with different acoustic impedance.
**Material and methods:** The multi-gate Doppler system was constructed. Initial investigations were performed on water with polymeric micro-particles (90 µm-250 µm). In-vitro experiments were conducted according to acute trombogenicity method. Blood was filtered (cascade filter, porosity 150, 105 and 40 µm) to assess micro-clots size and quantity. Final investigations were performed on animal's model (70 kg pig, 26 days, pulsatile, pediatric VAD). The spectrograms were analyzed off-line by means of following models: auto-regression, time-frequency and power spectrum assessment, in order to detect micro-embolus in all cases mentioned above.
**Results:** The micro-particle of 90 µm minimal size was detected. Micro-clots in blood-circulated in vitro were in various sizes (45 µm to 270 µm), types (small platelets aggregates, medium-size spherical micro-clots and larger filamentous structures), and quantities (from 1063 $L^{-1}$ for aggregates to 6 $L^{-1}$ for filamentous embolus). Auto-regression model detected micro-embolus with 92% sensitivity and 77% specificity. The spectrograms character correlated with clinical picture of supported animals. However, some cases appeared difficult for assessment.
**Discussion:** The ultrasound spectrogram analysis seems to be useful tool for non-invasive monitoring of thromboembolism in MCS. Further investigations are necessary in order to unambiguous assign spectrogram to phenomena occurring in coagulation system.
**Acknowledgement:** Project no. PBS1/A3/11/2012 supported by NCBiR.

**O28**
**INFLUENCE OF A THROTTLE IN HEMOLYSIS TESTS OF ROTARY BLOOD PUMPS**
*Affeld K, Lommel M, Rekus M, Thamsen B, Kertzscher U*
Biofluid Mechanics Laboratory, Charité - Universitaetsmedizin Berlin, Berlin, Germany

**Introduction:** Hemolysis testing is commonly performed during development of rotary blood pumps. Thereby, the pump operates in a model circulation composed of a blood reservoir, tubes and a throttle to adjust the operating point. Consequently, not only the influence of the pump itself as it would operate in the human body is quantified and the question arises if the throttle causes an additional hemolysis? Objective of this study therefore was to quantify the influence of the throttle on hemolysis.
**Material and methods:** For an isolated detection of the throttle impact alone, the flow loop setup had to be modified in a way that any kind of pump is avoided and the flow rate is generated externally. A throttle was placed on a tube connecting two reservoirs (volume capacity of 2 L). A pressure was build up in the reservoirs to produce a volume flow of 5 L/min from one reservoir to the other and switched over when a reservoir is empty. Fresh bovine blood was used to measure the normalized index of hemolysis (NIH). In addition, hemolysis of a Heartmate II pump was measured in a standard procedure.
**Results:** Preliminary results revealed a NIH of 0.019 for the HMII and 0.004 of the throttle alone where the damage of the test setup without throttle was subtracted.
**Discussion:** The hemolysis caused by a throttle might be in the same order of magnitude as what is commonly detected for a rotary blood pump. Further investigation is planned for the future.

**O29**
**INCIDENCE AND RISK FACTOR OF GI BLEEDING AMONG PATIENTS SUPPORTED WITH CONTINUOUS FLOW LEFT VENTRICULAR ASSIST DEVICE (CF-LVAD)**
*Miyamoto T, Nishinaka T, Umehara N, Ichihara Y, Tateishi M, Komagamine M, Katsube T, Saito S, Yamazak K*
Cardiovascular Surgery, Tokyo Womens Medical University, Tokyo, Japan

**Introduction:** Gastrointestinal bleeding (GIB) is a major complication among patient supported with cf-LVAD. Incidence and causes of GIB in our institute were evaluated.
**Material and methods:** From March 2011 to July 2015, 34 patients were implanted and supported by cf-LVAD for at least 6 months at our institute. Medical records were reviewed, and incidence and causes of GIB were evaluated. The parameters including PT-INR, platelet count, and von Willebrand factor were evaluated every 6 months after implant, and univariate analysis was performed for several risk factors.
**Results:** Mean age was 38 y. Mean support duration was 717 ± 395 days. 7 patients were female. Etiologies of heart failure were as follows (DCM:28, DHCM:4, ICM:1, others:3). 5 patients suffered from GIB. The causes of GIB were as follows (diverticulum of colon: 2, polyp: 1, unknown: 2). The patients were divided in two groups: GIB group (patients with GIB) and non-GIB group (patients without GIB). The rate of freedom from GIB was 91.3% at 1 year and 83.2% at 2 year. In comparison of two groups, platelet count was tended to be decreased in GIB group (GIB group: $14.8 \times 10^4$, non-GIB group: $21.2 \times 10^4$, p = 0.018 at 6 months). In univariate analysis, among several factors such as sex, age, antiplatelet therapy other than aspirin, and use of mucoprotective agent, over 45 y age was observed to be a risk factor of GIB (in patients of over 45 y age, OR:13.7, 95% CI:1.3-143.4, p = 0.10).
**Discussion:** Incidence of GIB was observed with relatively low rates, while low platelet count and older age were associated with incidence of GIB.

**O30**
**INCIDENCE OF NON-SURGICAL BLEEDINGS DECREASES OVER TIME AFTER CONTINUOUS FLOW LVAD IMPLANTATION**
*Jacobs S, Rega F, Meyns B*
Cardiac Surgery, KU Leuven, Leuven, Belgium

**Introduction:** Bleeding is one of the most frequent complications after LVAD implantation. Apart from the surgical bleeding in the immediate postoperative phase, nose bleedings and gastro-intestinal (GI) bleedings are the most frequent causes of bleeding. Research on bleeding events focuses primarily on the cause of bleeding and underlying coagulation disorders. The time course of these bleeding events is less well studied.
**Material and methods:** Hospital files of all patients who received a continuous flow LVAD implantation (HeartMate II, Thoratec Inc.) between 2007 and 2016 were reviewed (n = 118). All patients had exclusive follow-up in our centre and bleeding events were questioned and documented at every outpatient visit. Only non-surgical bleedings were included in the study. Mean follow-up of the population was 341 days (range 2 to 2046 days)
**Results:** Freedom from bleeding was 52% at one year. Nose bleedings (29.7%) were the most frequent, followed by GI bleedings (13.6%) and hemorrhagic strokes (4.2%). Forty percent of the patients had more than 1 bleeding episode. Bleeding events per 100 patient years decreased from 105 in the first year to 27 after the first year (p<0.0001).
**Discussion:** Non-surgical bleedings are frequent after LVAD implantation. We observed an impressive decline in bleeding incidence after the first year on assist device. This is most likely due to the combination of adapting anticoagulation protocols and treatment of the bleeding causes. This data indicate that bleeding risk varies in time and can be influenced. This is important in counselling patients about long term assist (i.e. destination therapy).

## Special Symposium - Biodegradable Polymeric Scaffolds for Advanced Tissue Engineering Concepts, O31-O34

**O31 (KL1)**
**FUNCTIONAL NANOFIBROUS SCAFFOLDS COMBINED WITH STEM CELLS FOR ADVANCED BIOMEDICAL DEVICES AND THERAPIES**
*Neves NM*[1,2]
[1]3B's Research Group - Biomaterials, Biodegradables and Biomimetics, University of Minho, Headquarters of the European Institute of Excellenceon Tissue Engineering and Regenerative Medicine, Guimarães, Portugal; [2]ICVS/3B's, PT Government, Guimarães, Portugal

**Introduction:** Among the various possible embodiements of Advanced Therapies and in particular of Tissue Engineering the use of temporary scaffolds to regenerate tissue defects is one of the key issues. The scaffolds should be specifically designed to create environments that promote tissue development and not merely to support the maintenance of communities of cells. To achieve that goal, highly functional scaffolds may combine specific morphologies and surface chemistry with the local release of bioactive agents.
**Material and methods:** Many biomaterials have been proposed to produce scaffolds aiming the regeneration of a wealth of human tissues. We have a particular interest in developing systems based in biodegradable polymers. Those demanding applications require a combination of mechanical properties, processability, cell-friendly surfaces and tunable biodegradability that need to be tailored for the specific application envisioned.
**Results:** Those biomaterials are usually processed by different routes into devices with wide range of morphologies such as biodegradable fibers and meshes, films or particles and adaptable to different biomedical applications. In our approach, we combine the temporary scaffolds populated with therapeutically relevant communities of cells to generate a hybrid implant. For that we have explored different sources of adult and also embryonic stem cells.
**Discussion:** We are exploring the use of adult MSCs, namely obtained from the bone marrow for the development autologous-based therapies. We also develop strategies based in extra-embryonic tissues, such as the perivascular region of the umbilical cord (Wharton´s Jelly).
This talk will review our latest developments of natural-based biomaterials and scaffolds in combination with stem cells for advanced biomedical devices and therapies.

**O32 (IL7)**
**BIO-INSPIRED INJECTABLE HYDROGELS AS IN SITU FORMING BIODEGRABLE SCAFFOLDS**
*Gallego-Ferrer G*
Centre for Biomaterials and Tissue Engineering, Universitat Politècnica de València, Valencia, Spain

**Introduction:** In situ forming hydrogels are advantageous scaffolds for tissue engineering due to their ability to encapsulate cells, injectability with minimal invasive surgeries and adaptability to the shape of the defect. Biomimetic structures inspired in the composition of the extracellular matrix can be obtained by the combination of proteins and polysaccharides. The protein provides adhesion sequences for cell interaction and the polysaccharide confers hydration and mechanical stiffness. The aim of this work is to explore the benefits of these combined structures on cell differentiation for the tissue engineering of soft tissues.
**Material and methods:** Fibrin-chitosan (Fbn-CHT) hybrids were produced by mixing chitosan microparticles with fibrinogen and subsequent crosslinking. Gelatin-hyaluronic acid (Gel-HA) matrices were obtained by enzymatically crosslinking previously synthesized tyramine conjugates.
**Results:** Dedifferentiated chondrocytes cultured in a nonchondrogenic medium on the Fbn-CHT hybrids recovered the phenotypic characteristics of hyaline cartilage chondrocytes. Proliferation was nearly suppressed after 7 days of culture and the cells actively produce collagen type II and sGAG. The alternance of chitosan microspheres and fibrin domains provides a nonflat topography that contributes to cellular redifferentiation. HA in the Gel-HA hybrids yield higher Young's modulus and swelling. Increased stiffness counterbalanced traction forces of cells and promoted myotube formation of encapsulated myoblasts. Chondrogenic differentiation was also promoted when mesenchymal stem cells were encapsulated in the Gel-HA hybrids, even in a growth medium.
**Discussion:** Bio-inspired injectable hydrogels are promising candidates for the tissue engineering of soft tissues.
**Acknowledgment:** EU-FP7 PIAP-GA-2012-324386, MINECO MAT2013-46467-C4-1-R projects and CIBER-BBN-Instituto de Salud Carlos III are acknowledged.

**O33 (IL8)**
**SILK FIBROIN-BASED HYDROGELS AS INSTRUCTIVE BIOLOGICAL MILIEU**
*Motta A*
Department of Industrial Engineering and BIOtech Research Centre, University of Trento, Trento, Italy; European Institute of Excellence on Tissue Engineering and Regenerative Medicine, Trento, Italy

**Introduction:** Hydrogels made from natural-derived polymers have become especially attractive in the field of tissue engineering for regenerating a wide variety of tissues and organs. Biologically inspired materials has become an increasingly platform towards innovative approaches in tissue engineering and regenerative medicine, because nature can provide a formidable set of "smart" materials.
**Material and methods:** Silk, a family of biopolymers is a tremendous example of structural material derived from self-assembly of relative simple molecular building blocks, with bio recognition capability, ability to self-assemble depending on the fabrication process and on the specific work-environment. Fibroin-based gels can be prepared by treating fibroin solutions with acids, with thermal treatments or addition of electrolytes to the fibroin solution, via shear stresses or sonication and, as recently reported, by supercritical carbon dioxide.
**Results:** Fibroin hydrogels depending on the processing method, showed different structures with unique properties in terms of crosstalk ability with the biological environment, so forming a tunable 3D instructive biological milieu for tissue regeneration field. Fine tuning fibroin-based gelation methods to better control hydrogel functional features, as well as incorporation with single or multi-components, are driving the improvement of SF hydrogel. Hydrogels have been validated in the last years in vitro and in vivo for several tissue engineering applications.
**Discussion:** Remarkable work has been made to control the structural and functional characteristic of silk hydrogels, integrating novel biological features with advanced processing techniques, to develop the next generation of functional silk fibroin hydrogels.

**O34 (IL9)**
**BIOMIMETIC SURFACE MODIFICATIONS FOR TISSUE ENGINEERING APPLICATIONS**
*Groth T, Koewitsch A, Zhao M, Yang Y, Esmaeilzadeh P*
Biomedical Materials Group, Institute of Pharmacy, Martin Luther University Halle-Wittenberg, Halle (Saale), Germany

**Introduction:** Biomimetic surface modification of tissue engineering scaffolds may promote not only attachment, but also growth and differentiation of primary and tissue-derived stem cells. Glycosaminoglycans (GAG) as components of extracellular matrix (ECM) and cell surface proteoglycans seem to be useful building blocks for such coatings due to their inherent bioactivity, abundancy and chemical stability.
**Material and methods:** GAG were activated either by oxidation or thiolation for covalent immobilization on surfaces. Furthermore native and activated GAG were used to make surface coatings with layer-by-layer technique with additional possibility for intrinsic cross-linking. Bioactivity studies were carried out with cultures of fibroblasts and mesenchymal stem cells.
**Results:** Surface analytical techniques showed that oxidized GAG can be successfully bound via imine bonds to amino-terminated surfaces, while thiolated were bound either photochemically to vinyl groups or directly on gold. Multilayer formation of activated GAG with polyamines was also successfully monitored by surface analytical techniques showing advantages of intrinsic cross-linking regarding layer mass and stability. Studies with human fibroblasts revealed that activated GAG immobilized on surface exhibited a bioactivity promoting adhesion, spreading and growth of cells. Multilayer coatings made of activated GAG promoted growth and differentiation of MSC.
**Discussion:** Activated GAG seem to be promising materials for stable, biomimetic surface coatings but also 3D systems in different tissue engineering applications promoting growth and differentiation of cells.
**Acknowledgment:** The work was funded partly by the European Commission, (FP7-PEOPLE-2012-IAPP) under grant agreement no. 324386 (FIBROGELNET).

## Special Symposium - Biomimetic Devices for Tissue and Organ Regeneration, O35-O39

**O35 (KL4)**
**OPEN AND CLOSED POLYMERIC THREE-DIMENSIONAL STRUCTURES FOR TISSUE ENGINEERING**
*Mano J*
Department of Chemistry, CICECO, University of Aveiro, Aveiro, Portugal

**Introduction:** The development of hybrid devices for tissue engineering is often inspired by the composition and complexity of native tissues. At the lowest level of such organization, one should select the adequate biomaterials to be used as the building block of the structure that will support cells and control their behaviour towards the production of new tissue.
**Material and methods:** We have been proposing the use of multilayered based arrangements prepared by the layer-by-layer technique (LbL) that could be then integrated in more complex porous macroscopic devices, often exhibiting a multi-scale organization. Using adequate templates, non-flat coatings can be fabricated with tuned compositions along the build-up assembly, including porous devices.
**Results:** This enables the production of very well controlled multifunctional and structural devices using mild processing conditions that could be useful in biomedicine, including in tissue engineering. In particular we have been interested in developing more complex/hierarchical porous structures using natural-based polymers that could fulfil specific requirements in such kind of applications. Often multiple cell types should be integrated in such hybrid devices to recapitulate relevant biological features necessary to trigger the regeneration process.
**Discussion:** Methodologies developed in our group will be exemplified, permitting the production of: (i) 3-dimensional (open) porous nanostructured scaffolds for tissue engineering, enabling the support of cells, by combining LbL and rapid prototyping technology; and (ii) multi-scale spherical objects to encapsulate cells, acting as "living" injectable or (closed porous) implantable devices.

**O36 (IL21)**
**LIVING BIOINTERFACES BASED ON NON-PATHOGENIC BACTERIA TO HARNESS STEM CELL BEHAVIOUR**
*Salmeron-Sanchez M*
Division of Biomedical Engineering, School of Engineering, University of Glasgow, Glasgow, UK

**Introduction:** The extracellular matrix (ECM) provides mechanical and biochemical support to cells, and plays a critical role in cell behaviour. Our aim is to engineer novel interfaces that mimic the dynamic behavior of the extracellular matrix, in particular in terms of integrin/receptor interactions as well as the presentation of growth factors. To do that, we have engineered biointerfaces between synthetic materials and cells that consist of genetically modified non-pathogenicn *Lactococcus lactis*. This layer of bacteria constitute a functional and dynamic interface that can be tuned to express adhesion proteins and growth factors, which constitutes an advanced and revolutionary way to control cell behavior in general and stem cell differentiation in particular.
**Material and methods:** *L. lactis* were modified to express FNIII7-10 as a protein membrane. Then, another strain was engineered to express BMP-2 either as a membrane protein or secreted to the cell culture media. Bacteria viability was characterisised as well as the interaction of stem cells with the functional interface (focal adhesions, viability) and stem cell differentiation towards osteogenic lineages.
**Results:** Bacteria were successfully modified and characterized to assess both the expression of FNIII1-10 as a membrane bound protein as well as the expression and secretion of BMP-2. Then, stem cell adhesion was studied on the engineered biointerfaces, and the formation of focal adhesions was quantified on the living interfaces. We show that the presence of BMP-2 induces stem cell differentiation towards osteogenic lineages on a layer of engineered *L. lactis*.
**Discussion:** We have shown that engineered non-pathogenic bacteria represent a dynamic functional biointerface able to direct stem cell differentiation.

**O37 (IL22)**
**FAST-DEGRADATION HYDROPHILIC-HYDROPHOBIC ENVIRONMENTS FOR CELL TRANSPLANTATION**
*Gámiz-González MA[1], Guldris P[1], Antolinos Turpín CM[2], Ródenas Rochina J[1], Vidaurrea A[2], Gómez Ribelles JL[1]*
[1]Center for Biomaterials and Tissue Engineering (CBIT), Universitat Politècnica de València, Valencia, Spain; [2]Networking Research Center on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Valencia, Spain

**Introduction:** Fast degradation polymer networks based on water-soluble chitosan derivatives have been produced using new biodegradable polycaprolactone cross-linkers. These networks combine hydrophilic chitosan domains with polycaprolactone chains that provide the obtained gel with adherent sites for protein adsorption and cell adhesion.
**Material and methods:** Aldehyde end capped low molecular weight polycaprolactone chains was used to cross-link carboxymethyl chitosan, in order to produce a block copolymer network of varying composition. Cross-linking reaction took place in a common solvent.
**Results:** It has been shown that polycaprolactone blocks are able to crystallize what probes phase separation between hydrophilic and hydrophobic domains. In spite of the hydrophobic component, even at high polycaprolactone contents the material behaves as a hydrogel with high equilibrium water content. Gels degrade in few days in hydrolytic or enzymatic media. Mesenchymal stem cells are viable when seeded in macroporous membranes made of these materials. The membranes disappear in cell culture after around one week showing continuous increase of cell numbers along this period.
**Discussion:** In this way the new materials are promising environments for cell transplant in regenerative therapies allowing cell delivering with very short-term resorption of the transplant vehicle.
**Acknowledgment:** MINECO MAT2013-46467-C4-1-R project and CIBER-BBN-Instituto de Salud Carlos III are acknowledged.

**O38**
**ENHANCEMENT OF ENDOTHELIAL CELL ADHESION ON EPTFE SUBSTRATE BY THE IMMOBILIZATION OF FIBRONECTIN-DERIVED PEPTIDE VIA SINGLE-STEP TYR OXIDATION**
*Kakinoki S[1], Suzuki S[1], Nishioka S[1], Yamaoka T[2], Hirano Y[1]*
[1]Department of Chemistry and Materials Engineering, Faculty of Chemistry, Materials and Bioengineering, Kansai University, Osaka, Japan; [2]Department of Biomedical Engineering, National Cerebral and Cardiovascular Center Research Institute, Osaka, Japan

**Introduction:** Expanded polytetrafluoroethylene (ePTFE) is widely used for cardiovascular prostheses due to its excellent anti-platelet adhesion property. Meanwhile, the adhesion of endothelial cells is also inhibited resulting in the lack of endothelialization and late thrombosis. In this study, we developed the high-efficient peptide immobilization technique and succeeded in the enhancement of endothelial cell adhesion on ePTFE substrate.
**Material and methods:** Fibronectin-derived cell adhesive peptide, Leu-Asp-Val with Tyr and positively-charged residues was manually synthesized by the typical Fmoc solid phase procedure. The peptide was immobilized on ePTFE substrate by just immersing into aqueous peptide solution with $CuCl_2$ and $H_2O_2$ used as catalyst and oxidant, respectively. Peptide-immobilized ePTFE surface was analyzed by water contact angle measurement and XPS spectra. Adhesive behavior of human umbilical endothelial cells onto peptide-immobilized ePTFE substrate was evaluated in vitro.
**Results:** After peptide immobilization, the water contact angle was remarkably decreased and the strong N1s peaks assigned to the peptide were detected in XPS spectra. These behaviors were remarkable in the peptide containing basic residues, suggesting that peptide adsorption and reaction of quinones produced by Tyr oxidation were promoted by the introduction of basic residues. Endothelial cell adhesion was greatly improved on peptide-immobilized ePTFE surface.
**Discussion:** We successfully immobilized cell adhesive peptide on ePTFE substrate by single-step Tyr oxidation. Especially, we found that the efficiency of peptide immobilization is drastically improved by the introduction of basic residues in the peptide sequence resulting in the enhancement of endothelial cell adhesion. This technique might be useful to accelerate the endothelialization on ePTFE prostheses.

**O39**
**MATERIAL-DRIVEN FIBRONECTIN NANONETWORKS PROMOTE MAINTENANCE OF MESENCHYMAL STEM CELL PHENOTYPES**
*Rico P[1,2], Mnatsakanyan H[1], Salmerón-Sánchez M[3]*
[1]Centre for Biomaterials and Tissue Engineering, Universitat Politècnica de València; [2]Biomedical Research Networking Center in Bioengineering, Biomaterials and Nanomedicine, Valencia, Spain; [3]Division of Biomedical Engineering, School of Engineering, University of Glasgow, Glasgow, UK

**Introduction:** Material systems mimicking natural environment of Mesenchymal Stem Cells (MSC) offer an approach to prolong MSCs multipotency. This is an alternative of strategies based on soluble factors in culture media. Material properties can direct lineage commitment. We previously demonstrate that subtle variations in surface chemistry modulates the conformation of adsorbed fibronectin (FN) that spontaneously organized into nanonetworks on Poly(ethyl acrylate) (PEA) while adsorbs in a globular morphology on Poly(methyl acrylate) (PMA). We hypothesise that FN nanonetworks assembled on PEA influence MSC behaviour.
**Material and methods:** Polymer films were obtained by spin coating on glass. Protein adsorption was performed and FN distribution was observed by AFM. Mouse MSCs were seeded at different densities and cell adhesion, differentiation and contractility were followed by immunofluorescence and qPCR analysis.
**Results:** Immunofluorescence and qPCR detection of markers for osteogenic and adipogenic commitment showed minimum levels after 15 days of culture under basal conditions whereas greater expression on PEA was obtained under differentiation stimulation. In addition, stemness marker expression was elevated in PEA under basal conditions after 15 and 30 days of culture.
**Discussion:** PEA induced FN-nanonetwork formation promotes enhanced, prolonged maintenance of self-renewal factors and retention of functional multipotency when basal media is used. However, when defined medias, traditionally used to induce specific differentiations is used, enhanced levels

of differentiation is noted; i.e. the cells were more sensitive to the defined medias when cultured on the FN nanonetworks.
**Acknowledgement:** The financial support of MAT2015-69315-C3-1-R (including the FEDER and CIBER) and ERC through HealInSynergy (306990) is acknowledged.

## Special Symposium - ALBUMIN - an Old Molecule with New Insights, O40-O43

### O40 (IL23)
### PROPERTIES AND ANALYSIS OF FUNCTIONAL CHARACTERISTICS OF HUMAN SERUM ALBUMIN

*Schnurr K, Waterstradt K*
MedInnovation GmbH, Berlin, Germany

**Introduction:** Albumin is the major plasma protein. It is a very flexible molecule with different affine binding sites for long chain fatty acids. It´s well known physiological functions are the maintenance of osmotic pressure and the transport function for fatty acids and other hydrophobic substances, trace elements and also medical drugs. Binding of these molecules can affect the ability of conformational mobility of human serum albumin. Detoxification is an important function of serum albumin either. Pathophysiological changes can influence this functionality efficiently. This albumin function correlates to dangerous illnesses, such as sepsis and SIRS. Serum albumin removes metabolites and toxins by transport to the liver, to help the organism to detoxify and regenerate.
**Material and methods:** The Albumin-functionality-test based on EPR spectroscopy can detect these modified binding and functional characteristics of serum albumin. The used radical supporting spin probe binds analogous other natural albumin ligands variably strong in different albumin binding sites and thus serves as indirect marker for serum albumin functionality.
**Results:** Compared to other tests for the assessment of the capacity to bind on the albumin molecule (e.g. ABiC) the Albumin-functionality-test makes additional statements regarding functional characteristics like transport quality and detoxification efficiency of albumin. Thus an “effective” albumin concentration could be determined, quantifying the amount of functional albumin in the patient.
**Discussion:** As a conclusion of results of various modules the Albumin-functionality-test can be used for disease progression monitoring and prognosis of SIRS, sepsis and liver diseases, for examination of efficiency of liver dialysis systems and for quality control of commercial albumins.

### O41 (IL24)
### MEASURING DEVICE FOR THE NON-INVASIVE DETERMINATION OF BILIRUBIN DURING EXTRACORPOREAL LIVER SUPPORT THERAPY

*Preussiger M[1], Tyczynski B[2], Kribben A[2], Jost U[3], Jungmann H[1]*
[1]MBR Optical Systems GmbH & Co. KG, Wuppertal, Germany; [2]Universität Duisburg-Essen, Wuppertal, Department of Nephrology, University Hospital Essen, Essen, Germany; [3]HepaNet GmbH, Hannover, Germany

**Introduction:** Hepatic diseases are wide spread and complicated to be handled due to secondary complications. Extracorporeal liver support therapies (ELST) are used to bridge the time to transplantation or to support liver function recovery. Since bilirubin is one of the prominent toxins to be removed, its actual status during ELST is a standard indicator for therapy efficiency. To enable monitoring of bilirubin during treatment, a device for point-of-care measurement of the bilirubin gradient is required.
**Material and methods:** A non-invasive device for measuring the transcutaneous bilirubin (TcB) concentration in blood circulation with visible reflection spectroscopy has been developed. Measurements during treatments with the fractionated plasma separation and adsorption system (Prometheus®, FPSA) assessed the function and reliability of the device and evaluated the gradient of bilirubin concentrations compared to serum bilirubin levels (SBR). SBR samples were taken at the beginning of the therapy and after every 2 hours; TcB readings every hour.
**Results:** Bilirubin was detected in the measured TcB-spectra from samples taken within 10 seconds. The gradient of calculated TcB-concentrations showed a good correlation ($r = 0.97$, $p<0.002$) to SBR, which decreased during therapy from 25 to 17 mg/dl.
**Discussion:** The developed non-invasive device enables the measurement of bilirubin gradient, even in the presence of high SBR of 25 mg/dl. Due to the short reading time, online monitoring during FPSA is feasible. The non-invasive device is a promising method to monitor effectiveness of toxic reduction during ELST. As a consequence the reduction of blood sampling in patients and related costs can be expected.

### O42 (IL25)
### THE ALBUMIN BINDING CAPACITY (ABIC): BIOMARKER OR THERAPEUTIC TARGET?

*Mitzner S[1,2], Stange J[1], Klammt S[2,3]*
[1]Division of Nephrology, Department of Medicine, University of Rostock, Rostock, Germany; [2]Fraunhofer Project Group EXIM, Rostock, Germany; [3]Charité Research Organisation (CRO), Berlin, Germany

**Introduction:** Human serum albumin (HSA) has multiple physiological functions in the human body, whilst the transport of water-insoluble metabolites and drugs is one of its most important features. Failure of liver or kidneys, as major organs of waste processing, results in overload of the albumin molecule with various ligands, such as bilirubin and bile acids (liver), or indoxyl sulfate and p-cresyl sulfate (kidneys). Currently, there is a lack of suitable biomarkers to detect albumin transport capacity failures in patients.
**Material and methods:** An assay was developed for the assessment of Albumin-Binding Capacity (ABIC) based on the capability of a ligand specific for a binding-site using the quantification of the remaining unbound fraction. ABIC was evaluated in various clinical situations, such as in acute decompensation of chronic liver failure, and at various stages of chronic kidney disease or sepsis.
**Results:** In all investigations a negative correlation between ABIC and the severity of disease was observed. Commercially available HSA-products show a decreased ABIC due to the addition of stabilizing ligands. Passage of commercial or HSA from patients over charcoal sorbents increased ABIC. There is good evidence that therapeutic cleansing of HSA in patients with liver failure with the MARS-method improves clinical parameters, such as hepatic encephalopathy, hepatic pruritus, circulatory or renal function.
**Discussion:** ABIC is a promising parameter to describe the status of patients with organ failures. Evidence suggests that the restoration of sufficient ABIC, either by albumin cleansing methods, such as MARS or the supply of fully functional albumin, is of therapeutic value.

### O43 (IL26)
### ALBUMIN IS HERE TO STAY … OR TO BE REMOVED: STILL OPEN QUESTIONS

*Vienken J[1], Baurmeister U[2]*
[1]Usingen, Germany; [2]Wuppertal, Germany

**Actual perceptions:** Current dialysis therapy moves towards an increasing use of high flux dialysis and its related treatment modalities, such as haemodiafiltration. Dialysis membranes with increased pores sizes are required for these treatment options. Depending on ultrafiltration rates, these membranes allow for the passage of even small peptides. The current dogma, designed by nephrologists, prescribes that these membranes should have a cut-off below the molecular weight of albumin, i.e., around 60,000, which reflects a sieving coefficient far below 0.1. As a consequence, only a 4 g loss of albumin is maximally accepted during a haemodialysis session. In contrast, treatments with peritoneal dialysis show a daily albumin loss of >10 g.
**Open questions:** Under the premise that “you can only control what you can measure!”, we are entitled to ask questions that may help to elucidate the role of the albumin molecule in more detail. Some of them are exemplarily listed here. How to describe the dynamics of the 3D-conformation of the albumin molecule during uraemia and during a treatment session? Do such changes affect the performance of the molecule? Can we expect a dynamic modification of molecule conformation? What is the impact of treatment aspects, such as anticoagulation, dialysis fluid composition and temperature? Do co-morbid conditions, such as diabetes and inflammation affect the performance of the albumin molecule as a molecular vacuum cleaner? Do we have to substitute albumin and compensate for its loss, given that modified albumin is removed?

**Consequences:** Clinical trials to answer these questions are needed and under way.

## Oral Session - Cardiovascular Implants for Children, O44-O48

### O44
### THE NEW POLISH PEDIATRIC VAD FAMILY DEVELOPMENT AND PRE-CLINICAL STUDIES

*Kustosz R[1], Gonsior M[1], Ścigała P[2], Czingon M[3], Kapis A[1], Pacholewicz J[4], Kuback Ki[4], Gawlikowski M[1], Bujok W[1], Głowacki M[1], Janiczak K[1], Cieśla P[1], Zawidlak-Węgrzyńska B[1]*

[1]Artificial Heart Laboratory, Zbigniew Religa Foundation for Cardiac Surgery Development, Zabrze, Poland; [2]Clinic for Animals Piotr Ścigała, Piekary Slaskie, Poland; [3]Clinic for Animals Michał Czingon, Zabrze, Poland; [4]Silesian Center for Heart Diseases, Zabrze, Poland

**Introduction:** The innovative family of pediatric extracorporeal, pneumatic ReligaHeart (RH) PED VAD was developed. RH-PED construction provides a low risk of thrombogenicity, no hemolysis and good hemodynamic features, confirmed during in-vitro and in-vivo pre-clinical studies.
**Material and methods:** RH-PED VAD was developed with different stroke volume: SV = 45, 30 and 20 $cm^3$. The device construction is based on asymmetric shape of adult device (RH-EXT) and is equipped with original tilting disc valves, designated for VAD application. The prototype of unique single-leaflet polyurethane inlet valve was developed for 20 $cm^3$ VAD. RH-PED manufacturing technology was developed, followed with prototypes production. The functional examination, long term durability and in-vitro acute thrombogenicity tests utilizing fresh animal blood were performed. The in-vivo studies were carried out, during 30 days of mechanical heart support using RH-PED 45 $cm^3$ and 30 $cm^3$, in domestic pig model (n = 7). VAD performance and animal health status were monitored. Presence of micro and macro biological material in VADs was examined during the experiment and after device explantation. Histopathological evaluation of animal vital organs was carried out.
**Results:** In-vitro and in-vivo pre-clinical studies results confirmed low thrombogenicity, no hemolysis and good overall physical performance of RH-PED VADs. In-vivo studies proved a lack of impact to vital organs and no sign of thrombus adhering to the pump. The RH PED prototype manufacturing technology could be upscale to the clinical device production.
**Discussion:** The RH-PED VADs pre-clinical examination results confirmed it reliability, opening prospect to introduce device-manufacturing technology for first clinical applications.
**Acknowledgement:** Project no. PBS1/A7/1/2012 supported by NCBiR.

### O45
### A NOVEL TEST BENCH TO SIMULATE THE INTERACTION OF VAD WITH THE FAILING SUPERIOR CAVO-PULMONARY CONNECTION

*De Gaetano F[1], Griselli M[2], Soos P[3], Costantino M[1]*

[1]Department of Chemistry, Materials and Chemical Engineering, Politecnico di Milano, Milano, Italy; [2]Department of Cardiac Surgery, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia; [3]Berlin Heart GmbH, Berlin, Germany

**Introduction:** Pulsatile Ventricular Assist Devices (VADs) offer different control strategies for mechanical circulatory support on patients with total cavo-pulmonary circulation. Great majority of research is focusing on these patients whilst children with failing superior cavo-pulmonary connection (SCPC) or Stage II Norwood remain an unsolved issue. Reasons are the scarcity of suitable assist devices for this small sub-group of univentricular patients and unsuitability for emergency types of mechanical cardiac support.
**Material and methods:** To understand the best way to treat these kind of patients, we developed a novel test bench of SCPC able to mimic both physiological (obtained from cardiac catheterization of 20 patients who have done well after SCPC) and pathological range of values. One modified Berlin Heart Excor (BHE) 15 ml pump was used to mimic the native heart behaviour, with ejection fraction of 66%.
**Results:** Setting the BHE rate at 130/min, we obtained in physiological conditions: cardiac output 1.3 l/min, upper body flow ~ 450 ml/min, common atrial pressure 6 ± 2 mmHg, SCPC pressure 12 ± 1 mmHg, mean arterial pressure 50-60 mmHg, pulmonary vascular resistance 1 WU. A BHE 10 ml pump was used as VAD with either atrial-arterial cannulation or ventricular-arterial cannulation.
**Discussion:** Four different failures were tested: systolic dysfunction, diastolic dysfunction, cavo-pulmonary intrinsic failure, and mixed. Although our test bench is only able to reproduce indirectly the neuro-humoral response noted in clinical practice, it allowed the investigation of VAD interaction with the SCPC in the different types of failures and the results obtained reproduced adequately the clinical scenarios of SCPC failure patients.

### O46
### OFF-LABEL USE OF STRETCHABLE POLYTETRAFLUOROETHYLENE: OVEREXPANSION OF SYNTHETIC SHUNTS

*Verbelen T[1], Famaey N[2], Gewillig M[3], Rega F[1], Meyns B[1]*

[1]Cardiac Surgery, University Hospitals Leuven, Leuven, Belgium; [2]Mechanical Engineering, KU Leuven, Leuven, Belgium; [3]Pediatric Cardiology, University Hospitals Leuven, Leuven, Belgium

**Introduction:** To describe our experience with balloon dilatation and stenting of modified systemic-to-pulmonary artery (PA) shunts in relation to an assessment and interpretation of the mechanical properties of thin-walled expandable polytetrafluoroethylene (ePTFE) stretch vascular grafts.
**Material and methods:** Our pediatric cardiology/cardiac surgery database was reviewed to identify all infants and children with a modified systemic-to-PA shunt who underwent cardiac catheterization. Reports and images were reviewed. Thin-walled stretchable and regular Gore-Tex vascular grafts were mechanically compared using tensiometry.
**Results:** 11 patients underwent dilatation or stenting procedures of a systemic-to-PA shunt. No major complications occurred and none of our patients died during or due to this intervention. High pressures in balloons and stents with diameters larger than the graft were used. Shunt diameters and oxygen saturation levels increased from 2.05 ± 1.25 mm to 4.75 ± 0.88 mm and with 12 ± 6.8%, respectively. In 6 patients re-catheterizations were performed. Four patients died, all with patent shunts. The fail-stress and the fail-strain in the circumferential direction of the stretchable graft were significantly higher than in the non-stretchable graft.
**Discussion:** Dilatation and stenting of stenosed modified systemic-to-PA shunts is feasible and safe. Dilatation and stenting of these shunts to calibers larger than those provided by the manufacturer is possible. Results of our technical study posit a great advantage for the use of the thin-walled stretch configuration of ePTFE.

### O47
### OBSTRUCTED MECHANICAL VALVE IN MITRAL POSITION IN SMALL CHILDREN: PROSTHETIC MANAGEMENT STRATEGIES

*Chan-Dominy A[1], Krupickova S[2], Ghez O[3], Michielon G[3], Burmester M[1], Casanueva L[1], Fraisse A[2]*

[1]Paediatric Intensive Care Unit, Royal Brompton & Harefield NHS Foundation Trust, London, UK; [2]Paediatric Cardiology, Royal Brompton & Harefield NHS Foundation Trust, London, UK; [3]Paediatric and Congenital Heart Surgery, Royal Brompton & Harefield NHS Foundation Trust, London, UK

**Introduction:** To report on management for thrombotic mechanical mitral valve (MV) complications in small children.
**Material and methods:** 2 case reports.
**Results:** A male neonate (3.8 kg) presented in heart failure secondary to MV endocarditis with ruptured chordae complicating group B streptococcal meningitis. He had mitral valve replacement (MVR) with 17 mm St Jude's HP prosthesis (MV area 3.8 $cm^2$, Z-score +1.3; MV annulus 13 × 14 mm, Z-score +0.5) at age 34 days, but developed blockage of leaflets despite thrombolytic therapy. At age 3-months, a supra-annular 17 mm St Jude's HP prosthesis was implanted. Prosthetic failure ensued with valve blockage refractory to repeated thrombolytic course, with mean transmitral gradient (TMG) of 20 mmHg. At age 7-months, a biological subsitute was surgically implanted with Melody valve, and serial dilation to 16 mm valve area. After 3 months of therapeutic range heparinisation, aspirin was instituted. Valve function

remained good with low TMG (10/2 mmHg, peak/mean) and no paravalvular leak at 12-month review.
A 15-month-old girl (8.3 kg) underwent MVR with 17 mm St Jude's mechanical valve (MV area 9.8 cm2, Z-score +4.9; MV annulus 13 × 16 mm, Z-score -0.7), after 2 previous mitral valvuloplastes for severe mitral regurgitation complicating bacterial endocarditis. Three months after MVR, she had acute MV thrombosis with prosthetic obstruction, and underwent urgent implantation of a 16 mm ATS Advanced-Performance (ATS-AP) prosthesis at annular position. She continued on warfarin as longterm anticoagulation. At 6-month review, TMG was 17/6 (peak/mean) with no paraprosthetic leak.
**Discussion:** In small children with challenging thrombotic mechanical MV complications, modified surgical implantation of bioprosthetic Melody valve or ATS-AP mechanical valve can offer alternative prosthetic strategies.

**O48**
**TREND OF ECHOCARDIOGRAPHIC AND ENERGETIC PARAMETERS IN LVAD PEDIATRIC PATIENTS**
*Di Molfetta A[1], Iacobelli R[2], Ferrari G[3], Filippelli S[1], Trivella M[4], Amodeo A[1]*
[1]Department of Pediatric Cardiology and Cardiac Surgery, Pediatric Hospital Bambino Gesù, Rome, Italy; [2]Medical and Surgical Department of Pediatric Cardiology, Pediatric Hospital Bambino Gesù, Rome, Italy; [3]Section of Rome, Cardiovascular engineering, CNR - Institute of clinical Physiology, Rome, Italy; [4]CNR - Institute of Clinical Physiology, Pisa, Italy

**Introduction:** To evaluate echocardiographic and energetic parameters trend in pediatric patients undergoing Berlin Heart EXCOR LVAD.
**Material and methods:** Children's data implanted were prospectively collected (2013-2015) before the LVAD and at the monthly follow-up till the LVAD explantation. Data were used to estimate ventricular energetic parameters.
**Results:** 12 patients were enrolled (75% idiopathic dilated cardiomyopathy, 17% non compacted myocardium, 8% restrictive cardiomyopathy). Average patients age and weight were 13.1 months and 7.2 Kg, respectively. Average LVAD staying was 226 days (59% transplanted, 8% recovered, 25% died, 8% on LVAD). Left ventricle was unloaded by the LVAD with a significant reduction in left ventricular end diastolic volume (average_p = 0.01), end systolic volume (average_p = 0.01) and a statistically significant improvement of left ventricular ejection fraction (EF) (average_p = 0.015) and left ventricular end systolic pressure-volume relationship (Emax) (p = 0.002). However, after the decrease, the LV volumes, atrial size, ventricular external work, potential energy, pressure-volume area, right ventricular systolic pressure, mitral valve annulus and regurgitation increase and then EF and Emax decrease. Right Ventricular Fractional Area Change (RVFAC) initially improves, but then right ventricular end systolic and end diastolic area and tricuspid valve anulus progressively increase and the RVFAC decreases. Left and right atero-ventricular coupling improve after the LVAD. Right ventricular external work, potential energy and pressure-volume area increase after the LVAD implantation. Finally, left (right) cardiac mechanical efficiency is improved (decreased, p = 0.02) by the LVAD.
**Discussion:** Left ventricular unloading decreases in time resulting in both left and right ventricular dilatation. A continuous and patient tailored LVAD setting could contribute to prolongue LVAD benefits.

## Oral Session - Clinical Aspects of Hemodialysis, O49-O54

**O49**
**CARDIAC FUNCTION AND SOME OTHER RISK FACTORS RELATED TO VITAMIN D DEFICIENCY IN PATIENTS WITH CHRONIC RENAL FAILURE (CRF) ON HEMODIALYSIS (HD)**
*Yonova D, Georgiev M, Antonov S*
Medical Faculty, Medical University, University Dialysis Center, Sofia, Bulgaria

**Introduction:** This study aimed to identify some additional risk factors for vitamin D deficiency (instead of the decreased calcitriol production due to CRF) in the patients on HD.
**Material and methods:** In a study of 72 HD patients some clinical and demographic factors, suspected to be related to deficit of vitamin D, were measured. Using logistic regression analysis (vitamin D deficiency as the dependent variable), we generated predictive models.
**Results:** Vitamin D deficiency was present in 85% of the studied patients. In the univariate analysis, the younger age, female gender, lower albumin level, and lower Heart Ejection Fraction (HEF), were strongly associated with lower levels of Vitamin D. In the final model as mightiest predictors of vitamin D deficiency remained female sex, gender and Cardiac function (r = 0.426, p<0.001, r = 0.283, p<0.01, r = 0.376, p<0.01), respectively.
**Discussion:** Additionally to CRF, some important clinical factors predict low Vitamin D levels. More factors should be tested (as nutrition, inflammation etc.) to discover how complexly to overcome vitamin D deficit in patients with CRF and HD treatment.

**O50**
**CHANGES IN PULSE WAVE THROUGHOUT HEMODIALYSIS SESSION**
*Dębowska M[1], Wójcik-Załuska A[2], Dąbrowski W[3], Poleszczuk J[1], Książek A[4], Załuska W[4], Waniewski J[1]*
[1]Nalecz Institute of Biocybernetics and Biomedical Engineering PAS, Warsaw, Poland; [2]Department of Physical Therapy and Rehabilitation, Medical University of Lublin, Lublin, Poland; [3]Department of Anesthesiology and Intensive Therapy, Medical University of Lublin, Lublin, Poland; [4]Department of Nephrology, Medical University of Lublin, Lublin, Poland

**Introduction:** Removal of water during hemodialysis (HD) session yields the decrease in total body overhydration and blood volume specifically with different possible effects on the cardiovascular system. We aimed to compare the pulse wave shape after the beginning and before the end of hemodialysis session.
**Material and methods:** Peripheral (radial artery) pulse wave was measured after the start and before the end of midweek, four hour long, HD session with 2.2 ± 1.1 L of ultrafiltration in 12 stable prevalent HD patients using applanation tonometry (SphygmoCor, AtCor Medical, Australia) and the central pulse wave was derived from the measurement.
**Results:** No change in measured (on arm), peripheral and central systolic (SP) and diastolic (DP) blood pressures was recorded throughout dialysis, however the heart rate increased from 68.2 ± 9.5 to 71.9 ± 9.6 per min and the ejection time decreased from 313.6 ± 39.9 to 284.1 ± 30.8 ms (p<0.05). The time of the start of the reflected wave decreased, and the increment in the peak of the primary left ventricular ejection pressure (P1) over diastolic pressure decreased. The central augmentation index was 148.7 ± 28.2 after the start and 146.8 ± 32.3 (p = 0.80) before the end of the session.
**Discussion:** During dialysis session the cardiovascular system changed mostly its characteristic times, but the augmentation index, an indirect measure of the arterial wall elasticity, did not change throughout the session. Therefore, our results suggest that during dialysis session with moderate ultrafiltration the elasticity of the arterial vessels does not change substantially according to its assessment by applanation tonometry.

**O51**
**INFLUENCE OF CLINICAL PARAMETER VARIATION ON IDH ONSET DURING THE FIRST MINUTES OF THE HD TREATMENT**
*Vito D, Casagrande G, Bianchi C, Costantino M*
Department of Chemistry, Materials and Chemical Engineering, Politecnico di Milano, Milano, Italy

**Introduction:** Intra-Dialysis Hypotension (IDH) is one of the main haemodialysis related complications, occurring in 25-30% of the sessions. IDH events can be difficult to manage because their etiology depends on several concurrent factors. The current study is aimed at analysing which clinical parameter, at the beginning of treatment, has an influence on the onset of hypotensive events during the dialysis session.
**Material and methods:** Clinical data on 122 patients enrolled in hospitals in Como, Lecco, Lugano and Varese have been analyzed. The enrolled patients have been classified in IDH prone or resistant, defining Hypotension Prone (HP), a patient who suffered of IDH in 2 or more sessioni and Hypotension Resistant (HR) a patient who suffered at most 1 IDH episode during the monitored period.
Mean Arterial Pressure (MAP), weight gain and the concentration of 4 blood electrolytes have been analyzed. Data have been firstly filtered in order to eliminate outliers. Shapiro-Wilk test have been applied to check for the normality

of data distributions. Parametric (t-test and one-way ANOVA) and nonparametric (Wilcoxon Test - Mann - Whitney and Kruskal - Wallis test) statistical tests were performed to define which parameters where different between the two groups.
**Results:** Data analysis showed that the MAP and the Na + concentration, Ca 2+ and Mg + were significantly different between HR and HP patients.
**Discussion:** MAP, and the concentration of Ca2+. Na+ and Mg+ considered at the beginning of the treatment appeared to be early Predictive parameters of hypotension onset during dialysis treatments.

**O52**
**CORRELATES OF CIRCULATING INTERFERON-λ3 (IFN-λ3) IN HEMODIALYSIS (HD) PATIENTS**
*Grzegorzewska A[1], Świderska M[2], Warchoł W[3]*
[1]Department of Nephrology, Transplantology and Internal Medicine, Poznan University of Medical Sciences, Poznan, Poland; [2]Student Nephrology Research Group, Poznan University of Medical Sciences, Poznan, Poland; [3]Department of Biophysics, Poznan University of Medical Sciences, Poznan, Poland

**Introduction:** IFN-λ3 plays a role in immune response by activation of T helper 1 pathway. We determined correlates of circulating IFN-λ3 among characteristics of HD patients.
**Material and methods:** Our study included 106 HBV vaccinated HD patients (88 developed anti-HBs) and 36 HBV infected HD subjects (27 developed anti-HBs). Plasma IFN-λ3 concentration was analyzed in respect to association with gender, age, causes of renal disease, dialysis vintage and modality (LF-HD, HF-HD/HDF), and anti-HBs titers.
**Results:** Circulating IFN-λ3 (ng/L) correlated with anti-HBs titers and dialysis modality. In vaccinated patients, each increase in plasma IFN-λ3 concentration per 10 ng/L was associated with 2.40 (1.16-4.97) higher probability of anti-HBs development (adjusted P = 0.018). Responders to HBV vaccination had higher IFN-λ3 compared with non-responders (120, 36-233 vs 53, 33-109, P<0.000001). IFN-λ3 was also associated with post-infection anti-HBs (1.44, 1.00-2.07, adjusted P = 0.049). Patients who generated anti-HBs after infection had higher IFN-λ3 compared with those who did not (133, 35-215 vs 71, 9-229, P = 0.043). In all patients, IFN-λ3 of 85.5 ng/L was a cut-off value in the prognosis of anti-HBs titer below vs. ≥10 IU/L (ROC sensitivity 68.7%, specificity 85.2%, AUC 0.827). Patients treated with HF-HD/HDF showed lower circulating IFN-λ3 than those using LF-HD (79.5, 20.4-227.5 vs 116, 9-232.7, P = 0.040). Treatment with HF-HD/HDF decreased IFN-λ3 by -28.4 ± 10.5 (β ± SE), adjusted P = 0.008.
**Discussion:** In HD patients, circulating IFN-λ3 strongly correlates with anti-HBs production after HBV vaccination and infection. The use of high-flux membranes decreases plasma IFN-λ3 levels what may weaken anti-HBs development.

**O53**
**CARDIOPULMONARY BYPASS: ASSESSING THE RISK OF RENAL INJURY**
*Abbasciano R, Mancini A, San Biagio L, Lucarelli C, Franzese I, Piani D, Onorati F, Tessari M, Menon T, Faggian G*
Department of Cardiac Surgery, University of Verona, Verona, Italy

**Introduction:** We sought to investigate whether continuous monitoring of peripheral oxidative balance during CPB by means of CDI can predict postoperative renal damage.
**Material and methods:** 101 consecutive patients undergoing cardiac surgery with CPB were continuously monitored with CDI. Do2, Vo2, ER were collected throughout CPB at 10-minutes intervals each and investigated with ROC curve analyses and logistic regression analysis for their potential predictive ability on postoperative acute kidney injury (AKIN-classification). Post-operative creatinine value, urine output, and estimated GFR were also collected.
**Results:** 18 cases of AKIN 1 or 2 (17.82%) were detected. At 50 minutes of CPB, VO2 of 68.5 ml/min/kg reported limited sensitivity and specificity (both 50%, AUC = 0.82, p = .008) for AKIN2, which improved at 60 mins of CPB (cut-off: 69 ml/min/kg, AUC = 0.89, p = .004; sensitivity 80% and specificity of 85%). ER ≥22.3% at 40 minutes reported 83% sensitivity and 84% (p<.003) for AKIN2 prediction. ER at 50 minutes (cut-off: 23.2%, AUC = 0.88, p = .002; sensitivity 83% and specificity of 86%) and 60 minutes (cut-off: 22.9%, AUC = 0.88, p = .005; sensitivity 80% and specificity of 82%) also predicted AKIN2. Logistic regression reported only VO2 at 40 mins to be independent predictor of AKIN2 (OR 1.35, 95% CI: 1.0-1.8, p = .05) or AKIN 1-2 (OR 2.3, 95% CI: 1.0-5.4, p = .04). A significant though weak linear correlation was ruled out between VO2 at 40 mins and serum creatinine at 12 postoperative hours ($R^2$ = .045, beta = 0.21 - p = .04).
**Discussion:** Continuous CDI monitoring may alert perfusion technicians about the potential for an ongoing and subtle renal damage during CPB, thus triggering countermeasures.

**O54**
**GLUCOSE-FREE DIALYSATE REDUCED SKIN AUTOFLUORESCENCE AS A MARKER FOR CARDIOVASCULAR DISEASES**
*Stegmayr B[1], Ramsauer B[1], Engels G[2], Graaff R[3], Sikole A[4], Arsov S[5], Hadimeri H[6]*
[1]Public Health and Clinical Medicine, Umea University, Umea, Sweden; [2]Haemoscan BV, Groningen, The Netherlands; [3]UMC Staff and Department of Endocrinology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; [4]University Sts Cyril and Methodius, Hospital of Nephrology, Skopje, The Former Yugoslav Republic of Macedonia; [5]PZU Diamed-Makedonija, Skopje, The Former Yugoslav Republic of Macedonia; [6]Department of Nephrology, Skaraborgs Hospital, Skövde, Sweden

**Introduction:** Hemodialysis (HD) patients suffer from an increased risk of cardiovascular disease (CVD) for which skin autofluorescence (SAF) is a strong marker by indirectly measuring tissue advanced glycation end products.
The aim of the study was to examine whether SAF is influenced by glucose in the dialysate.
**Material and methods:** SAF and plasma autofluorescence (PAF) where measured in patients before and after standard HD (ST) with a glucose containing dialysate (n = 24). Thereafter they switched to a glucose-free dialysate for 2 weeks. New measurements were performed on PAF and SAF after 1 week (M1) and 2 weeks (M2).
**Results:** The SAF value after HD increased non-significantly by 1.2%. When a glucose-free dialysate was used during HD, at M1, a decrease of SAF by 5.2% (p = 0.002, Wilcoxon paired) was found. One week later (M2) the reduction of 1.6% after the HD was not significant (p = 0.33). The PAF was significantly reduced during all HD sessions. Free and protein-bound PAF decreased similarly whether ± glucose in the dialysate (total PAF by -15%; free -20%; protein-bound -10%). The protein bound part of PAF corresponded to 56% of the total reduction. The protein bound PAF values after each HD showed the lowest value after 2 weeks using glucose free dialysate (p<0.05) indicating a progressive lowering of protein-bound substances.
**Discussion:** When changing for a glucose-free dialysate SAF was reduced by HD indicating that such measure may halter the accumulation and progression of deposits of AGEs to protein in tissue, and thereby also the development of CVD. Glucose-free dialysate needs further attention.

## Oral Session - Mechanisms of Blood Trauma, O55-O59

**O55**
**ON THE SIGNIFICANCE OF EXPOSURE TIME IN COMPUTATIONAL BLOOD DAMAGE ESTIMATION**
*Pauli L, Haßler S, Behr M*
Chair for Computational Analysis of Technical Systems, RWTH Aachen University, Aachen, Germany

**Introduction:** The reliability of common stress-based power law models for hemolysis estimations in blood pumps is still not satisfying. Stress-based models assume that a red blood cell (RBC) deforms immediately due to the action of forces. Therefore, the development of a new strain-based model, accounting for the time-dependent deformation of RBCs, is the focus of our research.
**Material and methods:** We use an Eulerian or field variable approach to predict free plasma hemoglobin with a power law correlation. Instead of an instantaneous stress distribution, the strain-based model considers the deformation history of RBCs for the stress computation. For the deformation modeling, the analogy of RBCs to droplets in high shear regimes is used. The

model is calibrated with mechanical properties of an RBC and fitted to the experimental data by Zhang et al. (Artificial Organs, 35(12):1180-1186, 2011).
**Results:** Comparisons of stress-based and strain-based models in a benchmark blood pump by the FDA show very significant differences. Stress peaks with short exposure contribute to the overall hemolysis in the stress-based model, whereas regions with long exposure time are responsible for damage in the strain-based model. For example, the gap between impeller and pump bottom is identified as a critical region due to a long residence time of the blood.
**Discussion:** The strain-based model introduces more biophysical phenomena into the simulation process and identifies different critical regions in the pump compared to the stress-based model. The Eulerian approach allows simple identification of such regions, which is useful for computer-aided design optimizations.

## O56
## THE IMPACT OF ARTIFICIAL SHEAR STRESS ON LEUKOCYTES AT A BIOMATERIAL INTERFACE

*Radley G[1], Pieper I[2], Chan C[2], Moriarty C[2], Foster G[2], Hawkins K[1], Thornton C[1]*
[1]Medical School, Swansea University, Swansea, UK; [2]Calon Cardio-Technology Ltd, Swansea, UK

**Introduction:** To mimic the foreign surface and artificial shear introduced to the body by ventricular assist devices (VADs) using both a rheometer and the Calon shear device.
**Material and methods:** Discs of biomaterial: diamond-like carbon coated stainless steel (DLC); single crystal sapphire (Sap); and titanium alloy (Ti) were attached to parallel plates on a rheometer. Whole human blood was sheared for 5 min between the discs at $0s^{-1}$ and $1000s^{-1}$. For the Calon shear device, bovine blood was circulated at different shear rates with and without biomaterial sleeves inserted. Leukocyte activation through L-selectin shedding, up-regulation of CD11b, and leukocyte microparticle production were measured with flow cytometry as well as viability.
**Results:** Preliminary rheometry data (n = 6) as percentage from baseline have shown that shearing on a Sap surface at $1000s^{-1}$ significantly reduces the number of total leukocytes compared to $0s^{-1}$ (76 ± 22%, p = 0.002). L-selectin expression on neutrophils was decreased significantly in the presence of Sap at $0s^{-1}$ (80 ± 13%, p = 0.03) and $1000s^{-1}$ (75 ± 8%, p = 0.004) and with Ti at $1000s^{-1}$ on neutrophils (74 ± 20%, p = 0.003) and monocytes (55 ± 22%, p = 0.02). CD11b expression and viability of the leukocytes was not affected by the biomaterial nor the shear. Data from the shear device is not available at this time.
**Discussion:** Initial results from the rheometer model indicate that shearing blood on a Sap surface may cause higher levels of leukocyte activation whereas DLC shows minimal activation.

## O57
## ENERGY DISSIPATION RATE AS ALTERNATIVE HEMOLYSIS METRIC IN STRESS-BASED MODELS

*Engel S, Janiga G, Thévenin D*
Laboratory of Fluid Dynamics & Technical Flows, Otto-von-Guericke-University Magdeburg, Magdeburg, Germany

**Introduction:** Flow-induced damage on red blood cells (RBC) remains a problem of blood flows in artificial devices. Increasingly complex models have been developed to estimate Hemolysis. The predominant part of rather simple models takes an equivalent stress as primary metric. This work proposes the usage of the energy dissipation rate (EDR) as alternative metric. The EDR offers the opportunity to correlate RBC damage with a fluid dynamical quantity that is independent of the flow to be modeled. Both laminar as well as turbulent flow behavior can be considered.
**Material and methods:** By transforming a known power-law based model, an alternative form is obtained. This new model is then fitted to experiments found in literature, which represent a wide range of EDR and exposure time. Subsequently, the calibrated model is tested on 3D benchmark cases with computational fluid dynamics (CFD) simulations.
**Results:** An acceptable fit for the new model was achieved and tested. Due to the limited amount of available information there is an impact on the confidence interval of that fit.
**Discussion:** An alternative power-law based model to estimate the flow-induced damage on red cells is proposed. A discussion of the model and its assumptions will be presented during the congress, supported by a comparison with related macroscopic damage models for laminar and turbulent flows.

## O58
## COMPARISON OF HEAT TRANSFER DYNAMICS IN A MODEL OF THE ARTERIAL SYSTEM DURING CONTINUOUS OR PULSATILE EXTRACORPOREAL CIRCULATION

*Casagrande G, Costantino M*
Department of Chemistry, Materials and Chemical Engineering, Politecnico di Milano, Milano, Italy

**Introduction:** The use of continuous or pulsatile perfusion during cardiopulmonary bypass implies variations in micro-vessels diameters due to the action of peripheral controls (myogenic, metabolic, endothelial) that can also influence the cooling and heating dynamics during the different phases of the procedure. Several models of the body heat transfer have been developed to study thermal regulation, but they do not consider the possibility to vary the central body temperature as it happens during extracorporeal circulation. Aim of this work is to develop a model allowing the simultaneous description of heat transfer and peripheral controls effects.
**Material and methods:** Control mechanisms and heat transfer dynamics have been integrated in a model of the circulation, comprising large artery segments and peripheral networks. Heat transfer from each vascular segment to both body tissues and the operatory room environment was modeled. The model was developed using Visual C++ while LabVIEW™ software was used for the graphical interface.
The model was used to study the differences in the cooling and heating processes during continuous or pulsatile cardiopulmonary bypass. Different cooling and heating transients at different operatory room temperature were evaluated.
**Results:** The developed integrated model allows evaluating differences in cooling and heating transients due to the perfusion modality and to the patient size. According to the experimental evidences, the model highlighted faster heat exchange dynamics when pulsatile perfusion was performed.
**Discussion:** The developed model appears flexible and reliable allowing the study of different surgery conditions, comparing the heat exchange dynamics with different perfusion modality, taking into account the action of peripheral controls.

## O59
## LONG TERM EVALUATION OF A NOVEL VERSATILE BIOPROSTHETIC VALVE MADE BY AUTOLOGOUS TISSUES

*Takewa Y[1], Nakayama Y[2], Sumikura H[1], Iizuka K[1], Katagiri N[1], Takeshita D[1], Tatsumi E[1]*
[1]Department of Artificial Organs, National Cerebral and Cardiovascular Center, Osaka, Japan; [2]Medical Engineering and Materials, National Cerebral and Cardiovascular Center, Osaka, Japan

**Introduction:** A novel autologous bioprosthetic valve (Biovalve) is developed with a unique in-body tissue engineering. This enables us multi-purpose valve replacement and tailor-made therapy for each patient. In this study, we made 3 types of heart valves and tested their feasibility and durability in large animal experiments.
**Material and methods:** We created many kinds and sizes of molds for Biovalves using plastic rods with 3D printer easily and quickly. We selected 3 types (a conventional type, a full-root type and a valve with a metalic stent for transcatheter implantation) and embedded them in the subcutaneous spaces of adult goats for 1-2 months. After extracting the molds with the tissue and removing the plastic rods only, Biovalve with tri-leaflets as the native valves were constituted from completely autologous connective tissues and fibroblasts. Five cases of conventional Biovalves were implanted under cardiopulmonary bypass, 12 cases of fullroot type were implanted, and 25 cases of stent-valve type were implanted with transcatheter technique into in situ the aortic or pulmonary valves (17 and 8, respectively).
**Results:** In each type, Biovalves were successfully implanted and showed smooth movement of the leaflets with a little regurgitation in angiogram, and the maximum duration reached to 8 months in fullroot type and 17 months in stent valve type. Histological examination of the Biovalves showed the autologous cells covering the laminar surface of the valves and also getting into the connective tissues.

**Discussion:** The Biovalves have a potential for tailor made therapy in valve surgery and satisfy the higher requirements of the systemic and pulmonary circulation maintaining the histological character as autologous tissues.

## Oral Session - Cells and Polymers for Tissue Engineering, O60-O64

### O60
### A NOVEL PERFUSION BIOREACTOR FOR MAMMALIAN CELL CULTURE

*Wawro B, Kruk J, Dudziński K, Kazimierczak B, Zakrzewska K, Samluk A, Kowalska A, Pijanowska D, Torbicz W*
Nalecz Institute of Biocybernetics and Biomedical Engineering PAS, Warsaw, Poland

**Introduction:** Cell culture technique is commonly used in many areas of biomedical research, including tissue engineering. Cells are highly sensitive to their surrounding that in traditional static cultures significantly differ from native cellular environment. The advantage of using perfusion bioreactors for culturing cells in vitro include ability to create cellular environment more resembling in vivo conditions. Here we present a novel, macro-scale perfusion bioreactor for culturing mammalian cells that enables microscopic observation of cells throughout the culture. Construction of bioreactor with direct access to the cells allows application of standard assay protocols for the end point analyses.
**Material and methods:** Elements of bioreactor were fabricated in polydimethylsiloxane (PDMS) by replica molding, on 3D PMMA master. The device was tested on several cancer–derived cell lines and isolated human liver cells. Proliferation rates of cancer cells (C3A, U87, Caco-2) and functional activity of primary hepatocytes (by means of albumin synthesis) were compared in perfusion and conventional static cultures.
**Results:** Cells were able to attach, and grow in collagen I-coated bioreactor. Depending on the cell type, proliferation rates of cancer cells in perfusion bioreactor were similar or partially inhibited comparing to standard static culture conditions.
Primary hepatocyte function of albumin secretion, quickly lost under standard static culture condition, was preserved for a longer time in perfusion bioreactor.
**Discussion:** Results of our experiments confirm that cellular responses to perfusion conditions are cell-type specific.
Usability of perfusion bioreactor was particularly demonstrated by slowing down dedifferentiation process of primary human hepatocytes.

### O61
### ESTABLISHMENT AND CHARACTERIZATION OF HUMAN RENAL PRIMARY CULTURES TO USE IN MICROFLUIDIC DEVICES

*Sánchez-Romero N, Giménez I*
Instituto Aragonés de Ciencias de la Salud, Zaragoza, Spain

**Introduction:** To establish and characterize a human renal primary culture enriched in proximal tubular cells (hPTPC).
**Material and methods:** Renal primary cultures enriched with hPTPC are generated from healthy tissue isolated from nephrectomies. Cell characterization was performed by RT-PCR, immunofluorescence (IF), immunocytochemistry, FACS, functional assays and different transporters´ activity. The presence of progenitor cells was determined by specific markers analyzed by FACS and IF.
**Results:** Morphologically, cells showed classic cobblestone appearance of epithelial cells. When cells reached confluence, expression of ZO-1 protein and acetylated tubuline was confirmed by IF, indicating the development of tight junctions and presence of primary cilia. The cell population was also positive for megalin. Additionally, hPTPC specific brush-border enzymes like CD13 and CD10 were confirmed by FACS and GGT-1 and DPPIV activity by functional assays.
Apical efflux transporter p-glycoprotein and multidrug resistant protein 4, and baso-lateral influx transporter organic cation transporter 2 and organic anion transporter 1 activities were detected. Multiplex RT-PCR analysis showed that these cells retain the most significant proximal tubule markers, although with the presence of some markers from cells from other segments of the nephron. A population of cells positive for CD133, CD24 and lactate dehydrogenase (FACS), CK19 and vimentin (IF) was also detected, suggesting the presence of kidney progenitor cells.
**Discussion:** The cell characterization confirmed the putative markers of proximal tubule and expression of multiple organic ion transporters, mimicking renal reabsorption and excretion. These primary cells constitute a powerful tool for future adoption in microfluidic platforms for in vitro transport studies in pharmacology, physiology and kidney bioengineering.

### O62
### FIBRIN GEL AS NATURAL SCAFFOLD FOR HUMAN STEM CELLS (WJ-MSC AND HIPSC-NPS) IN NEURODEGENERATIVE DISEASES TREATMENT

*Zychowicz M, Figiel- Dąbrowska A, Lech W, Obtułowicz P, Winiarska H, Domańska-Janik K, Bużańska L*
Stem Cell Bioengineering Unit, Mossakowski Medical Research Centre Polish Academy of Sciences, Warsaw, Poland

**Introduction:** The increasing need of novel therapeutics for neurodegenerative diseases cause searching for alternative treatments. The 3D biomaterial scaffolds as therapeutic cell carriers are widely used in preclinical and clinical cell transplantations. They should provide the appropriate conditions for encapsulation and transplantation of disease-relevant stem cell types. To address this issue we present two types of fibrin based cell-biomaterial hybrids that can be considered for neurorestorative treatments. The mesenchymal stem cells derived from Wharton Jelly (WJ MSC) could be induced in vitro to different stages of development including neural lineage phenotypes with desired paracrine and adjuvant characteristics. The more matured neural progenitors, derived from human induced pluripotent stem cells (hiPSC-NPs), would be designed to personalized, patient specific repopulation of injured tissue.
**Material and methods:** WJ MSC or hiPSC-NPs cultured in our lab were seeded into natural fibrin gel scaffold comprised of fibrinogen crosslinked with thrombin and checked for the cell viability, proliferation and migration.
**Results:** Applied fibrin scaffold provides good adhesion and proliferation, however the cell viability decreased during 7 days of culture. Over the culture time the gel was gradually degraded, releasing cells for migration outside the scaffold, however the degradation rate and migration activity was grater for WJ MSC than hiPS-NPs. The estimation of gel degradation made at 1, 3 and 7 day by measurement of AlexaFluor546 showed over 60% of fibrin releasing into the solution at day 7.
**Discussion:** Stem cell migration capability from the scaffold can provide good prognosis after transplantation of biomaterial-cell hybrid in the neurodegenerative disorders.
**Acknowledgement:** The work was supported by National Centre for Research and Development grant No Strategmed 1/234261/2/NCBR/2014 and statutory funds to MMRC.

### O63
### USE OF DECELLULARIZED TRACHEAS FOR AIRWAY ENGINEERING

*Sancho-Tello M[1], Milián L[1], Carda C[1], Garzón I[2], Foschinni G[3], Galán G[3], Mata M[4]*
[1]Departamento Patología, Universidad de Valencia; INCLIVA, Instituto Investigación Sanitaria Hospital Clínico Universitario de Valencia, Valencia, Spain; [2]Histology Department, Universidad de Granada, Granada, Spain; [3]Thoracic Surgery Unit, Hospital Clínico Universitario de Valencia; INCLIVA, Instituto Investigación Sanitaria Hospital Clínico Universitario de Valencia, Valencia, Spain; [4]Departamento Patología, Universidad de Valencia; INCLIVA, Instituto Investigación Sanitaria Hospital Clínico Universitario de Valencia; Centro de Investigaciones en Red de Enfermedades Respiratorias (CIBERES), Valencia, Spain

**Introduction:** The Hospital Clínico Universitario de Valencia (Spain) is a reference hospital for the treatment of patients with airway problems exhibiting complex tracheal stenosis. Actually, we are evaluating the usefulness of decellularized tracheas for the treatment of that complex stenosis with large extension where surgery is limited. We have studied the effect of detergents in the extracellular matrix (EM) as well as its capability to support cell growth in porcine SDS decellularized tracheas.
**Material and methods:** Tracheas were cut in 3 cm rings and exposed to 2% SDS for up to four weeks. Cell content was evaluated by DAPI weekly.

Haematoxylin-Eosin, Masson Trichrome, Orcein and PAS stainings were performed in paraffin-embedded formalin-fixed tissues or OCT-frozen tissues to analyze the effect of the detergent in the EM. When decellularization was achieved, tracheal rings were cultured with human airway epithelial cells and chondrocytes for up to three weeks.
**Results:** SDS completely removed cells from the tracheas analyzed. No changes related to elastic fibers were observed while a moderate loss of collagen and GAGs content was evident compared to non-decellularized samples. After culture, epithelial cell attachment was observed in the surface of the tracheal rings as well as chondrocytes in the cartilage layer of the tracheas analyzed.
**Discussion:** SDS treatment not only removed cells in the different tissues forming the trachea with a minimal disturbance of the EM, but also allows the attachment and proliferation of airway epithelial cells and primary chondrocytes.
**Acknowledgement:** This study was supported by Spanish Ministerio de Economía y Competitividad (project MAT2013-46467-C4-4-R).

**O64**
**POLYMERS WITH MICRO- AND NANOSTRUCTURED SURFACE FOR IMPLANTS AND FOR TISSUE ENGINEERING**
*Thormann A[1], Rudolph M[2], Heilmann A[1]*
[1]Biological and Macromolecular Materials, Fraunhofer IMWS, Halle, Germany; [2]Electrotechnics and maschine builiding, Anhalt University of Applied Sciences, Bernburg, Germany

**Introduction:** Polymers with micro- or nanostructured surfaces can improve the incorporation of implants by supporting cell adhesion. In addition, these surfaces stimulate cell adhesion and cell growing for tissue applications. One suitable method to get micro- and nanostructured polymer surfaces is hot embossing.
**Material and methods:** UHMWPE (ultrahigh molecular weight polyethylene) plates were vacuum laminated with HDPE (high density polyethylene) foils. Micro- and nanostructured surfaces at HDPE were made by hot embossing with an aluminum stamp having a combined micro- and nanostructure. The microstructures were made by laser structuring, the nanostructures by anodic oxidation. Surface morphology was investigated by scanning electron microscopy (SEM), cell growing experiments were performed with fibroblasts and chondrocytes.
**Results:** Peel test demonstrates that an almost perfect adhesion of HDPE on UHMWPE was achieved. By hot embossing, HDPE surfaces with different micro- and nanostructures were achieved. Embossing temperature, time and pressure have strong influence to the pin- or filament-like nanostructures on the HDPE surface. Depending on the realized micro- and nanostructure, surface properties like surface tension or wettability are modified. In addition, the surface structure has a substantial influence to the cell growing. SEM micrographs show that cell morphology depends on the combined micro- and nanostructures.
**Discussion:** Polymers with imprinted micro- and nanostructured surfaces are very suitable to improve cell adhesion and growing. The stamping technology is relevant for various technical polymer forming processes, e.g. for manufacturing of flat or three-dimensionally preformed implant plates or for implants made by injection molding. Further, with structured rolls imprinting can be performed as roll-to-roll process.

## Oral Session - From Bench to Bedside, O65-O70

**O65**
**THE INNOVATIVE MATERIAL TECHNOLOGIES APPLICATION FOR THE IMPLANTABLE ROTARY BLOOD PUMP RELIGA HEART® ROT**
*Gonsior M[1], Darłak M[1], Altyntsev I[1], Wierzchoń T[2], Antonowicz M[1], Kustosz R[1]*
[1]Artificial Heart Laboratory, Zbigniew Religa Foundation for Cardiac Surgery Development, Zabrze, Poland; [2]Faculty of Materials Science and Engineering, Warsaw University of Technology, Warsaw, Poland

**Introduction:** The innovative surface layers created on titanium and polymer elements of the Polish ReligaHeart® ROT LVAD were evaluated, including tribological and biocompatible properties, especially in high shear stress contact with blood.
**Material and methods:** The titanium blood pump components were modified in process of plasma potential glow discharge, resulting with diffusive titanium nitride surface layer TiN+Ti2N+αTi(N). The blood pump dielectric elements made of polyetheretherketone (PEEK CF) were modified with a-CNH surface layers, manufacturing in RFCVD process. The biomaterials studies were performed: friction coefficient, scratch test, contact angle, surface topography (AFM, SEM), hemolysis and trombogenicity (in physical model simulating high shear stress to blood). The 6 hours trombogenicity test with fresh animal blood was performed to validate pump embolization risk.
**Results:** The tribological tests confirmed that diffusive TiN layers improves tribological properties of titanium elements. The surface topography of 3D pump components showed high homogeneity of TiN layers. The best result was obtained for TiN layers of Ra 0.08 μm roughness. The a-C:N:H layers tests proved: high wear resistance, very good adhesion to the PEEK surface and low friction coefficient in contact with TiN. The biological studies showed that both: TiN and a-CNH layers do not damage erythrocytes, don't activate platelets adhesion neither aggregation, during blood exposure to high shear stress occurring in rotary pumps.
**Discussion:** Biomaterials assessment results promise the good properties of the innovative TiN and a-CNH layers for the rotary pump elements application, where the blood velocity and shear stresses are very high increasing thrombosis risk.
**Acknowledgement:** Project no. PBS1/A5/20/2012 supported by NCBiR.

**O66**
**THE ABILITY OF REMOTELY MONITORING THE OPERATION OF PULSATILE VENTRICULAR ASSIST DEVICE ON THE EXAMPLE OF SET: RH PED – DUO CONTROLLER**
*Czak M, Gawlikowski M, Kustosz R*
Artificial Heart Laboratory, Zbigniew Religa Foundation for Cardiac Surgery Development, Zabrze, Poland

**Introduction:** Investigation and practical implementation methods of remote monitoring the operation of assist in the treatment of patients with extracorporeal cardiac support system, along with the observation of selected hemodynamic parameters using the controller ReligaHeart® DUO modified for the purpose of supporting the operation of PED VADs.
**Material and methods:** The RH-DUO controller comes with a dedicated interfaces: Bluetooth and WiFi has been modified to assist small volume pulsatile VADs. The 2MOOP separated USB connector was a reserve communication interface. The data carried out of the heart support process are recorded by dedicated software on PC. The synchronous file sharing mechanism allows data transfer from PC to central database. Controller redundant sensors in conjunction with algorithms in the software provide a high level of detection and partial prediction states of emergency that are transferred to the central database. The DUO controller has been designed for use with blood ultrasonic flowmeter, allowing to correlate measurement of blood flow to the current operation of controller.
**Results:** The system has been verified in animal trials. Total time of monitoring was more than 8000 h. Data post-processing allowed observation of blood mean flow falling accidents, and detection of pump suction events.
**Discussion:** Remote monitoring can improve the mobility of treated clinically patients and helps to improve their quality of life. The data collected in the central database could permit to develop indicators for improve treatment of subsequent patients. Small size and increased mobility of controller allows to consider the use of non-clinical patient's rehabilitation.
**Acknowledgement:** Project no. PBS1/A7/1/2012 supported by NCBiR.

**O67**
**INFLUENCE OF AORTIC VALVE REGURGITATION UNDER LVAD SUPPORT ON HEMODYNAMICS AND CARDIAC METABOLISM IN ACUTE ANIMAL EXPERIMENTS**
*Iizuka K, Naito N, Sumikura H, Mizuno T, Tsukiya T, Takewa Y, Tatsumi E*
Department of Artificial Organs, National Cerebral and Cardiovascular Center, Osaka, Japan

**Introduction:** Aortic valve regurgitation (AR) is a serious complication under left ventricular assist device (LVAD) support. We made animal model of LVAD with AR, and investigated change of hemodynamics and cardiac metabolism under LVAD support with AR in acute animal experiments.

**Material and methods:** 5 goats (55 ± 9.3 kg) were investigated. Centrifugal type LVAD, EVAHEART implantation was performed with inserting inflow cannula to the left ventricular apex and suturing outflow graft to the descending Aorta. The AR model was established by placing a vena cava filter in the aortic valve. Aortic pressure (AoP), left ventricular pressure (LVP), LVAD pump flow, pulmonary artery flow (PAF) and coronary artery flow (CoF) were recorded as well as myocardial oxygen consumption (VO2), oxygen delivery (DO2), and oxygen extraction ratio (O2ER = VO2/DO2). We evaluated these values with changing pump rotation speed and controlling AR. AR+ was defined Sellers classification 3 or more.
**Results:** Though PAF didn't increase with increasing pump rotation speed, LVAD pump flow increased over systemic flow in AR+. Comparing AR+ and AR-, mean AoP was lower in AR+. LVP decreased with increasing pump rotation speed, but this decreasing tendency was weaker in AR+ than AR-. CoF was lower in AR+ than AR-, and this tendency became more marked with increasing pump rotation speed. O2ER in AR- decreased with increasing pump rotation speed, but O2ER in AR+ increased.
**Discussion:** Increasing pump rotation speed lead to increasing LVAD-left ventricular recirculation via AR and didn't contribute effective systemic circulation. AR caused disturbing cardiac assistance of LVAD support.

## O68
## SINGLE PULMONARY ARTERY SUPPORT FOR THE FAILING FONTAN CIRCULATION IN SHEEP

*Van Puyvelde J[1], Rega F[1], Nix C[2], Hazekamp M[3], Rijnberg F[3], Siess T[2], Claus P[4], Cools B[5], Gewillig M[5], Meyns B[1]*
[1]Cardiac Surgery, University Hospitals Leuven, Leuven, Belgium; [2]Abiomed Europe GmbH, Aachen, Germany; [3]Department of Cardiothoracic Surgery, Leiden University Medical Center, Leiden, The Netherlands; [4]Department of Cardiovascular Imaging and Dynamics, University Hospitals Leuven, Leuven, Belgium; [5]Department of Paediatric Cardiology, University Hospitals Leuven, Leuven, Belgium

**Introduction:** The Fontan circulation is associated with distinctly abnormal haemodynamics and a significant risk of progressive failure. We hypothesized that mechanical support from the cavopulmonary connection to a single pulmonary artery could restore haemodynamic stability. Our study evaluated the effects of single pulmonary support in an ovine failing Fontan model.
**Material and methods:** A total cavopulmonary connection (TCPC) was established in nine sheep. The superior vena cava was connected to the main pulmonary artery (PA). The inferior vena cava was connected to the PA by an ePTFE conduit. The Impella RP (Abiomed Europe GmbH, Aachen, Germany) was modified to form a cavopulmonary support system. After 12 weeks, we placed a modified Impella RP, inserted through the main PA, with the inlet lumen in the main PA, distally from the TCPC, and the outlet lumen in the right PA, with flow adjusted to 2.8 ± 0.7 L/min.
**Results:** The TCPC induced almost a doubling of the central venous pressure ($p<0.0001$). Five sheep died because of progressive failure of the Fontan physiology. Implantation of the modified Impella RP in four sheep resulted in a significant increase in left atrial pressure (+163%, $p = 0.05$). Central venous pressure decreased and arterial pressure increased during pump-supported Fontan circulation.
**Discussion:** To our knowledge, this is the first chronic ovine model of a total cavopulmonary diversion which provides all hallmarks of the failing Fontan physiology. Mechanical support from the cavopulmonary connection to a single PA can reverse the substantial decrease in left atrial pressure associated with Fontan circulation and might be able to restore normal haemodynamics.

## O69
## POSTOPERATIVE LEFT VENTRICULAR FUNCTION IN DIFFERENT TYPES OF PULMONARY HYPERTENSION: A COMPARATIVE STUDY

*Verbelen T[1], Van De Bruaene A[2], Cools B[3], Van Raemdonck D[4], Delcroix M[5], Rega F[1], Meyns B[1]*
[1]Cardiac Surgery, University Hospitals Leuven, Leuven, Belgium; [2]Cardiology, University Hospitals Leuven, Leuven, Belgium; [3]Pediatric Cardiology, University Hospitals Leuven, Leuven, Belgium; [4]Thoracic Surgery, University Hospitals Leuven, Leuven, Belgium; [5]Pneumology, University Hospitals Leuven, Leuven, Belgium

**Introduction:** Temporary left ventricular (LV) dysfunction after pulmonary endarterectomy (PEA) for chronic thromboembolic pulmonary hypertension (CTEPH) is well described. True LV-failure has only been described after bilateral lung transplantation (bLTx) in pulmonary arterial hypertension (PAH) patients. We sought to identify factors that cause LV-failure and preventive strategies.
**Material and methods:** From our database all PAH patients that underwent bLTx (n = 24) and all CTEPH patients that underwent PEA, with a minimal reduction of 800 dynes.s.cm$^{-5}$ (n = 27), were selected. Perioperative demographic and echocardiographic data were analyzed. MRI before and after right ventricular (RV) mechanical support in our sheep model of chronic RV pressure overload was analyzed.
**Results:** Pulmonary hypertension was diagnosed at significant younger age and time between diagnosis and surgery was significantly longer in pulmonary arterial hypertension patients. Atrial septostomy for PAH caused increases of LV dimensions and cardiac index. PAH patients had significant larger right ventricular (RV) dimensions, but a similar preoperative LV diastolic dysfunction. Surgery caused significant decreases in RV dimensions, to a lesser extent in CTEPH patients, and significant increases in LV dimensions. Three PAH patients developed postoperative LV-failure. Compared to other PAH patients their age at diagnosis was significantly younger, and their time between diagnosis and surgery was significantly longer. RV support significantly improved LV dimensions and function.
**Discussion:** In PAH, age at diagnosis is younger and LV preload deprivation lasts longer. This might explain the occasional development of LV-failure after bLTx. Preoperative atrial septostomy or a right ventricular assist device might train the LV, by increasing its preload, and avoid postoperative LV-failure.

## O70
## HIGH-DOSE ADENOSINE-LIDOCAINE-MAGNESIUM POLARIZED ARREST IN ELECTIVE CARIDAC SURGERY: RESULTS OF THE FIRST HUMAN RANDOMIZED CONTROLLED TRIAL

*Abbasciano R[1], Onorati F[1], San Biagio L[1], Lucarelli C[1], Fanti D[1], Dobson G[2], Menon T[1], Gottin L[3], Biancari F[4], Tessari M[1], Mazzucco A[1], Faggian G[1]*
[1]Department of Cardiac Surgery, University of Verona, Verona, Italy; [2]College of Medicine and Dentistry, Australian Institute of Tropical Health and Medicine (AITHM), James Cook University, Townsville, Australia; [3]Division of Cardiac Surgery and Postoperative Intensive Care Unit, University of Verona, Verona, Italy; [4]Division of Cardiac Surgery, University of Oulu, Oulu, Finland

**Introduction:** Potassium depolarization has been linked to myocardial and endothelial injury, left ventricular dysfunction and reperfusion arrhythmias. Our aim was to examine the potential benefits of normokalemic 'polarizing' cardioplegia comprising adenosine, lidocaine and $Mg^{2+}$ (ALM) compared to 'depolarizing' Buckberg-cardioplegia a prospective, randomized trial.
**Material and methods:** Two-hundred-eight patients undergoing low-risk elective CABG or AVR were randomized to traditional 4:1 cold blood Buckberg-cardioplegia (High-$K^+$-Group) or "polarizing" high-dose ALM normokalemic cold blood cardioplegia (ALM-Group). Perioperative troponin I, peripheral lactate, and hemodynamic status (thermodilution method) were compared. Time-to-cardiac arrest (TtCA), spontaneous recovery of sinus rhythm at declamping (sSRr) and clinical outcome were recorded. Troponin I, lactate, $SvO_2$%, and Base Excess (B.E.) were measured in coronary sinus blood before aortic cross-clamping and at reperfusion.
**Results:** Longer TtCA ($p = .03$) but higher sSRr ($p<.001$) were found after ALM cardioplegia. The ALM-Group at 10 min reperfusion had significantly lower coronary sinus troponin ($p = .002$), lower lactate ($p<.001$), higher SVO2 ($p<.001$) and higher base-excess ($p = .001$). Improved ALM cardioprotection was reflected in significantly lower peripheral troponin I (between-group $p = .003$), higher cardiac index (between-group $p<.001$) and lower PCWP (between-group $p<.001$) and one day less in the ICU ($p<.01$), suggesting improved flows and less whole body ischemia (peripheral lactate release between-group $p = .01$). Other clinical outcome variables were comparable.
**Discussion:** We show for the first time that full-polarized ALM arrest is safe and potentially efficacious in elective cardiac surgery, leading to significantly improved myocardial protection, perioperative hemodynamics, less whole body ischemia and lower ICU stays.

## Oral Session - Adsorption and Uremic Toxins, O71-O76

### O71
### POLYETHERSULFONE AND SLIPSKIN BLEND MEMBRANES FOR DIALYSIS TREATMENT

*ter Beek O, Pavlenko D, Suck M, Stamatialis D*
Biomaterials Science and Technology, University of Twente, Enschede, The Netherlands

**Introduction:** Prolonged dialysis can significantly increase toxin removal. When performed via a portable or wearable artificial kidney or via nocturnal dialysis, such treatment can result in improved quality of life of patients. Current membranes are mostly based on polyethersulfone (PES) and polyvinylpyrrolidone (PVP) blends for which long-term hemocompatibility is not optimal. Besides, their properties can be influenced based on sterilization methods. Here, we investigate development of PES and SlipSkin™ blends for dialysis. SlipSkin™ is a copolymer of N-vinylpyrrolidone and N-butylmethacrylate with superior hemocompatibility compared to benchmark membranes.
**Material and methods:** PES and SlipSkin™ (N-vinylpyrrolidone:N-butylmethacrylate ratio 50:50) were blended to enhance hollow fibers' hydrophilicity. Membranes were prepared by immersion precipitation and characterized by scanning electron microscopy and Fourier transform infrared spectroscopy. Furthermore, clean water permeance, as well as, membrane sieving coefficients and fouling resistance were studied using model solutions of bovine serum albumin (BSA) and creatinine. Commercial low-flux dialyzer (Fresenius F8HPS) was used for comparison.
**Results:** The new PES/SlipSkin™ hollow fibers present an asymmetric morphology; a selective layer with dense, finger-like pores and a macro porous layer. Their clean water permeance and creatinine clearance is similar to F8HPS dialyzers. The low ultrafiltration membranes have high BSA fouling resistance and excellent BSA retention. The investigation of the long-term membrane performance as well as possible effects of sterilization to the membrane are currently in progress.
**Discussion:** PES/SlipSkin™ blends give promise to the development of better membranes for prolonged dialysis by combining excellent hemocompatibility profiles and fouling resistance.
**Acknowledgement:** LSH Impuls KidneyPort project and EU Marie Curie ITN BIOART.

### O72
### CONFORMATION AND DYNAMICS AT A MESOSCOPIC LEVEL OF BIOMACROMOLECULES ADSOPTION: A COARSE-GRAINED MOLECULAR SIMULATION

*Sabater i Serra R[1,2], Constantino T[2], José María M[1], Gómez Ribelles J[1], Molina-Mateo J[2]*
[1]Networking Research Center on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Universitat Politècnica de València; [2]Centre for Biomaterials and Tissue Engineering, Universitat Politècnica de València, Valencia, Spain

**Introduction:** The aim of this work is to develop a model for studying the conformation and dynamics of linear macro macromolecules with different length on an adsorbing surface at a mesoscopic level of detail. This model can be applied to biological macromolecules with elongated structure, such as collagen, a fibrous protein with a linear chain as primary structure, which is used to modify biomaterial surfaces, such as titanium implants or biopolymers, in order to enhance their bioactivity.
**Material and methods:** Monte Carlo simulation by means of the Bond Fluctuation Model (BFM) has been applied. Three interaction potentials between the segments of the chain have been employed: a Lennard-Jones, a bond length and a bond angle potential. Also, a Lennard-Jones potential has been introduced to induce the adsorption of the macromolecules on the surface. The system was characterized by means of structural parameters through the simulation.
**Results:** Adsorption of macromolecules is a very complex process, which is driven by different polymer-surface forces. After applying thermal treatments, the results show that there is an optimum size range to maximise adsorption. The highest levels of adsorption were found in chains with intermediate size. Furthermore, the isothermal treatments show the close dependence between the polymer glass transition and the adsorption process.
**Discussion:** After applying different thermal treatments, changes in conformation and dynamics have shown how the macromolecule length affects the adsorption process.
**Acknowledgment:** The support of the project MAT2015-69315-C3-1-R (including the FEDER financial support) as well as CIBER is acknowledged.

### O73
### STRATEGIES FOR DIALYSATE REGENERATION USING MIXED MATRIX MEMBRANES

*Geremia I, Stamatialis D*
Department of Biomaterials Science and Technology, University of Twente, Enschede, The Netherlands

**Introduction:** Hemodialysis is a life-saving therapy, which however has quite high environmental impact. More than one hundred liters of ultra-pure water are used per session per patient and every session has to be performed usually three times per week. The environmental reasons, as well as the advantages of having continuous patient treatment, stimulated research towards development of portable or wearable artificial kidney systems with the regeneration of the dialysate. In this work we focus on strategies for removing urea from the dialysate via adsorption using mixed matrix membranes (MMM) where sorbent particles are incorporated into membrane matrix.
**Material and methods:** Flat sheet MMM membranes were prepared via phase inversion by casting polyethylene vinyl alcohol polymer solution containing functionalized chitosan beads. Membrane morphology was investigated via scanning electron microscopy and adsorption of urea to the beads was investigated via the detection of ammonium ions obtained by the hydrolysis of urea using urease.
**Results:** The beads are very well distributed in the MMMs. Their embedding to the membrane prevented their aggregation and decreased the pressure drop which is a typical problem of columns with beads. Comparison of urea adsorption isotherms for beads alone and for the MMMs indicates that the accessibility of the beads in the MMMs is very good.
**Discussion:** New MMMs for urea sorption for dialysate regeneration were developed. In the future, efforts will focus on the optimization of the membrane transport properties, increase of the sorption capacity and possible upscaling.
**Acknowledgement:** This work is financed by EU Marie Curie ITN-TheLink (grant agreement 642890).

### O74
### SUCCESSFUL TRANSPLANTATION IN ABO- AND HLA-INCOMPATIBLE LIVING KIDNEY-TRANSPLANT PATIENTS: A REPORT ON 12 CASES

*Rostaing L[1], Karam B[2], Congy-Jolivet N[3], Hage V[2], Sallusto F[4], Esposito L[2], Doumerc N[4], Debiol B[5], Guilbeau-Frugier C[6], Game X[4], Allal A[2], Kamar N[2]*
[1]Faculté de Médecine de Rangueil, Université Toulouse III Paul Sabatier, Toulouse, France; [2]Department of Nephrology and Organ Transplantation, CHU Toulouse Rangueil, Toulouse, France; [3]Department of Immunology, CHU Toulouse Rangueil, Toulouse, France; [4]Department of Urology and Organ Transplantation, CHU Toulouse Rangueil, Toulouse, France; Etablissement Français du Sang, CHU Toulouse Purpan, Toulouse, France; [6]Service d'Anatomie et Cytologie Pathologiques, CHU Toulouse Rangueil, Toulouse, France

**Introduction:** Few studies have assessed the outcomes of ABOi/HLAi living-kidney transplantation. We report a single-center experience of 12 ABOi/HLAi living-kidney recipients.
**Material and methods:** Twenty-seven donor-specific alloantibodies (DSAs) were found (1-6 per patient) with fluorescence intensities of 1,500-15,000. Desensitization was based on IV-Ig, two doses of rituximab (375 mg/m$^2$), tacrolimus-based (0.2 mg/kg) immunosuppression (started on day-10 pretransplant), and 11 (6-27) pretransplant apheresis sessions (plasmapheresis, specific or semi-specific immunoadsorption).
**Results:** By day 0, 17 of the 27 DSAs had become undetectable. After 19 (3-51) months, patient- and graft-survival rates were 100% and 91.6%, respectively. One patient had an acute humoral rejection whereas three had a chronic antibody-mediated rejection (CAMR). At the last follow-up, kidney biopsies

were nearly normal in seven cases (58.3%) and renal function was excellent except for the three cases of CAMR. Four patients had a BKV infection.
**Discussion:** ABOi/HLAi living-kidney transplantation is a reasonable option for highly sensitized patients.

### O75
### SPERMATOZOA INITIALLY INCREASE MOTILITY AS TO ESCAPE UREMIC TOXIN ENVIRONMENT

*Vollmer T[1], Glorieux G[2], Jankowski V[3], Jankowski J[3], Stegmayr B[1]*
[1]Division of Nephrology, Department of Internal Medicine, Medicine centre, University Hospital of northern Sweden, Umea, Sweden; [2]Nephrology Section, Department of Internal Medicine, University of Ghent, Ghent, Belgium; [3]Institute for Cardiovascular Research, RWTH Aachen University, Aachen, Germany

**Introduction:** Substances retain in the body of patients with chronic kidney disease and are denominated uremic toxins. Since not all substances may cause toxic effects, we described a method that estimates this by motility analysis of human spermatozoa. Here we aim to elucidate if the immediate response of spermatozoa after exposure to uremic substances is related to the outcome in the long term.
**Material and methods:** 12 uremic substances were tested for their motility effect on spermatozoa over time. A blank approach was used as control. Semen was obtained from healthy donors and progressive motility counted after direct exposure to uremic substances and at 1-2, 90, 180 minutes of incubation. For time effect on motility was adjusted, median is shown. Toxic effect was defined, if motility decreased at ≥90 minutes. Wilcoxon signed ranks test was used- matched pairs with controls.
**Results:** One substance stimulated motility over time, whereas 11 showed toxic effect. Uremic substances added to the semen caused a significant rise in sperm motility initially by 47% ($p = 0.003$) and by 22% at 1 to 2 minutes ($p = 0.003$). A decreased motility was found at 90 minutes (-22%, $p = 0.01$) and 180 minutes (-11%, $p = 0.008$). If motility at start increased by <50%, a pronounced reduction was found at 180 min ($rho = 0.69$, $p = 0.019$).
**Discussion:** Uremic substances cause a significant initial stress to spermatozoa, over time their motility impairs. We figure that this mechanism could be thought of as an escape mechanism for the cells to try to 'actively avoid' toxic input from environment. Not all retained substances have a toxic effect.

### O76
### ESTIMATED GFR POORLY REFLECTS CONCENTRATIONS OF VARIOUS URAEMIC TOXINS IN PAEDIATRIC CKD PATIENTS: NEW TOOLS ARE NEEDED TO IMPROVE DIAGNOSIS

*Snauwaert E[1], Van Biesen W[2], Raes A[1], Vande Walle J[1], Eloot S[2]*
[1]Paediatric Nephrology, Ghent University Hospital, Ghent, Belgium; [2]Department of Nephrology, Ghent University Hospital, Ghent, Belgium

**Introduction:** Chronic kidney disease (CKD) in childhood is a devastating disease characterised by a decreased life expectancy and important comorbidities. Retention of uraemic toxins is accepted to play a major role, but studies in children are lacking. In a four years project (IWT; started 1/10/2015), we want to provide the clinician with new diagnostic and therapeutic tools for the management of children with CKD, based on improved understanding of uraemic toxicity. As a first step, we evaluated whether the index of kidney function eGFR (estimated Glomerular Filtration Rate) is representative for various uraemic toxin concentrations in CKD children.
**Material and methods:** To date, we included 43 children (10.5 ± 5.5 year; 79.1% boys) with CKD stage 1-5, and investigated linear associations between eGFR (Schwartz) and the natural logarithm of serum concentrations of small solutes [uric acid (UA), urea, creatinine], middle molecules [beta-2-microglobulin (B2M), complement factor D (CfD)], and protein-bound solutes [p-cresylglucuronide (pCG), hippuric acid (HA), indole acetic acid (IAA), indoxyl sulfate (IS), p-cresylsulfate (pCS), and 3-carboxy-4-methyl-5-propyl-furanpropionic acid (CMPF).
**Results:** Mean eGFR was 45.1 ± 24.0 mL/min/1.73 m (range 4.9-102.7). eGFR variance was the highest ($R^2 = 0.80$) for creatinine and CfD, followed by B2M (0.68) and urea (0.63). In contrast, $R^2$ was low (0.20-0.40) for UA, total pCG, free and total HA, free and total IAA, free IS and free pCS. Even lower $R^2$ values (<0.20) were found for free pCG, total IS, total pCS and CMPF.
**Discussion:** The concentration of protein-bound solutes, toxins with proven pathophysiological effects, were extremely poor related to eGFR, such that eGFR cannot be considered representative for evaluating accumulation of solutes in the course of CKD.

## Oral Session - Implants and Scaffolds, O77-O81

### O77
### ELECTROSPUN COLLAGEN NANOFLEECES FOR APPLICATIONS IN THE FIELD OF REGENERATIVE MEDICINE

*Milosevic J[1], Kürbitz T[2], Heine C[1], Hasan S[1], Herbst C[1], Meisel H[1], Heilmann A[3]*
[1]SpinPlant GmbH Leipzig, Leipzig, Germany; [2]Electrotechnics and maschine builiding, Anhalt University of Applied Sciences, Bernburg, Germany; [3]Biological and Macromolecular Materials, Fraunhofer IMWS, Halle, Germany

**Introduction:** The aim of our studies was to produce biological nanofiber fleeces on collagen basis, which can be used for bone and cartilage repair and as scaffolds for soft tissue regeneration in various fields of Regenerative Medicine. The challenge of the current investigation was to preserve collagen's unique properties and native features that are defined, for example by its molecular structure, the collagen triple-helix. Moreover, the assembly of the collagen into fibrils and the cross-links of the fibrils provide the high tensile and mechanical strength of collagen that is required for tissue integrity.
**Material and methods:** To produce fleeces with preserved native collagen structure a unique electrospinning process was used. By means of different techniques the spun fleeces were characterized, with regard to maintenance of the triple helix, nanostructure, biocompatibility as well as cell adhesion, proliferation and migration.
**Results:** We developed protocols of spinning collagen fleeces on a nanoscale, while preserving the triple helical native collagen structure. We further established protocols to modify the spun collagen nanofibers by using cross-linkers, in order to make them stable and applicable for in vitro and in vivo trials. Moreover, our fleeces have been proven to be biocompatible, non-toxic, completely biodegradable, and stable for many weeks with preserved porosity and nanofiber structure.
**Discussion:** Native and stable collagen nanofiber fleeces have been produced within a unique and scalable electrospinning process. These nanostructured fleeces maximize interaction and attachment with cells and demonstrate sufficient porosity and permeability favoring the use of this material in Regenerative Medicine.

### O78
### 3D NANOMATERIALS FOR REGENERATION OF CONNECTIVE TISSUE, SUCH AS CARTILAGE

*Gerasimenko A[1], Podgaetsky V[1], Ichkitidze L[1], Telyshev D[1], Eganova E[2], Pavlov A[2], Selyshchev S[1]*
[1]Biomedical systems, National Research University of Electronic Technology, Moscow, Russian Federation; [2]Department of development and research of micro and nanosystems, Institute of Nanotechnology of Microelectronics of the Russian Academy of Sciences, Moscow, Russian Federation

**Introduction:** New possibilities of tissue engineering are connected with the development of 3D nanomaterials creation with functional properties of cartilage. Such materials can be created using the technique of carbon nanotubes (CNTs) structuring in albumin matrix.
**Material and methods:** Possibilities of medical application of CNTs increase with the information of its self-organization, growing and branching of bone, nervous and stem cells on CNTs, which allow different tissues of organism to regenerate. CNTs structuring in water matrix of albumin is provided by laser. Laser radiation evaporates water and the frame solid nanomaterial is created. When radiating the CNTs are being wrapped in the albumin layer with thickness of 20-40 nm. 3D nanomaterial phase state varies from elastic to solid state.
**Results:** The frame porous structure (10 nm-100 μm) of 3D nanomaterial is proved using spectral and microscope techniques. The hardness of nanomaterials was 200-300 MPa. The performed in vitro experiments on the cells have shown the absence of toxic effect of the nanomaterial. The experiments

on the laboratory animals have shown the absence of allergic reactions after nanomaterial injection into the rabbit perichondrium. The substitution of the removed cartilage segment for nanomaterial implant has caused its regeneration under the stimulation of active fission of usually passive chondrocytes.
**Discussion:** 3D nanomaterial can provide conditions for functional tissue regeneration similar to the influence of biological matrix. The carbon frame provides conditions for tissue self-organization which is maintained by non-covalent bonds under the hydrophobic tissue interacting. Such organization of biological macromolecules is realized in phospholipids that are basic components of plasma cell membrane.

### O79
### DEVELOPMENT OF BIODEGRADABLE INJECTABLE SYSTEM BASED ON CHITOSAN AND CALCIUM PHOSPHATE

*Rogina A[1], Matic I[2], Ressler A[1], Gallego Ferrer G[3], Ivankovic M[1], Ivankovic H[1]*
[1]Faculty of Chemical Engineering and Technology, University of Zagreb, Zagreb, Croatia; [2]Faculty of Science, University of Zagreb, Zagreb, Croatia; [3]Center for Biomaterials and Tissue Engineering (CBIT), Universitat Politècnica de València, Valencia, Spain

**Introduction:** Injectable gels have gained great importance due to their potential to minimize invasive manner during that surgical therapy. Injectable gels have ability for gelation under physiological conditions and as such are used for cell delivery and nutrients and growth factors diffusion. Injectable hydrogels based on chitosan as a biodegradable polymer matrix and hydroxyapatite as a bioactive inorganic phase are prepared in this study. The gelation of chitosan-hydroxyapatite hydrogels has been initiated by sodium hydrogencarbonate ($NaHCO_3$).
**Material and methods:** The composition of dried injectable hydrogels was determined by X-ray diffraction analysis and Fourier transmission spectroscopy, while morphology of lyophilized gels was investigated by scanning electron microscopy. Reological behaviour of hydrogels was determined by amplitude and frequency sweep experiments. Cytotoxicity of injectables was evaluated using MTT method.
**Results:** The characterization of prepared hydrogels has confirmed formation of hydroxyapatite within chitosan matrix. The reological measurements of chitosan-hydroxyapatite gels have indicated rapid thermogelling of prepared system and confirmed formation of 'strong physical gel' with suitable shear modulus. Biological evaluation confirmed the non-cytotoxicity of the prepared hydrogels.
**Discussion:** The composition of prepared hydrogels is favourable for bone tissue regeneration, while gelation rate makes those gels applicable as a cell carrier.

### O80
### BIOCOMATIBILITY STUDY OF AN INNOVATIVE ELASTOMER FOR LONG TERM IMPLANTS APPLICATION

*Zawidlak-Węgrzyńska B[1], Ścigała P[2], Gonsior M[1], Janiczak K[1], Gawlikowski M[1], Cieśla P[1], Kustosz R[1], El Fray M[3], Piegat A[3]*
[1]Artificial Heart Laboratory, Zbigniew Religa Foundation for Cardiac Surgery Development, Zabrze, Poland; [2]Emergency and Specialty Animal Medical Center, Piekary Slaskie, Poland; [3]Polymer Institute, Biomaterials and Microbiology Technologies Department, West Pomerania University of Technology, Szczecin, Poland

**Introduction:** The complete in vitro and in vivo biocompatibility study of the new elastomeric biomaterial for long term implants application was performed. Investigated material consist of the poly(terephthalate ethylene) (PET) and dimerized parts of fatty acids (DLA) - (PET/DLA) modified by D-glucitol.
**Material and methods:** The in vitro and in vivo examinations necessary for the biocompatibility confirmation according to ISO-10993 were carried out. The biocompatibility was determined by in vitro evaluation of cytotoxicity, hemolysis, thrombogenicity, biodegradation, and in vivo test of irritation in rabbits, skin sensitization in guinea pigs (GMPT test), tissue reaction after implantation in dorsal muscle and intraperitoneal implantation in the rabbits.
**Results:** Cytotoxicity tests showed that the PET/DLA materials do not cause toxicity on the cells, the cytotoxicity graduation for investigated materials was 0. No haemolysis reaction, nor platelets and leukocytes activation was observed in the blood after contact with the biomaterial surface. The degradation studies showed excellent stability of the studied polymer. PET/DLA polymer extract did not induce any skin sensitization in guinea pigs, nor irritation skin in the rabbit. Moreover, histological studies after implantation in dorsal muscle and intraperitoneal implantation in the rabbits showed that the materials did not elicit an inflammatory response.
**Discussion:** Standardized tests to detect sensitization, irritation, tissue reaction, hemocompatibility, cytotoxicity, biodegradation and thrombogenicity, demonstrated the safety and biocompatibility of PET/DLA polymer in accordance with the ISO-10993 requirements. The performed studies confirmed that PET/DLA modification by D-glucitol can be safely use as a construction material for a long term implants application.
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### O81
### IN VITRO CALCIFICATION: ADVANCING THROUGH THE DEVELOPMENT OF AN ACCURATE MODEL

*D'Alessandro C[1], Badria A[1], Ratna Tuladhar S[2], Gerosa G[2], Korossis S[3], Koutsoukos P[4], Mavrilas D[1]*
[1]Mechanical and Aeronautical, University of Patras, Patras, Greece; [2]Cardiac Thoracic and Vascular Sciences, Universitá degli Studi di Padova, Padova, Italy; [3]Cardiothoracic, Transplantation and Vascular Surgery, Hannover Medical School, Hannover, Germany; [4]Chemical Engineering, University of Patras, Patras, Greece

**Introduction:** Calcification is one of the main causes for long-term dysfunction of biological heart valves. The aim of this work is to develop an in vitro model for assessing the calcification potential of biomaterials.
**Material and methods:** The work developed an improved constant supersaturation system aimed at the evaluation of the mineralization potential of tissue engineered scaffolds. The kinetics of the process was monitored on-line by a computer-controlled syringe pump supplying ions of the mineralized phase at the appropriate stoichiometric ratio in a way that solution supersaturation was maintained throughout the mineralization process. The chemical and morphological identification of the deposits was done by energy dispersive analysis (EDS) and scanning electron microscopy (SEM) respectively.
**Results:** Three tissue types were examined: Fresh porcine pericardia, glutaraldehyde treated bovine pericardia (BPGL) and decellularized bovine pericardia. The BPGL showed increased calcification rates (41.8 ± 10.7 mol $m^2$ $s^{-1}$, n = 3) compared to the fresh pericardium (n = 4), which did not show any detectable crystallization process. Experiments with decellularized bovine pericardium are in progress.
**Discussion:** A novel model for in vitro screening of the calcification potential of tissue engineered scaffolds was developed. The model allowed for precise and highly reproducible kinetics measurements. Current experimental work focuses on the statistical assessment of the mineralization potential of tissues of interest. A dynamic in vitro model involving a quasi-physiological circulatory loop was constructed in parallel, in order to assess the effect of mechanical loading in the calcification of tissue engineered valvular scaffolds.

## Oral Session - Modelling *in silico* and in vivo, O82-O87

### O82
### IMPACT OF ROTARY BLOOD PUMP SPEED STEPS ON INTRAVENTRICULAR FLOW PATTERNS

*Aigner P, Moscato F, Schima H*
Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Ludwig Boltzmann Gesellschaft, Vienna, Austria

**Introduction:** Adverse events in mechanical cardiac support patients are still a crucial problem and thromboembolic events are probably related to altered blood flow patterns and stasis. Therefore areas of low flow with a high degree of stagnation during ventricular assist support are of special interest. The impact of different pump speed steps was investigated in an in-vitro setup to measure the effects on the flow patterns and washout of the ventricle.
**Material and methods:** In a left ventricular model flow behaviour was analysed with Particle Image Velocimetry and different pump speed steps were

evaluated. The standard deviation of the flow velocities in the ventricle and a stagnation index SI were used to characterize the effects of speed steps ranging from 3.5% to 18% of the baseline speed (2800 rpm).
**Results:** Overall the flow patterns for the investigated speed steps were similar. However with bigger speed steps, a positive effect on the flow variation and the washout was found. The SI improved from 5.54s at a speed step of 3.5% to 2.39s at a speed step of 18% indicating an overall lower stagnation. Also the standard deviation of the velocities showed an improvement from 0.045 m/s to 0.068 m/s indicating higher variations in the flow patterns.
**Discussion:** The use of rotary pump speed steps in an in vitro left ventricular model resulted in improved ventricular washout. With increasing pump speed step sizes higher flow variations were induced and this could reduce areas of stasis. Additionally increase in the flow variation might improve the ventricular washout and thromboembolic patient outcome.

**O83**
**IMAGE BASED FITTING OF NEW INFLOW CANNULA FOR THE EVAHEART LVAS**
*Sonntag S[1], Neidlin M[1], Groß-Hardt S[2], Benkowski R[3], Motomura T[4], Steinseifer U[2], Kaufmann T[2]*
[1]Enmodes GmbH, Aachen, Germany; [2]Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, RWTH Aachen University, Aachen, Germany; [3]B-Squared Medical Device Solutions LLC, Fort Worth, USA; [4]Evaheart Medical USA Inc, Houston, USA

**Introduction:** Two novel inflow cannula designs for the EvaHeart LVAS were developed with the aim of reducing risk of inflow obstruction, reducing pump pocket size and avoiding RV compression by the outflow graft. Using scans of six representative patients and virtual implantation, anatomical fitting of the original and novel cannula was analyzed. The novel designs were iteratively adjusted to achieve ideal fitting for a wide range of patients.
**Material and methods:** The CT scans were segmented and reconstructed to 3D models. Virtual implantation was performed by translating and rotating the pump. The preferred cannula position was at the anterior wall 2 cm lateral to the left anterior descending artery allowing cannula placement parallel to the septum. Parameters for design optimization were the bending angle, the inflow/outflow offset and the cannula length.
**Results:** Implantation of the original configuration at the optimal implantation position was not possible for patients with LVEDV <400 ml due to rip interference. After repositioning, the inflow tip was facing towards the septum, which may lead to obstruction. After several design iterations, optimal placement and orientation of the new inflow cannula were possible for all patients. RV compression was avoided with an inflow/outflow offset of 30°. Reduced pump pocket depth and size was achieved.
**Discussion:** Virtual fitting allowed analyses and design adjustments of two new inflow cannula in realistic anatomies. With the final designs the heart remains in its natural anatomic position assuring long-term unobstructed pump flow and therefore reducing the risk of adverse events for a wide range of patients.

**O84**
**INFLUENCE OF LVAD INFLOW CANNULA POSITIONING ON VENTRICULAR HEMODYNAMICS WITH A FLUID-STRUCTURE INTERACTION MODEL**
*Neidlin M[1], Sonntag S[1], Groß-Hardt S[2], Steinseifer U[2], Kaufmann T[2]*
[1]Enmodes GmbH, Aachen, Germany; [2]Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, RWTH Aachen University, Aachen, Germany

**Introduction:** Cannulation during LVAD support introduces an interference with intraventricular flow patterns. As various positions of the inflow cannula are possible, it is important to gain a better understanding of the occurring hydrodynamic phenomena.
**Material and methods:** Analysis of hemodynamics was performed with a numerical model of the left ventricle. The geometry was extracted from CT scans of two patients with an LVEDV of 124 ml and 420 ml. The inflow cannula was positioned with three different insertion lengths and two angles in the apical location. Movement of the ventricular wall was included. Full support and partial support conditions were investigated. Results were evaluated regarding flow configurations, wall shear stresses (WSS) and thrombus risk.
**Results:** Collision between the atrioventricular jet stream and the cannula tip was observed for higher insertion lengths and lead to increased WSS values. The occurring disruption of the mitral vortex ring reduced the kinetic energy of the left ventricle. An unfavorable cannulation angle increased the probability of suction due to close proximity of the cannula tip to the myocard. Finally, existence of recirculation areas underneath a far inserted cannula caused a higher thrombus risk. All effects were more distinct for the patient with a dilated ventricle. Observations were similar for both support conditions.
**Discussion:** Positioning of the VAD inflow cannula affects the ventricular hemodynamics and may obstruct the physiologic flow field. The conserved cardiac energy is reduced which ultimately deteriorates the hydraulic performance of the heart. Consequently, location of the inflow cannula should be chosen carefully with respect to the ventricular hemodynamics.

**O85**
**HEMODYNAMIC CHANGES IN RESPONSE TO IMPROVED VENTRICULAR CON-TRACTILITY DURING CONTINUOUS FLOW LVAD SUPPORT: IN-VITRO STUDY**
*Suciu A, Khir A*
Brunel Institute for Bioengineering, Brunel University London, Uxbridge, UK

**Introduction:** To investigate hemodynamic parameters changes during continuous flow VAD support with changes in left ventricular (LV) contractility, in-vitro.
**Material and methods:** A continuous flow pump to mimic continuous flow LVAD and a piston pump to mimic the LV were used to generate respectively 4 flow rates ($Q_c$, 2-5 L/min) and 5 single compression pulse strengths to simulate LV contractility (ps, 8-12 volts), in a mock circulation. Wave Intensity Analysis (WIA), a technique that determines the ventriculo-arterial interaction was applied to calculate the forward compression wave intensity (*FCW*). Also, maximum pressure ($P_{max}$), velocity ($U_{max}$) and their pulse magnitude ($P_p$, $U_p$) associated with the various ps and $Q_c$ were determined.
**Results:** $P_{max}$ increased proportionally with ps (13.65 vs. 14.66, kPa) but decreased at higher $Q_c$ (14.64 vs. 13.65, kPa). $U_{max}$ increased proportionally with both ps (0.35 vs. 0.42, L/min) and $Q_c$ (0.36 vs. 0.42, L/min). $P_p$ and $U_p$ increased with increasing ps (9.17 vs. 10.12, kPa), (0.17 vs. 0.23, L/min), but decreased with increasing $Q_c$ (13.39 vs. 10.12, kPa), (0.29 vs. 0.23, L/min). FCW decreased and increased respectively with increasing $Q_c$ (8.1E-0.4 vs. 5.2E-04, W/m$^2$) and increasing ps (1.9E-04 vs. 5.2E-04, W/m$^2$).
**Discussion:** During continuous flow LVAD support, an increase of LV contractility is associated with increase in $P_{max}$, $U_{max}$, $P_p$, $U_p$ and *FCW*. Also, changes in arterial hemodynamics are substantial when changing $Q_c$. *FCW* can be used for assessing LV contractility, in-vivo studies are required to confirm the current in-vitro results.

**O86**
**A COMPUTER MODEL OF A HEART MUSCLE - CORONARY SYSTEM INTERACTION FOR IABP ASSISTANCE HYBRID SIMULATIONS**
*Zieliński K[1], Kozarski M[1], Górczyńska K[1], Ferrari G[2], Darowski M[1]*
[1]Nalecz Institute of Biocybernetics and Biomedical Engineering PAS, Warsaw, Poland; [2]Section of Rome, Cardiovascular engineering, CNR - Institute of clinical Physiology, Italy

**Introduction:** Analysis of a real-time computer model of a heart muscle - coronary system interaction in the case of stenotic coronary disease.
**Material and methods:** The model consists of four functional sections: a lumped parameter model of the coronary circulation, closed loop circulatory model, model of the intra-aortic ballon pump (IABP) function including mechanisms of a balloon inflation and deflation as well as flows outside the balloon and a model of the heart muscle and coronary circulation interaction - a crucial point of the analysis. A model of the heart muscle - coronary system interaction, as dedicated for real time hybrid model applications, is numerically solved in time beneath 0.5 ms and contains well clinically defined parameters. The heart muscle - coronary circulation interaction mechanism is represented by a function connecting maximal left ventricular elastance (Emax) with the coronary flow decrease caused by the coronary artery stenosis. The presented model gives more realistic description of the IABP assistance than models taking into account only mechanical effects and neglecting a contribution of the coronary circulation.

**Results:** Some numerical simulation have been done corresponding to the following numerical cases: a) the closed loop circulatory model including coronary circulation with or without stenotic changes, b) the closed loop model assisted by IABP with and without interaction mechanism. The results in the form of selected transient pressure characteristics and left ventricular pressure-volume loops are presented.
**Discussion:** The simulations results correspond well with clinical IABP assistance results.

**O87**
**IN-VITRO TESTS RESULTS PROVIDE NEW INSIGHT INTO PROSTHESIS BEHAVIOR: A HELP FOR CLINICIANS TO CHOOSE PROSTHESIS AND SIZE IN AORTIC VALVE REPLACEMENT**
*Egron S[1], Fujita B[2], Ensminger S[2], Doose C[1], Pott D[1], Steinseifer U[1]*
[1]Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Aachen, Germany; [2]Department for Thoracic and Cardiovascular Surgery, Heart and Diabetes Center NRW, Ruhr University Bochum, Bad Oeynhausen, Germany

**Introduction:** In aortic valve replacement procedures, the choice of prosthesis-type and -size greatly impacts patient outcome. Recent market-entry of new prostheses has broadened this choice. Yet technical information is lacking to easily compare the prostheses.
Clinicians have a complex situation to assess. Prosthesis-oversize is wanted for safe anchoring and sealing, while annulus rupture and conductance disturbances have to be avoided; the risk of prosthesis ovalization is also critical. It is hence crucial to provide information about the prostheses radial force profiles and ovalization-sensibilities to predict performance in clinics. In this study, we analyzed five commercial valves -3 fully-crimpable prostheses and 2 sutureless prostheses.
**Material and methods:** In-vitro tests were performed to measure the radial forces and pinch force resistances of all five prostheses. Test-protocols were designed to provide quantitative comparison of the prostheses. Additionally, results were collected such that they can be directly translated into clinical case discussions.
**Results:** The prostheses present highly different radial force profiles. In several cases, the radial force value changes drastically in the passage from one size to the next bigger size. The ovalization-sensibilities of the valves are also very distinct from one type to the other.
**Discussion:** The manufacturers' sizing-recommendations seem to be based on different strategies. One prosthesis requires a very precise anatomy-sizing due to its stiff radial force profile, and the difference in ovalization-sensibilities is to be considered in patients with uneven calcification patterns. These new technical insights may help decision-making for clinicians and thereby improve patient outcome.

## Special Symposium - Implantable Biosensors, O88-O91

**O88 (KL5)**
**CONTINUOUS GLUCOSE MONITORING IN HUMANS USING A LONG-TERM IMPLANTED SENSOR/TELEMETRY SYSTEM**
*Gough DA[1], Routh TL[2], Lin JT[2], Lucisano JY[2]*
[1]Department of Bioengineering, University of California, La Jolla, San Diego, USA; [2]GlySens Incorporated, San Diego, USA

**Introduction:** A fully implanted sensor/telemetry system for long-term monitoring of subcutaneous tissue glucose has been tested in individuals with diabetes.
**Material and methods:** The sensor is based on a membrane containing immobilized glucose oxidase and catalase coupled to a differential electrochemical oxygen detection system and transmits signals every 3 minutes to an external receiver. The sensor system has functioned for over 520 days in normal and STZ diabetic pigs, and for over one year in clinical trials in humans with diabetes, with only occasional recalibration. The data include recordings of blood glucose clamps and spontaneous glucose excursions matched to reference blood glucose and finger-stick values.
**Results:** As the sensor signals indicate dynamic tissue glucose, for which there is no independent standard, and were not expected to exactly match instantaneous blood glucose, a dynamic mass transfer model describing the relationship between blood and tissue glucose has been developed. The values of all model parameters have been estimated, including the permeability to glucose and oxygen of tissues adjacent to the implant.
**Discussion:** Correlation coefficients indicate strong associations between sensor signals and reference glucose values. This fully implanted, long-term sensor system may make possible new approaches for improved management of diabetes.

**O89 (IL37)**
**MONITORING OXYGEN WITH OPTICAL SENSORS IN CELL CULTURE, ARTIFICIAL AND NATIVE TISSUE**
*Meier R, Liebsch G*
PreSens Precision Sensing, Regensburg, Germany

**Introduction:** Monitoring oxygen supply in cell culture, native or engineered tissue is crucial. Proliferation, migration and differentiation highly depend on the local oxygen supply. Cells seeded on scaffolds for tissue engineering often are subjected to hypoxic conditions, because of uneven oxygen supply within the constructs. These gradients in oxygen availability impede uniform cellular growth on scaffolds and can cause cell death in anoxic regions. Native tissues can have natural diffusion barriers, such as the skin or other epithelia, or spatially limited supply in tissue.
**Material and methods:** PreSens sensors measure oxygen directly using optical sensors (optodes).
**Results:** Contrary to electrodes that need direct sample contact, optodes can be even read out in a non-contact mode e.g. through transparent walls in cell culture vessels or, in principle, through the optical window of the skin. Thereby, they do not interfere with the sample, avoid contaminations, do not consume analyte during measurement, and are fully reversible. Further, they can measure in non-stirred solutions or non-perfused tissue constructs. These sensors can be applied as minimally-invasive or implantable fiber-optic sensors with high precision and spatial resolution, or as non-invasive planar sensors for 2D visualization. The use of optical oxygen sensors in cell culture, engineered and native tissue that all depict temporal and spatial changes in oxygen availability to the tissue or cells will be presented.
**Discussion:** This technique enables insights in processes in artificial and native tissue and enables monitoring to further pave the way towards artificial organs.

**O90 (IL38)**
**IMPROVED PLATINUM ANODES FOR THE OPERATION OF IMPLANTABLE GLUCOSE FUEL CELLS IN REAL PHYSIOLOGICAL FLUIDS**
*Frei M, Bühler M, Erben J, Kerzenmacher S*
IMTEK - Department of Microsystems Engineering, University of Freiburg, Freiburg, Germany

**Introduction:** Implantable glucose fuel cells based on platinum catalysts are a promising approach to realize a battery-independent power supply for medical implants. Their main advantages are continuous power generation, biocompatibility, and a theoretically unlimited lifetime. However, so far the poisoning of platinum anodes by tissue fluid constituents (e.g. amino acids) limits their lifetime to a few days. One strategy to overcome this limitation is the significant increase in specific electrode surface area available for the electro-oxidation of glucose.
**Material and methods:** To achieve this, we chose electrospun carbon-nanofiber mats as 3-D substrate for the electrodeposition of highly porous platinum. Correspondingly fabricated anodes were continuously operated in artificial body fluids containing amino acids and horse serum.
**Results:** Using the new approach, so far a roughness factor (RF; ratio of surface area to geometrical area) of 16500 ± 2300 has been reached. Compared to our previous state-of-the-art electrodes, this corresponds to an almost 3-fold increase. After 800 h of continuous operation in horse serum, the new anodes exhibited stable potentials of 9 ± 7 mV vs. SCE at a current density of 5 µA/cm². Compared to state-of-the-art this corresponds to an approximately 100 mV lower polarization loss.

**Discussion:** We demonstrated that the use of electrospun carbon-nanofibers as a 3-D substrate is a promising strategy to increase the specific anode surface and improve its functionality in real physiological environments. The projected power density of a correspondingly fabricated fuel cell would already be in the range of 0.3 μW/cm². We expect that this value can be increased by further optimization.

**O91 (IL39)**
**ADVANCES IN NANOTECHNOLOGY FOR ORGAN REPLACEMENT: A SUMMARY OF 15 YEARS OF RESEARCH AND COMMERCIALIZATION**
*Webster TJ*
Department of Chemical Engineering, Northeastern University, Boston, USA

**Introduction:** Nanotechnology (or the use of materials with one dimension less than 100 nm) has been revolutionizing the field of organ replacement for several decades due to the ability of nanomaterials to mimic natural features of healthy tissues. However, issues remain such as toxicity, assembling nanomaterials into functional organs, efficacy, drug loading, cost, and lengthy FDA approval times have still proven to be significant obstacles. The objective of this talk is to summarize recent advances in developing nanostructured artificial organs for quick regulatory approval.
**Material and methods:** Approaches such as top-down and bottom-up nano approaches along with 3D printing, cast-molding, and other techniques to create artificial organs will be covered. Approaches have been shown to be versatile using ceramics, metals, polymers, and composites thereof. In vitro and in vivo studies will be covered.
**Results:** Such approaches have led to improved interactions with mammalian cells (such as bone, cartilage, vascular, neural, bladder, etc. cells) and decreased interactions with immune cells (such as monocytes, macrophages, etc.) to regenerate organs. Lastly, a new approach to medicine focused on controlling picoscale events will also be introduced where one can dictate electron interactions within a material to improve cellular functions leading to greater organ regeneration.
**Discussion:** In summary, this presentation will cover what has been learned over the past several decades of translating nanotechnology to improve organ replacement while emphasizing future developments that we should expect for the field to grow (such as picotechnology).

## Special Symposium - Liver Decellularization: a Second Life for Liver Bioengineering, Bioartificial Livers and Extracorporeal Liver Perfusion Machines, O92-O93

**O92 (IL42)**
**EXTRACORPOREAL LIVER PERFUSION MACHINES: THE GOOD, THE BAD AND … THE FEASIBLE?**
*Sanchez Del Arco R, Gutierrez-Gutierrez J, Del Cañizo J*
Department of Surgery, Laboratorio de Circulacion Artificial, Hospital General Universitario Gregorio Maranon, Universidad Complutense de Madrid, Madrid, Spain

**Introduction:** Extracorporeal liver perfusion devices offer many advantages over current organ preservation techniques. In the last decade, this subject has become a hot topic and several research groups have got involved into the development of this technology. At the moment there are various machines on the market and some others in development, provided with different features.
**Material and methods:** Despite the potential of perfusion systems, many issues remain unsolved and further development is still required on this field. Some technical constraints include transportation difficulties, excessive size and insufficient power autonomy. Furthermore the introduction of a hitherto unseen technology often must lead to consider some other and no less important aspects. Examples of that are the need of staff specific training and continuous human surveillance. Moreover the high cost resulting from the implementation of this technology could be itself a major concern for some healthcare systems. It is therefore necessary to assess its economic impact and evaluate the eventual development of more efficient protocols.
**Results:** For the last three years our group has been developing a new normothermic liver perfusion system. Along this time we faced some problems not reported in the literature we reviewed.
**Discussion:** Hence we believe appropriate appraise the adequacy of different perfusion protocols and the goals they pursue as well as try to determine the role that this technology would play in current clinical practice.

**O93 (IL44)**
**LIVER DECELLULARIZATION: A SECOND LIFE FOR LIVER BIOENGINEERING, BIOARTIFICIAL LIVERS AND EXTRACORPOREAL LIVER PERFUSION MACHINES**
*Baptista P[1], Del Cañizo J[2]*
[1]Instituto de Investigacion Sanitaria de Aragon, Zaragoza, Spain; [2]Cirugia Experimental, Hospital Universitario Gregorio Marañon, Madrid, Spain

**Introduction:** According to the latest World Transplant Registry, in 2012 nearly 24,000 livers were transplanted. However, donor shortage is becoming a critical issue. Different strategies have been explored to face this problem, including expanded criteria, deceased and living donors. Unfortunately, they have not met expectations, and their impact on the number of available grafts has not alleviated the ever-growing liver transplant waiting lists.
**Material and methods:** Current organ preservation techniques, mainly based on static hypothermic storage, appear to have peaked. Moreover, bioartificial liver devices still present significant limitations and are not a definitive alternative to transplantation yet. Furthermore, whole organ bioengineering is still years away of presenting itself as a tangible alternative to organ donation. It is therefore necessary to transversally develop novel methods that enable a better and more prolonged conservation and even the recovery of suboptimal grafts (steatosis, elderly donors, systemic infection, etc), as well as increase the function and clinical impact of bioartificial and bioengineered whole livers.
**Results:** At the core of this might be organ decellularization, a fairly novel technique with the potential to provide complex substrates for richer cell-matrix interactions in these machines, increasing function and clinical relevance. Also, the integration of bioreactor know-how from bioartificial organs and extra-corporeal perfusion machines is key to accelerate and improve the development and maintenance of bioengineered whole organs.
**Discussion:** Hence, this symposium intends to provide a meeting place for professionals of these three fields, and through discussion, accelerate potential collaborations that can effectively improve the outcome and the future of organ support and transplantation.

## Special Symposium - Extracellular Vesicles: Markers of Cellular Activation and Contributors to Coagulation and Inflammation, O94-O95

**O94 (IL58)**
**PRO-COAGULANT POTENTIAL OF PLATELET-DERIVED MICROVESICLES**
*Tripisciano C, Weiss R, Eichhorn T, Weber V*
Christian Doppler Laboratory for Innovative Therapy Approaches in Sepsis, Department Health Sciences and Biomedicine, Danube University Krems, Krems, Austria

**Introduction:** We investigated the pro-coagulant potential of microvesicles (MVs) from human platelets and the role of phosphatidylserine (PS) and tissue factor (TF) exposed by MVs. The pro-coagulant activity of these MVs was compared to MVs enriched after stimulation of human monocytic THP-1 cells with lipopolysaccharide (LPS) from *E. coli*.
**Material and methods:** Platelet concentrates were obtained from healthy volunteer donors using a Trima Accel® blood collection system (Version 5.0, Gambro BCT). MVs were enriched via centrifugation (20,000 g, 30 min, 4°C)

after removal of cells (1,500 g, 15 min, RT). Samples were characterized via flow cytometry using annexin V as MV marker and CD41 as platelet marker, by nanoparticle tracking analysis, and by cryo-electron microscopy to define cellular origin, size distribution, and morphology. Pro-coagulant potential was quantified via thrombin generation (Technoclone GmbH) and detection of thrombin-antithrombin complex (Enzygnost TAT micro, DADE Behring).
**Results:** The mean size of isolated MVs was 173 ± 15 nm. Flow cytometry detected 70 ± 9.7% $CD41^+AV^+$ events in the MV gate (300-900 nm). Platelet-derived MVs supported the generation of thrombin in a dose- and PS-dependent manner. MVs derived from platelets and LPS-stimulated THP-1 showed differences in the time to onset of thrombin generation, but not in the maximal amount of thrombin, as confirmed by the TAT complex quantification over time.
**Discussion:** Our data clearly demonstrate the pro-coagulant potential of MVs derived from physiological platelets and suggest that quantitative and qualitative differences of MV-associated TF reflect its activity in physiological and pathological settings.

**O95 (IL59)**
**INFLUENCE OF ANTICOAGULATION ON CELL ACTIVATION AND MICROVESICLE GENERATION DURING LIPID APHERESIS**
*Weiss R[1], Fischer M[2], Weber V[1]*
[1]Christian Doppler Laboratory for Innovative Therapy Approach, Danube University Krems, Krems, Austria; [2]Center for Biomedical Technology, Department for Health Sciences and Biomedicine**,** Danube University Krems, Krems, Austria

**Introduction:** In this study, we aimed to assess the influence of citrate anticoagulation on platelet activation, MV generation and cell adhesion to acrylamide-polyacrylate adsorbents for low density lipoprotein (LDL) apheresis.
**Material and methods:** Blood was drawn from healthy volunteer donors and anticoagulated with citrate (2, 4 and 13 mM final concentration). Aliquots of 50 mL were recirculated over columns (3.5 × 1.8 cm) containing adsorbents for LDL apheresis at a flow rate of 1.2 ml per min for 4 hours. Samples were taken every hour, and blood cells in the flow-through were quantified using a blood cell counter. MVs were determined with a Gallios Flow Cytometer (Beckman Coulter) after calibration with fluorescent beads to cover the MV (0.3 and 0.9%u013Em) and the cell size (0.9 and 3%u013Em) ranges. Lactadherin staining was used to identify MVs. The following markers were used to differentiate cell-derived MVs: CD45+, CD14+ (monocytes); CD45-, CD41+ (platelets); CD45-, CD235a+ (red blood cells). Platelet activation was monitored by expression of CD62p (p-selectin), platelet factor-4 (PF4) and PAC-1 (activated GPIIb/IIIa).
**Results:** Platelet activation markers CD62p, PF4 and PAC-1 were significantly elevated for citrate concentrations below 4 mM, which was accompanied by significantly higher adhesion of platelets and white blood cells to the adsorbents. Likewise, the release of MVs was dependent on citrate concentration and higher amounts of MVs (red blood cell-and platelet-derived MVs) were released at lower citrate concentration.
**Discussion:** Our data show that citrate suppresses cellular activation and generation of MVs during contact of whole blood with adsorbent polymers.

## Oral Session - Liver and Cardiovascular Tissue Engineering, O96-O101

**O96**
**HOW TO DETERMINE THE CONCENTRATION OF CELLS ENCAPSULATED IN ALGINATE-POLYETHERSULFONE MICROCAPSULES**
*Lewińska D, Kupikowska-Stobba B, Grzeczkowicz M*
Nalecz Institute of Biocybernetics and Biomedical Engineering PAS, Warsaw, Poland

**Introduction:** Microcapsules containing living cells (b-cells, hepatocytes, genetically modified bacteria) and biologically active material (including enzymes, hormones, vaccines) have been investigated as potentially implanted hybrid organs or very sophisticated drug delivery systems for the last 40 years. In addition to classical alginate-polylysine-alginate (APA) microcapsules, also hydroxyethyl methacrylate-methyl methacrylate (HEMA-MMA) and alginate-polyethersulfone ones have been proposed. As the second kind of microcapsule is not transparent, the examination of their inner structure and their interior is very hard and requires appropriate techniques. In the presentation, we propose a special method, designed for determining the concentration of cells encapsulated inside this kind of microcapsule.
**Material and methods:** Alginate polyethersulfone microcapsules containing living cells were prepared using a one-step electrostatic technique designed by our lab, through which we obtain cell-loaded, biocompatible hydrogel cores that are surrounded by semipermeable polyethersulfone membranes. The method for determining cell concentration consists of three stages: chemical dissolution of the polymeric membranes, chemical liquefaction of cell-loaded alginate cores, and counting of the released, gel-free cells (e.g. using a cytometer or a Neubauer counting chamber).
**Results:** The method has been experimentally tested and used for quantitative assessment of the growth rate of yeast cells encapsulated in AP microcapsules and cultivated for 24 hours.
**Discussion:** The proposed method allows quantitative assessment of encapsulated cells without affecting their viability and can be easily applied in any microencapsulation-based technology in order to evaluate the concentration and growth rate of encapsulated cells.

**O97**
**LIVER TISSUE DECELLULARIZATION AS A TECHNOLOGY OBTAINING POROUS SCAFFOLD FOR TISSUE ENGINEERING AND REGENERATIVE MEDICINE**
*Bobrova M[1], Safonova L[1], Agapova O[2], Krasheninnikov M[3], Shagidulin M[2], Agapov I[2], Gautier S[2]*
[1]Biologocal Faculty, Lomonosov Moscow State University, Moscow, Russian Federation; [2]Academician V.I. Shumakov Federal Research Center of Transplantology and Artificial Organs, Moscow, Russian Federation; [3]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation

**Introduction:** Using the methods of regenerative medicine and tissue engineering for the creation of a bio-artificial liver is an actual problem. Investigation of mechanical and biological properties of decellularized liver tissue which is used as a porous matrix for creating cell engineering constructions (CEC) of liver.
**Material and methods:** Wistar rats (n = 30) were used as donor liver. Three groups of liver samples were prepared by decellularization using a perfusion solution with different concentrations of Triton X-100. The vascular network was visualized by perfusion of 0.5% blue dextran solution. Histological tissue staining, optical microscopy and scanning electron microscopy were used. Human hepatocellular carcinoma cell line $HepG_2$ was used to assess the proliferative cell activity on the obtained matrix.
**Results:** Decellularization of whole organ does not lead to changes in the specific structure of the tissue scaffold, the vascular network also does not damaged. Decellularized liver with 3% Triton X-100 solution has the highest tensile strength and elasticity. Microparticles with a mean size 200 µm were prepared from decellularized liver matrix. The cell compatibility of $HepG_2$ was significantly higher on microparticles from decellularized liver scaffold with 3% Triton X-100 solution.
**Discussion:** Decellullarization-produced liver matrix was found to preserve the native three-dimensional structure of liver tissue and vascular network. Decellularized matrix is biocompatible. It maintains the adhesion and proliferation of human hepatocellular carcinoma cell line $HepG_2$ and has mechanical properties appropriate for Tissue Engineering.

**O98**
**GENETICALLY MODIFIED FEEDER LAYER CELLS IN HEPATIC CELLS CULTURE**
*Zakrzewska K, Samluk A, Kowalska A, Pijanowska D, Pluta K*
Nalecz Institute of Biocybernetics and Biomedical Engineering PAS, Warsaw, Poland

**Introduction:** Generally, within two weeks the culture of isolated human hepatocytes loses its morphological and physiological features. Among many methods used to slow down the hepatocytes' dedifferentiation process, coculture with feeder layer cells is the most promising. Due to their ability to produce large amounts of extracellular matrix proteins and secret many

types of growth factors, fibroblasts are the most appropriate feeder layer cell types. The aim of this study was an attempt to coculture liver cells and genetically modified human skin fibroblasts (HSF), characterized by stable expression of epidermal growth factor (EGF), as feeder layer cells.
**Material and methods:** The generation of genetically modified feeder layer cells included: lentiviral vectors production, HSF transduction, and evaluation of the genetic modifications impact on the fibroblasts viability. Next, the fibroblasts with the proved overproduction of EGF were cocultured with hepatoma cells, followed by the culture status evaluation: albumin and α-1-antitrypsin production, cells viability, and *bile canaliculi* formation.
**Results:** The human fibroblasts with the stable overproduction of EGF improved parameters of the liver cells in the coculture. Albumin secretion was increased by 70% and *bile canaliculi* formation by 50%, compared to monoculture. Moreover, albumin production in C3A cells cocultured with this type of fibroblasts was the highest throughout the experiment, which is particularly important for a long-term culture of liver cells.
**Discussion:** Summarizing, the results confirmed the positive effect of modified fibroblasts on hepatic cells constitution and viability. In the future we plan to transduce HSF with other growth factors or cytokines to create better environment for liver cells.

**O99**
**PROCESSING OF HUMAN EXTRACELLULAR MYOCARDIAL MATRIX PRESERVES ITS CYTOPROTECTIVE EFFECTS**
*Becker M[1], Kappler B[1], Ma N[1], Falk V[2], Stamm C[2]*
[1]Berlin Center for Regenerative Therapies, Berlin, Germany; [2]Deutsches Herzzentrum Berlin, Berlin, Germany

**Introduction:** Freshly isolated human cardiac extracellular matrix sheets (cECM) have been shown to support stem cell proliferation and tissue-specific lineage commitment. We now developed a protocol for standardized production of durable, bio-functional hcECM microparticles and corresponding hydrogel, and tested its cytoprotective effects on contractile cells subjected to ischemia-like conditions.
**Material and methods:** Human ventricular myocardium was decellularized by a 3-step protocol, including Tris/EDTA, SDS and serum incubation (cECM). Following snap-freezing and lyophilization, microparticles were created and characterized by laser diffraction, dynamic image analysis (DIA), and mass spectrometry. Moreover, cECM hydrogel was produced by pepsin digestion. Baseline cell-support characteristics were determined using murine HL-1 cardiomyocytes, and the cytoprotective effects of ECM products were tested under hypoxia and glucose/serum deprivation.
**Results:** In cECM, glycoproteins (thrombospondin 1, fibronectin, collagens and nidogen-1) and proteoglycans (dermatopontin, lumican and mimecan) were preserved, but residual intracellular and blood-borne proteins were also detected. The median particle feret diameter was 66 µm (15-157 µm) by laser diffraction, and 57 µm (20-182 µm) by DIA with crystal violet staining. HL-1 cells displayed enhanced metabolic activity (39+/-12%, $p<0.05$) and proliferation (16 ± 3%, $p<0.05$) when grown on cECM microparticles in normoxia. During simulated ischemia, cECM microparticles exerted distinct cytoprotective effects (MTS conversion, 240 ± 32%; BrdU uptake, 45 ± 14%; LDH release, -72 ± 7%; $p<0.01$, each). When cECM microparticles were solubilized to form a hydrogel, the cytoprotective effect was initially abolished. However, modifying the preparation process (pepsin digestion at pH 2 & 25°C, 1 mg/ml final cECM concentration) restored the cytoprotective cECM activity.
**Discussion:** Extracellular matrix from human myocardium can be processed to yield standardized durable microparticles that exert specific cytoprotective effects on cardiomyocyte-like cells. The use of processed cECM may help to optimize future clinical-grade myocardial tissue engineering approaches.

**O100**
**IL-6 PRESENT IN HEART FAILURE SERUM FACILITATES SERUM FACILITATES THE ADAPTATION OF CORD BLOOD MESENCHYMAL STROMAL CELLS TO HYPOXIC ENVIRONMENTS**
*Xu Z[1], Nazari-Shafti T[2], Bader A[2], Falk V[2], Stamm C[2]*
[1]Berlin Center for Regenerative Therapies, Berlin, Germany; [2]Deutsches Herzzentrum Berlin, Berlin, Germany

**Introduction:** Cord blood mesenchymal stromal cells (CB-MSCs) protect cardiomyocytes from ischemic injury both in vitro and in vivo. Howewer, cell loss upon transplantation into the ischemic and failing heart remains a major obstacle to clinical translation. We investigated the effects of oxygen and nutrient deprivation and of soluble heart failure serum factors on CB-MSCs in order to develop strategies to improve engraftment efficacy.
**Material and methods:** Serum was collected from patients in end-stage heart failure (HFS, n = 12) and healthy controls (CS, n = 12) and added to CB-MSC culture instead of FBS. CB-MSCs incubated with 10% serum were and exposed to normoxia or hypoxia/no glucose conditions. MTS conversion, BrdU incorporation, poly-caspase activity and cell number were quantified using an Operetta high content screening system. Serum cytokine levels were determined by ELISA, and the key factor IL-6 was modified in respective experiments by adding recombinant protein or neutralizing IL-6R antibody.
**Results:** HFS exerted anti-apoptotic and pro-metabolic effects on CB-MSCs under hypoxia/glucose deprivation over time ($p = 0.004$ and $p = 0.029$, respectively). The peak effect on day 5 was a 30% decrease of poly-caspase activity in HFS ($p = 0.022$). In normoxia, HFS-cytoprotection was not observed, but BrdU incorporation was elevated (105% vs. CS, $p<0.001$). IL-6R antibody (0.02%ug/ml) depressed viability of CB-MSCs in HFS under hypoxia/glucose deprivation (-12 ± 4%), and HFS-equivalent concentrations of recombinant IL-6 protein (8 pg/ml) increased CB-MSC viability in CS under hypoxia/glucose derivation by 34% ($p = 0.003$).
**Discussion:** Serum from heart failure patients protects CB-MSCs from oxygen and glucose deprivation, mediated at least in part by IL-6. This phenomenon may be exploited in order to develop cytoprotective strategies in the context of cell therapy and tissue engineering.

**O101**
**CONTRIBUTION OF MESENCHYMAL STEM CELLS TO FIBROSIS**
*Fischer F*
Health Sciences and Biomedicine, Danube University Krems, Austria

**Introduction:** Tissue and organ regeneration is mediated by local self-repair of fully differentiated cells as well as by mesenchymal stem cells (MSCs) that can differentiate to osteoblasts, chondrocytes, adipocytes, muscle cells and neurons. The environmental hallmark of individual tissues with its extracellular matrix (ECM) composition and the cytokine profile released can determine MSC fate.
**Material and methods:** Immunohistochemistry and laser scanning microscopy (LSM), as well as qRT-PCR and western blotting was used to investigate suppressor of cytokine signalling (SOCS) 2, and the signaling molecules STAT1/3/5 in MSCs from different tissues. LSM and atomic force microscopy was used to investigate stress fibers, focal adhesions and micro-tubular structures and mitochondrial pattern during MSC development.
**Results:** SOCS2, a cytokine inhibitor and key regulator inhibiting signal transduction mediated by cytokines and growth factors that use type I and type II cytokine receptors by inhibit the JAK/STAT signaling pathway, was shown to be important for maintenance of MSC stemness. When MSCs were adhered to plastic surfaces in culture, MSCs downregulate SOCS2 and upregulate stress fiber production which induces substantial tension forces via focal adhesions anchored at both ends to the actin filaments.
**Discussion:** In the absence of SOCS2 MSCs tend to differentiate into the fibroblastoid lineage ex vivo.

## Special Symposium - Vascular Tissue Engineering, O102-O107

**O102 (IL60)**
**ADHESIVE AND CYTOTOXIC PROPERTIES OF POLYCAPROLACTONE, LACTIDE AND THEIR COPOLYMERS**
*Golovkin A[1], Bolbasov E[2], Tverdohlebov S[2], Sinev A[3], Mishanin A[3], Malashicheva A[3]*
[1]Institute of Molecular Biology and Genetics, Federal Almazov Medical Research Centre, St. Petersburg, Russian Federation; [2]Tomsk Polytechnic University, Tomsk, Russian Federation; [3]Federal Almazov Medical Research Centre, St. Petersburg, Russian Federation

**Introduction:** Biodegradable polymer nanofibrous scaffolds are believed to be the most perspective trend for small diameter blood vessel graft

development. After implantation the scaffolds serve as bypasses and are progressively infiltrated by host cells, thus forming autologous vessel. Promising materials for the implants are aliphatic polyesters (Polycaprolactone, Polylactic Acid etc.), however each particular material needs to be tested individually in terms of its application in potential grafting. The aim of this study was to compare several biodegradable polyesters by its compatibility with biological functions of living cells.

**Material and methods:** 4 types of biodegradable aliphatic polyesters were used: 1. Polycaprolactone (PURASORB® PC 12, PURAC), 2. L-lactide/DL-lactide copolymer (PURASORB® PLDL 8038, PURAC), 3. Poly-L-lactic acid (PURASORB® PL 38, PURAC), 4. L-lactide/Caprolactone copolymer (PURASORB® PLC 7015, PURAC). Nanofibrous scaffolds were made using electrospinning NANON-01A (MECC Co., Japan). Biocompatibility of the materials were tested using mesenchyme stem cells and measuring their adhesion and necrosis/apoptosis rate.

**Results:** L-lactide/DL-lactide copolymer demonstrated cytotoxic properties with low adhesion rate (6.17 ± 0.70 cells/mm$^2$) and low viability (11.52 ± 2.38% living cells). Polycaprolactone had the highest adhesion - 136.83 ± 11.82 cells/mm$^2$. The optimal balance of tested parameters was proved in Poly-L-lactic acid and L-lactide/Caprolactone copolymer with 94.83 ± 19.66 and 49.66 ± 12.83 cells/mm$^2$ and 86.92 ± 4.38 and 88.78 ± 2.46% of live cells respectively.

**Discussion:** Poly-L-lactic acid and L-lactide/Caprolactone copolymer could be the candidate materials for development of small diameter blood vessels grafts because of their low cytotoxic and high adhesion properties. At the same time additional aresearch is needed to choose optimal copolymer ratio and electrospinning process to achieve ideal physical and mechanical properties for vessel graft.

**O103 (IL61)**

**ENGINEERED VASCULAR TISSUES BY MIMICKING THE NATIVE EXTRACELLULAR MATRIX**

*Zhao Q, Kong D*

Key Laboratory of Bioactive Materials (Ministry of Education), Nankai University, Tianjin, China

**Introduction:** Vascular graft has proven to be an effective strategy for the treatment of cardiovascular diseases. However grafts made solely from synthetic polymers cannot satisfy the clinic requirements in terms of low long-term patency, because they only provide a simple structural or physical replacement without the biological functions.

**Material and methods:** In order to resolve this problem, we aim to fabricate vascular grafts which could mimic native extracellular matrix (ECM) in terms of both physiological structure and bio-functions. Different types of strategies and techniques have been explored to realize this purpose, including structure optimization, surface/interface functionalization, and controlled delivery of bioactive molecules.

**Results:** Up to now, we have successfully fabricated a kind of vascular grafts with dual surface functions of anti-thrombogenicity and rapid endothelialization.

**Discussion:** Through structural optimization, the problem of limited cellularization in vascular grafts has been effectively resolved, and thus the vascular tissue regeneration as well as the homeostasis has been improved. In addition, novel biomaterials with enzyme-controlled NO releasing property has been successfully prepared, therefore controllable and on-demand NO delivery has been realized, which is very important for the regeneration of vascular tissue and regulation of vascular homeostasis, especially in aged/diseased model.

**O104 (IL62)**

**MODIFICATION OF POLYMER SURFACE USING RFMS TECHNIQUE FOR INCREASED BIOCOMPATIBILITY**

*Malchikhina A[1], Bolbasov E[1], Shesterikov E[1], Golovkin A[2], Anissimov Y[3], Tverdokhlebov S[1]*

[1]Institute of Physics and Technology, National Research Tomsk Polytechnic University, Tomsk, Russian Federation; [2]Institute of Molecular Biology and Genetics, Federal Almazov Medical Research Centre, St. Petersburg, Russian Federation; [3]School of Biomolecular and Physical Sciences, Griffith University, Brisbane, Australia

**Introduction:** The aim of the research was to reduce poly (L lactide) (L-PLA), polycaprolactone (PCL) and thermoplastic vinilidene fluoride and tetrafluoroethylene copolymer (VDF–TeFE) hydrophobicity and increase surface free energy for improved living cell affinity.

**Material and methods:** Hydroxyapatite target radiofrequency magnetron sputtering (RFMS) was used for surface properties modification of biodegradable and biostable polymers such as L-PLA, PCL and VDF–TeFE. Atomic force microscopy was used to study polymers surface roughness and morphology characteristics. Chemical and structure composition changes were revealed by infrared spectroscopy, fluorescent X-ray spectroscopy and X-ray diffraction. Cell adhesion and viability were studied with bone marrow multipotent stromal cells and cell line EA-hy 926.

**Results:** It was shown that RFMS significantly changes the polymeric substrates surface morphology, electrical, chemical, contact properties and phase structure. Polymers contact properties were changed from highly hydrophobic to hydrophilic after the modification. Surface roughness increased significantly with the sputtering hydroxyapatite target elements (Ca, P and O) appearing in the chemical composition, which is important for the polymer materials application in bone surgery and tissue engineering. In case of polylactic acid surface modification, polymer crystallization occurs, as demonstrated by infrared spectroscopy and X-ray diffraction spectroscopy. The L-PLA and PCL biocompatibility increased as demonstrated by bone marrow multipotent stromal cells and cell line EA-hy 926 experiments.

**Discussion:** We hypothesize the formation of a (bio-) ceramic/(bio-) resorbable polymer interface as the result of plasma-surface interaction. The reported complimentary (bio-) target sputtering approach is not exclusive to L-PLA, VDF–TeFE and PCL polymers, it can potentially aid in modification of other bioresorbable and biostable materials.

**O105 (IL63)**

**DECELLULARIZED SMALL-DIAMETER VASCULAR PROSTHESIS FROM HUMAN PLACENTA CHORION**

*Schneider K[1], Enayati M[1], Grasl C[2], Walter I[3], Andreas T[4], Redl H[5], Wojta J[6], Bergmeister H[1]*

[1]Department of Biomedical Research, Medical University of Vienna, Vienna, Austria; [2]Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Vienna, Austria; [3]Department of Pathobiology, University of Veterinary Medicine Vienna, Vienna, Austria; [4]Institute for Biochemical Engineering, University of Applied Sciences, Technikum Wien, Vienna, Austria; [5]Ludwig Boltzmann Institute for Experimental and Clinical Traumatology, Vienna, Austria; [6]Ludwig Boltzmann Institute of Cardiovascular Research, Vienna, Austria

**Introduction:** Patients suffering of vascular diseases often have no suitable autologous vessels for harvesting leading to an increased need for alternative vascular substitutes. Decellularized matrices can be considered as an alternative to create small diameter conduits for in-vivo applications. The placenta represents human tissue source that can be readily harvested without any harm to the donor. In this study we investigated vessels isolated from the placenta chorion for their potential to be used as small diameter vascular grafts (SDVG).

**Material and methods:** Arteries (50 × 1.5 mm) from placenta chorionic plate were decellularized using a pulsatile perfusion setup with two different detergents (Triton X-100 or SDS). The luminal surface of grafts was modified by heparin crosslinking. Topography, structure, and tensile strength of the grafts have been studied. Expression of pro-and anti-inflammatory cytokines and macrophages was evaluated using PCR in-vitro (macrophage culture) and in-vivo (subcutaneous implants in nude rats (n = 28, 1 and 4 weeks). The phenotype of the host cells which populated the graft was characterized by immunohistochemistry.

**Results:** The acellular conduits of both groups showed appropriate tensile and suture retention strength and compliance. Pro-inflammatory expression of TNF-a and IL-1a were down-regulated in both grafts. IL-10 anti-inflammatory cytokine and CD163 M2 macrophage expression were up-regulated in both grafts but this was significant just in Triton X-100 grafts. Both implants showed no foreign body reaction and the grafts were repopulated by host cells.

**Discussion:** Placental decellularized vessels could be an excellent alternative to synthetic graft materials for small diameter applications.

**O106 (IL64)**
**TAILORING THE FOREIGN BODY RESPONSE FOR IN SITU VASCULAR TISSUE ENGINEERING**
*Rothuizen TC, Damanik FFR, Lavrijsen T, Visser MJT, Hamming JF, Lalai RA, Duijs JMGJ, van Zonneveld AJ, Hoefer IE, van Blitterswijk CA, Rabelink TJ, Moroni L, Rotmans JI*
Department of Nephrology, Leiden University Medical Center, Leiden, The Netherlands

**Introduction:** There's a large clinical need for novel vascular grafts. Tissue engineered blood vessels (TEBVs) have great potential to improve the outcome of vascular grafting procedures. This study describes a screening platform for a guided *in situ* vascular tissue engineering approach.
**Material and methods:** Polymer rods were developed that upon subcutaneous implantation evoke a controlled inflammatory response culminating in encapsulation by a tube shaped autologous fibrocellular tissue capsule, which can form a basis for a TEBV. First, a set of different polymer compounds as well as physical, chemical and biological surface modifications were tested on their ability to actively steer this tissue capsule formation using a rat model as testing platform.
**Results:** While tissue capsules were mainly composed of circumferentially aligned collagen and myofibroblasts, the different implant materials resulted in distinct differences in tissue capsule formation. Chloroform etched rods provided the most homogenous and densely packed tissue capsules that were completely populated by myofibroblasts. Next, we implanted these rods in the subcutaneous space of pigs. Again, the obtained tissue capsules capsules were mainly composed of matrix proteins, fibroblasts and macrophages at the 'luminal' side of the tissue capsules. Mechanical assessment of tissue capsules revealed a mean burst pressure of >1900 mmHg, sufficient to allow vascular grafting. We then grafted the tissue capsules as carotid interposition grafts and harvested these TEBV 4 weeks later. The patency rate was 87% and immunohistochemical analysis of the TEBV showed that the tissue capsules after grafting were mainly composed of desmin+ smooth muscle cells-like cells whereas no inflammatory cells were present any more. Furthermore, the lumen was largely covered with a confluent single endothelial layer as demonstrated with a lectin stain with similar staining pattern as endothelial cells in a native artery.
**Discussion:** In conclusion, using the subcutaneous space as in vivo bioreactor, autologous tissue engineered blood vessels were rapidly developed with sufficient mechanical strength to allow safe implantation in the arterial circulation. Within 4 weeks, the TEBV remodeled into an adequate vascular conduit. Future experiments should reveal the long-term patency of these TEBVs.

**O107**
**IBTA-FABRICATED MICROBIOTUBE VASCULAR GRAFTS MET 1 YEAR'S PERFECT PATENCY IN A RAT MODEL**
*Ishii D[1], Enmi J[2], Iida H[2], Kurisu K[1], Nakayama Y[3]*
[1]Department of Neurosurgery, Hiroshima University Graduate School of Biomedical and Health Sciences, Hiroshima, Japan; [2]Department of Investigative Radiology, National Cerebral and Cardiovascular Center, Osaka, Japan; [3]Division of Medical Engineering and Materials, National Cerebral and Cardiovascular Center, Osaka, Japan

**Introduction:** Biotubes are autologous tubular connective tissues formed by in-body tissue architecture technology (IBTA), which is a novel and practical approach in regenerative medicine. In last ESAO congress, we reported that Microbiotubes (MBs) with diameter of 0.6 mm had high patency (83.3%) in a 1-month follow-up magnetic resonance angiography (MRA). In this study, long-term patency of MBs was evaluated by MRA in a rat model.
**Material and methods:** The mold for multiple preparing of MBs was assembled by several stainless wires covered with silicone tubes. The molds were surgically embedded into the dorsal subcutaneous pouches of rats. After 2 months, the molds were harvested with surrounding tissues and MBs were obtained by removing the molds. MBs (length, 10 mm; internal diameter, 0.6 mm) were implanted in rat femoral arteries (diameter, ca. 0.5 mm) in allogenic manner by end-to-end anastomosis without use of any anticoagulant agents. Ten patent MBs after 1-month implantation were observed by follow-up 7- Tesla MRA until 6 months (n = 8) or 1 year (n = 2) after implantation.
**Results:** In all follow-up periods, all MBs were patent with little changing in vascular shape without stenosis, aneurysmal dilation, or elongation. The native-like vascular structure reconstructed after 1 month of implantation was histologically maintained for 1 year.
**Discussion:** High quality and long-term patency of MBs as the world's smallest vascular replacement grafts were established in this study. We confirmed that MBs could be useful as an alternative ultra small-caliber vascular substitute in the not too distant future.

## Oral Session - Biomaterials in Contact with Blood, O108-O112

**O108**
**INSPIRED BY NATURE BILAYERED POLYURETHANE NANOFIBROUS SCAFFOLDS FOR SMALL DIAMETER TISSUE ENGINEERED VASCULAR GRAFTS**
*M. Wojasiński M, Ciach T*
Faculty of Chemical and Process Engineering, Warsaw University of Technology, Warsaw, Poland

**Introduction:** In the last decade, researchers in the field of vascular prosthesis focused on small inner diameter (under 6 mm) devices. Moreover, they combined synthetic and biological materials, using tissue engineering approach, to build vascular grafts. However, still, there is no versatile and affordable method allowing vascular prosthesis scaffold to be produced.
**Material and methods:** We introduce solution blow spinning for the production of nanofibrous vascular graft scaffold with small diameter. Changing processing parameters in the process: polymer concentration, working distance, and processing time, we produced bilayered polyurethane nanofibrous vascular scaffolds. Scaffolds were tested for leaks in self-designed chamber. Investigation of the cytotoxicity of the scaffolds on L929 cell line was performed, according to ISO standard. Subsequently, scaffolds were investigated for cells penetration through the scaffold wall - from the outside to the inside – using confocal laser scanning microscope.
**Results:** Polyurethane nanofibrous vascular scaffolds with wall thickness in the range from about 100 µm to about 1 mm were produced. The inner wall thickness of scaffolds was: from about 10 µm to about 100 µm; porosity: from about 45% to about 70%; and mean fiber diameter: from about 200 nm to 600 nm. Scaffolds show now leakage of PBS, and no cytotoxic response in culture with L929 cell line. What is more, L929 cells migrated from the outside surface of the scaffolds inside of the wall during 21 days of culture.
**Discussion:** We report nanofibrous polyurethane vascular graft scaffolds produced with affordable solution blow spinning technique in 30 minutes, maximum. Scaffolds show adequate physical and bioactive properties for vascular grafts.

**O109**
**IMMOBILIZATION STRATEGIES FOR GLYCOSAMINOGLYCANS ON BIOMATERIALS FOR ANTI-INFLAMMATORY PURPOSES**
*Al-Khoury H*
Biomedical Materials Group Institute of Pharmacy, Martin Luther University Halle-Wittenberg, Halle, Germany

**Introduction:** Biomaterial implantation launches a series of interactions jointly called the foreign body response, which can impair the functionality of the biomaterial. Hence, efforts toward the modulation of the immune response to implants are promoted through the incorporation of anti-inflammatory drugs. Since the anti-inflammatory potential of glycosaminoglycans (GAG) is well known together with their ability to bind chemokines and cytokines, different approaches are investigated here to modify biomaterial surface, hence reducing the inflammatory response.
**Material and methods:** One approach aimed at the immobilization of hyaluronic acid (HA), chondroitin sulfate (CS), and heparin (Hep) by covalent binding to amino-functionalized substrata by 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC)/ N-hydroxysuccinimide (NHS) chemistry. In the second approach, the layer-by-layer (LbL) technique was used to physically adsorb the polyanions together with chitosan (Chi) in multilayers. The different systems were investigated regarding their surface charge, wettability as well as influence on macrophage adhesion and foreign body giant cell (FBGC) formation.

**Results:** Macrophage adhesion, morphology, FBGC formation, as well as IL-1β production were all significantly decreased on GAG modified surfaces at both methods in contrast to the positive controls. Thereby, Hep-Chi multilayers showed the most significant anti-inflammatory properties, which could be due to the physical adsorption of GAGs. The reduced binding strength in contrast to covalent binding would allow the uptake of Hep molecules by macrophages, which could lead to a reduction of NF-κB nuclear translocation and, thus, lower inflammatory responses.
**Discussion:** The two techniques for immobilization of GAG on biomaterial surface are promising approaches for designing novel anti-inflammatory coatings used for tissue engineering applications.

### O110
### SURFACE THROMBOGENICITY EVALUATION OF NEW INNOVATIVE BIOMATERIAL

*Janiczak K[1], Zawidlak-Węgrzyńska B[1], Cieśla P[1], Gawlikowski M[1], Kościelniak-Ziemniak M[1], El Fray M[2], Kustosz R[1]*
[1]Artificial Heart Labolatory, Zbigniew Religa Foundation for Cardiac Surgery Development, Zabrze, Poland; [2]Polymer Institute, West Pomerania University of Technology, Szczecin, Poland

**Introduction:** The aim of investigation was to assess the thrombogenicity risk of new copolymer PET/DLA developed for heart prosthesis construction.
**Material and methods:** The test was performed utilizing Impact-R analyzer with fresh human blood. Before examination blood count was measured to qualified the blood for analysis. The investigated material was a PET/DLA aliphatic-aromatic polyester copolymer consisting of poly(ethylene terephthalate) (PET) hard segments and ethylene dilinoleate (DLA) soft segments modified with D-glucitol. Additionally Bionate polyurethane was investigated as it has a low thrombogenicity potential and a polystyrene cell from the Impact R test kit as a reference material. The material samples were in form of 14.4 mm diameter discs. The test was performed in dynamic conditions where blood flows above the investigated surface with determinate speed and time. After the experiment activation of CD61, CD62P and CD45 cell receptors utilizing flow cytometry was determined to assess the number of activated blood platelets and platelet-leukocyte aggregates. Also an analysis of adhered cells to the biomaterial surface with active receptor (CD62P, CD45) utilizing fluorescent microscopy was performed.
**Results:** The number of activated platelets (CD62P) and aggregates platelet-leukocyte (CD62P-CD45) in blood circulating above the biomaterials surface was similar in all tested groups. The number of adhered platelets (CD62P) and platelet-leukocyte aggregates (CD62P-CD45) to investigated biomaterial surface was slightly lower than the number of activated elements on polystyrene. The number of adhered CD62 and aggregates in other test groups was comparable.
**Discussion:** The investigated biomaterial PET/DLA characterizes similar low thrombogenicity properties as Bionate polyurethane.
**Acknowledgement:** Project no. PBS1/A5/2/2012 supported by NCBiR.

### O111
### A DUAL DRUG DELIVERY SYSTEM (DDS) MADE BY ELEC-TROSPINNING AGAINST THROMBOSIS IN CARDIOVASCULAR DISEASES

*Repanas A, Mueller M, Al Halabi F, Bode M, Glasmacher B*
Institute for Multiphase Processes, Leibniz Universität Hannover, Hannover, Germany

**Introduction:** Life-threatnening thrombosis incidents after a stroke or myocardial infarction are very frequent. Therefore, novel strategies have been implemented to develop biomimetic materials that can provide local delivery of anti-coagulant agents. Electrospinning is an electrohydrodynamic method that can fabricate non-woven formulations, used as drug delivery systems (DDSs). A successful combination of anti-coagulants is aspirin and dipyridamole. The fabrication and characterization of a dual delivery system made by polycaprolactone and the aforementioned anti-coagulants, was the aim of this study.
**Material and methods:** Polycaprolactone (PCL) 20wt%, Aspirin (ASA) 1.5wt% and Dipyridamole (DIP) 1.5wt%, were dissolved in 2,2,2-Trifluoroethanol (TFE). Electrospinning was performed at a flow rate of 4 mL/h and an electrical field of 1 kV/cm. Fibers' morphology was studied via Scanning Electron Microscopy. In vitro drug release experiments were performed in PBS (pH = 7.4, T = 37°C) using UV-Vis spectrophotometry. The cumulative release of both pharmaceuticals was calculated and the release mechanism was determined.
**Results:** Cylindrical fibers with random orientations were created. ASA only, DIP only and ASA&DIP fibers had an average diameter of 0.92 ± 0.32 μm, 0.71 ± 0.28 μm, and 0.66 ± 0.23 μm, respectively. The cumulative release of both agents exhibited a bi-phasic profile over two months with an initial burst phenomenon and a subsequent gradual phase. Both pharmaceuticals followed a Fickian diffusion release mechanism that was confirmed after mathematical fitting of the experimental data.
**Discussion:** Taken together, these preliminary results indicate that electrospun PCL fibers could be further examined as a DDS in cardiovascular diseases-related applications.
**Acknowledgement:** REBIRTH(EXC 62/1)

### O112
### IN-VITRO EVALUATION OF THE POLISH PAEDIATRIC VAD RELIGA HEART PED THROMBOGENICITY

*Gawlikowski M, Janiczak K, Głowacki M, Cieśla P, Kustosz R*
Artificial Heart Laboratory, Zbigniew Religa Foundation for Cardiac Surgery Development, Zabrze, Poland

**Introduction:** The Polish, paediatric heart assist system has been evaluated in preclinical study. Goal of work was to assess paediatric VADs thrombogenicity in-vitro, and compare it with results carried out in-vivo.
**Material and methods:** Paediatric, pulsatile VADs ReligaHeart PED (SV = 45, 30, and 20 $cc^3$) equipped with original tilting disc valves as well as one-leaflet polyurethane inlet valve (for 20 $cc^3$ VAD only) have been tested in-vitro, by means of acute thrombogenicity method. Extended blood tests panel (morphology, platelets aggregation, acid base balance) was applied, in order to qualify blood for experiment and monitor blood coagulation during circulation. VADs thrombogenicity assessed in-vitro was compared with clinical picture of VADs in animal trials (swine model, n = 8, supporting duration from 8 to 27 days). The clots morphology (E&H staining) was compared.
**Results:** The ACT self-decreasing, as well as decreasing of platelets quantity and platelets aggregation were observed in all in-vitro tests. It caused clots forming in certain regions of VAD. The map of adhered material location was created for each VAD. The comparison of in-vitro and in-vivo circulation maps pointed out that clots were forming at similar regions. However, the mass of thromboembolic material was different while the morphology of thromboembolic material was similar.
**Discussion:** The ReligaHeart PED blood pumps low thrombogenicity have been showed. Qualitative in-vitro results have been confirmed in-vivo. Acute thrombogenicity method allows to find regions particularly subjected to clotting, however the size of clots cannot be treated as direct factor of thrombogenicity rate.
**Acknowledgements:** Project no. PBS1/A7/1/2012 supported by NCBiR.

## Special Symposium - Advances in Regional Citrate-Calcium Anticoagulation, O113-O115

### O113
### MODELLING AND SIMULATION OF A TARGET-ORIENTATED ALGORITHM FOR RCA

*Brandl M[1], Kellner K[1], Strobl K[2], Hartmann J[2]*
[1]Center for Integrated Sensor Systems, Danube University Krems, Krems, Austria; [2]Center for Biomedical Technology, Danube University Krems, Krems, Austria

**Introduction:** Anticoagulation is a necessary treatment procedure in extracorporeal blood purification. There are two main methods for anticoagulation: Systemic anticoagulation; is easy to handle but has several disadvantages for the patient and regional anticoagulation; needs additional technical equipment and some expertise by the operation staff but has a lot of advantages for the patient. Especially for patients with high bleeding risk and patients with an allergic reaction to heparin, a systemic anticoagulation

with e.g. heparin is dangerous or not possible. For these patients, regional anticoagulation with citrate and calcium is the first choice.
**Material and methods:** A mostly automated algorithm for regional citrate-calcium anticoagulation was developed. With this algorithm the infusion rate of citrate is controlled to archive a desired target ionized calcium concentration (level of anticoagulation) within the extracorporeal circuit and the substitution of calcium chloride into the venous blood line to restore the iCa level onto a physiological concentration is regulated.
**Results:** To calculate the desired target iCa level in the extracorporeal circuit, the initial patient's hematocrit and the initial patient's arterial iCa level must be considered. The desired target iCa level can be adjusted by the user in the range of 0.2 to 0.5 mmol pre-dialysis filter.
**Discussion:** Citrate anticoagulation can be optimized by achieving iCa-concentrations equal or lower than 0.2 mmol. Nomograms involving Hct-values for citrate-infusion management should be provided in order to handle an optimized citrate anticoagulation. The results of this study will be the base of a newly developed device for citrate-calcium anticoagulation as add-on device for dialysis machines.

### O114
### CITRATE ANTICOAGULATION IMPROVES BLOOD COMPATIBILITY IN DIALYSIS AND AHPERESIS – DATA FROM IN VITRO EXPERIMENTS

*Harm S, Hartmann J*
Center for Biomedical Technology, Danube University Krems, Krems, Austria

**Introduction:** Citrate inhibits the coagulation cascade by lowering the ionized calcium concentration in the extracorporeal circuit and is recommended as anticoagulant for continuous renal replacement therapy in critically ill patients. Contact of blood to materials of the disposable system initiates the coagulation and the activation of platelets and monocytes. The aim of this study was to compare heparin with citrate anticoagulation in regard to blood compatibility of different polymers.
**Material and methods:** Different polymer materials which are commonly used in extracorporeal therapies were incubated in blood from healthy volunteers and the activation of thrombocytes and leucocytes was determined. For the characterisation of the blood compatibility in the extracorporeal system, blood was recirculated in miniaturized setups for several hours. The disposable system consisted of a paediatric dialyzer, an albumin filter or a haemoadsorption column. Anticoagulation was carried out with trisodium citrate (6 mM) or heparin (3 IU/ml). Cell activation was evaluated by measurement of β-thromboglobulin and platelet factor 4 by ELISA. Cell adhesion of blood cells to the tested materials was visualized by SEM.
**Results:** The results show that cell adhesion to the materials was significantly lower when anticoagulation was carried out with citrate. Furthermore it could be shown that activation of leucocytes as well as thrombocytes was lower when citrate was used.
**Discussion:** Citrate anticoagulation improves the biocompatibility of materials used in extracorporeal therapies.

### O115
### INFLUENCE OF MAGNESIUM ON COAGULATION DURING CITRATE ANTICOAGULATION: AN IN-VITRO STUDY

*Strobl K, Hartmann J*
Department for Health Sciences and Biomedicine**,** Danube University Krems, Krems, Austria

**Introduction:** Regional citrate anticoagulation is a promising method for anticoagulation in extracorporeal blood purification. Citrate acts by chelation of the divalent cations calcium ($Ca^{2+}$) and magnesium ($Mg^{2+}$). While chelation of $Ca^{2+}$ is well accepted as anticoagulation mechanism, the role of $Mg^{2+}$ in coagulation is unclear. In the literature, synergistic as well as antagonistic effects of $Mg^{2+}$ are discussed. The aim of this in-vitro study was the evaluation of the effect of $Mg^{2+}$ in $Ca^{2+}$ free dialysis solutions on the activated clotting time (ACT) in citrate anticoagulation.
**Material and methods:** Citrated (6 mM) whole blood from healthy volunteers was dialysed against 0.9% NaCl with or without $MgCl_2$ (0.6 mM) solution resulting in blood without bivalent cations or $Ca^{2+}$ free blood with physiological $Mg^{2+}$ concentration. We compared kaolin-induced ACT of $Mg^{2+}$ free versus $Mg^{2+}$ containing blood after restoring $Ca^{2+}$ to different levels (0.2 to 1.2 mM).
**Results:** ACT increased with decreasing $Ca^{2+}$ concentration. ACT was comparable in both groups at physiological $Ca^{2+}$ (1.22 mM). However, with decreasing $Ca^{2+}$, $Mg^{2+}$ free blood showed an increasingly prolonged ACT compared to $Mg^{2+}$ containing blood.
**Discussion:** This study suggests that $Mg^{2+}$ in dialysis solution might contribute to activation of coagulation in citrate anticoagulation. $Mg^{2+}$ seems to be able to replace $Ca^{2+}$ if the latter is reduced, but the impact of $Mg^{2+}$ on coagulation is low under physiological conditions. However, the possible advantage of $Mg^{2+}$ free dialysis solution (with restoration of $Mg^{2+}$ concentration at the end of the extracorporeal circuit) has to be confirmed by in vivo studies.

## Oral Session - VADs in Daily Activity and Excercise, O116-O121

### O116
### FULL OR PARTIAL LEFT VENTRICULAR ASSIST DEVICE SUPPORT: COMPUTATIONAL ASSESSMENT OF HEMODYNAMICS

*Caruso M[1], Renzulli A[2], Fragomeni G[2]*
[1]DIMEG, University of Calabria, Rende, Italy; [2]Medical and Surgical Science Department, Magna Graecia University of Catanzaro, Catanzaro, Italy

**Introduction:** Left ventricular assist device (LVAD) is highly used for the advanced heart failure treatment. In the standard procedure, a full hemodynamic VAD support is implanted, even if nowadays partial supports are available, obtained with very small pumps implanted with less-invasive procedures and alternative outflow graft (OG) anastomosis site. The aim of this study was to compare the hemodynamics generated by Heartware, one of the most used full supports, and by the Synergy MicroPump, the smallest partial support.
**Material and methods:** A computational fluid dynamic analysis was carried out using a 3D aorta model reconstructed from CT. In case of Heartware, all flow (6.8 l/min) was provided with the OG anastomosed in the ascending aorta, whereas the Synergy ensured a flow of 3.8 l/min (OG anastomosed in the right subclavian artery) since there is a cardiac output of 3.0 l/min. In both cases, the outflow graft was virtually added to the patient-specific aorta model, and a MAP of 75 mmHg was considered.
**Results:** The cerebral perfusion remains the same considering the two VADs, whereas in case of Synergy a high flow rate (19% vs 4% of the total flow) and a high wall shear stress (>2 Pa) in the arms, a lower perfusion of the remaining part the organism (65% vs 80% of the total flow) occur.
**Discussion:** Synergy modifies the hemodynamics more than the Heartware: it removes the swirling flow in the ascending trunk but generates a retrograde flow in the right subclavian and innominate arteries, with an iper-perfusion of arms and higher hemolysis risk.

### O117
### EXERCISE PHYSIOLOGY IN HEART FAILURE: A SIMULATION STUDY

*Fresiello L[1], Meyns B[1], Di Molfetta A[2], Ferrari G[3]*
[1]Cardiac Surgery, KU Leuven, Leuven, Belgium; [2]Medical and Surgical Department of Pediatric Cardiology, Pediatric Hospital Bambino Gesù, Rome, Italy; [3]Institute of Clinical Physiology, National Research Council, Rome, Italy

**Introduction:** Exercise intolerance is a hallmark of heart failure (HF) and is the result of a multiple physiological impairments. We developed a simulator able to reproduce exercise in healthy and HF conditions.
**Material and methods:** A lumped parameter simulator was developed and adapted to reproduce graded bicycle exercise. The simulator includes heart, pulmonary and systemic circulations, gas exchange, baroreflex control, metabolic regulation and ventilation. The simulator was adapted to reproduce HF impairments: ventricular systolic/diastolic impairment, systemic and pulmonary hypertension, sympathovagal unbalance, reduced metabolic control, increased respiratory quotient and reduced perfusion of ventilated lungs.
**Results:** Simulation results were compared with literature data. From rest to exercise we observe that: cardiac output increases (4.9-9.3 l/min for healthy, 4.6-7.0 l/min for HF) peripheral resistance decreases (0.97-0.37 mmHg·s/cm$^3$ for healthy, 1.25-0.6 mmHg·s/cm$^3$ for HF) and arteriovenous oxygen difference increases (4.8-11.6 ml/dl for healthy and 5.6-14.4 ml/dl for HF). At peak exercise in HF ventricular contractility does not improve (1.7 mmHg/cm$^3$ for

healthy and 3.0 mmHg/cm$^3$ for HF), legs perfusion is reduced (6.2 l/min for heathy, 2.4 l/min for HF) and ventilation increases more to overcome the reduced perfusion of lungs (25.2 l/min for healthy and 40.3 l/min for HF).
**Discussion:** The simulator can reproduce exercise intolerance in HF as the results of several ventilation and hemodynamic limitations. The simulator will be used in the future to test the effects of therapies (i.e. assist devices, medications) aimed at improving exercise in HF.
**Acknowledgement:** This work is supported by Marie Curie Scholarship (PIEF-GA-2013-624296).

**O118**
**PRESSURE AND VOLUME UNLOADING DURING RAMP TESTS IN PATIENTS SUPPORTED WITH A LEFT VENTRICULAR ASSIST DEVICE: A MODEL STUDY**
*Moscato F[1], Gross C[1], Dimitrov K[2], Zimpfer D[1], Schima H[1]*
[1]Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Vienna, Austria; [2]Department of Cardiac Surgery, Medical University of Vienna, Vienna, Austria

**Introduction:** Ramp tests in patients with a left ventricular assist device are used to evaluate ventricular unloading and device function. The relationship between speed, pulmonary capillary wedge pressure (PCWP) and left ventricular end-diastolic diameter/volume (LVEDD/V) varies, however, for different patients making this evaluation difficult. Aim of this study was to investigate in a mathematical model the factors influencing the relationship between PCWP and LVEDV during ramp tests.
**Material and methods:** A model of the assisted circulation was adapted to reproduce hemodynamic data measured in 10 patients undergoing a ramp test (Jung MH et al. ASAIO J 2015:61:307-12). Once the "average patient" response was reproduced by the model, a subset of parameters was modified to simulate two extreme responses observed after speed increase: a) proportional decrease of PCWP and LVEDD; b) decrease of PCWP at an almost constant LVEDD.
**Results:** At lowest, baseline, and highest speed the model lead to a PCWP of 18, 16 and 10 mmHg compared to the clinical data of 20 ± 4, 14 ± 4 and 7 ± 3 mmHg. The LVEDV change at lowest and highest speed from baseline was 3% and -15% compared to the clinical LVEDD change of -1 ± 15% and -18 ± 25%. The factors influencing the PCWP vs. LVEDV relationship were the left ventricular end-diastolic pressure-volume relationship, the circulatory volume load, and to a less extent the left atrial and the mitral valve function.
**Discussion:** The mathematical model suggests that ramp tests might indicate differences in the diastolic properties of the assisted ventricle and in circulatory volume load. Echocardiographic evaluations to test this hypothesis are required.

**O119**
**TEMPORARY CARDIAC UNLOADING DURING EVOLVING MYOCARDIAL INFARCTION DRASTICALLY REDUCES MORTALITY: PERSPECTIVES FROM A SWINE MODEL**
*Trivella M[1], Piersigilli A[2], Bernini F[2], Pelosi G[1], Burchielli S[3], Puzzuoli S[2], Kusmic C[1], L'Abbate A[2]*
[1]Department of Biomedicine, CNR-Clinical Physiology Institute, Pisa, Italy; [2]Institute of Life Sciences, Scuola Superiore Sant'Anna, Pisa, Italy; [3]Fondazione Toscana Gabriele Monasterio, Pisa, Italy

**Introduction:** Acute myocardial infarction (AMI) with cardiogenic shock (CS) remains the leading cause of in-hospital death in acute coronary syndromes. In a pig model of AMI-CS we tested the efficacy of temporary cardiorespiratory assist device (CRA) in rescuing failing heart and reducing early mortality.
**Material and methods:** In open chest pigs we induced AMI by proximal left anterior descending (LAD) coronary artery ligation. Eight animals without CRA (C Group) were compared with 12 animals otherwise treated with CRA (T Group), starting at 60 min post-occlusion and lasting 120 min. In three animals of T Group, we also imaged regional myocardial oxygen content by 2D near infrared spectroscopy (2D-NIRS) with and without CRA, before and after LAD reperfusion.
**Results:** Animals without CRA all died in spite restless resuscitation maneuvers. Conversely, animals treated with CRA showed prompt reversion of heart dilatation and hypotension, as well as reduction of arrhythmias, allowing interruption of CRA in all cases, with recovered hemodynamics at the end of the observation period. During LAD occlusion, NIRS showed severe de-oxygenation of LAD territory that improved with CRA. After CRA suspension and LAD reperfusion, residual de-oxygenated area resulted smaller than the initial risk area.
**Discussion:** In AMI, CRA initiated during advanced CS, drastically reduced early mortality from 100% to zero within the observation period. CRA favored oxygenation of the ischemic area during LAD occlusion. Results support the use of CRA in AMI-CS to unload the heart favoring myocardial rescue and short-term survival.

**O120**
**WHAT DETERMINES EXERCISE CAPACITY IN LVAD PATIENTS? A MULTIPLE REGRESSION ANALYSIS STUDY**
*Fresiello L[1], Jacobs S[1], Timmermans P[2], Meyns B[1]*
[1]Clinical Cardiac Surgery Department, KU Leuven, Leuven, Belgium; [2]Department of Cardiology, University Hospital of KU Leuven, Leuven, Belgium

**Introduction:** Exercise capacity in patients with a left ventricular assist device (LVAD) is reduced as compared to control subjects. Aim of this work is to identify the underlying causes and the factors that predict exercise capacity in LVAD patients.
**Material and methods:** We analyzed the data of 35 patients, 2 HVAD and 33 HeartMate II, 26 males and 9 females performing a maximal cardiopulmonary exercise test at 196 ± 44 days after hospital discharge. We considered as patient's exercise outcome the peak oxygen uptake expressed as a percentage of age/weight/gender matched expected value (VO2p = 53.1 ± 13.1%). We identified variables reflecting patients' general condition (plasma albumin, rehabilitation etc.), left/right ventricular function (valve insufficiency, underlying diagnosis, peak heart rate etc.), renal function (creatinine, urea), initial INTERMACS class, plasma hemoglobin level and ongoing medication. Variables were explored for univariate correlation (Pearson). A linear multiple regression was used to identify predictors of VOp2 using a backward selection method.
**Results:** Variables significantly correlated with VO2p ($p<0.05$) are: body mass index at the time of LVAD implantation, INTERMACS, aortic valve opening and insufficiency, peak heart rate, NT-proBNP, rehabilitation, creatinine, urea and implantable cardioverter-defibrillator. The multiple regression analysis retained as independent predictors of VOp2: peak heart rate, INTERMACS, rehabilitation, aortic valve opening. All variables except INTERMACS are positively correlated with VO2p.
**Discussion:** Exercise impairment in LVAD patients is a complex problem involving several physiological mechanisms. Most of the predictors of exercise capacity are linked at the degree of the underlying cardiac function.
This work is supported by Marie Curie Scholarship (PIEF-GA-2013-624296).

**O121**
**MONITORING OF PHYSICAL ACTIVITY IN PATIENTS WITH A LEFT VENTRICULAR ASSIST DEVICE IMPLANTED**
*Gross C[1], Haller M[1], Zimpfer D[2], Schima H[1], Moscato F[1]*
[1]Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Vienna, Austria; [2]Department of Cardiac Surgery, Medical University of Vienna, Vienna, Austria

**Introduction:** Monitoring of daily physical activity is an emerging tool to assess health status both in normal and pathologic conditions. Such monitoring can be also important in patients with a left ventricular assist device (LVAD) implanted. This study aims at the validation of activity detection based on accelerometer data and at its first application to monitor post-implant patient activity.
**Material and methods:** Preliminary validation of the accelerometer activity and protocolled activities was performed with 9 datasets from 8 patients and resulted in a sensitivity of 96.3 ± 3.3% and a specificity of 92.5 ± 6.5%. An average of 152 days of activity data were recorded in 7 patients within the first 200 days post-implant. At post-operative days 50, 100, 150, 200 average daily physical activity was 60, 77, 88, 65 min/day. Two rehospitalizations in one patient were correlated with a drop in detected activity.
**Results:** Preliminary validation of the accelerometer activity and protocolled activities resulted in a sensitivity of 96.3 ± 3.3% and a specificity of 92.5 ± 6.5%. An average of 152 days of activity data were recorded in 7 patients within 200 days post-implant. At post-operative days 50, 100, 150, 200 average

daily physical activity was 60, 77, 88, 65 min/day. Two rehospitalizations in one patient were correlated with a drop in detected activity.
**Discussion:** Activity derived from the accelerometer can be useful to examine LVAD therapy. Combined with hemodynamic pump monitoring, it will give a more comprehensive picture of the interaction between LVAD and the remaining cardiac function during daily living.

## Oral Session - Computer Modelling in Hemodialysis, O122-O127

### O122
### FINITE ELEMENT MODELING OF SODIUM EXCHANGE IN THE HOLLOW FIBER OF A HAEMODIALYZER

*Ravagli E[1], Perazzini C[2], Severi S[1]*
[1]Department of Electrical, Electronic and Information Engineering, University of Bologna, Bologna, Italy; [2]Health Sciences and Technology Interdepartmental Center for Industrial Research, University of Bologna, Bologna, Italy

**Introduction:** Different spatially-distributed models have been proposed to describe diffusion along the hollow fibers of the haemodialyzer, focusing mainly on urea removal and on steady-state behaviour. Our objective is the development of a model of the single hollow fiber able to reproduce time-dependent sodium dynamics during simulated haemodialysis sessions.
**Material and methods:** A 2D hollow fiber model based on the finite-element method (FEM) was developed on COMSOL Multiphysics employing commercially-available haemodialyzers as reference. An ordinary differential equation (ODE) was employed to describe the time-dependent dynamics of systemic plasmatic sodium concentration, coupling this lumped-parameters model to the response of the spatially-distributed model. Time-dependent properties of our model were investigated by simulating steps in inlet dialysate sodium concentration. In-vitro haemodialysis sessions with bovine blood have been carried out for the purpose of model validation, gathering blood gas samples and recording dialysate inlet and outlet conductivity.
**Results:** The outlet sodium concentration reproduced by our model is highly correlated with outlet conductivity recorded throughout the experimental sessions (R-squared = 0.99). The coupling of plasmatic sodium ODE dynamics with the FEM model allowed for a correct reproduction of plasmatic sodium concentration recorded throughout the sessions (RMS error = 0.9 mM).
**Discussion:** FEM modelling is a suitable tool for the study of solutes exchange along the haemodialyzer fibers. Sodium concentration time-dependent dynamics can be correctly modelled for both blood plasma and dialyzer outlet port by coupling a simple one-pool model to the fiber FEM model.

### O123
### ANALYSIS OF THE EFFECT OF GEOMETRICAL AND OPERATIONAL PARAMETERS ON SOLUTE TRANSPORT IN HOLLOW FIBER DIALYZERS WITH A TWO-DIMENSIONAL TRANSPORT MODEL

*Donato D[1], Boschetti-de-Fierro A[2], Zweigart C[2], Eloot S[3], Storr M[2], Krause B[2], Leypoldt K[4], Segers P[1]*
[1]IBiTech – bioMMeda, Department of Electronics and Information Systems, iMinds Medical IT, Ghent University, Ghent, Belgium; [2]Research and Development, Gambro Dialysatoren GmbH, Hechingen, Germany; [3]Nephrology, Dialysis unit 1P8, Ghent University Hospital, Ghent, Belgium; [4]Baxter Healthcare Corporation, Deerfield, USA

**Introduction:** In the development of mathematical models of transport in hollow fiber dialyzers, dimensional analysis helps predict the complex interplay among the parameters controlling dialyzer efficiency. Since a systematic and in-depth analysis of the different dialyzer-related factors affecting solute transport has not been reported yet, the effect of relevant geometrical and operational dimensionless groups on dialyzer clearance was investigated with a two-dimensional axisymmetric transport model in the hollow fibers of a dialyzer.
**Material and methods:** Steady momentum transport in blood and dialysate compartments, and across the membrane, was described with Navier-Stokes and Darcy-Brinkman equations, respectively. Transport of urea, creatinine, phosphate and myoglobin in all three dialyzer compartments was described with convection-diffusion equations. The effect of non-newtonian blood behavior and concentration polarization was accounted for. Dimensional analysis provided the complete set of dimensionless groups determining dialyzer efficiency. Their effect on ultrafiltration flux profile along fiber length and solute clearances was studied by solving model equations for values typical in clinical practice.
**Results:** Model-predicted clearances agree with those found by experimental results. At zero net ultrafiltration, forward and backfiltration occurred close to blood inlet and blood outlet, respectively. Ultrafiltration rate and solute clearances generally increase with increasing pressure moduli, for fixed dialyzer geometry and operational conditions. Furthermore, ultrafiltration rate and solute clearances increase for increasing Reynolds numbers at blood inlet and increasing dialysate-to-blood inlet flow rate ratio, for given dialyzer geometry and pressure modulus.
**Discussion:** Model predictions may help optimize the design of hollow fiber dialyzers for blood purification.
**Acknowledgment:** Financial contribution supported by Baxter Inc.

### O124
### INTEGRATED MODEL FOR PHOSPHATE AND CALCIUM KINETICS DURING WEEKLY CYCLE OF HEMODIALYSIS

*Waniewski J, Dębowska M*
Nalecz Institute of Biocybernetics and Biomedical Engineering PAS, Warsaw, Poland

**Introduction:** The kinetics of phosphate ion (P) and calcium ion (Ca) during hemodialysis sessions were analyzed previously using simplified description that was reduced to single dialysis session and modeling of only one of these two ions. The aim of this study was to formulate an integrated model of P and Ca removal during and between dialysis sessions for the whole weekly hemodialysis cycle.
**Material and methods:** Kinetic equations describe the rate of change in the mass of Ca and complexed calcium in extracellular compartment, protein bound calcium in plasma and interstitial fluid, P in extracellular and intracellular compartments, protein bound phosphate in plasma and interstitial fluid, Ca and P in fast compartment. The computer simulations were performed for three sessions with interdialytic breaks of 2-2-3 days and 1.35 mmol/L calcium in dialysis fluid.
**Results:** The profiles of P concentration in plasma tended early to a constant value during HD and rebounded quickly to the pretreatment value after hemodialysis due to the phosphate exchange with the fast compartment and negligible exchange with the intracellular compartment. The model without the fast compartment was not able to describe the clinical profiles of plasma P. The predialysis concentration of P in plasma was higher than the equilibrium concentration for the exchange between the extracellular and fast compartments. The model predicted some increase in plasma Ca, and more pronounced increase in plasma total calcium due to hemoconcentration.
**Discussion:** The model correctly described the clinically observed profiles of Ca and P during the whole weekly cycle of hemodialysis.

### O125
### IN VIVO CHARACTERIZATION OF FRACTIOPES® 200, A NEW PLASMA FRACTIONATOR MEMBRANE FOR LIPID APHERESIS

*Krieter D[1], Lange F[1], Bonn F[2], Sauvant C[3], Lemke H[3], Wanner C[1]*
[1]Division of Nephrology, University Hospital Wuerzburg, Wuerzburg, Germany; [2]Membranes Business Unit, 3M, Wuppertal, Germany; [3]R & D, eXcorLab GmbH, Obernburg, Germany

**Introduction:** FractioPES 200 is a new polyethersulfone/polyvinylpyrrolidone-based plasma fractionator membrane for lipid apheresis. To avoid the often varying treatment conditions in humans, its in vivo permselectivity was assessed in a large animal experiment.
**Material and methods:** In a prospective, randomized, controlled, crossover trial, each of four sheep (39.0 ± 1.4 kg) was subjected to double filtration plasmapheresis with three specimen of FractioPES 200 (FPES; surface area 1.9 sqm; SelectiCure H19, 3M Membranes Business Unit) differing slightly in the in vitro sieving coefficient (SK) for HDL (FPESa, 0.300, FPESb, 0.261 and FPESc, 0.218) versus a control fractionator (EVAL, 2.0 sqm; Kawasumi Evaflux 5A20). Plasma filter (0.6 sqm; PlasCure 0.6; 3M), treated plasma volume

(1500 mL), blood (120 ± 0 mL/min) and plasma (30 ± 0 mL/min) flow rates were always identical. SK between 300 and 1200 ml and reduction ratios (RR) were determined for LDL (2,500-3,000 kDa), HDL (175-360 kDa), fibrinogen (305-385 kDa), IgG (150 kDA) and albumin (67 kDa).
**Results:** FPESc demonstrated lower (P<0.05) SK for HDL (0.30 ± 0.04 to 0.49 ± 0.10) versus EVAL (0.42 ± 0.04 to 0.74 ± 0.08) and FPESa (0.36 ± 0.06 to 0.64 ± 0.04). SK for fibrinogen of FPESb (0.05 ± 0.02 to 0.26 ± 0.34) and FPESc (0.01 ± 0.01 to 0.21 ± 0.16) were inferior (P<0.05) to EVAL (0.02 ± 0.01 to 0.40 ± 0.08). FPESa and EVAL did not differ in any SK. No significant differences in RR were determined between the filters.
**Discussion:** The permselectivity of FPESa and EVAL can be regarded as equivalent. The animal model was suitable to distinguish from the slightly inferior permeability of FPESb and FPESc, which did not translate into different solute RR.

### O126
### DOES THE PERITONEAL FLUID ABSORPTION DEPEND ON THE TONICITY OF DIALYSATE? – INSIGHTS FROM THE TWO-PHASE DISTRIBUTED MODELING

*Stachowska-Pietka J[1], Lindholm B[2], Waniewski J[1]*
[1]Nalecz Institute of Biocybernetics and Biomedical Engineering PAS, Warsaw, Poland; [2]Divisions of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Stockholm, Sweden

**Introduction:** During peritoneal dialysis bidirectional, concomitant transport of fluid and protein occurs through the tissue underlying peritoneal cavity. Clinical data suggest an increase in fluid absorption with increased dialysis fluid tonicity. We investigated to what extent the process of fluid absorption from the peritoneal cavity depends on dialysate tonicity and fluid ultrafiltration occurring in the opposite direction.
**Material and methods:** The expandable two-phase structure of the interstitium was described by the distributed model (Stachowska et al, 2016) for transport through the PhaseF (water-rich, colloid-poor region), PhaseC (water-poor, colloid-rich region), and between them. The capillary wall was described using the three-pore model, and the conditions in the peritoneal cavity were assumed as during the initial phase of dwell with glucose 3.86%, 2.27%, and 1.36% fluids with the same intraperitoneal hydrostatic pressure.
**Results:** Numerical simulations demonstrated that peritoneal absorption of fluid into the tissue occurs via PhaseF, whereas glucose-induced ultrafiltration from blood occurs via PhaseC, increasing with the increase of glucose concentration in dialysis fluid. The rate of fluid absorption was 1.77, 0.99, and 0.70 mL/min for glucose 3.86%, 2.27%, and 1.36% fluids, respectively. The increase of the absorption rate for higher glucose concentrations was related to the decreased hydrostatic pressure in PhaseF due to better fluid removal from the tissue via PhaseC with the ultrafiltration flow in the opposite direction.
**Discussion:** Computer simulations suggest a new mechanism for the change of peritoneal fluid absorption rate with the change in the tonicity of infused dialysis fluid.

### O127
### A NOVEL ANALYTICAL MODEL PREDICTING THE COURSE OF HEMATOCRIT ALONG THE LENGTH OF DIALYZER'S FIBERS

*Poorkhalil A[1], Mouzakis F[1], Amoabediny G[2], Kashefi A[1], Mottaghy K[1]*
[1]Institute of Physiology, RWTH Aachen University, Aachen, Germany; [2]Research Center for New Technologies in Life Science Engineering, University of Tehran, Tehran, Islamic Republic of Iran

**Introduction:** Contemporary therapies for ESRD patients encompass a wide range of Hemodialysis treatments, most of which rely heavily on dialyzers and hemofilters. The filtration process taking place in those devices with respect to the hemodynamic characteristics of the flow, remains relatively unclear. This study aims at improving the understanding of hemodynamics in a dialyzer by the utilization of experimental methods and mathematical models.
**Material and methods:** Based on the principles of blood flow, a mathematical model has been formulated, taking into consideration the dominant phenomena of filtration and backfiltration, and the driving forces behind them (transmembrane pressure, oncotic pressure etc.). An in vitro hemodialysis circuit was accordingly assembled using two sequentially connected dialyzers, in order to obtain satisfactory experimental data, necessary for the validation of the mathematical model. Fresh heparinized porcine blood was used throughout the course of this study.
**Results:** Pressure and flow data obtained from in vitro investigations with the hemodialysis circuit were used as an input for the mathematical model. In turn, the model predicted the development of hematocrit, pressure, and blood flow rate along the length of the hollow fibers, predicting the impact of filtration and backfiltration on the dialysis process.
**Discussion:** Validation of the model's predictions with experimental data, yields a very good agreement, which confirms the model's accuracy. The present model could serve as a tool for the optimization of hemodialysis treatments through parameter fine-tuning, in furtherance of reducing patient strain. Furthermore, it can be implemented for the prediction of blood trauma originating from prolonged hemodialysis sessions.

## Oral Session - Artificial Pancreas and Diabetes Treatment, O128-O133

### O128
### NANOTECHNOLOGY FOR TARGETED DRUG AND GENE THERAPIES

*Kost J*
Department of Chemical Engineering, Ben-Gurion University, Beer-Sheva, Israel

**Introduction:** Advances in biomedical engineering sciences have contributed to the development of novel nanoscale targeting approaches that may revolutionize treatment and bring new hope to patients.
**Material and methods:** Several nanocarriers have been approved for clinical use. However, to date, there are only a few clinically approved products to selectively bind and target cancer cells. An effective approach for achieving efficient drug delivery and targeting would be to develop nanosystems based on the understanding of their interactions with the biological environment. Reduced efficacy could be due to instability of therapeutic agent, intracellular transport barriers, toxicity of the carrier, changes in signaling pathways with the progression of disease, or drug degradation.
**Results:** Better understanding of the mechanism of uptake, intracellular trafficking, retention, and protection from degradation inside a cell are required for enhancing the efficacy of the therapeutic agent. Physical approaches to increase efficacy and targeting to specific tissues have been also studies.
**Discussion:** In the presentation the drug delivery aspects of nanomedicine, the molecular mechanisms underlying the interactions of nanoparticles with cell-surface receptors, biological responses and ultrasound as a targeting tool and its effect on cellular transport would be discussed.

### O129
### THE INFLUENCE OF THE VOICEDIAB SYSTEM ON METABOLIC CONTROL IN PATIENTS WITH TYPE I DIABETES

*Foltyński P[1], Ładyżyński P[1], Pankowska E[2], Mazurczak K[2]*
[1]Nalecz Institute of Biocybernetics and Biomedical Engineering PAS, Warsaw, Poland; [2]Department of Pediatrics, The Institute of Mother and Child, Warsaw, Poland

**Introduction:** Patients with diabetes treated with insulin need to estimate insulin boluses based on amount of carbohydrates, proteins and fat in the meal. To facilitate this the VoiceDiab system was developed in IBBE PAS (Warsaw, Poland) and its effectiveness was tested.
**Material and methods:** Forty four patients (mean age of 16.5 ± 10.4 years) having diabetes for 8.1 years (on average), were enrolled to the randomized cross-over study. Blood glucose was monitored continuously in two periods: when insulin boluses were calculated manually by a patient or when the VoiceDiab system was supporting bolus calculation. Mean blood glucose (MBG), standard deviation of blood glucose ($SD_{BG}$), time with glycemia above 180 mg/dl ($BG_{Hiper}$), time of glycemia in the range 70-180 mg/dl ($BG_{Norm}$) and time with glycemia below 70 mg/dl ($BG_{Hipo}$) were analyzed.
**Results:** The MBG increased from 160.8 mg/dL in the period with the VoiceDiab system to 163.0 mg/dL in the manual period. $SD_{BG}$ was also

lower in the VoiceDiab period than in the manual period (75.4 mg/dL v. 80.6 mg/dL, respecively). $BG_{Hiper}$ decreased from 36.3% in the manual period to 35.6% in the VoiceDiab period. $BG_{Norm}$ increased from 55.2% in the manual period to 56.1% in the VoiceDiab period. The $BG_{Hipo}$ did not change significantly (8.3% and 8.5% in the VoiceDiab and manual periods, respectively).
**Discussion:** The support of the VoiceDiab system resulted in significant decrease of mean blood glucose, increase of time in the normoglycemia range, and decrease of time in hyperglycemic range, therefore the VoiceDiab system may be used in support of patients with diabetes.
**Acknowledgement:** The study was financially supported from the grant No. PBS1/B9/13/2012 from the National Centre for Research and Development.

**O130**
**BED SIDE ARTIFICIAL PANCREAS WITH CLOSED-LOOP SYSTEM AND SURGICAL DIABETES TREATMENT**
*Hanazaki K[1], Munekage M[1], Kitagawa H[1], Yatabe T[2], Asano T[3], Kinoshita Y[3], Namikawa T[1]*
[1]Surgery 1, Kochi Medical School, Nankoku, Japan; [2]Anesthesiology, Kochi Medical School, Nankoku, Japan; [3]Nikkiso Co LTD, Tokyo, Japan

**Introduction:** Entity of surgical diabetes associated with operation is surgical stress induced hyperglycemia, which is trigger of postoperative infection (POI). It is well known that appropriate glycemic control will lead to good surgical outcomes via reduction of POI. This study aimed to evaluate the effects of surgical diabetes treatment using an artificial pancreas (AP).
**Material and methods:** From 2006 to 2015, more than 600 surgical patients underwent perioperative glycemic control using a bed side AP with closed-loop system (STG-22 or STG-55, Nikkiso, Tokyo). Peripheral venous blood is sampled continuously at less than 2 mL/h for glucose monitoring, with the AP able to continuously measuring blood glucose. Among them, almost patients performed tight glycemic control (TGC) including intensive insulin therapy (IIT) targeting blood glucose range of 80-110 mg/dL. Data were collected prospectively and were reviewed or analyzed retrospectively.
**Results:** All patients undergoing TGC had no hypoglycemia less than 70 mg/dl. Consecutive 305 patients undergoing IIT had not only no hypoglycemia but also high achievement rate of targeting blood glucose range, approximately 90%. Of note, this novel glycemic control revealed stable continuous blood glucose monitoring with less variability of blood concentrations. Also two prospective randomized controlled trials demonstrated that this novel TGC using an AP had better surgical outcomes after hepatectomy and pancreatectomy including POI compared with conventional glycemic control.
**Discussion:** Perioperative TGC using an AP is an effective and a safe surgical diabetes treatment to avoid not only hyperglycemia and hypoglycemia but also variability of blood glucose levels.

**O132**
**CHALLENGES AND RESULTS FOR THE ARTIFICIAL PANCREAS: THE CONTROL SYSTEMS PERSPECTIVE**
*Cusimano V, Palumbo P*
CNR - Institute of Systems Analysis and Computer Science A. Ruberti, Rome, Italy

**Introduction:** The Artificial Pancreas refers to the set of glucose control strategies aiming to cope with most malfunctioning of the endogenous insulin feedback action by means of exogenous insulin administration.
**Material and methods:** A model-based glucose control strategy is considered, with insulin intravenously administered. The control law is synthesized according to a reliable mathematical model of the glucose-insulin systems.
**Results:** Performances are evaluated by means of a population of virtual patients, modelled by a computer simulator recently approved by the Food and Drug Administration as a substitute of animal trials. Results (achieved by means of 10,000 MonteCarlo simulations) show an excellent level of safety (no cases of glycemia below 3.3 mM) and a very good level of efficiency: accounting for a 24 h simulation during which 3 standard meals are supposed to be administered, we manage (percentage of success >97%) for each meal to constrain plasma glycemia below 11 mM within the 2 h from the meal administration and during the period before the successive meal.
**Discussion:** Simulations are carried out by properly addressing the available technological limits and the unavoidable uncertainties in real-time continuous glucose sensors. Because of the intravenous administration of the insulin therapy, the clinical application relates to the somewhat niche problem of glycemia stabilization in critically ill subjects, such as can be found in surgical Intensive Care Units after major procedures. However, the robustness of the method suggests the extension to the application in wider contexts, such as insulin administration by means of subcutaneous infusions.

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## Oral Session - Computer Modelling in Respiratory System and Others, O134-O139

### O134
### COMPARISON OF AEROSOL ACCESSORIES PERFORMANCES BY A FLUID DYNAMIC COMPUTATIONAL APPROACH

*Possenti L, Casagrande G, Costantino M*
Department of Chemistry, Materials and Chemical Engineering, Politecnico di Milano, Milano, Italy

**Introduction:** Aim of this work is to compare aerosol accessories through a Computational Fluid Dynamic (CFD) method in order to evaluate their performances and to improve next CFD models of airway particles deposition providing boundary conditions at the mouth closer to reality.
**Material and methods:** Interaction between three commercial accessories and face (a mouthpiece and two masks – A and B) was analysed on the basis of output flow rate, fraction of particles delivered, particles velocity and direction at the outlet. A lumped parameter RC model was implemented to simulate the patient, instead nebulization rate and flow rate conditions at the interface with the device were experimentally determined with four different device-nebulizer couples. Pulmonary deposition site of particles was determined referring to UNI EN 13544-1. Multiple analyses were conducted on mask varying input parameters and position to evaluate their influence on the delivery performances.
**Results:** The model allowed to compare the delivery performances of the masks referring to the mouthpiece (99% of particles delivered to the mouth at the peak flow). The fraction of particles delivered by both the two mask at the peak flow was 95%. Result showed that performances of one of the mask (A) strictly depended on its position on the face.
**Discussion:** The computational setup allows a quantitative analysis of fluid dynamics of aerosol accessories also classifying particles by their diameter. The results are suitable to be used as boundary conditions in airway CFD analysis, and the computational method can be used to improve accessories evaluation or design.

### O135
### VIRRESPIR - A VIRTUAL PNEUMONOLOGICAL PATIENT IN THE FORM OF WEB APPLICATION

*Gólczewski T, Zieliński K, Stecka A, Ładyżyński P*
Nalecz Institute of Biocybernetics and Biomedical Engineering PAS, Warsaw, Poland

**Introduction:** Although there are several comprehensive models of the cardiovascular system, their pulmonary parts are usually extremely simple. The aim of the project was to develop a pneumonological virtual patient as a Web application available to authors of such models.
**Material and methods:** The VirRespir system was developed using Silverlight technology and hosted on IBBE server. It was based on the previously developed virtual pneumonological patient being a complex system of comprehensive models of: (a) the respiratory mechanics, (b) the pulmonary circulation, (c) gas transfer, transport and exchange.
**Results:** VirRespir is accessible from web browsers and it is executed on local workstations. It consists of four functional components activated by tabs in the graphical user interface. The 'patient' component can be used to define the virtual patient main data (such as age and height) and simulation scenario; 'simulation' - to fit virtual patient's parameters, to perform simulations and to observe the courses of chosen physiological variables; '*spirometry*' - to diagnose the respiratory system for the fitted parameters; '*external*' - to join end-users' numerical models of spontaneous breathing or respirator as well as more comprehensive models of heart and systemic circulation (instead of the embedded ones).
**Discussion:** VirRespir, a system accessible for free, can be both a useful self-reliant model for simulations of various pulmonary phenomena and a support of end-users' cardiovascular models (VirRespir join with an Italian model of the systemic circulation is shown in another presentation).
**Acknowledgement:** The project was partly supported by the grant POIG 02.03.00-00-003/09 co-financed by EU from ERDF.

### O136
### NUMERICAL SIMULATIONS OF THE LUNG AND HEART DISEASES COMORBIDITY

*Zieliński K[1], Gólczewski T[1], Ferrari G[2], Górczyńska K[1], Kozarski M[1], Darowski M[1]*
[1]Nalecz Institute of Biocybernetics and Biomedical Engineering PAS, Warsaw, Poland; [2]Section of Rome, Cardiovascular engineering, CNR - Institute of clinical Physiology, Rome, Italy

**Introduction:** A numerical study of the interaction between the respiratory and cardiovascular systems using a virtual patient (VP) suffering from the congestive left ventricular failure (CHF) and/or chronic obstructive lung disease (COPD).
**Material and methods:** The VP - a previously developed system of cardiovascular-respiratory numerical models, was used in simulations. It consists of two models: the respiratory system mechanics with gas transfer and exchange, and the cardiovascular system mechanics (pulmonary circulation, heart, systemic circulation) with gas transport and metabolism. VP parameters were adjusted to simulate the standard healthy patient as well as CHF and/or COPD of various severities. Several physical activity levels characterized with carbon dioxide production were considered. The following simulation data were analyzed: minute ventilation, ventilation to perfusion ratio, the arterial and venous oxygen and carbon dioxide tensions as well as cardiac output and left ventricular pressure-volume loop; those data were compared with the literature data.
**Results:** An increase in pulmonary blood volume and pressure related to CHF caused pulmonary edema, which impaired the efficiency of gas exchange in VP. In consequence of that impairment, the minute ventilation/carbon dioxide production slope was elevated in VP suffering from CHF, which is observed in real patients. Such elevation has been proven to be a strong prognostic marker in the CHF population. On the other hand, the slope was elevated in COPD.
**Discussion:** The presented VP is a valuable tool to study the cardio-respiratory interaction for comorbid lungs and heart diseases; it might also be used for educational purposes.

### O137
### GEOMETRY FACTOR IN CONTINUOUS INDUCTIVE POWERING AND INDUCTIVE RECHARGING OF IMPLANTED MEDICAL DEVICES

*Danilov A, Mindubaev E, Selishchev S*
Biomedical Engineering Department, National Research University of Electronic Technology (MIET), Moscow, Russian Federation

**Introduction:** The purpose was to investigate the performance of an inductive powering unit for various geometric configurations in continuous powering and recharging of implanted medical devices.
**Material and methods:** Numerical modeling was performed to calculate transmitted power as a function of the coils geometry and operating frequency. Geometry was chosen as specific for inductive powering of an implanted medical device: distance between coils is 10 … 30 mm, lateral displacements is 0 … 50 mm, diameter of the coils is 70 mm. Two operating modes were analyzed: system with preset resonant frequency and system autotuned to the odd splitting frequency.
**Results:** It was found that autotuned system has much more stable output for a wide range of values of the distance between coils and lateral displacement. Transmitted power variations due to changes in the distance in range 5 … 25 mm were less than 10% for the autotuned system and more than 50% for the system with preset operating frequency. On the other hand, for chosen parameters the amount of a power transferred on a preset resonant frequency is 2 … 3 times higher for a wide range of geometric parameters.
**Discussion:** There is a tradeoff between the stability and amount of a transferred power for autotuned inductive systems. Such a tradeoff is unavoidable for devices which require a continuous power supply (e.g., mechanical circulatory support). However, results of our simulation suggest that for a rechargeable device (e.g., spinal cord stimulators) another option exist: the critical coupling operation mode with coils positioning means, which provide stable geometric configuration during the course of the recharging.

**O138**
**FINITE ELEMENT ANALYSIS OF MINI-PLATE STABILIZATION OF MANDIBLE FRACTURE**
*Wądołowski P[1], Krzesiński G[1], Gutowski P[2]*
[1]The Faculty of Power and Aeronautical Engineering, Warsaw University of Technology, Warsaw, Poland; [2]Department of Cranio-Maxillo-Facial Surgery, Medical University of Warsaw, Warsaw, Poland

**Introduction:** The aim of presented analysis is to recognize the possible mechanical issues of mini-plate connection used to treat mandible fractures. There were prepared FEM analysis on healthy and treated mandible bone to obtain the stress and strain distribution within the bone and connecting mini-plate with screws under masticatory loads at multiple configurations.
**Material and methods:** The bone geometry was restored on the base of CT scans of hospitalized patient during the treatment, then the solid geometry consisting of cortical and cancellous bone was created. There were also simulated temporomandibular joint and muscle system. As a mini-plate was used sample device used in the treatment of mandible fracture. Finite elements mesh and analysis were performed by ANSYS software. To simulate realistic connection behavior there were used nonlinear contact conditions between the mini-plate and bones, also orthotropic material properties of the bone tissue were applied. Multiple mini-plate locations, angle positions and clearance between bone factions were considered.
**Results:** Performed calculations show that the bone-mini-plate system is able to stabilize properly the fractured mandible bone. There is visible strong dependecy between the mini-plate location and stress distribution within the connecting element and surrounding bone tissue. Results provide a strong basis for the mechanical optimization of the mini-plate cnnections. In order to medical validation, outcomes were compared to clinical observation.
**Discussion:** Details of achieved results provide the information helpful for better understanding the load transfer in the mandible with the stabilizer and to predict the behavior of the structure to prevent possible stabilization system damage.

**O139**
**SIMULATION OF MASS TRANSPORT DURING INTRAPERITONEAL CHEMOTHERAPY: A PARAMETRICAL MODEL OF SINGLE TUMOR NODULES**
*Steuperaert M[1], Falvo D'Urso Labate G[2], Debbaut C[1], Ceelen W[3], Segers P[1]*
[1]IbiTech-BioMMeda, Ghent University, Ghent, Belgium; [2]Department of Environmental and Chemical Engineering, University of Calabria, Rende, Cosenza, Italy; [3]Department of Surgery, Ghent University, Ghent, Belgium

**Introduction:** Patients with peritoneal carcinomatosis suffer from a widespread metastatic growth of tumor nodules in the peritoneal cavity. Although Intraperitoneal (IP) chemotherapy allows for higher intratumor concentrations of the cytotoxic agent compared to intravenous administration, actual application of IP chemotherapy is limited due to poor drug penetration in the tumor tissue. It is thus essential to better understand the drug transport during IP chemotherapy.
**Material and methods:** A 3D computational fluid dynamics model of a tumor nodule with necrotic core was created in Comsol® (COMSOL, Inc., Burlington, USA) describing the drug transport occurring during IP chemotherapy, including convective/diffusive/reactive drug transport in two tumor geometries (a spherical baseline model with radius $r_{sphere,large}$ = 1 cm/$r_{sphere,small}$ = 2 mm and $r_{necrotic,large}$ = 5 mm/$r_{necrotic,large}$ = 1 mm). To assess the efficiency of drug administration, a penetration depth (PD) was defined as the percentage of the total radius in which the drug concentration resulted to be over 6.6E-3 mol/m$^3$. These baseline models were subsequently adapted to evaluate the effect of therapy-related parameters (different drugs, vascular properties etc.) on drug penetration.
**Results:** Large differences in PD (PD; % of total radius) were found in the baseline cases for the two different scales ($PD_{sphere,large}$ = 4.04%; $PD_{sphere,small}$ = 20.82%). Vascular normalization therapy yielded different outcomes ($\Delta PD_{sphere,large}$ = 2.95%; $\Delta PD_{sphere,small}$ = 17.95%). Both cases showed less penetration when paclitaxel was used as opposed to cisplatin. This effect was more pronounced in the smaller geometry ($\Delta PD_{sphere,large}$ = -1.91%; $\Delta PD_{sphere,small}$ = -10.25%).
**Discussion:** The model is able to predict drug penetration depth for different sets of IP chemotherapy-related parameters, which may lead to optimization of drug transport during IP chemotherapy.

## Special Symposium - Extracorporeal Lung Support and Lung Transplantation, O140-O144

**O140**
**OXYGEN DIFFUSION THROUGH LUNG SURFACTANT USING FLUOROCARBON IN AN ARTIFICIAL ALVEOLAR CHAMBER**
*Khachab A[1], Hahn A[2], Mottaghy K[1]*
[1]Institute of Physiology, RWTH Aachen University, Aachen, Germany; [2]Federal Institute for Risk Assessment (BR), Berlin, Germany

**Introduction:** Lung surfactant is a surface-active lipoprotein complex, known among others for lowering surface tension at the air-liquid interface of the alveoli during respiration, and for stabilizing the alveoli against collapsing atelectasis. Presently, we report on the impact of a direct effect of pulmonary surfactant on the degree of $O_2$ diffusion rate, through a membrane surface area under constant gas exchange conditions.
**Material and methods:** A gas exchange device is designed to mimic the physiological conditions of the alveolar gas exchange process. Perfluorocarbon(FC-43) is used as a blood substitute. Fluorocarbons are biologically inert fluids, have higher density than blood, high oxygen solubility (up to 19 ml/dl), and are already used for liquid ventilation, artificial blood and liquid oxygenation. A thin layer of oil or silicon membrane is used alternatively as blood/air barrier. The space over the layers is continuously flushed with oxygen. A micro oxygen sensor (UNISENSE®) is continuously measuring $pO_2$ diffusing from the gas phase to the fluid compartment. A clinically implemented surfactant emulsion (Curosurf®) is applied.
**Results:** The results demonstrate that the surfactant does not impose any further resistance to the diffusion process, as it might be expected from an additional diffusion barrier. On the contrary, it surprisingly improved $O_2$ diffusion velocity over FC-43.
**Discussion:** The presented technique can be considered as a tangible artificial imitation, which mimics the gas transport properties of lung surfactant. The observed improvement of $O_2$ diffusion could play therapeutically a significant role in the treatment of gas exchange insufficiencies of the diseased lung.

**O141**
**ENDOXY: ENDOTHELIAL CELLS IN BIOHYBRID LUNGS PROMOTE NOT ONLY HEMOCOMPATIBILITY BUT ALSO GAS TRANSFER PERFORMANCE**
*Menzel S[1], Jockenhoevel S[2], Cornelissen C[3]*
[1]Department of Tissue Engineering and Textile Implants, Institute of Applied Medical Engineering, RWTH Aachen University, Aachen, Germany; [2]Department of Tissue Engineering and Textile Implants, Institut für Textiltechnik and Institute of Applied Medical Engineering, RWTH Aachen University, Aachen, Germany; [3]Section of Pneumology, Department for Internal Medicine, Medical Faculty, RWTH Aachen University, Aachen, Germany

**Introduction:** Extracorporeal membrane oxygenation (ECMO) can ensure adequate gas exchange for patients with respiratory insufficiency but its application is restricted by poor hemocompatibility. Hence, lining biohybrid lungs with endothelial cells (EC) should enable prolonged application. Regarding the design of biohybrid lungs, the aim of this study was to evaluate the gas exchange of endothelialised flat membranes in order to optimize performance while retaining an integral monolayer.
**Material and methods:** EC derived from human umbilical cord veins were seeded on gas permeable membranes. Based on the oxygen transfer rate (OTR) subsequent gas transfer tests of blank and endothelialised membranes were performed with culture medium (EGM-2, Lonza) in a custom-made bioreactor system optimized for gas transfer and flow rates inducing physiological shear stress. Cell morphology was assessed by microscopy and immunohistochemistry.
**Results:** During all experiments an integral monolayer has been maintained. Both setups provided oxygenation of the test fluid featuring small deviations with each one yielding an optimal operating point. For perfusion-limited OTR the performance of the endothelialised membrane exceeded the blank membrane.
**Discussion:** This study presented a bioreactor system suitable for the evaluation of the gas transfer performance of endothelialised membranes. The test fluid enabled microscopic control of cell integrity and extended trial periods.

According to the results, the EC seem to promote gas transfer to a certain extent. Although the underlying principles hereof still need to be clarified, the results represent a significant step towards the development of a biohybrid lung and might influence the prospective design of such devices.

**O142**

**SURFACE MODIFICATION OF SILICONE TUBES BY FUNCTIONAL CARBOXYL AND AMINE, BUT NOT PEROXIDE GROUPS, AND COLLAGEN IMMOBILIZATION IMPROVES CELL STABILITY**

*Salehi-Nik N[1], Zandieh-Doulabi B[2], Amoabediny G[3], Klein-Nulend J[1], Mottaghy K[4]*

[1]School of Chemical Engineering, College of Engineering, University of Tehran, Tehran, Islamic Republic of Iran; [2]Oral Cell Biology, Academic Centre for Dentistry Amsterdam, University of Amsterdam and VU University Amsterdam, MOVE Research Institute Amsterdam, Amsterdam, The Netherlands; [3]Department of Biomedical Engineering, Research Center for New Technologies in Life Science Engineering, University of Tehran, Tehran, Islamic Republic of Iran; [4]Institute of Physiology, Medical Faculty, RWTH Aachen University, Aachen, Germany

**Introduction:** Surface modification by functional groups promotes endothelialization in biohybrid artificial lungs, but whether it affects endothelial cell stability under fluid shear stress, and release of anti-thrombotic factors, e.g. nitric oxide (NO), is unknown. We aimed to test whether surface-modified silicone tubes containing different functional groups, but similar wettability, improve collagen immobilization, endothelialization, cell stability and cell-mediated NO release.
**Material and methods:** Silicone tubes were plasma pre-modified to introduce peroxide groups acting as initiators for graft polymerization. Silicone tubes containing peroxide groups were graft polymerized with acrylic acid to introduce carboxyl groups, or with aminosilane to introduce amine groups. Collagen was immobilized on silicone tubes with peroxide, carboxyl, or amine functional groups.
**Results:** Peroxide, carboxyl, and amine-groups increased collagen immobilization (41-76%). Peroxide and amine enhanced (1.5-2.5 fold), but carboxyl-groups decreased (2.9-fold) endothelial cell number after 6 days. After collagen immobilization, cell number was enhanced by all group-modifications (2.8-3.8 fold). Cells were stable under 1 h fluid shear stress on amine, but not carboxyl or peroxide-group-modified silicone (>50% cell detachment), while cells were also stable on carboxyl-group-modified silicone with immobilized collagen. NO-release was increased by peroxide and amine (1.1-1.7 fold), but decreased by carboxyl-group-modification (9.8-fold), while it increased by all group-modifications after collagen immobilization (1.8-2.8 fold). Only amine-group-modification changed silicone stiffness and transparency.
**Discussion:** In conclusion, silicone-surface modification with carboxyl and amine, but not peroxide-groups followed by collagen immobilization allows formation of a stable functional endothelial cell layer. These findings could help to significantly improve current biohybrid artificial lungs, or design new types of implantable artificial lungs.

**O143**

**DEVELOPMENT OF AN ULTRA COMPACT AND DURABLE ECMO SYSTEM AND A LONG-TERM EVALUATION BY CHRONIC ANIMAL EXPERIMENT**

*Katagiri N, Tatsumi E, Takewa Y, Tsukiya T, Mizuno T, Taenaka Y*

Artificial Organs, National Cerebral and Cardiovascular Center Research Institute, Osaka, Japan

**Introduction:** In cases of severe respiratory/circulatory support, some cardiopulmonary support systems have been used for over days to weeks while taking risks of complications related to thrombus and handling of miscellaneous equipments. We have been developing an ECMO system for long-term use in order to solve the current problems. In this study, we made a prototype of a compact ECMO system and evaluated its long-term durability and antithrombogenicity by a chronic animal experiment.
**Material and methods:** A compact oxygenator (BIOCUBE6000), a novel hydrodynamically levitated centrifugal blood pump and tubes were connected and designed as a disposable unit in order for being mountable on a driver unit. Its entire blood-contacting surface was treated with heparin bonding material (T-NCVC). A pump motor and measurement instruments were integrated into the driver unit. Veno-arterial bypass ECMO with a prototype system was conducted for 18 days using a goat weighing 61 kg. Continuous heparin administration was conducted for keeping ACT in the range 150-200 sec.
**Results:** A dedicated pre-connected circuit design could provide one-touch mountable holder and reinforcement of kink-prone tubes. The driver unit had a small size (W290 × D205 × H260 mm) and lightweight (6.6 kg). ECMO experiment could run without device exchange. $O_2$ and $CO_2$ transfer rates were kept at sufficient levels (140 ± 14 and 90 ± 22 mL/min, respectively). After the experiment, no thrombi were observed in the ECMO circuit.
**Discussion:** The prototype of the ultra compact ECMO system indicated the possibility of durability for over 2 weeks.

Withdrawn