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ORAL SESSION – MODELLING, O1-O7

O1
MULTI-SCALE SIMULATIONS OF ASPIRATION THROMBECTOMY
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Aim: Ischemic stroke inflicts high morbidity and mortality. Endovascular aspiration of the blood clot is a common surgical technique for the recanalization of the occluded arteries. However, the hemodynamics in the cerebral vessel network (CoW) are not completely understood, which results in medical misjudgment and complications during surgeries. To improve treatment outcome, computational models derived from patient data can be used to investigate the blood flow conditions.

Methods: In this study, we established a multi-scale description of aspiration thrombectomy. Firstly, the CoW was modeled as a 1-D pipe network on the basis of real geometries and validated with literature values of physiological pressure/flow curves. Afterwards, a vascular occlusion was placed in the middle cerebral artery and the relevant section of the CoW was transferred to a 3-D computational fluid dynamic (CFD) domain. A suction catheter in different positions was included in the CFD simulations. The geometry was extracted from MRI scans. The boundary conditions of the 3-D domain were taken from the 1-D domain to ensure system coupling.

Results: The 1-3D model confirms the literature data of pressure/flow curves. Further on, anatomical variations, like hypoplasia and aplasia of cerebral vessels, can be investigated with respect to their influence on the cerebral blood flow. The CFD simulations can be used to calculate the optimal insertion length of the catheter for a successful thrombus aspiration.

Conclusions: The presented framework shows the possibility of a 1-3D-3D computational approach for surgical guidance support.

O2
VAD IN FAILING FONTAN: SIMULATION OF VENTRICULAR, CAVO-PULMONARY AND BIVENTRICULAR ASSISTANCE IN SYSTOLIC/DIASTOLIC VENTRICULAR DYSFUNCTION AND IN PULMONARY VASCULAR RESISTANCE INCREASE
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Aim: Due to the lack of donors, VADs could be an alternative to heart transplantation for Failing Fontan patients (PTs). Considering the complex physiopathology and the type of VAD connection, a numerical model (NM) could be useful to support clinical decisions. The aim of this work is to test a NM simulating the VADs effects on failing Fontan for systolic dysfunction (SD), diastolic dysfunction (DD) and pulmonary vascular resistance increase (PRI).

Methods: Data of 10 Fontan PTs were used to simulate the PTs baseline using a dedicated NM. Then, for each PTs a SD, a DD and a PRI were simulated. Finally, for each PT and for each pathology, the VADs implantation was simulated.

Results: NM can well reproduce PTs baseline. In the case of SD, LVAD increases the cardiac output (CO) (35%) and the arterial systemic pressure (ASP) (25%). With cavo-pulmonary assistance (RVAD) a decrease of inferior vena cava pressure (IVCP) (39%) was observed with 34% increase of CO. With the BIVAD an increase of ASP (29%) and CO (37%) was observed. In the case of DD, the LVAD increases CO (42%), the RVAD decreases the IVCP. In case of PRI, the highest CO (50%) and ASP (28%) increase is obtained with an RVAD together with the highest decrease of IVCP (53%).

Conclusions: The use of NM could be helpful in this innovative field to evaluate the VADs implantation effects on specific PT to support PT and VAD selection.

O3
TRANSIENT NUMERICAL ASSESSMENT OF THE RISK OF THROMBUS FORMATION IN ROTARY BLOOD PUMP
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Aim: Thrombus formation and haemolysis associated with the exposure to high levels of shear stress, strain rates and stagnation regions remain a challenge for rotary blood pumps (RBP). Numerical prediction of potential risk regions for thrombus aggregation, deposition and growth during the cardiac cycle allows for comparative prototype pump evaluation. Therefore, the aim of this study is the development of a flow dependent risk factor for the prediction of thrombosis in rotary blood pumps and optimization towards a more haemolysis and thrombus free design.

Methods: Transient assessment of the pump performance and flow during cardiac support is achieved using Computational Fluid Dynamics (CFD). A factor for the prediction of thrombosis based on the local platelet concentration calculated by various flow induced threshold weighted contributions is derived, followed by a risk analysis within the pump. Four significantly different impeller blade and three volute geometries are compared with regard to thrombosis formation risk.

Results: The results are in good agreement with experimental findings of thrombus formations from haemolysis tests, encouraging the application of numerical prediction for problematic regions of actual thrombus growth.

Conclusions: This study presents an approach to identify problematic regions of thrombus within a RBP. Furthermore, it allows for the comparative evaluation of risk potential for thrombosis within the pump and is applicable for future device optimizations.

O4
NOVEL APPROACH TO ACCOUNTING FOR TURBULENCE IN BLOOD DAMAGE MODELING
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Aim: To account for the impact of turbulence in blood damage modeling a novel approach based on the generation of instantaneous turbulent fields generated from RANS-simulations is proposed.

Methods: Turbulent flow in a mechanical heart valve was simulated using RANS-based (SST k-w) flow solver FLUENT. The Reynolds Shear Stress (RSS) field is transformed into a divergence-free random vector field of velocity fluctuations using procedural noise functions. To consider the random course of the blood cells, for each time step an instantaneous turbulent flow field was computed by adding the turbulent velocity fluctuations and the mean velocity at each cell of the computational grid. On this instantaneous flow field, path lines and corresponding point-wise instantaneous shear stresses were calculated. For a comparison, path lines based on mean velocity field and respective viscous shear stress together with RSS values were calculated. Finally, blood damage index was integrated along the path lines using a power law approach.

Results: We found that the use of RSS parameter is not appropriate to blood damage modeling because RSS overestimates damaging stress and does not reflect a distribution of damage in a volume.

Conclusions: RSS should be avoided in blood damage modeling. A novel approach to calculate blood damage without RSS in RANS based flow simulations is established.

O5
DESIGN OPTIMIZATION OF DIALYSIS CATHETERS USING CFD
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Aim: A virtual test bench is set for the evaluation of the fluid mechanics performance of new dual lumen catheters for hemodialysis using computational fluid dynamics (CFD).

Methods: Eight different catheter designs were evaluated. The risk for thrombogenic events was evaluated in terms of shear-induced activation of platelets, quantified by a Lagrangian-based model of blood damage (Platelet Activation State, PAS). Convection-diffusion equation was solved to quantify the detrimental recirculation of dialyzed blood from the venous to the arterial lumen. The effect of central tip and side holes geometry/position on thrombogenic fluid structures was evaluated.

Results: The analysis of flow separation regions generated by catheters holes and of the shear-induced platelet activation in both lumens and in direct and inverted configuration allowed to identify critical features in catheters design and to rank their performance. Among the main findings: (1) the presence of geometric asymmetry reduces the risk of thrombus formation, with number, position and dimension of side holes playing a major role; (2) PAS is higher in the venous lumen, and in the inverted configuration; (3) recirculation is negligible in all models. In conclusion, this comprehensive comparison allowed to select an appropriate design for the device, highlighting the benefits of side hole number and their geometric asymmetry in catheter performance. The output of the study is an asymmetric catheter design suitable for pre-market prototype testing.
O6 AN ELECTRICAL ANALOG MODEL FOR LIVER PERFUSION: VALIDATION AND CALIBRATION
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Aim: Hypothermic machine perfusion (HMP) is reviving as a better preservation method for donor livers than the gold standard of cold storage, but faces some potential hazards (e.g. endothelial damage, flow competition). For that reason, we previously developed an electrical analog model of liver perfusion to investigate the effect of different HMP settings. Since its performance was not experimentally verified before, we present a new method to validate and calibrate the model.

Methods: A human liver (discarded for transplantation after failed reanimation) was subjected to pressure-controlled HMP. Pressure and flow waveforms were recorded simultaneously at the hepatic artery (HA) and portal vein (PV) during varying pressure settings (5-99 mmHg). Signal processing enabled calculating hydraulic input impedances (Z) based on Fourier analysis. A two-step approach, involving reduced [Z]-element Windkessel models, was adopted to fit the measured Z spectra (coherence > 0.9; 0-10 Hz) to the electrical model (unconstrained nonlinear optimization).

Results: Calibrated Z spectra agreed well with experimentally acquired spectra. Notably, results showed that - to date - viscoelastic effects have been largely underestimated in models presented in literature (factor of ±10%), speculatively due to neglecting the viscoelastic effects of liver tissue surrounding blood vessels.

Conclusions: A novel methodology was developed to calibrate the electrical model of liver HMP to one specific liver. Future research may focus on other clinical applications (e.g. liver cirrhosis).

O7 COMPUTATIONAL FLUIDDYNAMIC DESIGN OF A NEW ENDOTRACHIAL TUBE FOR TOTAL LIQUID VENTILATION
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Aim: This work is aimed at designing an instrumented endotracheal tube (ETT) dedicated to neonatal Total Liquid Ventilation (TLV) with perfluorocarbons by means of computational fluidodynamics (CFD).

Methods: A 3D model of an ETT, interfaced with a model of tracheal bifurcation with the typical branching in infants, was developed. Unsteady-state simulations (k-ε) turbulent model) were performed (Fluent 14.0, ANSYS Inc.) to replicate the flow rate pumped by a new TLV prototype (Pro-Li-Ve) developed by our group. A lumped parameter model was coupled to the CFD model to simulate realistic lung impedance and pulmonary pressure. The fluidodynamic effects of different positions of the ETT tip with respect to the carina were evaluated to minimize wall shear stresses (WSS). The effects of different tip shapes and of the presence of a pressure transducer in the ETT lumen were also analysed on single or double lumen ETTS.

Results: The model allows reliable simulations of the tracheal pressure obtained during in vivo trials. Any ETT tip conveys the 57% of the flow rate to and from the right bronchus. Maximum WSS acts on the internal side of the carina during inspiration. A minimum distance (13 mm) between tip and carina is required to minimize WSS. The presence of the pressure transducer does not affect airways fluidodynamics. A double lumen ETT would reduce dead space improving gas exchange although increasing in WSS and pressure.

Conclusions: The use of an ETT designed according to the developed model outcomes, instead of commercial ETTS, would be a fundamental step for the optimization of the ventilator-patient interface during TLV treatments.

O8 DESIGN OPTIMIZATION OF AN ANATOMICALLY ADAPTED PERCUTANEOUS HEART VALVE FOR THE TRICUSPID POSITION
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Background: The concept of an anatomically adapted tricuspid heart valve (THV) prosthesis for percutaneous implantation was developed and assessed in an initial proof of principle study. The device consists of two functional elements, a Vena cava superior-stent for secure anchoring and a tricuspid annulus-stent containing a THV with pericardial leaflets. The elements are connected by flexible struts. Shortcomings of the first design included a difficult positioning and insufficient structural stability.

Methods: To address the structural stability of the valve-bearing annulus-stent and optimize integration of the valve, the design was altered from 72° to 60° degree symmetry. The number of struts connecting the two stents was decreased to three. Strains and stresses were assessed by finite element analyses (FEA) for crimping, expansion and interaction of leaflets and stent. The design was assessed in porcine hearts from a slaughterhouse to analyze the anatomical fit of the new design. The prosthesis was tested in a right heart mock-loop inside an anatomically correct silicone model.

Results: The design changes led to better device stability in FEA and in vitro tests. A good anatomical fit was achieved in anatomical fitting studies in porcine hearts.

Conclusions: Design optimization successfully addressed the issues of the first generation percutaneous THV prosthesis.

O9 DEVELOPMENT OF A NOVEL MODULAR HEART VALVE PROSTHESIS FOR THE PULMONARY POSITION
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Background: Due to the anatomical variance of the right ventricular outflow tract and resulting difficult anchoring, transcatheter pulmonary valve implantation (TPVI) has received little attention. In order to create anatomically fit, patient-customized prostheses, a modular TPVI prosthesis consisting of standardized connectable elements was developed.

Methods: Anatomical studies were performed to define the dimensions of the elements needed to provide satisfactory anatomical adaptation. Finite element analyses (FEA) were performed using Abaqus/CAE (Simulia, USA) to iteratively optimize the mechanical properties. The considered conditions include expansion from a 10 mm nitinol tube during fabrication, as well as the crimping and deployment processes. Stent-leaflet interaction was assessed, considering the physiological pressure curve in the RVOT during 3 cardiac cycles. The designs of the stent frame elements and leaflets were optimized until the strains and stresses met acceptable values.

Results: Maximum stresses were 800 MPa for crimping and deployment simulation at 37°C. The design changes led to better device stability in FEA and in vitro tests. A good anatomical fit was achieved in anatomical fitting studies in porcine hearts.

Conclusions: Using the approach of iterative stent frame optimization, satisfactory designs of all elements needed to assemble modular customizable TPVI prostheses were found.

O10 THROMBOGENICITY AND BIOCOMPATIBILITY STUDY OF REDUCED GRAPHEN OXIDE MODIFIED TISSUE AS A PROMISING VERSATILE MATERIAL FOR TISSUE ENGINEERED HEART VALV
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Aim: Background: The modern tissue engineering, combine the acellular scaffolds seeded with cells ex vivo or in vivo. The scaffold should be non thrombogenic and biocompatible. The aim of our study was to evaluate the platelet activation effect of acellular tissue scaffold, modified by reduced Graphen Oxide (rGO).

Materials/Methods: Graphene oxide was prepared by modified Hummers method. For the study the acellular pulmonary valve conduit modified by rGO was used. The tissue samples were subjected in vitro to the interaction with whole blood in the simulated laminar flow condition. The following receptors were analysed: CD42a, CD42b, CD41a, CD40, CD65p and PAC-1. As a reference the non-coated acellular tissue, Poli-L lysine and fibronectin coated tissue was used. Also the biocompatibility study was tested, for this purpose the cytotoxicity test, TUNEL assay and Cell Cycle analysis was performed.

Results: Platelet activation upon contact with the tissues modified with rGO was not significantly different from the level of activation observed in the control and reference group.

Conclusions: The studies indicate that rGO can be very attractive material used for the scaffold modification designed to create heart valves bioprosthesia.
O11 DEVELOPMENT OF CUSTOMIZABLE HEART VALVE PROSTHESIS FOR ACQUIRED AND CONGENITAL DISEASES OF THE RVOT

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Aim: Acquired and congenital diseases of the right ventricular outflow tract (RVOT) are commonly associated with complex anatomies requiring dedicated custom prostheses. In order to achieve safe and effective device based treatment options for patients in need of RVOT replacement or repair, the project INTER-Heart deals with the design and regulatory approval process of dedicated pulmonary valve and RVOT prostheses, specifically a transcatheter heart valve (THV) and a conduit.

Methods: A kit with connectable elements for the assembly of customizable patient specific prostheses was conceived. The elements include a central Nitinol valve element with pericardial leaflets, a range of custom Nitinol stentframes for anatomical adaptation of the shape and device anchoring of the THV as well as a polyeuthene vascular graft with sinuses to form a conduit. The process of choosing peripheral stentframes to connect to the central element relies on 3D analyses of the RVOT based on CT or MRI patient data.

Results: Prototypes of the customizable THV demonstrate the feasibility of the concept. Virtual anatomical fitting studies of the patient specific prostheses prove the adaptability of the prostheses using standardized elements.

Conclusions: By using a modular system it is possible to develop customized and still profitable prostheses. The approval process is facilitated by the lower risks.

O12 IN VITRO EVALUATION OF A NOVEL AUTOLOGOUS BIOVALVE WITH A STENT FOR PULMONARY VALVE

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Aim: Using “in-body tissue architecture” technology and a novel method for constructing a stent valve, an autologous heart valve-shaped tissue with a stent was developed as stent-biovalve. In this study, we evaluated the hydrodynamic performances of stent-biovalve by changing its leaflet size in vitro test in order to determine the appropriate stent-biovalve form for pulmonary valve (PV).

Methods: A specially designed stent-mounted cylindrical acrylic mold was placed in a dorsal subcutaneous pouch of a goat and the implant was extracted 1 month later. The acrylic mold was removed and a tube structure of connective tissue impregnated with the stent strut was obtained. The tube was folded in half inwards and 3 commissures were fabricated to form 3 leaflets and we obtained the stent-biovalve (25 mm ID). The stent-biovalve was connected to a specially designed pulsatile mock circulation in the PV position. The hydrodynamic performances of stent-biovalves with 6 different axial leaflet lengths (13, 14, 15, 17, 20 and 25 mm) were examined under pulmonary circulation conditions using saline.

Results: The leaflet length was found to significantly affect the hydrodynamics of these valves. The stent-biovalve with 15 mm leaflet length demonstrated improved flow characteristics compared to other and the flow rate ranged from 6.2 to 7.6 L/min at a mean PAP of 18 mm Hg as the HR was increased from 70 to 120 bpm. The regurgitation rate was approximately 11%. The developed completely autologous stent-biovalve with appropriate leaflet size may be potentially useful for PV.

O15 EVOLUTION OF MARS: HE MARS EVOLUTION OF MARS: HE MARS

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Aim: We carried out modifications to MARS (Molecular Adsorbent Recirculating System) in order to increase its efficiency in hepatic metabolite removal in liver failure.

Methods: Patients: 4 affected by liver failure, 2 with high bilirubinemia (52.50 and 48.75 mg/dL in patients A and B respectively) and 2 with high bile acid serum concentrations (92.0 and 98.5 mMol/L in patients C and D respectively).

Treatments: 1) a 5-hour session with standard MARS (flows: 220 ml/min for blood, 150 ml/min for albumin) (115 S); 2) a session with the same blood and albumin flows but modified albumin circuit with parallel double adsorber units...
**O16 PORTAL BLOOD ARTERIALIZATION WITH AN EXTRACORPOREAL DEVICE TO TREAT TOXIC ACUTE HEPATIC FAILURE IN THE SWINE MODEL**

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**Abstract:** The present study aimed to determine whether a controlled portal blood arterIALIZation by a liver extracorporeal device, called L.E.O2 NARDO which means Liver Extracorporeal Oxygen NARDO, is effective in treating acute liver failure (AHF) induced in swine by carbon tetrochloride (CCl4) administration.

**Materials and Methods:** Twenty swine with AHF induced by intraperitoneal injection of carbon tetrochloride (CCl4) in oil solution at a dose of 480 mg/kg of body weight were randomly divided into two groups: animals received L.E.O2 NARDO treatment 48 hours after the intoxication, and swine that were not treated (control group). Blood was withdrawn from the iliac artery and reversed in the portal venous system. An extracorporeal device was interposed between the outflow and the inflow in order to monitor the hemodynamic parameters. Each treatment lasted 6 hours. Serum and liver samples were collected in both groups. The survival was assessed at 7 days.

**Results:** L.E.O2 NARDO treatment yielded beneficial effects for CCl4-induced AHF: a significant decrease in the total bilirubin (TB) and total bile acids (TBA) was observed at the end of each session.

**Conclusions:** This preliminary investigation demonstrates the possibility of an evolution of MARS, joining the high tolerability of the standard method with high efficiency in hepatic metabolite removal.

**O17 HUMAN PLASMA TOXICITY IN THE AMC-BIOARTIFICIAL LIVER**

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**Background and Aim:** The AMC-BioArtificial Liver (BAL) facilitates the human liver cell line HepaRG. Previously we found that both acute liver failure and healthy rat plasma reduced hepatic transcript levels. Here, we studied the effect of human plasma on HepaRG cells in monolayer and BAL culture, and investigated the effect of plasma enrichment to test whether the observed damage is due to a lack of differentiation stimuli and/or oxidative stress.

**Methods:** Monolayers and BAL cultures kept in medium (control) were exposed to 100% plasma with a mix of antioxidants, a corticosteroid and an urea cycle enhancer (plasma+), or without plasma-). Subsequently, ammonia elimination, urea synthesis, and hepatic transcript levels were assessed. In BAL-cultures, additionally LDH/AST leakage and lactate elimination were quantified.

**Results:** Monolayer cultures showed a significant decrease in hepatic transcript levels and ammonia elimination, after 16 and 24 hours in both the plasma+ and plasma− group compared to control. In BAL-cultures (16 h plasma+) there was a trend towards lower hepatic gene transcription in both plasma groups compared to control. This effect was less pronounced in the plasma+ group. No change in functionality or cell damage was observed. There was a trend towards improved lactate elimination in the plasma+ group compared to the plasma− group (p = 0.053).

**Conclusions:** BAL culturing renders HepaRG cells more resistant to detrimental effects of human plasma, which may be caused by oxidative stress and/or lack of differentiation stimuli. Plasma enrichment may limit these negative effects.

**O18 NURSING INNOVATIONS IN CARDIOVASCULAR THERAPIES BY QUALITY AND PROJECT MANAGEMENT STRUCTURES AT A UNIVERSITY LEVEL**

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**Abstract:** Development of novel devices and treatment concepts at a university research level is essential in advancing therapeutic cardiovascular technologies. Bridging the gap between early university level device developments and clinical application is often complicated by incomplete documentation, disregard of regulatory requirements and poor organization. Our aims are the transfer to an industry standard is costly and detrimental to innovation.

**Methods:** Quality and project management structures were implemented in a university research. A main focus was placed on technical documentation, including design changes and setbacks to adhere to industrial standards. To prove the feasibility of the concept, QM and PM processes were incorporated into the everyday workflow of specific projects with the aim of clinical application.

**Results:** Implementation of QM and PM was well tolerated once the benefits like shortened processing times, ensured compliance with regulatory requirements, and improved sustainability in knowledge were noticeable. Defined organizational structures provided more transparency for complex and creativity-driven projects.

**Conclusions:** Our experience shows that integration of QM and PM standards at a university level is possible. It constitutes a solid basis for the transfer to clinical application. Since every research project needs and withstands different degrees of QM and P, an adapted and scalable QM system for university research projects is under development based on our findings and experience.

**O19 THE CALON MINIVAD – A NEW LVAD WITH SMALL SIZE, MECHANICAL SIMPLICITY AND HAEMOCOMPATIBILITY AS DESIGN GOALS**

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**Abstract:** The Calon MiniVAD™ is a new LVAD that utilises a novel layout to potentially improve implantability, manufacturability and haemocompatibility. It is hoped that this will lead to commensurate improvements to the device cost and complication rate, improving the overall health-economic proposition.

**Methods:** The MiniVAD comprises a novel ‘T’ shaped layout with a motor rotor incorporated into the inflow cannula (implanted into the LV), and a compact centrifugal impeller that (outside of the LV but inside the pericardium). The performance of the MiniVAD has been evaluated in-vitro against a series of well-established metrics and also against novel assays developed by our group to gain better insight into haemocompatibility.

**Results:** Current performance, size and haemocompatibility results are: Power: <1 W/1l @ 100 mmHg

**Hydraulic characteristics:** 0-8 L/m average flow range with ‘flat’ curve (low shut off pressure and good preload/afterload sensitivity).

**Physical size:** <100 g weight; 15 mm depth x 35 mm diameter package (outside of heart, inside pericardium); 30 mm length x 22 mm diameter inflow cannula (implanted into LV)

**Leakage:** <0.02 g/100 L NIH, (bovine blood, 6 hrs loop test, 500 ml loop, 5 l/m)

**Platelet activation:** 11% compared to 9% in CentriMag and 6% in static control.

**Leukocyte damage:** 8% compared to 5% in Centri Mag and 6% in static control.

**Conclusions:** The haemocompatibility of the small, implantable MiniVAD is comparable to larger, extra-corporeal blood pumps such as the CentriMag and the Rotaflow. Further in-vitro evaluations are ongoing and in-vivo evaluations are planned for quarter four 2014.

**O20 DEVELOPMENT, VALIDATION AND USE OF A CFD MODEL FOR ITERATIVE DESIGN IMPROVEMENT OF THE CALON MINIVAD**

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**Abstract:** Develop and validate a computational fluid dynamics (CFD) model of the Calon MiniVAD, and use it to produce an impeller design with a flat pressure-flow (HQ) curve, maximum efficiency (η) and minimal shear stress.
Methods: A set of impellers were designed and built with identical blade shapes, but with differing heights. Flow domains were extracted from the CAD drawings and meshed. ANSYS CFX was used to calculate the blood flow. A discretization study was performed, and the effects of pressure-pressure vs pressure-flow boundary conditions, steady vs transient, time step and residuals sizes have been analysed. Flow fields were then calculated at points along the HQ curve and the estimated pressure heads were compared with those measured in an experimental flow loop. The validated numerical model was then used to implement a series of design improvements on the blade (shape, length, width, outlet/ inlet angle and number) and on the rotor geometry, volute, outlet pipe and secondary flow.

Results: As the height of the blades on the initial impellers increased from 1.5 to 4.5 mm the speed to reach the design point (100 mmHg and 5/6 min) decreased from 5,900 to 5,000 rpm. Characteristics at 10 l/min were: H<35 mmHg and η<12%. After the changes the design speed was reduced (4150 rpm) and the HQ curve was significantly flatter: at 10 l/min, H = 70 mmHg and η = 32%. Additionally pressure loss and shear stress have been decreased.

Conclusions: A validated numerical model of the Calon Mini/VAD has been developed and used to improve the characteristics of the pump.

O21 NUMERICAL SIMULATION OF A ROTARY PISTON TYPE TOTAL ARTIFICIAL HEART FOR THE DEVELOPMENT OF A NOVEL DRIVE AND BEARING CONCEPT S. J. Sonntag, J. Wappenschmidt, A. Goetzenich, U. Steinseifer, R. Autschbach
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Aim: In our concept study, a rotary piston pump is designed and evaluated for the use as Total Artificial Heart (TAH). The rotary piston design offers a pulsatile blood flow along with no need of heart valves. To support the development of a novel drive and bearing concept of the TAH design, a robust and efficient numerical Fluid-Structure-Interaction (FSI) model was developed. The simulation was used to identify the forces and momentums which must be applied to the rotary piston to meet the hydraulic needs for circulatory support.

Methods: The Immersed Boundary Method (IBM) was applied to simulate the piston motion. The model involves two immersed meshes (solid and fluid). During solving, the region of intersection is determined and the velocity inside the solid domain is constrained by applying a momentum source term.

Results: The hydraulic forces and momentums were concluded as the cause from the effect of the pressure and flow profiles and plotted as a function of the position of the rotary piston.

Conclusions: The proposed IBM method provides a robust and efficient alternative to computationally heavy and unstable mesh deforming techniques. Based on the simulation results, it was possible to determine the requirements for a suitable drive and bearing solution. Furthermore, critical locations in the design for hemolysis and thrombogenicity were identified and design optimization was performed accordingly.

O22 CIRCADIAN PUMP FLOW VARIATION IN ROTARY BLOOD PUMP RECIPIENTS M. Granegger1, T. Schliglohofer1, L. Muraldharan1, D. Zimpfer2, H. Schima1, F. Moscato3
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Aim: Overstimulation of the sympathetic system is typical for end-stage heart failure patients. For this reason the physiological circadian hemodynamic variability is diminished. Aim of this study was to investigate the circadian variability and long-term trends of the pump flow in the first 22 weeks after rotary blood pump (RBP) implantation.

Methods: In 20 RBP patients, estimated pump flow and speed signals, sampled every 15 minutes, were collected. The circadian variation in the pump flow signal was described by fitting a sine wave to each day’s pump flow signal and by determination of its amplitude. For the long-term trends, mean pump flow was calculated for each day.

Results: Mean hospital stay after implantation was 36 ± 10 days. Circadian variation in pump flow increased significantly during this first 5 weeks from a daily variation of 0.42 ± 0.16 L/min to 0.63 ± 0.25 L/min. After hospital discharge the mean circadian variation did not change significantly and was between 0.49 to 0.62 L/min. Mean pump speed did not change substantially throughout the whole observation period (range: 2760 to 2810 rpm), mean pump flow was between 5.2 and 5.5 L/min.

Conclusions: Circadian pump flow variability increased in the first 5 weeks after RBP implantation. This could indicate post-operative improvement of the cardiovascular function, which remains quite stable afterwards. However, it must be noted that the circadian rhythm could also be influenced by the daily physical activity which increases especially around the initial hospital discharge.

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Aim: The most critical component regarding the risk of the Reinhart total artificial heart (TAH) is the biocompatible membrane, which separates the drive unit from the ventricles. Hence a durability tester was designed to investigate its required 5 year lifetime. The aim of this study was to prove the validity of accelerated testing of this polyurethane membrane. Those in vitro tests are necessary, because animal trials will not permit sufficient prediction about a TAH’s lifetime.

Methods: The durability tester allows simultaneous testing of 12 membranes under physiological conditions. To accelerate the time of testing it operates with an increased speed at a frequency of 8 Hz. To prove the correctness of this acceleration, a servo-hydraulic testing machine was used to study the effect of different frequencies and their corresponding forces. Therefore the viscoelastic behaviour of the polyurethane could be investigated. Additionally, high-speed video measurements were performed.

Results: The force against frequency and the high-speed video measurements showed constant behaviour. In the range of 1 to 10 Hz the maximum resulting forces varied by 3% and the membrane movement was identical. A reduction of the membranes’ reset force from 8 h to 4.5 N after 220 million cycles was detected.

Conclusions: Frequencies below 10 Hz allow a valid statement of the membrane’s mechanical durability in the TAH. Viscoelasticity of the polyurethane in the considered frequency-range is negligible. The accelerated durability test is applicable to polyurethane membranes.

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Aim: Continuous flow ventricular assists device (VAD) drew the attention to VAD speed control development and testing. Aim of this work is to demonstrate the effectiveness of a hybrid (hydro-numerical) simulator (HCS) as a test bench for VAD autoregulation control.

Methods: The HCS is a computational cardiovascular model in which the left atrium and ascending aorta are connected in real time with the hydraulic part (impedance transformers). This permits to physically connect a Circuito Synergy® Micropump and to reproduce the HCS-VAD interaction in real time. The resulting inlet and outlet VAD pressures and VAD flow are sent to the ARU as inputs. This latter is a FPGA-based control unit allowing to adjust VAD speed remotely via Bluetooth or to automatically control VAD speed in order to keep VAD flow constant.

Results: HCS was used to reproduce an ischemic cardiomyopathy, the ARU was tested activating the VAD from 20000 to 26000 rpm via Bluetooth. Second, the ARU flow control was activated to 2 l/min and tested on the HCS reproducing ischemic cardiomyopathy, systemic hypertension and then hypotension. This caused a change of VAD afterload (74-94-49 mmHg) inducing ARU to automatically change VAD speed (25000-26000-24200 rpm).

Conclusions: The HCS, thanks to the connection to a real VAD and the reproduction of different pathologies, is a valid tool for testing different VAD speed control algorithms.

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Abstracts: XLI ESAO Annual Congress, 17-20 September 2014, Rome, Italy

**ORAL SESSION – TISSUE ENGINEERING AND REGENERATIVE MEDICINE 1, O25-O29**

**O25**

**ELECTROSPINNING OF SMALL DIAMETER VASCULAR PROSTHESES WITH FREELY ORIENTABLE FIBER DIRECTIONS**

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**Aim:** Conventional electrospinning suffers from uncontrollable fiber deposition. However, an increased control of fiber deposition would be beneficial for the fabrication of small diameter vascular prostheses to match the mechanical properties of the host vessel.

**Methods:** Vascular prostheses with an inner diameter of 2 mm were manufactured from a polyelectrolyteethane by our recently developed “dynamic deflection” electrospinning method. Four types of prostheses with longitudinal, circumferential, random and 30° fiber orientation were fabricated. Orientation effects were examined by optical means in the scanning electron microscope and by measuring the radial compliance of these constructs in the physiological range.

**Results:** Although complete straightness of the fibers was not achieved yet, macroscopic fiber alignment in the predominant direction of each selected orientation angle was observed. The grafts with longitudinal fiber orientation had a compliance of 15.6 ± 3.2%/100 mmHg, whereas the prostheses with circumferential orientation exhibit the lowest compliance of 6.1 ± 0.9%/100 mmHg.

**Conclusions:** Our work is focused on effects of DAG on vascular smooth muscle cells (VSMCs) and endothelial cells (ECs). In particular, the role of DAG on cell proliferation and differentiation, and also the anti-calcifying effect on VSMCs, have been studied.

**O26**

**LIPOSOME-ENCAPSULATED HEMOGLOBIN PRESERVES VO2 AND PROTECTS MYOCARDIAL AFTER MYOCARDIAL ISCHEMIA/INFARCTION AS A BIOLOGICAL ASSIST IN THE RAT**

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**Aim:** We tested the hypothesis that liposome-encapsulated hemoglobin (LEH) increases blood O2 content and maintains VO2 even at low cardiac output (LOS), simultaneously preserving hemodynamics and myocardium as assisting medication.

**Methods:** Effect of LEH was tested in 52 rats undergoing myocardial ischemia for 40 min and reperfusion for 40 min. Rats were randomly assigned to 3 groups after pretreatment with 10 mL/kg of LEH with high O2-affinity (P50 = 1 mmHg, n = 19), homologous RBC at the same amount as hemoglobin (RBC, n = 15) or saline (SL, n = 16). Cardiac function was determined by monitoring pressure-volume relationship, inspiratory and expiratory O2 and CO2 gas analyses, A-V blood gas analyses and evaluating endpoint immunohistochemically-determined area of myocardial infarction.

**Results:** After myocardial ischemia, stroke volume, ejection fraction, stroke work and cardiac output (CO) bounced back better in SL and RBC groups than LEH-treated rats, in which these variables remained suppressed during ischemia and reperfusion. The suppression in hemodynamic variables became significant in LEH rats compared with the SL group 20 and 40 min after reperfusion, when CO reversely correlated with A-V O2 difference as if it keep their products, or VO2, constant among the groups. LEH rats had a significantly smaller MI area (9.7 ± 9.1 mm2, P<0.05) than SL (20.8 ± 6.2 mm2) or RBC-treated animals (26.4 ± 14.2 mm2).

**Conclusions:** The results suggest that LEH pretreatment may preserve VO2 and spare cardiac compensation that further aggravates ischemia, thereby preserving myocardium undergoing ischemia and reperfusion, suitable for treating LOS and priming for mechanical ventricular assist device (VAO) as diagnostic assistance.

**O27**

**A SECOND-LOOK AT NERVE REGENERATION BY ARTIFICIAL NERVE-GUIDES IN HUMAN UPPER LIMB**

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**Aim:** Macroscopic observations of nerve regeneration in humans are rare. However, nerve-gap-injuries may be associated with lesions in other structures, like tendons or bones. In these cases, it is common to plan a second surgery to improve functional recovery. We exploited these second surgeries for the purpose of studying nerve regeneration in Humans.

**Methods:** We assessed the clinical outcome of 50 implants of collagen-based nerve-guides, which were implanted in the upper limb. We performed a “second-look” of 20, assessing macroscopically both nerve regeneration and collagen degradation.

**Results and Conclusions:** 1) pain was never recorded in these patients; 2) an adequate sensory recovery took place whenever a nerve-regenerate was found inside the guide; 3) motor recovery seemed to occur only when gap-lesion was shorter than 10 millimeters; 4) the degree of degradation appeared to be variable and not directly correlated with time; we make the hypothesis that it could be associated with the site of implantation.

**O28**

**EFFECTS OF DES-ACYL GHRELIN ON VASCULAR CELLS**

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**Aim:** Ghrelin is a 28-amino acid peptide existing in two major forms: n-Octanoyl-modified Ghrelin and Des-Acyl Ghrelin (DAG), an identical peptide in which the third amino acid serine is not acylated. Recently, ghrelin role in cardiovascular functionality has been discovered. Our work is focused on effects of DAG on vascular smooth muscle cells (VSMCs) and endothelial cells (ECs). In particular, the role of DAG on cell proliferation and differentiation, and also the anti-calcifying effect on VSMCs, have been studied.

**Methods:** VSMCs and ECs were isolated from porcine aorta and cultured with 10^-7 M DAG. Western Blot analyses were performed in order to evaluate the expression of proliferation and differentiation cell markers (PCNA, Myogenin and eNOS). Moreover, Real Time PCR was performed to evaluate the expression of the Osteocalcin gene (BGLAP). The anticalcifying effect was evaluated through a calcein assay on VSMCs cultured in calcifying medium with and without 10^-7 M DAG.

**Results:** Western Blot analysis showed the ability of DAG in controlling VSMCs’ proliferation while the expression of PCNA on ECs was not affected by DAG. VSMCs contractile phenotype was not affected by the presence of DAG, while ECs showed eNOS up-regulation in the presence of DAG. The expression of the BGLAP gene decreased in the presence of DAG with respect to control. Calcein assay confirmed the results.

**Conclusions:** Our work suggests an important role of DAG on VSMCs and ECs phenotype preservation. Moreover, also as an anti-calcifying effect for VSMCs has been established.

**O29**

**AMNIOTIC FLUID STEM CELLS AND CHRONIC KIDNEY DISEASE**

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**Aim:** Alport Syndrome (AS) is characterized by a hereditary form of glomerulonephritis, wherein an abnormal level of glomerular basement membrane is produced, gradually leading to interstitial fibrosis and eventual loss of renal function. At present, there is no definitive therapy to delay progression of renal failure. Current therapeutic options are limited to ACE inhibitors, dialysis and eventually transplantation, with end result that is far from being adequate. Stem-cell based therapies may provide alternative therapeutic opportunities. In this study we evaluate the role of amniotic fluid stem cells (AFSC) in a mouse model of AS.

**Methods:** AFSC were administered and blood and urine samples were analyzed for renal function. Kidneys were harvested at different time points and processed for histologic and molecular evaluation.

**Results:** Injected animals presented increased life span and lower albuminuria, creatinine and BUN along with lower levels of inflammatory cytokines. AFSC stimulated activation of M2 macrophages, involved in tissue remodel-ling. While preserving podocyte number, AFSC do not differentiate into podocytes and do not stimulate production of collagen IVα5, suggesting a paracrine/endocrine mechanism of action through modulation of the renin-angiotensin system.

**Conclusions:** AFSC are capable of slowing down the progression of AS by in-creasing structural and functional benefits to the kidney. These cells may present an alternative approach to treat medical conditions where currently therapeutic options are either limited or inadequate.
**O30** CREATION OF A BLOOD DAMAGE EVALUATION "HANDBOOK" – A SUITE OF IN VITRO HEMOCOMPATIBILITY TESTS FOR VENTRICULAR ASSIST DEVICES

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**Aim:** Our goal is to develop a comprehensive suite of blood damage testing methods that together amount to a handbook for the assessment of the overall in vitro safety profile beyond the standard haemolysis tests currently used. This could be used to optimise the design of blood-handling devices such as ventricular assist devices (VADs).

**Methods:** Multicolour flow cytometry (MFC) methods have been developed for: platelet activation, von Willebrand factor (vWF) activity as well as leukocyte viability/activation and microparticle formation. Biochemistry methods measure haemolysis and the contact-activation pathway of the coagulation caused by surfaces in the VAD. Finally immunoblotting is used to assess the degradation of high molecular weight vWF multimers. Absolute counting methods have been developed to quantify changes in the flow cytometry tests. All methods are developed from a multi-species approach for human/bovine/ovine/porcine blood to cover species normally used in the pre-clinical validation phase and to ensure results translate to the clinic. Species-specific differences are identified to ensure we chose the optimal species for the pre-clinical verification. The main instrument platform used is MFC because it is easily quantifiable, rapid and uses minimal sample volumes and all assays are validated using controlled levels of shear stress in rheometers.

**Results:** We have results that enable us to clearly show differences in haemo-compatibility between different blood pumps including RotaFlow, VentAssist, CentriMag and the Calon MiniVAD.

**Conclusions:** In summary, we herein present an approach to obtain a substantially better insight into damage to blood cells and proteins during in vitro testing of VADs.

**O31** FULL FACTORIAL MULTIVARIATE ASSESSMENT OF THE EFFECT OF PUMP GAP DESIGN PARAMETERS ON BLOOD TRAUMA

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**Aim:** Adverse events like bleeding, hemolysis and thrombosis are associated with the washout of pump gaps of rotary blood pumps (RBP). The aim of this study is to understand the quantitative effect in design parameters of pump gaps on blood trauma.

**Methods:** The flow in an axial gap is determined by the length, diameter, clearance, rotational speed, pressure difference and a potential force moving the impeller to an eccentric position. Assuming values for an LVAD, a full factorial investigation leading to 64 configurations was conducted by predicting the flow numerically. Due to the lack of eccentricity, 32 of 64 configurations are (Taylor-)Couette flows. A particle-based Lagrange-approach was employed estimating fluid and blood stress and residence time. Statistical significance was assessed by pooling effects of multi-factor interactions and quantifying the variance.

**Results:** The results correspond well to published experimental findings of comparable configurations of (Taylor-)Couette flows. Based on the experimental design, 34% of a statistical total damage is due to the gap size. Surprisingly, the pressure affecting the residence time plays an important role with 18% whereas the effect of a force (eccentricity) is not significant. Moreover, the relative effect of the diameter is more important than speed and gap size. Eight 2-factor interactions show significant results indicating the need to consider interdependencies.

**Conclusions:** The results yield substantial insight into the importance of design parameters for gaps in RBP. Further experimental investigations are planned to confirm and render the findings more precisely. The study suggests that an elaborate design of pump gaps can reduce adverse events and improve the patient's quality of life.

**O32** WALL SHEAR STRESS MEASUREMENTS IN A HEART MATE II VAD AT MULTIPLE STATES OF OPERATION

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**Aim:** During clinical application, blood pumps such as ventricular assist devices (VAD) can cause blood damage and thrombus formation due to shear loading of the blood. These adverse events occur mostly in the vicinity of walls. The objective is to assess the wall shear stress vector fields with an optical flow measurement method. This is taken as an indicator for the blood damaging potential, which is a function of the flow rate and rotational speed.

**Methods:** An upscaled model of a Heart Mate II VAD is investigated, which is based on the dimensions of an explanted HM II blood pump. The model is upscaled 3:1 in order slow down velocities. The wall particle image velocimetry (Wall-PIV) method permits to track particles moving with the flow close to the wall. From this movement wall shear stress can be assessed. In order to validate the assumed similarity between the original and 3:1 upsized model, throttle curves at three rotational speeds were estimated and compared applying Reynolds and Euler similarity.

**Conclusions:** This work demonstrates that the wall-PIV method can be used to obtain meaningful data at different states of operation of a commercially available LVAD.

**O33** A NEW COUETTE SHEARING DEVICE FOR THE INVESTIGATION OF SHEAR-INDUCED BLOOD DAMAGE

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**Aim:** Shear induced blood damage is the cause for complications in the clinical use of rotary blood pumps. Blood damage is known to be dependent on shear forces and exposure time. Both are highly dynamic and repetitive in blood pumps. Different concepts of Couette flow devices have been used to simulate the shear experienced by the blood. However, these investigations were focused on long exposure times and single stress exposure. Objective of this study is the design and experimental use of a device, which permits short exposure times of 25 ms and repeated use.

**Methods:** A rotational Couette flow chamber has been developed with a rotating outer cylinder to avoid Taylor vortices. The ranges of shear rates and exposure times were determined by Computational Fluid Dynamics (CFD) simulations of current blood pumps (Thoratec HeartMate II, Heartware HVAD). Geometric models have been obtained by dimensional measurement of explanted pumps.

**Results:** The shear device has a gap of 180 µm between two coaxial hollow cylinders and a diameter of 60 mm. It holds a blood sample of 4 ml. The outer cylinder is made of silicon coated precision glass. The inner cylinder is made of stainless steel. The drive is achieved by using torsion bars. By changing the number and twist angle of the torsion bars the stress exposure can be varied. With this shear device a field of high dynamic stresses in the range of these determined in the CFD simulations can be realized.

**Conclusions:** With the shear device concept highly dynamic and repetitive stresses as occurring in rotary blood pumps can be realized.

**O34** INVESTIGATION OF THE FLOW IN AN AXIAL BLOOD PUMP WITH THE PAINT EROSION METHOD

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**Aim:** Pump thrombosis and thromboembolic events are serious complications related to the clinical use of ventricular assist devices (VAD) and are also seen in the Thoratec® HeartMate II™VADs (8.4% after 3 months reported by Starling et al 2014). Thrombus formation is likely to happen in flow separation and stagnation zones. Objective of our study was to assess the near wall flow of the device.
This is achieved experimentally with the paint erosion method. Also, computational fluid dynamics (CFD) simulations were performed.

**Materials and Methods:** From an explanted VAD a CAD model was established, fabricated scaled up three times and integrated in an experimental setup. The surfaces of flow straightener, rotor and stator were painted with a mixture of turpentine and oil paint. In accordance with the similarity laws, different operating points corresponding to physiological pressure build-ups were investigated. A run of 6 min was recorded with a video camera. In addition, the pump was investigated by transient numerical simulations using sliding mesh and a k-omega SST turbulence model.

**Results:** With the paint erosion method typical flow patterns on the pump surface could be visualized. A recirculation zone downstream the flow straightener was identified. The experiments are in good agreement to the CFD results.

**Conclusions:** Recirculation regions in a HeartMate II model were shown experimentally by the paint erosion method and CFD calculations. These regions may be prone to thrombus formation.

Q35

**IN VITRO THROMBOSIS RESULTING FROM SHEAR RATE AND BLOOD COAGULABILITY**
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**Aim:** In vitro antithrombogenic testing with a mock circulation is a useful pre-evaluation for an ex vivo testing of a mechanical assist devices. In order to establish the in vitro testing, we have been making clear a quantitative thrombosis model resulting from shear rate and blood coagulability using a rheometer, and apply to experimental conditions of the in vitro testing.

**Methods:** Bovine blood was used as a testing blood, and the activating clotting time (ACT) was adjusted with trisodium citrate and calcium chloride from 200 to 1,000 s, and applied to a rheometer followed by sheared at between 100 and 2,880 s⁻¹. Blood coagulation time and the amount of thrombus was measured by the torque sensor of the rheometer. Prothrombin time (PT) and activated partial thromboplastin time (APTT) of the testing blood were also measured after sheared.

**Results:** The blood coagulation time increased and the degree of thrombus amount decreased, with an increase of shear rate at between 50 and 2,880 s⁻¹ for the testing blood with an ACT of 200-250 s. Then, the ACT of 200-250 s was considered to be appropriate coagulability condition for in vitro antithrombogenic testing, and the increasing shear stress generated in a mechanical assist devices reduce thrombosis through the intrinsic clotting system.

**Conclusions:** The ACT between 200 and 250 s was suitable condition for the in vitro antithrombogenic testing, and the increasing shear stress generated in the mechanical assist devices reduce thrombosis through the intrinsic clotting system.

Q36

**A NEW APPROACH FOR SEMI-EMPIRICAL MODELLING OF MECHANICAL BLOOD DAMAGE**
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**Aim:** Evaluation of blood trauma in devices e.g. internal artificial organs, is considered as one of the major parameters for modelling and designing. The current models, Continuous and Threshold models are defined based on empirical correlations. Also recently introduced two alternative semi empirical models (SEM) which are based on a “physical” problem description, demonstrate still deviation in comparison with experimental data. Here we introduce a modified semi-empirical approach in order to get closer to the already achieved experimental data on red blood cell (RBC) trauma.

**Methods:** A combined SEM is here applied as haemolysis caused by a) membrane permeation of RBC and b) membrane breakdown. This definition is as a weighted average damage index of both permeation and non-uniform threshold models. For experimental validation, we developed a high shear Couette device using native blood.

**Results:** The results demonstrate that here presented model predicts, by taking the dominated phenomena into account in a wide range of shear stress i.e. up to 610 Pa, a high fitting behaviour toward the experimental data. Furthermore, it is shown that the consideration of simultaneous effect of physical phenomena minimizes the deviations down to 5%.

**Conclusions:** Analysis of the presented model confirms its potential applicability for the prediction of blood damage in connection with development of blood contacting devices or artificial organs.

**ORAL SESSION – TISSUE ENGINEERING AND REGENERATIVE MEDICINE 2, O37-O43**

Q37

**INFLUENCE OF SURFACE ROUGHNESS PARAMETERS ON MG63 CELL VIABILITY: A STUDY ON LASER MICROTEXTURED Ti6Al4V SURFACES**
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**Background:** Surface roughness of biomedical implants is important in determining the biocompatibility of the implant. Average roughness (R_a) is the most commonly used surface roughness parameter, but it does not describe the exact nature of roughness of the surface. Though a range of the average surface roughness has been identified that is suitable for being suitable for implants, often contradictory results support. In this study, laser microtextured surfaces have been studied to find out the correlation between MG63 cell viability and different 3d surface roughness parameters.

**Methods:** Laser microtexturing was done on Ti6Al4V surface to create grooves with ~20 µm depth, ~200 µm width. MG63 cells were cultured on three types of microtextured surfaces, which had similar R_a value. Cell counts after 3 and 5 days, found from MTT assay, were correlated with the 3d surface roughness parameters like skewness, kurtosis etc.

**Results:** Statistical analysis showed that the consideration of simultaneous effect of physical phenomena for cell adhesion in case of surfaces having similar R_a, Projected area ratio, skewness, etc. also had strong correlation with cell viability.

**Conclusions:** Higher kurtosis value means sharp peaks are present at the surface profile. As a result, surface charge density will be higher in the peaks, which may lead to adherence of cells to those peaks. This can be a possible explanation of the higher adherence of cells to the surfaces with higher kurtosis, as found in this study.

Q38

**GENERATION OF HIGHLY PURE PHYSIOLOGICALLY AND PHARMACOLOGICALLY FUNCTIONAL SINUS-NODAL-BODIES FROM PLURIPOTENT STEM CELLS**
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**Aim:** The "sick sinus syndrome" comprises pathological, symptomatic sinus bradycardia, sinoatrial block, sinus arrest as well as the tachycardia-bradycardia syndrome. Therapy relies on electrical pacemakers. However, the latter lacks hormone responsiveness and bears hazards such as infections and battery failure. This may be overcome via "biological pacemakers" derived from pluripotent stem cells (PSCs).

**Methods:** Our group has previously shown that "forward programming" of pluripotent stem cells towards specific cardiomyocyte sub-types is feasible via overexpression of distinct early cardiovascular transcription factors such as Msx1 (early/intermediate type cardiomyocytes) and Nkx2.5 (ventricular cells). In order to generate pacemaker cells, we used the T-box transcription factor Tbx3, as it is required for normal size and function of the sinoatrial node (SAN). Tbx3 is a transcriptional repressor acting to suppress the atrial myocyte phenotype and therefore specifying SAN versus atrial cells.

**Results:** Here, we first demonstrate directed differentiation of PSCs which leads to cardiomyocyte aggregates consisting of over 80% physiologically and pharmacologically functional pacemaker cells. These induced sinoatrial bodies (ISABs) exhibited highly increased beating frequencies (300-400 bpm) for the first time close to mouse hearts. Additionally, performed Ca²⁺ measurements showed Calcium gradients typical of pacemaker cells. Our ISABs were able to robustly pace myocardium ex vivo. In addition, we have started RNA-Seq to define the ISAB transcriptome with the vast majority of ontologies related to heart function/development and to structures of contractile cells.

**Conclusions:** Overall, we provide the first example of highly pure functional cardiac pacemaker tissue derived from stem cells, a crucial step towards future cell therapy and drug-testing in vitro.

VASCULAR GRAFTS

TRITON-TRIPPLE NITINOL-CELLULOSE-MODIFIED SMALL DIAMETER O40 pericardium in cardiac surgery including congenital cardiac surgery. We evaluated the implanted beagle dogs 7 days (n = 2), 30 days (n = 2), and 3 months (n = 2) after the patch repair. No aneurysmal change was administrated after implantation.

Methods: Silicone rod molds (diameter 8 mm) were embedded into dorsal subcutaneous pouches of beagle dogs (10 kg). After 8 weeks, we harvested the molds covered with connective tissue, and obtained the connective tissue tube (Biostub) by removing the rod molds. The Biotubes were cut open and sheeted, which had almost equal strength compared to autologous pericardium. Under general anesthesia right thoracotomy was made. We created a right atrial defect (size: 20 mm × 10 mm) by using a side-binding aortic clamp and closed the defect with a Bio-Sheet patch. No antiplatelets or anticoagulants were administered after implantation.

Results: We evaluated the implanted beagle dogs 7 days (n = 30), 30 days (n = 2), and 3 months (n = 2) after the patch repair. No aneurysmal change was found in the Bio-Sheet patches macroscopically. In histological evaluation, the luminal surfaces of the Bio-Sheets were completely covered with endothelial cells without formation of intra-atrial thrombosis after 3 months.

Conclusions: Bio-Sheet, which can be made and implanted easily showing a fine mid-term result, may have potential to be used as a substitute for self-pericardium in cardiac surgery including congenital cardiac surgery.

O40

TRITON-TRIPPLE NITINOL-CELLULOSE-MODIFIED SMALL DIAMETER VASCULAR GRAFTS

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Objective: According to the WHO report in 2012, atherosclerosis-related diseases are known to cause over seven million deaths a year worldwide. For patients undergoing surgical treatment of diseases such as atherosclerosis, bypass material is urgently needed as to up to 25% of patients lack suitable bypass material. Previous materials and designs had shortcomings specific to small diameter application. This project aims to construct an artificial graft suitable for the small diameter clinical application in the near future. Clinical translation through design and practical handling are key points as well as in vivo endothermalization without preseeding.

Methods: A 3.5 millimeter nitinol mesh is coated in a novel rotation reactor with a specific type of inert and antithrombogenic cellulose synthesized by using an Acetobacter strain. Different series, in terms of media composition as well as culture settings, of total 35 vessels are analyzed according to burst strength, cell morphology, and a new prolyl-specific peptidase (PsP) from fungus 

Conclusions: The relative lacunarity function (RLF) was adopted to minimize the influence of varying porosity on scaffolds architecture heterogeneity.

Results: The presence of the BG component affects both (1) porosity, S1 is characterized by higher porosity (81%) than S2 (70%) and S3 (88%), demonstrating that the deposition of BG particles on the pore walls has the consequence to reduce the available void area, and (2) heterogeneity, in fact S3 presents higher spatial heterogeneity than S1 and S2, as confirmed by the RLF analysis, and a scale of randomness which is slightly wider than for S1. This higher heterogeneity could be ascribed to the higher content of BG particles with respect to S1 and S2, that cause micropore occlusion.

Conclusions: The adopted approach allows to investigate the scale-dependent spatial pore distribution over the 3D reconstructed scaffold models and to catch related structural heterogeneity features, providing a comprehensive characterization of the scaffold texture.

O42

CELL BEHAVIOUR IN SANDWICH-LIKE CULTURES

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Objective: The distribution of cell receptors anchored to the 2D surface of biomaterials highly differs from that observed in the extracellular matrix (ECM) in vivo, which triggers a different, less physiological, cell response. Hence we suggest that sandwich culture, that targets ventral and dorsal receptors, could be a robust system to study cell behaviour in 3D environment more similar to the ECM.

Methods: Cells were seeded on 2D substrates and immediately or after 3 hours of culture, sandwich-like cultures were obtained by gently laying the upper (dorsal) substrate. Cell morphology, adhesion, migration and differentiation were studied under different conditions by changing the substrates or protein coatings (both in the ventral and the dorsal side).

Results: Our results suggest that both biological and mechanical stimuli within sandwich-like culture play an important role in cell behaviour that resembles 3D systems. For example, the ability to reorganise the ECM in sandwich culture has been shown to influence cell adhesion and morphology similarly as in hydrogels. Cell migration also differs to 2D substrates and can be tuned according to the culture conditions (substrates and protein coatings). Finally, sandwich culture increased myogenic differentiation and further experiments are being carried out in order to better characterize the process.

Conclusions: Our results support the hypothesis that sandwich culture can be used as a versatile intermediate system between 2D and 3D cultures and has the potential to provide further insights into the role of dimensionality in cell-material interactions.

O43

NEW ENZYMES AND HARVESTING STRATEGIES FOR THE PRODUCTION OF HMSC THERAPEUTICS

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Objective: The cell harvest step is of great importance in hMSC manufacturing. In contrast to the manufacturing of other therapeutics (e.g. antibodies), hMSCs contrast to the manufacturing of other therapeutics (e.g. antibodies), hMSCs must stay viable and unaffected. As required by the authorities, detachment of culture, sandwich-like cultures were obtained by gently laying the upper (dorsal) substrate. Cell morphology, adhesion, migration and differentiation were studied under different conditions by changing the substrates or protein coatings (both in the ventral and the dorsal side).

Results: Our results suggest that both biological and mechanical stimuli within sandwich-like culture play an important role in cell behaviour that resembles 3D systems. For example, the ability to reorganise the ECM in sandwich culture has been shown to influence cell adhesion and morphology similarly as in hydrogels. Cell migration also differs to 2D substrates and can be tuned according to the culture conditions (substrates and protein coatings). Finally, sandwich culture increased myogenic differentiation and further experiments are being carried out in order to better characterize the process.

Conclusions: Our results support the hypothesis that sandwich culture can be used as a versatile intermediate system between 2D and 3D cultures and has the potential to provide further insights into the role of dimensionality in cell-material interactions.

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Results: Conventional trypsin showed disadvantages for hMSC harvest from dynamic bioreactor systems. New enzyme candidates like Accutase or the PsP showed comparable or even better results in detachment time and efficiency than standard trypsin. While harvest in a closed system was unproblematic for FBR expansion, a STR was modified to allow carrier-based expansion and enzymatic detachment of hMSCs from carriers within the same closed system.

Conclusions: The study showed that new promising enzyme candidates for hMSC detachment are available. Nonetheless, it is still necessary to study hMSC harvest in dynamic systems because the results from static culture experiments cannot be adapted to dynamic culture. Undoubtedly, hMSC expansion and harvest in dynamic systems is key to success of cell therapy.

O44 CRANIAL CRUCIATE LIGAMENT RUPTURE: A MULTI-BODY ANALYSIS COMPARING CORRECTIVE TIBIAL OSTEOTOMIES
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Aim: The aim of this study is to consider a new kind of tibial osteotomy for the treatment of Cranial Cruciate Ligament (CrCL) deficient stifles, that is the so-called Center Of Rotation of Angulation Cora Based Leveling Osteotomy (CBLO), and to compare its outcome with the Tibial Plateau Leveling Osteotomy (TPLO), one of the most currently used osteotomies.

Methods: A Sawbones® model of a canine right knee was used to generate the IGES geometries by means of a laser scanning system. The model included femur, tibia, fibula, menisci, patella, patellar ligament, medial and lateral femoro-patellar ligaments, tendon of insertion of the quadriceps muscle group, cruciate ligament. Solidworks® was used to perform the tibial osteotomies and to identify the insertion and origin points of the ligaments. Four multi-body models of the stifles were then created in Adams®. They included the femoro-tibial joint (FTJ), ligaments and contact forces. These four models represented a physiological, CrCL-ruptured, post-TPLO, post-CBLO stifle, respectively. Finally, a cranial drawer test was performed by applying a 44.5 N force to the tibia with or without applying a force to compress the femur against the tibia.

Results and Conclusions: There was no significant difference between the pathologic and post-surgery condition for a compressive force inferior or equal to 44.5 N, while only 30 N were reached, even when the CrCL is intact, unless the compressive force reached 150 N. Osteotomies outcomes are far better than pathologic condition. With reference to the comparison between TPLO and CBLO, the latter proved to be more stable.

O45 A NOVEL NON-FUSION SCOLIOSIS CORRECTION SYSTEM
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Aim: Surgical treatment of scoliosis generally results in an almost completely rigid spine and can only be done after growth. We developed a revolutionary non-fusion correction system which slowly, but persistently corrects. It is expected to correct the axial rotation of the spine. Due to coupled motion, lateral bending is corrected as well. To deliver the appropriate torque, the system is pre-stressed before final anchoring to the spine. The system is fixed to only three vertebrae via cross-bridges.

Methods: To test the mechanical strength and performance, the XS-TOR was anchored to three metal vertebrae containing 6D force sensors, after which several spinal configurations were simulated and the reaction forces and moments were recorded. Animal experiments were performed with an inverse version of the implant that induces scoliosis instead of correcting it, since animals do not have scoliosis.

Results: The XS-TOR generated a correction torque that remains constant during growth and correction, due to a special design feature. The increase in spinal stiffness is very limited, only 0.01-0.03 Nm/° in bending and 0.04-0.08 Nm/° in torsion. All animal experiments ended successfully. Scoliosis was induced, spinal growth was not inhibited and fusion of the spine prevented.

Conclusions: The XS LATOR is able to create scoliosis, a change in both torsion and lateral bending, is able to allow spinal motion and growth, and does not induce vertebral fusion. The XS-TOR induces torsion as well as lateral deviation and we expect that it is, therefore, also capable of correcting it. We expect that the system behaves as intended in scoliosis correction. This means that a new way of treating scoliosis is possible, starting already during growth when scoliosis is less severe and ending after growth by removing the system.
modulate the characteristics of these structures. These include electrospinning (espin) methods such as Coaxial E-spin which enables the encapsulation of various drugs into the core of the fibers.

Methods: Both single jet and coaxial jet E-Spin were use to produce fibers. Polycaprolactone (PCL) and Aspirin (ASA) were dissolved in 2,2,2-Trifluoroethanol (TFE) at concentrations of 150 mg/mL and 15 mg/mL respectively for the single jet E-Spin. For the coaxial jet E-Spin the same solution was used both for the core and the shell (without ASA in the shell solution). Structure and morphology of the fibrous scaffolds were examined by Scanning Electron Microscopy (SEM). Uniaxial dynamic mechanical testing was performed to investigate the mechanical properties of the fibers. To study the cumulative release of ASA, samples were incubated in PBS (pH 7.4) at 37°C inside a water bath and the absorbance was measured by using a UV-Vis spectrophotometer.

Results: The coaxial approach resulted in fibers with an average diameter of 680 nm and an average pore size of 9.09 µm while the values of Elastic Modulus and Stress at 30% Strain were 64.89 MPa and 6.63 MPa, respectively. Moreover, the amount of drug released in the first 8 hours was reduced from 58.32% to 33.14% and the encapsulation efficiency increased from 34.36% to 86.13% in contrast to single jet fibers following a Fickian diffusion in both cases.

Conclusions: Coaxial E-spin can be utilized as a technique to encapsulate hydrophobic pharmaceuticals inside biodegradable scaffolds for clinical applications in drug delivery.

O49 COMBATING INFLAMMATION AND INFECTION THROUGH TAILORED NANOSTRUCTURED DESIGN
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Aim: There are major global healthcare issues associated with the rising incidence of non-communicable diseases and the need to reduce dependence on antibiotics. Our aim has been to develop a range of pure and composite nanoporous sorbent systems in different structural forms which can absorb biological toxins and microbial contaminants. Such therapeutics offer the potential for cost effective and efficient treatments to target adsorption of the instigators of infection and inflammation.

Methods: A range of polymer resin derived adsorbents with nanoporous domains in bead and monolith form were characterised using SEM and porosimetry. Cell models were used to assess biocompatibility. Removal of toxins, including inflammatory cytokine TNF, microbial endotoxin, acetaldehyde were measured by HPLC, ELISA, LAL assay and flow cytometry.

Results: Nanoporous domains allowed adsorption of high molecular weight inflammatory molecule TNF and gram negative bacterial endotoxin. Low molecular weight and protein bound toxins were adsorbed to some extent by adsorbents with porous domains of less than 2 mm but adsorptive capacity was significantly increased (p<0.01, n = 3) using advanced nanoporous materials with superior surface area and porous domains for adsorption.

Conclusions: Pure and composite nanoporous sorbent systems may be designed in a range of structural forms for extracorporeal, oral and dermal delivery to adsorb biological toxins, microbial contaminants and suppress excessive inflammatory stimulus.

O50 POLYELECTROLYTE ASSEMBLY ON NANOSTRUCTURED BIOMATERIAL SURFACES
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Aim: A system with unique surface properties was designed here using nanosphere lithography (NSL) and layer-by-layer (LbL) technique. Owing to its ability to guide not only cell adhesion, but also growth and differentiation, a potential application in regenerative medicine is aimed.

Methods: Tetrahedral gold nanostructures of different dimension were obtained by varying the size of colloids during NSL. Dip as well as spray coating were employed to modify the nanostructures with polyelectrolytes (PEL) of different origin (e.g. poly (ethylene imine) (PEI), heparin (HEP), etc.) by controlling their pH value. Pristine and modified nanostructures were intensively characterized using various methods (AFM, SEM, and WCA). Further, the cellular response to such unique systems was investigated using immunochemistry.

Results: Nanostructure size and distance clearly influenced the surface wettability. Moreover, the effect was even more pronounced introducing PEL, which also affected the surface charge. Hence, the nanostructured surfaces could be rendered highly hydrophilic (HEP) or moderately wettable (PEI) controlling feature dimensions as well as the terminating molecule. Further, cells responded positively to the surface chemistry (HEP) as well as topography (PEI).

Conclusions: We show that gold nanostructures on planar surfaces could be specifically modified with a PEL system. Due to their economic effectiveness as well as simplicity, both techniques could be applied to develop unique systems for stem cell therapy.

O51 DESIGNING A NOVEL BIODEGRADABLE CYANOACRYLATE-BASED TISSUE PATCH
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Aim: Management of post-surgical leaks from different organ systems is a perennial concern. Existing tissue sealants are composed of fibrin-based sealants, synthetic compounds, or glutaraldehyde-albumin cross-linked systems. Each one of these compounds presents benefits and drawbacks for the surgical management of post-surgical leaks. This talk aims to report on a novel biodegradable tissue patch under development as another tool for the management of post-surgical leaks.

Materials and Methods: We synthesized and characterized a family of polyurethane copolymers composing polyethylene glycol and polycaprolactone to function as the patch backing. The bulk material was processed into films and fabrics and both were solvent welded together. Monomeric cyanoacrylate was added to the surface layer of the fabric and functioned as the active layer. The adhesive strength of the patch prototypes were tested on bovine tissue as a model. The degradation rate for the patch prototypes were tracked by placing them in PBS in a 37°C incubator.

Results: The synthetic tissue adhesive patches had a tensile modulus on the order of magnitude of soft tissue and displayed an adhesive strength of 10.1 ± 2.6 N, surpassing that of the biological glues.

Conclusions: The prototype patches exhibited adhesive strengths on par and better than the existing tissue adhesives, on a human tissue model. The in vitro patch degradation was tailored according to different material compositions to span a range of rates.

O52 HYDROPHOBICALLY-MODIFIED GELATIN BASED ADHESIVES WITH HIGH BONDING STRENGTH AND BIOCOMPATIBILITY
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Aim: Tissue adhesive is a biomedical material that can bond tissues together after surgical operations. However, these commercial adhesives still have disadvantages on bonding strength and biocompatibility. The aim of this study is to develop biocompatible tissue adhesives with high bonding strength using hydrophobically-modified gelatin.

Methods: Hydrophobically-modified gels with different hydrophobicity and introduction ratio were prepared by the reaction of active ester of fatty acid chloride or cholesteryl chlorofomate with the primary amine of gelatin. The measurement of bonding strength was performed using fresh arterial media as an adherent. Quantitative determination of tissue reaction after implantation of tissue adhesive was also performed using NF-kB/luciferase transgenic (NF-kB/luc tg) mice.

Results: Tissue adhesives composed of hydrophobically-modified gelatin and biocompatible crosslinker were developed. Resulting adhesives had 2-fold higher bonding strength compared with commercial adhesive. Cross sectional views revealed that developed adhesives still remained on the surface of arterial media even after bonding strength measurement. These adhesives also showed excellent biocompatibility, bioabsorbability and only mild tissue reaction in a rat subcutaneous tissue model.

Conclusions: Developed adhesives can be applied in the field of not only cardiovascular surgery but also chest surgery.
Abstracts: XLI ESAO Annual Congress, 17-20 September 2014, Rome, Italy

**O53 PROSPECTION OF IMPLANT BASED ON NONSTRUCTURED MEMBRANES ASSOCIATED WITH DOPAMINERGIC NEURONS - AUTOLOGUE PURPOSE FOR TREATMENT OF PARKINSON DISEASE**
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**Aim:** To develop of implant based on nonstructured membranes seeded with dopaminergic neurons from human adipose-derived mesenchymal stem cells (h-ADMSC) for treatment of Parkinson Disease.

**Methods:** Development membrane, the total mass based on dried films was performed according to the commercial samples donated by MEMBRACEL®. In addition, the inclusions of drugs (lysozyme-LZ and/or fluconazole-FZL), with antibacterial and antifungal properties, are also evaluated in these systems. The bioinonanocomposites were obtained after defibrillation using a never-used bacterial cellulose (BC) to form a pulp and the films of BC regenerated (RBC), in the presence or not of the hydrocolloids: tamarind xyloglucan-XG or gellan gum-GL or collagen-C (10% w/w) and/or drugs (10% w/w) were developed by dry casting (Patent). In vitro assays were performed to test for adhesion and proliferation with the h-ADMSC from human adipose liposuction. Then, those cells, 1 x 10⁵/cm² were seeded and differentiated to dopaminergic neurons in established medium conditions and time, maintained in an Incubator with 5% CO₂ at 37°C (Patent); thereafter, it was analyzed the dopamine production by ELISA assay for allowing the quantification of their production. Optical and Electron Microscopies were done in membrane and cells. The Flow Cytometric analysis was done in h-ADMSC fraction and tri-lineage pluripotency test. The immunassay was done to demonstrate the dopaminergic neuron differentiation by ß-tubulin and Tyrosine Hydroxylase.

**Results:** RBC-tamarind xyloglucan nanostructured membrane incorporated with lysozyme presented the best performance in adhesion and proliferation tests as 35.3% more efficiency than the control. The h-ADMSC has differentiated to dopaminergic neurons on the membrane and those cells were able to produce 1.0 ng/ml of dopamine.

**Conclusions:** The results allow the utilization the developed implant in preclinical studies of Parkinson Disease Model.

*Financial supports: CAPES.*

**O54 NEW GENERATION OF THE HOLLOW FIBRE MEMBRANES FOR DIALYSIS TREATMENT**
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**Aim:** Mixed matrix membranes (MMMs), which combine the benefits of adsorption and filtration in one step, represent a novel concept for blood purification. Current research is focused on fabrication and optimization of double layer hollow fibre membranes, which consist of a particle free inner layer attached to the MMM outer layer.

**Methods:** Polyethersulfone/polyvinylpyrrolidone polymer blend was used as membrane forming material for inner and outer layer of the hollow fibre. As the adsorptive particles, activated carbon was incorporated into the outer polymer matrix in order to provide enhanced removal of blood toxins. Membrane characterization was performed by scanning electron microscopy (SEM) and clean water flux (CWF). Additionally, adsorption experiments of various toxins under static and dynamic conditions were performed to estimate the adsorptive properties of newly fabricated membranes.

**Results:** Based on previous experience of our laboratory, double layer MMMs were fabricated and spinning parameters were optimized. Specifically, the diameter of the hollow fibre membranes was decreased by using different spinneret type. Additionally, influence of polymer and bore liquid composition and pumping speed was tuned to obtain membranes with properties suitable for dialysis. Conclusions: Decrease in hollow fibre diameter improves surface to volume ratio of hollow fibres, which results in improved efficiency of dialysis.

**Acknowledgements:** This work is financially supported by the EU Marie Curie ITN – BIOART Project.
O57 MONITORING OF GLUCOSE CONSUMPTION AND LACTATE PRODUCTION BY ENDOTHelial CELLS CULTURED IN CAPILLARY MEMBRANE BIOMATERIALS
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Aim: The objective is to monitor glucose consumption and lactate production by human umbilical vein endothelial cells (HUVEC) cultured in capillary membrane biomaterials to be used as a model of a blood vessel.

Methods: Isolated HUVECs were cultured in modified Medium 199. After the second passage, HUVECs were introduced into bioreactors in different quantities (2, 4, 6, and 15 x 10^4 cells per cm^2). Bioreactors were rotated for 4 h to seed cells on the inner surface of capillaries. We used original bioreactors with 14 polysulfone capillaries, inner diameter of 640 µm and total surface area of 16.3 cm^2 covered with fibrinectin to promote cells attachment. HUVECs were subjected to the shear stress resulting from medium flow generated by a peristaltic pump. Glucose and lactate were measured every 24 h in the circulating medium for 4 days.

Results: Glucose consumption was the highest during the first day of culture and then it stayed relatively stable. Lactate production was stable during the whole monitored period in all cultures but the one with 150,000 cells per cm^2. In this case, cells produced 3.5 times more lactate during the first day than in the other cultures, which might be attributed to a limited oxygen supply for such an amount of cells.

Conclusions: The obtained results suggest that HUVECs can be safely seeded in the assessed bioreactors with densities ranging from 2 to 6 x 10^4 cells/cm^2 and that cell cultures stabilize after 24 to 48 h.

O58 BIOPHYSICAL CHARACTERIZATION OF NATIVE WHARTON’S JELLY FOR TISSUE ENGINEERING APPLICATIONS
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Background: The mechanical properties of a regenerative biomaterial are fundamental to define critical design considerations for implant success. A natural biomaterial of great potential is native Wharton's Jelly (nWJ), rich in proteoglycans, collagens and perinatal stem cells. To date, little is known on its mechanical characteristics despite their importance in developing innovative nWJ-based therapies.

Methods: nWJ was harvested from 5 UCs and mechanical characterization was carried out using atomic force microscopy (AFM) and shear rheology. AFM indentation curves were measured using 5 µm ramp sizes at a scan rate of 0.5 Hz and Young's modulus was calculated using the Hertz model with a Poisson's ratio of 0.4. Dynamic and steady shear rheology experiments were performed to measure the viscoelastic moduli (G', G'') and shear viscosity (η), respectively.

Results: AFM of nWJ yielded a Young's modulus range consistent with that of some of the body's softest tissues (e.g., brain). Elastic and viscous moduli (G', G'') of nWJ increased with increasing frequency, indicating that the tissue stiffens in response to mechanical stress. Furthermore, the shear viscosity (η) showed an inverse dependence on shear rate, which indicates a shear thinning behavior.

Conclusions: nWJ is a natural 3D biomatrix with elastic and resilient thixotropic properties that are desirable for potential applications in tissue engineering.

O60 INTEGRATED BIOPATIBILITY CHARACTERIZATION OF TUBULAR SCAFFOLDS FOR VASCULAR TISSUE ENGINEERING
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Background: Scaffolds for vascular tissue engineering have to meet specific biocompatibility requirements regarding mechanical properties, cellular response and overall haemocompatibility. Since proper preparation and mounting of electroporations matrixes is crucial for the various analyses and particularly time-consuming, a reliable device needs to be developed for standardizing test procedures.

Methods: Three-layered electroporated tubular scaffolds with an inner diameter of 4 mm spun from PCL/PLA (I) or PCL/PLA/PEG (II) were used for all experiments. A single simplified mounting mechanism was developed and evaluated in a comprehensive sequence of experimental analyses regarding cell seeding, mechanical data, biocompatibility and cell viability.

Results: Mechanical properties decreased with the addition of PEG to the polymer blend, demonstrated by a reduction of tensile strength from 5.8 MPa (I) to 3.9 MPa (II). Young’s modulus increased in circumferential (7.6 MPa/7.5 MPa) as well as in longitudinal direction (40.1 MPa/29.8 MPa). Furthermore, an influence of fiber diameter on the haemocompatibility could be observed, since scaffolds with thinner fibers caused a significant decrease in number of platelets in dynamic haemocompatibility testing. Endothelial cell seeding (RBE-4) of PCL/PLA scaffolds led to a confluent monolayer after 7 days of cultivation, proved by fluorescence microscopy.

Conclusions: We developed a combination of methods and devices that enable a broad characterization with optimized work flow for parameter studies. The mounting mechanism provides a simplified, standardized interface not only for electroporated scaffolds but for all kinds of fragile porous scaffolds, e.g. from directional solidification.

O61 BIOREACTOR-BASED MODEL PLATFORM FOR CARDIAC TISSUE
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Aim: A bioreactor-based model platform was developed for culturing cardiac constructs in a native-like environment and for investigating cardiac tissue developmental aspects and factors that influence the generation of functional cardiac tissues.

Methods: The platform is composed of: (1) a stand-alone sensorized bioreactor, which provides cyclic stretch and on-line monitoring of culture parameters; and (2) 3D fibrin engineered heart tissue (iET) rings, acting as cardiac pseudo-tissues. The culture chamber is equipped with sensors (temperature, pH, and CO2%O2) and a heating strip, and can house up to three iET rings. The mechanical stimulation unit supplies controlled cyclic stretch (1-200% deformation, 1-6 Hz frequency). The monitoring/control unit allows real-time monitoring and control of the stimulation unit and chamber temperature. The operating conditions are set and monitored by a purposely-built software. As for the iET rings, neonatal rat cardiomyocytes were mixed with fibrin and medium, cast into circular moulds, incubated for 48 hours, and finally dynamically cultured.

Results: In-house tests confirmed the effectiveness of chamber isolation, mechanical stimulation unit, and monitoring/control unit. iET rings were obtained and characterized by histological analyses before and after physiological...
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O62 DESIGN AND QUALIFICATION OF A SINGLE-USE STIRRED BIOREACTOR FOR THE EXPANSION OF HUMAN MESENCHYMAL STEM CELLS AT BENCHTOP SCALE
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Objective: For a broad range of therapies there is clearly a growing interest in human mesenchymal stem cells (hMSCs) isolated from adipose tissue and bone marrow. However, this trend is accompanied by the need for a large number of cells of consistent quality and thus alternatives to the prevailing planar cultivation systems, which are non-instrumented and limited in scale. Stirred bioreactors operated with solid and porous microcarriers at benchtop and pilot scale have shown promising results. Recently, published results have indicated the advantages of single-use versions, even though these were originally designed to grow more robust continuous cell lines (e.g. CHO cell lines).

Methods: To improve cultivation conditions for human adipose tissue- and bone marrow-derived hMSCs when generating therapeutically relevant cell numbers for autologous cell therapies with microcarrier solid fractions exceeding 0.3%, we modified the fluid flow characteristics of the commercially available UniVessel® SU 2L using Computational Fluid Dynamics (CFD). The goal was peak cell numbers of approximately 1×10^9 cells within 10 days while maintaining stem cell marker profiles. For this purpose, 12 different models were investigated with regard to the impeller diameter and blade angle as well as the off-bottom clearance. The optimization criterion was to reduce required impeller speeds, and consequently shear stresses, while maintaining a homogenous microcarrier suspension.

Results: By increasing the impeller blade angle and reducing the off-bottom clearance, the required specific power inputs for microcarrier suspension were reduced by factors of between 2.2 and 4.6 in comparison to the standard version of the UniVessel® SU, depending on the microcarrier concentration. This finally resulted in 3.4 to 11.1 times higher peak cell densities (1.17×10^9 hBM-MSCs and 1.44×10^9 hADSCs) than in the standard version and the desired peak cell number of 1×10^9 cells in the modified UniVessel® SU under low-serum conditions.

O63 ENGINEERED SMART TOOLS FOR NEURODEGENERATIVE DISORDERS: CHONDROITIN SULPHATE DELIVERY IN NEUROPROTECTION
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Cell numbers of approximately 1×10^9 cells within 10 days while maintaining stem cell functionality were achieved using proprietary hydrogels composed of agarose and Carbomer 974P, to be further investigated for their use as a delivery system.

Aim: To study the neuroprotective effect of chondroitin sulphate (CSs) released from a hydrogel matrix. The presented numerical study demonstrated the system suitability for culture cardiotic constructs.

Conclusions: By controlling and monitoring of individual parameters to be separated from in vivo systemic effects, this closed automated platform provides a reliable model system, with high reproducibility and low contamination risk, to study the effects of chemical-physical stimuli on cardiac tissue maturation and function.

O64 DESIGN OF MICRO SLIT FOR CELL SORTING
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Aim: Biological cells might pass through a path narrower than their diameter in vivo. The spleen, for example, has the slits. The narrow path is able to sort cells, according to their size and deformability. The photolithography technique enables manufacturing a micro slit. In the present study, the micro slit has been designed to observe behavior of a biological cell passing through the narrow path in vitro.

Methods: A silicone disk was used for a photolithography mold. Both a laser drawing system and a dry etching process were used for the micro-fabrication. The slit, width 0.85 mm and height 0.001 mm, has been designed between two parts of transparent polidimethylsiloxane disks. The disks have rectangular micro ridges on the inner surface. The dimension of the fabricated micro ridges was measured with a laser microscope. A suspension of swine red blood cells or C2C12 (mouse myoblast cell line originated with cross-striated muscle of C3H mouse) was alternatively introduced into the slits by drawing with a syringe pump. The behavior of cells passing through the micro slit was observed with an inverted phase-contrast microscope.

Results: The mean height of the ridges measured with the microscope is 0.0010 mm, which keeps space of the slit. Several red blood cells can pass through the micro slit, although C2C12 cannot pass through the micro slit.

Conclusions: The experimental results show that the micro slit can be fabricated with photolithography technique and has the potential of sorting biological cells.
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sequential B-mode images are cross-correlated to calculate 2-D velocity vectors. UV results were compared with Doppler and transit-time flow measurements.

Methods: In vitro experiments were performed in a pulsatile flow loop. The working fluid was water/glycerol with ultrasound contrast agent (microbubbles). The latex tube was imaged using an Ultrasonix RP500 and a novel imaging sequence was used to interleave two ultrasound frames, enabling a short and variable (0.3-39 ms) interframe time separation (it). A rabbit was anaesthetised and imaged through the abdomen, with microbubbles administered via the ear vein. Radiofrequency data were post-processed offline using in-house code which calculates the local correlation between successive frames, then sums correlation results for identical phases of all cardiac cycles.

Results: Peak velocities >2 m/s were accurately measured across the entire field-of-view in vitro, while peak systolic velocities in the rabbit were 0.99 m/s and 1.04 m/s with UV and Doppler respectively. As it was increased flow instability during deceleration caused the UV velocity measurement to drop to zero. Comparing velocity measurements of decelerating flow with different values of it leads to a new method for investigating flow instability.

Conclusions: With short it UV and derived flow rates agreed excellently with Doppler and transit time flow rates.

O67 PERFORMANOE OF WALL-LESS CANNULAS FOR MINIMAL ACCESS PERFUSION

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Aim: The aim of this study was to assess whether smaller diameters of the wall-less venous cannulae are sufficient for venous drainage with augmentation, thus allowing in-situ cannula exchange.

Methods: Flow rate (Q) and negative pressure (P) were measured for the 24F wall-less (Smartcath) restricted to 23F and 17F, and the control (Biomedicus cannula) 23F and 17F, using centrifugal pump and an experimental bench set-up, with after load 60 mmHg.

Results: 288 measurements were recorded. At 1500, 2000, 2500, and 3000 RPM pump speed, the Q values for the 23F access were 2.62 ± 0.02, 4.66 ± 0.03, 6.47 ± 0.08, and 8.21 ± 0.09 lm/min for the wall-less cannula, versus 1.56 ± 0.03*, 2.77 ± 0.02*, 3.82 ± 0.05*, and 4.77 ± 0.05*: p<0.05* lm/min for the control cannula Q values were -28.58 ± 0.14, -76.62 ± 0.41, -124.64 ± 0.43, and -191.20 ± 1.11 mmHg, versus -37.38 ± 0.66*, -95.54 ± 0.61*, -170.25 ± 1.43*, and -257.55 ± 1.05* mmHg. The Q values for the 23F access were 3.40 ± 0.02, 6.25 ± 0.03, 8.65 ± 0.05, and 10.94 ± 0.02* lm/min versus 2.69 ± 0.02*, 4.86 ± 0.02*, 6.81 ± 0.02*, and 8.55 ± 0.03* for the 23F control cannula. The wall-less cannula provides a promising solution for improved venous drainage for scenarios, the 17F and 23F access. One single cannula dimension for various access vessel diameters simplifies minimal invasive surgery.

O68 DEVELOPMENT AND IMPLANTATION OF TISSUE ENGINEERED SELF-EXPANDABLE AORTIC STENT GRAFTS (BIO STENT GRAFTS) USING IN-BODY TISSUE ARCHITECTURE TECHNOLOGY IN BEAGLES

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Aim: The approach of regenerative medicine based on the tissue encapsulation phenomenon of foreign materials in living bodies. Using the technology, we firstly developed expandable aortic stent grafts which can assimilate to native aorta are desirable for avoiding endoleaks.

Methods: Porcine in-vivo blood trials using bowry chambers were performed with sprayed PCU samples and negative and positive references. The surface of the PCU samples was varied with regard to the density of the fibre structure. The bowry chambers were placed on a laboratory mixer roller for 2 hours conditions and the blood samples were taken before and after the experiment. Different parameters, for example thromboelastography, hemogram, various coagulation factors and platelet factors were analysed. The PCU samples were also evaluated using laser-scan microscopy.

Results: We found that surface properties have a great influence on the thrombogenicity of the sprayed PCU samples. Depending on the chosen surface, the thrombogenicity parameters ranged between the values of positive and negative references.

Conclusions: The parameter set-up of our spraying process, and the various coated surface properties has a high influence on its hemocompatibility. Further investigations are planned to fully understand the phenomenon and to achieve biocompatibility.

O7O IN-VITRO/IN-VIVO BEHAVIOUR OF THERMOPLASTIC POLYURETHANE GRAFT

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Aim: Vascular prostheses are widely used in medical applications, for example in conjunction with LVADs, TAHS and for conduits. At our institute, we developed a spraying process enabling the production of adaptable prostheses with a non-woven structure of polycarbonatetherethan (PCU). The process also allows the manufacturing of surfaces with different properties. In this study, the potential influence of these surface properties on the thrombogenicity is investigated.

Methods: Porcine in-vivo blood trials using bowry chambers were performed with sprayed PCU samples and negative and positive references. The surface of the PCU samples was varied with regard to the density of the fibre structure. The bowry chambers were placed on a laboratory mixer roller for 2 hours conditions and the blood samples were taken before and after the experiment. Different parameters, for example thromboelastography, hemogram, various coagulation factors and platelet factors were analysed. The PCU samples were also evaluated using laser-scan microscopy.

Results: We found that surface properties have a great influence on the thrombogenicity of the sprayed PCU samples. Depending on the chosen surface, the thrombogenicity parameters ranged between the values of positive and negative references.

Conclusions: The parameter set-up of our spraying process, and the various coated surface properties has a high influence on its hemocompatibility. Further investigations are planned to fully understand the phenomenon and to achieve biocompatibility.

Aims: Despite the intensive research in vascular graft development, an efficient small diameter vascular graft (SDVG) is still currently unavailable for clinical use. In this study, synthesis thermoplastic polyurethane (TPU) vascular grafts were fabricated via electrospinning. The in-vitro study was carried out by developing a macrophage/fibroblast (M/F) co-culture (CC) model. The in-vitro and in-vivo behaviour of the grafts were compared with polytetrafluoroethylene (ePTFE) conduits.

Methods: Structure and porosity of the grafts were characterized via SEM and liquid intrusion method. Crystal violet staining, XTT cell viability, PCR gene expression (CD163 and CD68 genes) and 3D cell distribution/IF microscopy studies were carried out in vitro. TPU and ePTFE grafts were implanted into infrarenal aorta rats for immunohistochemistry (ED1 and ED2 staining) studies.

Results: The porous structure of the TPU grafts supported cell attachment, viability and growth more than the ePTFE grafts. Macrophages were both CD68+ and CD163+ cells, in vitro. TPU grafts revealed notable early cellular ingrowth in-vivo compared to ePTFE. Also, CD68+ macrophages significantly migrated into all parts of the graft wall within 1 week. CD68+ cells were much less than CD163+ cells in both grafts.

Conclusions: The TPU grafts supported viability, attachment and distribution of the cells more than ePTFE grafts. Migration of the cells was more noticeable in TPU grafts in-vivo.
Abstracts: XLI ESAO Annual Congress, 17–20 September 2014, Rome, Italy

O71 SUCCESSFUL ONE-DEVICE-TREATMENT OF INTRACRANIAL GIANT AND WIDE NECK ANEURYSMS

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Aim: We have developed a microporous covered stent for the one-device-treatment of giant and wide neck intracranial aneurysms, which are particularly hard to complete treatment with existing clinical methods. The aim of this study is to establish animal experimental models for the establishment of pre-clinical functional evaluation to assess the feasibility of this stent for use in the characteristic intracranial vessels.

Methods: Three types of animal experimental models were prepared: 1) Canine carotid siphon model, which was made by fixed anastomosed CCAs into a skeletonized acrylic framework designed according to the geometry of human ICA based on 3D rotational angiography; 2) Canine sidewall aneurysm model with modification by creating curves using a part of acrylic casing noted above while capable of making wide necked aneurysms on its outer curvature; 3) Stent placement in rabbit aorta at the branching of lumbar arteries.

Results: 1) Our stents smoothly went through the canine carotid siphon model in all cases. 2) Our stents fitted well in the curved vessels in all cases and spontaneous occlusion was confirmed in all cases after stent placement. Follow-up angiography at 12 weeks revealed patency of the parent vessels with completely thin neo-intimal layering. The aneurysms completely disappeared and were replaced by connective tissue. 3) The flow of lumbar arteries, the ostia of which were even covered by the stents, was maintained for 12 weeks. This is also observed in overlapping stent placement.

Conclusions: These experimental models in combination seem feasible and sufficient to assess the devices designed for endovascular treatment of intracranial aneurysms on tortuous vessels with small branches. This will be useful as world standard for the development of intracranial endovascular devices.

O72 LONG-TERM OBSERVATION OF RABBIT CAROTID ANEURYSMS TREATED BY MULTI-POROUS COVERED STENTS

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Aim: Our covered stents can embolize aneurysms, prepared experimentally at rabbit carotid arteries, immediately after their placement with maintenance of side branch opening flow of vertebral arteries and internal carotid arteries. The aim of this study is the evaluation of long-term patency of parent arteries and branching arteries, and embolization of aneurysms for clinical application in the intracranial area.

Methods: The covered stents were prepared using the specially designed balloon-expandable stents with open cell structure (CoCr, 3 mm × 20 mm). The stents had thin polyurethane cover membrane (thickness: 20 mm), in which the strut was completely impregnated, with a larger amount of micro pores (diameter: 100–300 mm; opening ratio: 10–30%). Experimental aneurysms (10–15 mm) were created at rabbit brachiocephalic arteries (with 30° angle). In hoop tensile measurements rings of 2 mm length were load- ing was seen in longitudinally oriented type by a diameter change of 8.8% after 1000 cycles compared to 3.4% in circumferential oriented type.

Conclusions: Our covered stents performed well in that they yielded less intimal hyperplasia with maximum embolization effect without disturbing branching flow for over 2 years.

O73 ELASTIN-LIKE RECOMBINAMERS BIOSTENT

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Aim: Restenosis and thrombosis after stent implantation remain important clinical complications, which drive continuous development in the fields of percutaneous interventional cardiology and radiology. We explored the use of recently developed gels obtained by catalyst free click reaction of elastin-like recombinant polymers (ELR) to fabricate a new class of vascular stents, with the ultimate goal of creating endovascular devices that exclude the atherosclerotic plaque from the blood stream, prevent cellular ingrowth in the vessel’s lumen, have high biocompatibility, physiological hemocompatibility and elicit a reduced response of the immune system.

Methods: The approach consists in embedding bare metal stents in the ELR-gels by injection-molding, followed by endothelialization under dynamic pressure and flow conditions in a bioreactor.

Results: The elastin-like hydrogel-bioStents (ELR-bioStents) exhibited mechanical stability under high flow conditions in vitro and could undergo crimping and deployment without damage. The presence of RGD in the ELR supported full endothelialization in less than two weeks in vitro. Minimal platelet adhesion and fibrin adsorption were detected after exposure to blood as shown by immunostaining and scanning electron microscopy.

Conclusions: These results prove the potential of the proposed approach towards a new and more effective generation of stents.

O74 DYNAMIC MECHANICAL CHARACTERIZATION OF SMALL DIAMETER VASCULAR GRAFTS ORIENTATED FIBER STRUCTURES

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Aim: Electrospinning is a promising method to create small diameter vascular grafts. For good functionality mesh structure and mechanical behaviour are essential. Fiber orientation and mesh density influence tensile strength, elasticity and cell growth. Due to different structural requirements between inside (cell attachment) and outside (cell in-growth), multilayered grafts are favourable. In this work, the effect of highly oriented fibers on mechanical behaviour was investigated by dynamic tensile tests.

Methods: Four types of electrospun vascular grafts were investigated: Fibers oriented randomly, in circumferential, longitudinal and cross-wise direction (with 30° angle). In hoop tensile measurements rings of 2 mm length were loaded sinusoidally for 1000 cycles at 10 Hz between 0.03 and 0.06 N, corresponding to a blood pressure of 80 to 120 mmHg. Finally, a quasi-static tensile test until rupture was performed.

Results: Circumferential oriented fibers exhibited the highest tensile force but showed no compliance with 8.1 ± 0.9%/100 mmHg. The other types had significantly lower tensile force but exhibited compliance with best performance of longitudinally oriented types (15.6 ± 3.2%/ mmHg). However, continuous creeping was seen in longitudinally oriented type by a diameter change of 8.8% after 1000 cycles compared to 3.4% in circumferential oriented type.

Conclusions: Oriented fiber structures allow the adjustment of biomechanical properties in electrospun vascular grafts.

O75 HEMODYNAMIC EFFECTS OF PARTIAL RIGHT VENTRICULAR SUPPORT IN THE ACUTE VS THE CHRONIC PRESSURE OVERLOADED RIGHT VENTRICLE

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Purpose: Temporary right ventricular (RV) support for the acute pressure overload- ed RV after heart transplantation or acute lung edema is well described. Patients with a chronic pressure overload- ed RV might also benefit from this support. We wanted to assess the hemodynamic effects of RV support in the acute vs the chronic pressure overloaded RV.

Methods: The pulmonary artery was banded in 16 sheep. In 8 sheep we immediately [‘Acute’] implanted a CircuLiteSynergy® micro-pump draining blood from the right atrium to the pulmonary artery. In the second group, the same pump was implanted only 8 weeks after banding [‘Chronic’]. Hemodynamics were recorded before and after pump implantation.

Results: Only in ‘Chronic’, initiation of the pump resulted in a significant increase of left atrial pressure and a significant decrease of RV end systolic pressure. The pump generated flows of 1.40 ± 0.47 L/min in ‘Acute’ and 2.81 ± 0.12 L/min in ‘Chronic’ (p<0.0001), both at 22 kRPM. There was no difference in total cardiac output. However, the contribution of the RV in generating the
total cardiac output was significantly lower in ‘Chronic’ (19 ± 12 vs 59 ± 8%, p<0.00001).
Pressure-volume loop analysis showed that in supported ‘Chronic’ stroke volume, ejection fraction and end systolic pressure were significantly lower (15.4 ± 5.8 vs 25.4 ± 4.4 ml, p<0.01; 17 ± 6 vs 25 ± 4%, p<0.05 and 27.7 ± 7.4 vs 43.1 ± 12.0 mmHg, p<0.05, respectively), compared to supported ‘Acute’.

Conclusions: Supporting the pressure overloaded RV optimizes hemodynamics towards the same levels in ‘Acute’ vs ‘Chronic’. However, the contribution of the RV to the generation of the total CO is significantly lower in ‘Chronic’. Therefore, at our opinion, the failing RV might benefit even more from mechani-

O76 NEUROHORMONAL MARKERS DURING MECHANICAL CIRCULATORY SUPPORT
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Aim: NT-proBNP and plasma renin activity (PRA) are used as biomarkers in chronic heart failure. NT-proBNP levels are frequently used for follow-up during the first year of support. Renal function of the patient. PRA measurement during mechanical circulatory support might have added value in follow-up of patients with a left ventricular assist device (LVAD).

Methods: Between 2009 and 2013 PRA, NT-proBNP and renal function was measured prospectively in 55 patients undergoing LVAD implantation (HeartMate II, Thoratec), preoperatively and at fixed time points over the next 12 months. Renal function (Gomeruluer filtration rate, GFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula.

Results: PRA and NT-proBNP levels decreased significantly during the first 14 days (PRA: 32.3 µg/L/h vs. 0.0001 and 10356 ± 10807 ng/L vs. 4345 ± 7715 ng/L, p<0.01) and remained decreased during the first year of support. Renal function improved in the first 14 days (64 ± 35 mL/min vs. 106 ± 48 mL/min; p<0.0001), at 12 m this effect was no longer statistically significant (64 ± 35 mL/min vs. 73 ± 26 mL/min; p<0.12). There was no significant correlation between PRA and NT-proBNP (Pearson correlation coefficient = 0.063), p = 0.438 or PRA and GFR (Pearson correlation coefficient = -0.094; p = 0.190). There was a strong correlation between NT-proBNP and GFR (Pearson correlation coefficient = -0.249; p<0.0001).

Conclusions: PRA and NT-proBNP levels decrease significantly during LVAD support. NT-proBNP showed a strong correlation with renal function. PRA had no correlation with the renal function. Measuring PRA might have added value in the follow-up of patients with a LVAD.

O77 NUCLEO-MITOCHALD TRANSLOCATION OF PHOSPHORYLIZED PKCδ ASSOCIATES WITH TUNNEL-POSITIVE AND UROCORTIN NEGATIVE STAINING IN THE HUMAN HEART FROM DIABETIC PATIENTS UNDERGOING ON-PUMP CARDIAC SURGERY

Aim: We have previously developed a Native Heart Load Control System for a continuous-flow left ventricular assist device and demonstrated that the rotational speed (RS) in synchrony with the cardiac cycle can alter pulsatility and left ventricular (LV) load. In this study, we compared these effects with the fix pulsatile mode by changing the RS independently of the cardiac cycle.

Methods: We implanted EVaHEART via left thoracotomy in seven goats (52.9 ± 5.0 kg) with a normal heart. After the implantation, we administered propanolol to reduce heart rate around 60 bpm. In previous experiments, rotational speed of the pulsatile mode was increased during the initial 33% of RR interval of the systolic phase by an automatical control based on electrocardiogram. In the fix pulsatile mode, we made up-pulsed RR interval by temporary pacemaker and increased RS independently of the phase of systolic phase. We used three modes, the continuous mode (constant RS), the pulsatile mode (increase RS in systolic phase), and the fix pulsatile mode and shifted puls-eRR interval 500 ms, 600 ms, 750 ms and 1000 ms. In these modes, we assessed the change of pulsatility (pulse pressure and dP/dt max of aortic pressure) and LV load (stroke work and LV end-diastolic volume).

Results: There were significant increases in pulsatility and LV load of the pulsatile mode relative to the values of the continuous mode. However, in the fix pulsatile mode, there were much less increased in these values regardless of puls-eRR interval.

Conclusions: Fix pulsatile mode could produce less pulsatility and LV load than the pulsatile mode.
Abstracts: XLI ESAO Annual Congress, 17-20 September 2014, Rome, Italy

O80
ANALYSIS OF R WAVE AMPLITUDE DURING VAD IMPLANTATION, EXPERIMENTAL STUDY
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\textbf{Aim:} It is known in literature the coupling between the electrical and mechanical activity of the ventricle. This work is aimed at investigating if this relationship is still present during a ventricular assist device (VAD) and if it can be of help for VAD patient monitoring.

\textbf{Methods:} Data of 6 animals undergoing an atrio-aortic VAD implantation surgery were analysed, 5 with a Gyro Centrifugal pump 2, and 1 with a Circuite Synergy Micropump. In all experiments VAD was activated and then speed was increased progressively. Electrocardiographic (ECG) and left ventricular volume data were recorded and analyzed: the R wave peak (RWA) was individuated and the volume in the corresponding time was identified. After a moving average analysis on both signals, a regression and correlation analysis was performed.

\textbf{Results:} For all experiments the increment of VAD speed provoked a decrement of ventricular end-diastolic volume and a corresponding increment of RWA. This trend was confirmed by the correlation analysis, showing a strong negative relationship between the RWA and the corresponding ventricular volume ($r=0.8$ and $p<0.001$ for all experiments).

\textbf{Conclusions:} The present work evidences the potential usefulness of the ECG, a low invasive and low cost signal, in inferring information about the status of the ventricle during VAD. This may be a first step in a future remote monitoring of ventricular unloading and VAD therapy optimization.

\textbf{Acknowledgments:} This work was supported by SensorART (N. 248763) and CNR-CNRS bilateral project (N. 139804).

O81
APPLICATION OF THREE-DIMENSIONAL VISUALIZATION AND PRINTING METHODS IN THE PREOPERATIVE PLANNING OF COMPLEX CONGENITAL HEART DEFECT REPAIR
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\textbf{Background:} Congenital heart defects are diverse and often complex in form. Their repair requires surgical experience and skill as well as preoperative planning using medical imaging data. In order to provide operating physicians with all available data, virtual anatomical studies are performed using preoperative CT and MRI datasets.

\textbf{Methods:} Using the programs Mimics and S3matic (Materialise, Belgium), anatomical models are extracted and analysed. Measurements are performed along renal cell types, such as mesangial, podocytes and tubular cells were detected.

\textbf{Conclusions:} Complex congenital heart defects present a challenge for any operating physicians and any available method promising a potential improvement to outcome should be applied and optimized. 3D visualisation and printing should be available to physicians in the planning of complex cardiothoracic surgical procedures.

ORAL SESSION – BIOARTIFICIAL ORGANS, O82-O88

O82
THERAPEUTIC EFFECT OF NONWOVEN BIODEGRADABLE FILTERS WITH MESENCHYMAL STEM CELLS ON A RAT MODEL OF CHRONIC RENAL FAILURE
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\textbf{Aim:} Devices consisting of nonwoven filters and cells captured thereon have been investigated for regeneration or recovery of impaired kidneys. The cells on nonwoven filters were expected to serve as a local supply of growth factors and cell sources when they are placed near the injured kidney. In this study, biodegradable nonwoven filters made of polyacetic acid (PLA) were investigated in combination with rat mesenchymal stem cells derived from bone marrow (rBMSCs).

\textbf{Methods:} PLA filter disks were placed into cell-capturing devices, then, rBMSCs were passed through the filters. The filters/rBMSCs complex was cultured for evaluating growth factor production, or implanted in the kidney of 5/6 nephrectomy rats followed by resection of the kidney after eight weeks. This study was approved by the Institutional Animal Care and Use Committee of Fujita Health University.

\textbf{Results:} The capture rates of rBMSCs on five PLA filter disks were more than 85%. The production of hepatocyte growth factor (HGF) by rBMSCs was significantly enhanced by the interaction with PLAs filters. The PLA filters/rBMSCs complex decreased glomerulosclerotic lesions when it was attached to the surface of the injured kidney.

\textbf{Conclusions:} rBMSCs on PLA nonwoven filters enhanced their HGF production, and improved glomerulosclerosis of chronic renal failure models.

\textbf{Acknowledgments:} This work was partly supported by Aichi Kidney Foundation and JSPS KAKENHI grant number 25410232.

O83
AMNIOTIC FLUID RENAL PROGENITORS AND RENAL EXTRACELLULAR MATRIX: A NEW APPROACH FOR KIDNEY REGENERATION
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\textbf{Aim:} Renal congenital abnormalities still remain a significant contributing factor for chronic kidney disease. Current treatments aimed at slowing progression of the disease are insufficient and often dialysis and/or transplantation becomes necessary. Combination of a natural or biodegradable scaffold with cells could be a new approach to discover alternative tools for replacing significantly impaired or non-functional kidney tissues. Our laboratory has previously reported that human amniotic fluid (AF) is a source of renal progenitor cells.

\textbf{Methods:} A subpopulation of renal progenitor cells expressing were isolated from AF. Using a detergent-enzymatic method, we decellularized whole mouse kidney extracellular matrix (ECM) that was seeded with renal progenitor cells, implanted into the kidney of nude mice, and harvested for characterization.

\textbf{Results:} One month after surgery, implanted ECM showed angiogenesis and formation of renal tubular-like structures. In addition to formation of 3D renal structures in the scaffolds, cells positive for markers associated with essential renal cell types, such as mesangial, podocytes and tubular cells were detected.

\textbf{Conclusions:} These results suggest that AF renal progenitor cells seeded into renal ECM could represent a unique investigational approach for kidney regeneration that may be used to augment or replace damaged or compromised kidney tissue from either congenital or chronic disease.

O84
KIDNEY TISSUE ENGINEERING BASED ON DECELLULARIZED MATRIX SCAFFOLDS
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\textbf{Aim:} Chronic kidney disease progressively deteriorates kidney function. New therapies for severely damaged kidneys are needed due to limited regenerative capacity of the kidney and organ donor shortages. One possibility is to create new kidneys by tissue engineering with decellularization and recellularization processes.

\textbf{Methods:} For decellularization, rat and porcine kidneys were perfused by sodium dodecyl sulfate. Integrity of scaffolds and ECM structure and composition was investigated by optical microscopy, micro-CT and immunofluorescence. Acellular scaffolds were then seeded with HUVEC and mES cells through the renal artery and ureter, respectively. Cell distribution was investigated by immunofluorescence and H&E stainings.

\textbf{Results:} We obtained whole organ scaffolds with the intact 3D geometry by decellularization as shown by histological examination and SEM analysis. Micro-CT scan established integrity, patency and connection of the vascular network. The seeded cells infused through renal artery were uniformly distributed in the vascular network and in glomerular capillaries while cells infused through ureter reached the tubular compartments.

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Conclusions: Our findings indicate that rat and porcine kidneys can be successfully decellularized to produce intact renal ECM scaffolds able to support the engraftment of cells in glomerular and tubular structures. This study represents an initial step toward development of a transplantable organ.

Acknowledgments: The research was supported in part by the ERC Grant (RESET-268632).

O85 CREATININE TRANSPORT THROUGH HUMAN PROXIMAL TUBULE CELL MONOLAYERS ADHERENT TO BIOFUNCTIONALIZED PES MEMBRANES
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Aim: Membranes for bioartificial kidney (BAK) have to be an ideal scaffold for cell adhesion, proliferation and function expression. Poor renal cells bio-compatibility of polymer membranes calls for the need of their bio-function-alization. We investigated the optimization of collagen IV (cIV)-based double coating on polyethersulfone membranes (PESM) to favor functional monolayer formation of a conditionally immortalized proximal tubule epithelial cell line (cPTEC).

Methods: PESM were coated with 3,4-Dihydroxy-L-phenylalanine (L-DOPA) and cIV. Morphological and transport properties changes of differently coated PESM were investigated. cPTECs monolayer formation on coated membranes was examined by immunocytochemical stain of tight junction protein ZO-1. Transepithelial transport of 14C-creatinine (Papp) was measured by liquid scin-tillation.

Results: Double coated PESM presented progressively more stable cIV ad-hesion with increasing dissolution and exposure time to L-DOPA. Both ZO-1 expression and creatinine Papp through cPTEC monolayers was higher for cells cultured on double coated PESM than standard Transwells®. Transport inhibitors addition significantly reduced the creatinine Papp for all conditions.

Conclusions: Optimal performance of cPTECs on double coated PESM makes this a promising strategy for the development of BAK with functional cell monolayers.

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O86 INTEGRATION OF MULTI-PARAMETRIC SENSOR SYSTEMS IN BIOARTIFICAL LIVER SUPPORT SYSTEM
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Aim: Bioartificial liver support (BAL) technologies provide an option for tempo-rary bridging of the liver function in severe diseases. Multi-parametric monitor-ing of liver support systems could improve quality control and clinical safety of the systems.

Methods: Rat pancreatic progenitor-derived hepatocytes were cultured in a 3D multi-compartment bioreactor culture system. For non-invasive in-vitro monitor-ing foibase impedance sensors were integrated in the cell compartment. A new ammonium sensor, and also optical-chemical pH and O2 sensors were integrated into the perfusion circuit.

Results: The metabolic activity of the cells in the bioreactor system was not influenced by sensor integration, as shown in comparison with sensor-free control systems. The time course of impedance signals recorded at differ-ent positions in the cell compartment showed a comparable time course. Impedance signals reflected changes in the culture state and perfusion media. Online ammonia and O2 measurements correlated with daily taken samples. Online monitoring of pH allowed supporting constant culture conditions.

Conclusions: Successful integration of non-invasive multi-parametric sensors in the 3D bioreactor system resulted in real-time monitoring of the cell behav-iour. Thus, changes in the cell behaviour can be detected immediately and al- lows for early decision making regarding BAL application.
immune cells without compromising their insulin release in response to blood glucose.

Methods: Poly(ethersulfone)-based hollow fibre membranes were tested for encapsulation of islets of Langerhans. Hydraulic permeance and convective transport of glucose, insulin, BSA and IgG were determined. Islets viability and functionality in the bores were assessed by histology and response to glucose.

Results: Glucose and insulin permeance through the membranes is comparable to that of water. The permeance of BSA and IgG is lower especially at low transmembrane pressures, and the sieving coefficient of IgG is almost zero. The TUNEL assay showed hardly any apoptotic cells after 7 days of culture, while GIIST showed a moderate response to insulin changes due to relatively big bore size in comparison to islets.

Conclusions: Transport measurements indicate that islets are able to sense glucose and IgG is mainly blocked by the membrane suggesting that our device is suitable for islet encapsulation. The device dimensions still need to be optimized.

O90 A CFD ANALYSIS OF AORTIC FLOW DURING LINEAR AND PULSED EXTRACORPOREAL MEMBRANE OXYGENATION UNDER DIFFERENT INFLOW CONDITIONS

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Aim: Extracorporeal Membrane Oxygenation (ECMO) is a medical procedure used to supply oxygen to blood circulation of patient with cardiac/pulmonary failure. Since linear flow in ECMO is often responsible of some clinical problems, the aim of this study was to evaluate the hemodynamic modifications of blood behavior in aorta due to linear and pulsed ECMO.

Methods: A multi-scale study, realized coupling a 3D CFD analysis and a lumped-parameter model (0D boundary conditions), was carried out by using COMSOL 4.3a (COMSOL Inc, Stockholm, Sweden).

A 3D patient-specific model of the aorta with its three epi-aortic vessels (innominate or brachiocephalic artery, left carotid artery, left subclavian artery) was obtained from a series of in vivo CT-scan slices using a commercial software.

The developed flow meter quantified a flow rate using centrifugal force generated by flow in a curved cannula. The strain gauges in the flow meter measured the centrifugal force using the strain of the outer wall of the cannula. The zero compensation, which compensated the drift of the measurement data, was conducted at the initial driving condition and the ventricular suction condition, since the flow rate was determined to be 0 L/min under these conditions.

O91 MINIATURIZED FLOW METER WITH ZERO COMPENSATION USING A CURVED CANNULA IN AN ANIMAL STUDY

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Aim: For patients using a left ventricular assist system a reliable flow measurement system is required. The purpose of the present study is to develop a miniaturized flow meter with zero compensation using a curved cannula, and evaluate the measurement accuracy both in a mock circulation study and an animal study.

Methods: The developed flow meter quantified a flow rate using centrifugal force generated by flow in a curved cannula. The strain gauges in the flow meter measured the centrifugal force using the strain of the outer wall of the cannula. The zero compensation, which compensated the drift of the measurement data, was conducted at the initial driving condition and the ventricular suction condition, since the flow rate was determined to be 0 L/min under these conditions.

O92 POLYMER-PHOSPHOLIPID COMPLEXES FOR THE SOLUBILISATION AND DELIVERY OF DRUGS TO THE EYE

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Aim: Topical application of ophthalmic drugs is very inefficient; contact lenses used as drug delivery devices could minimize the drug loss and side effects. Stereylene-maleic acid copolymers (PSMA) can form polymer-phospholipid complexes with dipalmityl phosphatidylcholine (DMPC) in the form of nano-spherical vesicles, which can easily solubilise hydrophobic drugs. They can be dispersed on very thin contact lens coatings to immobilize the drug on their surface.

Methods: Two types of complexes stable at different pH values (5 and 7 respectively) were synthesized and loaded with drugs of different hydrophilicity.

Results: The mean size of the complexes obtained by light scattering were 50 nm and 450 nm respectively with low polydispersities. However, they were affected by the drugs load and release. An increase was observed in the duration of the release in the case of hydrophobic drugs, from days to weeks, avoiding initial "burst" and with a lesser amount of total drug released due to the interaction of the drug with the phospholipid core.

Conclusions: Polymer-phospholipid complexes in the form of nanoparticles can be used to solubilise and release hydrophobic drugs in a controlled way. The drug load and release can be optimised to reach therapeutic values in the eye.

O93 COMPUTATIONAL MODEL OF RED CELL FLOW IN MICRO-CHANNELS FOR PROBING MOLECULES ENCAPSULATION

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Aim: Preliminary experiments confirm the possibility to load Red Blood Cells (RBCs) with probing molecules (PM) by applying mechanical shear stresses ($\tau$) on RBCs stroma. This work is aimed at studying the optimal fluid dynamic conditions allowing the encapsulation of PM into RBCs flowing in a micro-channel (MC).

Methods: A computational model was developed by using COMSOL Multiphysics 4.2a (Stockholm, Sweden). A 50 x 50 µm cross-section and 58.5 mm length MC was considered. The mixture model was used to evaluate velocity ($v$), volume fraction of dispersed phase ($\phi$) and $r_{s}$ for a suspension of RBCs and PM (FITC-Dextran) in a Phosphate Buffer. When the pair of $r_{s}$ and $r_{t}$ values and duration lays in the sub-haemolytic portion of the shear stress characteristic time of PM into RBCs, encapsulation was promoted. The flow rate $Q$, and the haematocrit $Ht$ and MC size were tuned to optimise fluid dynamic conditions and increase encapsulation.

Results: The optimal conditions were $Q = 40 \mu$L/min and $Ht < 0.15$ with the modelled MC. The resulting high pressure drop suggests to increase MC width (2000 µm) and $Ht < 0.15$ with the modelled MC. The resulting high pressure drop suggests to increase MC width (2000 µm) by keeping constant height and length. The new optimal conditions were $Q = 1600 \mu$L/min, $0.05 < Ht < 0.30$. A normalized index ($I_{n}$) was defined as the product of $v$ and $\tau$; encapsulation is higher in the round crown region of the MC section, where $0.8 < I_{n} < 1.5$ is lower than $0.27 L/min$.

Conclusions: The developed model allows to characterize RBCs fluid dynamics in MC and to identify the optimal conditions to promote PM encapsulation into RBCs. This model will be used to design a new experimental set-up, defining appropriate test conditions.
Abstracts: XLI ESAO Annual Congress, 17-20 September 2014, Rome, Italy

O94
ESTABLISHMENT OF THE GUIDELINE FOR INNOVATIVE MEDICAL DEVICES: COLLABORATION WITH ACADEMIA, CLINICIANS, INDUSTRY AND REGULATORY AGENCY
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Aim: To promote the development of medical devices with new clinical concept, assessment in the guidelines would be useful for stakeholders; clinicians, manufacturers, patients and regulators. The guidelines would contribute to the acceleration of the approval process and safe clinical application. While government-led guidelines could not reflect the actual situation, few guidelines have been established by people in R&D field. In Japan, using ECMO for longer than approved periods (off-label use) increases, which can raise various risks for the stakeholders. To reduce the risks and enhance the development of next-generation ECMO system for long-term use, we propose new assessment guidelines.

Methods: We compiled guidelines of ECMO system for long-term use via discussion at a committee which consisted of experts of medical devices, including ECMO; academic experts, clinicians, manufacturers, and regulators.

Results: We drafted the assessment guidelines of ECMO system for long-term use. Academic experts examined non-clinical and clinical test issues. Clinicians shared the current clinical needs. Manufacturers showed the market situation and hurdles to approval application. Regulators requested that the guidelines be a reference for the review. Despite different backgrounds and standpoints, experts expanded their views and developed consensus towards the appropriate ECMO use.

Conclusions: Partnerships with all experts play a prominent role in establishing “reasonable” assessment guidelines of long-term use ECMO in Japan.

O95
STAGNATION AREAS AND A WASHOUT STUDY AS AN ASSESSMENT FACTOR FOR THE DESIGN PROCESS OF THE VAD
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Aim: Different assessment factors and a numerical flow analysis of the pneumatic VAD – Religa EXT – developed at the Foundation for Cardio-Surgery Development, Zabrze, under transient conditions are discussed. The main aim of the investigations was to assess a stagnation area and a washout method as valuable criteria for the VAD design process.

Methods: In the present study, a motion of the diaphragm and valve discs was simulated. The valves based on J. Moll’s design were used. The washout and the stagnation areas inside the Religa EXT VAD for two angular positions of valves were investigated. The first angular position was based on experimental tests, whereas the second one was found in the optimization process with an objective function based on minimization of the stagnation areas. Four full cycles of operation of the Religa EXT VAD were performed. The non-Newtonian blood viscosity model based on Power Law formula was applied in all numerical simulations. The stagnation areas were described as regions with a low value of velocity, below 0.01 m/s, close to the VAD walls. To investigate the washout of blood, two fluids were used. Both of them are based on the same blood model. The ANSYS CFX v14.5 code is used to perform the numerical experiment.

Results: The calculated flow field showed a high level of agreement between the stagnation areas and the washout method. An angular position of valves has a significant influence on the stagnation areas and the washout of residual blood.

Conclusions: The numerical study shows that the stagnation areas and the washout method are reliable factors for the design process of a new pulsatile VAD. Similar areas of the VAD, for both methods, were detected as potentially prone to coagulation.

O96
ORAL SESSION – RENAL ASSIST: VASCULAR ACCESS, O96-O102

O96-PHOSPHATE REMOVAL DURING NOCTURNAL HEMODIALYSIS: A STUDY WITH TOTAL DIALYSATE COLLECTION
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Aim: To quantify phosphate removal during nocturnal HD (NHD) by measuring concentrations in serum, hourly and total dialysate collection.

Methods: 8 patients (3 women) receiving NHD were studied for one session on the longest break between NHD. Serum and total dialysate phosphate concentration was measured every hour. Duration of the NHD was 8 hours in 3 patients and 7 in 5.

Results: Phosphate removal assessed in serum was more important during the first 2 hours, then a plateau was reached. Average serum concentration before NHD was 1.43 mmol/l and 0.78 mmol/l and 0.81 mmol/l after 7 and 8 hours, respectively. The reduction was statistically significant (p = 0.005 in p = 0.02, respectively). The highest average concentrations in total dialysate was in the 1st hour (0.31 mmol/l), then concentrations remained stable (0.23; 0.24; 0.25, 0.21, 0.21 and 0.18 mmol/l for every next hour, respectively). Average total reduced mass of phosphate quantified from hourly and total dialysate was 5195.7 mg and 5466.2 mg. Reduction ratio for 7 and 8 hours NHD was 45.3% and 43.1%.

Conclusions: Phosphate has been removed in a consistent manner during whole duration of nocturnal hemodialysis (despite the plateau in serum concentration), indicating phosphate transfer from intracellular space. Total reduced mass quantified from hourly and total dialysate in our study was more than four times higher than previously reported.

O97
RATE OF ACCUMULATION OF ADVANCED GLYCATION END-PRODUCTS: REPEATED SKIN BIOPSIES AND SKIN AUTOFLUORESCENCE MEASUREMENTS IN DIABETIC HEMODIALYSIS PATIENTS
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Aim: To measure the rate of accumulation of different Advanced Glycation End-products (AGEs) in the skin of diabetic hemodialysis (HD) patients over a period of one year and to find the factors that influence this process.

Methods: Twenty-two diabetic HD patients were enrolled in this study. The amount of pentosidine, carboxymethyl-lysine (CML) and carboxyethyl-lysine (CEL) in the biopsies was measured biochemically. Skin autofluorescence (SAF) was measured non-invasively to determine the AGEs accumulation in the skin. Dietary records from the HD patients were obtained to assess the AGEs, calorie and protein intake. Furthermore, BMI, as a measure of nutritional state, was obtained.

Results: The pentosidine, CML and CEL content of the biopsies correlated with SAF; but all four variables were not significantly different between the two time points. We found that the independent predictors of the one year increase of pentosidine were: one year increase of SAF and the SAF value at the first time point. The independent predictors of the one year increase of CML were: one year increase of SAF; the SAF value at the second time point and the 4th quintile of BMI. The independent predictors of the one year increase of CEL were: the one year increase of SAF and the 4th quintile of BMI.

Conclusions: Biochemically determined skin AGEs of the diabetic HD patients did not show a significant increase in one year time. The rate of skin AGEs accumulation is independently associated with the increase of SAF and BMI.

O98
HEPARIN-ALBUMIN PRIMING IN THE CLINICAL SETTING FOR HD PATIENTS AT RISK FOR BLEEDING
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Objective: Patients on haemodialysis (HD) may have an increased risk for bleeding when performing HD, i.e., before or after surgery, after brain haemorrhage or intestinal bleeding.

Material and Methods: We use a priming solution containing heparin (H), 10000 units, and 10 mL of albumin (A), 20%, added to 2 L of priming solution. This mixed solution is used to prime the dialysis circuit before connection of the patient. The residual fluid is removed when the blood fills up the circuit. A pilot study showed that it was possible to lower to extent of added anticoagulation by this measure. The aim of this study was to evaluate a larger cohort of patients treated either by standard dose of anticoagulation only (Group-S; n = 526) or a group that had initial HA priming performed before HD (Group-HA; n = 882) with the aim to reduce the dose of systemic heparin or low molecular weight heparin.

Results: Comparing baseline data between Group-S and Group-HA the mean age was higher (61.5 ± 16 yrs 59.5 ± 17, p = 0.021), dialysis time was longer (3.3 hours ± 0.7 yrs 3.2 ± 0.6, p = 0.002) while there was no difference in extent of ultrafiltration (1.76 vs 1.74 L), systolic blood pressure (141 vs 139), speed of blood pump (244 vs 243). The total dose of anticoagulation/ dialysis was
848 ± 1950 U vs 1844 ± 1794 U (p<0.001). In group-HA the total dose of anticoagulation (Units) was 0 Units/HD in 24%, and ≤1000 units/HD in 50% of procedures. Total clotting occurred to the same extent in both groups (4 versus 9 dialyses) and genders.

Conclusions: Heparin-albumin priming significantly reduces the extent of anticoagulation during HD in patients at risk for bleeding.

O95 CLINICAL ASSESSMENT OF HEMODIALYSIS ARTERIOVENOUS FISTULAS AT THE ELBOW
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Aim: When the superficial veins are unavailable in the forearm, we create an arteriovenous fistula (AVF) at the elbow using superficial or perforating veins, in order to extend the possibility of providing an autogenous vascular access. We examined two types of elbow AVFs to evaluate their clinical feasibility.

Methods: From January 2010 to June 2013 we created 60 AVFs at the elbow, including 43 AVFs with superficial veins (i.e., cubital-median, cephalic or basilic veins) and 17 AVFs with perforating veins, when the forearm veins were unavailable. The vein was anastomosed to the brachial or radial artery, according to topological conditions so as not to exert an excessive tension to the anastomosis. We followed the survival of respective AVFs to obtain primary and secondary patency rates. To estimate the access flow, we measured time-averaged blood flow rate of the inflow brachial artery by Doppler ultrasound.

Results: Primary patency rate was not significantly different between AVFs with superficial and perforating veins, whereas secondary patency rate was inferior in those with perforating veins; two-year survival was 89 and 80%, respectively (Log-Rank p = 0.04). Estimated access flow was 690 and 890 mL/min, respectively, which was not statistically significant, however AVFs created with the brachial artery showed greater blood flow, compared to those with the radial artery (1010 vs. 670 mL/min, p = 0.03).

Conclusions: AVF creation with perforating veins at the elbow seemed to be a feasible option when the superficial veins are poor in the forearm. The arterial anastomotic site was revealed to significantly influence the access flow.

O100 WHEN NATIVE ARTERIOVENOUS FISTULA FOR HEMODIALYSIS IS NOT POSSIBLE: PTFE GRAFTS VS TUNNELLED CUFFED CATHETERS
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cila
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Aim: Vascular access complications account for the high morbidity related to hemodialysis (HD). We compared vascular access and patient survival in patients with tunnelled cuffed permanent catheters (TCC) and with PTFE grafts.

Methods: We studied 87 HD patients, 56 with TCC and 31 with PTFE graft (follow-up = 2 years). Patients with TCC were older than those with PTFE graft (73.5 ± 11.3 vs 63.8 ± 14.6 years, p = 0.001). Atrial fibrillation was significantly more frequent in TCC group than in PTFE group (30.3% vs 6.5%, p = 0.01).

Results: In an unadjusted Kaplan-Meier analysis, TCC survival at 24 months was 5.4 months longer, but not significantly (log-rank = 1.3, p = ns). Cox regression analysis adjusted for age, sex, type and number of previous vascular accesses, diabetes, atrial fibrillation and smoking confirmed similar vascular access survival between the groups, with diabetes as an independent risk factor for the survival of both vascular accesses (p = 0.02). In an unadjusted Kaplan-Meier analysis a higher 24-month mortality was found in TCC group than in PTFE group (log-rank = 10.07, p<0.01). The adjusted Cox regression analysis showed that TCC was associated with a 3.2-fold increased risk of death.

Conclusions: When arteriovenous fistula is not possible, PTFE grafts can represent the vascular access of second choice.

O101 TRANSITIONAL FLOW IN PATIENT-SPECIFIC ARTERIOVENOUS FISTULAE FOR HEMODIALYSIS
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Aim: Radial-cephalic arteriovenous fistula (AVF) is the first choice for providing the life-line vascular access for hemodialysis patients. Nowadays, the surgical placement of AVFs still has high failure rates due to neointimal formation. We have shown in idealized AVF models that disturbed flow (i.e., low and oscillating shear stress) may develop in areas that locate well the sites of future stenosis. Our present study was aimed at investigating the nature of disturbed flow in realistic geometry models of AVFs.

Methods: We employed patient-specific, image-based computational fluid dynamics (CFD) simulations. To extract the blood vessel geometry we used MR images of subjects starting HD treatment, performed 40 days post-operatively. We performed transient CFD simulations with subject-specific blood rheology and flow boundary conditions. We then characterized the blood flow field by means of velocity and wall shear stress (WSS) plots and categorized disturbed flow by means of the oscillatory shear index (OSI).

Results: In all simulated cases, we observed transitional laminar-to-turbulent flow developing in the juxta-anastomotic vein (JAV), but not in the proximal feeding artery. The disturbed flow zones (high OSI) were located on the inner wall of the JAV, and along the distal artery wall.

Conclusions: We have found transitional flow developing in the JAV. The oscillations of the velocity vectors in these areas result in eddies that rotate WSS orientation. On these sites, the development of both oscillating and multi-directional disturbed flow on endothelial cells may be responsible for neointima formation in newly created AVFs.

O102 HEMODIALYSIS TUNNELED CENTRAL VENOUS CATHETERS: SINGLE CENTER EXPERIENCE
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e
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Aim: Central venous catheters used for hemodialysis are a common cause of complications. Catheter malfunction secondary to thrombosis or malpositioning of the catheter, and catheter-related bloodstream infections (CRBI) are common occurrences.

Methods: We looked at the outcome of a group of 185 patients (pts) receiving chronic HD treatment via tunneled-cuffed catheters during the 5-year period. Criteria for catheter removal were: (1) persistent bloodstream infection and (2) catheter dysfunction. Event rates were calculated per 1,000 catheter days, and Kaplan Meier analysis was performed to estimate THC cumulative survival.

Results: 282 THC were included in the analysis and were grouped by insertion site of the catheter: (TF) n = 155; (IJ) n = 68, (TSC) n = 59. Duration time of THC, average 129-429 days. Infection rates were: TFC ~ 3.1 episodes/1000 catheter days; TJC ~ 2.8, and TSC ~ 2.9. A total of 63 CRBI events in 35 pts were identified. The most common isolated microorganisms were Gram-positive. Antibiotic therapy was statistically significant for catheters survival in group with TSC. Risk factors were most likely to result in colonization or infection with multi-resistant species, age (odds ratio/OR, 1.2 to 14.1); prolonged hospital stay (OR, 1.3 to 17.5); and exposure to broad-spectrum antimicrobial drugs (OR, 1.6 to 25.1).

Conclusions: Our data showed a high survival rate of THC in pts undergoing HD, with low incidence of catheter dysfunction and CRBI. Careful application of standard protocols and well educated dialysis staff contributed to achieve these results.

ORAL SESSION – ECMO, O103-O109
O103 FLOW IN A CROSS LAYER FIBER OXYGENATOR: VALIDATION OF COMPUTATIONAL FLUID DYNAMICS USING PARTICLE IMAGE VELOCIMETRY
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Aim: Computational Fluid Dynamics (CFD) is routinely used for the investigations of the blood flow in fiber membrane oxygenators. For the experimental validation Particle Image Velocimetry (PIV) was applied on an up-scaled transparent model of an oxygenator with cross layered fiber arrangement.

Methods: The oxygenator was designated to be used as an artificial placenta with a flow range from 30 to 120 ml/min. Considering the similarity theory, a transparent and up-scaled model by a factor of 5.8 of the oxygenator was built that satisfies the requirements of the optical measurement method. 3C-PIV was performed to investigate the corresponding minimal and maximal flow rates. For the numerical approach the model was meshed unstructured in the original size and analyzed at the equivalent operating points. The fiber bundle was modeled as isotropic porous media.
Results: In comparison, the macroscopic flow field distribution, areas of high flow and stagnation show a good agreement. However, the view of the flow between the fibers differs in a microscopic level regarding the tortuosity that can be quantified by the path length of stream lines.

Conclusions: These first PIV measurements of an up-scaled model of a cross layer oxygenator show promising results to be used as a validation methodology for CFD of oxygenators in the future.

A NOVEL METHOD FOR IN-VITRO EVALUATION OF CO2 TRANSFER CAPACITY THROUGH MEMBRANE OXYGENATORS
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Aim: Membrane Oxygenators (MO) should have a sufficient physiological CO2 Transfer Rate (CTR). This is crucially important especially during the long-term applications of artificial lungs, e.g. ECMO and AVCO2R. While CTR evaluation with native blood is complex and time consuming, an adaptation of an analogous fluid instead of blood is still a challenging task for in-vitro investigations.

Methods: The proposed system is based on pH decrease as a result of CO2 dissociation in distilled and deionized ultra-pure water. Having the pH of this liquid, the total CO2 content could be calculated through a cascade of equations. Subsequently, the CTR of a MO is achieved by measuring the liquid flow rate and pH-value difference between liquid inlet and outlet. Using a fitting curve analysis, a new equation is designed, representing the ratio of $\frac{N_{CO2}}{V}$ used in the gas phase, considering the flow rate of the liquid phase, priming volume as well as membrane surface area of testing MO.

Results: In-vitro performance investigations of 2 different types of commercial adult and paediatric MOs up to their maximal liquid flow rates, show that the obtained results are in excellent accordance with those carried out with blood.

Conclusions: The presented method is suitable to predict the CO2 transfer capacity of MO in in-vitro studies as an easy handling and quick test, and can be considered a reliable alternative method to animal blood experiments.

THE EFFECT OF BLOOD CONTACT SURFACE AREA REDUCTION DURING CARDIOPULMONARY BYPASS IN A RAT MODEL
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Aim: Cardiopulmonary bypass (CPB), preserve patient’s life by providing adequate oxygen supply and blood flow to vital organs. However, previous studies have suggested that the interaction of blood and large artificial surface contributes to inflammatory response during CPB. As a result of a series of chain reactions, the numerous powerful inflammatory mediators are formed and released. We hypothesized that small CPB circuit which reduces priming volume and blood contact surface area attenuates the systemic inflammatory response with a re-distribution of inflammatory cytokine levels and organ tissue damage during CPB.

Methods: Rats were divided into the large surface area CPB (priming volume: 15 ml, surface area: 0.044 m²) group and the small surface area CPB (priming volume: 7 ml, surface area: 0.036 m²) group. CPB pump flow was maintained at 80 ml/kg/min. Blood samples were collected before (baseline), and at 60 min and 120 min after initiation of CPB. We measured the serum cytokine levels (TNF-α, IL-6, IL-10) and biochemical markers (LDH, ALT, AST).

Results: Pro-inflammatory markers (TNF-α, IL-6) and biochemical markers were significantly elevated in the high priming volume CPB group compared with the low priming volume CPB group at 60 min. At 120 min, however, none of the markers was statistically different between the 2 groups.

Conclusions: These data suggested that in addition to the blood contact surface area factor, the CPB exposure duration is also an important factor for causing the systemic inflammatory response.

COMPUTER TOMOGRAPHY OF AIRWAYS AND LUNGS DURING TOTAL LIQUID VENTILATION WITH PERFLUOROCARBONS
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Aim: The airway deformation and pulmonary distribution of liquid perfluorocarbons (PFC) were evaluated by computer tomography (CT) during Total Liquid Ventilation (TLV) performed with a new ventilator prototype (Pro-Li-Ve).

Methods: Spiral thorax CT scans (120 kV, 125 mA, ST 1.00 s, 3 mm thickness/index, 1.00 pitch) were run during conventional gas ventilation and TLV with PFC (FC-770, 3M) on 2 anesthetised New Zealand juvenile rabbits (weight 1.1 ± 0.08 kg). The time needed to fill the entire lungs at the beginning of TLV was evaluated. Series of 30 axial CT scans were also performed at the same section in 3 different airway regions (trachea, carina, first bronchi) to quantify airway deformation during normal breaths or expiration collapses.

Results: About 15 min after TLV start the PFC is homogeneously distributed in the trachea, bronchi, and alveoli. The attenuation level is always positive (from 269 to 509 Hounsfield Units (HU) in the independent and dependent pulmonary regions, respectively). Airway narrowing is induced by the negative expiratory pressure that can cause airway collapse (e.g. tracheal narrowing 20% during normal breaths, 48% during collapse).

Conclusions: This analysis proved PFC excellent properties as contrast medium, having linear attenuation coefficient similar to the contrast agents commonly used in radiology. This property permitted good anatomic details, highlighting airway deformation during TLV and proving PFC to homogeneously fill the lungs.

PRACTICAL TECHNIQUE OF VENO-VENOUS EXTRACORPOREAL MEMBRANE OXYGENATION FOR EFFECTIVE OXYGENATION AND CARBON DIOXIDE REMOVAL
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Aim: Recently, the number of cases of veno-venous extracorporeal membrane oxygenation (VWECMO) for adult respiratory failure patients increases. However, oxygenated blood by ECMO may recirculate into ECMO circuit. This is known as recirculation. And it may induce ineffective gas exchange. Although some factors such as cannula position or bypass flow are related to recirculation, the details are not clarified. The aim of this study is to investigate practical technique of VWECMO for effective gas exchange.

Methods: VWECMO was performed in 5 goats (mean body weight, 58 kg). We varied the position of return cannula in the superior vena cava (SVC), the right atrium (RA) or the inferior vena cava (IVC), whereas the position of drainage cannula was fixed in the IVC. We changed bypass flows from 1-4 L/min in all positions, and compared the recirculation rate. We checked whether oxygenation and carbon dioxide removal were enough by measuring the arterial oxygen saturation (SaO2), partial pressure of arterial oxygen (PaO2) and partial pressure of arterial carbon dioxide (PaCO2).

Results: In the SVC return cannula group, the recirculation rate was lowest, and SaO2 and PaO2 were highest. The bypass flow exceeded 2 L/min had SaO2 > 80% at SVC or RA position. PaCO2 approached the normal range when the bypass flow was more than 2 L/min.

Conclusions: Most desirable return cannula position is in the SVC, and both the cannula position and the bypass flow rate are important for effective oxygenation and carbon dioxide removal.

Impact of AT3 Infusion on Coagulation in a Porcine ECMO Model
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Background: Extracorporeal Membrane Oxygenation (ECMO) shows promise in supporting subjects with lung injury; however, the optimal method of anticoagulation during ECMO remains unknown. A continuous antithrombin III (AT3) infusion, as opposed to traditional bolus administration, may result in attenuation of hemorrhage and lung injury.

Methods: Anticoagulation is analyzed through use of 14 pigs on mechanical ventilation and ECMO using an oleic acid-induced acute lung injury animal model. An IRB approved protocol included cardiorespiratory monitoring for 32 hours of venovenous extracorporeal support. Experimental animals are randomly divided into two experimental groups (n = 6 per group): heparin + continuous AT3 and heparin, along with two control subjects. Serial laboratory analyses were obtained of bronchoalveolar lavage fluid and serum.

Results: The group receiving continuous AT3 infusion demonstrates a trend towards decreased thrombus formation including intracardiac and oxygenator clots (0% vs 40%). Analysis of lung histology suggests that a continuous AT3 may attenuate the inflammation and edema that attends acute lung injury. Subjects receiving AT3 received more crystalloid and colloid in response to...
hypotension due to blood loss (2880 mL vs 1805 mL; p = 0.018) and a trend towards more blood transfusions (1906 mL vs 1015 mL; p = 0.086).

**Conclusions:** Use of a continuous AT3 infusion may allow for minimization of ECMO related thrombotic complications and decreased pulmonary inflammation, but due to hemorrhage, as well as increased required blood products and fluid resuscitation may cause more harm than benefit.

**O109 ABYLACAP AS PROMISING DEVICE TO TREAT PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)**

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**Aim:** In patients with ARDS, gas exchange is impaired and mechanical ventilation is needed. The use of low tidal volumes is more lung protective but can be associated with hypercapnia and respiratory acidosis. Extracorporeal CO2 removal (ECOO-R) is a therapeutic option to correct pH. The aim of this study was to derive optimal working parameters for the ECOO-R.

**Methods:** A 56-year-old man with ARDS was treated 7 days by Abylacap (Bellco, Italy). The system consists of a pediatric polyethylene-pentene hollow fiber membrane oxygenator. The oxygenator and the incorporated heat exchanger are coated with a non-thrombogenic phosphorylcholine coating. Every 24 h during 5 days, blood was sampled at the Abylcap inlet and outlet under different conditions of blood (QO2: 200-400 mL/min) and 100% O2 flow (QO2: 0.5-8 L/min).

Blood samples were analysed for total CO2 content, partial O2 tension, O2 saturation range of our laboratory is 69-229 pmol/L. During the follow-up period of 1.05, APTT 36.2, AT 82.91, and Trc 208.66

Conclusions: Using optimal operating parameters with QO2 at 400 mL/min and QO2 at least 6 L/min, the ECOO-R is a promising device when treating patients with ARDS.

**O110 PROTHROMBIN FRAGMENTS F1+2 AND FIBRINOGEN ARE HIGHLY EL- EVATED IN PERITONEAL DIALYSIS PATIENTS, BUT ARE NOT ASSOCIATE- ED WITH CARdioVASCULAR COMPLICATIONS AND MORTALITY IN THE LONG-TERM FOLLOW-UP.**

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**Aim:** Recognition of the role of coagulation system in the pathogenesis of cardiovascular diseases has increased interest for investigations of the association of prothrombin fragments (F1+2) with cardio- and cerebrovascular complications which are the leading causes of death in the dialysis population. Few data exist about the coagulation parameters in dialysis population, with contradictory results. Aim of the present long-term follow-up prospective study was to investigate the plasma levels of F1+2 and antithrombin III (AT) in dialysis patients, and to determine their role in development of different complications after 7 years of follow-up.

**Methods and Results:** Two groups were included in the investigation: 28 clinically stable CAPD patients, (average age 45.33; range 19-75 years), who had not suffered from peritonitis during the last six months, and 18 patients (average age 53.7; range 18-74 years) on hemodialysis (HD) without signs of infection. The CAPD group had significantly elevated serum fibrinogen -7.3 g/L; PV was 1.34, APTT 27.9 s, and Tc 208.66 x 10^9/L. The HD group had fibrinogen 3.2, PV 1.05, APTT 36.2, AT 82.91, and Tc 150. Antithrombin III (AT); a potent inhibitor of coagulation cascade, was higher in the CAPD (101.63%) vs. 82.91% in the HD group; however, both values were within the normal range of our laboratory (75-125%). A statistically significant elevation was found in the levels of F1+2 in all patients, but significantly higher in the CAPD group, 3331.4 pmol/L vs. 514.38 pmol/L in the HD group (p<0.00001). Prothrombin F1+2 values reference range of our laboratory is 69-229 pmol/L. During the follow-up period of 7 years 16 patients died (11 from the PD, and 5 from the CAPD group), 7 from the cardiovascular causes. However, there was no correlation between the coagulation parameters and occurrence of cardiovascular complications or mortality.

**Conclusions:** Elevations of hemostasis activation markers may occur not only in the presence of overt thrombosis but also during the hypercoagulable state like is chronic kidney disease. Additionally, elevated F1+2 may reflect chronic inflammation in dialysis population. Further studies are urgently needed to precisely estimate role of coagulation cascade in development of cardiovascular disease in uremic patients.

**O111 TEMPORAL PATTERN OF AMYLASE-INDUCED DIGESTION OF GLUCOSE POLYMERS**

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**Aim:** The enzymatic activity of amylase determines the rate at which glucose polymers (GP), such as icodextrin (Ico, a mixture of GP used as osmotic agent in peritoneal dialysis fluids), are digested. We developed a mathematical model describing changes in the composition of Ico induced by amylase at concentrations characteristic for biological fluids including peritoneal dialysate.

**Methods:** Solutions with Ico (75 mg/mL) were spiked with synthetic porcine pancreatic α-amylase (PPA) at 12.5 - 200 U/L. The concentrations of GP fractions with molecular weight <1 to 66 kDa were determined by HPLC.

**Results:** A mathematical model based on Michaelis-Menten kinetics for the temporal evolution of concentration of GP was proposed. The model parameters were estimated using experimental data.

**Conclusions:** A mathematical model coupled with experimental data allowed accurate description of the temporal pattern of α-amylase-induced digestion of glucose polymers. Whether the observed changes in the composition of Ico induced by α-amylase, resulting in increase of low molecular weight GP, influences the osmotically driven ultrafiltration flow needs to be further studied.

**O112 HEALTHCARE SYSTEM ORGANIZATION IS A FACTOR FOR DIFFERENT PD USAGE IN EUROPE?**

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**Aim:** The usage of peritoneal dialysis (PD) varies across Europe. The reimbursement system for renal care has been suggested as an explanation for differences. However, PD usage differs within countries due to regional or centre level issues despite similar or identical reimbursement systems within the country. Therefore, other factors relating to the healthcare system organization may explain the PD variability within a country.

**Methods:** The ERA-EDTA report was examined to show the differences in PD distribution across Europe. Published literature and country specific health system data were examined to explore the variable PD utilization.

**Results:** Published data from France show that overall 14% of patients start with PD, but this varies from 0% to 45% among 59 districts included in the study. Data from the UK Department of Health shows differences in distribution of PD usage in specific centres across the country with range from 2.74% to 27.45%. Published data from Italy show that use of PD varies regionally and is strongly influenced by the number of private centres. In the seven regions with no private centres and in eight regions with <10% patients on dialysis in private centres the incident PD rate is 23.2% and 18.0% respectively. In the remaining regions with >10% of patients on dialysis in private centres the rate of PD usage declines to 9.5%.

**Conclusions:** Within countries there are large differences in PD usage which cannot be explained solely on reimbursement issues. Centre specific differences including individual nephrologists’ attitude, beliefs, PD knowledge and practice organisation/infrastructure must influence the choice of PD.
THE SELF-LOCATING CATHETER IS PREFERABLE TO A STRAIGHT TENCKHOFF FOR ACUTE ONSET OF PERITONEAL DIALYSIS

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Objectives: We are developing a technique for direct start of peritoneal dialysis after insertion of the dialysis catheter into the abdominal cavity without complications of obstruction or leakage.

The aim of this study was to investigate if the use of a self-locating PD catheter with a wolfram weight at the tip (di Paolo catheter) would result in different outcomes than a straight Tenckhoff catheter.

Material and Methods: The study included 106 operations. Three operations were excluded from analysis due to inability to insert a catheter due to extensive intra-abdominal adherences. Of the remaining 103 insertions, a straight Tenckhoff catheter was inserted in 60 and a self-locating catheter in 43 patients. In this clinical assessment study, in the first part we decided to start with insertion using a double cuffed straight Tenckhoff catheter. If reoperation was necessary, the first option was to change the catheter into a self-locating wolfram catheter. After the first 42 insertions we decided to randomize to insert either a straight Tenckhoff or a self-locating wolfram catheter. A previously described operation technique allows immediate postoperative start of dialysis in most patients.

Results: PD start was initiated the first postoperative day in 99% cases. We found that significantly less self-locating catheters had to be changed into standard straight Tenckhoff catheters due to less in- or outflow problems (p = 0.004). Long-term patency was better with the self-locating catheter.

Conclusions: The study showed that when using the self-locating wolfram catheter fewer outflow problems occurred. This type of catheter therefore can be recommended for acute start of peritoneal dialysis using an insertion technique tightening tissue in three layers.

PARICALCITOL THERAPY AND THE INFLAMMATORY MARKERS IN PERITONEAL DIALYSIS PATIENTS

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Aim: A few links between chronic kidney disease (CKD) and cardiovascular disease (CVD) have been discovered, among them inflammation. In the last years, a growing interest has been given the pleiotropic effects of vitamin D in CKD. Paricalcitol, a selective vitamin D receptor activator (VDR), has demonstrated in experimental studies a potential to modulate the inflammatory process. The aim of the study was to analyze the anti-inflammatory effects of oral paricalcitol, in peritoneal dialysis (PD) patients with secondary hyperparathyroidism (SHPT) and to compare the effect of paricalcitol to calcitriol.

Materials and Methods: 32 patients on CAPD were included in a 12 weeks study: 10 were on oral paricalcitol treatment (group P); 7 stopped oral paricalcitol (group NP); 7 were on oral calcitriol (group C) and 8 did not take any calcitriol (group N). No patient had treatment with anti-inflammatory or immunosuppressant drugs 4 weeks before and during the investigation. Serum concentrations of intact parathyroid hormone (PTH), high-sensitive C-reactive protein (CRP), interleukin (IL)-6, and tumor necrosis factor-alpha (TNFa) were measured at the beginning and the end of the study.

Results: At the end of the study, these parameters changed as follows: In the group P, treated with paricalcitol, mean levels of PTH, decreased significantly from 520.8 ± 53.3 to 276.33 ± 31.5 pg/ml (p < 0.001), mean serum IL-6 levels fall from 11.58 ± 3.2 pg/ml to 5.12 ± 2.2 pg/ml (p < 0.001); CRP experienced a significant decrease from 10.52 ± 2.5 to 7.68 ± 3.6 mg/l (p < 0.01) and mean level of TNFa had a less significant fall – from 22.3 ± 2.7 to 21.2 ± 2.3 pg/ml (p < 0.05). Interestingly after stop the treatment with paricalcitol (in group NP) IL-6 was significantly higher in all patients at the end and mean TNFa was increased as well. In the rest of the patients (groups C and N) the levels of CRP, IL-6 and TNFa did not change significantly.

Conclusions: The present study shows that oral paricalcitol administration to PD patients (but not calcitriol) is associated with modulation of inflammatory process, specifically with a reduction of CRP and IL-6.

PHASE ANGLE AND LEAN TISSUE INDEX ARE SLIGHTLY HIGHER IN HEMODIALYSIS THAN IN PERITONEAL DIALYSIS GROUP OF PATIENTS

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Background: Protein malnutrition is a common cause of morbidity and mortality in patients with renal replacement therapy. Determination of body mass composition with bioimpedance analysis is a useful tool for the evaluation of the nutritional status of patients on peritoneal dialysis and hemodialysis.

Methods: The aim of the study was to compare nutritional parameters in a group of dialysis patients using bioimpedance analyzing. We analyzed 12 patients on peritoneal dialysis and 17 hemodialysis patients. A negative selection of patients on peritoneal dialysis in our study is present. Phase angle, lean tissue index, fat tissue index, body hydration status and routine biochemical blood analysis were evaluated. Average values of parameters with standard deviation, statistical significance (p<0.05) and Spearman’s correlation coefficients were calculated.

Results: Phase angle was lower in the group of patients on peritoneal dialysis (4.49 ± 1.06) than in the group of hemodialysis patients (5.025 ± 0.89), but non-significant. Out of the whole group, three patients had phase angle less than 3.5 and all of them suffered from heart failure. Phase angle was lower in women than in men, and had a negative correlation with age, lean tissue index, body composition mass, albumins, creatinine, haemoglobin values and physical capacity in both sexes. Patients on peritoneal dialysis had lower values of albumins than hemodialysis patients (36.33 ± 3.42 vs. 39.05 ± 2.59 g/L, p = 0.019) and lower blood potassium values (4.42 ± 0.6 vs. 5.21 ± 0.97 mmol/L, p = 0.021). Lean tissue index values were lower in patients on peritoneal dialysis (13.98 ± 3.57 vs. 14.13 ± 2.78 kg/m², p < 0.05), but overhydration is more frequent in patients on peritoneal dialysis (2.68 ± 2.53 vs. 1.92 ± 1.14 L). Values of IPH is negatively correlated with lean tissue index (p = 0.026).

Conclusions: Bioimpedance body mass composition analysis showed a better nutritional status in hemodialysis patients than in patients on peritoneal dialysis.

PLASMA PENTOSIDINE, MALNUTRITION AND ALL-CAUSE MORTALITY IN CKD STAGE 5 PATIENTS

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Aim: Chronic kidney disease (CKD) patients exhibit increased levels of advanced glycation end-products (AGEs) due to hyperglycemia, oxidative stress, and inflammation. Accumulation of AGE’s like pentosidine may represent a risk factor for cardiovascular disease (CVD) and other complications. We studied the association between pentosidine and nutritional status and its impact on clinical outcome.

Methods: Plasma pentosidine (by reversed-phase HPLC using fluorescence detection), biomarkers of inflammation, and nutritional status were measured in conjunction with initiation of dialysis therapy in 366 CKD stage 5 patients (53 ± 12 years; 81% males; 30% diabetics; 35% CVD; median glomerular filtration rate (GFR) 6.4 (range 3.7-9.1) ml/min/1.73 m²). Nutritional status was assessed by subjective global assessment. We divided patients into four groups according to the median of plasma pentosidine and presence or not of malnutrition and analysed the relation between pentosidine, nutritional status, and all-cause mortality.

Results: The pentosidine levels associated positively with age (P<0.01), serum C-reactive protein (P<0.05), albumin (P<0.001), osteoprotegerin (P<0.001), vascular cell adhesion molecule-1 (P<0.001), homocysteine (P<0.001) and 8OHdG (P<0.001) levels, and total lean body mass (P<0.001), and negatively with GFR (P<0.05). Malnourished patients with high pentosidine had the worst survival (Log rank test, Chi square = 33.7 p<0.001).

Conclusions: Circulating pentosidine associates with markers of inflammation, oxidative stress, and nutritional status CKD stage 5 patients. Malnourished CKD stage 5 patients with elevated plasma pentosidine have an increased risk of death.