49th ESAO-IFAO Congress: August 29–September 1, 2023 Bergamo, Italy

Presidential Message

It is a great honor for me to welcome you to the annual Congress of the European Society of Artificial Organs, in conjunction with the International Federation of Artificial Organs. This occasion is particular in that I acted as Congress President and as Editor-in-Chief of the International Journal of Artificial Organs, the official journal of ESAO. Besides that, I have the privilege to welcome you in my own city, Bergamo. Our Congress will take place in this prestigious location of the University of Bergamo, where historical beauty is accompanied by the atmosphere of the old city of Bergamo. I am sure that you will have the opportunity to experience the scientific activities of the Congress and discover at the same time the beauty of the city and the surroundings.

With the help of the Congress Organizing Committee, and all the contributions reported in this issue of the journal, we assembled a scientific program that span from basic research and modeling to clinical applications. As you well know, the field of artificial organs is very multidisciplinary. For this reason, we aim to bring together scientists and clinicians for the discussion of new advances in the field.

We all know that research on artificial organs and clinical applications started more than 60 years ago, and that they are now routine clinical practice for the survival of a large population of patients. New developments in the field are always less evident, while industrial activities and organization are today providing efficient and safe artificial organs and medical technology in general. In this scenario, there are today different and new challenges that involve research and clinical use of artificial organs. We then aimed at extending our scientific program to these broader challenges. Among them, an important role is represented by the theoretical modeling that is today more powerful, based on increased computational power and on more clinical data than ever before. Digitalization in the medical field continuously generates a large body of clinical data that our community has the capability to analyze and use to render medical care more efficient. At the same time, this large body of data opens the possibility to use the artificial intelligence approach to obtain more reliable predictions and help to assist medical activities. In this context, the safety of artificial organs, and of medical devices in general, has to face the requirements of the new Medical Device Regulation of the European Union. This is a challenge that we would like to analyze during the Congress, to evaluate advantages and challenges of this important change in industrial production and clinical use of medical devices. Since the progress of technology and of biological science is always evolving, the scientific program contains communication on bioartificial devices and technology, as well as biofabrication.

All these aspects of our program will allow interaction of people with different backgrounds and expertise, young and more experienced scientists. We believe that direct interaction in in-person meetings is always fundamental for the growth of our competences and our relations. We are confident that you will be an active part of this process during the Congress.

A large number of scientific and clinical research investigations will be presented in our Congress. It would be important to spread these messages and results to the large scientific community at global level. For this task, I encourage you to submit contributions, in different forms, to our journal, the IJAO that receives contributions from different continents. The journal aims exactly at the dissemination of scientific and clinical research in the area of artificial organs. As mentioned previously, since different disciplines are now involved in the field of artificial organs and in medical technology, also IJAO is expanding the journal aims and related topics to cover the new challenges of this broad field of engineering and medicine.

Let me now join all the Organizers of the Congress to welcome you to the annual Congress of our Society, and to the city of Bergamo. We wish you a productive and enjoyable experience.

Andrea Remuzzi
Congress 2023 President and Editor in Chief
The International Journal of Artificial Organs

Welcome Message

Dear Colleagues,

on behalf of the European Society for Artificial Organs, it is my pleasure and honor to welcome you to the 49th ESAO Congress taking place in Bergamo, Italy, from August 29th to September 1st, 2023, organized by Prof. Andrea Remuzzi and his team, which is at the same time the 9th Congress of the International Federation of Artificial Organs.

The motto of the congress is “Biomedical Research to Improve Artificial Organs”. Organ support and artificial organs have found their way into clinical use and are routinely applied in many areas. Still, their continuous improvement and the development of new technologies are needed to support or replace deficient organs. As new technologies emerge, the different approaches have to be integrated, which requires a joint action of basic researchers, engineers, clinicians, as well as Regulatory Authorities and our Corporate Partners.

The ESAO Congress is the place where representatives from all these groups can meet to present their progress, to discuss clinical needs, and to focus on future developments. The view ahead is particularly supported by the very active participation of your yESAO members, which we highly appreciate.

Bergamo, located in the alpine Lombardy region of northern Italy, approximately 40 km northeast of Milano, and in close proximity to the lakes Como, Garda and Maggiore, is a perfect location to host the ESAO Congress. It mixes modern facilities with historical and very pleasant surroundings, and I am sure this combination will promote networking and fruitful encounters.

We are all confident that the conference will stimulate the exchange of experience between researchers, engineers, industry, and clinicians on an international level and will thereby inspire innovation in the field.

A warm welcome to ESAO 2023!

Viktoria Weber
ESAO President

49th ESAO Congress - Boards and Committees

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Scientific Program Overview

MONDAY, August 28			
START	**END**	Pre-congress meeting	AULA CASTOLDI - 5 Opening Words from yESAO coordinators
12:45	13:15		
13:30	14:30		AULA CASTOLDI - 5 Keynote 1
14:30	15:00		**Coffee Break**
15:00	18:00		AULA CASTOLDI - 5 Pitch session and networking
20:00	23:00		**Social Dinner yESAO**

TUESDAY, August 29			
START	**END**	Pre-congress meeting	**Visit at Mario Negri Institute for Pharmacological Research**
10:00	12:00		
12:30	13:30		**Lunch**
13:30	14:30		AULA CASTOLDI – 5 Keynote 2
14:30	15:00		**Coffee Break**
15:00	16:00		AULA CASTOLDI – 5 Workshop
16:30	18:00	AULA MAGNA **Opening Ceremony** **Presidential Address** **Welcome Addresses** **Awards Ceremony** **Opening Lecture** Grand challenges for dialytic kidney replacement therapy 2023 and beyond *Peter KOTANKO, Renal Research Institute, New York, NY, US* **Musical performance**	
18:30	21:00	**Welcome Reception and Buffet**	

WEDNESDAY, August 30				
START	**END**	**AULA CASTOLDI - 5**	**AULA 8**	**AULA 6**
8:30	10:00	A11 Blood Damage in Artificial Organs	B11 Hemodialysis and Uremic Toxins	C11 Symposium: Artificial Pancreas: New Challenges and Opportunities Towards Fully Automated and Personalized Diabetes Management
10:00	10:45	AULA MAGNA **Plenary Lecture 1:** The artificial pancreas, signals, models & control: shifting the paradigm of diabetes treatment *Claudio COBELLI, University of Padova, Padova, Italy*		
10:45	11:15	**Coffee Break**		
11:15	12:45	A12 Symposium: New Trends and Applications in Mechanical Circulatory Support	B12 Symposium: Artificial Kidney	C12 Tissue Engineering I
12:45	14:00	**Lunch** **Sponsor Symposium**: How to accelerate the development of mechanical circulatory support devices Magnus Ahlström - Hydrix		
14:00	15:30	A 13 Ventricular Assist Device I	B13 Symposium: Wearable Artificial Kidney	C13 Symposium: Advanced Biomaterials for Tissue Engineering
15:30	16:30	A FT Poster Flash Talk	B FT Poster Flash Talk	C FT Poster Flash Talk
16:30	17:30	**Poster Session 1 – Coffee Break**		
17:30	18:15	**Plenary Lecture 2** The Future of Organ Replacement Therapy: will Xenograft Eventually Help Clinical Practices *Giuseppe REMUZZI, Mario Negri Institute, Bergamo, Italy*		

THURSDAY, August 31				
START	**END**	**AULA 5 - Castoldi**	**AULA 8**	**AULA 6**
8:30	10:00	A21 Symposium: Rotary Blood Pump Design	B21 Symposium: Vascular Access for Hemodialysis	C21 Symposium: European Activities for 3D Printing in Hospitals
10:00	10:45	AULA MAGNA Plenary Lecture 3: Soft Robotic Technologies for Medical Applications *Ellen ROCHE, MIT, Cambridge, MA, US*		
10:45	11:15	**Coffee Break - AULA 1: IJAO Editorial Board**		
11:15	12:45	A22 Extracorporeal Life Support	B22 Symposium: Theoretical Models in dialysis	C22 Tissue Engineering II
12:45	14:00	**Lunch** Sponsor Symposium: 3D-bioprinted bionic pancreas as an innovative method of treating and preventing diabetes: how far are we from clinical application? *Michał WSZOLA, Polbionica*		
14:00	15:30	A23 Joint EuroELSO Symposium: Simulation and Artificial Intelligence in ECLS	B23 Modelling and Devices	C23 Symposium: Albumin, Scientific and Clinical Advances on a Versatile Protein
15:30	17:00	**Poster Session 2- Coffee Break**		
17:00	18:00	A24 Ventricular Assist Device II	B24 New Methods for Biological Applications	C24 Organ on Chip
18:00	19:00	**AULA 5 - ESAO General Assembly**		
20:30	23:00	**Social program - Gala Dinner**		

FRIDAY, September 1				
START	**END**	**AULA 5 - Castoldi**	**AULA 8**	**AULA 6**
8:30	10:00	A31 Symposium: Computational Fluid Dynamics	B31 Symposium: Big Data and CKD	C31 Symposium: A New technology as a Booster for Transplantation
10:00	10:45	AULA MAGNA **Plenary Lecture 4**: EU Regulatory framework on medical device regulation: state of play on the implementation *Mario GABRIELLI COSSELLU, Bruxelles, BE* Opportunities and challenges for medical devices, from conception to market Fabrizio PIZZUTILO, Milan, IT		
10:45	11:15	**Coffee Break**		
11:15	12:45		B32 Organ Preservation and Medical Device Regulation	C32 Tissue Engineering III
12:45	13:30	**Closing Ceremony / Awards**		
13:30	14:30	**Farwell Lunch**		

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Scientific Program - Oral Presentations

Session: Blood Damage in Artificial Organs

O1

GHOST BLOOD- A NOVEL FLUID FOR VISUAL MONITORING OF COAGULATION IN AN OCCLUSION SYSTEM

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Objectives: Water-glycerol mixtures are primarily used as blood-substitute fluids for in-vitro studies of flow dynamics in the investigation of biomedical devices. Although such fluids have the advantage of full transparency, they cannot reproduce the natural rheology and coagulation of blood. With our new approach of using a mixture of erythrocytes with reduced hemoglobin content (ghost cells) and blood plasma, we were able to mimic the rheology and coagulation properties of whole blood.

Methods: The coagulation properties were tested by thromboelastometry (ROTEM), and the dynamic viscosity was measured at high shear rates from 2650 s-1 down to 5 s-1 in exponential steps by a cone-plate rheometer at 22 °C and 37 °C, both analyses showed similar behavior compared to whole blood.

Results: However, ROTEM results regarding natural coagulation indicate accelerated coagulation at the same clot strength. The typical pseudoplastic property of blood was achieved at 22 °C without any additives, but at 37 °C, xanthan had to be added to increase the viscosity, especially at low shear rates $<$ 50 s-1. In addition, the so-called "ghost blood" showed an approximately 120-fold reduction in light absorption. For this purpose, a model of the left atrial appendage was used to visualize the occlusion during PIV measurements. Thus, we were able to visualize the forming of a thrombus in an occlusion system in real-time during perfusion.

Conclusions: The increased transparency and blood-like behavior in terms of coagulation and rheology opens new possibilities for studying the flow dynamics in blood-carrying medical devices that are designed to shield the blood flow in specific areas. In the future, the ghost blood allows for the investigation of other thrombus-prone regions due to stagnation such as aneurysm occluders, left atrial appendage occluders, or the neo-sinus after transcatheter aortic valve implantation.

O2

HEMOLYTIC PERFORMANCE OF EXTRACORPOREAL BLOOD PUMPS USING COMPUTATIONAL MODELS AND PATIENT COHORT DATA

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Objectives: Hemolysis is a major complication in the application of extracorporeal blood pumps (ECBPs).
In recent years, many studies were conducted on the hemolytic performance of ECBPs, but these focused only on specific operating points and neglected the entirety of the clinical operating point (COP) range. The aim of this study was to investigate blood damage potential of commonly used ECBPs under common (COPs).

Methods: We used CFD models of the Xenios DP3 and Getinge Rotaflow ECBPs to predict hemolysis over a wide range of operating points by training reduced order models (ROMs) via non-intrusive polynomial chaos expansion allowing the rapid calculation of hydraulic and hemolytic parameters over the entire range of COPs. Additionally, we analyzed clinical data of 790 patients admitted to Intensive Care Unit from 2012 to 2021 undergoing extracorporeal membrane oxygenation (ECMO) therapy. We extracted 97052 data points of pressure and flow and calculated the likelihood of each pump operating point occurring within the cohort range. By combining the reduced order models with the clinical likelihood of each operating point the clinically relevant blood damage potential of each pump was investigated.

Results: Our model shows continuous characteristics of hemolysis performance over the entire operating point range of an ECBP. We identified the operating point of 3.94 l/min and 201 mmHg as the most common one within our cohort data range. Additionally, we compared the ECBPs within the 99 percentile of cohort operating points and showed that overall the Rotaflow had a lower blood damage potential then the DP3.

Conclusions: We present a novel approach to combine clinical patient cohort data with numerical simulations in order to deduce hemolytic performance in ECBPs. Our results outline differences across ECBPs, which could help to find the most critical operating points in terms of blood damage in the development and approval process of ECBPs.

O3

HEMOLYSIS INDUCED BY HIGHLY DYNAMIC STRESSES: INFLUENCE OF STRESS TYPE AND NUMBER OF REPETITIONS IN AN ELONGATIONAL FLOW SETUP

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Objectives: The broad use of rotary blood pumps is limited by its induced blood damage, which leads to a high number of adverse events. Most of the blood damage is generated in the gap between the rotor blades and the housing wall, the area with the highest stress load and very short exposure times. The damage is caused by both shear and normal forces on the blood components. The objective is to investigate the blood damage in this region by examining different gap geometries. The focus is the damage caused by high dynamic normal stresses and the comparison with the blood damage models.

Methods: To measure the influence of highly dynamic normal and shear stresses on hemolysis, this study performed experiments with human whole blood in three different shaped microchannels representing three flow scenarios. The test setup allows a high number of stress loads with low hemolysis beside the microchannels. For the level and duration of the applied stress loads, parameters of typical critical areas of rotational blood pumps were used as a basis. In addition, flow simulations were performed to capture the flow fields and various stress-based hemolysis models were applied to estimate the hemolysis.

Results: We measured hemolysis in the physiological range for unphysiological shear stresses up to 2000 Pa, normal stresses up to 1176 Pa with exposure times in the range of milliseconds and up to 1200 stress load repetitions. The hemolysis was independent of the geometry of the microchannel and of the same order of magnitude as the reference channel. The applied models estimated higher hemolysis levels and significant differences between the microchannels.

Conclusions: The results suggest that short-term, highly dynamic stresses play a smaller role in hemolysis than assumed by the applied stress-based models.

O4

HAEMOLYSIS MODELLING OF A POSITIVE-DISPLACEMENT TOTAL ARTIFICIAL HEART

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Objectives: Total artificial hearts (TAHs) are used for treatment of end-stage biventricular heart failure where a suitable donor heart is unavailable. Haemolysis is the damage to red blood cells with potentially harmful side effects. Mechanical circulatory support devices, like a TAH, create flow conditions that may give rise to haemolysis. Most haemolysis models are developed for rotary blood pumps. The aim of this study was to assess the appropriateness of available haemolysis models on a positive-displacement TAH.

Methods: A CFD model of the Realheart TAH V11.2 was created in Ansys Fluent V2022R2, using the same previously developed fluid-structure interaction modelling strategy that predicted valve motion for the legacy device V11C. The haemolysis index (HI, %) was calculated by assessing a shear-dependent power-law model using both an Eulerian scalar transport and Lagrangian particle tracking approach, using empirical constants established for rotary blood pumps. The model was solved until outlet HI values were constant. Three conditions were simulated: a baseline systemic condition at 5 L/min was compared against a systemic flow at 7 L/min and pulmonary flow at 5 L/min, achieved by varying heart rate and downstream two-element Windkessel parameters. Haemolysis was experimentally determined according to ASTM standard F1841-97.

Results: Pulmonary HI was 29% and 16% smaller than the baseline systemic HI for both Eulerian and Lagrangian models respectively. Systemic HI at 7 L/min was 24% and 30% greater than baseline for both Eulerian and Lagrangian models respectively. Experimentally, a 29% decrease and 80% increase between baseline, pulmonary and systemic flow at 7 L/min respectively was observed.

Conclusions: Eulerian and Lagrangian HI was the same order of magnitude. The relative change in HI between pulmonary and systemic baseline was the same as experiments, but the model did not exactly capture the same increase at 7 L/min. Future work will focus on model optimisation and parameter investigation.

O5

MICROFLUIDIC STUDY ON A TRANSPARENT BLOOD MODEL FLUID WITH ALGINATE MICROSPHERES

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Objectives: The reduction of blood damage is still a big challenge in blood-carrying medical devices. In vitro experiments are performed to investigate the damage-causing effects, but due to the opaqueness of blood cells, only near-wall flows can be observed. Thus, several transparent blood models to visualize the rheologic behavior of blood have been proposed and examined. Nevertheless, two-phase blood models with added particles still represent the properties of blood inadequately or are very expensive and complex to produce.

Methods: In this in vitro study, the viscosity, the flow behavior and the cell deformation of human red blood cells have been compared to a novel, easy-to-produce, two-phase blood model fluid with deformable alginate microspheres. The comparison has been performed in a cone-plate rheometer, a straight and a hyperbolic converging microchannel.

Results: The viscosity of the blood model fluid with a particle fraction of 30 % shows a shear-thinning behavior, comparable to that of blood at room and human body temperature within shear rates from 7 – 1000 s-1. In high shear rates the blood model fluid reaches an almost constant value of 4.6 mPas at 22 °C and 3.7 mPas at 37 °C. The size of the alginate microspheres is 8.37 µm ±1.87 µm in diameter. They are deformable in an extensional flow with a deformation index of 0.44 ± 0.14 that is 14 % lower than the one of the red blood cells. In a straight microchannel the blood model fluid forms a cell free layer comparable to that of blood. The experiments show a good optical accessibility of the two-phase flow with traceable movements of individual microspheres in the center of the microchannel.

Conclusions: With this study it could be shown that the blood model fluid is well suited to be used in experimental setups to mimic the two-phase flow behavior of blood.

O6

IN-VITRO HEMOCOMPATIBILITY ASSESSMENT OF BLOOD PUMPS UNDER REALISTIC OPERATING CONDITIONS

Bender M.[1], Escher A.[1], Röhrich M.[1], Fischer M.[1], Hametner C.[2], Laufer G.[1], Kertzscher U.[3], Zimpfer D.[1], Jakubek S.[2], Granegger M.[1]

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Objectives: Conventional mock circulatory loops (MCLs) cannot replicate realistic hemodynamic conditions without inducing blood trauma. This constrains in-vitro hemocompatibility examinations of blood pumps to

static operating conditions that do not reflect clinical scenarios. The aim of this study was to develop an atraumatic MCL based on a hardware-in-the-loop concept (H-MCL) that enables hemocompatibility assessment under realistic pressure and flow conditions.

Methods: The atraumatic H-MCL was designed for 450±50 ml of blood with the sole blood-contacting components being the two polycarbonate reservoirs, the silicone/polyvinyl chloride tubing and the blood pump under investigation. An advanced control strategy was chosen to control the hemodynamic pressures (calculated in real time by a numerical cardiovascular model) while maintaining a constant blood level: To ensure physiologic reference tracking and to account for inherent coupling effects a decoupling pressure control was derived by feedback linearization. The level control was addressed by an optimization task, to overcome periodic loss of controllability. The HeartMate 3 (HM3) was showcased to evaluate the HMCL's accuracy at typical hemodynamic conditions and to demonstrate the H-MCL's atraumatic properties. Pilot hemolysis experiments were conducted with bovine (n=2) and human (n=2) blood, and evaluated in terms of the normalized index of hemolysis (NIH).

Results: Typical hemodynamic scenarios of patients with full and partial support were replicated with marginal coupling effects and root mean square error (RMSE) of 1.74±1.37 mmHg and 0.94±0.83 mmHg, respectively, while the fluid level was not exceeding a range of ±4% of its target value. The initial examinations of hemolysis demonstrated the atraumatic characteristics of the novel H-MCL, as evidenced by levels of NIH (bovine: 5.1-7.2mg/100L; human: 1.6-1.8mg/100L) that are consistent with those reported in existing literature.

Conclusions: Collectively, these findings indicated the H-MCL's potential for in-vitro hemocompatibility assessment of blood pumps within realistic hemodynamic conditions.

Session: Hemodialysis and Uremic Toxins

O7

REAL-TIME OPTICAL MEASUREMENT OF CARDIORENAL TOXIN URIC ACID DURING HEMODIALYSIS

Holmar J.[1], Arund J.[1], Luman M.[2], Adoberg A.[2], Leis L.[2], Paats J.[1], Pilt K.[1], Tanner R.[1], Fridolin I.[1]

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Objectives: Chronic kidney disease (CKD) patients are at higher cardiovascular risk than the general population. Vascular calcification (VC), one of the cardiovascular complications, is mediated by oxidative stress, inflammation, and accumulation of uremic toxins during CKD. Uric acid (UA) is a cardiorenal toxin that accumulates in the case of CKD. Therefore, effective removal of UA is crucial. The primary therapy for replacing kidney function and removing toxins from end-stage CKD patients is hemodialysis. Effective removal of toxins can be estimated by blood or dialysate lab analysis or optical monitoring.
In this study, the authors tested a miniaturized optical sensor for monitoring UA levels and removal.

Methods: Twenty-two patients were included, and concentration, removal ratio, and total removed amount of uric acid were observed during 88 hemodialysis sessions in Tallinn, Estonia. Four treatments for each patient were performed with different dialysis settings with two different dialysis modalities (HD and HDF) and various blood and dialysate flows and types of dialyzers according to predefined treatment settings. Optical multi-component monitor (MCM) sensor (Optofluid Technologies OÜ, Tallinn, Estonia), developed in the frame of European Commission project 767572 "Online Dialysis Sensor Phase2 (OLDIAS2), was connected with the dialysate outlet drain for uric acid measurements. As a reference, spent dialysate samples were collected and analyzed in the clinical chemistry laboratory.

Results: The results (Mean±SD, Lab vs. Sensor) of the uric acid concentration 57.20±34.05 vs. 57.22±33.09 µmol/L, reduction ratio 68.72±10.91 vs. 67.89±12.48 %, and total removed amount 7.00±2.10 vs. 7.33±2.29 mmol did not differ significantly from the values obtained from the clinical laboratory ($p<0.05$).

Conclusions: The study demonstrated a good concurrence between concentration and removal parameters of uric acid in the spent dialysate from the clinical laboratory and the miniaturized optical real-time sensor. The study indicates that the optical sensor is reliable for on-line monitoring of uric acid removal during hemodialysis.

O8

EFFECTS OF FILTRATION ON THE REMOVAL CHARACTERISTICS OF DIALYSIS MEMBRANES WITH ADSORPTION PROPERTIES

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Objectives: Dialysis membranes made of polymethyl methacrylate (PMMA) have been used for hemodialysis for a long time, and PMMA has specific adsorption removal characteristics due to its adsorption properties. Currently, PMMA membranes are also beginning to be used for hemodiafiltration in Japan. We conducted the present study to clarify whether the adsorption properties of PMMA membranes are altered by filtration.

Methods: The solute removal characteristics for β-lactoglobulin (β-LG; molecular weight 18.4 kDa, 36.8 kDa as dimer, large middle molecule) were examined at different filtration flow rates using three PMMA membrane filters (PMF-21A, NF-2.1US, NF-2.1HS) with different pore sizes. Bovine blood (2.9-3.6 L) was adjusted to a hematocrit of 30% ± 1% and a total protein concentration of 6.5 ± 0.1 g/dL, and β-LG was added at 30 mg/L. The experimental conditions were HD (filtration rate: 0 mL/min) and post on-line HDF (filtration rate: 42 mL/min and 63 mL/min). The amount of β-LG removed by adsorption was calculated from the difference between the amount of β-LG removed from the blood side and the amount permeated to the dialysate (filtrate) side.

Results: Under all conditions, β-LG was removed only by adsorption to the membrane, and there was almost no leakage to the dialysate side. The amount of β-LG adsorbed was smaller for the membranes with the smaller pore sizes, while it increased with increasing filtration flow rate for all membranes. When the pore size or the filtration flow rate was increased, the amount of β-LG that could enter the membrane increased, that is, the amount of β-LG removed by adsorption increased.

Conclusions: PMMA membranes with adsorption properties show a greater amount of adsorption of large middle molecules during HDF when the pore size and filtration flow rate are increased.

O9

ANTICOAGULATION STRATEGY IS ASSOCIATED WITH BLEEDING AND QUALITY OF LIFE IN CHRONIC HAEMODIALYSIS PATIENTS

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Objectives: In haemodialysis (HD), prevention of circuit clotting is a concern, but tools to monitor anticoagulation strategies are lacking. Also, data on bleeding complications and the eventual impact on Quality of Life (QoL) in this population are scant. We therefore investigated bleeding incidence, dialyser clotting and QoL in relation to anticoagulation doses in maintenance HD patients.

Methods: This prospective longitudinal observational study included all chronic HD patients. Bleeding tendency was scored with ISTH-BAT and HAS-BLED questionnaires at week 0, 4, and 8. Patient's limbs were visually scored for bruises and haematomas, and QoL was assessed using EQ5D-3L and Visual Analogue Scale (VAS) questionnaires. At week 0, the used haemodialyser was scanned in a micro-CT scanner to quantify the number of patent fibers.

Results: The 70 included patients used either enoxaparin (n=48), tinzaparin (n=17), direct anti-Xa inhibitors (n=1) or no systemic anticoagulation (n= 4) for dialysis. Bleeding scores were 0[0;1] and 3[2;4] for ISTH-BAT and HAS-BLED, respectively, and visual scoring showed 2[0;4] bruises and haematomas. QoL was 0.85[0.77;1.00] for the EQ5D and 70[60;80] for the VAS. Fiber patency was 81[70;90]%, but was not associated with anticoagulation dose (p=0.103). Patients in the highest versus lowest tertile of anticoagulation dose had a worse VAS score (p=0.027), and patients identified as having versus not having a bleeding tendency by ISTH also had a worse VAS score (p=0.010). Cluster analysis showed 49 patients in cluster 1, characterised by lower anticoagulation dosing (P=0.008), lower fiber patency (borderline P=0.067), lower ISTH bleeding scores (P=0.002) and visual scoring (P=0.004), and higher QoL with EQ5D ($P<0.001$) and VAS ($P<0.001$), as compared to 21 patients of cluster 2.

Conclusions: While dialyser fiber blocking was limited, the substantial degree of minor bleeding suggests that current anticoagulation dose regimens are potentially too exaggerated. This was associated with a negative impact on quality of life.

O10

PREVENTION OF POST-TRANSLATIONAL MODIFICATIONS (PTMS) IN CHRONIC KIDNEY DISEASE (CKD) WITH FREE AMINO ACID SUPPLEMENTATION

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Objectives: Chronic kidney disease (CKD) affects >10% of the population wordwide. In CKD patients the plasma concentration of uremic mediators is increased due to reduced kidney function. These increased concentrations cause numerous post-translational modifications (PTMs) like carbamylation, guanidinylation or oxidation of proteins, which can lead to an alteration of conformation, activity or function. Specifically PTMs of proteins like albumin are undesired, since their high mass prevents them to be cleared by the kidney or hemofiltration. Therefore, preventing PTMs beforehand is of high interest. Here we analyse the effect of amino acid supplementation and their capability to protect peptides from PTMs.

Methods: Three different peptides were analyzed for PTMs (carbamylation, guanidinylation, oxidation) after incubation with small molecules like urea, o-methylisourea and hydrogen peroxide by mass spectrometry. After reliably inducing PTMs, lysine, serin, or cysteine were added before the incubation.

Results: After incubation with urea, the peptides showed an additional signal in mass spectrometry caused by carbamylation, which was completely prevented by amino acid supplementation. Incubation with o-methylisourea led to single and double guanidinylation of the peptides. Lysine and serine supplementation prevented most of the guanidinylation, but cysteine could fully protect all three peptides. Lastly, incubation with hydrogen peroxide caused oxidation. Depending on the peptide, low or high amount of oxidation was detected. Low amount of oxidation could be prevented by all three amino acids, but high amount of oxidation was only reduced by cysteine.

Conclusions: Here we were able to induce uremic toxin specific PTMs. The degree of PTMs changed between the peptides. The presence of free amino acids showed an amino acid depending protection from PTMs, with cysteine having the best protective properties. The underlying mechanism will be further elucidated, as amino acid supplementation might be a promising therapy option to prevent PTMs in CKD to improve patient outcome.

O11

IDENTIFICATION AND CHARACTERIZATION OF A NOVEL INHIBITOR OF VASCULAR CALCIFICATION: CALCIFICATION BLOCKING FACTOR

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Objectives: Vascular calcification is a common comorbidity in patients with chronic kidney disease (CKD) undergoing dialysis, leading to various cardiovascular complications. Cardiovascular physiology and pathophysiology is influenced by adrenal glands via the synthesis and secretion of well-known compounds like mineralocorticoids, glucocorticoids and amine peptides. Therefore, in the current study, we investigated a previously unidentified adrenal gland mediated systemic regulation of the vascular calcification processes.

Methods: Chromatographic fractionation was used to separate the bovine adrenal gland homogenate. The resulting fractions were tested for their impact on vascular calcification processes in cells, aortic rings, and a rat model of vascular calcification induced by vitamin D3 and nicotine. Potential mediators were identified using mass spectrometry and by comparing them with relevant databases.

Results: We identified a 19 aa peptide, named "calcification blocking factor" (CBF), which reduces vascular calcification by hindering the transformation of aortic smooth muscle cells into osteoblast-like cells. CBF is released from the adrenal gland secreted parent protein Chromogranin A through enzyme-mediated cleavage by calpain 1 and kallikrein. Under calcifying culture conditions, CBF decreased the calcium content of aortic smooth muscle cells and aortic rings, as well as in the aortas of animals treated with vitamin D and nicotine (VDN). Pulse pressure as a marker of arterial stiffness of VDN animals treated with CBF significantly decreased. We show that CBF reduces vascular calcification via PIT-1/NF-κB/BMP2/p-SMAD pathway. Furthermore, individuals with end stage renal disease undergoing dialysis have notably lower levels of CBF, highlighting its role in the increased risk of vascular calcification in these patients, supporting our preclinical data. To determine the active site of CBF, we analyzed smaller fragments of the 19 aa peptide.

Conclusions: To conclude we identified and characterized a new 19 amino acid peptide, known as CBF, that regulates vascular calcification and is derived from the adrenal glands.

O12

POST-TRANSLATIONAL MODIFICATION OF APO A1 IN CHRONIC KIDNEY DISEASE

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Objectives: High-Density Lipoprotein (HDL) is a well-established cardioprotective agent and the dysfunctions of HDL contribute to the excess cardiovascular mortality in patients with chronic kidney disease (CKD). Post-translational modifications (PTMs) of HDL proteins can lead to functional impairments of HDL. There is a lack of conclusive mass spectrometric data on the occurrence of PTMs in HDL from the CKD collective compared to HDL from healthy persons. The aim of this study was to investigate the presence of PTMs in the major HDL protein apolipoprotein A-I (apo A-I) in CKD patients and healthy controls.

Methods: In this study, the prevalence of PTMs in HDL-associated Apolopoprotein A-1 from patients with different CKD stages as well as from healthy volunteers is investigated by application of MALDI-TOF/TOF mass spectrometry. The plasma of CKD patients (KDIGO stages 1-5 according to GFR) and healthy control subjects were purified and desalted and with Mass spectrometry methods MALDI-TOF-MS and following MS/MS-analyses for result validation. Analysis of mass spectra by comparison of identified peaks with matched proteins in the MASCOT data base (Matrix Science, UK). Additional MS-Analyses of human apo A-I (Sigma, Germany) that was in vitro modified before by incubation with urea.

Results: Guanidinylations of apo A-I are identified for the first time with high accuracy and sensitivity utilizing the MALDI-TOF-MS method. The frequency of apo A-I guanidinylations in CKD patients is increased comparatively stronger in advanced disease stages. Results are reproducible when modifying apo A-I in vitro, suggesting a urea-dependent mechanism of protein guanidinylations in uremic patients. Pathophysiological consequences of guanidinylated apo A-I remain to be elucidated.

Conclusions: In an ongoing clinical study, the pathophysiological consequences of guanidinylated apo A-1 are analyzed.

Symposium: Artificial Pancreas: new Challenges and Opportunities Towards fully automated and Personalized Diabetes Management

O13-K
ARTIFICIAL PANCREAS: FROM AN INVASIVE DEVICE TO A PORTABLE, PATIENT-TAILORED AND ADAPTIVE CONTROL SYSTEM ENSURING PATIENT'S SAFETY

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Objectives: Type 1 Diabetes is an autoimmune disease which requires exogenous insulin treatments to maintain the glycemia in the safe range. The conventional therapy is far from being optimal due to the absence of a feedback action. The so-called Artificial Pancreas (AP) is a closed-loop system composed of a glucose sensor, an insulin pump and a control algorithm which defines the optimal therapy. All over the years, the AP has become increasingly portable and less invasive, allowing longer trials outside the hospital environment still guaranteeing the patient's safety. However, the significant inter and intra-patient variabilities call for a patient-tailored and adaptive control system ensuring patient's safety.

Methods: The Pavia teams developed a Model Predictive Control (MPC) algorithm that was gradually improved during the last decade exploiting the results obtained in vivo, from the inclusion of a posteriori constraints based on clinical experience to the adaptation of the controller over the time to face the physiological changes of the patient.

Individualized models have been identified to consider the inter-patient variability, using both classic identification techniques and newer machine learning approaches. The periodical adaptation of the controller to the patient evolution over the time has also been explored to deal with the inter-day variability and multiple-model predictors to handle the intra-day variability.

Results: Promising results have been obtained in silico and in vivo during monthly trials with the Pavia's MPC and with its adaptive version. The HbA1c was significantly improved with respect to conventional therapy. In silico study shows that the use of patient-tailored and adaptive systems can improve the glucose prediction and the overall control.

Conclusions: New machine learning approaches are currently under study to design new generation alarm systems for hypo and hyperglycaemia prevention. New advanced intraperitoneal (IP) sensors and pumps are currently under development to design an IP-IP-AP with a more physiological route.

O14
TAILORED TYPE 2 DIABETES SIMULATOR FOR OPTIMALLY IN SILICO TESTING INSULIN TREATMENTS IN TARGET POPULATIONS

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Objectives: In silico trials have shown an important role in developing and testing type 1 diabetes (T1D) treatments, including artificial pancreas (AP). Interestingly, AP technology has recently being used also in people with type 2 diabetes (T2D). Compared to T1D, T2D pathophysiology is more complex and variable, e.g., due to different ethnicity and stage of disease progression. Thus, AP optimization around a specific T2D target population might be more challenging than T1D. To support this phase in silico, we propose a method for tailoring the existing early-stage Padova T2D simulator (T2DS) to a target population.

Methods: In order to illustrate the method functioning, an illustrative case study is provided, where the T2DS is tailored to insulin-naïve Caucasian T2D subjects who start insulin therapy. Toward this end, first the T2DS is identified on available average data of the target population. The outcoming estimated model parameters are used as reference for generating a new cohort of virtual subjects describing the Caucasian T2D pathophysiology. A model of insulin degludec (iDeg) is also incorporated into the T2DS in order to enable basal insulin therapy. The in-silico Caucasian population is finally validated by simulating an insulin titration trial, with iDeg dose individually adjusted for optimal glucose control, and by comparing the simulated study outcomes with the clinically available counterparts.

Results: Simulated distributions of fasting plasma glucose (FPG) and iDeg dose are statistically similar to the respective clinical outcomes: at the end of the basal insulin titration period, in silico vs. clinical FPG is 102 ± 22mg/dL vs. 106 ± 40mg/dL, iDeg dose is 0.56 ± 0.43U/kg vs. 0.59 ± 0.35U/kg.

Conclusions: The tailored T2DS is representative of insulin-naïve Caucasian T2D subjects, thus it can effectively support therapy optimization for the target population. The tailoring methodology can be applied to other T2D stages, offering a reliable platform for extensively in silico testing different treatments before human trial.

O15
AN ANNOUNCEMENT-FREE SINGLE-/DUAL-HORMONE ARTIFICIAL PANCREAS CUSTOMIZABLE ACCORDING TO THE PATIENT'S PREFERENCES

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Objectives: The automatic regulation of blood glucose with artificial pancreas (AP) systems outperforms other insulin treatments for type 1 diabetes. Commercial devices require mealtime and estimated carbohydrate content to handle meals and anticipative actions like reducing basal infusion or increasing glucose targets to compensate for exercise. These manual actions can be burdensome for most patients. Although announcement-free systems have been researched, they may not fit more proactive patients wanting to intervene. Concerning hypoglycemia mitigation, either carbohydrate suggestions or continuous glucagon reduce the exercise-related hypoglycemia risk. Pen-based glucagon micro-dose administration can also be a feasible option in patients more concerned with weight gain without the increased complexity of pump-based delivery. This work proposes a new user-customizable single-/dual-hormone AP that accommodates different user preferences in interacting with the system.

Methods: The proposed AP was conceived for a meal-announcement-free operation, albeit including a non-interacting feedback scheme that enables optional meal announcements without overdelivery risk. Moreover, the users can choose between carbohydrate suggestions or glucagon delivery to mitigate hypoglycemia. Glucagon can be administered continuously (pump) or impulsively (pen). All configurations were simulated with the virtual adult cohort of the UVa-Padova simulator in a two-week scenario with meals and aerobic exercise sessions.

Results: In all the cases the percentage time in range exceeded the recommended 70%. Announcing meals reduced the percentage time above 180 mg/dL by more than 5% without significantly increasing the percentage time below 70 mg/dL. Furthermore, glucagon delivery results in a similar percentage time below 70 mg/dL to carbohydrate suggestions with the advantage of being a non-caloric action.

Conclusions: These positive results in silico motivate further validations of the proposed AP in clinical trials.

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O16

REMOVING THE PATIENT FROM THE LOOP: FROM HYBRID TO FULLY AUTOMATED INSULIN DELIVERY IN TYPE 1 DIABETES

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Objectives: There is enough evidence showing the safety and efficacy of current commercial hybrid closed-loop (HCL) automated insulin delivery (AID) systems in improving glucose control in people with Type 1 Diabetes (T1D). However, these systems remain highly dependent on announcement and quantification of meals and physical activity. Fully Closed-Loop (FCL) offers a way to remove this dependency.

Methods: In two randomized crossover supervised clinical trials of T1D and adults, we assessed the feasibility of removing the announcement of meals and aerobic physical activity, respectively. Two unannounced meal- and exercise-aware FCL systems (mFCL and eFCL) were compared with their respective announced meal- and exercise-unaware HCL systems (mHCL and eHCL). A separate analysis, showing the potential of removing such announcements is presented and hence reduce the disease burden in this population.

Results: (Study 1: mFCL vs mHCL) Thirty-five adults with T1D were randomized for the meal study. In a representative meal, the TIR for the 5h-postprandial period was 63±19% and 75±23%; overall, 24-h control was 86±10% and 77±12%, both outcomes with significant difference favoring mHCL. TBR remained low in both interventions. (Study 2: eFCL vs eHCL) Fifteen adults with T1D were randomized for the exercise study. The eFCL system reduced the number of hypoglycemic events to 5 vs. 15 during a 45-min bout of aerobic exercise and 2 vs 11 in the 4-hour following the challenge, both with statistical significance. Overall, in the 24-h control, TIR remained acceptably good for both interventions.

Conclusions: While postprandial control remained best with mHCL, mFCL offered overall TIR above 70% with similar or lower exposure to hypoglycemia. In the case of exercise, reduction of participant's hypoglycemia was achieved with no exposure to hyperglycemia. Larger studies in uncontrolled environments are needed to extend the domain of validity of these technologies.

O17

COORDINATING MANUALLY ACTUATED CONTROL ACTIONS WITH AUTOMATIC BASAL INSULIN ADJUSTMENTS IN AN ARTIFICIAL PANCREAS FOR TYPE 1 DIABETES TREATMENT

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Objectives: Type 1 diabetes is a chronic disease caused by the autoimmune destruction of the pancreatic beta cells. The consequent lack of insulin compromise glucose homeostasis, forcing patients to perform multiple therapeutic actions to maintain their blood glucose in a nearly normal range (70-180 mg/dl). One of the primary actions is the administration of exogenous insulin to reduce blood glucose concentration. Unfortunately, insulin overdosing might cause hyperglycemia, a dangerous condition that must be treated immediately with the ingestion of fast acting carbohydrates (CHO) to increase blood glucose concentration. An Artificial Pancreas (AP) is a closed-loop insulin delivery system that assists the patients in the formidable daily challenge of managing their blood-glucose concentration. AP systems currently on the market acts only on insulin as a control variable. Here, we present a Model Predictive Control algorithm for glucose regulation that jointly plans insulin delivery and CHO ingestions.

Methods: While insulin delivery can be automatically actuated by commanding an insulin pump, CHO must be ingested by the patient and thus require manually intervention. Frequent CHO intakes are therefore impossible. To address this problem, we model CHO ingestion with Boolean variables and enforce sparsity in time of these manual actions with suitable constraints. The MPC optimization problem becomes a Mixed-Integer Quadratic Program, that can be efficiently solved with commercial software based on branch-and-bound strategies. The proposed control strategy was tested on the UVA/Padova T1D simulator, a FDA-accepted simulator of T1D subjects.

Results: With respect to an insulin-only strategy, the newly proposed algorithm increases the time spent of the nearly normal range in the majority of the patients, with larger benefits in those poorly controlled. This is achieved while simultaneously reducing time spent in hypoglycemia.

Conclusions: Coordinated planning of insulin and CHO can improve blood glucose, although at the cost of an increased patient involvement.

O18

FULL INSULIN INDEPENDENCE AFTER TRANSPLANTATION OF BIONIC PANCREATIC FLAPS.FIRST RESULTS OF PRECLINICAL STUDIES IN LARGE ANIMALS

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Objectives: The first milestone of a new therapy for the treatment of T1D is the development of 3D bioprinted petals consisting of pancreatic islets and biomaterials. The aim of the study was to demonstrate the functionality of pancreatic islets in in vivo studies on large animals.

Methods: Domestic pigs were the research model. The animals were divided into 4 groups:(1)healthy pigs (Control; n=3);(2) animals with T1D after pancreatectomy, treated with insulin (T1D;n=3);(3) animals after pancreatectomy and autotransplantation of pancreatic islets to the liver (LIVER; n=3);(4) animals with T1D after pancreatectomy, which were autotransplanted with bionic petals (3D-PETALS; n=3).The effectiveness of the transplantation (TX) was assessed by the concentration of glucose, insulin intake and C-peptide. The observation lasted 1 month.

Results: The results showed that in the LIVER group, insulin intake within 3 weeks decreased by 71% compared to the demand before TX. Whereas 1 month after TX, the demand was lower by 62%. The 3D-PETALS group showed that the insulin intake in 3 weeks after TX decreased by 65%, and within a month decreased by 84%. In the 4th week after TX, the insulin intake average in the T1D group was 8.17U, while in the LIVER group=2.44U and in the 3D-PETALS group=1.06U. Islet TX significantly reduced insulin intake (T1D vs LIVER; p=0.0001 and T1D vs 3D-PETALS; $p<0.0001$). Glucose measurement showed significant changes. After 1 month of follow-up, glucose levels were significantly lower in the LIVER vs T1D (265.8mg% vs. 310.2mg%; $p<0.0001$) and 3D-PETALS & T1D (198.3mg% vs 310.2mg%; p=0.0354). Most importantly, glycemic levels were also significantly lower between the LIVER & 3D PETALS groups (265.8mg% vs. 198.3mg%; p=0.0021). The concentration of C-peptide during the study was 0.14ng/ml.

Conclusions: Bioprinted petals with dECM-based bioink significantly reduces diabetic parameters. Thus, it seems to be an effective therapy for people with T1D.

Symposium: New Trends and Applications in Mechanical Circulatory Support

O19-K
SUBPULMONARY SUPPORT OF FONTAN PATIENTS - FROM COMPUTER SIMULATION TO CLINICAL APPLICATION

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Objectives: A novel venous cannula (VC) was designed as an additional component of the EXCOR-VAD™ (Berlin Heart) to improve sub-pulmonary hemodynamics as a bridge to transplant of patients suffering a failure of their subpulmonary Fontan-circulation. After clinical implementation, the need for an adjustment of the VC to address a larger number of smaller patients became obvious. We like here to describe the crucial part of different techniques of computer simulation in this process.

Methods: After having interviewed several experts, their suggestions regarding an adjustment of the VC-shape for smaller patients were summarized by a computed model. In a three-dimensional simulation, its morphological compatibility with the anatomy of small patients (Body Surface Area: < 0.6 m2; Body Weight: < 15kg) was examined by a virtual fitting. The resultant model was subjected to a hemodynamic flow-simulation to assure proper function.

Results: The virtual fitting revealed an optimal adjustment of the VC to smaller patients not only by a true-to-scale minimization of the former model, but also by the reduction of shape as crucial step. The hemodynamic flow-simulation demanded only a minimal modification.

Conclusions: We achieved by this computer-simulated workflow a suitable approach for a new design of a VAD-cannula that allows optimal results in size, shape and function in the very specific issue of small patients suffering a failure of their subpulmonary Fontan-circulation.

O20
DEVELOPMENT AND TESTING OF THE CORWAVE MEMBRANE PUMP

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Objectives: Continuous-flow left ventricular assist devices (LVADs) are associated with serious adverse events including stroke and bleeding, notably due to absence of physiologic pulsatility, lack of pump adaptation to patient activity, and ongoing blood trauma. CorWave is developing a unique LVAD employing an undulating membrane to propel blood. The membrane oscillation frequency and magnitude can be modulated to generate a physiologic pulse synchronized to the native LV. Herein, we present the development and testing of the membrane pump and adaptive control algorithms.

Methods: Algorithms for pulsatility, suction detection, arrhythmia detection, and physiologic adaptation were developed, then tested in a mock circulation loop (MCL). Pumps and control algorithms were evaluated in sheep implants, up to 3 months in duration, including in sheep with heart failure, to evaluate hemodynamic performance. Additional implants were completed without post-op anticoagulation to evaluate thrombogenicity. Long-term durability studies have been started on individual membranes and complete pumps.

Results: MCL tests indicated that in synchronous pulsatile mode, the pump could generate pulse pressures up to 30 mmHg allowing aortic valve (AV) opening every beat, compared to 10 mmHg for continuous-flow LVADs with AV opening once every 3-5 beats. During acute implants in sheep with heart failure, the pump autonomously responded to changes in pre-load and afterload. In chronic implants, the algorithm synchronized with the native LV in over 97% of heart beats. Thrombo-provocative implants showed no evidence of thromboembolism. In durability tests, membranes have reached 2 years, while long-term pump durability tests remain ongoing.

Conclusions: The development and testing of the CorWave LVAD and physiologic control algorithms demonstrated the pump could generate physiologic pulsatility and adapt to altered hemodynamics. The robustness of the algorithms was confirmed in chronic implants. Comprehensive testing demonstrated that the CorWave pump can deliver pulsatility, adaptability, and hemocompatibility required to improve LVAD therapy.

O21
IS IT TIME TO RETHINK THE ROLE OF CHRONIC ANIMAL STUDIES IN MCS DEVELOPMENT?

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Objectives: In 2022, the FDA Modernization Act 2.0 was passed, relieving the need for animal testing in drug development. At the same time, in MSC development a big share of effort is still put in chronic animal studies. Herein, the authors review the efficient use of animals and in vitro models for MCS development.

Methods: The new act encourages alternative testing methods for preclinical drug development, while ISO 14708-5 still recommends validating many endpoints in animals that can potentially better be assessed using in vitro or in silico studies. Looking at past studies from different MSC developments, the effort on in vivo trials (up to hundreds per device) does not correlate with the impact on validation. A huge discrepancy between in vivo and clinical findings exists.

Results: In vitro biocompatibility testing has significantly advanced in recent years. Several research groups are developing in vitro thrombogenicity assays. CFD can be used to determine hemolysis and thermal impact of design or operating condition. Medical imaging facilitates washout analysis and hybrid simulators provide hemodynamic characterization across a wide range of operating conditions including suction models. Human blood is 2 to 3 times more hemolytic than blood from large animals and should be used for in vitro hemolysis studies. Human cadavers and virtual patients enable anatomical fitting studies. What remains is the surgical procedure which can be developed on cadavers and acute animals.

Conclusions: Although hemolysis, stroke, pump thrombus and GI bleeding have not been an issue in in vivo studies of several MCS devices to date, they remain an issue in the clinic. Since several approved MCS devices have available clinical data, we should use these to develop better standardized in vitro tests using these devices as baseline controls aiming to develop devices that are at least equal to or better than our community's past performance.

O22
MECHANICAL SUPPORT FOR FAILING LYMPHATIC FUNCTION: A CONCEPTUAL STUDY

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Objectives: Cardiovascular diseases often coincide with lymphatic dysfunction: Elevated central venous pressures, for instance, may lead to both increased lymphatic preload (lymph production) and elevated lymphatic afterload (impeding lymph return to the cardiovascular system). Collectively, this may cause lymphatic overload with potential lymphatic failure. This study aimed to model the central lymphatic system, to identify key requirements for lymphatic support and to develop a prototype of a lymphatic assist device.

Methods: A lumped-parameter model was developed to simulate the largest lymphatic vessel connecting the lymphatic system to the cardiovascular system – the thoracic duct – as a chain of individual contractile units (i.e. lymphangions). The model accounts for key mechanisms of lymphatic pumping including signal propagation between adjacent lymphangions, refractory periods upon contractions, and shear-mediated modulation of contraction strength. The thoracic duct model was examined across various pre- and afterload conditions (Pin: 5-25mmHg; Pout: 5-25mmHg) to identify key prerequisites for lymphatic support. Corresponding findings served to devise a soft robotic assist device for mechanical support of the thoracic duct near the junction with the subclavian vein.

Results: Elevated preloads (>10mmHg) with low afterloads (5mmHg) resulted in high lymph flow (>8.2mL/min). These conditions led to shear-mediated inhibition of contraction strength (with a >10% reduction) to minimize flow resistance, enabling passive fluid flow behavior with persistent valve opening. In contrast, when afterload considerably exceeded preload, lymph flow was significantly hampered (<0.06mL/min), signifying the need for lymphatic assistance. To address this, a miniaturized lymphatic assistance device (L=10mm; D=5mm) was realized, comprising a fabric material embedded with Velcro and concave pneumatic pockets appropriate for extravascular wrapping around the thoracic duct.

Conclusions: The numerically identified design requirements for lymphatic support could be translated toward a prototype of a lymphatic assist device that may hold the potential for lowering lymphatic afterload and restoring lymph flow by peristaltic pumping.

Symposium: Artificial Kidney

O23
CARBON FOOTPRINT OF A FRENCH HEMODIALYSIS FACILITY

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Objectives: The objective of this work was to evaluate the carbon footprint of a hemodialysis unit in France using the Bilan Carbone approach developed by The French Agency for Ecological Transition and the Bilan Carbone Association.

Methods: Activity data associated with hemodialysis treatment at the Charles De Gaulle facility in 2021 was collected and converted to unit of tonnes of CO2 equivalents (t CO2-eq) via specific emissions factors. This facility provides hemodialysis through a total of 56 hemodialysis generators.

Results: Over the year 2021, the Charles de Gaulle facility provided a total of 25270 hemodialysis treatments ensuring the care of approximately 162 patients (at a rate of 3 sessions per week). The associated annual carbon footprint for the facility was 1436 t CO2-eq. Annual carbon footprint amounted to 8.9 t CO2-eq/patient/year corresponding to 57 kg CO2-eq /treatment. The main sources of emissions were products and services purchased (30% of total emissions), patients and staff travels (25% of total emissions), and fixed assets (21% of total emissions).

Conclusions: Our results confirm the high carbon footprint associated with in-center hemodialysis, showing that it is mainly attributable to purchases, travels, and fixed assets. These empirical data will serve as a basis for reflection in the development of a strategy to reduce GHG emissions associated with hemodialysis.

O24
EFFECT OF THE PARTICLE SIZE OF PHOTOACTIVE POROUS COORDINATION POLYMERS ON NITRIC OXIDE RELEASE

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Objectives: One of the reasons for the development of complications during hemodialysis therapy is platelet activation due to contact between the blood and artificial materials. We found that addition of nitric oxide (NO) to the dialysate inhibits blood coagulation, and potentially reduces complications. However, NO gas is difficult to handle for clinical use due to the need for a high-pressure gas cylinder. In the present study, we used a nitric oxide framework (NOF), a photoactive

porous coordination polymer as the NO-releasing agent that is easily produced and releases NO in response to light, and attempted to clarify the effect of the particle size of NOF on NO release.

Methods: To produce different sizes of NOF, the stirring or diffusion method with the reaction time set at 18 hours, 4 days, 1 week, or 2 weeks were used. The particle size of the NOF was measured on SEM images. NOF was activated by light in distilled water, and the amount and rate of NO release from the sample were evaluated by the Griess method.

Results: The particle size of NOF produced by the stirring method was the smallest (<10 μm), and the size increased with increasing reaction times when produced by the diffusion method (10 to 100 μm). The amount and rate of NO release from NOF produced by the diffusion method decreased with increasing particle sizes. Longer reaction times increased the particle size, which showed less efficient NO release, either because NO is not released from the center or not formed NOF at all.

Conclusions: The diffusion method allows NOF with large particle sizes to be produced, depending on the reaction times, but very large particle sizes were associated with a reduced NO release capacity.

O25

NEXT GENERATION OF EXTRACORPOREAL ALBUMIN DETOXIFICATION (ECAD) IMPROVES SURROGATE SURVIVAL BIOMARKERS WHEN COMPARED WITH MARS IN A RANDOMIZED TRIAL

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Objectives: Meta analysis have concluded that Extracorporeal Albumin Detoxification (ECAD) using MARSTM provides a short term survival benefit. In order to further improve survival, the next generation of ECAD adsorbents, („HepalbinTM“) was investigated in a clinical trial.

Methods: Subjects with an indication for ECAD were randomized to receive either MARSTM first and HepalbinTM second or vice versa. Serum samples investigated for reduction of bilirubin, bile acids and improvement of albumin binding function. Clinical parameters, hepatocyte and granulocyte function were measured.

Results: Total bilirubin was reduced from 360±165 to 285±131 umol/l by 21% by HepalbinTM and from 354±178 to 287±149 umol/l by 19% by MARSTM ($p<0.05$ pre-/post). Bile Acids were reduced from 95.75(21.4-333) to 37.8(7.7-106) umol/l (61%) by HepalbinTM and from 99.45(31.5-309) to 62.35(17-185) umol/l (37%) by MARSTM. Albumin Binding Capacity-(ABiC) improved significantly in 6 hour treatment from 52.9±11.7 to 62.3±12.4 % by HepalbinTM ($p<0.05$) and from 55.44±14.4 to 59.0±13.3% (n.s.) by MARSTM. Detoxification Efficacy (DTE) was unchanged during MARSTM (12±7vs.11 ± 8%;n.s.) while it was significantly increased after HepalbinTM (9.7± 8.4vs.17± 18%;$p<0.05$). Binding Efficacy (BE) was unchanged during MARSTM (23±9vs.22 ± 9%;n.s.) while it was significantly increased after HepalbinTM (20±8vs.25±6%;$p<0.05$). During a single treatment, HepalbinTM improved HE in 22%vs.5% in MARSTM and in Pruritis, response was seen in both treatments, but on 15% more of the patient`s during HepalbinTM. In the Bioassay tests, HepalbinTM resulted into a significant reduction of plasma`s hepatotoxicity and improvements of hepatocyte growth and granulocyte function (phagocytosis) while MARSTM was not associated with significant changes.

Conclusions: Significantly increased detoxification dose, effects on surrogate markers for survival, effects on prognostic scores and bioassays suggest that improvement of detoxification dose will contribute to the extension of survival benefits already seen with MARS now by the introduction of the next generation of ECAD based on HepalbinTM technology.

O26

LESS MICROBUBBLES ENTERED THE PATIENTS USING THE VENOUS CHAMBER EMBOLESS DURING HAEMODIALYSIS

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Objectives: The extracorporeal circuit (ECC) enables hemodialysis (HD) but air contamination of the blood appears and microbubbles (MBs) pass as microemboli into the return bloodline of the patient and deposit in lungs, heart and brain. Venous chambers aim to reduce contamination of MBs but chambers in clinical use have limited capacity to eliminate MBs. This clinical study intended to compare a new, Emboless®, chamber to the standard venous chamber of Fresenius 5008 (F5008).

Methods: Thirty-eight HDs were performed as 19 paired HD sessions. Eleven patients were included. Venous chambers used were either F5008 or Emboless, in a randomised order. Dialyzers, blood-pump speed, HD or HDF and ultrafiltration was kept similar between the pairs. Microbubbles were measured at the 'Inlet' and 'Outlet' of the venous chamber with an ultrasound device adjusted for HD (hil mode, BCC200, GAMPT). Measurements were made for MBs between all sizes 20μm-500μm diameter. If HDF was performed the first 30min measured were by HD and the subsequent 30min by HDF (extended time if less than 1000 detected inlet MBs). The percentage of change in 'MB-Outlet' versus 'MB-Inlet' counts were compared (paired Wilcoxon test). Maximum reduction could be -100% while increase of MBs (worsened) caused unlimited raise (+) percentage.

Results: The median overall change of MBs were for F5008 a reduction by -33% (mean -20 ±76%, N =8544) and for Emboless -69% (mean -56 ±54%, N=8402; and pairwise N=8093, $p<0.001$). The reduction was more efficient for Emboless vs F5008 for small (20-199μm) MBs (-50% vs -14%, $p<0.01$), medium (200-299μm) MBs (-73% vs - 36%, $p<0.01$) and large (300-500μm) MBs (-100% vs -67%, $p<0.01$).

Conclusions: Less MBs and subsequently less microemboli entered the patient using the Emboless® compared to using the Fresenius 5008 venous chamber during haemodialysis. Considering our previous autopsy studies, the results support less tissue damage of the patients using Emboless®.

Session: Tissue Engineering I

O27

INVESTIGATION OF THE POSSIBILITY OF SUBSTITUTING AN AUTOLOGOUS BIOLOGICAL HEART VALVE FOR VARIOUS VALVE DISEASES

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Objectives: We have been developing a novel autologous biological heart valve (biovalve) using a unique technique, called in-body tissue engineering, in which tissue is formed by applying the encapsulation reaction of connective tissue. In this study, we evaluated the performance and tissue structure by implantation experiments using large animals (adult goats) and examined whether the biovalve could be an option for various valve diseases.

Methods: The biovalve molds were made of acrylic and metal, implanted subcutaneously in the back of an adult goat, and the molds were

removed around 8 weeks after implantation to obtain the biovalve. The biovalve was surgically implanted into the aorta and pulmonary arteries of adult goats and its performance was evaluated.

Results: The biovalves could be implanted in the aortic or pulmonary valve positions by conventional open-heart surgery or transcatheter valve implantation, respectively. Postoperative angiographic and blood pressure waveform monitoring showed good mobility of the valve leaflets and no significant stenosis or regurgitation. The biovalves remained well beyond the maximum observation period of 3 years. At the end of the experiment, the biovalves showed good preservation of valve leaflet structure with little thrombus formation or calcification. Histologically, cellular invasion was observed in the connective tissue of the removed biovalves after 4 weeks, and neovascularization was also observed. A layer of vascular endothelium-like cells was also seen on the blood contact surface. In addition, these tissues were found to change into a structure resembling normal valvular tissue at the level of several weeks after implantation.

Conclusions: The biovalve is expected to be a promising alternative valve for various valve diseases because of its good histocompatibility in regenerative medicine, ease of application in artificial organs, and the advantage of being able to fabricate planned shapes.

O28

AN INNOVATIVE CULTURE SYSTEM TO INVESTIGATE VASCULAR TISSUE ENGINEERING BIOMECHANISMS

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Objectives: Vascular tissue engineering aims to regenerate vessels "at the target site" using cell-free scaffolds supporting endogenous regeneration. Despite encouraging in vivo proof-of-concept studies, intimal hyperplasia and early stenosis remain prevalent complications in graft implantation.
With the aim of investigating these phenomena, we succeeded in developing an innovative and versatile culture system able to perform cell seeding and mimic in vivo-like stimuli (pre-tensioning, wall shear stress (WSS) and cyclic pressure) for long-term experiments.

Methods: The developed system main components are: 1) a culture chamber; 2) a rotating mixer for semi-automatic cell seeding; 3) a pinch-valve to generate a pulsatile stress; 4) two fluid dynamic circuits (luminal and extraluminal compartments). Three-layered electrospun grafts (Øin=6 mm, l=60 mm), composed of a nanometric mesh of silk fibroin (SF) and polyurethane (PU) enclosed within SF layers, were manufactured, and used. Human umbilical vein endothelial cells (HUVECs) were seeded through an ad hoc semi-automated procedure (10^6 cells/ml), combining discrete and continuous rotations. After the seeding phase, the sample was maintained under culture condition for 3 days. Cell morphology was investigated by immunostaining.

Results: The developed culture system was successfully subjected to bench tests to verify cytocompatibility, adaptability with the assembly procedures under laminar flow hood and maintenance of sterility inside an incubator for long-term. We observed that HUVECs almost completely covered the graft and established a complex cell-graft and cell-cell interaction network, resulting in a compact endothelial cells monolayer. All these observations endorse the possibility to obtain a functional cell-populated graft to subject to physio-pathological environments of fluid flow.

Conclusions: The encouraging biological results represent a preliminary, but crucial step. Indeed, obtaining a reproducible graft colonization is fundamental for the exploitation of a custom-made device.
In perspective, through the developed innovative system, it will be possible to establish an accurate culture model that allows to investigate the complex biological interactions that occur in vascular tissue engineering.

O29

3D-BIOPRINTED BIONIC PANCREAS AS AN INNOVATIVE METHOD OF TREATING AND PREVENTING DIABETES - HOW FAR WE ARE FROM CLINICAL APPLICATION?

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Objectives: Type 1 diabetes (T1D) affects millions of patients. Islet or pancreatic transplantation is a method of treating complicated T1D. The limitation of these methods is the lack of organs for transplantation. 3D-bioprinting using living cells could be a solution. We present results of bioprinted bionic pancreas on animal model.

Methods: Research was carried out on 60 mice (SCID) and 24 pigs. The mice were divided into 3 groups: control; IsletTx (porcine islets transplanted under the kidney capsule); 3D-bioprint (3D-bioprinted petals with porcine islets transplanted). Petals were transplanted into the dorsal part of the muscles under the skin. Daily glucose measurement was performed, and the level of C-peptide was tested every 7-days. The pigs were divided into 4 groups: control; diabetic group (pancreatectomy-T1D); TX-petals group (transplanted 3D-bioprinted bionic petals with previous pancreatectomy); TX-BP group (pigs with transplanted 3D-bioprinted bionic organ with full vasculature). The animals were measured daily with blood glucose levels and c-peptide. 3D-bioprinted bionic pancreas were transplanted to the large vessels: aorta and vena cava.

Results: MICE: Fasting glucose was significantly lower in the IsletTx and the 3D-bioprinted groups compared to the control group since 7th day post-Tx. On day 14, decreased values were observed only in the 3D-bioprint group. PIGS transplantation: pigs in TX-petals group received full insulin independence after six weeks post transplantation with detectable c-peptide. Pigs in TX-BP had a stable flow through the organ in vivo up to two weeks post-tx. Transplantation of bionic petals resulted in full insulin independence post-tX in pigs.

Conclusions: Transplantation of a fully vascularized organ created with 3D-bioprinting technology can achieve stable blood flow in vivo.

O30

DEVELOPMENT OF A TESTING SYSTEM FOR THE CALCIFICATION POTENTIAL OF FULL-SIZE CELLULARIZED BIOMATERIALS IN VITRO

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Objectives: One of the significant problems associated with bioprosthetic heart valves is structural degeneration. Although novel anti-calcification treatments are improving the longevity of the heart valves, the mechanisms of structural valve degeneration (SVD) are poorly understood. One of the significant mechanisms of SVD is the formation of calcium deposits on and in the leaflets. Novel biohybrid prosthetic heart valves may reduce the risk of SVD through self-renewability, but their calcification potential remains to be fully explored.

Methods: We have developed an in-vitro test system adapted to the requirements of biohybrid implants or cellularized materials to investigate the calcification behavior. With this new tester, the calcification of complete implants can be assessed under physiological cardiac pressure in an accelerated setting. The calcification is induced by a cell-compatible fluid with a high physiological range of calcium and phosphate.

Results: Moreover, cytotoxicity assays demonstrated the device's cell compatibility. Additionally, a sterility test showed no evidence of bacterial growth after 2 weeks of incubation. In addition, in a proof-of-concept study with pericardium tissue, we were able to induce calcification and identify calcification initiation sites and visualize them by labeling with tagged fetuin-A and Von Kossa staining.

Conclusions: Our new test system will contribute to a better understanding of the different mechanisms of (early) calcification and will reveal the calcification potential of biohybrid implants without the need for animal experiments. Furthermore, the test system can be used for cell culture, so native heart valves or new systemic anti-calcification treatments can also be investigated.

O31

HIGH-THROUGHPUT GENERATION OF HYDROGEL MICRODROPLETS FOR MICROTISSUE ENGINEERING APPLICATION

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Objectives: Droplet microfluidics-based strategies are gaining popularity recently for various applications in biotechnology and therapeutics. However, achieving high throughput in producing cell-laden microbeads is still a challenge. Our research shows a reliable, single-run approach for the high-throughput generation of hydrogel cell microcarriers (the “cores” of,200 µm) using photo-crosslinking ‘on the fly’ followed by re-encapsulation in another hydrogel layer to form the “shell” (400-600 µm) for multi-type microtissue engineering.

Methods: Firstly, the system included a bead-generation chip with multiple parallel channels. The hydrogel containing a particular cell line was used to form water-in-oil emulsions with a combination of fluorinated oil and surfactant in an external circular track (HFE 7500 and PFPE-PEG-PFPE). The generated microbeads subsequently traveled through a crosslinking chip in front of a LED UV lamp to form crosslinked “cores”. Post-washing, the “cores” were remixed with a hydrogel containing the other cell type to create the “shell” in a broadened channel T-junction chip.

Results: The system facilitated high throughput and frequency of monodisperse microbeads. The microstructures produced by re-encapsulation showed significant cellular viability (~90 %) with efficient cell compartmentalization. The created platform enabled the culture of the different cell lines to form their niche and maintain crosstalk through the porous hydrogel. The cell-laden droplets are used for micro-tissue engineering to explore various applications. We generated a tumor-stromal model with breast cancer cells forming the tumoral “core” while the “shell” comprised fibroblasts to mimic the tumor microenvironment.

Conclusions: In the context of oncology, the 3D cancer-stromal model can help explore the cancer architecture and facilitate the study of the interaction between cancer cells and other components of the tumoral environment. Attempts are currently being made to extend the application of these “core”-“shell” microbeads to generate organoids (artificial pancreatic islets).

O32

SIRNA DELIVERY AND MICROTISSUE ASSEMBLY VIA GELATIN MICROPARTICLES FOR BONE TISSUE REGENERATION

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Objectives: Bone tissue engineering using human mesenchymal stem cells (hMSCs) is a promising strategy to support regeneration of bone defects. The cultivation and differentiation in a three-dimensional environment preserves cell-cell interactions and results in enhanced biological functions. However, the densely packed cell layers lead to an oxygen and nutrient gradient resulting in necrotic core formation [1]. In this study, we used gelatin microparticles cross-linked with an oligomer (cGM) than can serve for two purposes: 1) as a cell-adhesive biomaterial to reduce necrotic core formation and 2) as a siRNA delivery system to decrease expression of anti-osteogenic targets.

Methods: hMSCs were aggregated with various amounts of cGM and stimulated with osteogenic supplements to form microtissues. We analyzed the impact of different cGM amounts on cell viability and osteogenic differentiation markers. siRNA-loading of cGM was done via oligomer-stabilized calcium phosphate nanoparticles (CaP-NP). These showed to be a highly effective siRNA transfection reagent with a high siRNA loading efficiency in a previous project [2]. We determined siRNA silencing efficiency using the BMP-2 antagonist Chordin as a molecular target and evaluated effects on the osteogenic differentiation.

Results: Analysis showed that cultivation of hMSCs with cGM significantly increased cell viability and osteogenic differentiation. In comparison to monolayer cells, the loading of cGM with siRNA-carrying CaP-NP resulted in an increased silencing efficiency of Chordin in hMSCs that led to a remarkable increased mineralization of the microtissues.

Conclusions: Here, we present cGM as a promising biomaterial to improve bone tissue regeneration. As a cell-adhesive material, cGM increased cell viability and osteogenic differentiation of hMSCs. The loading of cGM with a Chordin siRNA via oligomer-stabilized CaP-NP showed a successful silencing of the BMP-2 antagonist Chordin with a remarkable increased mineralization.

[1] Schmitz, C. et al.: Front. Bioeng. Biotechnol. 2021, 9: 611837. [2] Mitrach, F. et al.: Pharmaceutics 2022, 14(2): 326.

Session: Ventricular Assist Device I

O33

MECHANISTIC INSIGHTS INTO HF-RELATED MORTALITY OVER PROLONGED HEARTMATE 3 SUPPORT

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Objectives: Recurrence of heart failure (HF) emerged as the main cause of long-term mortality in patients implanted with the HeartMate 3 (HM3) left ventricular assist device (LVAD). We aimed at deriving a possible mechanistic rationale of reported clinical outcomes and investigated the effects of prolonged HM3 support on left ventricular (LV) mechanics.

Methods: Data on pump parameters (i.e., pump speed, estimated flow, and pulsatility index) were prospectively recorded in consecutive HM3 patients. Data were first recorded following post-operative rehabilitation (baseline) and then at 6, 12, 24, 36, 48 and 60 months of support.

Results: Data of 43 consecutive patients were analyzed. Pump parameters were set according to regular patients' follow-up, including clinical and echocardiographic assessment. We recorded a significant progressive increase in pump speed over the course of support: from 5200 (5050-5300) rpm at baseline to 5400 (5300-5600) rpm at 60 months of support (p=0.0007). Consistent with the increase in pump speed, a significant increase in pump flow (p=0.007) and decrease in pulsatility index (p=0.005) were also recorded.

Conclusions: Our study reveals unique features of the HM3 on LV activity. The need for progressive increase in pump support reflects indeed lack of recovery and progressive worsening of LV function, which might contribute to the reported high incidence of recurrence of HF in the HM3 population. We speculate that these phenomena might be the result of intrinsic detrimental effects of the pump on LV mechanics: in particular, desynchronized pump speed modulation algorithm (the Artificial Pulse, AP) might induce prolonged periods of excessive LV distension and, eventually, deterioration of LV contraction capacity. Synchronization of the AP might conversely improve LV unloading driven by the pump and preserve spontaneous LV activity. In turn, this might reduce incidence of LVAD-related adverse events and, ultimately, further extend patients' expectations for survival with this pump.

O34

LEFT ATRIAL DECOMPRESSION WITH THE HEARTMATE3 IN HEART FAILURE PATIENTS WITH PRESERVED EJECTION FRACTION

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Objectives: The heterogeneous condition known as heart failure with preserved ejection fraction (HFpEF) accounts for around 50% of all heart failure (HF) diagnoses with a lack of effective medical therapies. Left ventricular chambers of HFpEF patients are relatively small and inappropriate for implantation of the contemporary mechanical circulatory support (MCS) device – the HeartMate3 (HM3). However, previous in-silico studies have shown that a MCS device implanted in the left atrium (LA) may alleviate pulmonary congestion. Therefore, the aim of this study was to evaluate the virtual anatomic compatibility and hemodynamic effectiveness of HM3 in the enlarged LAs of HFpEF patients.

Methods: The retrospective study included 10 HFpEF patients with accessible high-resolution computed tomography (CT) images for the construction of the 3D cardiac model. The computer aided design model of HM3 was virtually implanted into the LA through the left atrial appendage (LAA) and left atrial posterior wall (LAPW). As measures to assess device fit, inflow cannula location and overlapping volume with surrounding structures were examined. Moreover, the impact of left atrial unloading in both rest and exercise hemodynamic situations was assessed in a hybrid mock circulatory loop.

Results: In 9/10 patients, virtual implantation of the HM3 was achieved through the LAA, and in 10 /10 patients through the LAPW without any severe intersection with surrounding tissues. In the in-vitro hemodynamic simulations, the optimal pump speed setting to maintain normal LA pressure and avoid backflow through the pump was 5400rpm at rest and 6400-7400rpm during exercise.

Conclusions: LA decompression with the HM3 may be feasible in the HFpEF collective. However, optimal pump speed settings of the HM3 are crucial to ensure sufficient support and to avoid backflow at rest and exercise.

O35

CHALLENGES IN EXPERIMENTAL FLOW VALIDATION FOR THIRD-GENERATION VENTRICULAR ASSIST DEVICES

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Objectives: Computational fluid dynamics (CFD) has been established as a valuable technique for the in-silico flow analysis in rotodynamic blood pumps (RBPs). Corresponding experimental validation of CFD-simulated flows in RBPs, however, is typically limited to easily accessible quantities such as flow rate and pressure head. This study aimed at evaluating the feasibility and challenges associated with enhanced in-vitro validation for third generation RBPs.

Methods: In a novel in-vitro testbench for enhanced flow validation, the original HeartMate 3 (HM3) geometry had to be modified to enable high-precision acquisition of impeller torques and to grant access for optical flow measurements. These modifications were necessary for the validation of global hydraulic losses and for the future validation of local flow structures, both important measures to comprehend global and local determinants of blood trauma. The modified HM3 geometry was equivalently employed for in-silico flow analysis, and global flow computations were validated across 15 operating conditions. Further, the validated flow in the modified testbench geometry was compared to simulated flows in the original HM3 geometry in order to assess the impact of the necessary modifications on global and local hydraulic properties.

Results: Global hydraulic properties in the modified HM3 testbench geometry were successfully validated (pressure head: r=0.999, RMSE=2.92mmHg; torque: r=0.996, RMSE=0.134mNm). Comparing the modified geometry with the original HM3 geometry through in-silico analysis showed good agreement in terms of global hydraulic properties ($r>0.999$, relative errors $<11.97\%$). However, the necessary geometric modifications led to substantial deviations in local hydraulic properties (errors up to 81.78%) and hemocompatibility predictions (deviations up to 21.03%).

Conclusions: This study indicated that the significant local effects arising from necessary geometric modifications may hinder the transferability of local flow measures obtained from advanced in-vitro testbenches to original pump designs.

O36

SURFACE ROUGHNESS MODELLING FOR RAPID-PROTOTYPED NEOVAD BLADES

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Objectives: The NeoVAD is a proposed paediatric Left Ventricular Assist Device for infants. Rapid prototyping via 3D printing has been utilised to explore the blade geometry design space , however prototypes exhibit surface roughness which effects hydrodynamic performance [1]. This effect is amplified for the NeoVAD as the miniaturised design brings geometric length scales to the same order of magnitude as roughness measurements and this study aims to numerically model these effects.

Methods: Numerical modelling techniques were investigated for capturing the hydrodynamic behaviour of 3D printed geometries using Ansys CFX 2021 R1 (Ansys Inc.) to solve the Reynolds Averaged Navier-Stokes equations utilising the k-ω SST turbulence model. Computational fluid dynamics simulations of smooth walled pumps were carried out across multiple flow rates ranging from 0.5 to 4 L/min to produce pressure-flow and efficiency-flow curves that could be compared to experiments. Wall roughness for a range of equivalent sand-grain roughness values was then included using two methods: a shift of the wall nodes and use of a modified wall function [2], and the use of non-zero eddy viscosity on the wall (icing) [3]. Experimentally, the roughness was measured using a 3D microscope (Keyence VHX 6000).

Results: Surface roughness measurements of 3D printed blades showed a range of finishes with arithmetic mean roughness values from 20-120 μm. Including surface roughness effects improved simulation accuracy: the RMSE between simulation and experiment using icing simulations with sand-grain equivalent roughness of 1 mm (which is not a physical roughness measure) was less than a third of RMSE with smooth walls.

Conclusions: The ability to numerically capture surface roughness effects allows performance predictions of smooth walled machined pumps inferred from 3D rapid printed prototypes.

[1] He X et al., IEEE Access; 2019; [2] Lechner R, Menter FR, Technical Report ANSYS/TR-04-04; 2004; [3] Aupoix B, ASME. J. Fluids Eng.; 2015.

O37

AN EXTRA-AORTIC SOFT ROBOTIC CARDIAC SUPPORT DEVICE: PATIENT-SPECIFIC IN-VITRO AND IN-VIVO EVALUATION

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Objectives: Heart failure is a serious cardiac condition currently treated with continuous flow implantable pumps that are blood contacting, dampen blood flow pulsatility, and lack patient-specific design. Here, we report the design and function of a soft robotic counter pulsation device that smoothly conforms externally to the aortic vessel wall. Cuff geometry and size was scaled to subject aortic diameter.

Methods: In a patient-specific mock loop, we accurately recreate hemodynamic conditions of a patient with high blood pressure and clinically diagnosed diastolic heart failure (cardiac output: 5.17 L/min, peak flow: 266 mL/s, blood pressure: 150/69 mmHg) in interaction with a compliant model of the patient's aorta. We assessed intra-vessel systolic pressure reduction resulting from various actuation paradigms and we recorded time-resolved blood flow as well as wall deformations using magnetic resonance imaging (MRI). The device was subsequently implanted on the ascending aorta of two healthy pigs to assess the physiological response of the healthy heart to counter-pulsation support.

Results: In vitro, the soft robotic device decreased afterload in the simulated patient by 10mmHg, while preserving blood flow pulsatility. High resolution MRI experiments showed anatomically favorable deformations of the vessel wall, efficient physiological flows, and minimal flow disturbance. In vivo, aortic pressure reduction was 3mmHg, and cardiac output increased instantaneously by 64% and 4% in the two animals respectively upon aortic counter-pulsation support.

Conclusions: In this proof-of-principle study, soft robotic extra-vascular support effectively lowers afterload, which is expected to reduce strain on the heart. The device has low risk for thrombus due to no blood contact and low flow disturbances. The soft design renders the device adaptable to different vessel sizing and implantable using minimally invasive surgery. Further studies are necessary to elucidate the physiological mechanisms of counter-pulsation as means to increase cardiac output and for assessing applicability as durable support for patients with heart failure.

O38

EXCEEDING THE LIMITS OF CURRENT PUMP MONITORING: NON-INVASIVE DIAGNOSIS OF LEFT VENTRICULAR UNLOADING WITH THE HEARTMATE 3 SNOOPY

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Objectives: Limited patient monitoring overshadows improved clinical outcomes with the HeartMate 3 (HM3) left ventricular assist device (LVAD). Intrinsic pump data proved valuable to optimize left ventricular (LV) unloading and patient management. Therefore, this study aims to investigate HM3 pump behavior using a non-invasive monitoring system (HM3-Snoopy).

Methods: Pump data was obtained with HM3-Snoopy (1Hz sampling rate) in a clinical, prospective, single-center study (ClinicalTrials.gov ID: NCT04641416) from 34 patients, 24 patients during echocardiographic speed-ramp-tests and Valsalva-maneuvers; 10 long-term cohort patients during index-hospitalization. Pump data were analyzed for collinearities and sensitivity to hemodynamic changes, data patterns reflecting undesired LV unloading were identified, and results were applied to the long-term cohort.

Results: For all patients, the HM3-Snoopy successfully recorded 39 pump parameters. 35 echocardiographic speed-ramp-tests were performed on 24 patients (age: 58.9±8.8 years, BMI: 28.1±5.1 kg/m², female: 20.8%, SpeedBaseline = 5443±244 rpm, BP = 75±12 mmHg) with speed changes of 1000 (IQR: 1000) rpm. Provocation testing resulted in echo-determined suction-events in 7 (14%) tests and PI-events (automatic pump speed reduction, standard monitoring) in 5 (71.5%) of these tests. Based on novel identified pump parameters, three mechanisms associated with PI-events were identified: a) LVAD speed changes, b) suction or c) loss of flow pulsatility. Application of these parameters to the long-term cohort (age: 60.1±9.2yrs, BMI: 27.1±3.2kg/m2, female: 10.0%), revealed 216 (0.6 to 1085) data points of undesired pump flow conditions per hour, corresponding to an undesired data points prevalence of 6% (0.02% to 30.1%) for HM3 Snoopy and 0.3% (0.0% to 2.4%) for standard monitoring (PI-events and low-flows).

Conclusions: HM3 Snoopy demonstrated the ability to record more pump parameters including unloading-sensitive waveform features at a higher sampling rate than standard monitoring. PI-events had different triggering mechanisms, which were not sufficiently sensitive to clinically undesired unloading conditions, therefore suction may be underestimated based on standard monitoring.

Symposium: Rotary Blood Pump Design

O39

NUMERICAL EVALUATION OF A NOVEL TWO-STAGE VENTRICULAR ASSIST DEVICE FOR PEDIATRIC PATIENTS

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Objectives: Currently, no intracorporeal left ventricular assist device (LVAD) is commercially available for small pediatric patients. The requirements of small size and excellent hemocompatibility at low-flow conditions pose a distinct challenge for the development of a pediatric LVAD. This study aimed to assess the feasibility of a novel, miniaturized two-stage pump to meet these specific requirements.

Methods: The design of the novel pediatric LVAD features two pump stages with a back-to-back impeller as a single rotating part. The impeller is hydrodynamically suspended in the radial direction and axially centered through reluctance forces. This enables miniaturization together with a reduction in circumferential velocity while achieving the required pressure head. Computational fluid dynamics was used to evaluate the pump performance. Washout of the priming volume was assessed through a passive scalar transport and pump-induced blood trauma through a power law model for the normalized index of hemolysis (NIH). Results were compared to the performance of the state-of-the-art LVAD HeartMate3 under the same pediatric operating conditions.

Results: The two-stage pump shows a pressure head of 55mmHg at a flow rate of 1.5L/min with a circumferential velocity of 3.7m/s at a hydraulic efficiency of 33%. With a total priming volume of 3.7mL a washout of 95% is obtained in 0.17s, and the predicted NIH is 4.0mg/100L. In comparison, the HeartMate3 reaches a 95% washout of its 14.5mL priming volume after 0.86s with an NIH of 6.7mg/100L at a circumferential velocity of 4.1m/s.

Conclusions: The proposed two-stage pump builds up the required pressure head at a smaller size and reduced circumferential velocity, resulting in improved numerical hemocompatibility metrics compared to the HeartMate3 at pediatric operating conditions. Further in vitro experiments will be performed to validate the numerical results. Overall, the two-stage pump may successfully tackle the low-flow challenges for pediatric LVADs.

O40

IN-SILICO INVESTIGATION OF GAP SIZE IMPACT ON ROTARY BLOOD PUMP PERFORMANCE AND HEMOCOMPATIBILITY IN LOW FLOW RATE OPERATION CONDITIONS

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Objectives: Hemocompatibility remains the biggest challenge in rotary blood pumps and more information on the relationship between pump design, hemodynamics and blood trauma is necessary. The aim was to systematically analyze influences of axial gap and radial gap sizes between the impeller and the outer housing on performance and hemocompatibility markers of a rotary blood pump under low flow conditions (flow rates $Q \leqslant 2$ L/min).

Methods: We developed a fully parametric generic CAD blood pump model (ParaPump) with a total of 40 adjustable parameters to generate the fluid volumes of the investigated design variations. Furthermore, the design allows for quick prototyping and bench testing. The impeller's geometric parameters were adapted to mimic the Getinge RotaFlow-32 blood pump. We used a computational fluid dynamics model to calculate device hemodynamics and evaluate the performance and hemocompatibility for each design. A total of 36 simulations were carried out, varying the axial and radial gap sizes between 0.5mm and 3mm in 0,5 mm increments in various combinations.

Results: The ParaPump shows good agreement regarding hydraulics, recirculation and hemolysis estimations when compared to in-vitro and in-silico studies of the RotaFlow-32. Results show a strong non-linearity of hemolysis, with a maximum difference in hemolysis of 9.6% between the most blood damaging design (axial gap 0.5 mm and radial gap 1 mm) and the most blood compatible design (axial and radial gap 3 mm). In contrast, we see a 9.3% higher recirculation rate for the 3 mm axial and radial gap design compared to the 0.5 mm axial and 1 mm radial gap design.

Conclusions: Our results show a counterintuitive inverse relationship between recirculation rate and blood trauma during low flow. At first sight, this contradicts recent findings from literature and poses the need for further investigations of hemodynamics in rotary blood pump particularly in off-design operating points.

O41

TOWARDS AN ADJUSTABLE BLOOD PUMP FOR WIDE-RANGE OPERATION – IN-VITRO RESULTS OF PERFORMANCE AND HYDRAULIC EFFICIENCY

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Objectives: Rotary blood pumps in Extracorporeal Life Support (ECLS) applications are designed for a single design point but are usually applied over a wide range of operation points. Studies showed that a deviation from the design point in rotary blood pumps lead to an unexpected rise of hemolysis with corresponding clinical complications. In other industrial branches, rotary pumps are usually built adjustable, such that critical parameters for the flow (e.g. in- and outflow angle of the blades) can be adjusted during operation in accordance to the individual operation point. However, conventional mechanisms of impeller geometry adjustments are usually not suitable for the operation with blood. In this study, we present a novel, potentially hemocompatible mechanism to adjust the impeller geometry of a blood pump during operation with the aim to ensure hemocompatibility over the wide range of operation points used in ECLS. In-vitro data of hydraulic performance and efficiency are presented.

Methods: 3D printed prototypes of the adjustable blood pumps were manufactured, and the hydraulic performance and efficiency were measured (n=3) in a test stand using a water-glycerol mixture.

Results: The adjustment of the in- and outflow angles of the blades in the adjustable blood pump resulted in a substantial change of the

performance curve (e.g. an increase of the pressure head of 68%) and the hydraulic efficiency.

Conclusions: The study proved that the novel mechanism of the impeller geometry adjustment presented here changes substantially the performance and hydraulic efficiency of the pump. It is now possible to tailor the overall performance of the pump over the range of operation points. The influence on the hydraulic efficiency, as an indirect indicator for hemocompatibility, shows the potential to also influence the hemocompatibility of the pump and ensure a best setting in each operation point during ECLS.

O42
DESIGN OF THE NEOVAD FLOW PATH USING COMPUTATIONAL FLUID DYNAMICS AND COUPLED 0D-3D MODELLING

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Objectives: The NeoVAD is a paediatric LVAD aiming to provide safe, long-term, bridge-to-transplant therapy for infants 5-20 kg. The pump uses axial flow with the rotating impeller powered by a blood washed motor. To reduce blood damage, such as haemolysis, a higher secondary flow is desirable, so the aim of this study was to investigate the influence of geometric design choices on flow through the motor-gap.

Methods: The flow path was extracted from the CAD and NeoVAD was situated in an ellipsoid representative of a paediatric ventricle. The main impeller-diffuser was simulated as a momentum source. Fluid dynamic comparisons included: prototype contact bearing versus eventual mag-lev; dimensions of the main windows; and momentum of the secondary impeller located near the inlet bearing value. Ansys CFX was used for solving the equations of fluid motion with computational fluid dynamics (CFD) and for pulsatile flow the 3D CFD model was coupled to a 0D lumped parameter model of the circulation implemented in Matlab Simulink.

Results: The bearing design determined the direction of the secondary flow: the contact bearing created forward flow while the mag-lev bearing created reverse flow. Smaller inlet windows created a pressure drop helping to drive forward flow with the contact bearing but working against the reverse flow of the mag-lev bearing. With a pump flow rate of 2 l/min the secondary flow with the mag-lev bearing was 32 ml/min; this could be increased with a secondary impeller. Residual pulsatility of the native ventricle may help to wash out the motor-gap.

Conclusions: The mag-lev bearing may have sufficient flow to prevent blood damage but the reverse direction could result in multiple motor-gap passes. There is a complex interplay between the geometric features of the NeoVAD which influence the secondary flow through the motor-gap and further analysis is required to make design decisions.

Symposium: Vascular Access for Hemodialysis

O43
WALL VIBRATIONS IN THE ARTERIOVENOUS FISTULA FOR HEMODIALYSIS: A NOVEL MECHANOBIOLOGICAL STIMULUS?

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Objectives: Native arteriovenous fistula (AVF) is the preferred vascular access for haemodialysis treatment, but it still has a high failure rate due to stenosis formation. Convincing evidence suggests that disturbed flow conditions may play a key role in vascular remodeling. We recently demonstrated that AVFs harbor transitional flows and the aim of the present study was to investigate whether these hemodynamic conditions could promote aberrant mechanical stresses within the vascular wall.

Methods: We acquired non-contrast-enhanced fast spin echo magnetic resonance images 3 days after radio-cephalic AVF surgery in a 72-year patient and we generated a 3D patient-specific model. An external layer with a constant thickness of 0.3 mm was added to the AVF model to include the vascular wall, which was modeled using three-term compressible Mooney-Rivlin. Robin boundary conditions were used to model the viscoelastic behavior of the perivascular tissues. We imposed pulsatile blood flow waveforms derived from US examination at the proximal and distal radial artery. A validated and formally 2nd order accurate fluid structure interaction solver developed upon FEniCS Finite Element Model library was used to solve for the flow field and wall deformation.

Results: High-fidelity fluid structure interaction simulations revealed the presence of wall vibrations in frequency bands up to 150 Hz and wall vibrations amplitude of about 10 micrometers. A sensitivity analysis to assess the impact of flow rates, and vascular wall stiffness and thickness, changes that typically occur during AVF maturation, confirmed the robustness of the results. Interestingly, areas of high-magnitude vibrations were always predominant at the anastomosis floor and on the inner venous side, locations that correlate with regions where stenosis typically develops.

Conclusions: The same location of vascular wall vibrations and vessel stenosis may suggest an unknown mechanobiological process linking high-frequency mechanical stresses within the vascular wall and adverse vascular remodeling.

O44
THE DESIGN OF A DYNAMIC ARTERIOVENOUS FISTULA, A VASCULAR ACCESS ONLY WHEN THE PATIENT NEEDS IT

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Objectives: The durability of arteriovenous fistulae (AVFs) in providing high-flow vascular access is far from optimal. A major limiting factor affecting durability is stenosis and occlusion of the venous outflow tract induced by the supraphysiological and turbulent flow. Another limitation of AVFs in the substantial cardiac burden of the constantly elevated cardiac output. The high flow caused by the AVF is always present, but only necessary during dialysis sessions. By enabling opening and closing of the AVF, the necessary high flow for dialysis will only be present during the,12 hours of dialysis per week. Circulation can return to close to normal outside these sessions, removing the core of the issue in vascular access. A novel, fully implantable device to allow opening and closing of the AVF has been developed.

Methods: A short piece (<1cm) of standard vascular graft is anastomosed between the vein and artery creating a configuration similar to an side-to-side AVF. The device is sutured to this graft and can reduce the cross-sectional area to zero, normalizing the circulation and minimizing the risk of thrombus formation. A magnetic drive mechanism placed directly under the skin allows actuation with an external set of magnets. This enables non-invasive control to open and close the anastomosis to stop and start anastomotic flow.

Results: The system has been tested in a benchtop setting and implemented in a cadaver, illustrating that non-invasive control is feasible. Through a 5mm thick layer of silicone skin model, the graft can be non-invasively manipu-

lated to block fluid exceeding pressures of 200mmHg, and accurately controlled to any state between open and closed.

Conclusions: If proven valid, the device should improve AVF outcomes, and reduce cardiac burden and costs of AVF interventions due to stenosis and high flow issues. Ongoing preclinical studies are pivotal to establish long-term functionality and cardiovascular effects.

O45

THE FUTURE OF VASCULAR ACCESS SURVEILLANCE: ACOUSTIC ANALYSIS OF ARTERIOVENOUS FISTULA SOUNDS

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Objectives: The sounds generated by blood flowing through vascular access could offer a possible non-invasive strategy for monitoring arteriovenous fistula (AVF) function. The purpose of our study was to detect differences in sound frequency spectrum of non-functioning and well-functioning AVFs.

Methods: We acquired the sounds of 159 AVFs, 145 routinely used for hemodialysis and 14 not used due to significant stenosis. The sounds were recorded with a 3M Littmann 3200 Electronic Stethoscope in extended mode and pre-processed to obtain 4s recordings, high-pass filtered at 50 Hz. The ratio of maximum peak amplitudes in the low (100-250 Hz) and high (500-750 Hz) frequency ranges, labelled as low-high peak ratio (LHPR), was computed in Matlab for each recording. Sound recordings of functioning AVFs were also grouped by AVF complications, assessed by Doppler Ultrasound. The non-normal distribution of populations and the significance of the difference between groups were evaluated with Shapiro-Wilk and Wilcoxon's nonparametric tests, respectively. Data are reported as median and interquartile range.

Results: Statistically significant differences were found in sound recordings of non-functioning and functioning AVFs, with a median LHPR of 1.18 [0.65-1.65] and 2.34 [1.15-4.72], with higher frequencies in non-functioning AVFs. Among functioning AVFs, the presence of complications such as vessel restriction or aneurysms (n=46) resulted in higher contribution of high frequencies, with a median LHPR of 1.4 [0.97-2.07], close to the values found in non-functioning AVFs. Furthermore, there were also different acoustic characteristics among complications: stenotic AVFs produced higher frequency peaks than aneurysm sounds, with a median LHPR of 1.05 [0.78-1.46] as compared to 1.97 [1.42-2.50].

Conclusions: Sound analysis revealed unique characteristics in the frequency spectra of AVFs, allowing objective discrimination between well-functioning and failing AVFs. Our results suggest that acoustic analysis can be used as a valuable, fast, easy and low-cost monitoring technique to predict AVF failure and complications.

O46

EVALUATION OF THE VASCULAR ACCESS FUNCTION BY SOUND ANALYSIS USING A PSEUDO-VESSEL STENOSIS MODEL WITH DIFFERENT STENOSIS DIAMETERS AND LENGTHS

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Objectives: In hemodialysis therapy, a vascular access (VA) is created to facilitate removal and circulation of the blood in the dialysis circuit for purification. However, the criteria for assessing the VA function by sound analysis have not yet been standardized and a method for quantitative analysis is still lacking. The aim of the present study was to quantitatively evaluate the VA function by sound analysis using an in-vitro pseudo-vessel stenosis model with different stenosis diameters and lengths.

Methods: An in vitro-vessel model was created by inserting stenosis-inducing parts ranging in diameter of from 5.4 to 0.6 mm and in length of from 5 to 20 mm in the outflow downstream from a Y-shaped connector simulating an arteriovenous anastomosis site. Time-frequency analysis of the sounds obtained at the outflow was performed using wavelet transform, and the normalized cross-correlation coefficient (R), which represents the change in the frequency over time, was calculated. The sound in the absence of stenosis was used as reference, and the sounds emitted at the sites of stenosis were compared with the reference.

Results: A high-frequency component of the vascular sound was emitted as the diameter at the stenotic site decreased. The R was about 30% lower than the reference when the diameter decreased to 50% and about 72% lower than the reference when the diameter decreased to 80%. No change in R was observed with change in the length of stenotic site. Thus, the diameter at the stenotic site can be quantitatively evaluated from the values of R calculated from the time-frequency analysis.

Conclusions: R calculated from time-frequency analysis for vascular sounds can detect changes in the diameter at the stenotic site. This method could be used for quantitative and objective evaluation of the progression of stenosis.

Session: Extracorporeal Life Support

O47

CAN A DIALYZER EXPEDITE EXTRACORPOREAL GAS EXCHANGE?

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Objectives: Hollow fiber membrane oxygenators (HFMO) made out of polypropylene (PP) and poly-4-methylpentente (PMP) have established themselves as cornerstones of extracorporeal life support over the past few decades. A novel method of producing competitive gas exchangers by handling hollow fibers with silicone is bound to send ripples around the oxygenator industry.

Methods: As part of the feasibility study, commercial dialyzers of varying surface area and fiber diameter have been treated with silicone to create a purely diffusive coating that prevents plasma leakage and the migration of gas bubbles into the bloodstream, without hindering gas exchange. The quality of the silicone film has been evaluated by diverse methods especially developed for this purpose (e.g. pressurization of the intracapillary space); later corroborated by scanning electron microscopy (SEM). The fluid dynamic behavior and the gas transfer of the new devices have been investigated in vitro using porcine blood.

Results: SEM images reveal a homogeneous silicone film coating the capillary lumen, while gas pressurization affirms the purely diffusive nature of the silicone layer. Fluid dynamic investigations indicate that blood pressure drop remains within physiological values. Gas exchange efficiency has been equivalented to that of commercial HFMOs, whereas zero plasma leakage has been observed.

Conclusions: The technique introduced here, is suitable for coating whole dialyzer modules in a single act, instantly transforming an affordable, readily available blood filtration product into a reliable, fully functional gas exchanger. Furthermore, as they have the standard dialyzer shape, these innovative oxygenators can be directly operated by dialysis machines – an ideal combination for Low-Flow applications, such as extracorporeal carbon dioxide removal (ECCO2R). Nevertheless, the potential of silicone-coating microporous hollow fibers can be further expanded to cater for High-Flow applications such as cardiopulmonary bypass, ECMO, etc. after undergoing the necessary adaptation/optimization (e.g. symmetric capillary membranes, i.e. PP, as scaffold for exterior coating).

O48

UMBILICAL CORD CANNULATION SETUP FOR ECMO CANNULATION

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Objectives: Respiratory failure is a leading cause of neonatal morbidity and mortality especially among preterm newborns. The use of extracorporeal membrane oxygenation (ECMO) in neonates opens perspectives as rescue treatment as well as standard treatment of prematurity in the future. An exceptional opportunity in neonates is the connection of an oxygenator via the umbilical vessels, mimicking the native in-utero situation. Because umbilical vessels develop vasospasm soon after cord clamping, the cannulation needs to be performed as an ex-utero intra partum (EXIT) procedure on the perfused cord. For ethical reasons, this cannot be done for experimental purposes on living human subjects. We developed a test stand as a simulation environment for EXIT procedures on human umbilical vessels.

Methods: A test stand for the reperfusion of donated human umbilical cords was developed. Human umbilical cords and placenta-blood, which were donated to our biobank after written informed consent were collected after cesarian section. The vessels of the umbilical cords were reperfused in order to reestablish blood flow within the umbilical vessels. Firstly, the the vasospasm was antagonized using papaverine. This permitted mid-bore cannulation of all vessels from both ends of the off-cut thereafter. The cannulae were sealed, and the umbilical vessels were reperfused using a centrifugal pump. After stabilization, a test circuit was connected to the cannulae, the process and the quality of the cannulation were tested.

Results: We report test results for the tightness of the sealing and the corresponding compliance dependent on the volume flow from N= 24 umbilical cords. The setup allows for the insertion of pediatric ECMO cannulae into every umbilical vessel, and the establishment of physiological flow parameters in donated human umbilical cords.

Conclusions: This is the first test environment which provides a platform for testing cannula designs and the training of cannulation techniques in donated human umbilical cords.

O49

A HYBRID IN SILICO – IN VITRO CARDIORESPIRATORY SIMULATOR FOR IMPROVED EXTRACORPOREAL MEMBRANE OXYGENATION SUPPORT

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Objectives: Extracorporeal membrane oxygenation (ECMO) provides lifesaving support for patients affected by acute and severe cardiovascular and/or respiratory failure. Optimal patient-specific tailoring of ECMO requires proper understanding of patient – device interaction, which is inherently complex and involves multifaceted critical care aimed at prevention and recovery of (multi-)organ failure. This works aims at providing a high-fidelity hybrid in silico – in vitro simulator for improved insights into individual patient – ECMO interaction.

Methods: The in-silico component of the simulator includes: a lumped parameter model of the closed loop cardiocirculatory system (atria, ventricles, systemic and pulmonary circulations), baroreflex and metabolic controls, a mechanical lung model featuring mechanical ventilation, O2 and CO2 gas exchange in the lungs and peripheral tissues. The in vitro component includes active hydraulic chambers, filled with water, that mimic aorta and vena cava, all being connected with the in-silico model in real time. An ECMO circuit is connected between the in vitro aorta and vena cava, accordingly. As clinical scenario we simulated a severe cardiorespiratory failure due to left ventricular dysfunction: cardiac output (CO) 3.7 L/min, blood pressure 74/50/(62) mmHg, arterial blood O2 saturation (SataO2) 77% and mixed venous O2 saturation (SatvO2) 45%.

Results: After setting baseline conditions of cardiorespiratory failure, ECMO is initiated at 3.2 L/min circulatory support resulting in: CO 5.1 L/min, blood pressure 90/71/(80) mmHg, SataO2 95% and SatvO2 61%, where the SataO2 is the computed balance between fully-oxygenated ECMO flow and the pulmonary venous flow, where gas exchange is suboptimal due to functional pulmonary impairment.

Conclusions: The hybrid simulator captures the intricate patient – ECMO interaction and provides clinically realistic hemodynamic and respiratory parameters vital for optimal critical care. An attractive future perspective is to substitute the water by an artificial blood-like fluid that would allow realistic gas exchange in the ECMO oxygenator.

O50

A NOVEL GAS-EXCHANGE-AREA-ADJUSTABLE OXYGENATOR FOR EXTREMELY PRETERM INFANTS

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Objectives: Every year, 600,000 infants worldwide are born extremely prematurely (EP). The lungs of these smallest patients are still underdeveloped, so conventional mechanical ventilation can cause severe damage. As an alternative treatment, extracorporeal blood oxygenation (ECMO) functioning as an "artificial placenta" is expected to allow sufficient maturation of the lungs. However, long-term use in these fast-growing patients requires increasing gas exchange performance, which would necessitate device changes with major risks to the patient. Therefore, we propose a new type of “growing” oxygenator.

Methods: We developed a gas-exchange-area-adjustable oxygenator that operates at two different sizes without changing the device nor increasing the flow resistance. It consists of two concentric oxygenator cavities, each equal in volume. When only the outer cavity is connected, the oxygenator provides the gas exchange area required by an EP infant at 24 weeks of gestational age (GA) with blood flow rates $\dot{V}$blood of 50 ml/min – 125 ml/min. As the child grows, the inner cavity can be added by rotation. Together, both cavities cover the needs of an EP infant at 26–28 weeks of GA with $\dot{V}$blood above 125 ml/min. We performed gas-transfer measurements according to ISO 7199 to verify our novel design.

Results: Starting at V̇blood=50 ml/min, gas transfer performance increased until V̇blood=100 ml/min was reached. From here, a drop in performance was observed. Switching on the second chamber at a flow rate of V̇blood=125 mL/min yielded an improvement in gas transfer performance of about 50%.

Conclusions: Our novel gas-exchange-area-adjustable oxygenator design proved effective in improving gas transfer performance at increasing blood flow rates. A first milestone was set for the oxygenation of growing EP infants while avoiding the risks associated with a device change.

O51
FLUID DYNAMICS ANALYSIS THROUGH NUMERICAL SIMULATION OF EXTRACORPOREAL MEMBRANE OXYGENATION

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Objectives: Veno-Arterial Extracorporeal Membrane Oxygenation (VA ECMO) is a vital tool in the management of severe cardiorespiratory dysfunction. Although VA ECMO it is widely used, the effect given by its interaction with the failing heart is not yet fully understood, in terms of hemodynamic and perfusion. Multiphysics numerical simulations are a powerful tool that would allow us to better understand these aspects. This work deals with the design and the multiphysics simulations of patient-specific VA ECMO treatments and the development of a platform for their use in a clinical setting, to localize the so-called mixing-zone (MZ) and evaluate oxygen distribution inside blood vessels, with timescales appropriate to medical needs.

Methods: A patient-specific aorta model was created starting to a male's computed tomography chest dataset. Various cardiopulmonary deficit-ECMO support level conditions were evaluated using computational fluid dynamics and diluted gas transport theory, within a multiphysic approach. Thus, reduced order modelling (ROM) was used to develop the clinical-use platform.

Results: MZ shift to aortic arch when increasing ECMO support level, as well as oxygen saturation increase inside cerebral blood vessels. ROM use allows to significantly reduce computational times.

Conclusions: The results agreed with clinical observations, although no in-vivo nor in-vitro validation was do. Although still embryonic, the developed platform would allow the use of numerical simulations in the clinical setting for VA ECMO treatments.

O52
ENDOSPRAY: DEVELOPMENT OF AN ENDOTHELIALIZED OXYGENATOR MODEL FOR LONG-TERM CLINICAL APPLICATION

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Objectives: Conventional oxygenators have a short life span due to low hemocompatibility and unspecific protein absorption. To overcome this limitation, membrane endothelialization is proposed. It can extend the application period and has already been proven effective in small laboratory models. Here, we present research on the design, construction, and optimization of a flat sheet membrane oxygenator suitable as a laboratory prototype for a biohybrid oxygenator. We evaluate the procurement of suitable membranes, spacing materials, testing of the fabricated housing as well as functionalizing the gas exchange membrane for endothelial cell adhesion.

Methods: The gas exchange membrane is in contact with gas and blood. Polydimethylsiloxane (PDMS) is used as a liquid-tight membrane. To support the gas phase, a combination of a 3D-air fabric and fiberglass sheet is used. The housing is fabricated of Polymethyl methacrylate (PMMA). Gas transfer tests are performed via blood tests according to ISO 7199:2016. Furthermore, optimization of the PDMS membrane functionalization with Sulpho-SANPAH (SS) and the cell adhesive peptide motif gRGD for cell adhesion is performed.

Results: An optimized oxygenator model for endothelialization is successfully designed, manufactured, and tested. A PDMS membrane of 50 µm thickness has sufficient strength for practical handling and processing. The gas exchange membrane has a total surface area of 0.4 m². The oxygenator is leak-proof up to a flow rate of 1.300 ml/min. The priming volume reaches up to 245 ml. Pressure drop on the gas and liquid side is relatively low. Regarding surface functionalization, it was observed that cell adhesion is also possible when the PDMS membrane is treated just with Sulpho-SANPAH without RGD under static conditions.

Conclusions: The oxygenator model is cheap to manufacture, and the design allows easy upscaling. Here, the first step towards a non-microfluidic oxygenator laboratory model based on flat-sheet membranes for endothelialization is achieved.

Symposium: Theoretical Models in Dialysis

O53
OPTIMISATION OF VANCOMYCIN DOSING IN PATIENTS ON CHRONIC HIGH-FLUX HEMODIALYSIS

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Objectives: Vancomycin is frequently prescribed to hemodialysis (HD) patients using empirical dosing regimens. Vancomycin pharmacokinetics (PK) in these patients is however different due to impaired kidney function, decreased protein binding, and HD removal. We aimed to optimise vancomycin dosing in patients on chronic high-flux hemodialysis.

Methods: This prospective observational study included 23 HD patients in whom vancomycin was prescribed. Blood samples were taken inter- and intradialytically (n=234) to measure total and free vancomycin concentrations. A population PK model was developed using non-linear mixed effects fitting the observed time-concentration data. Monte Carlo simulations were performed over 1 week, simulating different doses with a fixed infusion speed of 1000mg/h, and using different schemes (i.e. administered during, during/after, and after HD). PK/pharmacodynamic (PD) target was set at trough values 15-20mg/L (i.e. predialysis), and 400＜AUC24h/MIC＜600 with MIC=1mg/L. Finally, interdialytic protein binding was calculated and compared to that in an average healthy population.

Results: Forty % had subtherapeutic (＜15mg/L) and 25% supratherapeutic trough values (＞20mg/L), and 57% reached supratherapeutic values (AUC24h/MIC ＞600). A two-compartmental model with between-subject variability for volume of distribution of central compartment (V1), total body clearance (CL) and dialysis extraction ratio (ER) fitted best the measured vancomycin concentration data. ERs of

total vancomycin were 49±26%. For infusions 100% during dialysis, Monte Carlo simulations revealed that 1500mg was best practice with AUC24h/MIC=569[508;653]. For infusions 50/50% during/after dialysis or 100% after dialysis, a dose of 1000mg was found most appropriate with medium AUC24h/MIC equal to 434[488;554] and 454[511;590], respectively. Our study population significantly differs in protein binding (32.2±8.3%) compared to an average population (55%) ($p<0.001$).

Conclusions: In general, it is difficult to make a standard dosage regimen for this patient population, which is a plea for individualized dosing. One may also wonder if another PK/PD target is needed in this patient population considering the decreased protein binding.

O54

H^+ MOBILIZATION DESCRIPTION TO IMPROVE THE ACCURACY OF A PATIENT-SPECIFIC MODEL FOR THE PREDICTION OF SOLUTES' EXCHANGES DURING HEMODIALYSIS

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Objectives: The acid-base equilibrium during dialysis has been extensively studied since the 70s, even by using mathematical models. The maintenance of a proper acid-base balance in the organism depends on bicarbonate exchanges among dialysate, plasma, and the extravascular compartment. No one until now has introduced a detailed description of the involved phenomena in patient-specific models. This work wants to fill this gap, introducing a detailed description of bicarbonate exchange and of H+ mobilization in a patient-specific model, as a propaedeutic step for acid-base studies.

Methods: H^+ mobilization description, as from a literature model, has been introduced in the multi-solute, multi-pool patient-specific model, developed at LaBS of Politecnico di Milano. After the model training by using clinical data pertaining to 3 consecutive sessions, it can be used to predict patients' responses by simply knowing the patient's condition and the machine settings at the treatment start. The mobilization coefficient mH has been introduced as a patient-specific parameter, modulating H^+ bonding to $HCO3^-$. A total of 628 dialysis sessions (referred to 133 patients dialyzed in 4 different centers) were used. Model accuracy in describing plasmatic concentrations of Na^+, K^+, Cl^-, Ca_2^+, HCO_3^-, and urea has been evaluated in terms of percent Root Mean Square Error (RMSE%) comparing simulated output and clinical data.

Results: Accounting for the H+ mobilization implies a median RMSE% improvement of 13.75% for bicarbonate when compared to the original model. An improvement of 5.55% ($p<0.001$) is observed when all the solutes were considered.

Conclusions: The implementation of H^+ mobilization in the current model, by introducing a new patient-specific parameter, allows an overall improvement of the model accuracy. The next step would be the identification, in a wide set of patients, of the peculiar characteristics of the subclasses of patients with similar behavior.

Session: Tissue Engineering II

O55

EFFECT OF THE IN VITRO EXPOSURE OF ENDOTHELIAL CELLS TO MECHANICAL VIBRATIONS

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Objectives: The mechanobiology of vascular cells plays a key role in vascular remodeling. Recent numerical simulations investigated the effect of mechanical stresses on vessels remodeling, but the biological effect on cellular functions remains unclear. Therefore, this preliminary study aims at investigating the effects of vibrations on endothelial cells by exposing them to mechanical vibrations obtained by a 50Hz sound-generated pressure wave.

Methods: Human umbilical vein endothelial cells (HUVECs) were seeded and cultured in two 150mm gelatin-precoated cell culture dishes at a density of 106 cells. After 4 days, a dish was mounted on an aluminum support structure equipped with a speaker and a digital power amplifier that received a 50Hz input sound recording, while the other one was maintained in static conditions as control for 48 hours. The sounds emitted by the speaker and cell vibrations were recorded at 0, 24, and 48 hours with an in-house microphone-equipped device and with an accelerometer. Data were collected with Coolterm and analyzed in MATLAB-R2022a. At the end of the experiment, the morphology of stimulated and static control cells was investigated by phase-contrast microscopy. Cell counting and Alamar Blue assay were performed to determine HUVECs' viability in both conditions.

Results: The stimulated plate received over time a sound characterized by the main frequency of 50Hz and its odd harmonics and was subjected to a movement of 71microns (2sigma) perpendicular to the culture dish. The analysis showed that sound-induced vibrations changed HUVECs typical morphology and determined their detachment. The number of cells cultured under vibrations was about 80% compared to static control and Alamar Blue assay revealed a decrease in cell viability greater than 50% for HUVECs exposed to mechanical stimulus.

Conclusions: Preliminary results suggest the great potential of our simple but reliable framework for the investigation of vascular remodeling and related cell dysfunctions responsible for vascular diseases.

O56

PHYSICAL AND AUGMENTED PATIENT-SPECIFIC SIMULATORS FOR THE TRAINING OF UNRUPTURED INTRACRANIAL ANEURYSM CLIPPING

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Objectives: The good outcome of microsurgical clipping of complex Unruptured Intracranial Aneurysms (UIAs) is mainly dependent on surgeon's experience. Residents and neurosurgeons can build experience and gain confidence through training on animal or human cases. Alternatively, physical and digital physio-pathological models are available, but they are limited by low haptic or visual realism. The aim of this study was to develop high-realism training platforms of microsurgical clipping of UIAs.

Methods: Two complementary physical and digital patient-specific training simulators based on additive manufacturing and augmented reality have been developed. The physical simulator consists of a 3D printed hard skull compatible with interchangeable, perfused and fluorescence compatible modules including the silicone 3D printed aneurysm phantoms. The holographic clipping simulation employs a real-time finite-element-model

simulating the deformation of the UIA anatomy when interacting with a controlled virtual clip. In order to assess the realism and usefulness of the simulations in training, a clinical Likert-like questionnaire study has been conducted with neurosurgical residents and specialists (n=14).

Results: Haptic feedback of the physical phantoms was indicated as realistic during the simulation (good/excellent = 93%), with the phantoms having realistic dome thickness (0.44 ± 0.11 mm) and complete occlusion confirmed by both the fluorescence angiography and CT scan. On the other hand, the holographic simulation aided the understanding of anatomy (good/excellent = 100%). Both the physical and the holographic simulators also resulted useful in selecting or discarding clips for proper occlusion.

Conclusions: The developed simulators represent affordable platforms for the training of neurosurgical residents' skills in a realistic clinical scenario.

O57

DEVELOPMENT OF AN INTEGRATED IN VITRO-IN SILICO MODEL TO PREDICT THE INTERACTION OF IMMUNE CELLS WITH SOLID CANCERS

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Objectives: Immune cells play a crucial role in the development and progression of cancer [1]. To better understand this interaction, we developed an in vitro model that combines a millifluidic bioreactor called MOAB (MOAB Srl, Milano, Italy) [2], that provides a controlled environment for cell circulation and mass transport [3], and 3D bioprinted constructs, which act as physical structures for cancer cells to grow in [4]. In parallel, we developed an in silico model to provide insights into multiphysics interactions between immune cells and cancer cells and help to better understand the mechanisms of the immune response to cancer.

Methods: Gelatin methacrylamide 3D scaffolds containing lung cancer primary cells were designed to obtain 3x6x0,5mm3 constructs with 0,1mm thick fibers laid in a woodpile fashion. Samples were statically cultured for 2 days before perfusing them with suspended lymphocytes from healthy donor buffy coat. In parallel, an in-silico model was developed to retrieve adequate perfusion and mass transport parameters through CFD analyses and particle tracing.

Results: The scaffolds promoted viability and proliferation of the cancer cells for a few weeks of perfusion inside the bioreactor. The results of the in silico simulation helped the fine tuning of the perfusion and mass transport parameters of the 3D bioprinted constructs, yielding optimal shear stress ranges and concentration profiles of factors to cultured cells, while allowing efficient circulation of immune cells.

Conclusions: Our model to recapitulate and analyze the cancer-immune cells interaction using an in silico and an in vitro model resulted in a reliable and cost-effective platform for conducting the in-depth investigation of the molecular mechanisms that regulate the cancer-immune cells interaction. Our work helps to bridge the gap of currently popular in vitro models in providing controlled perfusion of solid cancers, enabling the focusing on molecular interplay.

References: [1]10.7554/eLife.69015; [2]10.1007/s10544-011-9600-0; [3]10.3389/fbioe.2021.799594; [4]10.1088/1758-5090/ABDACF

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O58

DURABILITY TESTING OF WOVEN SCAFFOLDS FOR A NEW GENERATION OF ARTIFICIAL HEART VALVE LEAFLETS

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Objectives: The current state of the art in the treatment of heart valve disease is bioprostheses with leaflets made from animal pericardium. These leaflets are subject to biological variability, prone to calcification and structural degeneration, which limits their lifespan and requires repeated surgical interventions. The goal of this project is to investigate a leaflet scaffold based on a load-oriented woven textile. It is designed to provide structural integrity and can be further processed with a hemocompatible and bioactive coating. An important milestone is the achievement of fatigue strength of the leaflet scaffold integrated into a valve ring.

Methods: Pre-selection of the weave configuration was done by mechanical testing (tensile strength, bending stiffness, thread shift) and microscopic assessment of porosity. Woven scaffolds were coated with TPU-chloroform (Carbothane PC-3585A, Lubrizol) and mounted in a valve ring. Accelerated wear tests were performed under simulated physiological load in a LinA testing device (AME-HIA) and run for 20 million cycles at 37° C. Leaflet function and indications of wear were assessed by slow motion movie, photographic and microscopic inspection. Resulting favorite textile scaffold-valve ring constructs were tested with a higher number of load cycles.

Results: Labtypes of woven leaflet valves have undergone sequential design optimization and currently withstand more than 90 million load cycles (tests are ongoing). Critical failure zones near the commissures could be addressed by weave modification and the pattern of weave attachment to the valve ring. New R&D results regarding both aspects will be presented.

Conclusions: Preliminary results support the achievement of adequate durability of leaflet scaffolds composed of load-oriented warp and weft threads. A milestone will be 200 million cycles, with a further increase in perspective.

O59

FIRST ANALYSIS OF DURAL FIBROBLASTS AND STEM CELLS MONOCULTURE ON ELECTROSPUN SCAFFOLDS WITH DIFFERENT COMPOSITIONS FOR MENINGEAL TISSUE ENGINEERING

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Objectives: Dura mater is the most external meninge, a half-rigid membrane located between central nervous system and bone tissues. Upon injury, complications are frequent because of its inefficient regeneration and scar tissue formation. Dural tissue engineering could lead to better understanding of this interface and help developing an in vitro model and innovative implantable scaffolds as artificial dura. Our goal is to develop a multiphasic biomaterial mimicking the dura mater thanks to electrospun scaffolds cultured with stem cells and/or

dural fibroblasts. We present here the results of the impact of different scaffold's compositions on the adhesion, proliferation, and viability of both cell types.

Methods: Primary human dural fibroblasts (HDuF) and immortalized adipose-derived stem cells (ASC52telo) were each monocultured in their respective media for 1 week on 3 electrospun scaffolds: 12% pure PCL (polycaprolactone), 12% PCL/Silk Fibroin and 12% PCL/Hydroxyapatite. For each condition, two fiber orientation were tested: random and aligned. Metabolic activity (Alamar Blue) was measured at day 1, 4 and 7 and cell viability (MTS, Live/Dead) at day 7. ALP staining was performed at day 7 on the ASC52telo for a first insight on osteogenesis.

Results: The ASC52telo attached and proliferated on every scaffold with no significant difference regarding cell viability. As expected, ALP staining showed that the presence of hydroxyapatite in the scaffold initiated an early osteoblast differentiation compared to the other conditions. On the contrary, the HDuf attached and proliferated significatively better on the scaffold with silk fibroin than the others.

Conclusions: From these results we have determined that 12%PCL/Hydroxyapatite and 12%PCL/Silk fibroin could be optimal for the culture of ASCs and HDuf, respectively. The cell functionality at longer term needs now to be assessed further, for each cell type and in co-culture. The impact of fiber orientation will also be analyzed more closely.

O60

ASSEMBLING CATALYTIC NANOCOMPARTMENTS INTO ARTIFICIAL SIGNALING CASCADES

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Objectives: The spatiotemporal separation of biochemical processes by compartmentalization plays a fundamental role in nature. Reproducing, but also manipulating hierarchically organized compartments with regard to their responsiveness and communication provide crucial information towards understanding biological systems.

Methods: We organized artificial organelles into an integrated signaling system that performs a cascade of molecular events via DNA hybridization.

Results: The latter afforded the attachment of such "artificial organelles" to the cell surface, endowing the cell with non-native extracellular functions and a unique exogenous signaling pathway. Our work represents a significant advance in the field of communicative networks by combining compartmentalization with controlled inter-compartment distance to promote efficient cascade reactions. In addition, the combinatorial and functional diversity of catalytic nanocompartments (CNCs) assembled into various supramolecular architectures can be exploited either in bulk or on a surface, whereby surface immobilization offers the advantage of highly controlled spatial organization. As an example, we developed a reusable biomolecular signaling platform comprising catalytic nanocompartments whose geometrical arrangement enabled effective communication. The chip promoted the transfer of signals between neighboring nanocompartments, resulting in a complex cascade reaction (DNA synthesis, PPi and ATP production) that ultimately produced light. The simple removal and reloading of catalytic compartments rendered the platform suitable for multiple cycles of cascade reactions.

Conclusions: We demonstrate that polymer-based nano-compartment assemblies offer an ideal scaffold for the development of the next generation responsive and communicative soft-matter analytical devices for applications in catalysis and medicine.

Session: Modelling and Devices

O61

URINARY BLADDER VOLUME MONITORING WITH IMPLANTABLE SENSORS

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Objectives: Several pathologies (e.g., spinal injuries) lead to the loss of bladder sensation. As a consequence, patients are not able to perceive the urge to urinate and define the moment for voiding. Although self-assessments based on abdomen palpation and pre-programmed toilet programs were proposed, there exist high risks of side effects due to excessive use of voiding assistive devices (e.g., catheters), or bladder overdistension due to delayed voiding. This applies both to native and artificial bladders (AB). To cope with this need, we propose three sensing technologies: bioimpedance sensors for volume monitoring of the native bladder, and a comparison between resistive textile and magnetic sensors for AB volume.

Methods: Bioimpedance monitoring through implantable electrodes may allow native bladder monitoring. Measurements are performed by suturing electrodes on bladder tissue. The amount of urine in the bladder is the main factor inducing measurements variations. When the native tissue is replaced by a synthetic counterpart, deformation and distance sensors might prove more efficient depending on the AB design. Exploiting a hexagonal-shaped prototype, resistive textile and magnetic sensors are used to monitor folds openings and walls distances, respectively. The proposed monitoring strategies have been tested on bench with gradual filling and using porcine ex vivo tissue in case of native bladder. The systems performance is evaluated as percentage errors in volume estimation.

Results: Bioimpedance measurements proved volume estimation errors around 20% for the native bladder. Slightly better results are obtained for AB monitoring using resistive and magnetic textile sensors with volume estimation errors around 15% for both.

Conclusions: Equipping the bladder with sensors could provide the patient with fullness feedback. However, further miniaturization is required for future chronic implantation.

O62

SMARTPHONE-BASED PARTICLE IMAGE VELOCIMETRY AND PARTICLE TRACKING VELOCIMETRY FOR IN VITRO CHARACTERIZATION OF CARDIOVASCULAR FLOWS

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Objectives: Particle Image Velocimetry (PIV) and Particle Tracking Velocimetry (PTV) are widely used for the experimental characterization of cardiovascular flows. PIV and PTV measurements present challenges with respect to cost, maintenance, energy consumption, and safety. We aim here to demonstrate the feasibility of accessible and inexpensive PIV and PTV cardiovascular flow measurements based on a smartphone camera as image acquisition device and a low-power laser.

Methods: Measurements were conducted in healthy and stenosed phantoms of the left anterior descending coronary artery under steady-state flow condition at different flow regimes (inflow Reynolds number from 20 to 200). The smartphone-based setup adopted a Samsung

Galaxy S9+ (12800x720 pixels, 960 Hz camera) and low-power continuous laser. Smartphone-based PIV and PTV measurements were compared with PIV measurements obtained using a conventional setup with a HiSense Zyla camera (CMOS, 2560x2160 pixels) and a dual pulsed Nd:Yag laser (Dantec Dynamics). Displacement errors and uncertainties were estimated applying the particle disparity method.

Results: Displacement errors and uncertainties were ≈5% and <1.2 pixels, respectively, for both smartphone-based and conventional PIV measurements, indicating the reliability of the former. Velocity fields from smartphone-based PTV and PIV substantially agreed with conventional PIV, presenting average percentage differences in the velocity magnitude in the range 4.7%-10.5% (smartphone-based PTV) and 8.0%-10.7% (smartphone-based PIV) in the healthy phantom. In the stenosed phantom, these differences raised to 28.6%-53.1% (smartphone-based PTV) and 35.3%-49.8% (smartphone-based PIV), with discrepancies mainly located at the stenosis throat, where the fixed smartphone acquisition frequency led to image blur and velocity underestimation. Post-stenotic flow features like flow separation and recirculation were successfully captured at all flow regimes.

Conclusions: The proposed smartphone-based setup lowers the barriers of PIV and PTV measurements reducing costs, safety risks and energy consumption. This enables its use for educational, industrial or research investigations, or as a first-line tool to guide more accurate measurements.

O63

FUNCTIONAL POLYMERIC MODELS OF ATRIOVENTRICULAR VALVES FOR CLINICIANS TRAINING

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Objectives: The spread of transcatheter techniques to treat valvopathies increases the treatable patients as these techniques reduce invasiveness of conventional surgery, lowering operatory risks. Nevertheless, these procedures are extremely challenging for clinicians, as devices interact with complex anatomy in beating heart conditions and surgeons are guided only by medical imaging. Hence the need for platforms capable of simulate the cardiac structures in terms of hemodynamics and anatomical realism to provide adequate procedure simulation environments for operator training. In this work, we developed a method to realize polymeric functional models of atrioventricular valves, starting from patient specific or paradigmatic anatomies, featuring adjustable chordae tendineae as a tool for hands on-training on percutaneous valve interventions.

Methods: A paradigmatic 3D model of mitral valve and a patient-specific 3D model of tricuspid valve were recreated exploiting silicone casting technique with 3D printed moulds. Models were enriched with tissue patches to make leaflets suturable. Chordae tendineae were reproduced through PE thread that was sutured into the models, and a chordae-adjuster system was developed to control chordae length, modelling pathological and physiological behavior. Valve models were incorporated into a pulsatile flow mock-loop to evaluate their hemodynamic behavior and the chordae-adjuster efficacy. Echocardiographic tests were performed to assess system compatibility with medical imaging.

Results: Pulsatile flow tests proved the correct functioning of the models, valves opened and closed following transvalvular pressure, and recorded hemodynamic indexes were comparable to in-vivo settings. Sutured leaflets withstood many cardiac cycles at high heart rates without damage or tearing. The chordae-adjuster allowed recreating physiological and pathological valve configurations: correct coaptation, leaflet bulging or tethering. Furthermore, the models were visible under echocardiography, proving echogenicity of material and compatibility with operatory environment.

Conclusions: These models were able to mimic morphology and functioning of atrioventricular valves and could represent a promising tool for clinicians training on novel percutaneous strategies.

O64

DESCRIPTION OF DIRECTION DEPENDENT GAS TRANSFER IN OXYGENATORS

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Objectives: Oxygenators play an important role in lung rehabilitation, however, gas exchange efficiency needs to be improved. A priori estimation of gas exchange in oxygenators is not possible with existing methods. Therefore, more detailed knowledge and systematic investigations of gas transfer on fiber level is necessary to locally resolve gas transfer inside the devices. The aim of this study was to quantify and better understand the influence of fiber orientation and blood flow on gas transfer using computational modelling and in-vitro experiments.

Methods: We performed CFD simulations in periodic sections of oxygenators containing fibers with an outer diameter of 380 µm which are woven to mats of 18 fibers per 10 mm. Three main flow directions (x, y, and z) were determined for two types of fiber bundles (90° and 24° angle between stacked and cylindrically wound fiber mats, respectively), resulting in five different configurations. We used a validated numerical model to evaluate gas transfer along the flow path of 5 mm length. In parallel, small experimental oxygenators were developed matching these configurations. In in-vitro experiments with porcine blood, blood-gas concentrations were analyzed before and after the oxygenators. Simulations and experiments were performed at five flow rates with Reynolds numbers between 1 and 10.

Results: Numerical results indicate separation of concentration boundary layers between fibers depending on flow distribution inside different fiber bundles. Fiber-configurations influence gas transfer by factor 2 (24° x vs. 90° z). The resulting gas transfer rates can be parametrized in a dimensionless number (Sherwood number) as a function of the Reynolds number for each configuration.

Conclusions: Gas transfer in membrane oxygenators is strongly dependent on fiber orientation and flow direction. On the fiber scale, complex fluid mechanical effects were observed requiring further investigation. In the ongoing study, the parametrization shall be used to model fiber bundles of whole oxygenators.

O65

PRELIMINARY ASSESSMENT OF AN INNOVATIVE AORTIC VALVE DECALCIFICATION DEVICE IN EX VIVO HUMAN MODEL

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Objectives: Aortic valve (AV) stenosis is one of the most prevalent valvular heart diseases in the elderly population. Transcatheter aortic valve implantation (TAVI) has emerged as the gold standard for patients with severe AV stenosis. However, TAVI is not without complications, including periprocedural neurological events and long-term bioprosthetic durability. New strategies for slowing disease progression and delaying

prosthetic AV implantation are being developed. With the aim to break up calcium deposits and restore the AV leaflets' flexibility and mobility, a new transcatheter debridement device (TDD) exploiting ultrasonic pulse waves is under development. Preliminary ex vivo investigations on human hearts were carried out to understand if biomechanical modifications in leaflets treated with TDD could influence AV hemodynamic.

Methods: Four human cadaveric hearts with AV stenosis were incorporated into an ex-vivo beating heart platform. Each heart sample was characterized under pulsatile flow conditions before (baseline) and after TDD treatment (post-treatment). The following parameters were evaluated: transvalvular pressure drop (ΔPsys), backflow volume (BV), and effective orifice area (EOA). Images of the leaflets were captured after the TDD procedure for a macroscopic qualitative examination.

Results: The treatment induced a reduction in ΔPsys in all tested samples (19.4±9.5%). An average improvement in EOA of 17.8±6.6% and an average reduction in BV of 16.6±57.5% were obtained. However, no statistically significant changes were observed in ΔPsys (p-value=0.1076), EOA (p-value=0.0649), and BV (p-value=0.8385) values between baseline and post-treatment conditions, probably due to the low number of heart samples used. Furthermore, valve integrity was maintained in all experiments.

Conclusions: These tests are a preliminary demonstration of TDD' potential to improve AV hemodynamics without damaging the valve's integrity. TDD may be a promising tool to treat patients with AV stenosis without valve replacement intervention.

O66

INTER-MODEL AND INTER-MODALITY ANALYSIS OF LEFT VENTRICULAR HEMODYNAMICS: COMPARATIVE STUDY OF CFD APPROACHES, ECHOCARDIOGRAPHIC AND MRI DATA

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Objectives: The analysis of intra-ventricular hemodynamics is of high interest in current cardiovascular research to improve the understanding of occurring diseases. Computational fluid dynamics (CFD) based on medical imaging can be used to derive high-resolution hemodynamic information. However, different approaches exist in the literature to assess hemodynamics based on altering imaging methods and in-silico approaches. Within this study, two different approaches based on two imaging modalities, namely ultrasound (US) and magnetic resonance imaging (MRI) will be compared, and their applicability exposed.

Methods: Time-resolved three-dimensional cardiovascular US and MRI were performed on a human proband, resulting in 4D-images (3D in space + time) of the left ventricle (LV) and 3D-images of the left atrium, mitral valve, and ascending aorta. Within one cardiac cycle 25 timesteps were captured which describe the time-discrete LV movement. Based on these multimodal images, two existing approaches were used to assess the hemodynamics in the moving ventricle. First, a moving mesh method based on an interpolation between the 25 geometries resulting in a continuous movement was applied. Second, a sophisticated CFD approach using the systolic and diastolic LV geometry and the prescribed continuous ventricular movement based on the volume curve was applied. A verification of the two methods was taken out by comparison to the MRI flow fields and the US velocities, respectively.

Results: Initial results reveal differences in the movement of the ventricular wall captured with US and MRI which already causes different vortex formation. The blood flow reveals a good agreement with MRI flow data when MRI is used as a basis for both methods. Between the two methods, both reveal similar hemodynamics and can be verified by MRI.

Conclusions: Patient-specific blood flow can be modeled using different implementations in CFD. Attention should be paid to high-resolution imaging and high-fidelity segmentation to assess realistic and comparable results.

Symposium: Albumin, Scientific and Clinical Advances on a Versatile Protein

O67-K

THE ROLE OF ALBUMIN´S BINDING CAPACITY IN VIVO AND IN VITRO

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Objectives: Data from X-ray analyses of human serum albumin reveal a heart-shaped molecule with an □-helical content. Considered as an inert protein, it mainly participates in sustaining blood pH and osmotic pressure. However, albumin also acts as a carrier and transporter for ligands, drugs and toxins and its role as an inert protein must be questioned.

Methods: Due to its binding of glucose by non-enzymatic glycosylation (AGEs), of pharmaceutical agents and toxins, such as uremic retention solutes as well as bacterial endotoxins it can be called a “molecular vacuum cleaner”. Current investigations show that binding happens through molecular forces, such as hydrogen bonds and hydrophobic interactions to different HSA subdomains, such as IA, IB, IIA, IIB, IIIA, and IIIB.

Results: Binding in vivo depends on its 3D-conformation and is controlled by pH, temperature, ionic conditions and 17 molecular disulfide bridges. In vitro, stabilizers added to albumin infusion solutions determine its binding capacity. Albumin half-life in plasma can be prolonged when fatty acids are bound to the protein. Many commonly used drugs with acidic or electronegative features, such as Warfarin, Diazepam, Ibuprofen bind to HSA. Albumin-binding may be desirable to solubilize such agents that would otherwise aggregate and be poorly distributed in blood circulation. Therefore, dugs with a high affinity for the protein (>95% bound) would require higher doses to achieve the effective concentration in vivo. In addition, such drugs will be slowly distributed to the required sites in the human body and may not be efficiently eliminated by either kidney or liver.

Conclusions: Albumin´s binding capacity for toxins and drugs is reduced under pathological conditions, such as in liver- and kidney-disease. This phenomenon can be attributed to a change in the protein´s 3D-conformation. Whether such modified albumin molecules should be removed by hemodialysis is still a matter of debate.

O68

THE ALBUMIN-FUNCTIONALITY-TEST (AFT) AS A NEW VALUABLE TOOL TO ASSESS HUMAN ALBUMIN FUNCTION IN PATIENTS WITH LIVER AND KIDNEY DISEASE

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Objectives: Influence of liver and kidney disease on both morbidity and mortality in the population is becoming increasingly important. The analysis of albumin function offers a suitable platform for early detection of possible stages of escalation of these diseases. Albumin as the major plasma protein has several physiological functions with binding and transport being one of them. Binding of different molecules can affect the ability of conformational mobility of human serum albumin, which can be detected by Albumin-functionality-test (AFT). This albumin function correlates to dangerous illnesses like liver and kidney failure.

Methods: The Albumin-functionality-test based on electron paramagnetic resonance (EPR) spectroscopy uses a spin labeled fatty acid which binds analogous other natural albumin ligands variably strong in different albumin binding sites and thus serves as indirect marker for the serum albumin functionality.

Results: Thus an "effective" albumin transport function could be determined, which quantifies the amount of functional albumin in the patient in comparison to healthy population. Parameters obtained from Albumin-functionality-test like binding efficiency (BE) and detoxification efficiency (DTE) correlate with severity of disease and show prognostic information.

Conclusions: Data from three different studies are presented showing reduced binding efficiency of less than 40% for liver patients with acute-on-chronic liver failure (ACLF) and BE of about 50% for kidney disease-patients treated with hemodialysis. In both conditions oxidative state of albumin is changed. Our results show significantly reduced BE of reversibly oxidized albumin, not irreversibly. As a conclusion of these results Albumin-functionality-test seems to be an eligible diagnostic tool for patients with liver and kidney disease, respectively.

O69

ASPECTS OF ALBUMIN FUNCTION IN CLINICAL APPLICATION

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Objectives: Albumin may be considered the most essential protein in human blood, playing a pivotal role as transport protein for protein-bound, water-insoluble drugs and uraemic toxins. Its transport capacity decreases in patients with advanced stages of critical illnes, and unbound fractions of uraemic toxins are associated with major complications. Albumin binding capacity (ABiC) is a dye-based method to quantify the remaining binding capacity at one of the major binding sites (site II) of the albumin molecule. We investigated how far this decline is quantifiable and how it correlates with different stages of critical illness.

Methods: Blood samples from 70 critically ill patients were incubated with a binding site-specific fluorescent marker, and the amount of unbound marker was determined after filtration by fluorescence detection. Measurements in a pooled human plasma served as a reference.

Results: ABiC levels significantly correlated ($p = 0.001$) with KDIGO stages for acute kidney injury. Septic patients had a significantly reduced ABiC compared to non-septic patients ($p < 0.001$). Patients who died during hospitalisation had a significantly lower ABiC on the first day ($p = 0.038$) than survivors.

Conclusions: Albumin represents a target molecule for pharmacological and physicochemical therapies to improve toxin excretion and reduce mortality in critically ill patients. To date, however, the functional properties of albumin in these patients and its alterations are poorly understood. Advancing knowledge of albumin binding competitors to promote removal of protein-bound toxins along with the value of understanding the functional properties of albumin for clinical decision-making, especially for individualized therapeutic regimens, needs to be further explored and cross-integrated.

Session: Ventricular Assist Device II

O70

INVESTIGATION OF A PROTOTYPE FOR A PULSATILE MECHANICAL CIRCULATORY SUPPORT SYSTEM FOR RIGHT HEART FAILURE SITUATIONS IN A LARGE ANIMAL STUDY

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Objectives: Isolated right heart failure is much rare than RHF due to left heart failure. In the last decade, treating RHF with temporary mechanical circulatory support (MSC) came into focus. MCS is an alternative to intra-aortic balloon pump (IABP) counterpulsation or surgically placed ventricular assist.

Methods: This study investigates a prototype of a pulsatile, percutanous MCS in a porcine model. The MSC's membrane pump is connected to a T-splitter, which directs the blood flow either through the inlet catheter into the pump or out of the pump into the outlet catheter. A catheter in the jugular vein aspirated the blood. Bypassing the right ventricle, the blood is ejected into the pulmonary artery (PA). The pump was driven by an IABP console providing the pump rate. To simulate an RHF, the PA was obstructed by clamping. Subsequently, the MSC was activated, providing a blood flow of 3.2 L/min. The hemodynamic pressures (systolic and diastolic aortic and PA and central venous pressures) and the pump flow were measured before and after the device was activated.

Results: The MSC can provide an output of 38ml per pump beat, directly proportional to the pump rate investigated from 55 bpm to 85 bpm. PA obstruction drastically worsened the hemodynamic state, which is reflected by decreasing the pressure in the aortic and PA by around 25%. When the MCS was activated, the pressures recovered up to 95% of the healthy initial conditions. The pressure in the central venous system was increased by 25% compared to the initial healthy state. After activation, the CVP recovers to health conditions.

Conclusions: The data provided by this experiment show that the MCS improves the Hemodynamics in the presence of acute RV failure. More tests need to be performed to clarify the occurrence of hemolysis caused by the T-Splitter.

O71

TRANSLATABILITY OF ANATOMICAL COMPLIANCE IN VIRTUAL FITTING TO LARGE ANIMAL TRIALS - CHALLENGES IN CAVOPULMONARY ASSIST DEVICE DESIGN

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Objectives: Pre-clinical in-silico assessments of anatomical compliance have become pivotal in medical device design. However, translation of virtual device implantability in humans to subsequent development stages, such as animal trials, may be limited. We thus aimed to evaluate the potential of analysing in-silico device implantation in virtual animal

models prior to animal testing to predict in-vivo anatomical device compliance.

Methods: Double- and single-outlet cavopulmonary assist device (CPAD) designs were virtually implanted into computed tomography models of both a Fontan patient and a native ovine anatomy. Anatomical device compliance was compared between human and sheep, along with an exploratory analysis of correlations between in-silico and in-vivo anatomical compliance in acute sheep trials.

Results: Given the diverse human and ovine anatomical conditions, the double-outlet CPAD was posited spatially replacing the Fontan pathway in the human model, while optimal implantation into a sheep anatomy was achieved in-parallel to the main-to-right pulmonary artery course. In-silico implantation of the single-outlet CPAD design revealed an enhanced versatility to adapt to the differing human and sheep cardiovascular anatomy. The resulting device fit comprising respective in- and outflow graft shapes demonstrated superior anatomical compliance compared to a double-outlet device configuration. The optimized double-outlet device position and graft configuration identified in virtual fitting appeared both anatomically accurate and surgically feasible upon implantation in 6 acute animal trials, while in-vivo results of the single-outlet pump are currently pending.

Conclusions: Virtual fitting of novel device designs into animal models facilitated the characterization of anatomical implantability for optimized surgical planning prior to in-vivo CPAD trials.

O72

PLATELET MIRNA PROFILE IN PATIENTS WITH LVAD: A NEW MARKER TO PREDICT BLEEDING EVENTS?

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Objectives: MicroRNAs (miRs) emerged as promising diagnostic and therapeutic markers in heart failure. To date, few studies investigated miR patterns in LVAD patients, but none focused on the association between platelet miRs and the development of adverse events. We investigated for the first time the potential clinical utility of platelet miRs in the setting of durable LVAD support.

Methods: We prospectively determined by quantitative real-time polymerase chain reaction the expression levels of selected platelet miRs known to be involved in platelet activation, coagulation, and cardiovascular diseases in consecutive LVAD patients. Data were longitudinally measured before LVAD implant and after 1, 6, and 12 months of LVAD support. Data were compared with those measured in healthy volunteers (controls). In silico analysis was also performed to identify pathways related to differentially expressed miRs.

Results: Data from 15 consecutive LVAD patients and 5 controls were analyzed. The pre-implant expression levels of platelet miR-126, miR-374b, miR-223 and miR-320a were significantly different in patients vs. controls. Following LVAD implantation, the expression levels of platelet miR-25, miR-144, miR-320 and miR-451a changed significantly over the course of LVAD support. In silico analysis revealed that these miRs are implicated in both cardiac- and coagulation-associated pathways. Of note, patients who suffered from bleeding (n=5, 33%) had significantly higher pre-implant expression levels of platelet miR-151a and miR-454 with respect to patients who did not. The same miRs were also differentially expressed in bleeders following LVAD implantation early before the clinical manifestation of the events.

Conclusions: This study provides proof-of-concept evidence of significant modulation of platelet miRs expression driven by LVADs. Importantly, our data suggest the possible existence of a platelet miRs signature predictive of bleeding events and open the perspective for the development of novel therapeutic strategies targeted to platelet miRs modulation in patients identified at high risk of LVAD-related adverse events.

O73

ACUTE IN-VIVO EVALUATION OF A DOUBLE-OUTFLOW PUMP FOR CAVOPULMONARY SUPPORT

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Objectives: Recently, both single-outflow and double-outflow cavopulmonary assist devices (CPADs) have been proposed for the Fontan population. Although large animal trials have been conducted to evaluate single-outflow configurations, an equivalent in-vivo assessment for double-outflow concepts is yet missing. Therefore, the aim of this study was to evaluate the hemodynamic benefit of a previously proposed double-outflow CPAD in an acute sheep model.

Methods: The examined pump denotes a previously developed double-inflow double-outflow rotodynamic blood pump tailored for the implantation in the total cavopulmonary connection of Fontan patients. The two inflow cannulae of the double-outflow CPAD were connected to the caval veins. The two outflow cannulae were connected to the right and main pulmonary artery via an end-to-side graft anastomosis. Caval flows, cardiac output (CO), central venous pressure (CVP), pulmonary artery pressure (PAP), and left atrial pressure (LAP) were measured during speed ramp protocols to monitor hemodynamic changes.

Results: A total of six experiments were conducted (53.35 ± 5.1kg). In three of these experiments, the CPAD was evaluated, and biventricular equivalency restored in terms of venous return. The results indicate that venous pressures (CVP) decreased linearly with increasing pump speed setting ($r > 0.879$), whereas caval flow ($r > 0.973$), cardiac output (CO) ($r > 0.993$), PAP ($r > 0.973$), and LAP ($r > 0.408$) increased.

Conclusions: Despite the substantial complexity of the sheep model given the pulmonary arterial configuration that necessitates significant graft bending, the CPAD was assessed in three acute experiments and exhibited the potential to entirely replace a subpulmonary ventricle.

Session: New Models for Biological Applications

O74

DEVELOPMENT OF A DECM-BASED HYDROGEL FOR THE PRODUCTION OF STABLE AND FUNCTIONAL ARTIFICIAL PANCREATIC ISLETS PRODUCED BY THE INK-JET METHOD

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Objectives: There are clinical trials report using stem cell-derived β-cells as an innovative treatment of T1D. However, one should remember about the possibility of their clinical application. Transplantation on β-cells, into the portal vein carries a high risk of undetermined final location of the cells. The aim of this experiment was to evaluate the survival and functionality of β-cells in artificial pancreatic islets, bioprinted with ink-jet method.

Methods: INS-1E cells were used in the study. Two types of encapsulation hydrogels were used: 2% HAMA + 20% GelMA (H-G_INS) and 2% HAMA+20% GelMA + dECM (ECM_INS). The GSIS assay and FDA/Pi staining were used to assess cell functionality and viability.

Results: Functional analysis showed that the addition of dECM significantly affected β-cells functionality. Control group showed a significantly reduced viability at time points (7,14 and 21 days) compared to day "0" ($p<0.005$). The ECM_INS group has demonstrated stable functionality for more than 14 days. There was also a significant increase in cell functionality in the ECM_INS group relative to the control group ($p<0.005$). This relationship persisted throughout the experiment.

Conclusions: The use of dECM for bioprinting of artificial islets is crucial for maintaining their full functionality. The developed composition of the bioink and the method used enable the production of stable 3D-structures that can be safely transplanted, because they retain their structure in physiological conditions.

O75

INFLUENCE OF ELECTRICALLY CHARGED POLY(VINYLIDENE FLUORIDE) SUBSTRATES ON HUMAN BONE MARROW MESENCHYMAL STEM CELLS RESPONSE

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Objectives: The aim of this study was to analyse the proliferation, maintenance of multipotentiality and differentiation of bone marrow-derived human mesenchymal stem cells (hBMMSCs) cultured on flat poly(vinylidene fluoride) (PVDF) substrates, which present different crystallization phases, and different electrical charge on the biomaterial surface. The electrical properties of bone are relevant not only as a hypothesis of the bone adaptation and remodelling control mechanism, but also in the context that external electrical stimulation of bone promotes healing and repair.

Methods: Human mesenchymal cells from non-neoplastic bone marrow aspirates were first isolated and characterized. Then, cells were cultured for 5 days in basal medium on flat substrates crystalized in alpha or beta phase (non-polarized, positively and negatively polarized). The culture medium was then changed to osteogenic medium. Cell viability, proliferation, morphology and multipotentiality were analysed after 5 and 28 days of culture. Markers associated with multipotentiality (CD90, CD105 and CD73) were assessed by flow cytometry (FC) and the expression of genes (LPL; SOX9, COL1A1 and RUNX2), related to early differentiation into adipocytes, chondrocytes and osteoblasts, were studied by quantitative PCR (Q-PCR).

Results: Flow cytometry showed significant differences in CD90 and the gene expression of COL1A1 and SOX9 when cultured on PVDF with different phase crystallisation and electric charge. In addition, the production of alkaline phosphatase was also influenced by the substrate charge.

Conclusions: This study shows that proliferation and immunophenotypic markers were greatly influenced by the electrical charge of PVDF substrates. hBMMSCs cultured on negatively charged PVDF substrates showed higher rates of proliferation compared to positive or neutral charge. In addition, hBMMSCs differentiation was importantly influenced by the positive charge of the substrates.

O34

DEVELOPMENT OF A SIMPLE AND SHORT-TERM DECELLULARIZATION PROCEDURE FOR IN VIVO ALLOGENEIC TISSUE-ENGINEERED VASCULAR GRAFTS

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Objectives: We have been clinically applying in vivo tissue-engineered vascular grafts composed of autologous collagen and fibroblasts constructed in subcutaneous tissues of the pediatric patients with heart diseases. Since there is a concern about the strength of autografts in high-risked children, we devised to use the more reliable decellularized allograft constructed in healthy adult individuals. To avoid infection as well as deterioration due to long-term storage, it would be desirable to decellularize the harvested graft simply in a short time and transplant it to the patient on the same day. We have previously achieved adequate decellularization with detergent treatment by a very simple and short-term horizontal shaking method. This time, we evaluated their histological findings and mechanical properties after treatments under several conditions to investigate their suitability as allografts.

Methods: Cylindrical silicon rods (diameter: 5mm, length: 30mm) were implanted in the subcutaneous tissue of beagle dogs for several months to construct tubular vascular grafts. The harvested grafts were decellularized by horizontal shaking (2h/1h/30min) using 1% sodium lauryl ether sulfate (SLES). These were cut into tubes with a length of 5mm, passed through two shafts through the lumen, and stretched unidirectionally at a speed of 100 mm/min in wet conditions. The traction strength curve at that time was measured, and the maximum strength until just before the tissue rupture was recorded.

Results: After more than one hour of treatment, grafts were adequately decellularized. No statistically significant difference was observed between the decellularized and the non-decellularized groups in the average maximum strength in the traction test.

Conclusions: Non-decellularized autologous vascular grafts have already been successfully applied clinically. Since the decellularized grafts have suitable mechanical properties as well as autologous vascular grafts, they are expected to be used as reliable allografts for high-risk pediatric patients.

O77

POLYZWITTERIONIC COATING OF POROUS ADSORBENTS FOR THERAPEUTIC APHERESIS

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Objectives: Blood compatibility is crucial in hemapheresis, where adsorbent polymers are in direct contact with whole blood. Here, we present blood compatible zwitterionic polymers that can be applied as surface coatings on porous adsorbents to enhance blood compatibility, i.e., to minimize the activation of blood cells on the biomaterial surface.

Methods: We developed blood-compatible matrices by surface modification with polyzwitterionic polysulfobetainic and polycarboxybetainic coatings. Photoreactive zwitterionic terpolymers were synthesized by free-radical polymerization of zwitterionic, photoreactive and fluorescent monomers. Upon UV irradiation, the terpolymers were photodeposited and mutually crosslinked on the surface of hydrophobic polystyrene-co-divinylbenzene (CG161c, Amberchrom) and hydrophilic polyacrylamide-co-polyacrylate (DALI, Fresenius Medical Care) beads. Blood compatibility was evaluated by assessing polymer-induced hemolysis, coagulation parameters, and cell adhesion to the material surface under batch and flow conditions. The remaining adsorption capacity of coated adsorbents was studied in human whole blood.

Results: Fluorescence microscopy revealed coatings with an average thickness of 5 µm, which were limited to the bead surface. The plain synthesized polyzwitterions (1.0 mg/mL), as well as coated adsorbents (10% v/v), did not induce hemolysis (Hb $<$5 mg/dL). Polyzwitterionic coating of the hydrophobic CG161c adsorbents improved coagulation parameters by significantly shortening prothrombin time (PT), activated partial thromboplastin time (aPTT), and diminishing the adsorption of antithrombin (AT)-III and protein C. In the case of DALI, the coating effect was less pronounced. Coated CG161c maintained an adsorption capacity of 39-67% for IL-6 and 25-35% for TNF-α, while the coated DALI beads preserved 80% of the adsorption capacity for low-density lipoprotein.

Conclusions: Coating enhanced the blood compatibility of hydrophobic, but not of hydrophilic adsorbents. The most pronounced effect was observed on coagulation parameters (PT, aPTT, AT-III, protein C) and neutrophil count. Polycarboxybetaine with a charge spacer of 5 carbons was the most promising polyzwitterion for the coating of adsorbents for whole blood apheresis.

Session: Organ-on-Chip

O78

INVESTIGATION OF OLEIC ACID, PALMITIC ACID AND THEIR MIXTURE ON THE DEVELOPMENT OF HEPATIC STEATOSIS USING LIVER-ON-CHIP TECHNOLOGY

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Objectives: Nonalcoholic fatty liver disease (NAFLD) is a metabolic and progressive disease whose incidence has dramatically increased in recent years with the rise of obesity. It is characterized by the process ranging from simple steatosis to hepatocarcinoma. However, a deep understanding of NAFLD progression remains challenging due to the lack of relevant in vitro human disease models. In this work, we investigated the effect of several free fatty acids on our HepG2/C3A based liver-on-chip.

Methods: We used a PDMS-based liver-on-chip model designed to ensure the dynamic culture of the hepatic cells with an optimal shear stress. To induce steatosis, hepatic cells were exposed to oleic acid, palmitic acid and a mixture of oleic and palmitic acids, as far as they are common dietary products. Fatty acids exposure last 2 or 7 days to mimic an acute and chronic exposure, respectively. HepG2/C3A cells functionalities was assessed by staining or/and measuring the levels of albumin and urea. In addition, mRNA levels of hepatic and steatosis markers were also investigated. Finally, intracellular lipid accumulation was evaluated by staining cytoplasmic lipid droplets.

Results: We found that palmitic acid treatment led to most advanced toxicity. Oleic acid exposure was associated with a mild inflammation at the gene level associated with a lipid accumulation in the cells. Co-exposition of oleic acid with palmitic acid seemed to reduce the palmitic acid's hepatoxicity and restored the levels of several lipidic and glycolytic genes.

Conclusions: Thus, the present study characterized the effect of several free fatty acids on liver cells and revealed the potential of our liver-on-chip to generate a hepatic steatosis model to investigate the development and the key aspects of NAFLD progression.

O79

DESIGN AND VALIDATION OF A DEVICE FOR HIGH-THROUGHPUT DRUG SCREENING ON PATIENT-DERIVED ORGANOIDS 3D CULTURES

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Objectives: Organoids are in vitro-cultured structures derived from stem cells that self-organize three-dimensionally (3D) and recapitulate the structure and functions of the organs of origin. They represent useful models for studying development processes, regenerative medicine, pharmacological research, and disease modelling. Patient-derived organoids (PDOs) represent an easy-to-use and more realistic alternative to 2D and xenograft models and hold promise for developing personalized medicine.

Methods: Here we present a device to culture organoids for drug screening purposes. This platform is designed to host 288 independent units. Each independent unit is composed of an 8 µl Matrigel® drop containing patient-derived organoids. Drops are hanging to custom 3D printed supports and cultured in immersion, each one in single wells of a 384 multiwell plate.

Results: Validation of the platform has been performed by exploiting a biobank of genomically and clinically annotated organoids, generated from surgical resections of colon cancer metastasized to the liver. Extensive testing has confirmed that organoids grow and proliferate in the platform as their counterpart cultured in standard conditions. Moreover, drug screening on organoids with reference compounds, performed in parallel in the platform and in the standard 96 multiwell plate, gave comparable results.

Conclusions: Our tool allows a 3-fold reduction of the reagent used to perform drug screening compared to a standard 96 multiwell and shortens the time to obtain clinically relevant information on drug sensitivity.

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O80

MECHANICAL AND BIOCHEMICAL CHALLENGES IN A NOVEL DYNAMIC BIOREACTOR FOR OVARIAN CORTICAL TISSUE CULTURE

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Objectives: Multi-step in vitro culture of cryopreserved ovarian tissue strips, i.e., tissue culture until antral follicles develop, oocytes maturation, fertilization and embryo transfer, could permit to exploit fertility potential of women with ovarian tumors or premature ovarian failure. We recently showed that culture in novel dynamic bioreactors providing enhanced O2 transport and mechanical challenges on tissue enclosed in permeable nets permits to enhance follicle viability and development over conventional dish culture. Herein we characterize the extent of O2 transport enhancement and of mechanical ovarian tissue stimulation.

Methods: Reference was made to bioreactors optimized with 3D CFD flow transport models hosting 10 strips 1x1mm2 large, 0.6mm thick of ovarian cortical tissue operated at 4ml_medium/min under steady compression. Strains were characterized by 3D laser profilometry on orthodontic wax strips. Fluid-mechanical shear stresses and dissolved O2 concentration profiles were estimated with 3D models of fluid and O2 diffusive and convective transport.

Results: Compressive solid strain pattern mirrored strip-holding net structure, and was consistent on either strip surface yielding total strains in -13%/-3% range. Flow and O2 transport models showed that tissue strips are challenged with shear stresses in the 10-3-10-2Pa range and that the medium layer adherent to tissue, where O2 concentration decreases, was significantly thinner than in conventional dishes even with O2-permeable bottom.

Conclusions: Culture in the novel dynamic bioreactors permits to exert on ovarian tissue solid strains and fluid-mechanical shear stresses in ranges eliciting tissue biochemical response without any damage, while significantly enhancing O2 transport from medium bulk to tissue thanks to bioreactor convenient geometry. The synergic effects of enhanced oxygen supply to follicles, due to disruption of the stagnant medium layer adherent on strips, and mechanical cues exerted on strips, e.g., compressive strains and shear stresses, likely preserved follicle viability and promoted progression to secondary follicles better than static culture.

O81

VERIFICATION OF A NOVEL PLATFORM TECHNOLOGY FOR THE ISOLATION OF RARE CELLS

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Objectives: Circulating endothelial cells (CECs) are rare cells in the bloodstream. A proteomic and transcriptomic analysis of these cells enables the diagnosis and analysis of cardiovascular diseases, like heart failure. It remains a technical challenge to isolate them in large enough quantities for a precise diagnosis and downstream analysis. We introduce the BMProbe™, a platform technology for the minimal invasive isolation of rare circulating cells.

Methods: The probe is a medical grade stainless steel wire that can be coated with any Immunglobulin G antibody for the isolation of specific cells in the venous bloodstream. To target CECs, the probe is coated with anti-CD105 antibodies. Experiments were performed to determine a geometry that has improved conditions for cell deposition. Different probe geometries were tested in a developed flow system that was filled with a dextran solution and endothelial cell culture cells (HUVEC). Further, ex vivo experiments with patient-blood were performed to validate the ex vivo functionality of the platform technology.

Results: The flow system experiments indicate a 31 times greater cell binding efficiency of the BMProbe™ compared to a flat geometry. Further, the functionality to isolate rare cells from the patient blood was verified. It was possible to differentiate the 9 healthy controls from 7 patients with disease. The sensitivity is 86% and the specificity is 88%.

Conclusions: This is a promising method to isolate rare cells in large quantities directly from the venous bloodstream without removing blood from a patient. An additional advantage is the isolation of the cells from their natural habitat, reducing the stress on the cells caused by blood withdrawal and subsequent blood sample processing. The future step is to verify the functionality in vivo.

Symposium: Computational Fluid Dynamics

O82

A LONGITUDINAL STUDY IN A PATIENT-SPECIFIC AVF: VASCULAR REMODELING AS A PROTECTIVE MECHANISM FOR FLOW STABILISATION?

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Objectives: The mechanisms underlying vascular stenosis formation in the arteriovenous fistula (AVF) for haemodialysis (HD) remain mostly unknown. This study aims at investigating the relation between hemodynamic conditions and vascular remodelling in an AVF failed 1.5 years after surgery due to stenosis formation.

Methods: Non-contrast-enhanced magnetic resonance imaging (MRI) and Doppler Ultrasound (US) examinations were acquired at 3 days, 40 days, 6 months, 1 year and 1.5 years after surgery in a 72-year male referred for native radio-cephalic AVF at the Unit of Nephrology and Dialysis of Bergamo Hospital. Three-dimensional surface models were generated using the Vascular Modeling Toolkit (VMTK) and high-fidelity computational fluid dynamic simulations were solved using pimpleFoam (OpenFOAM suit), prescribing patient-specific boundary conditions derived from US in the proximal and distal radial artery. Morphological and hemodynamic changes over time were then investigated.

Results: The AVF had a successful maturation process, characterised by a massive arterial and venous dilatation and a huge increase in blood flow volume within the 6 months after surgery. Between 6 months and 1 year, a juxta-anastomotic vein stenosis caused a cross-sectional area (CSA) reduction of 62.51%, becoming very evident at 1.5 years (-78.82% in CSA). The changes in the vessel lumen were accompanied by a decrease of the blood flow rate, which did not allow HD anymore at 1.5 years. The development of the stenosis in the venous segment was paralleled by the regularisation of blood flow velocities and consequent decrease in the near-wall disturbed flow metrics, i.e. Oscillatory Shear Index and Spectral Power Index.

Conclusions: Our results show that local flow instabilities may have induced progressive intimal hyperplasia during time and suggest that this adverse inward remodelling could act as a protective mechanism towards blood flow stabilization.

O83

ANIMAL-BASED CFD ANALYSIS OF HEMODYNAMICS IN PULMONARY ARTERY WITH AN IMPLANTED PRESSURE SENSOR

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Objectives: Pulmonary artery pressure sensors (PAPS) are proposed for the monitoring of heart failure patients.

Methods: To proof an ability of an in-silico study to assess a risk of the sensor thrombogenicity a chronic animal study using pigs was conducted. Computed tomography (CT) data was acquired before and immediately after implantation, as well as one month follow-up. Devices were implanted into 10 pigs, each one in the left and right pulmonary artery (PA). The implantation procedure aimed at facilitating favorable and non-favorable positioning of the devices to increase chances of thrombus formation. Eight devices were positioned non-optimally. Pre-interventional PA geometries were reconstructed from the respective CT images, and the devices were virtually implanted at the exact sites and orientations indicated by the follow-up CT. Transient intra-arterial hemodynamics were calculated using computational fluid dynamics. Wall shear stresses (WSS) and oscillatory shear indices (OSI) before and after device implantation were compared.

Results: Simulations revealed no relevant changes in any investigated hemodynamic parameters due to device implantation. Even in cases, where devices were implanted in a non-favorable manner, no marked differences compared to devices implanted in an optimal position were found. Before implantation WSS was 2.35 $\pm$ 0.47 Pa, whereas OSI was 0.08 $\pm$ 0.17. Areas affected by low WSS magnitudes were 2.5 $\pm$ 2.7 cm², whereas the areas affected by high OSI were 18.1 $\pm$ 6.3cm². After device implantation, WSS and OSI were 2.45 $\pm$ 0.49 Pa and 0.08 $\pm$ 0.16. Surface areas affected by low WSS and high OSI were 2.9 $\pm$ 2.7 cm², and 18.4 $\pm$ 6.1 cm².

Conclusions: The results indicates that no clinically relevant differences in hemodynamics are occurring after device implantation, even at non-optimal positioning of the sensor. Simultaneously, no embolic events were observed, suggesting that the risk for thrombus formation after device implantation is low.

O84

IMAGE-BASED SIMULATION OF LEFT VENTRICULAR HEMODYNAMICS: A NUMERICAL FRAMEWORK TOWARDS CLINICAL FEASIBILITY

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Objectives: Left ventricular hemodynamics are hypothesized to serve as an early indicator for the manifestation of cardiovascular diseases. In the analysis of hemodynamics, computational fluid dynamics (CFD) can complement medical imaging methods for in-depth flow investigations. To obtain information about individual conditions, a high level of patient-specific input into the model is required. Considering the variety of data sources, medical imaging modalities, and the range of data quality, this leads to demanding case processing with a lot of manual effort.

Methods: We therefore standardized the workflow by coupling the individual anatomical representation in form of a statistical shape model (SSM) with a fluid structure interaction (FSI) workflow. Thereby, we obtain a high degree of individuality in our simulations while keeping the case-specific effort involved at an acceptable level. To test the simulation pipeline, we processed data of healthy volunteers and patients with isolated or combined aortic stenosis and mitral regurgitation. For patients with ventricle aneurysms after myocardial infarction, we compared pre- and post-treatment situations.

Results: We used the healthy volunteer data for a proof-of-concept by comparing CFD results to 4D flow MRI measurements. Further, simulations of mitral regurgitation patients revealed characteristics of altered kinetic energy and specific energy dissipation during diastole as also seen in previous MRI studies. As expected, simulations of the pre- and post-surgical hemodynamics of left ventricular aneurysms showed significantly improved flow conditions after surgery.

Conclusions: To conclude, we could prove that our workflow is robust and easy to use while including a lot of patient-specific details. This allows for representation of individual flow features, which can perspectively be used in clinical routine to support diagnostics, therapy planning, and outcome prediction. A profound validation study must follow to test the approach on a sufficient amount of data.

O85

ASSESSING THE HEMODYNAMIC EFFECTS OF BYPASS SURGERY ON GIANT INTRACRANIAL ANEURYSMS USING FLUID-STRUCTURE INTERACTION SIMULATIONS

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Objectives: The term GIA means intracranial aneurysm larger than 25 mm whose rupture usually leads to death or serious brain damage. Among all methods of treating these cerebrovascular pathologies, one can distinguish bypassing. It means that neurosurgeons cut off the blood inflow to the aneurysm sac and they create an additional connection to distal arteries. Such a connection preserves proper blood supply to all efferent arteries. However, there is one question that remains unanswered – which cerebral perforator should be chosen as the vessel to which the bypass should be anchored. It is impossible to predict the outcomes of each possibility in clinical practice, whereas with computational fluid dynamics (CFD) tools obtaining such an answer becomes feasible. Therefore, the main objective of this research was to perform virtual bypassing procedures and observe which configuration was optimal for the given patient.

Methods: The geometry of the arterial system, including the giant aneurysm, was reconstructed basing on biomedical imaging scans. Then, two variants of the bypass were proposed. After conducting a series of fluid-structure interaction (FSI) simulations with elastic walls assumption, flow hemodynamics in the cerebral region was assessed (including shear stress, blood distribution, pressure distribution and aneurysm volume).

Results: A comparative analysis of three cases showed a strong effect of the bypass configuration on the flow conditions inside the aneurysm. Differences in WSS, OSI, TAWSS and viscosity were noted. A significant decrease in pressure and consequently aneurysm shrinkage was observed. Additionally, areas susceptible to thrombosis were identified.

Conclusions: Results obtained from in-silico analyses can be used as an additional source of knowledge about the circulatory system affected by the bypassing surgeries. Conducted simulations indicated a beneficial effect of bypassing procedures on the mechanical load on the vessel walls. Moreover, they proved that a degree of affinity to possible thrombus formation depends on the bypass localization.

Session: Organ Preservation and Medical Device Regulation

O86

BIO-ELECTRICAL MARKERS OF CARDIAC FUNCTION FOR DONOR HEARTS ON NORMOTHERMIC MACHINE PERFUSION

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Objectives: Normothermic ex-situ heart perfusion (ESHP) enables qualitative assessment of hearts donated after circulatory death (DCD) prior to transplantation. However, additional and sensitive parameters of cardiac function of DCD hearts on ESHP are needed. The aim of this study was to present electrophysiological (EP) parameters from electrical mapping as novel bio-electrical markers of post-ischemic cardiac performance.

Methods: Porcine slaughterhouse hearts (PSH) were divided in two groups based on duration of warm ischemic time (WIT) (short WIT (<5 min.) vs. long WIT (ca. 10 min.). Hearts were instrumented on a Langendorff-perfusion device and electrical mapping of the right (RV) and left ventricle (LV) was performed 60 minutes after start of reperfusion. EP parameters including potential voltages, slopes and conduction velocities were calculated from these measurements and correlated to lactate trends and visual contractile performance of the PSH.

Results: Unipolar voltages were lower in the long WIT group compared to the short WIT group (RV: 3.8 vs. 16.4 mV, p=0.057. LV: 10.8 vs. 23.6 mV, p=0.029). In addition, more low-voltage, lower potential slopes, slower conduction velocities and more conduction block was found in the LWIT group. Unipolar voltages and potential slopes of the RV strongly correlated with the visual contractile performance of the PSH. In addition, less correlation was observed between these EP parameters and lactate trends.

Conclusions: Prolonged WIT was associated with lower potential voltages, decreased potential slopes and slower conduction in a porcine DCD model and unipolar voltage appeared the strongest marker of cardiac performance. These bio-electrical markers can hopefully aid transplantation teams in decision-making on transplantability of DCD hearts on ESHP.

O87

LIVER DONATION AFTER CIRCULATORY DEATH WITH VERY PROLONGED WARM ISCHEMIA: A PILOT EXPERIENCE OF ABDOMINAL NORMOTHERMIC REGIONAL PERFUSION ALONE

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Objectives: Over the last two decades, liver donors from controlled donation after circulatory death (cDCD) have become a precious resource to face organ shortage in many countries. In Italy, a legally obliged stand-off period of 20 minutes necessarily leads to very prolonged warm ischemia. In this particular national context, the use of abdominal normothermic regional perfusion (aNRP) is systematic; the addition of ex-situ machine perfusion (MP) is almost systematic, but not supported by evidence. We report a pilot experience of extended criteria cDCD liver transplantation (LT) with very prolonged warm ischemic time (WIT), with aNRP alone, at our high-volume transplant center. We investigated whether our results were comparable to the best possible outcomes in low-risk cDCD LT.

Methods: Prospectively collected data on 24 cDCD LT, with aNRP alone, were analyzed.

Results: The median total and asystolic WIT were of 51 and 25 minutes, respectively. Measures within benchmark cut-offs were: median duration of surgery (5.9 hours); median intraoperative transfusions (3 units of red blood cells); need for renal replacement therapy (8.3%); intensive care unit stay (3 days); incidence of primary nonfunction, ischemic cholangiopathy, bile leak, and vascular thrombosis (0%); incidence of bleeding (8.3%) and anastomotic strictures (25%); overall morbidity up to 12 months (the median comprehensive complication index was of 16.6 points at discharge and at 3 months, of 24.4 points at 6 months, and of 27.2 points at 12 months); the rate of graft loss (8.3%) and retransplantation (0%) up to 6 months; 12-month mortality (9.5%). Hospital stay (33 days, due to logistics) and mortality up to 6 months (8.3%, due to graft-unrelated causes) exceeded benchmark thresholds.

Conclusions: This pilot experience suggests that livers from cDCD with very prolonged WIT that appear viable during adequate quality aNRP may be safely transplanted, with no need for ex-situ MP, with considerable resource savings.

O88

ANALYSIS OF THE EFFECTS OF THE AORTIC CONDUIT GEOMETRY AND MECHANICAL BEHAVIOUR ON HEART VALVES PROSTHESES TEST BENCH CHARACTERISATION

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Objectives: Any medical device, before reaching the market, has to follow a precise path: first pre-clinical trials that involve in-vitro and in-vivo tests and then clinical trials. For heart valve prosthesis (HVP) the information on the required procedures is contained in the ISO 5840:2021 Standard in which are available the descriptions of all the tests to be performed on a new prosthesis. Performing in-vitro pulsatile test is mandatory, however, no indications are given on the characteristics of the tube downstream of the HVP to test.

Methods: Two conduits characterized one by the presence of the Valsalva sinuses, and the other by the ascending aorta's compliance were 3D printed. Thus, a complete characterization is performed on a commercial polymeric material, the Elastic 50A resin by Formlabs. Several tests were performed including a tensile test to find the elastic modulus and cyclic tests to ensure survival to testing. The results obtained were used to 3D print the conduit with the correct thickness and compliance. Then, according to the Standard, pulsatile tests were performed on three heart valve prostheses: a mechanical, a polymeric, and a biological one; in three configurations: standard, rigid with Valsalva sinuses and compliant with Valsalva sinuses.

Results: From the performed tests emerged that the introduction of the Valsalva sinuses led to a decrease in regurgitation, due to vortex formation, and an increase in MSPD, likely due to the diameter reduction downstream of the valve. The compliance instead reduced the diameter effect, decreasing the MSPD, but led to an increase in regurgitation due to backflow from the tube's pulsatile behavior.

Conclusions: From these results, we can see how the lack of precise directions on the aortic downstream conduit in the Standard leaves everyone the freedom to test the HVP in conditions that cannot properly predict how the valve will perform in the human body.

O89

DE-RISKING MEDICAL DEVICE DEVELOPMENT: ON THE WAY OF BECOMING THE FIRST FULLY DIGITAL CRO BY USING DIGITAL PATIENT TWINS

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Objectives: Virtonomy is becoming the first fully digital CRO by transforming medical device development and approval using a web platform that leverages digital patient twins and simulation to enable in-silico R&D and clinical trials. Virtonomy helps medical device developers significantly reduce time, cost and risk associated with getting a new device to market by shifting testing from in vivo and in vitro to in silico.

Methods: Regulatory approval is a crucial and demanding part of bringing medical devices to market. Regulators around the world have recognized the potential of this so-called in silico testing to not only prevent post-market failures but also to reduce health inequalities in the current development process. By providing a more efficient and cost-effective way to test medical devices and reducing the risk to fail in a later stage, the in-silico approach has the potential to significantly support the regulatory process. Virtonomy has created the first digital twin cloud-based technology v-Patients that enables medical device manufacturers to perform virtual testing in the web-browser by simulating the device in their target population based on real-world evidence data of humans and animals.

Results: Virtonomy's in silico technology has been successfully applied in preclinical studies, allowing researchers to simulate the behavior of medical devices in animals and the human body before beginning clinical trials, but also to generate digital evidence to substitute clinical studies. Virtonomy has successfully collaborated with leading medical device companies from implantable cardiovascular devices to wearable sensors, helping them to streamline their product development process and bring innovative new products to market more quickly.

Conclusions: The virtual studies have proven to give results that may not have been possible with conventional approaches, reduce the risky and expensive trial-and-error process, and increase evaluation confidence to ensure product safety prior to clinical trials.

O90

QUICK AND RELIABLE TEST TO SCREEN TOXICITY OF MATERIALS FOR TISSUE AND CELL ENGINEERING AND REGENERATIVE MEDICINE

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Objectives: The high sensitivity of reproductive tissues to chemical toxicants and recent evidence showing that even medical-grade 3D printing polymers might contain ovo-toxicants highlight the limits of current protocols to screen material toxicity for medical applications. We report on development of a quick and reliable toxicity test based on reproductive tissue culture with material extracts. Test reliability was proven with respect to leachables from food/medical-grade and technical polymers as candidates to build dynamic bioreactors for long-term culture of ovarian tissue strips for reproductive purposes.

Methods: Slab samples of medical-grade polypropylene (PP), untreated and treated polyamide (uPA & tPA), dental resins, technical polycarbonate (PC), professional and basic resins, low-density polyethylene (LDPE), and ABS-like resin (ABS-L-R) were either kindly provided by manufacturers or 3D printed by SLA and were tested without post-treatment. Toxicity was evaluated in two-steps: 1. leachable-containing medium was incubated with bull spermatozoa and spermatozoa motion kinetics was characterized in time; 2. strips of bovine ovarian tissue were cultured in dynamic bioreactors made of three selected biomaterials (ABS-L-R, uPA, PP) and follicle viability was evaluated at D7 vs. static dish culture and fresh tissue.

Results: Culture with spermatozoa suggests that food-grade PP, medical-grade uPA and dental resin, together with the technical pro and basic resins had the least detrimental effects on spermatozoa that behaved similar to conventional culture dish polystyrene. Culture of ovarian tissue strips in dynamic bioreactors made of the least toxic material significantly enhanced follicle development and viability over static cultures. Use of the most toxic material caused the total absence of viable follicles after 7 days, suggesting the better reliability of the spermatozoa test than those used by the norms.

Conclusions: Biomaterial tissue-compatibility strongly conditioned bioreactor performance, evidencing the importance of material choice for reproductive tissue culture and the limits of current material toxicity tests.

O91

A RETROSPECTIVE STUDY FOR COST-BENEFIT COMPARISON OF ROBOTIC AND MINIMALLY INVASIVE SURGERY FOR MITRAL VALVE REPAIR

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Objectives: A retrospective comparison of three surgical methods for mitral valve repair was conducted, considering patients operated by a single surgeon at the Cliniche Humanitas Gavazzeni in Bergamo, Italy.

Methods: The populations included 128 patients operated with robotic surgery by means of the Da Vinci robot (May 2019 to September 2022); 147 patients with minimally invasive surgery with external clamp (March 2014 to September 2022); 109 patients with minimally invasive surgery with endoclamp (March 2014 to September 2022). Based on the adopted inclusion and exclusion criteria, 118 patients operated with robotic surgery, 133 with external clamp, and 101 with endoclamp were suitable for the analysis. The t-test or the Wilcoxon Rank Sum test was applied to continuous metrics, while the Fisher exact test to binary metrics, all including the Bonferroni correction for multiple comparisons.

Results: The robotic surgery, in which small incisions are made, is associated with less patient bleeding in the first 24 hours, with a consequent reduction in the number of transfused blood units. It is also associated with reduced intensive care and extubation times. Patients operated with robotic surgery, thanks to special extubation protocols, are often disconnected from lung ventilators in the operating room, thus allowing a rapid mobilization of the patient. Therefore, these patients can start the rehabilitation program in a shorter time, which reduces hospital stay times. They also have better ejection fractions, pressure drops and mitral regurgitations. Moreover, less radiographic examinations and post-operative consultations are performed on patients operated with robotic surgery. Finally, most patients operated with robotic surgery are not discharged to a rehabilitation facility but sent home.

Conclusions: The reported significant results on the studied populations support the evidence for improved surgical outcomes and better postoperative conditions of robotic surgery.

Session: Tissue Engineering III

O92

NOVEL THERAPEUTIC APPROACH FOR OSTEOARTHRITIS BASED ON AN INJECTABLE GLYCOSAMINOGLYCAN FOR VISCOSUPPLEMENTATION WITH CHONDROPROTECTIVE EFFECT

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Objectives: The recommended procedure to treat osteoarthritis (OA) according to the ESCEO depends on the extent of damage of joint tissues. Treatments based on anti-inflammatory drugs require persistent injections and rarely contains the degeneration over the course of the years. More severe stages involve substituting the articular structure for an artificial prosthesis. Halfway, viscosupplementation therapies are based on the injection of hyaluronic acid (HA) to reduce friction. Here we present a viscosupplement gellable on demand that mimics the actual macrostructure of the proteoglycan, by including biomolecules that support hydration of the cartilage and stimulate its native cells.

Methods: By using EDC/NHS chemistry, it is possible to obtain a crosslinkable HA hydrogel with chondroitin sulfate (CS) grafted to it in a straightforward rection in aqueous media and without the need of catalysts. The crosslinking potential and the grafting efficiency has been determined by spectrophotometric or fluorometric reference assays. Conditions under which the SOL-GEL transition happens have been studied with a parallel-plates rheometer. The biological characterization of the grafting macromolecule and the hydrogels, as well as biodegradation tests of the gels for analysing the controlled release are currently in progress.

Results: The resulting solution can be turned into a gel at will under physiological pH, in presence of oxygen. Rheometric assays of the hydrogels revealed similar properties than commercial, top-of-the-range viscosupplementation alternatives that do not have the chondroprotective counterpart. A preliminary biological characterization, with human chondrocytes, suggests that the CS grafting to the HA does not compromise its biocompatibility, as compared to the bare macromolecules.

Conclusions: We developed a protein-free biomimetic proteoglycan with the ability to make the SOL-GEL transition on an osteoarthritic joint that will have a controlled and sustained release of chondroprotective biomolecules.

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O93

ENHANCING PRINTABILITY OF HYDROGELS BASED ON METHACRYLATED BIOPOLYMERS BY PRE-CROSSLINKING APPROACH

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Objectives: Methacrylated hyaluronic acid (HAMA) and methacrylated alginate (ALGMA) are widely used as additives to hydrogel-based bioinks. Those materials were found to by higly biocompatible, biodegradable and non-toxic thus supporting cell cultures. Moreover, due to the presence of methacrylic groups in their structure, addition of appropriate photoinitiator can trigger polymerization upon UV-Vis light exposure. The limitation for these materials are inadequate visco-elastic properties, which play a significant role in extrusion-based printing. Fibers extruded from low-concetrated HAMA and ALGMA solutions do not allow to obtain a high-resolution construct. In order to use the biological potential of hyaluronic acid and alginate, it is necessary to develop a method that improves the rheological and extrusion properties of materials.

Methods: Low-percentage solutions of methacrylates were applied for the research, focusing on the hydrogels based on HAMA and ALGMA. Both variants contained the various concetration of photoinitiator (LAP), enabling for cross-linking at UV-Vis light. The materials were pre-crosslinked by short-time exposing of solutions using visible light with a both wavelength of 405nm and 365nm. Then, the prepared solutions were used in printability tests on an extrusion-based bioprinter. Furthermore, NMR measurements of hydrogels in established time intervals were performed to determine the dependence of cross-linking degree on exposure time.

Results: Conducted reaserch revealed that the pre-crosslinking of low-percentage solutions of methacrylated biopolymers significantly impact on printability. The parameters used for initial cross-linking of the solutions resulted in only partial cross-linking of the material, which was shown by NMR tests. In printability tests, firm and homogeneous fibers were obtained, enabling the printing of high-resolution models.

Conclusions: Application of pre-crosslinked of low-percentage methacrylate solutions allows to improve their printability. The application of the presented method of preparing HAMA and ALGMA solutions gives new possibilities in using them for precise extrusion-based 3D printing.

O94

VALIDATION OF A MICROGEL-BASED IN VITRO 3D BONE MARROW MODEL FOR MULTIPLE MYELOMA

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Objectives: Multiple myeloma (MM) is a haematological malignancy involving monoclonal plasma cells within the bone marrow (BM). Interactions between MM cells and the BM niche significantly affect MM development and drug resistance. We aimed to develop a biomimetic 3D platform to study MM behaviour. We included commercial dextran microspheres (Cytodex 1) functionalised with extracellular matrix (ECM) biomolecules. As the cellular component of the BM niche, we co-cultured MM cells and human mesenchymal stem cells (hMSCs).

Methods: Layer-by-Layer (LbL) technique was used to functionalise microspheres with heparan and chondroitin sulphate, hyaluronic acid and collagen. The morphological and physicochemical properties of the coatings were assessed. Cell culture was carried out in suspension and lasted up to three days. We used three MM cell lines (RPMI8226, MM1S and U226) in co-culture with hMSCs, introduced in the model as an agglomerate of cells and non-functionalised microspheres. Cell cycle

distribution, apoptosis and proliferation assays were assessed to validate the culture platform and to study co-culture interactions.

Results: We confirmed the presence of the biomolecules on the microspheres' surface. Good cell proliferation was obtained in all the conditions and MM cell lines, RPMI8226 being the one with the highest cell growth. Apoptosis and cell cycle assays showed that culture conditions affect the viability and percentage of active cells in the RPMI8226 cell line. Regarding the U226 cell line, viability was barely affected; but the rate of active cells increased significantly.

Conclusions: Microsphere characterisation demonstrated the LbL technique is suitable for functionalising Cytodex 1 with biomolecules of the BM ECM. Our platform allows the growth of all three MM cell lines. Future research will address using this model as a study platform for selecting and evaluating new drugs against MM, which could improve response and personalised therapy for this disease.

O95
TOWARDS ARTIFICIAL BLOOD: RHEOLOGICAL CHARACTERIZATION OF HYDROGEL BEADS AS ARTIFICIAL ERYTHROCYTES FOR MULTIPHASE BLOOD FLOW MEASUREMENTS

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Objectives: Hemodynamic flow models needed for cardiovascular applications frequently rely on data obtained from Particle Image Velocimetry (PIV) experiments. A single-phase glycerin/water-substitute is commonly used to visualize a simplified blood flow. To overcome these limitations, a multiphase blood substitute for PIV measurements was introduced. Hydrogel particles (beads) from poly-sodiumarcylate-co-arcylamide P(SA-Am) were successfully fabricated in a biconcave shape. They are suspended in the glycerin/water-mixture which imitates blood plasma. To enhance bead detectability for PIV experiments, liposomes, containing the fluorescence dye uranin, are to be integrated into the beads as markers. The rheological behavior of beads with and without liposomes is characterized via rheometer.

Methods: Microfluidic systems (MFS) where used to produce biconcave beads. As the continuous phase olive oil was used. Liposomes were produced via thin film hydration and extrusion. The liposomes were dispersed into the hydrogel solution in concentrations from 0,5 to 10vol.%. Integration was confirmed via cryo-SEM. For the rheological experiments, the beads were dispersed into the glycerin/water solution in concentrations from 2-20vol.%, to investigate their flow behavior. A rheometer with a plate-plate-configuration is used to measure the dynamic viscosity. Therefore, shear rates between 5 and 20001/s were tested. To investigate the rheological influence of glycerin/water-solutions, different concentrations between 0,5 and 36 vol.% were tested.

Results: Biconcave P(SA-Am) beads with an average diameter of 250µm were produced. Successful integration of liposomes into the hydrogel beads could be confirmed for concentrations of 5vol.% and above. Rheometric experiments confirmed shear thinning behavior of the blood substitute fluid. The glycerol concentration influences the absolute viscosity of the artificial blood.

Conclusions: Liposomes were successfully integrated into the hydrogel beads. The artificial fluid exhibited blood-like flow behavior throughout the shear rate range investigated. By adjusting glycerol and bead concentrations the overall viscosity behavior can be precisely adjusted. The detectability of the artificial erythrocytes is currently tested via PIV.

O96
HUMAN DENTAL PULP STEM CELLS (HDPSCS) INCREASE VASCULARIZATION OF 3D-PCL SCAFFOLDS

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Objectives: 3D PCL scaffolds in combination with alginate had probed effectiveness for cartilage regeneration. PCL scaffold would serve as structural support, for example, for the regeneration of the airway. For those applications, the vascularization of the substitutes to be implanted determines their success or failure. Mesenchymal stem cells have probed their utility for the induction of vascularization of different scaffolds. Our objective is to incorporate hDPSCs into PCL-alginate scaffolds to improve their vascularity in vivo.

Methods: PCL scaffolds were prepared by a mixed particle leaching/freeze extraction process. The following experimental groups were considered: PCL (control group), PCL + alginate and PCL + alginate + hDPSCs. These constructs were implanted subcutaneously, on the back of nude mice. Three weeks after the implantation, a standard histopathological evaluation of the scaffolds was performed, and angiogenesis was assessed by CD31 immunohistochemistry detection. Vascularization was evaluated based on the total number of vessels detected in the scaffold and their size, considering large ($>$ 20 µm), medium (10-20 µm), and small ($<$ 10 µm) vessels.

Results: All the implanted scaffolds showed good biocompatibility. A perichondrium-like tissue surrounding the PCL discs was also observed. It was possible to observe the generation of a system of vessels of greater diameter on the periphery of the scaffolds and of smaller diameter within it. Likewise, it was possible to appreciate the partial degradation of the PCL trabeculae. The groups that contained mesenchymal cells showed better vascularization with an abundance of smaller caliber vessels than in the rest of the groups.

Conclusions: The use of hDPSCs could improve the vascularization of PCL-alginate scaffolds.

Scientific Program - Poster Session 1-2

Extracorporeal Life Support and Artificial Lung

P1
ASSESSMENT OF FLOW DISTRIBUTION IN HOLLOW FIBER AND 3D TPMS OXYGENATOR MEMBRANES USING TIME RESOLVED CONTRAST ENHANCED COMPUTED TOMOGRAPHY

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Objectives: Additively manufactured 3D-membrane structures based on triply periodic minimal surfaces (TPMS) are a novel approach for oxygenator design. In contrast to hollow fiber membrane oxygenators, TPMS structures allow for local variation of membrane geometry to homogenize flow distribution lowering the risk of thrombosis. In our study, we establish a new method for flow homogeneity assessment using contrast enhanced computed tomography (CT) and compare the perfusion of a commercial oxygenator and an anisotropic TPMS membrane.

Methods: A computational fluid dynamics model was set up to simulate flow inside oxygenators. Using this model, a TPMS membrane was modified iteratively homogenizing the flow inside the device. The TPMS oxygenator prototype was then manufactured using 3D-printing. Finally, flow distribution inside a commercial predicate and the TPMS prototype

were investigated by injecting a contrast agent (CA) bolus into continuous water flow through the devices whilst performing time resolved CT scans in a next generation photon counting scanner.

Results: The traversing of CA through the membrane structures can be clearly visualized in the imaging data. The commercial oxygenator shows a homogenous CA distribution with slightly decreased perfusion of the top corner. Inside the TPMS membrane, an increased perfusion of this top corner, where its flow resistance is the lowest, is observed.

Conclusions: Time resolved CT scans using CA bolus injection are an effective method to investigate the homogeneity of membrane perfusion. In our study, the numerical model underpredicted the effect of local variation inside the TPMS membrane which led to a top shifted perfusion in the final prototype. This is likely to be caused by geometrical inaccuracies of the 3D-printing process with corresponding exponential growth of flow resistances. However, the proposed effect of local TPMS geometry adjustments for a tailored overall device perfusion could be clearly demonstrated using our proposed method.

P2

DEVELOPMENT OF AN AGGRESSIVE THERAPY TO ADMINISTER DRUGS DIRECTLY INTO THE TRACHEA TO IMPROVE SURVIVAL AND ACHIEVE EARLY WEANING OF PATIENTS ON ECMO

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Objectives: With the increasing number of patients suffering from acute respiratory distress syndrome caused by new coronaviruses, the demand for extracorporeal membrane artificial lungs (ECMO) is increasing, and early weaning from ECMO and improving the life-saving rate is an urgent issue. We have drafted a new treatment modality that promotes early pulmonary recovery by administering drugs directly into the lungs through the trachea. The purpose of this study was to establish a large animal model that would allow us to evaluate an aggressive lung treatment method that administers drugs transairway under ECMO.

Methods: Adult goats fitted with VA-ECMO were injected intravenously with endotoxin to create a model of respiratory failure due to sepsis. Blood and lung tissue were sampled over time to measure inflammatory status. Only one lung was injected with the drug to check for differences in inflammation between the left and right lungs.

Results: Twelve animal studies have been conducted. After endotoxin administration, pulmonary hypertension due to vasoconstriction and a decrease in pulmonary blood flow and a marked decrease in blood oxygen saturation were induced. Histological evaluation showed plasma leakage from the peribronchial vessels after LPS administration, and findings of thickening of the alveolar walls around the vessels over time. Comparison of the left and right lungs showed a difference in the degree of inflammation, allowing evaluation of the effect of the therapeutic agent

Conclusions: We have succeeded in establishing a model of acute severe lung disease caused by endotoxin and in creating an animal model in which new therapies can be evaluated.

P3

ENDOXY IN FLAME: ENDOTHELIAL AND IMMUNE CELL INTERACTIONS DURING BIOHYBRID LUNG APPLICATION

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Objectives: Extracorporeal membrane oxygenation (ECMO) therapy faces challenges such as limited hemocompatibility and an increased inflammatory reaction. One promising solution to these challenges is endothelialization of the gas exchange membrane. This study aims to investigate interaction between endothelial cells (ECs) and immune cells for biohybrid lung application, which has been poorly investigated so far.

Methods: Human umbilical vein endothelial cells (HUVECs) were seeded on polydimethylsiloxane gas exchange membranes and cultured in a microfluidic system with wall shear stress of 20 dyn/cm2. After 24-hour pre-cultivation, peripheral blood mononuclear cells (PBMCs, 1.5 x 106 cells/mL) activated with lipopolysaccharides (LPS, 100 ng/mL) were added to the dynamic system for 24 hours. Cultures without LPS and/or PBMCs served as controls. Cell layer confluency was analyzed by immunohistochemical staining with CD31/PECAM-1 and von Willebrand factor. Flow cytometry analysis was performed on HUVECs to determine expression of vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1) and E-selectin. Leukocyte adhesion assay was conducted to determine the number of adhered PBMCs.

Results: Treatment with LPS-activated PBMCs caused a reduction of cell layer confluency and a change in HUVEC morphology towards a prolonged, aligned cell shape, as opposed to controls with non-activated PBMCs without LPS. Here, HUVECs showed typical cobblestone morphology. Flow cytometry analysis revealed significantly increased expression of VCAM-1, ICAM-1 and E-Selectin for HUVECs treated with LPS-activated PBMCs in contrast to controls. Increased adherence of PBMCs on HUVECs layer was observed after LPS-treatment.

Conclusions: In conclusion, the study provides valuable insights into the interaction between ECs and blood immune cells during inflammation, which is relevant for biohybrid lung application. The results raise the question whether gas exchange membrane endothelialization is a feasible way to overcome current challenges of ECMO systems. Further studies are necessary to investigate this interaction and develop strategies to optimize the effectiveness of endothelialization for biohybrid lung application.

P4

EVALUATION OF ARTERIAL AND VENOUS CANNULAE PERFORMANCE IN SIMULATED PULSATILE PEDIATRIC ECMO CIRCUIT

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Objectives: The use of extracorporeal membrane oxygenation (ECMO) support has doubled in the last decade. Differences in indication, settings, as well as implantation site, occur in ECMO when comparing pediatric patients to adults. To optimize the ECMO-support for this heterogeneous group of critically ill patients, each component of the circuit should be considered. Most studies are carried out with water, and although latest studies introduced blood as priming solution, no investigation has been performed for pulsatile flow conditions.

Methods: Four arterial cannulas (8Fr, 10Fr, 12Fr, 14Fr) and five venous cannulas (12Fr, 14Fr, 16Fr, 18Fr, 20Fr) (Medtronic DLP) are tested in twelve combinations (8A-12V, 8A-14V, 8A-16V, 10A-12V, 10A-14V, 10A-16V, 12A-14V, 12A-16V, 12A-18V, 12A-20V, 14A-18V, 14A-20V). The ECMO-setup consisted of an oxygenator (Hilite 800 LT), diagonal-pump (DP III), and ¼in standardized length arterial/venous tubing with cannula pressure transducers. A validated left-heart mock loop driven by a computer-controlled piston pump was used to simulate pediatric conditions. The circuit was

primed with blood mimicking fluid. The cardiac output was set to 3l/min, the mean aortic pressure to 40mmHg, and the heart rate to 120bpm. Limits of 200mmHg for pressure drop, -70mmHg for pressure loss, and 8500RPM for pump speed were set to resemble a clinical scenario.

Results: We found that larger arterial cannula yielded a lower pressure drop and provided higher hemodynamic energy, independent of the venous cannula size. Larger venous cannula reduced the afterload of the pump and allowed to reach an equivalent flow rate with a reduced RPM. Finally, the efficiency of the ECMO in supporting the circulatory system was reduced for increasing pump speed.

Conclusions: The major limiting factor of the ECMO circuit appears to be the pump. These results show that pulsatility plays an important role in the evaluation and optimization of a complex system such as the ECMO.

P5
HOW THE ASSEMBLY OF HOLLOW-FIBRE BUNDLES AFFECTS THE MICROSTRUCTURE OF AN ARTIFICIAL LUNG: A COMBINED STRUCTURAL AND FLUID DYNAMICS STUDY

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Objectives: In view of studying new design solutions for artificial lungs, computational fluid dynamics (CFD) simulations prove to have a relevant role in investigating the local fluid dynamics and the device performance. Although local phenomena are highly influenced by bundle microstructure, micro-scale models tend to neglect geometric and structural aspects such as compact fibre arrangement and fibre deformability. Indeed, during the device assembly, both press-fitting the bundle to avoid fluid dynamic shunts and having random staggered configuration between fibre layers could affect the fluid domain geometry and then the fluid dynamics. The aim of this work is to evaluate the impact of bundle press-fitting and fibre layer staggering on micro-scale fluid dynamics through a combination of structural and CFD simulations.

Methods: Experimental tests on commercial fibres were used to calibrate the fibre material model. Structural simulations of compression loading on a periodic cell at different degrees of press-fitting and staggering conditions were performed. Starting from the deformed fibre geometry, a CFD periodic cell was defined. CFD simulations on deformed and staggered geometries and on idealized geometries were carried out to assess the impact of these aspects.

Results: CFD analysis on idealized fibre cells proves to give a relevant overestimation of bundle permeability and underestimation of local shear stresses compared with equivalent analysis on deformed fibre cell. Differences grow as the degree of press-fitting increases, with permeability overestimated by about twice for 10% bundle compression. In contrast, fibre staggering result in no significant differences when high fibre density is involved.

Conclusions: Fibre bundle assembly, specifically with regard to press-fitting, seems to be a relevant aspect to considered for a correct estimation of fluid dynamics in terms of both permeability, of interest for macro-scale simulations with porous approach, and local quantities, of interest for estimating gas transport and flow-induced blood trauma.

P6
INCREASING OXYGENATION USING MICROSPHERES - A CONCEPTUAL STUDY

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Objectives: This study aims to evaluate the effect of microspheres on blood oxygenation.

Methods: For this small in vitro study, scaled-down prototypes consisting of a glass tube and 5 capillary membranes were constructed. The space between the membranes was filled with silicate microspheres of 0.2 - 0.25 mm diameter. Additionally, unfilled prototypes were constructed for comparison. In parallel tests, blood was pumped through both prototypes while oxygen flowed through the membranes. After one pass, the oxygen content of the blood was measured by blood gas analysis.

Results: In the setup with the Sphere-filled prototype, blood oxygen levels increased significantly more (median: 39.4%, 0.25 percentile: 28.7%, 0.75 percentile: 80.9%) than in the setup with the unfilled prototype (22.6%, 18.8%, 31.1%), while oxygen levels were generally low, ranging from 40 to 70 mmHG.

Conclusions: It was shown that microspheres can be used to increase the oxygenation rate in the used setup . Whether the results can be transferred to full-size oxygenators needs to be investigated. In addition, the effect of the microsphere surface on blood damage is of great interest and is part of ongoing experiments.

P7-FT
OPTIMIZATION OF A SINGLE-LUNG TRANSPLANTATION MODEL ON A RAT MODEL

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Objectives: To develop a method of orthotopic single-lung transplantation in an experiment on a rat model.

Methods: In our study, we used Wistar rats. As a preservative, we used a solution of Celsior in a volume of 15 ml. The lung removal procedure was performed under inhalation anesthesia of 3.5% Isoflurane. After tracheal intubation by direct laryngoscopy, we underwent median sternotomy, the wound edges were separated by a retractor. We injected 500 IU of heparin solution into the cavity of the right ventricle and cannulated the pulmonary artery with an 18-gram catheter. We isolated the anatomical structures of the left lung to prepare for the application of cuffs for subsequent anastomosis. Lung transplantation: access was performed through a left-sided anterolateral thoracotomy in the 4th-5th intercostal space. The elements of the root of the left lung were separated in a blunt and sharp way. After that, an angular vascular clamp was applied with simultaneous clamping of all elements of the lung root. After applying the clamp, the lung was cut off in the pleural cavity.

Results: The rat survival before the end of the experiment was 80%, 2 rats died on the first day after transplantation due to massive hemothorax. The Pa02/FiO2 index at selective sampling was 437 $\pm$ 25 mm Hg. Morphological examination of lung samples showed intact architectonics of the lung parenchyma in all cases. Microatelectatic zones were distributed heterogeneously and occurred on separate segment.

Conclusions: The developed model of orthotopic transplantation is simple to perform, cuffs using excluded surgical complications associated with the imposition of an anastomosis in the classical way. The proposed technique for performing transplantation on a rat model has shown its effectiveness and reliability.

P8-FT
PEDIATRIC LUNG TRANSPLANTATION ON EXTRACORPOREAL MEMBRANE OXYGENATION SUPPORT WITH PERIPHERAL CANNULATION: A SINGLE CENTER EXPERIENCE

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Objectives: No specific recommendations about mechanical circulatory support in pediatric lung transplantation (LT) exist. Data from small series suggest that the benefits of extracorporeal membrane oxygenation (ECMO) in adults may also apply to the pediatric setting. At our institution, the use of mechanical circulatory support is selective, and ECMO with peripheral cannulation has become the preferred strategy. We reviewed our experience, focusing on the feasibility and safety of this approach.

Methods: A single center series of pediatric LT performed on ECMO support with peripheral cannulation was retrospectively analyzed.

Results: Between 2012 and 2023, 9 LT, including 1 early retransplantation, were performed using ECMO with peripheral cannulation. 7/9 LT were bilateral, sequential; 2/9 LT were monolateral, including 1 living donor LT. 5/9 grafts were lobar. The median (range) recipients' age and weight were: 11 (6-15) years, 27 (20-37) Kg. Intraoperative ECMO was: veno-arterial in 5/9 cases, including 2 cases of preoperative bridging with veno-venous ECMO; veno-arterial-venous in 3/9 cases; veno-venous in 1/9 case with preoperative veno-venous ECMO. Arterial cannulation was: surgical in 5/8 cases, percutaneous in 3/8 cases. ECMO was maintained after LT, and the median (IQR) duration of intra- plus postoperative ECMO was 25 (16-51) hours. Three arterial thromboses occurred as a complication of percutaneous cannulation: 2 were successfully treated, 1 had long-term sequelae. The rates of bleeding, requiring reoperation, and acute kidney injury, necessitating renal replacement therapy, were 22%. In-hospital mortality was 12.5%: 1 patient, bridged to LT and retransplantation with veno-venous ECMO, died of multiorgan failure. 6/8 patients are alive, with a median (IQR) follow-up of 38 (10-55) months.

Conclusions: Our experience suggests that ECMO with peripheral cannulation is feasible also in the pediatric setting, and may be convenient for ECMO maintenance after LT. Surgical cannulation seems safer than peripheral cannulation.

P9-FT
POLYURETHANE BLEND MEMBRANES FOR BLOOD OXYGENATION

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Objectives: Extracorporeal Membrane Oxygenation (ECMO) is essential in critical care for the management of severe respiratory and cardiac failure. Responsible for maintaining O2 and CO2 levels in the blood, the membrane blood oxygenator (BO) is considered the most important part of the ECMO circuit. Despite the considerable progress during the last decades, efficient BOs for prolonged ECMO do not exist, contributing to the higher rates of thrombosis seen in patients supported by ECMO. To improve the O2 permeability our research group have been focused on the development of new blend polyurethane-based (PUR) membranes, using polyether and polyester-based segmented PURs, which exhibit enhanced hemocompatibility, in association with a good flex-life and mechanical strength.

Methods: In this work, two groups of dense symmetric membranes were prepared by the solvent evaporation technique: pure polyurethane (PU) membranes and polyurethane blend membranes using different total polymer/solvent and polyurethane/second reagent weight ratios. The mechanical properties of the membranes were studied through tensile tests. Single gas, O2 and CO2 permeation studies were carried out by the constant volume method at 37°C in an in-house built experimental set-up.

Results: The permeability coefficients obtained from the permeation curves ranged from 239 to 347 Barrer for CO2 and 26 to 30 Barrer for O2. The ranges obtained for the diffusion coefficients by the time-lag method were between 1.4 and 3.0 x 10-6 cm2/s for CO2 and between 2.0 and 2.5x10-6 cm2/s for O2. The solubility coefficients varied between 116 and 186 x 10-4 cm3/cm3.cmHg for CO2, and between 11 and 13 x 10-4 cm3/cm3.cmHg for O2.

Conclusions: Our data suggests that the introduction of a second component affected not only the mechanical properties by increasing the molecular mobility, thus reducing stiffness but also, that the higher degree of mixing between hard and soft segments leads to higher CO2 and O2 permeation rates.

Blood Damage in Artificial Organs

P10
A METHOD OF PREVENTING BLOOD VOLUME DECREASE DUE TO HIGH GAS FLOW RATE DURING ECMO HEMOCOMPATIBILITY EVALUATION

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Objectives: During ECMO development, the blood cell damage shall be evaluated by its claimed maximum blood flow rate and maximum gas flow rate according to ISO 7199. However, the required high gas flow would induce reduced blood loop volume during the tests. This study aims to optimize the test method while minimizing blood volume change due to the high sweep gas flow rate.

Methods: The head-to-head comparison was conducted with 3 sets of loops. All blood loops were kept with the same blood volume (700ml per loop), same operating condition, and same blood condition (meet ISO 7199 standard). The difference between the three sets of loops is in the gas condition. Pure gas was applied to the first gas line. For the second loop, we added a pure water-filled gas washing bottle into the gas line, so that the gas will be moistened. In the third gas line, we kept the gas washing bottle at the same temperature as the blood. The study was performed for 3hrs. We merged the blood bag into a big beaker filled with water, marked and maintained the water height. Then the volume of the added water is the blood loss volume.

Results: The blood volume was reduced by 50ml/h, 30ml/h, and 0ml/h for the pure gas loop, moistened gas loop, and warm moistened gas loop respectively. Volume change of blood may due to the humidity and temperature difference between the gas and blood, which may cause the water exchange through the membrane. The influence of humid gas on hemocompatibility results should be further evaluated with quantified gas humidity.

Conclusions: The experiments indicated that the humidity and temperature of the sweep gas will influence blood volume change during ECMO hemolysis tests. If possible, applying warm humid sweep gas during ECMO clinical use might help maintain the patient's fluid balance.

P11
ASSESSING LAGRANGIAN HEMOLYSIS MODELS: APPLICATION TO FDA NOZZLE BENCHMARK

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Objectives: Nowadays, the hemolytic behavior of cardiovascular devices is assessed through in vitro procedures. Nevertheless, numerical models

for mechanical hemolysis estimation are being developed using computational fluid dynamics (CFD) to reduce experimental tests and related costs, improving design and optimization processes. In this study, five approaches for hemolysis prediction were tested starting from a CFD model of the Food and Drug Administration (FDA) Nozzle benchmark and assessed employing the experimental data available in literature.

Methods: The FDA Nozzle hemodynamic was assessed with ANSYS Fluent and employing two configurations: Sudden Expansion (SE) and Conical Diffuser (CD). The predictions of mechanical hemolysis were determined implementing five Lagrangian stress-based approaches and an equivalent shear stress formulation available in literature. Four sets of constants for the power law equation were taken from previous studies and tested.

Results: The experimental data for the SE configuration present high variability therefore, even if the computational results fall within the standard deviation range, they do not allow the accuracy assessment of the numerical models considered. On the contrary, the comparison of hemolysis predictions for the CD configurations shows that the use of Giersiepen and Ding's constants typically overestimate hemolysis while two of the Lagrangian models substantially deviate from in vitro findings. The best outcomes were obtained with the hemolysis models that incorporate damage history, especially if combined with Heuser's constants.

Conclusions: The accuracy of hemolysis prediction is influenced by both the Lagrangian approach and the set of constants implemented. The hemodynamic of the sudden diameter change of the FDA Nozzle is complex to simulate and affects the precision of calculated shear stresses and thus the hemolysis estimations. Both models of hemolysis incorporating the damage history had high correlation coefficients, despite showing discrepancies with respect to the experiments. This high correlation indicates their adequacy for design optimization by relative comparisons of hemolysis risk.

P12-FT

COMPARING WETTABILITY PROPERTIES OF MICROSCALE SURFACE PATTERN MODIFICATIONS OBTAINED VIA 2-PHOTON-POLYMERIZATION

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Objectives: Blood-contacting medical devices are widely used; however, they can cause hemocompatibility-related issues. Surface wettability modifications might positively impact the hemocompatibility profile of these devices. The aim of this work is comparing wettability properties of different surface patterns obtained by means of two-photon polymerization.

Methods: Microscale-roughness promotes hydrophobicity through the so-called "Cassie-Baxter state". 3 patterns (cones, spheres, riblets) in 4 microscale dimensions (nominal 2-3µm, small 6-9µm, medium 12-18µm, large 24-36µm) were designed respecting geometrical constrains needed to maintain the Cassie–Baxter state. Micro-structured surfaces were manufactured by UpBrix-resin via two-photon polymerization 3D-printer (NanoOne, UpNano GmbH, Austria) with a 40x objective. Wettability was evaluated with water contact-angle measurement using a goniometer (DSA25, Krüss GmbH, Germany).

Results: A comparative analysis was conducted between micro-structured and flat surfaces, and different dimensions within each microstructure type (Welch's ANOVA). Following results were obtained as average of 5 measurements per sample. Flat surface: 74°± 4, (N=3); cones: nominal 108°±12 (N=2), small 108°±8 (N=3), medium 127°±8 (N=3) and large 125°±7 (N=3); spheres: nominal 90°±9 (N=1), small 110°±7 (N=2), medium 111°±8 (N=2), and large 123°±0.6 (N=1); riblets: nominal 106°±10 (N=2) , small 121°±5 (N=2), medium 122°±5 (N=3), and large 134°±17 (N=3). All micro-structured surfaces showed a contact-angle significantly higher compared to flat surface ($p < 0.01$). Also, a significant increasing of contact-angle was observed for medium and large cones vs. nominal and small cones, for large and medium riblets vs. nominal riblets, and for large spheres vs. all other spheres dimensions ($p<0.01$).

Conclusions: The proposed micro-structures show high efficiency in promoting hydrophobicity with respect a non-textured surface. Larger micro-structures improve surfaces water-repellency which could turn in a blood-repellent behaviour. However, shape and dimension of microstructures can affect the platelet-adhesion which is a focus on ongoing investigations. Furthermore, super-hydrophobicity would be even better, for which surface-topography must be combined with suitable coating currently under investigation.

P13

DYNAMIC IN VITRO CALCIFICATION OF BOVINE PERICARDIUM PATCHES

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Objectives: Calcification is a major issue affecting the durability of biological heart valve prostheses. It refers to the formation of mineral deposits containing calcium phosphate on the surface (extrinsic) and inside (intrinsic) of the prostheses. Dynamic in vitro methods are crucial for a time- and cost-saving analysis of the calcification process. Therefore, we developed a compressed air-based method for the dynamic in vitro calcification of bovine pericardium patches. Furthermore, hyperspectral imaging was evaluated as a technology to visualize calcified areas.

Methods: Three glutaraldehyde crosslinked bovine pericardium patches were calcified in vitro under dynamic conditions. Patches were dynamically loaded using compressed air at a frequency of 1 1/s for nine weeks. The calcification solution was weekly replaced. The composition of crystalline phases was investigated by Raman spectroscopy. Hyperspectral imaging in the near infrared light region (NIR) and short wavelength infrared light region (SWIR) was performed to visualize deposits of calcium phosphate. Calcium content of the patches was measured using ethylenediaminetetraacetic acid titration.

Results: White crystalline phases could be observed on all patches after nine weeks of in vitro calcification. Crystalline phases exhibited peaks at wavenumbers of 959 1/cm to 962 1/cm in Raman spectroscopy, indicating the presence of hydroxyapatite. Those peaks could not be found in apparently non-calcified areas. Both extrinsic and intrinsic calcified areas of the patches could be detected and localized through SWIR hyperspectral imaging. Calcium content of the patches was 5,41 mg ± 1,89 mg according to titration.

Conclusions: The test bench developed was able to successfully reproduce the process of calcification in vitro, even by using relatively low loading frequencies of 1 1/s. Our findings indicate that SWIR hyperspectral imaging is a promising approach for two-dimensional mapping of extrinsic and intrinsic calcified areas in biological heart valve prostheses or patches. Future work will address surface modification of patches to prevent calcification.

P14

IMPACT OF CONNECTOR DESIGN ON IN VITRO HEMOLYSIS TESTING USING THE BPX-80® CONTINUOUS-FLOW PUMP

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Objectives: The ASTM F1841 standard for evaluating hemolysis induced by blood pumps does not specify the technicalities of the test rig components used for testing. Connectors used to attach pumps to test rigs must be designed efficiently to evaluate device impact on blood to obtain its true performance. The clinically used centrifugal flow BPX-80 Bio-Pump® Plus (Medtronic) was chosen for this study due to its low hemolysis rates, extensive clinical use and ease of access to cost-efficient disposable pump heads.

Therefore, the aim of this study was to evaluate the impact of connector design on human blood using the BPX-80® in the Aachen test rig.

Methods: In vitro hemolysis testing was performed using the Aachen test rig for the systemic circulation according to the ASTM standards, F1830–97 and F1841–97 (2017). Two different connectors, DM410 (PA12, 3D-printed) and AB6260 (PVC, milled), were tested with pooled, cross-matched human whole blood anticoagulated with citrate phosphate dextrose diluted to a hematocrit of 30 ± 2%. Plasma-free hemoglobin (pfHb) was measured using the Harboe spectrophotometric assay.

Results: The mean flow, pressure head and temperature (n=3) for DM410 tests were 4.91 ± 0.08 L/min, 100.74 ± 0.98 mmHg and 36.39 ± 1.65 °C respectively, while for AB6260 tests were 4.94 ± 0.08 L/min, 99.17 ± 1.1 mmHg and 36.11 ± 0.68 °C respectively. DM410 tests showed an increased mean pfHb over time compared to AB6260 tests. The average mgNIH and MIH for DM410 tests were 11.02 ± 0.38 mg/dL and 0.99 ± 0.16, while for AB6260 tests they were 3.63 ± 0.93 and 0.33 ± 0.09, respectively.

Conclusions: Connector design has a clear impact on hemolysis results and should ideally be standardised in full measure. Relevant topics for future studies include broadening the analysis to additional parameters such as platelet characterization and viability of other blood components.

P15-FT
IMPACT OF OPERATING CONDITIONS ON HEMOCOMPATIBILITY-RELATED ADVERSE EVENTS IN HEARTMATE 3 LEFT VENTRICULAR ASSIST DEVICE RECIPIENTS

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Objectives: Despite considerably improved clinical outcomes with the HeartMate3, hemocompatibility-related adverse events (HRAEs) remain an interdisciplinary challenge. Previous in-silico and in-vitro studies suggested an association between blood trauma and pump operation, with compromised hemocompatibility towards lower flows and higher pump speeds. To assess the clinical relevance of these findings, we aimed to investigate the interrelation of operating conditions and HRAEs in patients supported with the HeartMate3.

Methods: This retrospective single-center study included 149 consecutive recipients of the HeartMate3 implanted at University Hospital Vienna between 2014 and 2022. Endpoints involved one-year survival and HRAE incidence, including stroke, gastrointestinal bleeding (GIB) and pump thrombosis (PT). Pump flow (Q) and speed (ω) were collected for each patient, and pressure head (ΔP) was computed using a mathematical model of HeartMate3 and its graft. Two groups were defined according to Q and ΔP [A= Q⩾4.4, ΔP⩽75mmHg, n=67; B= Q<4.4, ΔP>75mmHg, n=82]. Group differences were analyzed using chi-squared-, t-test and Kaplan-Meier analysis.

Results: The one-year survival rate was 80.5% with significant differences amongst the groups (A=88.0% vs. B=74.3%; p=0.036). HRAEs were observed in 31.5% of the patients, including 26.8% in group A and 35.5% in group B (p=0.267). The stroke incidence was significantly higher in group B (A=11.9% vs. B=30.4%; p=0.007), with emphasis on ischemic (p=0.016) compared to hemorrhagic strokes (p=0.075). Moreover, lactate dehydrogenase (LDH) was significantly higher in group B (p=0.021). No significant differences were observed concerning GIBs (p=0.627) and PTs (p=0.445). However, GIBs occurred more frequently in patients with pulsatility indices (PI) ⩾ 2.5 (p=0.015).

Conclusions: These clinical results indicate significant effects of hydraulic pump characteristics at different operating conditions on clinical outcome. High pressure head and low flow operation may be associated with increased mortality rates and stroke incidences. Further research is needed to delineate the observed effect of PI on GIB.

P16
MULTISPECIES, MULTISCALE MODELLING OF THROMBOSIS POTENTIAL IN BLOOD CONTACTING MEDICAL DEVICES

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Objectives: As a result of interactions between blood, non-physiological material surfaces and flow structures, implanted medical devices, are prone to thrombosis: the formation of blood clots. These can be either in the bulk flow, or on material surfaces in which case they may detach, causing a stroke or pulmonary embolism. The interactions between the various clotting species are complicated and a computational model could assist with understanding the impact of this interplay on clotting potential and subsequently be used in device design. The aim here was to create a numerical model based on the hypothesis for a prothrombotic state by Bartoli et al [1] that incorporates the effects of shear stress on erythrocytes and von Willebrand factor (vWf).

Methods: Computational fluid dynamics (CFD, Ansys Fluent) with a series of convection-diffusion-reaction equations incorporated using user-defined functions was used to model the interactions between: platelets, activated platelets, platelet agonists, plasma free haemoglobin, inactive vWf, shear stress, haemostatically active vWf, enzymatic cleavage by ADAMTS13 and vWf fragments. Results for platelet adhesion were compared with experimental results from literature [2]. Separately OpenFOAM with the RheoTool extension was used to model Brownian motion of vWf molecules under fluid shear stress. Total extension length was compared with experimental measurements from literature.

Results: There was some spatial correlation between normalized platelet density simulated using the convection-diffusion-reaction equations and with experimental values, with the peaks being in similar locations. The molecule extension length from the Brownian motion model increased with increasing fluid shear, in agreement with experiment, however the magnitude of the extension differed.

Conclusions: The two models embody novel ideas for computing thrombosis in medical devices and have promising preliminary results. Future work will require tuning the models individually before combining them into one multiscale approach.

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P17-FT
OPTICAL ANALYSIS OF GHOST CELLS UNDER MECHANICAL HEMOLYSIS USING FLUORESCENCE HEMOLYSIS DETECTION

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Objectives: The amount of hemolysis in circulatory support systems is measured as free plasma hemoglobin with standardized tests; the position of hemolysis is estimated with numerical models. A method to combine the two approaches and measure the position of hemolysis is missing. Therefore, we developed the 'fluorescent hemolysis detection'. An optical measurement, where hemolysis in a two-phase blood model fluid results in a fluorescent signal. The measurement is proven feasible for chemical hemolysis but yet not transferred to lower amounts of mechanical hemolysis. Therefore, we are working on an experimental setup for the fluorescent hemolysis detection where mechanical hemolysis can be applied while an optical measurement is possible.

Methods: The two-phase blood model fluid consists of hemoglobin-depleted erythrocytes (Ghost Cells) loaded with calcium diluted in a sodium chloride solution with a calcium-indicator (Cal590 potassium salt, AAT Bioquest). Upon destruction of the Ghost Cells, the indicator binds to the calcium and its fluorescence increases. We introduced mechanical hemolysis with up to 1000 ultrasonic shockwaves to Ghost Cells and whole blood. For both, the free plasma hemoglobin is measured, additionally for the Ghost Cells the extracellular calcium and the fluorescence are measured.

Results: The free plasma hemoglobin rises for the Ghost Cells and whole blood with increasing repetitions of shockwaves. For the Ghost Cells, the extracellular calcium stays constant while the fluorescence increases up to 500 shockwaves.

Conclusions: The amount of hemolysis can be measured as free plasma hemoglobin in whole blood as well as in Ghost Cells. Free plasma hemoglobin values of Ghost Cells are lower than whole blood because they are hemoglobin-depleted. Extracellular calcium cannot be used as a Ghost Cell equivalent to free plasma hemoglobin because no elevation could be measured. However, it has to be determined if the increasing fluorescence is enough to optically measure the position of hemolysis in single shockwaves.

P18

INVESTIGATION OF PLATELET DEPOSITION ON TITANIUM WITH DIFFERENT HARD MATERIAL COATINGS AND ROUGHNESS VALUES IN A FLOW CHAMBER

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Objectives: The formation of thrombi is still a challenge in ventricular assist devices (VADs). This can be caused by the subsequent deposition of proteins and platelets on foreign surfaces. In VADs, the blood contacting components are mainly made of titanium alloys. This study aims to investigate the potential for platelet deposition of (1) five different hard material coatings on titanium, which are used to prevent surface scratches and (2) titanium with four different degrees of roughness to determine the influence of the degree of polishing.

Methods: An in-vitro test bench was developed to optically investigate the deposition of fluorescent labelled platelets on the protein layer of different surfaces. Samples included (1) coatings: Titanium Nitride, Titanium Niobium Nitride, two types of Diamond-Like Carbon and Wolfram Carbid and (2) titanium with Ra values between 0,122µm and 0,021µm. Human whole blood was incubated with Mepacrine (fluorescent dye) and then pumped with a defined shear rate condition through a flow chamber over the samples. The adhered platelets were visualized via inverted fluorescence microscopy. The analyzation of the green values and the binary image of the generated fluorescent picture offers conclusions about the platelet accumulation and the percentage of the covered surface area, respectively.

Results: Statistical analysis only showed significant lower potential for platelet deposition for Titanium Nitride compared to titanium without any coating. Furthermore, all rougher surfaces showed significant higher potential for platelet deposition compared to the most polished surface (Ra=0.021µm).

Conclusions: It can be concluded that none of these coatings have a higher potential for platelet deposition than uncoated titanium, pointing towards suitability for blood contacting components. Moreover, high efforts for polishing titanium surfaces are shown to be of high importance in terms of platelet deposition.

Ventricular Assist Devices

P19

DEVELOPMENT OF A PEDIATRIC CENTRIFUGAL BLOOD PUMP: THEORETICAL AND EXPERIMENTAL RESULTS

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Objectives: It is largely recognized that mechanical circulatory support devices may improve hemodynamic conditions in heart failure patients. The development of VADs to treat heart failure in children and infants faces several challenges. This work presents the design and tests of a pediatric rotary pump for temporary circulatory support of children with a target flow range of 1,5 - 3,0 L/min.

Methods: A centrifugal blood pump was designed considering $<$ 15 mL priming volume, outer diameter of 30 mm and 12 mm inflow and outflow ports. A topology optimization formulation was developed for this application considering pressure, vorticity and energy dissipation profiles. A set of pump prototypes with impeller blades and volute geometries defined by the method of topology optimization were compared by computational analysis to pumps with blades and volute defined using traditional design concepts. The impellers and volutes with the best simulated results and those obtained by traditional design were 3D printed and used to assemble centrifugal pumps with ceramic bearings. Pump operation was provided by an external motor magnetically coupled to the impeller in a radial configuration. Hydrodynamic performance of prototypes based on both designs were compared using a computer controlled hydraulic mock loop of the pediatric circulation.

Results: Hydrodynamic performance tests using blood analog solution showed that centrifugal pumps designed by both methods generate flows within the target range under 100 mmHg afterload at speeds varying from 3000 to 5000 rpm. Computational results comparing both designs showed better performance of the optimized pumps. At 2,0 L/min water mass flow pumps generated similar pressure (85 vs 90 Pa) with smaller vorticity (280 vs 400 m3/s2) and energy dissipation (0,25 vs 0,35 W) in optimized and traditionally designed pumps, respectively.

Conclusions: The results obtained suggest that the performance of the pumps designed are compatible with the hemodynamic necessities of pediatric patients.

P20

BRUSHLESS SPEED CONTROL FOR A NOVEL BRAZILIAN AXIAL VENTRICULAR ASSIST DEVICE

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Objectives: The reduction in size of these systems, which increases their reliability, biocompatibility and robustness, is essential to the complete implantation of the VADs, which is the main focus of the current state of art. Continuous flow VADs are actuated by brushless motors due to their reliability. The objective of the current project was to implement and simulate sensorless speed control in order to actuate VAD.

Methods: In order to increase the robustness of the system even further, a strategy that does not use Hall sensors can be implemented. The sensorless strategy to control speed that was implemented in this work aims to detect the position of the rotor by using the coil of the inactive phase in order to sense the variation in magnetic flux, which comes in the form of back-electromotive forces.

Results: A three phase inverter to electrically commute the motor's phases, a conditioning circuit that obtains the back-electromotive forces and a speed controller were developed. The speed control and the commutation logic were implemented by using a microcontroller. The results that were obtained in computational simulations indicated that the three-phase inverter, the commutation logic and the controller reached the project requirements. The implemented microcontroller commutation logic presented the expected behavior. Commutation signals were obtained in six stages, necessary for the correct activation of the phases of the brushless motor. The controller was validated in terms of its step response, demonstrating low overshoot and fast control action in the system.

Conclusions: To further enhance the robustness of the system, an alternative strategy that eliminates the use of Hall sensors can be employed. The sensorless speed control strategy, implemented in this study, detects the position of the rotor by measuring variations in magnetic flux through the coil of the inactive phase, thus relying on back-electromotive forces for detection.

P21

CENTRIFUGAL PUMP DEVELOPMENT FOR ECMO SYSTEM.S

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Objectives: Development the extracorporeal centrifugal pump, which use as a consumable component in the method of ECMO.

Methods: The main components of a centrifugal pump are: a compact housing, rotor with an optimized impeller, an articulated suspension and a magnetic suspension system. The main advantage of the product is the advanced pump vane system, which allows increasing the flow rate and reducing the impeller speed parameters. Thus, the product design solves the main problem - minimizing the traumatic effect of the patient's blood.

Results: The limiting shear stresses were 112 Pa at 4000 rpm, with the maximum allowable values of 150 Pa, while the normalized hemolysis index was at the minimum allowable values. The product is integrated into the ECMO , providing controlled oxygenation under schemes conditions: "veno-venous" and "arterio-venous". The product is controlled by an extracorporeal autonomous and semi-autonomous unit. The average rate of blood cells damage by the pump, controlled by the amount of free hemoglobin in blood plasma (PHb), does not exceed 50 mg% when the system is operated for 6 hours (in vitro) under blood flow rate of 3 l/min and back up outlet pump pressure from 100 to 300 mmHg. Working parts of the pump in contact with blood are made of a biocompatible material, which ensures that there are no wall clots in the pump. The pump has a minimum filling volume (60 ml) and is easy to install and operate. The product is designed for maximum hydraulic efficiency for ECMO mode and will provide the stable blood circulation characteristics required for the functioning of the oxygenator.

Conclusions: Centrifugal pump implementation will provide consumables for the intensive cardio resuscitation and perfusion department, providing the possibility of therapy for patients with pathologies of the cardiovascular system and associated complications in the form of low oxygen content in the blood.

P22

DESIGN AND DEVELOPMENT OF AN IMPLANTABLE INTRA-VENTRICULAR BALLOON PUMP

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Objectives: Mortality remains unacceptably high amongst severe heart failure patients. A major contributing factor is the high cost of mechanical circulatory support devices, therefore the development of lower-cost alternatives will improve access to treatment for patients in lower socio-economic status. The present research project aimed to develop a low-cost Intra-Ventricular Balloon Pump (IVBP).

Methods: The IVBP was designed for implantation through the left ventricle apex, off-bypass, for conduction of in vivo animal studies into device feasibility. An ovine cohort-specific IVBP was designed, using computed tomography data, to avoid impinging upon the mitral valve structures. Three left ventricle models were analysed to identify the volume available for the balloon to safely operate within. Balloon manufacture comprised a mixture of polyurethanes poured over a latex balloon mould, which upon cure, was collapsed to release the polyurethane balloon. A cannula was inserted into the polyurethane balloon and fixed using an adhesive, with a catheter line attached to allow inflation to occur. The balloon was inflated using an Intra-Aortic Balloon Pump console, with a delayed ECG signal input to ensure inflation during systole. The balloon was then placed inside of an introducer sheath to allow for implantation.

Results: IVBPs were successfully manufactured and tested to ensure 24 hours of support with no rupture to the membrane. Balloons could collapse to fit inside the sheath and were easily deployable. ECG input could be delayed so that inflation could occur at any portion of the cardiac cycle . The inflation volume could also be independently controlled for synchronisation of the inflation timing and systole, prior to full support.

Conclusions: The IVBPs achieved each of the desired goals for ease of implantability, control of the inflation timing, and reliability of the device. The authors are confident that this device is able to proceed to conduction of live ovine model studies.

P23

DEVELOPMENT AND VALIDATION OF A MOCK CIRCULATORY LOOP WITH BAROREFLEX RESPONSE

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Objectives: The baroreflex response maintains homeostasis in the cardiovascular system (CVS) by regulating blood pressure through changes in heart period, contractility and peripheral resistance. The incorporation of the baroreflex response into a mock circulatory loop (MCL) is crucial for the evaluation of cardiac assist device (CAD) performance.

However, the literature lacks studies on the implementation and validation of this mechanism. Therefore, this study aimed to develop and validate a MCL with baroreflex response against dog data.

Methods: The MCL comprised of a left ventricle simulator, compliance chamber, automated vascular resistance, reservoir, and baroreflex response regulating heart period and vascular resistance. To assess the dynamic performance of the baroreceptor response, an arterial occlusion was simulated using a Hoffman clamp between the compliance chamber and the resistor. Data were collected before and during the occlusion of the tube. The mean pressure, flow, and heartbeat period of five consecutive heartbeats were compared for normal and clamped conditions against arterial occlusion data of a dog.

Results: Under normal conditions, the MCL mean pressure, flow, and heart period were 38mmHg, 2.8L/min, and 0.65s, respectively, while the corresponding in vivo dog data were 41mmHg, 1.8L/min, and 0.65s. Under clamping condition, the MCL values changed to 100mmHg, 0L/min, and 0.84s, respectively, while the corresponding dog data changed to 76mmHg, 1.2L/min, and 0.60s. Between the normal condition mock and dog, the mean pressure, flow, and heart period showed a difference of -9%, 59%, and 15%, respectively. For the clamped condition, there was a difference of 31%, -103%, and 39%, respectively.

Conclusions: In conclusion, the MCL simulated the baroreflex response during the clamping of the tube. However, significant differences in flow were observed, which may result from the simplified lumped representation of the complex CVS. Further studies should be conducted to improve the accuracy of the MCL.

P24

DEVELOPMENT OF A GENERIC AND COMMERCIALLY TRANSLATABLE MOTOR CONTROLLER AND DRIVER FOR MECHANICAL CIRCULATORY SUPPORT DEVICES: BENCHTOP TO BEDSIDE

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Objectives: Mechanical Circulatory Support (MCS) device development often starts with an emphasis on pump design. Electronics and software are often developed quickly to provide core functionality only. These prototype pumps generally do not consider the selection of safety-critical microcontrollers, long-term manufacturer chip support, system redundancy options and the management of software risks. The project aimed to develop a generic commercially translatable motor controller and driver platform for MCS devices that de-risks commercial development.

Methods: Voice of Customer research was conducted on industry personnel in the US and EU to identify the need for a generic motor controller and driver platform. The market insights generated and prioritised a matrix of features and use cases to be included in the platform. Hazards analysis of other MCS motor controllers and drivers guided the system architecture. The generic motor controller and driver platform, LUDO, was offered to MCS developers.

Results: Based on market insights, the generic platform features included six independent half-bridge outputs capable of driving two brushless direct current motors up to 90 W. Depending on pump requirements, I2C, SPI, GPIO, ADC and UART connections were made available. Online configuration and data display suitable for engineers to clinicians were implemented by a Windows-based framework. The architecture allows motor control algorithms to be implemented via Simulink Code Generation. A Texas Instrument RMS57L843 and a Field Programmable Gate Array were included to facilitate Class C software implementation following IEC 62304. Developers utilising LUDO have successfully customised and reduced the motor controller and driver form factor to fit within their unique product vision in the implantable and external assemblies.

Conclusions: The study has developed a generic and commercially translatable motor controller and driver for safety-critical applications. The developed LUDO platform could improve the efficiency in taking novel MCS ideas to commercial realisation.

P25

DEVELOPMENT OF AN IMPEDANCE BASED NON-INVASIVE AND PULSATILE RVAD

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Objectives: This study explores the feasibility of using an impedance pump as a right ventricle assist device, which is non-invasive, pulsatile, valveless and potentially suits single ventricular defect patients undergone total carvopulmonary connection (TCPC) procedures.

Methods: A laboratory experimental set-up was built to test parameters in physiological range, in particular, flow rates in a variety of adverse pressure head changes, pumping mechanism frequencies, and varying tube diameters and lengths and material properties. The pumping mechanism was realised by a programmable solenoid. Accurate measurements were achieved by a Millar PCU-2000 Dual Channel Pressure Control Unit with a Mikro-tip catheter transducer for pressure, and Transonic Systems T206 Dual Channel Small Animal Blood Flow Meter with Transonic Flow Probes for flow rate.

Results: Significant results were obtained, e.g. valveless unidirectional pulsatile pumping against adverse pressure gradient. Some of the results validated previous research papers, while others provided new significant potentials that could be essential for the development of the impedance pump for future uses in cardiovascular functions.

Conclusions: The results are considered to be significant in developing the understanding of the system's performance, with changes in fluid flow magnitude, direction, and behaviour presented as well as new observations and correlations between some parameters of the system detected.

P26-FT

IN-SILICO AND IN-VITRO ASSESSMENT OF A PHYSIOLOGIC CONTROL SYSTEM FOR A TOTAL ARTIFICIAL HEART

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Objectives: The ShuttlePump is a pulsatile, valveless total artificial heart featuring equal left and right stroke volumes and low pre- and afterload sensitivities. Therefore, to achieve left-right balance and avoid over- or underpumping, an active control strategy adapting the pumps output to the patients' need is required. The aim of this study was to design and assess a physiologic control system, with a minimum number of sensors and an intuitive way to set patient specific control parameters by physicians.

Methods: The proposed control strategy combines an active control feature which adapts the stroke rate based on changes in venous return and an interatrial shunt to equalize atrial pressures and prevent lung congestion. Stroke rate is adapted based on right atrial pressure (RAP) sensor readings and a proportional controller. The control strategy was established and evaluated in a lumped parameter model of the ShuttlePump within the cardiovascular system including a bronchial shunt flow. Optimal interatrial shunt resistance was determined and responses of the control strategy to hemodynamic changes investigated. Results were validated in a mock circulatory loop with the possibility to adapt the interatrial shunt diameter and venous pressures.

Results: In the numerical model, the pumps output increased linearly with rising RAP (0.3 L/min/mmHg). Independent from bronchial shunt flow (0-0.7 L/min), pressure difference between left and right atrium decreased linearly with shunt resistance (<1mmHg at 0.1mmHgs/ml). Similarly, in the mock circulatory loop left-right balance was achieved with interatrial shunts >6mm and the pump rate increased with rising RAP.

Conclusions: The proposed control strategy with a single sensor was successfully established and tested in-silico and in-vitro. Baseline pump rate and proportional controller gain are the only patient-specific parameters to adjust the pump output in resting condition and the sensitivity to changes in RAP. The results substantiate further development towards animal experiments with the entire system.

P27

KTAH: DESIGN AND SIMULATION OF A PERISTALTIC TOTAL ARTIFICIAL HEART

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Objectives: Heart failure affects 64.3 million people worldwide, with around 23 million suffering from the end-stage condition. Lack of heart donations motivates the development of total artificial hearts. KTaH total artificial heart is a novel peristaltically driven device that can work in both non-pulsatile and pulsatile modes. KTaH is composed of two compliant silicone-based chambers, enclosed inside a stable 3D printed case. Each chamber replaces native atria and ventricles. A motor between the soft chambers rotates driving four rollers that propel the blood forward by the compression of the chambers. KTaH aims at reducing shear-stress and consequent blood trauma thanks to low rotational speeds (18 - 75 rpm) and soft-biocompatible blood-contacting surfaces. The goal is to present numerical results of the expected flows achievable with the proposed design, aimed at a cardiac output of 5 L/min.

Methods: An analytical relationship between the KTaH operational parameters and the average flow was estimated, resulted from an ideal estimated chamber volume of 140 mL, speed of the rollers of 19 rpm and setting the chambers to empty twice per complete rotation of the motor. In the attempt of validating the analytical results, a 3D numerical simulation was carried out in Simscale. A mesh composed of 251885 cells was used, with a mean cell volume of 0.24 mm3.

Results: Analytically, the average flow was 5.32 L/min. Simulation shows a velocity profile similar to that of the expected output in a native aorta with a peak velocity of 1 m/s and a mean steady state flow of 5 L/min.

Conclusions: Preliminary results show the potential of KTaH to achieve natural flow profiles and compact design with adaptable chamber size. Further work will focus on developing the physical prototype and its evaluation under different physiological conditions using a Hybrid Mock Loop.

P28

MAVIS TOTAL ARTIFICIAL HEART

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Objectives: A new total artificial heart is under development to provide support for patients with advanced heart failure as a bridge to heart transplant. We aim to design an innovative durable TAH with low risk of thrombosis, hemolysis, infection and malfunction. The implantable component is planed to be small (up to 50 cc) in order to be easy to accommodate in different bodies, as women size, small adolescents and children.

Methods: We used mathematical modeling to calculate the pump characteristics to deliver variable flows at different pump diameters, turbomachinery design software CFturbo(CFturbo GmbH, Dresden, Germany) to create the conceptual design of the pump, Fusion 360 CAD software to further refine the design, computational fluid dynamics software Ansys for in silico test pump performance and 3D printing with stereolithography printer (Form 2, Formlabs, Somerville, MA, USA) for the prototype.

Results: We present the concept, design, and early prototyping of a fully implantable total artificial heart for long-term use containing two radial flow pumps actuated by a radial bearingless slice motor. The designed implantable system comprises an electronic control unit (ECU) responsible for receiving wirelessly the energy, driving the bearingless motor, storing the energy in a battery and to communicate with external controller.

The system pumps 10 liters/min at 100 mmHg on the left side and 2-5% less blood (9.8-9.5 l/min) at 20 mmHg on the right side.

Conclusions: In vitro testing will provide input for further optimization of the device before proceeding to a completely functional prototype that can be implanted in animals.

Designing a durable, wireless, safe and simple TAH we have created the premises for a new generation of TAH that may receive a larger acceptance in the field of advanced heart failure.

P29-FT

MULTI-OBJECTIVE OPTIMIZATION OF A ROTARY BLOOD PUMP FOR FONTAN PATIENTS

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Objectives: Rotodynamic blood pumps (RBPs) denote multimodal systems with hydraulic and electromagnetic designs. Pediatric applications require small device conceptions due to anatomical constraints. This study aimed at pump size reduction of an RBP for Fontan patients using multi-objective design optimization considering both hydraulic and electromagnetic performance.

Methods: Three design variables of the double inlet single outlet RBP were considered: outer impeller diameter (D=17,18,19mm), inner impeller diameter (d=9,9.5,10mm) and gap width (w=0.5,0.75,1mm). Computational fluid dynamics (CFD) were employed to evaluate 27 hydraulic designs in terms of energy dissipation, shear stress exposure and washout at a nominal operating point (4L/min, 12.5mmHg). Actuation systems were adapted for each design individually, and respective motor losses (hysteresis, conduction and eddy current losses) numerically described based on the required rotational speed and torque predicted by CFD. Geometric, hydraulic and electromagnetic properties were integrated into weighted objective functions to obtain a score for pump size, hemocompatibility and motor performance for each design.

Results: Design variations hold the potential for a 45% reduction of priming volume. Flow simulations revealed hydraulic efficiencies to drop with increasing gap size (up to 11%), while the gap volume flow increased (up to 1.92L/min) as well as the overall hemocompatibility score. Larger outer impeller diameters did also lead to higher hemocompatibility scores. In contrast, smaller outer diameters and larger gaps did not necessarily result in increased motor losses. The minimum losses (0.21W)

were indicated for the design with the smallest outer impeller diameter and 50% increase in gap size (D=17mm, d=9.5mm, w=0.75mm). Local blood temperature rise was well below the acceptable increase of 2K for all designs.

Conclusions: Pump miniaturization is feasible without deterioration of motor performance but adversely affects hemocompatibility. A multi-objective optimization is imperative to determine the ideal trade-offs between the partly conflicting requirements for low blood trauma and high motor efficiency.

P30

NUMERICAL PERFORMANCE EVALUATION OF HYDRODYNAMIC BEARING FOR A NOVEL TOTAL ARTIFICIAL HEART – THE SHUTTLEPUMP

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Objectives: ShuttlePump is a novel valveless pulsatile total artificial heart recently introduced as a potential solution for long-term support. The pumping principle utilizes a synchronized rotational and translational piston motion within a cylindrical housing with two in- and outlets. A hydrodynamic bearing has been designed to levitate the piston without mechanical contact with the housing. This study aimed to numerically evaluate the performance of this hydrodynamic bearing in terms of load-carrying capacity and to characterize the effect of the mechanical design and motion pattern of the moving piston.

Methods: Computational fluid dynamic simulations were performed to numerically predict the hydraulic forces for four eccentric (ε) positions for a bearing gap clearance of 140μm, considering only the piston's rotational motion (3Hz). Based on the results, the effective length of the bearing was identified by fitting through a nonlinear least square approach to solving the Sommerfeld equation. Further, the Lomakin effect was investigated by including the translational and rotational motion of the piston for two eccentric positions.

Results: The 140μm bearing gap exhibits an exponential increase in force with increasing eccentricity. A mean effective bearing length of 36.7mm was determined via extrapolation. Piston notches cause changes in pressure distribution, leading to fluctuations in effective bearing length during each cycle, ranging from 34.8mm to 38.1mm. The Lomakin effect is evident as the mean hydraulic forces under static pressure condition due to rotation and translation are 6.9N and 8.5N for 0.2ε and 0.4ε, respectively, while only rotational motion has 1.36N and 3.3N of load for the same eccentricities.

Conclusions: The results showed that the piston's mechanical design and motion pattern significantly impacts bearing performance. Future studies will use advanced fluid-structure interaction to evaluate the stability of the bearing and will be validated experimentally with a fully functional prototype of ShuttlePump.

P31

THE EFFECT OF DONOR VARIABILITY AND HAEMODILUTION ON IN VITRO HAEMOLYSIS TESTING

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Objectives: The American Society for Testing and Materials (ASTM) F1841 standard recommends the dilution of blood for in vitro ventricular assist device (VAD) testing to standardise haematocrit (HCT) levels. We previously showed that haemodilution with PBS can increase haemolysis, although haemolysis can be reduced when diluting with PBS + 4 g% BSA (bovine serum albumin) for large dilutions. However, donor variability impacts testing results, therefore, this study aimed to investigate the effect of variation in donor blood and the diluents used during in vitro testing.

Methods: Bovine blood was diluted with either PBS or PBS + 4g% BSA and pumped with the CentriMag centrifugal pump under haemodynamic conditions or subjected to VAD-like shear for 6 hours. Complete blood counts, plasma free haemoglobin, Normalised Index of Hemolysis (NIH), protein and viscosity levels were measured.

Results: Haemodilution impacted mechanical fragility depending on the diluent and blood parameters. Overall, PBS alone caused significantly higher haemolysis than with PBS + 4g% BSA. However, donors with high levels of MCH (mean corpuscular haemoglobin), MCHC (mean corpuscular haemoglobin concentration) or white blood cell (WBC) counts were associated with higher levels of haemolysis, regardless of the diluent used. In contrast, protein concentration and viscosity levels were not significantly different between tests with high vs. low levels of haemolysis. The identification and removal of fragile donors could, thereby, limit donor variability and improve the reproducibility of testing.

Conclusions: These findings could aid the development of in vitro haemolysis testing across laboratories and result in future considerations for the ASTM standards by maintaining physiological blood parameters (MCH, MCHC, WBC and haemoglobin). Moreover, since donor-donor variability is a crucial factor in determining the levels of haemolysis, these results highlight the need for standardisation in testing procedures to reduce bias and improve the accuracy of in vitro VAD testing.

Apheresis and Adsorption

P32

ENTERORRHAGIA PRESENTING IN PATIENT WITH GRANULOMATOSIS WITH POLYANGITIS- A CASE REPORT

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Objectives: ANCA-associated vasculitis(AAV) as a term includes: microscopic polyangiitis(MPA), granulomatosis with polyangiitis(GPA) and eosinophilic granulomatosis with polyangiitis(EGPA).GPA is characterised by formation of granulomas and inflammation of small and medium-sized vessels leading to organ dysfunction,with a predilection for respiratory tract and kidneys.Gastrointestinal(GI) involvement happens rarely in GPA but when affected,has a poor prognosis.

Methods: Case report:We report a case of 50-year-old male with GPA who presented with pulmonary renal syndrome and enterorrhagia due to GI vasculitis.The patient was treated with: hemodialysis,pulse methyl prednisolone,cyclophosphamide and plasmapheresis.Our systematic review of the literature found only a few case reports where gastrointestinal symptoms were one of the first signs of GPA,however,this entity might be more frequent if physicians would think of this possibility more often.

Results: From the examinations:Biopsy of hard and soft palate showed granuloma.Pseudomonas aeruginosa was isolated from the urine,the blood culture remained sterile.PCR test for Sars CoV2 infection,serological findings for infectious agents:anti Treponema pallidum IgG and IgM,Lowenstein culture,Fluorescent microscopy of sputum and Genexpert MTB/RF sputum: remained negative. Immunohematological analyses: IAT,DAT, Enzyme test, Cold autoagglutinins, Cold isoagglutinins, Coombs autoagglutinins and Isoagglutinins with Coombs: remained negative. The antinuclear factor (ANA) was negative and cytoplasmic anti-neutrophilic

cytoplasmic antibody (c-ANCA) was 3+ positive. Routine urine examination showed trace of proteins,8- 10 erythrocytes,plenty of leucocytes. Ultrasonography revealed that both kidneys were normal in size and slightly increased echogenicity. Gastroscopy was performed and upper digestive bleeding was excluded. Digital rectal examination showed that it was not melena but enterorrhagia.CT scan of the lungs was performed in addition to nodules and alveolar hemorrhage.Due to enterorrhagia CT angiography of the abdomen was done to localize the site of bleed,arterial phase of scans showed: hyperdense linear zone in part of the wall of the distal ileum with increased density compared to the native series,suspicious for hemorrhage.

Conclusions: In cases with high clinical suspicion of GI involvement in GPA,early aggressive immunosuppressive therapy and eventual surgical intervention remains the cornerstone of the management.

P33-FT
EXTRACORPOREAL IMMUNE CELL THERAPY OF SEPSIS

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Objectives: Immune cell dysfunction is crucial in sepsis. Granulocyte concentrate (GC) transfusions, as the only available immune cell concentrates, potentially induce tissue damage via local effects of neutrophils. Therefore, using the donor immune cells purely extracorporeally is an attractive option. Clinical trials with standard GC in an extracorporeal plasma treatment achieved beneficial effects. In this ex vivo study, purified GC with longer storability were investigated in a simplified extracorporeal plasma treatment system paving the way for a recently started clinical multi-center trial.

Methods: Purified GC were stored up to 3 days and used in a simplified two-pump plasma perfusion simulating a 6-hour treatment. The extracorporeal circuit consists of a blood circuit and a plasma circuit with 3 plasma filters (PF). PF1 is separating the plasma from the patient's blood, plasma is perfused through PF2 containing the donor immune cells. A PF3 is included in the plasma backflow as a redundant safety measure. 1000 ml donor plasma were used to simulate patients. Granulocyte efficacy was assessed by phagocytosis, oxidative burst and cell viability as well as cytokine release and metabolic parameters.

Results: The donor immune cells demonstrated very good performance throughout the whole 6-hour treatment as evidenced by high viability, phagocytosis and oxidative burst. Stable glucose consumption and lactate production underline the high metabolic activity of the cells and cytokine release, like IL-8 and MCP-1 further demonstrated full functionality. Cell performance was similar both after storage for 1 and 3 days demonstrating the longer storability of purified GC compared to standard GC.

Conclusions: Results demonstrate that granulocytes remain viable and active even after 3 days of storage and 6-hour treatments supporting the use of the system in clinical trials. In 2022 a multicenter randomized controlled trial with this one-way system has started in septic shock patients.

P34-FT
STABILIZATION OF THE CIRCULATING BLOOD VOLUME BY ADJUSTING THE SODIUM CONCENTRATION OF THE SUBSTITUTION FLUID IN DUAL FILTRATION PLASMAPHERESIS

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Objectives: Plasma exchange or dual-filtration plasmapheresis (DFPP) is used to remove anti-A/anti-B antibodies in ABO-incompatible kidney transplant recipients. However, the substitution fluid used for DFPP has a low osmotic pressure, which may cause a decrease in the blood pressure and discomfort due to a decrease in the circulating blood volume during treatment. The aim of the present study was to determine whether DFPP can be performed more safely by adding sodium chloride (NaCl) to the substitution fluid to avoid decrease of the circulating blood volume during treatment.

Methods: The study was conducted in 32 patients who needed elimination of anti-A/anti-B antibodies prior to renal transplantation. The first DFPP was performed using 800 ml to 1 L of conventional substitution fluid (a mixture of lactic solution and 20% albumin solution) (control treatment). The second DFPP was performed with substitution fluid to which 20 ml of 10% NaCl had been added (NaCl treatment). Changes in the circulating blood volume (⊿BV) in both treatments were measured every 30 minutes.The blood osmolality and total protein (TP), sodium and hemoglobin (Hb) concentrations were also measured before and after the DFPP.

Results: In the NaCl treatment, the osmolality of the substitution fluid increased from 194±12 to 266±18 mOsm. In addition, the ⊿BV was less pronounced from 120 to 210 minutes ($P<0.01$). The NaCl treatment prevented significant post-treatment plasma osmotic pressure decrease, TP decrease, and Hb increase observed in the control treatment; however, the plasma Na concentration did not change in either treatment. The NaCl treatment was associated with a less pronounced decrease of the blood pressure and less discomfort.

Conclusions: Addition of NaCl to the substitution fluid prevented a significant drop in the circulating blood volume during DFPP.

Modelling in Artificial Organ

P35
A COMPLEX MEASUREMENT SYSTEM FOR ACQUISITION OF DATA REQUIRED IN MODELING OF CARDIOPULMONARY SYSTEM SUPPORT AND TREATMENT

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Objectives: The use of models, either numerical, physical or hybrid, in initial testing of new equipments is a modern approach, which is of particular meaning in biomedical engineering due to ethical restriction related to experiments with humans or animals. However, reliable tests require reliable models which can simulate the work of living organs under different, unusual or sometimes unexpected conditions, e.g., leading to arterial oxygen saturation decrease with lung ventilation increase. In the case of the cardiopulmonary system, pleural effusion is a special factor influencing this system work.

Methods: To analyze this influence, we have elaborated a complex measurement system. A PC based computer with its own developed software (ToraceMon) is the core of the measurement system. It gathers signals from the following various devices: a pleural manometer and a detector of breaths (both of own construction), and the commercial devices that are a non invasive hemodynamic monitor (PhysioFlow), spirometer (Lungtest 1000), transcutaneous blood gases monitor (Radiometer TCM4) and finger pulse oximeter (IGEL).The mechanical Dirac delta is used for subsequent signals synchronization.

Results: The system is used during therapeutic thoracentesis to see how increased intrathoracic pressure (IP) caused by the pleural effusion and its decrease during fluid withdrawal impact the work of both the cardiovascular and respiratory systems. Particularly, we are interested in the dependence of the stroke volume (SV) on IP changes. Surprisingly, initial results seem to suggest that IP has influence on SV only in a small part of patients, which has to be explained by physico-physiological analyses and computer simulations.

Conclusions: This knowledge can be useful for improvement of our virtual and artificial (hybrid) cardiopulmonary patient used, among other, in tests of new ventricular assist devices.
The work was supported by the National Science Centre, Poland (Grant No 2012/05/B/NZ5/01343).

P36-FT
A NEW CONTROL ALGORITHM OF PRESSURE-CONTROLLED INDEPENDENT LUNG VENTILATION

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Objectives: In the case of respiratory failure and asymmetrical lung pathologies conventional mechanical ventilation or Extracorporeal Membrane Oxygenation can be applied. When these procedures give no patient improvements, the alternative can be Independent Lung Ventilation (ILV). ILV can be applied just by one ventilator but also with a special pneumatic divider. This study aimed to develop a new pressure-based algorithm for the pneumatic divider, enabling cooperation with the ventilator set in the pressure-controlled mode.

Methods: A previously developed system for ILV, named Ventil was modified. A new electronic control module, based on microprocessor architecture was developed and implemented in the Ventil. Input signals from pressure and flow sensors were acquired as inputs for the control algorithm. Its output was an electrical signal for the stepper motor's controller to drive Ventil's dividing head. The Ventil together with the ventilator was connected to 2 artificial lungs (ALs). The simulations were performed for different parameters set in the ventilator and Ventil along with various resistive and compliant properties of the ALs. The results were analyzed in terms of peak pressures (PPEAKs), tidal volumes (TVs) as well as pressure and flow profiles and the system's stability and compared with the results for the previous version of the control algorithm.

Results: The simulation results show that the new control algorithm provides better stability and optimization in comparison to the previous one. The PPEAKs in ALs are more efficiently managed and can be predicted in accordance with the PPEAK set in the ventilator. The Ventil covers a wider range of TV divisions when the new control algorithm is applied.

Conclusions: The new control algorithm improves the performance of the Ventil when used with the ventilator working in pressure-controlled mode. The work was supported by the National Science Centre, Poland (Grant No 2021/43/D/ST7/01912).

P37
CONSTRUCTION AND MANUFACTURING OF AN MRI-READY EXPERIMENTAL SETUP AND PHANTOM HEART MODEL

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Objectives: CFD simulations using patient-specific geometries are a promising tool for diagnostics and treatment planning of left ventricular and mitral valve diseases. To validate these simulations, extensive data on flow characteristics is necessary. This data can be obtained from patients or probands with a time-resolved 3D phase contrast imaging with three-directional velocity encoding (4D flow MRI). However, data quality can be limited due to movements, irregular heart frequency and low dwell times in the MRI. To obtain data without these disturbances, MRI-ready experimental setup using a phantom heart model made of silicone is developed.

Methods: The parts of the experimental setup which are inside the MRI scanner need to be metal free to exclude interference with the magnetic field of the scanner. The setup is constructed with a backup tank to ensure leakage free handling. The phantom heart model is planted into a fluid filled box which is connected to an MRI compatible piston pump. Therewith the pressure in the box can be changed to achieve physiological flow profiles in the ventricle and a ventricular movement in accordance with the probands MRI images.
The heart geometry of the phantom model was taken from proband MRI-data and adapted using CAD software such that all experiment requirements are met. The ventricle is cast from silicone into 3D-printed modules.
For aortic and mitral valve, 3D-printed manufacturing is evaluated against casting in molds, both with silicone material. They will be produced in an almost closed state to ensure a correct shape and proper closing, as well as to avoid manual separation of the leaflets manually after printing.

Results: Testing and optimization of the phantom is matter of current work and results will be presented at the latest state.

Conclusions: Our MRI-ready experimental setup can possibly replace in-vivo MRI messurements for validation of CFD simulations.

P38-FT
DESIGN OF A HIGH FIDELITY SIMULATOR AND 3D PRINTING OF THE AORTA: IMPLICATIONS FOR PREPROCEDURAL PLANNING IN CARDIOVASCULAR INTERVENTIONS

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Objectives: Simulation with functional anatomical models offers realistic conditions for training and preprocedural planning of cardiovascular interventions, possibly reducing complications. This work presents the design and construction of an aorta simulator with patient-specific anatomy connected to a computer-controlled mock loop of the circulation using a pulsatile ventricular assist device (VAD). The applicability of the simulator was tested using an intra-aortic balloon pump (IABP) mimicking hemodynamic conditions found in heart failure.

Methods: Vascular geometry was reconstructed after segmentation (Mimics.v21, Materialize) using cardiac CT scans of an anonymized adult patient. The aorta, subclavian and femoral arteries were printed (J750 DAP, Stratasys) using a Shore A30 material (Agillus©, Stratasys). The proximal end of the aorta was connected to the VAD outflow port and the femoral arteries to the inflow port by a Y connector and pulsatile flow obtained. Proximal and distal aortic pressure and flow were recorded. Assistance with a 40-cc IABP (CS100, Datascope) in counterpulsation was simulated. Systolic and diastolic pressures were adjusted to simulate progressive heart failure conditions and an external ECG generator synchronized the VAD and IABP in counterpulsation (1:1; 1:2; 60 cpm). Mechanical properties were obtained from 3D printed flat samples (ASTM D638-V type IV; Instron 3365) or tubular structures for compliance tests using volume displacement to transmural pressure ratio.

Results: IABP assistance (1:2) resulted in reverse flow due to volume displacement, inflection point at the onset of deflation and diastolic

pressure augmentation >100 mmHg, the later probably related to reduced compliance in the lower range of pressure pulses. Maximum stress of 0,56 ± 0,03 at strain of 130% was found for vessel wall material with an elastic modulus of 0,6 MPa at 0,2 MPa.

Conclusions: The proposed simulator reproduced hemodynamic conditions found in clinical practice. The 3D-printed vasculature improved perceptual and visual understanding of the anatomy allowing for preprocedural planning and training.

P39-FT
DEVELOPMENT AND CHARACTERIZATION OF CALCIFIC AORTIC VALVE MODELS FOR CLINICIANS TRAINING IN TRANSCATHETER CARDIOVASCULAR PROCEDURES

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Objectives: Calcific aortic valve (AV) stenosis represents the most common valvular heart disease in elderly and the leading cause of valve replacement in USA and Europe. Recently, minimally invasive transcatheter procedures have revolutionized its treatment by reducing patients' recovery and hospitalization. However, these approaches require adequate surgical training which currently involves use of biological cadaver samples resulting in ethical and availability issues. Therefore, the goal of this work was to develop a polymeric model of calcific AV that can provide surgeons with a reliable and realistic tool for training in transcatheter procedures.

Methods: Three-point bending tests were performed on five different epoxy resin (ER) and calcium phosphate (CP) solutions in water (W) to identify which calcification mixture replicates physiological mechanical properties. Paradigmatic polymeric aortic roots were designed and, with two different silicone hardnesses, manufactured by injection molding. Calcifications were embedded on AV leaflets, reproducing different calcification patterns (radial and arc) and severity (mild to severe). In pulsatile mock loop calcific AV models were tested simulating different working conditions (stroke volume of 50ml, 65ml and 80ml; mean aortic pressure of 100mmHg; frequency of 60bpm). Transvalvular pressure was acquired, and effective office area (EOA) was calculated. Finally, fluoroscopic imaging compatibility of the models was assessed.

Results: ER22%-CP67%-W11% calcification mixture exhibited maximum force (52.8N) and flexural strength (3.37MPa) comparable to literature results. At 80ml of stroke volume, calcific AV models with arc pattern and higher silicone hardness better replicated pathological values of transvalvular systolic pressure (63.6mmHg) and EOA (0.56cm2) than radial pattern (45.0mmHg and 0.67cm2, respectively) and with lower silicone hardness (14.6mmHg and 1.17cm2, for severe arc pattern model). Calcifications visualization under fluoroscopy was successfully verified.

Conclusions: This work provided a method to develop biomechanical realistic calcific AV models capable of replicating pathological conditions and a reliable tool for surgical training in transcatheter procedures.

P40
DEVELOPMENT OF A METHOD FOR NON-INVASIVE BLOOD PRESSURE MEASUREMENT AT THE CHEEK

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Objectives: Hypertension is a common condition that greatly increases the risk of developing cardiovascular disease. Non-invasive blood pressure measurements are the most important tool for the timely detection of hypertension. Current standard methods rely on the use of an upper arm cuff. However, these devices cannot be used for patients with amputated or malformed upper extremities. To address this problem, an alternative method of determining blood pressure at the cheek has been developed.

Methods: A photoplethysmogram (PPG) of the facial artery is measured via a mouthpiece to detect blood volume changes. The photodiodes are located in the oral cavity and the pressure pad with photodetectors is located on the outside of the cheek. During the measurement, the pressure pad is inflated to 200 mmHg to ensure the collapse of the artery, and then slowly deflated. The pressure in the pressure pad correlates with the systolic blood pressure during the deflation phase. The transmission of light through the facial artery correlates with the blood volume inside the artery and is recorded in parallel. The systolic blood pressure is determined by means of an algorithm that iteratively calculates sigmoid fits. The resulting systolic pressure is fed to a pre-trained neural network. A cuffed oscillometric device served as the reference method.

Results: A dataset comprised of 52 measurements was used for the evaluation of the method. The average error of the proposed method is 4.06 mmHg with a standard deviation of 3.75 mmHg. The systolic blood pressure of the subjects ranges from 100 – 150 mmHg.

Conclusions: Although the accuracy is within the normative requirement of 5 ± 8 mmHg, the significance of the results cannot be shown due to the lack of data set size.

P41
FLUID-STRUCTURE INTERACTION SIMULATION MIMICKING EXPERIMENTAL OPENING OF A BIOPROSTHETIC BOVINE AORTIC VALVE UNDER STEADY-STATE FLOW CONDITIONS

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Objectives: Fluid-structure-interaction (FSI) simulations are a powerful tool for studying prosthetic valves. In this study, an FSI simulation was performed to replicate an experimental setup in which a bioprosthetic bovine pericardium aortic valve was investigated under steady-state flow conditions.

Methods: A 21 mm Avalus™ Bioprosthesis (Model 400, Medtronic, Ireland) was placed in a mock circuit with a straight tubular test section. Using 40% glycerol, a range of steady-state flows were created. During the experiment the flow-rate and the transvalvular pressure were measured, and photos of the valve opening were taken and subsequently used to determine the effective orifice area (EOA). For the FSI simulation, a valve-specific geometric model was created by means of a µCT scan (voxel size 31µm). A literature-based anisotropic hyperelastic leaflet material was implemented, representing the decellularized matrix with embedded circumferential collagen fibers. The simulation fluid domain represented the experimental test section. The inlet velocity boundary conditions matched the measured experimental data. Three flow-rates were simulated: 3.85 L/min, 8.90 L/min, and 12.00 L/min. Simulated and experimental EOAs were subsequently compared.

Results: Simulations were performed on the Vienna Scientific Cluster supercomputer. The simulated and experimental EOA ratios were

39.2mm2/73mm2 = 0.535, 75.4mm2/100mm2 = 0.686 and 93.2mm2 /118mm2 = 0.790, respectively. In the experiment, an asymmetric opening was observed, with one leaflet showing more pronounced deformation. Simulated leaflet openings resembled those of the two partially opening experimental leaflets.

Conclusions: Simulated EOAs were smaller than experimental EOAs, particularly at low flow-rates. Deviations in measured flow-rates or in leaflet material properties could be the reason. The simulation material properties were based on averaged experimental literature data and identical for all leaflets. This does not consider variability of biological materials or property-altering chemical treatments. Prospectively, an introduced scaling factor might compensate for heterogenic leaflet material properties and achieve better matching EOAs.

P42

HEMODYNAMIC RUPTURE RISK PARAMETERS FOR INTRACRANIAL ANEURYSMS AND UNCERTAINTY

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Objectives: Even though they affect a substantial part of the population and the fact that both rupture and treatment of intracranial aneurysms (IAs) can result in considerable morbidity and mortality, the development of surveillance and treatment strategies remains difficult. Clinical adoption of geometric and hemodynamic rupture risk parameters remains limited, despite the large number of proposed parameters. Besides the ability to discriminate rupture status, any proposed parameter should be robust. This study looks at the influence image segmentation has on the uncertainty of hemodynamic rupture risk parameters.

Methods: Based on computational fluid dynamics (CFD) data from a previous study by Voß et al. (DOI: 10.1371/journal.pone.0216813), which was kindly provided by the authors, this study analyzed 19 hemodynamic rupture risk parameters on five IA geometries segmented by 26 research groups. Segmentations were obtained during the Multiple Aneurysms AnaTomy Challenge 2018 (MATCH). Spatially and/or temporally distributed parameters were averaged to obtain scalar quantities.

Results: Analysis of the CFD data is currently ongoing. Results will be presented at ESAO 2023 and will include inter-parameter correlations, measures of segmentation-related uncertainty, and histograms of parameter distributions.

Conclusions: Once finalized, the results will provide estimates of the sensitivity of individual hemodynamic rupture risk parameters to differences in image segmentation. They will further help to group parameters that capture similar hemodynamic features based on inter-parameter correlations. This will allow identification of parameter sets that are both robust and capture diverse hemodynamic features, while hopefully also helping in identifying what makes parameters robust.

P43

HYDRODYNAMIC BEHAVIOR OF VASCULAR STENOSES

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Objectives: According to federal health reporting in Germany, about 360,000 people suffered a stroke in 2020, of which 6.7 percent resulted in death [1]. The aim of this work is to get insight into the relationship between pressure and flow in pre-, intra-, and post-stenotic areas of vascular obstructions.

Methods: Pressure values at flow rates between 200 and 600 ml/min were recorded in vitro for different degrees of stenoses in the pre-, intra- and post-stenotic area. All pressure values were corrected to 120 mmHg (systole), 80 mmHg (diastole) and 100 mmHg for Mean Arterial Pressure (MAP) according to the normal human blood pressure as a basis.

Results: Stenoses with a degree higher than 83% show a distinct decrease in pressure due to increasing flow velocity in the intra-stenotic region. This can cause the stenosis to collapse spontaneously, resulting in occlusion of the vessel. A surprise is that the post-stenotic pressure no longer increases to the original pre-stenotic pressure as expected for ideal conditions according to Bernoulli's equation.

Conclusions: In case of lumen reduction above 83%, there is not enough potential energy remaining to increase the post-stenotic pressure to the expected value. This can be explained by large frictional energy in pulsatile flow systems, so that a large part of the kinetic energy of the fluid is probably converted into heat. Consequently, these so-called "symptomatic stenoses" are of high clinical relevance, as the patient is exposed to a high risk of myocardial infarction or stroke.

[1] Statistisches Bundesamt (2021): Fallrate von Schlaganfällen (tödlich und nicht-tödlich) je 100.000 Einwohner. Gesundheitsberichterstattung des Bundes

P44

MECHANISTIC INTERPRETATION OF ICODEXTRIN OSMOTIC PRESSURE DURING PERITONEAL DIALYSIS

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Objectives: Icodextrin, a mixture of glucose polymers, provides osmotic pressure to remove water during peritoneal dialysis (PD). The contribution of polymers of different lengths to this pressure was not previously compared to clinical data on kinetics of icodextrin fractions during long peritoneal dwells. We provide mechanistic interpretation of icodextrin kinetics and its transcapillary osmotic pressure using three pore model (TPM) of PD applied to clinical data.

Methods: TPM (large, small and ultrasmall – water only – pores) - extended to include degradation of icodextrin by alpha-amylase - was applied to clinical data from 11 PD patients during 16-hour peritoneal dwell with icodextrin-based dialysis fluid and frequent sampling of dialysate and blood. Icodextrin was theoretically described as 7 fractions of different molecular weights (Fr1: 835, Fr2: 2924, Fr3: 6804, Fr4: 14257; Fr5: 28872, Fr6: 52206, Fr7: 87833 Daltons) according to the measured polymer distribution.

Results: The effective osmotic pressure gradient (EOP, ideal osmotic pressure gradient times reflection coefficient) between dialysate and blood for all fractions decreased during the dwell. Fractions F2, F3 and F4 had the highest EOP, whereas EOP of F6 and F7 was negligible, and EOP of F1 changed sign because of accumulation of glucose oligomers in plasma with dwell time. EOP of small solutes (urea, creatinine, glucose, sodium, chloride) was negative until solutes equilibrated between plasma and dialysate after 6 hours. Transcapillary ultrafiltration to the peritoneal cavity due to EOP of icodextrin was mostly across small pores, while absorption of fluid from the peritoneal cavity due to EOP of small solutes was via ultrasmall pores.

Conclusions: The most important contributors to EOP are medium fractions with high concentrations (F2 – F4), while the largest polymers do not directly contribute substantially to EOP of icodextrin. Small solutes decrease the overall transcapillary removal of water, especially during the initial 6 hours of dwell time.

P45

MODELING RADIAL-FLOW PACKED BED BIOREACTORS (RPBBS) FOR LONG-BONE TISSUE ENGINEERING: THE ROLE OF EXTERNAL RESISTANCE TO SOLUTE TRANSPORT

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Objectives: Modelling flow and solutes transport in bioreactors for tissue engineering is generally approached with pseudo-homogeneous models or with models describing fine details of porous scaffold seeded with adherent cells. The former neglect solute concentration gradients near the cells and do not properly account for hypoxic or anoxic zones, but have not high computational requirements. The latter properly describe transport to cells but require powerful computers and long processing times. Poor predictions of severe culture conditions and long running times, respectively, make both models unfit for real-time monitoring and control of the pericellular culture microenvironment in TE bioreactor. Aim of this study was to propose how a pseudo-homogeneous transport model may be modified to account for solute transport resistance from medium bulk to cell surface in scaffold pores (i.e., external to cells) and become feasible for monitoring and control purposes.

Methods: The pseudo-homogenous model was built to describe the steady-state transport of momentum and dissolved oxygen through void spaces and scaffold in an rPBB according to the Navier-Stokes, Brinkman and convection-dispersion-reaction equations, respectively. The scaffold was modelled as a transport equivalent bed of Raschig rings and resistance to oxygen transport was accounted for with available semiempirical correlations for solute transport. Balance equations were solved numerically with the FEM Comsol Multiphysics software for conditions typical of long-bone TE.

Results: The model soundly predicted culture under hypoxic or anoxic conditions in scaffold zones where medium stagnates, as in poor bioreactor design, and/or when highly metabolically active cells are cultured at high concentrations, as when tissue matures. High radial perfusion rates could correct the imbalance between oxygen supply and increasing metabolic demand till scaffold maturation without excessive computational power and times.

Conclusions: Use of this type of model appears promising for monitoring and controlling the pericellular microenvironment in TE bioreactors

P46-FT

PATIENT-SPECIFIC SIMULATOR FOR PREOPERATIVE PLANNING IN CARDIOVASCULAR INTERVENTIONS

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Objectives: The clinical use of 3D printing has gained success in preoperative surgical planning, allowing clinicians to perform surgical treatments in a safe, realistic, and controlled environment. Therefore, the use of patient-specific simulators for preoperative training plays a key role in defining customized solutions for patients, increasing treatment efficiency and accuracy, and reducing surgical risks. In this work, we present the design and manufacturing of a 3D-printed patient-specific thoracic simulator equipped with modular and interchangeable components for multiple surgical procedures. Specifically, the thoracic simulator has been validated by the hands-on implantation of an innovative ventricular remodeling device for the treatment of tricuspid functional regurgitation (FTR).

Methods: A patient-specific thoracic simulator composed of ventricles, septum, atria, mammary arteries, aorta, lungs, diaphragm, and rib cage, was developed starting from CT images of an 86-year-old male with moderate FTR. To obtain a modular simulator, mesh models of anatomical structures were processed in Meshmixer and design solutions were implemented in Fusion 360. Anatomical structures were 3D-printed with PLA and connected via pin connectors, allowing them to be disconnected and interchanged with other anatomies. Furthermore, by integrating disposable silicone patches into 3D components, the simulation of the procedure can be performed multiple times. The simulator's usability was tested and validated by experienced cardiac surgeons.

Results: The usability test demonstrated the feasibility of using the thoracic simulator during preoperative planning. Specifically, surgeons were able to test different strategies to identify the optimal surgical treatment for the specific anatomy of the patient represented in the model.

Conclusions: The developed simulator has shown potential in preoperative planning of the device implantation procedure. Moreover, the simulator's modularity makes it versatile and adaptable to replicate different medical procedures by incorporating interchangeable and disposable anatomical components. Future developments could lead to the introduction of fluid dynamics by integration with a pulsatile flow mock loop.

P47

POSSIBLE PREDICTORS OF CEREBROVASCULAR ACCIDENTS IN PAEDIATRIC PATIENTS WITH PHACES SYNDROME: IN-SILICO INVESTIGATIONS

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Objectives: PHACES syndrome is a rare condition of associated disorders that affects multiple parts of the children's organism. It manifests its presence with cardiac and arterial anomalies, ocular anomalies or even dermatological issues. The risk of cerebrovascular accident (CVA) resulting from PHACES syndrome is multifactorial, however, the mechanistic principles are not fully known. Current literature lacks information on an influence of arteriopathy on the potential risk of CVA. Therefore, the main objective of this research was to assess an impact of arteriopathy present in PHACES syndrome to identify a possible reason of CVA.

Methods: An arterial system spatial model was prepared basing on biomedical imaging data. Then, this reference geometry was subjected to three modifications of the internal carotid artery: a) PHACES syndrome (severe tortuosity and high hypoplasia), b) just severe tortuosity, c) just high hypoplasia. Afterwards, the authors performed numerical investigations with the fluid-structure interaction (FSI) method to reliably predict flow hemodynamics under pulsatile flow conditions. Additionally, a blood washout study was taken into consideration.

Results: Numerical simulations proved that a simultaneous combination of severe tortuosity and high hypoplasia could create a thrombogenic environment, where hypoplasia seemed to be a more dominant factor. We noted a significant reduction of blood flow intensity in the syndrome-affected artery, an increase in the blood viscosity as well as an increase in the blood stagnation. Moreover, a non-negligible increase in a relative amount of "not-washed-out" blood was observed for PHACES syndrome case study.

Conclusions: It was proven that numerical simulations can support statistical analyses and they can provide information on the mechanistic background of possible CVA resulting from PHACES syndrome. In this research, PHACES syndrome geometry showed that several regions could be prone to possible thrombus formation which could detach and block farther cerebral arteries leading to CVA.

P48

PROOF OF CONCEPT FOR DESIGN AND DEVELOPMENT OF A SOFT BIOMIMETIC VENTRICLE

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Objectives: With the limited availability of donor hearts, Total Artificial Hearts and Ventricle Assist Devices have been used as a bridge therapy to transplantation. However, they do not sufficiently mimic the motion of the native heart, leading to complications among which also death. To address this issue, our aim is to design a soft robotic left ventricle that closely replicates the motion and function of the human left ventricle (LV) using pneumatic artificial muscles (PAM).

Methods: We developed a finite element model of an idealized human LV using a novel method to generate the myofiber architecture. The deformation of the ventricle was studied in a single beat and compared to clinical data.
We then computationally designed and modeled the artificial ventricle (AV) using PAMs and a passive matrix based on the proposed myofiber architecture. The PAMs and the passive matrix were modeled as linear elastic and neo-hookean hyperelastic materials, respectively. The global parameters and deformation of the Biomimetic LV were evaluated and compared to the LV model. Furthermore, we investigated the effect of varying muscle parameters on the performance of the model.

Results: The LV model closely matched physiological data, exhibiting thickening of walls, base-apex twist, and motion of the endocardial and epicardial walls. The AV model had an ejection fraction of more than 50%, with similar wall deformation and base-apex twist and shortening motions as the LV model. We found that increasing the stiffness of the PAMs led to a higher ejection fraction. These findings suggest that optimizing the PAM design can further improve the performance of the AV.

Conclusions: Our intricate design of a Biomimetic LV based on intrinsic myofiber architecture successfully replicates the native LV motion and function, and has the potential to serve as an effective and safe alternative to current TAHs and VADs for patients with end-stage heart failure.

P49

RENAL REPLACEMENT THERAPIES OPTIONS FOR HYPERKALEMIC CARDIOCIRCULATORY ARREST

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Objectives: During advanced life support, if the serum potassium is ⩾6.5 mmol/L early in the resuscitation, hyperkaliemia should be considered as the potential cause. When the pharmacological treatments to lower potassium levels are ineffective, renal replacement therapy (RRT) in combination with high-quality cardiopulmonary resuscitation should be considered, especially if the return of spontaneous circulation is not achieved within 15 minutes or with an initial serum potassium ⩾9.5 mmol/L.

Both intermittent hemodialysis (HD) and continuous renal replacement therapies (CRRT) have been used with good outcomes in hyperkalemic cardiocirculatory arrest (HCA). HD usually ensures faster potassium removal, but the defibrillation compatibility of CRRT machines removes the need for disconnection of the extracorporeal circuit during resuscitation. However, published guidelines only give generic prescribing indications for RRT. We compared the benefits of the two treatments using mathematical modeling.

Methods: Using a two-compartment model we simulated potassium kinetics during one HD and two CRRT sessions with different modalities: continuous venovenous hemodialysis (CVVHD) and hemodiafiltration (CVVHDF). HD was modeled with blood flow Qb = 200 mL/min and dialysate flow Qd = 500 mL/min. CRRT had Qb = 200 mL/min and Qd = 80 mL/min. Dialysate concentration of potassium was the lowest commercially available for both therapies. CVVHDF had, in addition, a replacement fluid infused with 0 mmol/L potassium concentration at a rate of 24 mL/min. Initial potassium concentration was 9.5 mmol/L in all cases.

Results: The simulated results showed that CRRT is significantly less efficient than HD, with the need for an additional 23 minutes in CVVHDF and 38 minutes in CVVHD to reach a safe potassium concentration of 6.5 mmol/L.

Conclusions: The difference is enough to offset the defibrillation compatibility advantage of CRRT, leading to support the proposition of HD as the therapy of choice in HCA, whenever available.

P50

THE HYBRID CARDIOVASCULAR SIMULATOR TO STUDY VALVULAR DISEASES

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Objectives: To better understand the impact of valvular heart disease (VHD) on the hemodynamics of the circulatory system a hybrid cardiovascular system (HCS) can be used. The aim of this study was to develop physical models of VHD, namely aortic stenosis (AS) and mitral regurgitation (MR), as well as to perform simulations with them and assessment of the severity of VHD.

Methods: A previously developed HCS was used in conjunction with physical models of VHD. The MR model was a chamber connected two adjacent sections of the simulator and served as a bypass with the ability to change the diameter of the passage orifice and. The AS model was a mechanical device for restricting blood flow through the aortic valve by placing a diaphragm with a specific orifice diameter next to the aortic valve. Several simulations were performed for varying degrees of AS and MR by using diaphragms with different orifice diameters. The results were analyzed in terms of transvalvular pressure gradients, flow rates as well as estimates of aortic valve area and mitral valve area using the Gorlin's and Aaslid equations.

Results: The preliminary simulation results showed that the system is behaving correctly. Namely, in the case of AS - the mean pulmonary arterial pressure was increased due to increased preload of the left ventricle and the decrease in right ventricular preload was caused by a decrease in systemic arterial pressure. For the case of MR - with increasing severity of MR, there was a decrease in the left ventricular pressure and an increase in the left atrial pressure.

Conclusions: The HCS was adapted to perform simulations of the circulatory system using two artificial valves – mitral and aortic. Moreover, two physical models of VHD were developed, namely valve stenosis and regurgitation. The simulation results are generally consistent with the literature data.

P51

VIRTUAL TREATMENT PLANNING AND OUTCOME PREDICTION FOR PATIENTS WITH COMPLEX UNIVENTRICULAR PHYSIOLOGY

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Objectives: Several congenital heart defects result in the need for univentricular palliation of patients. In those patients, the superior and inferior vena cava are connected to the pulmonary artery via the staged Fontan procedure, facilitating the so-called total cavopulmonary connection (TCPC). This intervention is associated with several sequelae, such as the formation of pulmonary arteriovenous malformations (PAVM), that is assumed to be associated with the distribution of hepatic blood (HFD) towards the left and right pulmonary artery. In patients with uneven HFD, surgical or interventional treatment facilitating even HFD is a promising approach to achieve remodeling of PAVM. Here, computer-based approaches might allow outcome prediction of different treatment strategies.

Methods: The patient-specific anatomies of the TCPC of three Fontan-palliated patients with PAVM were reconstructed using CT or a combination of CT and MR images. First, numerical simulations of the pre-interventional hemodynamics were performed. Based on the patient-specific anatomy and these simulation results, different treatment strategies were identified by pediatric cardiologists and congenital heart surgeons. The patient-specific models were altered virtually to mimic these treatment strategies. Finally, for each virtual treatment the resulting HFD was calculated.

Results: Reconstruction of the complex anatomy of the TCPC was possible in all three patients despite presence of metallic stents. To facilitate this, combined approaches using both CT and MRI were required in two patients. For each patient at least one treatment strategy that was considered viable and the treatments effect on HFD was estimated.

Conclusions: Virtual treatment planning is a promising approach for patients with complex anatomies, such as the TCPC, which do not allow intuitive assessment of the post-operative changes. Especially as treatment strategies vary widely with respect to their respective risk, an objective outcome assessment might help to identify the ideal patient-specific treatment strategy.

P52
A COMPLIANT 4D IN VITRO MODEL OF A LEFT VENTRICLE TO TEST MECHANICAL CIRCULATORY SUPPORT SYSTEMS

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Objectives: Mechanical Circulatory Support (MCS) systems are characterized by a constant flow of innovations. The use of mock loops could speed up the validation process of MCS. However, they usually offer realistic representations of ventricular hemodynamics, but not of its anatomy, limiting their testing capabilities. We propose an innovative cardiovascular simulator that includes a physiologically activated 3D model of the left ventricle (LV), suitable to test MCSs under different (patho-)physiological conditions.

Methods: The cardiovascular simulator includes an in silico lumped parameters model of the cardiovascular system (right ventricle, atria, pulmonary and systemic circulations). The in vitro system consists of a compliant 3D model of the LV, hydraulically activated by gear pumps and DC motors to recreate pressure-volume (PV) loops following the loading conditions resulting from the in-silico model. Starting from the CT scan of a patient, the compliant 3D LV was created in polyvinyl alcohol using the molding technique (inner chamber volume 125 mL). At first the hemodynamic of a healthy patient with a cardiac output of 5.0 L/min was simulated. Then afterloads, preloads, heart rates and ventricular contractile states were changed, to mimic different heart failure conditions.

Results: The PV loops measured in the 3D LV model range between the systolic and diastolic values of the cardiac cycle for each considered case scenario. PV loops reflect the changes in the afterload and/or preload applied in the in-silico model and the intrinsic mechanical properties of the considered LV.

Conclusions: The proposed cardiovascular simulator represents a realistic anatomical and physiological replication of the LV interacting with the remainder closed loop circulatory in silico model. The result is a 4D LV model that can work as a reliable test bench for MCSs under different (patho-)physiological conditions.

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Hemodialysis and Uremic Toxins

P53
A TWO-COMPARTMENT EXPERIMENTAL MODEL CAPABLE OF EVALUATING THE PERFORMANCE OF ADSORPTION-BASED BLOOD PURIFICATION

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Objectives: The performance of a recirculating dialysate system and blood purification system using an adsorbent change over time depending on the solute concentration. Therefore, conventional evaluation methods such as the single-pass method are not applicable to evaluate the performance of these systems. In the present study, we attempted to establish a method to evaluate the performance of a blood purification system using bovine blood using a two-compartment experimental model, in which solutes are distributed between the blood and extravascular fluid.

Methods: Mass transfer between the body fluids and blood was simulated in a body-side circuit consisting of an extravascular fluid tank (28 L) and bovine blood tank (3.7 L) connected through a high-permeable dialyzer. The dialysate on the treatment machine side was calcium-free, to avoid blood coagulation. The solute concentrations of urea, creatinine, uric acid, and potassium were measured during the 240-min hemodialysis session and until 60 minutes after the session.

Results: During the hemodialysis session, the differences in the concentrations of urea, creatinine, uric acid, and potassium between the blood and extravascular fluid decreased, and the concentrations reached an equilibrium between the two solutions at 30 min after the end of the treatment. A rebound phenomenon was observed and the rebound rate at 300 minutes was 49%, consistent with the values reported in clinical practice. The time-course of the urea concentrations during hemodialysis and the rebound phenomenon that ended about 30 min after the treatment indicated that this model well simulated solute transfer occurring in the body during hemodialysis.

Conclusions: A two-compartment experimental model using blood and an extravascular fluid tank connected by a high-permeable dialyzer showed similar decreases and rebounds in the blood concentrations of solutes to those observed in clinical practice, so that this model is suitable for evaluating the performance of adsorption-based blood purification.

P54-FT
BLOOD FLOW CONDITIONS AND SOUNDS IN ARTERIOVENOUS FISTULA FOR HEMODIALYSIS

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Objectives: Arteriovenous fistula (AVF) is the preferred vascular access for haemodialysis but is still associated with a high failure rate. The purpose of this study was to investigate the relation between hemodynamics and sound recordings in AVFs and their possible role in vascular remodelling.

Methods: Four patients with primary radio-cephalic AVFs underwent follow-up at 3 days, 3 weeks and 1 year after surgery. MRI scans, blood viscosity analysis and blood flow volume (BFV) ultrasounds assessments were acquired and exploited to reconstruct patient-specific 3D geometries and to perform computational fluid dynamics (CFD) simulations. AVFs sound recordings were acquired with a 3M Littmann 3200 Electronic Stethoscope and their spectral features were analysed. The low-high peak ratios (LHPR) between peak amplitudes in the low (100-250Hz) and high (500-750Hz) frequency ranges were calculated. Then the relation between computed hemodynamics and sound recordings was investigated.

Results: The results show that the intensity of AVF sounds was directly proportional to the measured blood flow, with an accurate (R=0.7) and significant ($p<0.01$) correlation between the venous BFV and the sound maximum frequency peak. The relation between blood flow and AVF sounds was confirmed by the correlation between longitudinal changes in brachial BFV and in LHPR for single patients ($p<0.01$, R=0.68). CFD simulations showed that models characterised by turbulent-like velocity phenotype presented important high frequency peaks in sound recordings. Significant differences were found in the median LHPR values of subgroups characterised by extended or reduced areas of Oscillatory Shear Index > 0.1 (1.51 vs 3.20, respectively).

Conclusions: This preliminary work investigated the relationship between CFD-computed hemodynamics and sound recordings in AVFs, highlighting that complex flow, usually associated with vascular remodelling, could be related to high-frequency vibrations and opening up new scenarios to improve AVF monitoring during clinical practice.

P55-FT
EARLY PROGNOSIS OF ARTERIOVENOUS FISTULA MATURATION

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Objectives: The blood flow (BF) is one of the crucial tool for assessment functionality of arteriovenous fistula (AVF). The aim of our study was to determine the association between blood flow at day 1 and preoperative diameter of blood vessels with maturation of the AVF at 4th and 8th week.

Methods: Eighty Caucasian patients with chronic kidney disease (CKD) stage 4/5 and CKD stage 5 on hemodialysis (CKD5D), with newly-created radiocephalic AVF for hemodyalisis (HD), were enrolled in this prospective study. Hemodynamics and morphological evaluation of the blood vessels by Doppler ultrasound (DUS) were performed in all patients. The diameters of the blood vessels were measured before AVF creation. The blood flow (BF) of AVF was calculated by DUS on 1st day, at 4th and 8th week. The successful maturation of AVF was defined as BF $\geqslant$600 mL/min.

Results: The mean age of the patients was 59,89 $\pm$ 13,45 years, with 46 (57,50%) men and 34 (42,50%) females. The successful rate of AVF maturation was 43,75% (N:35/80) at 4th week and 62,5% (N:50/80) at 8th week. The results of the six adjusted models in multivariate analyses showed that BF at day 1 as a predictor for AVF maturation at 4th and 8th week was associate with best model indices and lowest p-values. To be even more specific, calculation of BF at day 1 data was performed by ROC (receiver operating characteristic) to establish the best cut-off point as a predictor of AVF maturation at 4th and 8th week. The preoperative diameters of the blood vessels were significantly larger in patients with maturated AVF at 4th and 8th week.

Conclusions: Our study showed that BF at day 1 was a great predictor of AVF maturation at the 4th and 8th week.

P56
EVALUATION OF THE SOLUTE REMOVAL PERFORMANCE AND BIOCOMPATIBILITY OF A REUSED DIALYZER

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Objectives: Dialyzer reuse refers to the practice of using the same dialyzer for multiple hemodialysis treatments. The concept of dialyzer reuse was introduced primarily for economic reasons in the 1960s. The practice, however, declined steadily, although it remains widespread in some developing countries. Currently, both the solute removal performance and biocompatibility of dialyzers have improved, as also the cleaning solution or reprocessing method used for dialyzer reuse. The present study was conducted to evaluate changes in the solute removal performance and biocompatibility of a reused dialyzer as compared with those of a single-use dialyzer to clarify the advantages and disadvantages of dialyzer reuse under the current circumstances.

Methods: We compared the characteristics of previously unused dialyzers and dialyzers that had been clinically used and reprocessed 5 or 15 times in Thailand. The endotoxin (ET) concentrations and viable bacterial counts in the dialyzer priming solution were determined. The hydraulic permeability (Lp) of the dialysis membrane and sieving coefficient for β-lactoglobulin (β-LG, MW 36,800 as dimer) were measured. Circulation experiments using porcine blood were also performed to compare the reactivity of leukocytes in response to the lipopolysaccharide (LPS) coming in contact with the dialyzer.

Results: No viable bacteria were detected in either dialyzer, although ET was detected in some priming solutions, indicating possible bacterial contamination occurring during the reprocessing. The Lp and sieving coefficient for β-LG were lower for reused dialyzers. Reused dialyzers were also associated with increased reactivity of leukocytes in the blood after treatment, suggesting that reused dialyzers may have altered membrane surface properties, which may increase the risk of complications in the long term.

Conclusions: Reuse of dialyzers was associated with deterioration of the removal performance for middle molecules and increase in the reactivity of leukocytes, which represent some of the potential disadvantages of reuse of a dialyzer.

P57
INTRADIALYTIC INFUSION OF DIALYSATE BOLUS FOR THE ESTIMATION OF ABSOLUTE BLOOD VOLUME IN HAEMODIALYSIS PATIENTS

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Objectives: A relatively simple method has recently been proposed for the estimation of absolute blood volume (ABV) in haemodialysis (HD) patients, which involves intradialytic infusion of a dialysate bolus and visual assessment of the subsequent increase in the relative blood volume (RBV) displayed on the screen of the dialysis machine. The aim of this study was to propose an algorithm for an automated and more accurate assessment of such RBV increase, taking into account the possible noise and short-term variability in the RBV signals.

Methods: The study was based on data collected during maintenance dialysis in 98 patients of the Vienna General Hospital, Austria performed with Fresenius 5008 machines. After 1 h of treatment, the dialysis was temporarily stopped in order to infuse 240 mL of dialysis fluid at the rate of 200 mL/min using the hemodiafiltration module. The RBV signals were recorded by the Blood Volume Monitor integrated in the dialysis machine. The performance of the algorithm was evaluated on data from patients with relatively undisturbed RBV signals available from two HD sessions from the same week of treatment.

Results: We proposed an algorithm consisting of interpolation of the RBV signals and fitting them with 5th degree polynomials for up to 30 min before and after the bolus infusion. The intra-patient spread of the ABV estimated in two sessions from the same week using the fitted RBV curves was 182 mL, thus significantly lower ($p < 0.001$) compared with the simple two-point approach (462 mL).

Conclusions: The proposed algorithm has the potential to be used in clinical practice for an automated estimation of ABV to support the proper ultrafiltration settings, although it needs to be validated on larger datasets and requires some improvements on the technical side of bolus infusion and RBV signal recording.

P58

IN-VITRO EVALUATION OF THE EFFECTS OF UROKINASE COATING OF INDWELLING CATHETERS ON THE RISK OF THROMBUS FORMATION ON THE SURFACE OF THE CATHETER

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Objectives: Thrombus formation in the flow paths of indwelling hemodialysis catheters impairs catheter function. Urokinase-coated catheters were manufactured with the expectation that the urokinase immobilized on the catheter surface would have long-lasting antithrombotic properties due to its fibrinolytic properties. The aim of the present study was to determine the effect of urokinase coating of catheters on the risk of thrombus formation on the surface of the catheters in vitro.

Methods: Fresh porcine blood was circulated in a simulated body circulatory circuit at a flow rate of 1.5 L/min. Three types of catheters (all 11 Fr) were inserted into the circulatory circuit: a urokinase catheter with urokinase coating (UK), a catheter with the same structure, but without urokinase coating (non-UK), and a catheter with a different structure without urokinase coating (GamCath). The indwelling catheter was used for 4h of extracorporeal circulation simulating hemodialysis, and for the remaining time, the flow paths of the catheter were filled with saline solution. The residual hemoglobin (Hb) level and residual blood lactate dehydrogenase (LDH) activity in the eluate from the blood cells attached to the catheter were measured.

Results: Thrombus formation was identified on the outside of all the catheters after both short-term (48 h) and long-term (144 h) circulation. There were no differences in the Hb levels in the eluate among the three types of indwelling catheters. On the other hand, the LDH activity was lower when in the UK catheter rather than the non-UK catheter was used, indicating that platelet adhesion was lower on the UK catheter. The eluate LDH activity was also lower for GamCath than for the non-UK catheter, indicating that the structure of the catheter was also important to decrease the propensity for thrombus formation.

Conclusions: Urokinase coating was effective for decreasing thrombus formation on indwelling catheters.

P59

IN-VITRO EVALUATION OF THE SOLUTE REMOVAL PERFORMANCE OF THE HEMODIAFILTER CLEARUM HSF

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Objectives: It is important to evaluate the basic performance of hemodiafilters under varying operating conditions, so that the removal characteristics can be determined prior to their use in a clinical setting. The present study was conducted to clarify the solute removal characteristics of the hemodiafilter Clearum HSF by varying the filtration rates under the pre-dilution or post-dilution mode in an in-vitro hemodiafiltration (HDF) experiment.

Methods: Circulation experiments were conducted using 3.6-3.8 L of bovine blood containing 30-40 μg/mL of β-lactoglobulin (β-LG) for 4 hours, by varying the filtration flow rates in the pre-dilution or post-dilution mode in online HDF. Experiments were conducted at filtration rates (QFs) of 10, 12.5, and 15 L/h for pre-dilution HDF, and QFs of 2.5, 3.75, and 5 L/h for post-dilution HDF. The sieving coefficient (SC) for β-LG, the amount of β-LG removed, and the amount of albumin leakage were measured.

Results: The SC for β-LG decreased with time and was higher in the post-dilution mode than in the pre-dilution mode. The amount of β-LG removed and amount of albumin leakage increased as the filtration flow rate increased. β-LG removal was the highest in the post-dilution HDF at QF = 5 L/h. The amount of albumin leakage was also the lowest in the post-dilution HDF at QF = 5 L/h. Albumin leakage increased as the filtration flow rate increased, but was less than 1 g/session under all the conditions; thus, the albumin leakage was not excessive, regardless of the filtration flow rate.

Conclusions: Clearum HS 20 is a hemodiafilter that allows both increased β-LG removal and increased albumin leakage as the filtration flow rate is increased in both pre-dilution and post-dilution HDF; however, it does not cause excessive albumin leakage, irrespective of the filtration flow rate.

P60

NEUROLOGICAL DISORDERS IN CHILDREN TREATED BY CONTINUOUS HEMODIALYSIS FOR INHERITED METABOLIC DISEASES

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Objectives: Two common inherited metabolic diseases, namely, ornithine transcarbamylase deficiency (OTCD) and methylmalonic acidemia (MMA), manifest as hyperammonemia and require blood purification (BP) to remove the excess ammonia (NH3). The objective of the present

study was to explore the factors that might be associated with persistent neurological deficits.

Methods: We retrospectively investigated the data of four infant cases.

Results: Case 1) OTCD, 0 year old, weight 3.12 kg, continuous hemodialysis (CHD) was performed for 11 days. The BP therapy was started 2 days after the onset. Serum NH3 level: 104 mg/dL at the start, 99 mg/dL at completion.
Case 2) OTCD, 0 year old, weight 2.90 kg, CHD was performed for 6 days. The BP therapy was started 2 days after the onset. Serum NH3 level: 7270 mg/dL at the start, 115 mg/dL at completion.
Case 3) MMA, 3 years old, weight 12.3 kg, CHD was performed for 7 days. The BP therapy was started 3 days after the onset. Serum NH3 level 384 mg/dL at start, 31 mg/dL at completion.
Case 4) MMA, 0 year old, weight 2.89 kg, CHD was performed for 4 days. The BP therapy was started 5 days after the onset. Serum NH3 level 234 mg/dL at start, 69 mg/dL at completion.
Cases 2 and Case 4 unfortunately showed persistent neurological deficits. Case 2 had a high NH3 level at the start of the therapy and in Case 4, a relatively long period of time (5 days) had elapsed from the onset until the start of the BP.

Conclusions: To avoid persistent neurological deficits, it would be desirable to start the BP therapy as early as possible to rapidly decrease the serum NH3 level and reduce the duration of exposure to elevated NH3 levels.

P61

PREDICTION, INCIDENCE AND OUTCOME OF ACUTE KIDNEY INJURY IN COVID-19 HOSPITALISED PATIENTS

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Objectives: In COVID-19 patients, acute kidney injury(AKI) is recognized as a cause of high mortality. The aim of our study was to assess the rate, predictors of AKI and survival among COVID-19 patients.

Methods: We analysed clinical and laboratory admission data, predictors of AKI and outcomes including the need for renal replacement therapy(RRT) and mortality at 30 days.

Results: Out of 115 patients 62(53.9%) presented with AKI: 21(33.9%) in stage 1, 7(11.3%) in stage 2, and 34(54.8%) in stage 3. RRT was required in 22.6% of patients and resolved in 76 %. Pre-existing CKD was associated with a 13-fold risk of AKI (p= 0.0001). Low albumin (p = 0.017), thrombocytopenia (p = 0.022) and increase of Creatine kinase over 350UI (p = 0.024) were independently associated with a higher risk for AKI. Mortality rates were significantly higher among patients who developed AKI compared to those without (59.6% vs 30.2%, p= 0.003). The low oxygen blood saturation at admission and albumin were found as powerful independent predictors of mortality (OR 0.937; 95%CI: 0.917 – 0.958, p = 0.000; OR 0.987; 95%CI: 0.885–0.991, p= 0.024, respectively). Longer survival was observed in patients without AKI compared to patients with AKI (22.01± 1.703 vs 16.69 ± 1.54, log rank p= 0.009).

Conclusions: Renal impairment is significant in hospitalised COVID-19 patients. The severity of the disease itself is emphasized as main contributing mechanism in the occurrence of AKI, and the lower blood saturation at admission is the strongest mortality predictor, outreaching the significance of the AKI itself.

P62

THIN FILMS WITH COMPETITIVE BINDING SURFACES FOR ENHANCED REMOVAL OF PROTEIN-BOUND UREMIC TOXINS

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Objectives: Hemodialysis (HD) is inefficient in the removal of protein-bound uremic toxins (PBUTs), which circulate in the blood bonded to human serum albumin (HSA). The cut-off of conventional HD membranes is lower than the molecular weight of HSA (66.5kDa) and therefore UT-HSA complexes are retained and accumulate in the body of patients with end-stage renal disease (ESRD) for the rest of their lives. Direct intravenous infusion of protein-binding competitors, like ibuprofen (IBF), has been explored to enhance PBUTs removal and results seem promising, however, concerns about their toxicity and long-term administration have triggered the search for new approaches, specifically adsorption- and displacement-based techniques. In this work, we propose the covalent bonding of IBF to cellulose actetate (CA)/silica (SiO2) to produce thin films capable of displacing PBUTs from HSA at the surface. If successful, this approach will promote competitive binding locally at the surface of the membranes inside the hemodialyzer, rather than have the drug circulating in the bloodstream.

Methods: Design and synthesis of competitive binding CA/SiO2 films by i) chemical modification of silica precursors with IBF, and ii) reaction of the modified precursor with CA/SiO2 by sol-gel reactions to produce monophasic hybrid CA/SiO2-IBF thin films.

Results: Design and synthesis of competitive binding CA/SiO2 films by i) chemical modification of silica precursors with IBF, and ii) reaction of the modified precursor with CA/SiO2 by sol-gel reactions to produce monophasic hybrid CA/SiO2-IBF thin films.

Conclusions: These findings suggest that CA/SiO2-IBF are promising membrane materials for future HD membranes capable of displacing PBUTs from HSA and thus enhance the clearance of PBUTs. Furthermore, this approach eliminates concerns regarding toxicity and long-term administration of pharmaceutical drugs, making it a promising alternative treatment to ESRD.

P63

TREATMENT WITH HIGH CUT OFF MEMBRANES IN LONG HEMODIALYSIS SESSIONS IN PATIENTS WITH MULTIPLE MYELOMA: OUR EXPERIENCE

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Objectives: Multiple myeloma(MM) presents a malignant proliferation of plasma cells,with a significant volume release of serum free light chains(sFLCs),which can cause acute kidney injury(AKI).As complication AKI can arise in more than 20% of patients with MM and half of them may require dialysis.The key to treating AKI is rapid reduction of sFLCs levels using specific chemotherapy and extracorporeal removal of sFLCs with high cut-off hemodialysis(HCO-HD),with membrane cut-off pore size (45-60kDa).

Methods: Case series:We report on two cases with MM who developed AKI and were treated with HCO-HD on our clinic.The first patient, a 74-year-old male,was admitted to our clinic after developing AKI due to MM relapse with anuria,elevated values of serum degradation products and FLC:κFLC 1770mg/l, λFLC 11.7 mg/l,rFLCk/λ152.The second patient,a 68 year old female,was referred to our clinic after started hemodialysis treatment with conventional HF dialyzers due to AKI. Because of history of lumbar pain,investigations were made and MM was diagnosed.At that time the values of FLC were: κFLC 35 mg/l, λ FLC 2420mg/l,FLC k/λ 0,0148,the values of serum creatinine and urea

remained high.Abdominal ultrasound showed kidneys with regular shape,echogenicity,secondary deposit in the liver and an ovarian cystic hiformation highly suspicious for ovarian cystadenocarcinoma. Combination of specific chemotherapy and HCO-HD sessions was started in both patients.At the beginning,6-h sessions were performed using a 2.1m2 HCO filter.Afterwards, further 7 to 8-h sessions were continued for five days in the first week,followed by 8-h per day alternate daily.

Results: The treatment proved to be effective in removing both k and λsFLCs.Mean reduction ratio(mRR) of k sFLCs of the first patient was 53% and mRR of λsFLCs of the second patient was 66%.

Conclusions: The combination of chemotherapy plus long HCO-HD was effective in reducing the level of sFLCs in both patients and recovering a sufficient degree of kidney function in the first patient, allowing significant savings and better quality of live.

P64

TWO YEARS KIDNEY FUNCTION DECLINE PREDICTING FACTORS IN LIVING KIDNEY TRANSPLANTATION DONORS

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Objectives: The study aimed to identify pretransplant donor related factors associated with renal function decline.

Methods: We retrospectively studied LDKT donors from one transplant center in the period 2013 -2022. Demographic characteristics as age, gender and relation to the recipient, patients preference to donate the kidney with higher measured split GFR, the presence of diabetes, hypertension, hyperlipidemia and BMI ＞30kg/m2 were analysed. Estimated GFR by CKD EPI was notified prior donation, one and two years afterwards. In a multivariate regression analysis the reduction ratio (RR) of CKD EPI was explored as dependent variable.

Results: We studied 121 donors. CKD EPI declined to 68.17±18.62ml/min at first and 66.01±21.29ml/min at the second year. The RR of 24.53 ± 20.60 % and 27.62±18.76% raised on yearly bases, respectively. In the univariate analysis of the GFR declination at the first year BMI＞30kg/m2 was associated with higher reduction of GFR (δ=0.318, p=0.003). At the second year the presence of diabetes emerged as worsening factor of GFR (δ=0.227, p=0.034) and BMI＞30kg/m2 kept its significance (δ=0.426, p=0.000). All the other parameters showed no significant associations to the GFR decline. In the multivariate analysis BMI＞30kg/m2 remained as most powerful predictor at 12 months reduction of eGFR.

Conclusions: Patients with diabetes and especially with obesity are at higher risk of rapid decline in kidney function after kidney donation. Careful assessment prior kidney donation should weight the risks.

Organs-on-chip

P65

A NOVEL IN VITRO MODEL TO APPLY CONTROLLED MULTIDIRECTIONAL HYDRODYNAMIC STIMULI ON HUMAN ENDOTHELIAL CELLS

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Objectives: Atherosclerosis is a chronic-degenerative occlusive disease. Alteration of the blood flow is a main pathogenic risk factors, acting on mechanotransduction mechanisms. Vascular endothelial cells (EC) are extremely sensitive to tangential stress occurring in the vessel wall (wall shear stress, WSS), related with local changes of hemodynamic. Altered WSS is a trigger of endothelial dysfunction and permeability increase. Despite this, the phenomena remain elusive.
In this scenario, we have developed a novel in vitro model allowing to apply multidirectional, complex WSS patterns in controlled conditions for investigating the effects of specific WSS on vascular EC behavior.

Methods: The bioreactor rationale is based on the combination of an input flow rate and sample rotation: thanks to this is possible to generate complex multidirectional stresses by instantly varying both the magnitude and the direction of the WSS vector.
During preliminary biological experiments (n=5) we investigated two different atherogenic condition: one unidirectional (WSS=0.1Pa, OSI=0) and one multidirectional (WSS=0.1Pa, OSI=0.2). Primary human aortic ECs were seeded (250000 cells/mm2) on custom cartridge for at least 5 days. Cell viability, distribution and morphology were assessed at fluorescence microscope.

Results: Through in silico analysis, we verified that the cartridge rotation doesn't affect the fluid dynamic inside the flow channel.
Preliminary biological results applying atherogenic WSS showed a local decrease of pseudo-capillary organization of the ECs. The phenomenon was more evident after multidirectional atherogenic stimuli, with ECs detachment, and change of EC shape in favor of more spread cells.

Conclusions: The developed in vitro model represents an innovative device with respect to the current state-of-the-art enabling the possibility to investigate different stress patterns effects. In perspective we will exploit this device to examine the complex mechanobiological interactions that occur in the sub-endothelial tissue in the early stage of the atherosclerosis pathology evolution.

P66

ANALYTE SENSORS FOR BIOLOGICAL FLUID MONITORING

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Objectives: Chemical sensors are indispensable tools for quality monitoring and analysis across a wide range of applications from the water industry, food and agriculture to health. At IMEC, using our strengths in silicon chip technology, we have achieved highly miniaturized and mass (re)producible chemical sensing solutions to adapt to existing and emerging technological markets. The next step is to bring this silicon technology enabled sensing to the health domain.

Methods: Electrochemical

Results: Over the years we have developed a variety of chip-based sensors, of dimensions ＜1cm2, for electrical conductivity and a wide range of ions, including a built-in microfluidic reference electrode on a chip, a key component to any electrochemical based system. These sensors have been demonstrated in real world applications such as surface water quality monitoring and nutrient monitoring in greenhouses. For example, in the Flanders region, real time continuous conductivity and pH data was obtained for over 6 months, demonstrating the reliability of the sensor chip technology for demanding applications.

Conclusions: Our vision is to expand our sensing expertise towards biomedical applications, like organ-on-chip (OoC), bioprocess analytics, artificial organs (AO) and eventually implantables. Such a sensor must comply with more stringent requirements, for instance, biocompatible and non-cytotoxic materials and packaging. Within NextGen High Tech Project funded by the Dutch Growth Fund Initiative, IMEC the Netherlands will be defining the (bio) chemical sensor roadmap for miniaturized inline sensing with first applications foreseen in OoC and AO

(artificial kidney). Our first sensor designs target to bring up to 100 sensing electrodes in a space of 7.5mm × 7.5mm (industrial standard for OoC), to allow for multiple analyte detection, giving higher throughput and replicate measurements.

P67
ORGANS-ON-CHIP WITH AN INTENDED MEDICAL PURPOSE: REGULATORY ISSUES

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Objectives: Organ-on-chip (OoC) devices have great potential in fulfilling the promises of personalized medicine, by recapitulating a specific person's physiology. This study's objective is to clarify the regulatory framework for OoCs with a medical purpose.

Methods: Depending on the intended use of the device, regulatory requirements for OoCs (which do not have yet a specific regulation) can be derived. European regulations have been considered, in order to determine their applicability to OoCs.

Results: OoC devices with diagnostic purposes are functionally similar to in vitro diagnostic (IVD) medical devices (MDs): they may provide information on physiological/pathological processes; predict treatment response/reactions; monitor therapeutic measures. However, IVD MDs cannot contain viable cells/tissues of human or animal origin (according to MD regulation (MDR), "'non-viable' means having no potential for metabolism or multiplication"), which hinders the applicability of the IVD regulation (IVDR) to OoCs.
An OoC may also have a therapeutic intended purpose: e.g., the availability of an implantable liver-on-chip, capable of substituting liver functions upon implantation, cannot be ruled out, in the future. This would require the demonstration of its safety and efficacy. OoCs of this category are similar functionally to a MD, according to the latter's definition. The scope of the MDR, though, excludes the use of viable cells/tissues (either of human or animal origin) in the fabrication of MDs, therefore such OoCs cannot be not regulated exclusively by the MDR.
A more appropriate regulatory framework is the Advanced Therapy Medicinal Product (ATMP) Regulation 1394/2007. In particular, OoCs can fit well, at certain conditions, into the definition of "combined ATMP", since it incorporates, as an integral part of the product, one or more MDs, besides the cellular component.

Conclusions: There is a need to adapt the current regulatory frameworks to the case of OoCs with diagnostic/therapeutic functions, in order to assure safety and efficacy of such devices.

Tissue Engineering and Biofabrication

P68-FT
DESIGNING ELASTIC PROPERTIES OF 3D PRINTED MULTIMATERIAL SCAFFOLDS

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Objectives: 3D printing enables the rapid production of many complex structures, such as porous scaffolds for bone reconstruction or orthopedic applications. However, for applications where specific elastic properties are required, there may not be suitable materials available on the market. Material jetting, a 3D printing method that processes multiple materials together in a printed part, allows the creation of multimaterials with new properties and the creation of mechanical gradients. This study focuses on how to predict the resulting Young's modulus and Poisson's ratio of 3D printed matrix-inclusion composites with varying volume fractions.

Methods: Measurement data was obtained from tensile tests performed in accordance with ISO 527 using commercially available materials (VeroClear, RGD8530, RGD8430, Stratasys Ltd., USA). The matrix inclusion composites that were tested had cubic inclusions with volume fractions of f=10%, 30%, 45% RGD8530/RGD8430 in a VeroClear matrix. In addition, the geometry of the printed parts was examined using optical coherence tomography (OCT). Multimaterial homogenization and finite element (FE) simulations have been evaluated and compared with the measured data to create a model that is capable of predicting the multimaterial properties from the knowledge of the pure material properties.

Results: Measurements showed that the Young's moduli of the multimaterials were lower than the weighted average of the pure materials (up to 26.5±2.7% softer for f=45%). OCT scans showed deviations from the digital design, most notably the rounding of the edges of the cubic inclusions. A valid simulation can be obtained taking into account modified geometries and non-ideal bonding of the printed materials.

Conclusions: In conclusion, this study has investigated how 3D printed multimaterials behave and what aspects need to be considered when predicting their elastic properties. This knowledge allows for the design of structures with precisely defined properties and even gradients in Young's modulus for advanced structures and scaffolds for bone grafting.

P69-FT
ADDRESSING CHALLENGES IN 3D MODELING AND PRINTING FOR VIRTUAL AND RAPID PROTOTYPING OF DEVICES FOR SUBSTITUTIVE MEDICINE AND TISSUE ENGINEERING

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Objectives: The increasing demand for the timely availability of biomedical devices in laboratories and clinical practice requires expedited design and development processes through 3D modeling. Simply having a 3D model does not guarantee a functional printed object, because properties such as surface quality, morphological conformity, stability, and biocompatibility must be considered. This study aims to propose a protocol for generating comprehensive 3D models that can be adapted throughout all stages of medical device development, from concept to fabrication to utilization, without compromising the overall design integrity.

Methods: Advanced 3D modeling tools were used in the study, such as CAD software PTC Creo release 8, CAE software Comsol Multiphysics, and Zortrax Inkspire 3D printer with basic and medical-grade resins. Focus was on addressing geometric complexity challenges, particularly in rounded areas with merged surfaces, when transferring models between different applications using interchange file formats such as IGES, STEP, and STL. Various medical device models were produced. Particular attention was given to bioreactor design for ovarian tissue culture, which required a thorough investigation of arising specific issues.

Results: Modifications were made to geometry to minimize distortions in Multiphysics simulations, with a focus on tissue perfusion with the medium in bioreactors. Adjustments were also made to export and processing parameters for 3D printing, resulting in a set of recommendations for defining a protocol based on best practices. Notably, parameter adjustments were made after measuring the printed part's geometry in the metrology laboratory.

Conclusions: Developing a single 3D model meeting the requirements of CAE simulations, 3D printing, and other fabrication techniques is challenging. Even if successfully generated, the model needs to account for way too many factors and variables that influence the final outcome. In such cases, the expertise and capability of the operator play a crucial role in the virtual and real prototyping of custom-made medical devices.

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DETERMINATION OF SALIVA CONTENT IN AEROSOLS RELEASED BY DENTAL PROCEDURES

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Objectives: The SARS-CoV-2 pandemic has created a great demand for a better understanding of the spread of aerosols. Especially the aerosol released during dental treatment may be contaminated with infectious saliva. However, the risk of an infection during dental treatments caused by aerosol transmission from patient to dentist is currently unclear. The aim of this investigation is to create a model to evaluate the amount of potential infectious saliva in dental aerosol as well as droplets to estimate the risk for dental staff.

Methods: To create the dental aerosol the attending dentist is using a dental turbine (DT), contra angle high-speed handpiece (CAH) and an ultrasonic scaler (US) in an artificial oral cavity. To measure the amount of saliva in the aerosol, the patients saliva flow is simulated by a tracer fluid (20% NaCl, 1 ml/min) while the dental tool coolant is ultrapure water (50-80 ml/min). To determine the full amount of produced aerosol, in a reference measurement, the tracer fluid (20% NaCl, 50-80 ml/min) is used as coolant. Above the artificial oral cavity, the aerosol-enriched air is sucked into the absorber. The absorber consists of a reservoir with ultrapure water, whose electrical resistance is measured to determine the amount of dissolved NaCl tracer from the aerosol. There were 10-11 measurement repetitions per dental tool. Methods to reduce the aerosol, such as room air filters and dental suctions devices, were also considered.

Results: The total amount of aerosol has a significant difference with 121 mg CAH 69 mg DT and 10 mg US. Nevertheless, there is an insignificant difference in the dissolved saliva outcome of the three tools with 0.137 mg ($\pm$0.0025).

Conclusions: The presented model can determine the amount of contaminated Aerosol released by dental procedures. It shows that the amount of saliva in the detected aerosol is insignificant.

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3D PRINTABLE HYDROGELS OF HYALURONIC ACID AND GELATIN BASED ON ENZYMATIC CROSSLINKING

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Objectives: The aim of this study is the development of bioinks of hyaluronic acid (HA) and gelatin (Gel) based on enzymatic crosslinking to build structures with high fidelity and good cell viability for liver tissue engineering

Methods: Two compositions were explored: HA and HA-Gel 80-20, which were optimized for extrusion bioprinting from different solutions in a cell friendly buffer, from 1% to 5% w/v. Grid structures were prepared. Viscosity was analyzed by oscillatory rheology. Fiber uniformity and pore ratio were evaluated to assess the printing resolution by ImageJ software. HepG2 cells viability was assessed post-printing and after 1 day of culture using 4% and 5% bioinks and two types of nozzle 20g and 22g.

Results: Viscosity of HA bioinks 3% to 5% and HA-Gel 4% and 5% was similar to Cellink standard bioink, which made them promising as bioink candidates. Uniformity and pore ratio revealed that highly viscous bioinks were more suitable for bioprinting, HA 4%, and HA-Gel 4% and 5% produced more precise and well-shaped constructs. HepG2 cells were alive after the printing process in all conditions. Cells within the HA-Gel 5% bioink were less viable than in HA-Gel 4% due to the higher-pressure requirements on the printing process as the viscosity increases. After 1 day of cell culture, cell viability was similar in both hydrogels, HA-Gel 4% and HA-Gel 5%. Nozzle diameter had no influence on cell viability for any condition

Conclusions: Enzymatic HA-Gel bioinks were optimized for bioprinting purposes. 4% and 5% solutions can be extruded with great resolution, incorporate cells, and print them without compromise cell viability.

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A SYSTEM FOR AUTOMATIC MIXING OF TWO COMPOSITIONS OF CULTURE MEDIA AND MEDIUM EXCHANGE IN THE ARTIFICIAL BLOOD VESSEL MODEL

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Objectives: This work aimed to develop a system for automatic mixing of two compositions of culture media in order to produce a culture medium with an intermediate composition, and medium exchange in culture vessels. The effectiveness of the system was assessed in two parallel cultures of endothelial cells seeded in bioreactors on the inner surface of semi-permeable membrane capillaries.

Methods: The developed system automates the exchange of medium in several culture vessels during static cultures or in flow bioreactors. The system takes fresh media of different compositions from two containers mixing them in a controlled proportion. The system consists of: the computerized control unit, peristaltic pump for medium replacement, two containers with culture medium and two independent circulation circuits with the multi-channel peristaltic pump supplying two bioreactors seeded with cells. The system removes the same volume of medium from the circulation circuit that it delivers during the medium exchange, regardless of the differences in the accuracy of the pump channels.

Results: We assessed effectiveness of the system in the simplest case scenario when no media mixing was required. We used media with two different glucose concentrations, i.e. 5 mM and 30 mM, investigating what volume of circulating medium needs to be replaced in order to achieve a new target glucose concentration with a relative error lower than 10%. Threefold exchange of the circulating medium volume (3 x 23 mL) was sufficient when increasing the glucose concentration, whereas the decrease in the glucose concentration required a fourfold exchange of the circulating medium volume.

Conclusions: The developed system exchanges culture medium, ensuring that new target concentrations of medium components are achieved with adequate accuracy. It can be used to automatically stimulate cultured cells using time varying stimuli.

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P73-FT

ANALYSIS OF FILTRATION AND BACKFILTRATION IN HOLLOW FIBER MEMBRANE BIOREACTORS

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Objectives: Hollow fiber cell reactors provide a huge surface area for cell attachment on the outer fiber bundle within a cartridge. Cells are supplied with substances flowing through the inner fiber volume, and the dominant transport process for this feeding is diffusion. Cell lines grow around the fibers and are not in contact with the media flow. However, filtration and backfiltration across the fiber membrane due to the pressure gradient along the fiber length is always present during operation of a cell reactor. The objective of this study is to look at possible consequences for the cell lines.

Methods: Data of Schneditz et al. about internal filtration in high-flux dialyzers during simulated hemodialysis were analyzed with regard to the mean transit time of an albumin-bound, non-diffusive indicator. The average fiber flow QB was quantified by integration of modeled local flow over the fractional length of the hollow fiber bundle.

Results: Flow of the medium in the hollow fiber continuously decreases in the first half of the hollow fiber. After reaching a minimum close to the center of the cartridge module, flow continuously increases again because of backfiltration and finally gets back to the original value when reaching the fiber exit.

Conclusions: Within the cartridge, cells are exposed to shear stress. In the middle zone, shear stress is minimal but diffusion through the membrane wall is lowered due to viscosity increase of the fluid inside of the hollow fiber. In the rear zone, cells are living in a depletion environment because cell degradation products from the front zone have to pass these cells to follow backfiltration into the hollow fiber.

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P74

APPLICATION OF NMR SPECTROSCOPY TO MONITOR METABOLIC PROFILES OF ENDOTHELIAL CELLS CULTURED IN VITRO

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Objectives: This study aimed to assess the feasibility of using NMR spectroscopy to investigating metabolic profiles in human umbilical vein endothelial cell (HUVEC) culture medium under in vitro conditions.

Methods: HUVECs were isolated, grown in culture flasks, mixed from 10 donors, and cultured in culture plates for 14 days in three variants of culture medium, i.e. with 5 mM glucose (N), with 5 mM glucose and 50 µM ascorbic acid (N+VitC), and with 30 mM glucose and 50 µM ascorbic acid (H+VitC). The culture medium was changed daily. Medium samples after the 1st, 3rd, 5th, 7th, 10th and 14th day were used to acquire NMR spectra. The signals in the 1H NMR spectra were assigned to 30 compounds. We analyzed the intensity of signals that correspond to the concentrations of the compound in the sample.

Results: We analyzed intensities of the NMR signals of: Formate, Histidine, Phenylalanine, Tyrosine, alpha-D-Glucose, beta-D-Glucose, Myo-inositol, an unidentified component of endothelia cell growth supplement (ECGS), Glycine, scyllo-Inositol, Glucose, Creatinine/Creatine, Citrate, Glutamine, Pyruvate, Glutamate, Acetate, Lysine, Alanine, Lactate, Valine, Leucine, and Butyric acid. We noticed that unidentified component of ECGS was released by cells to medium in very large amounts (32, 24 and 30 times higher than in the pure medium in N, N+VitC and H+VitC, respectively). The level of glucose and VitC in the culture medium influences the metabolic profile of HUVECs. For example, the average concentration of Phosphorylcholine decreases from 161% in N to 129% in N+VitC and 91% in H+VitC, whereas concentration of Phenylalanine is almost not affected (118%, 118% and 112%, respectively).

Conclusions: NMR spectroscopy is a feasible technique, which can be used to monitor metabolic profiles in samples of HUVEC culture medium under in vitro conditions.

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P75

BIOMATERIALS USED FOR CLINICAL 3D BIOPRINTING OF BIONIC ORGANS WITH A FLOW SYSTEM: ASSESSMENT OF HEMOCOMPATIBILITY

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Objectives: Hemocompatibility of blood-biomaterial interactions is one of the most important criteria for their success in vivo applicability. Blood-biomaterial interaction can activate the coagulation cascade. Therefore, it is crucial for medical devices, as well as bioinks used for 3D bioprinting of bionic organs to be hemocompatible. Biomaterials should allow direct contact with blood without a clotting effect. The regulation of blood coagulation is then a key issue in the development of biomaterials for medical applications.

Methods: The experiment was conducted on porcine whole blood without anticoagulant. The following biomaterials were used: methacrylate gelatin (GELMA), methacrylic hyaluronic acid (HAMA); methacrylate alginate (ALGMA), methacrylate chitosan (CHIMA), biomaterials based on extracellular matrix (dECM), pluronic (PLU), alginate (ALG), hyaluronic acid (HA) and positive control. The blood was added to the surface of the cross-linked biomaterials. The samples were incubated during 1,3,5,8,10,12,15,20,25 and 30 minutes intervals. Then 1ml of water was added. Samples were shaken for 30sek at 300rpm. The absorbance was reading at 540nm. The higher the absorbance value, the higher the concentration of hemoglobin, which means less blood clotting on the surface of the biomaterial.

Results: The analyzed biomaterials are significantly different in terms of hemocompatibility. PLU was characterized by immediate clot formation. At the 10th minute, the degree of hemolysis was also significantly lower in the case of ALG. Advantageously, the highest degree of hemolysis was found in dECM-based bioinks, regardless of their concentration. Thus, it was shown that dECM does not increase the coagulability of the tested blood.

Conclusions: Not every biomaterial due to the material composition despite preferential physicochemical properties and a beneficial effect on the viability and functionality of cells in vitro tests, will be suitable for bioprinting of bionic organs having direct contact with blood after implantation.

P76

CONSTRUCTION OF THE MODEL OF BIOLOGICALLY ACTIVE FUNCTION BLOCK OF IMPROVED BAL DEVICES

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Objectives: Liver diseases are one of the most frequent causes of death worldwide. Currently, liver transplantation (LT) is the only cure for its failure. Unfortunately, donor shortage is a great limitation to this therapy. One of the most promising alternatives for LT are bioartificial livers

(BALs). These hybrid devices constitute a bridging therapy for patients waiting for LT. The most advanced system is ELAD, which came to the third phase of clinical trials. However, ELAD did not live up to expectations. The device utilizes the C3A human hepatocellular carcinoma cell line, which has non-functional urea cycle (lack of ARG1 and OTC genes expression) and this could be a reason for its clinical trials failure. Here we show the construction of the model of the biologically active function block, based on genetically modified hepatic tumor cell lines, that can be applied in an improved BAL.

Methods: In order to restore urea cycle we conducted genetic modification of C3A cells using lentiviral vectors. We proposed two different approaches – transgenes were carried on by the same lentiviral vector or by two different vectors. After establishment of the new cell lines we compared them with their parental C3A cells in dynamic culture. These conditions were ensured by flow system constructed in our laboratory, based on polysulfone hollow fiber bioreactors. At the end of the experiment cells' viability was determined using trypan blue exclusion method. Then glucose consumption (colorimetric method) and albumin production (ELISA test) in collected media samples were measured.

Results: Obtained results showed that in dynamic culture both genetically modified cell lines were characterized by higher albumin secretion and increased glucose consumption than their unmodified counterparts. Comparison of stationary and dynamic conditions indicated that flow culture ensured better environment for hepatic cells growth.

Conclusions: Summarizing, genetically modified cells outperformed their unmodified counterparts.

P77
DEVELOPMENT OF LIPOPLEX-LOADED SURFACE COATINGS FOR CONTACT-TRIGGERED TRANSFECTION

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Objectives: The release of bioactive substances from smart biomaterials after implantation holds great potential in regenerative medicine due to its ability of precisely targeted, local application. Layer-by-Layer (LbL) material deposition provides the possibility to build thin-film coatings with controlled thickness on various surfaces. Therefore, it is widely used in the field of surface functionalization. The development of LbL coatings loaded with biological active substances is of special interest to control cell behaviour. An upcoming field is the functionalization with nucleic acids to achieve an in situ transfection for controlled protein expression.
In this study the LbL technique is applied to generate lipoplex embedding surface coatings that are composed of hyaluronic acid and chitosan [1]. By using LbL deposition it is intended to create a surface coating which results in high transfection efficiency. Our aim is to get insights in the properties and the control of the transfection activities.

Methods: Basal polyelectrolyte multilayers (PEM) are prepared by alternating incubation of the surface with the oppositely charged polyelectrolytes. After a stable basal PEM is fabricated, the lipoplexes are adsorbed and cover layers are added, which have a protecting effect on the lipoplexes. The gene expression analysis is performed by encapsulating a GFP-encoding pDNA in the lipoplexes, allowing a quantification of transfection events by fluorescence microscopy and flow cytometry.

Results: Investigations of the kinetic of the transfection achieved with the lipoplex functionalized PEMs has were carried out and the effect of the number of cover layers on the transfection kinetics was studied, which opens up the possibility to engineer in situ transfection systems with a time-controlled mode of action.

Conclusions: This work demonstrates that gene-functionalised surface coatings are a smart strategy to provide growth factors and other signalling proteins in the field of regenerative medicine.
[1] C. Husteden et al. ACS Applied Materials and Interfaces 2020, 12, 8963–8977

P78
ELECTROSPUN PCL AND PLA SCAFFOLDS FOR TISSUE ENGINEERING FOR HYPOTHERMIC STORAGE

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Objectives: In tissue engineering, cell seeded scaffolds aim to regenerate tissue defects. In this regard, electrospun scaffolds demonstrate a suitable approach since they can mimic the native extracellular matrix. Compared to the cryogenic storage of tissue and tissue engineered constructs, hypothermic preservation is sufficient to store living material for short duration at lower technical requirements. Before preserving cell seeded scaffolds under hypothermic conditions, we analyzed their general properties.

Methods: Fibrous scaffolds were fabricated by electrospinning. Briefly, polycaprolactone (PCL) and polylactic acid (PLA) were dissolved in hexafluoroisopropanol (HFIP). Four different ratios were chosen: (1) PCL 150 mg/ml, (2) PCL/PLA 100/50 mg/ml, (3) PCL/PLA 75/75 mg/ml, and (4) PCL/PLA 50/100 mg/ml. Electrospinning was performed in vertical and horizontal set-ups. The morphological, thermal and chemical properties of the obtained fiber mats were characterized with SEM, DSC and FTIR, respectively.

Results: FTIR measurements of the electrospun scaffolds have shown the characteristic bands and confirmed that no residual solvent could be detected. Additionally, the DSC investigations showed that the electrospinning process did not majorly change the thermic properties of the materials. Exceptions were the crystallinity of PCL which was in the range of 44% and 71% and PLA being between 40% and 50%, depending upon the blend ratio and electrospinning set-up. SEM analysis confirmed a mean fiber diameter between 1,68 µm and 4,19 µm. Fibers were randomly aligned.

Conclusions: PCL/PLA blended scaffolds were successfully manufactured and can be manipulated by influencing the process parameters. Ongoing investigations will reveal the cytocompatibility and the preservation outcome of hypothermic preserved cell seeded constructs in different preservation media.

P79
EVALUATION OF BETA CELL VIABILITY AND FUNCTIONALITY DEPENDING ON DECM CONCENTRATION IN BIOINK

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Objectives: The key element of bioprinting is the use of appropriate biomaterials that provide appropriate conditions for the diffusion of nutrients and oxygen exchange. Thus, they will allow you to maintain maximum cell viability and functionality. One of the most popular biomaterials are biomaterials based on dECM. The purpose of this study was to check whether the upper limit in the dECM content of bioink.

Methods: The final bioink contained 2% to 16% dECM. Functionality (GSIS) was assessed and histological analysis was performed. In addition, cytotoxicity tests were performed.

Results: All tested variants enabled bioprinting of stable constructs. Depending on the dECM content, the pressure was 6-48kPa and the temperature was 16-25°C. Cytotoxicity analysis showed that cell viability is reduced for variants with more than 13% dECM. The best results were obtained for bioinks containing up to 11% dECM. Moreover, the addition of dECM in the range of 8-11% showed up to 25% higher cell growth than in the group of untreated cells. Cell functionality was also highest with bioink containing up to 11% dECM. However, the highest results were obtained for the 5% and 8% variants. Histological analysis showing 3-fold increase in insulin signal in bioinks up to 11%. Keeping the best result for 5% and 8% dECM.

Conclusions: It has been shown that the concentration of dECM should be selected experimentally. In the case of beta cells, it should not exceed 11%. However, it should be noted that in vitro and in vivo results may differ. It is related to the process of diffusion of nutrients. Once implanted in the body, a fully compatible construct becomes vascularized. In this way, the exchange of nutrients takes place more easily. Therefore, the concentration of dECM in the final bioconstructs may be higher.

P80

DEDIFFERENTIATED HUMAN HEPATOCYTES – CELLS CHARACTERIZATION

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Objectives: Currently, the only effective treatment of patients with liver failure is organ transplantation. However the main problem of this therapy is donor shortage. Scientists are searching for the alternative therapies to extend patients' life till transplantation. The most promising results were obtained for hybrid devices called Bioartificial Liver (BALs). The best possible source of cells for these systems are human isolated hepatocytes.

Methods: In our laboratory, we have elaborated human hepatocyte isolation method, which is based on mechanical defragmentation and enzymatic digestion of liver tissue. This method enables isolation of the whole spectrum of liver cells. Using a special culture medium dedicated to hepatocytes we obtained dedifferentiated fibroblasts-like cells which can divide and still produce markers characteristic for hepatocytes. These new cells, called Liver Derived Fibroblasts (LDF), are designated to be used for seeding our self-manufactured hollow-fiber flow bioreactors. This culture module constitutes our model of the novel biologically active function block of improved BAL.

Results: Preliminary Results obtained from flow cytometry, immunostaining, and ELISA tests clearly showed that our new cells could still produce albumin, a characteristic protein for hepatocytes, even after dedifferentiation. Moreover, we could also observe urea production by the LDF.

Conclusions: We concluded that this biological material, capable of proliferation and expressing some liver-related features, is suitable for further use in our model.

P81

GELATIN-HYALURONIC ACID SCAFFOLDS FOR THE TREATMENT OF ACUTE LIVER FAILURE

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Objectives: Liver transplantation is widely used as a definitive therapeutic option for acute and chronic liver diseases. However, the shortage of liver donors has encouraged the development of alternative approaches. Cell-based liver therapies are a good alternative to liver transplantation. Nevertheless, the low engraftment capability and the reduced functional quality of primary human hepatocytes (PHH) limits its broader application. Three-dimensional materials containing PHH have been proposed to improve cell therapy outcomes, as they preserve the in vivo extracellular environment by enabling cell-matrix and cell-cell interaction. The aim of this study is to explore the suitability of an optimized scaffold of gelatin-hyaluronic acid (Gel-HA) seeded with PHH for the treatment of liver failure.

Methods: Scaffold was prepared by enzymatic crosslinking. Mechanical properties and morphology were analyzed. Human hepatocytes were seeded within the scaffold and their functionality was assessed. Scaffold seeded with PHH was implanted in mice with acute liver failure induced by an overdose of acetaminophen (APAP). Animal survival, transaminases levels, ophthalmic acid and cytokine levels were analyzed after transplantation.

Results: The mechanical properties of the scaffold were close to the human liver with an interconnected porosity of 102 μm pores size. PHH cultured in the Gel-HA scaffold exhibited increased albumin and urea secretion and enhanced metabolic capacity compared to standard monolayer cultures. The transplantation of the scaffold containing PHH led to an improvement in liver function (transaminase levels, necrosis) and ameliorated damage in a mouse model of APAP-induced liver failure. Further, the study provided mechanistic understanding of APAP-induced liver injury and the impacts of transplantation by analyzing cytokine production and oxidative stress induction to find suitable biomarkers of cell therapy's efficacy.

Conclusions: The GEL-HA scaffold is a promising material for liver tissue engineering as it enhances hepatocyte functionality and improves the outcomes after implantation in an animal model of liver failure.

P82

IN PURSUIT OF BIODEGRADABLE ALTERNATIVES TO SILICONE FOR ENDOTHELIAL TISSUE REGENERATION OF THE DIGESTIVE TRACT

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Objectives: Poly (glycerol sebacate) (PGS) is a biodegradable polymer that is synthesized by polycondensation between glycerol and sebacic acid. It is a polyester with suitable characteristics for tissue regeneration such as good mechanical properties and biocompatibility. Furthermore, it is biodegradable, a very important characteristic that makes it a perfect candidate for its use in biomedical applications. Due to the flexible and elastomeric nature of PGS, it's been typically oriented towards replacement and engineering of soft tissues. In addition, its mechanical properties and degradation kinetics can be modified and adjusted to suit the requirements of the application in which it is to be used.

Methods: To do this, PGS is combined with other biodegradable materials (such as gelatin, polyethylene glycol, polycaprolactone, polylactic

acid, etc.). In this sense, characterizations of the materials obtained have been carried out referring to their mechanical, thermal and physicochemical properties.

Results: In this study we have synthesized and characterized a copolymer that combines PGS with gelatin to suit the challenging scenario presented within the digestive tract. A Design of Experiments has been used to understand how to improve the percentage of gelatin present in the material, and the reaction time. It was possible to maintain the standardization of the samples used in these tests, as described in the UNE EN ISO 527-2, by making a 3D printed mold for tensile specimen.

Conclusions: The physicochemical characterization confirmed the copolymerization reaction. In addition, the thermal behavior of the copolymer meets the requirements of the application keeping its integrity around physiological temperature.

P83

LIVER BIOCONSTRUCTS CREATED WITH INK-JET TECHNOLOGY FOR TESTING DRUG ACTIVITY AND TOXICITY

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Objectives: In the process of pharmacological research, a reproducible model representing the complex microenvironment of the human liver is still missing. Studies typically use 2D cultures, co-cultures, or spheroids that meet most testing needs but do not address the toxicity in the microenvironment of human tissues. This problem can be solved with bioprinted tissue models. The creation of such a bioconstruct is conditioned by the properties of the biomaterial, such as the stimulation of gas exchange and the distribution of nutrients, while maintaining the printability to create complex structures, such as hepatic lobules. We characterized the biocompatibility of biomaterials intended for the production of bioconstructs mimicking the microenvironment of human liver tissue.

Methods: We developed two formulations of biomaterials. The first consisted of methacrylates: gelatin and hyaluronic acid. The second was additionally enriched with decellularized extracellular matrix. Both variants contained the LAP photoinitiator. Hepatocyte and endothelial lines were suspended in culture medium and then mixed with the biomaterial. The hydrogel drops were created using ink-jet technology and crosslinked at 405 nm. The bioconstructs were cultured for 21 days on inserts. Microscopic imaging was performed using a live/dead staining, and the material was preserved for histological analysis.

Results: FDA/Pi staining showed high viability of the bioconstruct, staining more than 90% of viable cells with FDA, and only a few cells were stained with Pi. In addition, direct microscopic observation and histological examination showed an uniform distribution of the spherical cells with the ability to proliferate. Therefore, cells tend to form spheroids and migrate towards the surface of the bioconstruct.

Conclusions: Both bioinks showed biocompatibility with the liver cell line and therefore will be used for the bioprinting of liver tissue models with the flow system. The generated models will be applied in cytotoxicity and activity studies of biologically active substances.

P84

MANUFACTURING OF PLLA/PVA ELECTROSPUN MEMBRANES USING GREEN SOLVENTS FOR OCULAR AUTONOMOUS DRUG DELIVERY SYSTEM

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Objectives: Around 14 million cataract operations are performed globally per year, and this number has increased steadily over the past few decades due to population ageing among other reasons. All cataract patients will have to use various medications eye drops after surgery with different dosage regimen to protect them from infection, inflammation, and pain. This treatment requires a regimen of drops in a descending pattern, not easy for the elderly who may need the help of someone else and/or been dependent. For this reason, the average noncompliance rate for eyedrop treatment has been shown to be approximately 30%. Poor compliance can impact clinical outcomes and can lead to complications such as endophthalmitis or macular edema. Our approach is to synthesize biodegradable membranes for postoperative ocular insert that allow controlled drug release at different time points.

Methods: Electrospinning (ES) was selected since it is versatile method which provides the ability to encapsulate multiple drugs and control their release profiles. This technology produces micro/nanometer diameter fibers with a large surface area, high flexibility and superior mechanical properties. Polylactide acid (PLLA) and Polyvinyl alcohol (PVA) membranes were synthetized by diluting their monomeric compounds into green solvents, such as DMSO and ethyl acetate, in different proportions and then used for electrospinning. Thermal, physicochemical, and mechanical analysis were performed, together with degradation studies.

Results: PLLA and PVA membranes based on microfibers were obtained by using greener solvents dilutions. Fiber diameter were around 1-2 µm depending on the material and solvent composition. Physicochemical techniques confirmed no solvent remain in the membrane after synthetized. Differences were obtained regarding degradation times, directly related to its thermal and mechanical properties.

Conclusions: Biodegradable membranes of PLLA and PVA were obtained with properties that suits our demands to be used as an ocular insert for postoperative autonomous drug delivery system.

P85

MULTIPOTENCY AND OSTEOGENIC DIFFERENTIATION OF HUMAN BONE MARROW MSC CULTURED ON PROTEIN OR POLYSACHARIDE FUNCTIONALIZED SUPPORTS

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Objectives: The aim of this work was to demonstrate the effect of protein or polysaccharide substrates on the adhesion, proliferation, and osteogenic differentiation of human bone marrow mesenchymal stem cells (hBMMSCs) cultured in 2D or 3D environments.

Methods: Synthetic flat substrates or microspheres around 150 microns were prepared using a random copolymer of ethyl acrylate (EA), ethyl methacrylate (EMA), and acrylic acid (AA), poly(EA-EMA-AA). Heparin or gelatin was grafted on the surface of the substrates using carbodiimide chemistry. The hBMMSCs were isolated from normal bone marrow aspirates of non-neoplastic patients under informed consent, and expanded

until passage five. Flow cytometry was used to assess the presence of the characteristic multipotency markers CD73, CD90, and CD105, while gene expression was studied by RT-qPCR.

Results: hBMMSCs cultured in expansion medium in monolayer showed a decrease of adhesion and viability as the AA content augmented, due to the increase in the hydrophilicity of the substrate, and they were found not viable in the substrates containing 10% AA. In 3D environments, cells actively proliferated even with microspheres with the highest contents of AA. Both functional coatings supported osteogenic differentiation in osteogenic medium, as evidenced by the expression of characteristic genes. Gelatine favoured spontaneous osteogenic differentiation while heparin induced the loss of multipotency markers in basal medium.

Conclusions: Grafting of functional protein or polysaccharide on the culture substrate strongly affected the biological response of hBMMSC.

P86

NON-WOVEN ELECTROSPUN SCAFFOLDS WITH CONTINUOUS GRADIENT FROM HONEYCOMB-LIKE TO ALIGNED STRUCTURES FOR OSTEOTENDINOUS JUNCTION TISSUE ENGINEERING

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Objectives: Microstructures in electrospun scaffolds are known to guide the differentiation of stem cells. We already showed that honeycomb-like structures and aligned fibers seem to promote the fate of C3H10T1/2 cells line as bone and tendon cells respectively. In order to propose a continuous gradient of those structures mimicking the tendon insertion to bone, a novel electrospinning system has been developed combining micropatterning and gap-spinning. This biphasic structured non-woven scaffold has to be both mechanically and biologically characterized in order to engineer a continuous junction from bone to tendon.

Methods: Photolithography was used to manufacture microstructures on wafer used as a part of the electrospinning collector. Solutions of 10 and 12%wt/v polycaprolactone were used to produce fibers with/without beads, respectively. Elastic moduli of each phase of the material were determined thanks to uniaxial tensile test with Region Of Interest. C3H10T1/2 cells were then seeded on the scaffolds without any differentiation factor during one week in static and dynamic conditions. The viability and proliferation were evaluated by Live/Dead kit, MTT assay and the early differentiation by ALP Activity. Immunostaining and ALP staining were used to observe the fate of C3H10T1/2 cells line as bone and tendon cells respectively. Moreover, the scaffolds and the cells were observed on SEM.

Results: This new collection system permitted to create two microstructured phases with a continuous gradient from honeycomb-like structure to aligned fibers. The honeycomb-like phase reached an elastic modulus of 80-100 MPa whereas the aligned phase reach 130-150 MPa. Confocal microscopy has shown tendon differentiation in the aligned region. Similarly, ALP has been denser on the honeycomb region than the aligned region, corresponding to the early differentiation of cells to bone.

Conclusions: We have validated this new production technic leading to a novel biphasic structured non-woven scaffold to achieve tissue engineering of enthesis.

P87

OPTIMIZATION OF ELECTRO-SPINNING PROCESS FOR PRODUCTION OF SMALL TUBULAR STRUCTURES WITH HIGH FIBRE YIELD AND STABLE PROPERTIES

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Objectives: In order to create small tubular structures with an inner diameter less than 1 mm for tissue-engineered constructs, the electrospinning technique is commonly used. However, the use of a small collector means that process parameters greatly affect the yield of fibres and the structure of the scaffold. The purpose of this study is to optimize the electro-spinning process to produce stable and high-yield small tubular structures.

Methods: During the study, the effects of various electro-spinning parameters were analysed and a new setup was designed to control climatic conditions and apply negative potential to the collector. By optimizing control variables through statistical experimental design, maximum fibre yield and process stability were achieved. Structural characterization was carried out to determine the mass, thickness, and fibre structure of the scaffold, and SEM images were taken for further characterization. Statistical analysis and regression models were implemented to determine correlations between manufacturing parameters and fibre yield, as well as scaffold structure properties.

Results: The study resulted in a significant increase in fibre yield from less than 25% to over 90%, and a stable and reproducible process was established. Additionally, scaffold properties could be adjusted based on the investigated parameters.

Conclusions: The study's methodology and the new setup have cost-effective implications for further process establishment, and are transferable to other applications such as the production of nerve channels and scaffolds that guide the growth of nerve fibres.

P88

OVERCOMING OF PHOTOINITIATOR LIMITATIONS. SELF-CROSSLINKING MATERIAL FOR BIOPRINTING APPLICATION

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Objectives: Main aim of presented research is to develop photocurable material basing on gelatin derivatives which do not demand polymerization initiator for efficient crosslinking of polymer fibers.

Methods: One of the stages of creating 3D scaffolds from hydrogels is polymer cross-linking using a photoinitiator such as LAP or Irgacure. It is commonly known that the by-products of photoinitiator degradation show cytotoxicity, which is a very undesirable effect in biomaterials engineering.
Facing the problem of photoinitiators cytotoxicity we initiated research on materials capable of crosslinking without using of photoinitiator. The key of the research was to find compounds containing appropriate groups sensitive to UV-Vis irradiation, incorporated them into polymer structure and optimize working parameters for application in bioprinting.
In order to create new materials, a series of reactions was carried out to create active esters of appropriate acids and attach them to gelatin. Due to presence of functional groups such as primary amine groups and hydroxyl groups in the gelatin structure, it was possible to functionalize peptide chains.

Results: As a result of the conducted experiments a wide group of materials was obtained. These materials can crosslink under the UV-Vis irradiation using a selected wavelength. In addition, they do not require the

use of any photoinitiator, and the cross-linking process is caused by the reaction within the substituents. Optimization of the synthesis reaction allowed to regulate the degree of substitution in the range of 20-100%.

Conclusions: The use of gelatin fibers as the basic biopolymer paved the way for the new group of materials expansion. It is possible to find new applications for the above materials, which would allow for a significant development of the biomaterials chemistry. In addition, using various synthesis methods, it is possible to functionalize the most important part of the polymers in bioprinting such as chitosan or hyaluronic acid.

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QUANTITATIVE ANALYSIS OF LIVER-RELATED GENE EXPRESSION LEVELS IN HUMAN HEPATOCELLULAR CARCINOMA CELLS AND IN THEIR GENETICALLY MODIFIED COUNTERPARTS

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Objectives: For years, research has been conducted to obtain a cellular model to assess the hepatotoxicity of drugs, as well as to elaborate biological material to be applied in the construction of a bioartificial liver supporting patients with acute liver failure. In both applications, the liver parenchymal cells play a crucial role. These cells must perform a number of liver-specific functions, e.g. produce proteins, especially albumin, metabolize xenobiotics, eliminate urea, maintain a balance between glutamine production and glutamate consumption.

Methods: Our research is focused on establishing the practical model of hepatic cells. Therefore, the expression of selected liver-related genes in the three hepatocellular carcinoma-derived cell lines was compared: (1) C3A, a commonly used model of hepatocytes, which is also characterized by a low level of expression of genes encoding urea cycle enzymes: Arginase I (ARG1) and Ornithine transcarbamylase (OTC); (2) C3A_AO - a newly developed cell line genetically modified in the Tissue Engineering Laboratory of IBBE PAS, to bear additional copies of the hARG1 and hOTC genes; (3) HepaRG – an immortalized liver cell line that retains many features of the human hepatocytes.

Results: Quantitative analysis of the levels of expression of selected genes (GLUL, CYP1A2, ALB, CYP3A4, PXR, HNF1A, HNF4A, CPS1, ARG1) by RT-qPCR shows that C3A_AO cells have an advantage over the unmodified cells in the expression of two genes: HNF1A and CPS1. The higher level of expression of the PXR in C3A and C3A_AO cells as compared to HepaRG is also statistically significant. It is worth emphasizing that C3A_AO and HepaRG cells express the same levels of ARG1 and HNF4A genes.

Conclusions: The research should be extended, but based on the already obtained results, the C3A_AO cells constitute a potentially new model for hepatotoxicity studies or a material for the construction of biologically active function block of a bioartificial liver.

P90-FT

SHORT TERM RELEASE BEHAVIOUR OF MODEL PHARMACEUTICALS FROM HYDROGEL BEADS FOR THE DEVELOPMENT OF ARTIFICIAL BLOOD

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Objectives: Blood donations represent an increasingly finite resource in medical care. A common problem of large-scale wounds is contamination with pathogens. Current transfusion solutions do not yet offer the possibility of extended antibiotic first-line protection. Thus, we propose the development of drug-eluting artificial erythrocytes from hydrogels containing vesicles to regulate the release kinetics of aspirin as a model drug.

Methods: DSPC/cholesterol-liposomes (25 mg/ml, 1:1 w/w) were produced by thin-film hydration with aspirin solution (5 mg/ml) and extrusion (1 μm pore size). Electro-spraying (7 ml/h, 5 kV, 10 cm distance) was used to produce alginate beads (B, 2 wt% medium viscosity or 4 wt.% low viscosity) containing 0.5 ml aspirin solution (BA) or 2.5 ml liposome solution (BLA). 100 mg beads were stored under static conditions in 1.4 ml SBF at 37 °C for 72 h and analysed spectroscopically and photometrically.

Results: Mean diameters of 1796.6 μm (B), 1768.1 μm (BA) and 1820.8 μm (BLA) were measured. Release from BA showed limited increase with saturation after 10 hours (final concentration 0.46 mg/ml). This corresponds to 92% of the active substance load. The control B showed no release over the investigated period of time. From BLA, no significant release of the active substance compared to the control could be measured over the period investigated.

Conclusions: Release of aspirin was successfully demonstrated from BA. The absence of release from BLA may indicate that the liposomes were successfully used as a diffusion barrier and slowed the release. Liposomes could be a promising way to control the release behaviour of drugs from artificial erythrocytes. However, it could also indicate that the drug concentration in the beads is too low, which needs to be investigated further.

P91

SURFACE MODIFICATION OF A TITANIUM ALLOY: EFFECTS ON THE ADHESION OF A POLYMER-BASED COATING

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Objectives: This work aims to critically identify how different textures generated on a titanium alloy through mechanical and thermal processing affect the adhesion of a polymer-based coating, for application in tissue-contacting implants.

Methods: Four preparation processes were studied on the Ti6Al4V titanium alloy: polishing, face milling, grit-blasting, and electrical discharge machining. Surface contact angle after processing was probed employing the sessile drop technique, supported by surface composition mapping and surface topography analysis performed in preliminary works. Chitosan-bioglass coatings were deposited via drop casting, in triplicates for each surface processing condition. Coating adhesion was measured via scratch testing.

Results: Best performance is found for grit-blasted surfaces, ensuring mechanical interlocking with the coating due to their peculiar surface topography. The worst adhesion is given by the electrical discharge machined surfaces: the coating is easily detached due to a detrimental oxide layer, although the texture being similar to grit blasted samples. Coating on milled samples has slightly improved behavior compared to polished ones.

Conclusions: The tests demonstrated a marked influence of titanium alloy surface processing and related texture on coating adhesion. The processes investigated in this work involve a wide range of surface modification mechanisms. Thus, this work is a step forward towards deepening of the correlation between texture parameters and adhesion of polymer-based coatings.

P92-FT

THE WETTABILITY PROPERTIES OF MICROTOPOGRAPHY ON POLYCAPROLACTONE

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Objectives: Implant materials mainly interact with biological tissues at the materials surface, which affects protein adsorption and consequentially cell response, such as cell attachment and proliferation. An array of surface modifications have been developed over the past decades, e.g. to achieve enhanced osseointegration (i.e. cell adhesion). Microtopography can influence cell adhesion through mechanobiology and biophysical cues. The aim of this study was to investigate the effect of microtopography on the biophysical surface property of wettability.

Methods: Four different microtopographies (Pillars, Grooves, Inverted Pyramids and Osteon-like structures) were created as a negative inside a mold using 3D-CAD modelling. These designs and a negative control (flat surface) have been then manufactured using the two-photon-polymerization (2PP) NanoOne (UpNano GmbH, Austria). Polycaprolactone (Mn 80k, Sigma Aldrich) was then hot extruded into the molds. Water contact angle measurements were performed five times per microtopography with a contact angle goniometer (DSA25E, Krüss, Germany).

Results: The contact angle measurements showed that all microtopographies lead to an increase in the water contact angle compared to the flat surface (Pillars Δ=0.1°$\pm$11.7°, Osteon-like Δ=8.5°$\pm$11.3°, Grooves Δ=12.5°$\pm$17.9°, Inverted Pyramids Δ=21.6°$\pm$11.2°, $p<0.05$). Structures with cavity/pits like geometry tended to show an increased contact angle compared to structures with a protrusion like character, possibly because of the creation of a Cassie-Baxter state in which air is trapped in the cavities.

Conclusions: Microtopography decreases wettability of Polycaprolactone surfaces which might not be favorable for cell adhesion with geometry of the surface playing a crucial role regarding the extent of this decrease. Other surface property-changing methods, like plasma treatment, might be considered to circumvent the decrease in wettability. However, detailed investigations to evaluate the influence of microtopography on cell adhesion in relation to wettability need still to be performed.

P93

TUBULAR SCAFFOLDS WITH REDUCED SURGICAL POROSITY FOR TISSUE-ENGINEERED CONSTUCTIONS OF SMALL DIAMETER BLOOD VESSELS

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Objectives: To develop a technology of formation of porous tubular scaffolds with reduced surgical porosity for tissue-engeneering constructions of small-diameter blood vessels.

Methods: Frameworks in the form of 3 mm inner diameter tubes were formed by electrospinning from a 10% solution of polycaprolactone (PCL) with the addition of 5–30% gelatin (PCL-G) in hexafluoroisopropanol (voltage between electrodes 25 kV, solution flow rate 4 ml/h, distance up to the collector 100 mm, the speed of the substrate rod rotation 1000 rpm).
The surface of the scaffold was coated with a bioactive coating consisting of successive layers of bovine serum albumin, heparin and platelet lysate stabilized by glutaraldehyde.
Surgical porosity (SP) was measured at a pressure of 120 millimeters of mercury.

Results: When applying 1 ml of PCL-G solution, the SP of scaffolds drops from 30.4 $\pm$ 1.5 ml cm-2 min-1 in the case of pure PCL to 2.8 $\pm$ 0.5 ml cm-2 min-1 at a concentration of gelatin in PCL equal to 20%. Scaffolds formed by applying 2 ml of PCL-G, regardless of the concentration of added gelatin, showed SP in the range from 1.7 to 1.9 ml cm-2 min-1. At the same time, the addition of 10% gelatin provides a defect-free surface structure both from the outer and inner sides, as well as the best mechanical properties among the samples studied (Young's modulus 6.7 $\pm$ 2.1 MPa, force to break 26.7 $\pm$ 4.9 N and elongation to break 423 $\pm$ 80%). It has been shown that a scaffold made of PCL-G and coated with a bioactive coating is able to support adhesion and proliferation of endothelial cells of the EA.hy926 line.

Conclusions: PCL-G scaffolds treated with a bioactive coating is a potential candidate for the formation of a tissue-engineered design of a prosthesis for small-diameter blood vessels.

P94

CHONDROGENIC DIFFERENTIATION OF MSCS FROM VARIOUS SOURCES DURING CULTIVATION ON MATRIX FROM DECELLULARIZED PORCINE ARTICULAR CARTILAGE

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Objectives: To compare the chondrogenic potential of mesenchymal stromal cells (MSCs) from various sources (adipose tissue (hADSC), dental pulp (hDPSCs), umbilical cord stroma (hUMSCs)) during their cultivation on a microdispersed matrix from decellularized porcine articular cartilage (MDC matrix).

Methods: For decellularization sodium dodecyl sulfate, Triton X-100, ultrasound and DNase were used. 5$\times$105 MSCs were cultivated in a chondrogenic medium for 21 days with 5 mg of MDC matrix dispersed in it, followed by a histological study of the morphology of the formed cell-engineered constructs (CECs).

Results: During the cultivation of hDPSCs on the 21st day a single cell-matrix conglomerate was formed, fibroblast-like cells grew, multicellular clusters appeared, and there were practically no visible signs of extracellular matrix (ECM) production by the cells. The proliferation of hUMSCs and hADSC on the matrix surface was also accompanied by the association of cartilage microparticles into large aggregates but, as opposed to hDPSCs, multilayered cellular zones of cells were formed inside the aggregates, which actively synthesized the ECM. The highest production of glycosaminoglycans by hUMSCs and hADSC in the composition of the MDC matrix indicates the differentiation of cells in the chondrogenic direction. And only in CECs with hADSC by day 21 we had visualized the highest production of collagen with a positively staining for collagen type II.

Conclusions: CECs based on MDC matrix and hADSC are the most promising for the formation of a tissue equivalent of cartilage.

P95
MORPHOLOGICAL CHARACTERIZATION OF HUMAN LUNG CANCER ORGANOIDS CULTURED IN TYPE I COLLAGEN HYDROGELS.A HISTOLOGICAL APPROACH

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Objectives: Cancer organoids are a valuable approach for the manufacture of 3D in vitro model for drug screening. We propose to standardize morphological characterization of organoids composed of CAFs and lung tumor cells cultured in a 3D-system generated from collagen hydrogels.

Methods: A549 cells and CAFs were cultured, and suspensions of 150.000 cells/ml were generated, according to the following ratios: 100% A549, 25% A549 and 75% CAFs and 100% CAFs. Cell suspensions were cultured according to the drop slope method for 72 h. The organoids generated were collected and cultured in type I collagen (4 mg/ml) hydrogels drops for 72 h. The size and morphology of the organoids were evaluated every 24 h, using a phase contrast microscope. Organoid and cells morphology was evaluated by fluorescent F-actin staining. Vimentin and pankeratin were evaluated by immunofluorescence. 3D morphology of organoids was evaluated by confocal microscopy. Ultrastructural characterization of cells in the organoids by transmission electron microscopy.

Results: The generated organoids acquired an alveolar morphology with the appearance of cell expansions that were more abundant and branched in relation to the origin of the stromal cells and their abundance when generating organoids. These structures were formed by branches of A549 cells flanked by fibroblasts, which seemed to direct their growth. Ultrastructural analysis of the organoids revealed that all cells had a secretory phenotype. The cells included in the organoids showed an epithelioid morphology, with abundant junctional complexes and interdigitations. On the periphery and migrating outward from the organoid, fibroblastic cells appeared with abundant processes rich in actin filament bundles.

Conclusions: The study of the morphology of organoids and the characterization of their growth depend on the cell types they incorporate and therefore their characterization is important when generating relevant pharmacological models.

Organ Preservation for Transplantation

P96-FT
DEVELOPMENT OF A SIMPLE ORGAN PERFUSION SETUP FOR INVESTIGATING THE EFFECT OF THERAPEUTIC METHODS ON MARGINAL ORGANS

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Objectives: There is a major shortage of donor organs worldwide. Surgeons are already increasingly using marginal organs to expand the donor pool. Normothermic machine perfusion (NMP) is a promising technique for keeping organs alive outside the body for extended periods of time. It thus opens up the possibility of applying a variety of therapeutic procedures that could help improve organ function in the future, thus helping to further expand the donor pool. Our goal was to develop a simple, comparatively low-cost organ perfusion setup that can be easily adapted and implemented by many scientific research groups to facilitate the broad application and investigation of potentially therapeutic methods on marginal organs in large animal models.

Methods: We present a perfusion setup using commercially available medical components (oxygenator, tubing, connectors), sensors (pressure, flow, temperature), and actuators (heating pads, laboratory roller pumps) controlled by rapid control prototyping software. Other important parameters during perfusions (pH, O2/CO2 saturation, electrolytes, liver enzymes, bilirubin, urea) are determined externally with a blood gas analyzer or a clinical chemistry analyzer. Iterative development of the perfusion system is performed in an animal experiment using pig livers.

Results: To date, nine pig livers have been perfused with the system for up to 6 hours. During perfusion, we observed a significant increase in lactate and liver enzymes and a decrease in hematocrit, indicating suboptimal perfusion of the livers.

Conclusions: We attribute the decrease in organ viability during perfusion with our system to inadequate flow via the hepatic artery and portal vein. We are confident that optimization can be achieved in the next 1-2 trials. Once stable perfusion is achieved for 6 or more hours, we will begin testing different therapeutic approaches developed in our group or by collaborators to improve organ viability compared to standard NMP in animal studies with different organ damage models.

P97-FT
SPLIT RENAL FUNCTION, RENAL VASCULAR VARIATIONS AND DONOR PREFERENCES: CHALLENGE AND CROSSROADS TOWARDS RIGHT KIDNEY CHOICE

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Objectives: Renal vascular variations, split renal function and potentional donor's preferences interplay on the donation decisions in living donor kidney transplantation (LDKT). This study aimed to assess the challenges in decisions for choosing the proper kidney for donation.

Methods: Retrospective study was performed through a review of the medical history charts and national electronic database of LDKT from 2013 – 2022, in one transplantation center. Those with significant missing data, were excluded from the final analysis. Demographic characteristics, CT angiographic findings and Tc-99m DTPA renal scan for SRF and donor preferences were analysed. The bilateral presence and number of accessory renal arteries, their hilar or polar position in respect of the renal artery, early artery branching, variations of the veins number and left vein course were assessed. Significantly different SRF was defined as more than 10%.

Results: Out of 137 consecutive LDKT, 124 donors were included in the study. The mean age of donors was 59.00 ⌖11 years, 40 (32%) were male and 14 (11%) were unrelated. There were no variations in 88(64%) renal arteries on the right and 69(56%) on the left. The most common variation on both sides was an accessory hilar artery in both sides in 15%. An accessory inferior renal polar artery was observed in 15% and superior in 13% of patients. Three renal arteries or three veins on one side were observed in one patient. Variation of renal arteries on both sides was 13(10%). Early artery branching was found in 25%. In 41 (33%) of donors SRF was significantly different and 8 (18%) of those donated the better kidney because of donors preference.

Conclusions: Variations in renal vascular anatomy and different SRF are very often in kidney donors. The quality of the decision process relies on good institutional policy and adequate pretransplant donor evaluation.

Robotic Surgery

P98-FT

LEARNING CURVE FOR ROBOTIC MITRAL VALVE REPAIR SURGERY IN A BERGAMO HOSPITAL DURING THE COVID-19 PANDEMIC: A RETROSPECTIVE STUDY

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Objectives: We determined the learning curve of an experienced mitral valve repair surgeon when he started using the Da Vinci robot to perform the same mitral valve repair surgeries. We also considered that, during the learning period, the hospital where the study was conducted had to deal with the severe COVID-19 pandemic, resulting in a slowdown in surgical activity and the recruitment of doctors to deal with the pandemic.

Methods: We modelled the surgery duration time by means of a log-linear model whose input variables include the classical covariates used in the learning curves for surgery but also input variables that model the presence and intensity of the COVID-19 pandemic. Descriptive statistics were performed on the data collected from these patients, and the log-linear learning curve was fitted to them. The outputs were analysed in terms of the time trend of the surgical duration and, as far as the learning curve is concerned, in terms of the goodness of fit and of the covariates that significantly influence surgery duration time.

Results: Data included a total of 138 surgeries performed from May 2019 to February 2023 at the Cliniche Humanitas Gavazzeni in Bergamo, Italy. The first 19 patients were operated before the onset of the COVID-19 pandemic in Bergamo, up to February 18th, 2020, while the following 57 patients in the period from June 9th, 2020 to December 21st, 2021 during the first pandemic waves, and the remaining 62 patients after January 2022, 11th when the situation returned almost to normal. The results showed the negative impact of the COVID-19 pandemic on learning the new technique, which would have been faster without the interruptions and slowdowns due to the pandemic.

Conclusions: Our work provided a quantitative analysis on the impact of the COVID-19 pandemic on the learning process for robotic mitral valve repair surgery

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