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POSTERS

Poster Session I

Cardiac Assist Devices in Clinical Application I

P1

DESTINATION THERAPY LVAD AND CANCER: A CASE AGAINST DARWIN'S SURVIVAL OF THE FITTEST

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Background: End-stage heart failure and advanced cancer carry an extremely poor prognosis with a disabling quality of life (QOL). Anecdotal reports are beginning to appear in the literature of DT-LVAD patients who subsequently are found to have malignancies.
Aim: To bring awareness to the combination of DT-LVAD patients with cancer and the challenges associated with these two conditions.
Methods: A 72 year-old man with end-stage heart failure was implanted with a Heartmate II® LVAD as Destination Therapy. The surgery was uneventful and he was discharged on postoperative day 16. Seven months later, he developed melena and was found to have an ulcerated mass at the gastroesophageal (GE) junction that was pathologically adenocarcinoma. CT/PET scanning and upper endoscopic sonography staged the disease at III (T3N1M0). Subsequent imaging showed a lytic L4 lesion that was biopsy proven metastatic disease. Due to the presence of the LVAD, the patient was not a surgical candidate for resection. Treatment consisted of chemoradiation therapy.
Results: Serial PET scans showed a range of complete absence of abnormal 18F-FDG uptake to occasional uptakes in various locations with mild to moderately elevated maximal SUV units. The patient is alive with a good QOL approximately 3.5 years from LVAD implantation and 3 years from esophageal cancer diagnosis.
Conclusions: End-stage heart failure and cancer can be successfully treated with combination DT-LVAD therapy and aggressive cancer therapy. A multispecialty and multi-modality approach is necessary to manage these complex cases. With the growing number of DT-LVAD patients worldwide, it will be imperative for healthcare providers to be aware of non-cardiac conditions - such as malignancy - and to address to address them in a collaborative fashion.

P2

PREDICTOR FOR WEANING FROM EXTRACORPOREAL MEMBRANE OXYGENATION IN INFANTS WITH HEART FAILURE

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Background: Extracorporeal membrane oxygenation (ECMO) is commonly used for circulatory support in pediatric cardiac surgical patients and other diseases with low cardiac output and hypoxemia.
Aim: This aim of study was evaluated the efficacy of ECMO support for respiratory and heart failure in infants and children.
Methods: From April 2002 to February 2017, 34 patients aged 13 days to 9 years old (average 21.1 months), bodyweight 1.7 kg to 28.5 kg (median 4.1 kg) underwent ECMO support for failing cardiac function, hypoxemia and low cardiac output syndrome. In 30 patients, ECMO was introduced after operation for congenital heart disease (11 complete repair including Fontan circulation and 19 palliative repair). Recently, we incorporate continuous renal replacement therapy. (CRRT) in ECMO circuit with or without renal failure to control the balance of moisture and the electrolyte.
Results: 22 patients (65%) were successfully weaned from ECMO and 18 patients (53%) discharged from the hospital. The mean duration of ECMO support was 264 hours (range 4.3-2029 hours). Although activated clotting times (ACTs) were generally maintained in the range of 150-250s, it was difficult to control the bleeding. 24 patients, 12 (54%) patients weaned from ECMO and 12 patients (100%) unweaned from ECMO, required renal replacement therapy during ECMO support using peritoneal dialysis or continuous renal replacement therapy. There was no bleeding weaned from ECMO patients. Eight patients had additional operative procedures; Re-VSD patch closure in a one, arch plasty in a one, systemic-pulmonary shunt in four and Fontan takedown in two.
Conclusions: ECMO for heart and respiratory failure in infants and children is effective and allows time for recovery of cardiac dysfunction and acute respiratory failure. The combination of ECMO and CRRT were safely undergone for the management of fluid balance and electrolyte.

P3

THE EXPERIENCE ON TECHNICAL SUPERVISION OF PATIENTS SUPPORTED BY HVAD SYSTEM

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Background: HVAD is the most popular MCS system in Poland. It has been applied in 90 adults and 2 children in 5 hospitals, till the date. The longest support is 3.5 years (n = 7, still pending), with 2 cases of recovery reported. Technical team supports clinicians during periodic patients' follow-up visit and in emergency cases. Research was performed in the project RH-ROT/266798/STRATEGMED-II.
Aim: Aim of work was to develop methodology for technical supervision of patients supported by HVAD.
Methods: Developed methodology consists of log-file analysis, waveform evaluation and acoustic assessment of pump operation. Log-file analysis is led in order to detect pump embolization (rising or falling power trend) as well as assessment of course of assistance (flow, flow pulsation, minimum flow and its' circadian rhythm). Mean power is compared with range of acceptable power in respect to pump speed.
Waveform analysis is led in order to find retrograde flow and/or to assess AoV opening. Acoustic evaluation of pump operation is carried out in order to early detection of embolization (the amplitude of 3rd harmonic is measured). During every follow-up visit the technical condition of system is evaluated. In each case technical assessment is complemented by medical data (INR, LDH, NIBP, wound condition, echo etc.).
24/7 emergency hotline as well as remote log-file assessment has been introduced.
Results: 710 follow-up visit, emergency and remote controls have been performed. Developed methodology allowed to recognize pump embolization (n = 17), monitoring of tPA treatment (n = 10), ventricular fibrillation (n = 4), flow drop due to serious cardiac arrhythmia (n = 8), driveline plug contamination (n = 5) and minor technical malfunction. 2 and 3 years surviving is 0.70 and 0.55, respectively.
Conclusions: Presented methodology is a valuable addition to routinely medical examination of patients supported by HVAD. Good cooperation between medical and technical teams has led to reach high patients' surviving. Routine acoustic pump evaluation has been proved as sufficient tool for early VAD embolization detection.

P4

BLOOD PRESSURE CONTROL IN HEART FAILURE PATIENTS SUPPORTED BY A CENTRIFUGAL LEFT VENTRICULAR ASSIST DEVICE

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Background: Blood pressure control in pts with left ventricular assist device (LVAD) can present unique challenges. Centrifugal pumps, such as the

HeartWare, are known to be more afterload sensitive in comparison to axial flow pumps and therefore are more susceptible in response to hypertension.
Aim: In the present study we describe the long-term blood pressure management and the incidence of adverse events in HeartWare LVAD pts.
Methods: This was a retrospective study of 28 pts (26 men, 2 women, mean age 63 yrs) with NYHA class IV heart failure who were being supported by a HeartWare HVAD (HeartWare International, Framingham, MA). All pts underwent 3-5 weeks inpatient cardiac rehabilitation (CR) with sophisticated blood pressure adjustment according the ISHLT Guidelines. In the further course pts presented every 12 weeks in VAD ambulance. Adjustment of blood pressure medication was performed when MAP was >90 mmHg during repeated measurements. The mean follow-up was 865 days.
Results: At the end of CR all pts were on antihypertensive drugs (14% required 1 medication, 64% were on 2, 21% were on 3). ACE-inhibitors or angiotensin II receptor blockers (86%) and beta blockers (75%) were the most commonly prescribed medications. In the context of a quarterly clinic visit 20 of 28 patients (71%) needed additional antihypertensive therapy (9 pts within 6 months after implantation, 7 pts within 1 year and 4 pts later). 7 patients had more than 1 hypertensive derailment. In total there were 4 neurological events (stroke n = 1, TIA n = 2, intracranial hemorrhage n = 1 (pt died)).
Conclusions: Early after LVAD implantation blood pressure control can be achieved in pts with HeartWare LVADs, with the majority of patients requiring 2 antihypertensive drugs. Nevertheless, after discharge from the hospital a high percentage of LVAD patients need additional antihypertensive treatment. Adequate blood pressure control in the home environment seems to be essential to prevent severe esp. neurological complications.

P5

EFFECTS OF VENTRICULAR ASSIST DEVICE ON CARDIAC TROPONIN T ISOFORM EXPRESSION IN PEDIATRIC PATIENTS WITH HEART FAILURE

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Background: HF is a syndrome that results from structural and functional derangements of heart. During HF, an altered production of sarcomeric proteins, such as cardiac troponins (cTn), could induce an increase of ventricular cavity dimensions and systolic dysfunction. Four different isoforms of cTnT, including fetal (1, 2, 4) and adult (3) variants, exist and present different Ca2+ sensitivity with effect on cardiac function: the fetal cTnT4, shows decreased Ca2+ sensitivity, while the adult cTnT3 higher. The re-expression of cTnT fetal isoforms in the adult hearts contributes to the functional remodeling of HF. VAD as bridge to cardiac transplantation is used for the treatment of adults with HF and represents a possible therapy also in pediatric HF. VAD unloads the failing heart and may modify phenotype of HF, including structural proteins.
Aim: We aimed at investigating the effects of VAD on the expression of cTnT isoforms in the heart of HF children.
Methods: Ten HF children submitted to VAD [62 ± 23 ms (mean ± SD), 7 males, 23 ± 4.5 LVEF%] were enrolled. mRNA expression levels both fetal and adult cTnT isoforms were determined in 10 cardiac ventricle biopsies collected at VAD implant (preVAD) and 7 at transplantation (postVAD).
Results: mRNA expression of cTnT1 did not change after VAD. Levels of cTnT4 and 2, the lesser expressed variants during embryonic life, increased after VAD treatment (cTnT4:0.105 ± 0.021 vs 0.402 ± 0.08; p = 0.0026; cTnT2:0.11 ± 0.018 vs 0.35 ± 0.077, p = 0.005; preVAD vs postVAD). cTnT3, the adult isoform, significantly increased in postVAD compared to preVAD (0.25 ± 0.045 vs 0.55 ± 0.081, p = 0.005; preVAD vs postVAD).
Conclusions: In HF children, the increased expression of cTnT3 and 4 isoforms after VAD could modify Ca2+ sensitivity with consequences on cardiac function thought the modulation of synchronized activation of ventricular muscle.

P6

OUTCOMES OF HEART TRANSPLANTATION FOLLOWING SUPPORT BY MICROMED® DEBAKEY VAD® VERSUS HEARTWARE® HVAD® – A SINGLE CENTER STUDY

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Background: We retrospectively compared all heart transplanted patients following support with an axial flow (MicroMed® DeBakey VAD®) versus a rotary flow (Heartware® HVAD®) left-ventricular assist device (LVAD) at the Medical University of Vienna.
Methods: Between 1999 and 2009, 41 Patients (mean age 52 ± 10.8 years, 92.7% male) were transplanted following axial flow support. Between 2007 and 2015, 46 patients (mean age 53.6 ± 11 years, 80.4% male) were transplanted following rotary flow support. Pre-transplant variables as well as post-transplant mortality and morbidity were compared between both groups using Student T-test, Log-Rank test and Chi-Square test, respectively.
Results: Patients supported by the axial flow pump had significantly higher systolic pulmonary artery pressure (axial: mean 48.3 ± 14.8 mmHg; rotary: mean 36.9 ± 14.8 mmHg, p = 0.002) and shorter time on the waiting list (mean 223.8 ± 414.7 days vs 445.7 ± 469.5 days, p = 0.023) than the rotary flow group. Donor age was higher in the rotary flow group (mean age 34.8 ± 10.4 vs 40 ± 14 years, p = 0.053), but there were no differences in organ ischemic time. There were no between-group differences in survival at 30 days (95.1% vs 100%, p = 0.13), 1 year (85.4% vs 91.3%, p = 0.386), overall survival (p = 0.577), and renal replacement therapy (24.4% vs 30.4%, p = 0.529). The axial flow group showed higher rates of primary graft dysfunction (22% vs 6.5%, p = 0.037) and ventilation over 7 days (34.1% vs 15.2%, p = 0.039).
Conclusions: Post-transplant survival was excellent and did not differ between the axial and rotary flow groups. However, higher rates of primary graft dysfunction and ventilation over 7 days were found in the axial flow group, most likely due to transplant era differences between both groups.

P7

MINIMALLY INVASIVE BIVENTRICULAR SUPPORT WITH PERCUTANEOUS EXTRACORPOREAL MEMBRANE OXYGENATION AND LEFT VENTRICULAR ASSIST SYSTEM THROUGH MINI-THORACOTOMY

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Background: Mechanical circulatory support with percutaneous extracorporeal membrane oxygenation (ECMO) is widely applicable for the treatment of fulminant myocarditis (FM). However, it may increase afterload of left ventricle (LV) by direct perfusion of the blood with insufficient drainage, which result in delayed myocardial recovery and poor systemic perfusion. To overcome this disadvantage of percutaneous ECMO, we utilized combined use of ECMO and LV venting system using direct cannulation into LV cavity.
Aim: The aim of this study is reporting our experience of combined use of percutaneous ECMO and our direct LV venting system in FM.
Methods: We utilized this system in three patients with refractory FM developing organ dysfunction and pulmonary edema despite of ECMO support. Through left thoracotomy, direct drainage cannula of 18 French was inserted into the LV cavity with double purse-string suture on the surface of LV apex under fluoroscopic guidance. Two drainage cannulae from LV cavity and femoral vein were connected to the two ECMO circuit with centrifugal pump and oxygenator individually and they were connected to the same perfusion cannula of femoral artery. Cardiac function was evaluated by serial echocardiography.
Results: After establishment of venting system, total ECMO flow was increasing from 3.2 to 4.6 L per minute with LV venting flow of 1.2 L per minute. Improvement of pulmonary edema and LV decompression was observed soon after the operation in the all patients. In two patients, we observed good cardiac recovery and LV venting and peripheral ECMO were successfully weaned off on day 8 and 16 and day 13 and 15, respectively. One patient died due to multi organ failure after the 30 days of ECMO support and. During the

support periods, no cerebrovascular event and limb ischemia was observed in all patients.
Conclusions: This system may be a less invasive and useful alternative to the biventricular support in the patients with cardiogenic shock due to FM.

P8
MAPPING AND ABLATION DURING MECHANICAL CIRCULATORY SUPPORT (BERLINHEART) IN A CHILD WITH DIAGNOSED TACHYCARDIA-INDUCED CARDIOMYOPATHY. IS THIS THE WAY TO WEAN?
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Background: Tachycardia-induced cardiomyopathy, as cause of heart failure and impaired left ventricular function, is considered reversible.
Aim: We present a case of a 11 years old boy diagnosed with cardiomyopathy and recurrent tachycardia of uncertain origin. Left ventricle assist device (Berlin Heart EXCOR 30 cc) was implanted in a standard manner as a treatment of heart failure with left ventricle ejection fraction of 15%.
Methods: After 4 weeks on support free from arrhythmia and confirmed rise in ejection fraction up to 60% the weaning protocol was started and again induced tachycardia. We decided to proceed with electromapping and potential ablation of the arrhythmia origin.
Results: Under general anesthesia, using Seldinger method, 10-pole coronary sinus diagnostic and contact force sensing ablation catheter (Navistar Thermocool SmartTouch SF) were introduced. In order to avoid unnecessary radiation exposure, only basic fluoro images of heart (AP, LAO, RAO) were taken and integrated with electroanatomical system. Local activation time (LAT) fast anatomical map (FAM) was made using Carto 3 system. During mapping, earliest activation area was identified in posterio-left aspect of RVOT. Electrograms projection from that area represented arrhythmia morphology recorded during tachycardia episodes. Radiofrequency (RF) ablation applications were performed in that area, during which arrhythmia was terminated. Acute success was confirmed by stimulation protocol with no arrhythmia induction.
Conclusions: Actually the child is prepared for the next try of weaning scheme. If we confirm the persistent effect of ablation and reversed cardiomyopathy following the BerlinHeart's and own weaning protocol the explantation of the system will be the next step.

Cardiac Assist Devices in Clinical Application II

P9
CARDIAC REHABILITATION OF LEFT VENTRICULAR ASSIST DEVICE PATIENTS REQUIRING RENAL REPLACEMENT THERAPY - A MAJOR CHALLENGE
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Background: With an increasing number of left ventricular assist device (LVAD) patients requiring renal replacement therapy (RRT) the need for adequate cardiac rehabilitation (CR) regimes meeting the special demands of this patient group arises.
Aim: The aim was to evaluate the characteristics, therapeutic needs and scopes of LVAD patients requiring RRT at admission to CR, in order to identify their special CR needs.
Methods: This was a retrospective mono-centre study. Patients with implanted LVAD requiring RRT who completed inpatient CR (11/2008-02/2017) were included. A sample of 6 patients (mean age 55.6 years; 5 male; 5 HVAD; 1 HeartMate3) met the inclusion criteria. Hemodialysis was performed in the CR hospital affiliated dialysis center.
Results: Pts were admitted to CR after a mean interval of 51 days after implantation. 5 of 6 pts had a preexistent renal disease requiring RRT (mean RRT time before LVAD 6.4 years; glomerulonephritis n = 2, diabetic nephropathy n = 1, polycystic renal degeneration n = 1, chronic renal failure after septicemia n = 1). 1 pt developed acute kidney injury after a second pump exchange. 4 pts were under long-term hemodialysis, 2 pts performed peritoneal dialysis. 4 of the 6 pts presented markedly reduced physical condition and extreme muscular deconditioning at the time of admission and were not able to perform initial 6 MWT and maximal isometric strength test for M. quadriceps. The other 2 pts showed 6 MWD of 390 m and a peak torque of M. quadriceps of 1085/845 N. These 2 pts were able to perform cardiopulmonary exercise testing (peak VO^2 7 ml/kg/min and 17 ml/kg/min, respectively). At least, at the of CR (mean duration 31 days) all pts showed significant improvement of physical capacity.
Conclusions: The results demonstrate a heterogeneous group of LVAD pts requiring RRT. There is a need for a highly individualized approach in the somatic, but also in the educative, psychosocial and social therapeutic regimes.

P10
THE EXPERIENCE OF USING ECMO ON AN INFANT AFTER MODIFIED NIKAIDOH PROCEDURE
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Background: Surgical treatment of complete transposition of the great arteries (TGA), ventricular septal defect (VSD), and left ventricular outflow tract obstruction (LVOTO) is still a challenge. Nikaidoh procedure is an alternative method, but most patients need reoperation for conduit degeneration and pumonary valve regurgitation or stenosis. TO preserve the pulmonary valve can avoid reoperation, so Modified Nikaidoh procedure may be the optimal selection for these patients, but the technique is more complex.
Aim: To present the experience of using ECMO on an infant after Modified Nikaidoh Procedure.
Methods: A 2-year-old boy weighing 12.3 kg was diagnosed with complete transposition of the great arteries (TGA), ventricular septal defect (VSD), left ventricular outflow tract obstruction (LVOTO) and pulmonary valve stenosis. A procedure of double-root translocation by use of a valve-spared pulmonary root was underwent. After the operation, the patient complicated serious low cardiac output Syndrome (LCOS), extracorporeal membrane oxygenation (ECMO) were performed for 8 days untill cardiac function improved. Acute renal failure lasted for 35 days during when abdominal cavity infection, pneumonia and gastrointestinal dysfunction occurred. Peritoneal dialysis (PD) and many other therapies were performed.
Results: The patient recovered well and discharged after 104 days postoperation. Follow-up echocardiography showed no LVOTO, no aortic valve regurgitation, no pulmonary stenosis and mild pulmonary valve regurgitation.
Conclusions: Nikaidoh procedure is an alternative choice for TGA/VSD/LVOTO, and the better long term outcome can be achived when the pulmonary valve is preserved. But this procedure may associate severe comlications. ECMO support in time is necessary for some patients, and it is very important to manage these patients properly in intensive care unit (ICU).

P11
THE USEFULNESS OF PERIPHERAL ECMO AS A BRIDGE TO IMPLANTABLE LVAD IN PROGRESSIVE DECLINE HEAT FAILURE PATIENTS
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Background: In Japan, implantable continuous-flow LVAD is only indicated for "stable" heart failure patients listed for heart transplantation. Generally, mechanical circulatory support including peripheral ECMO is used to stabilize hemodynamics, as a bridge to implantable LVAD in patients with critical cardiogenic shock (INTERMACS level 1).
Aim: We investigated whether peripheral ECMO support is useful to not only "critical cardiogenic shock (level 1)" but also "progressive decline (level 2)" patients.
Methods: Two patients with severe heart failure were waiting for heart transplant with INTERMACS level 3 (stable but inotrope dependent). However, their hemodynamics as well as renal and liver function progressively

deteriorated and right ventricular dysfunction became noticeable. Urgent biventricular assist device implantation was indicated, however it was deemed very high risk. Therefore, we introduced peripheral ECMO and intra-aortic balloon pumping with local anesthesia before implantable LVAD insertion.
Results: After PCPS and IABP installment, their hemodynamics became stable and renal and liver function recovered. Central venous pressure decreased from 27 and 35 to 6 and 5 (mmHg), respectively. After 9 and 15 days of PCPS and IABP support, implantable LVAD (EVAHEART) insertion and concomitant tricuspid annuloplasty were performed and RVAD was not required. ECMO and IABP were removed at the same time. Their postoperative course was uneventful.
Conclusions: The bridge-to-LVAD use of peripheral ECMO could stabilize hemodynamics and recover organ function in INTERMACS level 2 patients. Despite prior right ventricular dysfunction, our aggressive introduction of ECMO could be helpful to escape RVAD support.

P12
CLINICAL COURSE, FUNCTIONAL CAPACITY AND DISCONTINUATION OF RVAD AFTER PLANNED AND UNPLANNED BIVENTRICULAR SUPPORT SYSTEM IMPLANTATION
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Background: 10-20% of VAD candidates still cannot be treated with an LVAD alone. Implantation of biventricular support systems - planned or unplanned - remains more challenging with lower survival, offers limited quality of life and may be proposed as bridge to transplant.
Aim: The aim of this study was to characterize the clinical course and the functional capacity of BVAD pts after implantation.
Methods: Eight pts (4 male, 4 female, mean age 49.5 years; DCM n = 4, ICM n = 1, myocarditis n = 1, cardiomyopathy after chemotherapy n = 2) underwent HeartWareR BVAD implantation. In three pts RVAD was implanted later in previously non-expected severe right heart failure. Mean inpatient stay was 91 days followed by inpatient rehabilitation (IR; mean duration 38 days).
Results: The clinical course after implantation was burdened with major complications (renal insufficiency n = 5, liver insufficiency n = 2, long-term ventilation n = 4, re-exploration n = 4, ECMO implantation n = 1, severe necrosis D II-V hand). During IR the 6-MWD improved from 226 m to 333 m. The maximal isometric strength of M. quadriceps femoris also improved (293 Nm vs. 399 Nm). Starting from markedly lower values same levels were reached at the end of a prolonged IR in the unplanned group (45 vs. 33 days). One female pt (53 years) developed pump thrombosis of RVAD 18 months after implantation. In nearly recovery of the right ventricle RVAD was stopped and left in place without complications. Two further pts underwent successful HTx.
Conclusions: Postimplant treatment of BVAD pts represents a special challenge because of numerous complications and severe muscular deconditioning. Pts who receive a RVAD only days after LVAD insertion fare much worse than those who receive an RVAD simultaneously with LVAD implantation. After prolonged IR both planned and unplanned BVAD pts reached the same level of physical capacity. RV function may recover even after months on BVAD support. The RVAD then may be stopped and left in place without complications.

P13
SHORT AND LONG TERM LEFT AND RIGHT VENTRICULAR MECHANICS AFTER LVAD IMPLANTATION IN PEDIATRIC PATIENTS: A 2D AND 2DSPECKLE TRACKING ECHOCARDIOGRAPHIC STUDY
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Background: Two-dimensional speckle tracking echocardiography (2 DSTE) is an angle-independent method for myocardial strain measurement that has been used to characterize cardiac function in children.
Aim: To study the ventricular interdependence in LVAD pediatric patients (pts) by conventional 2D echocardiographic (ECHO) and 2D-strain during short-term and long-term support.
Methods: ECHO and clinical data of pediatric pts implanted with a pulsatile-flow LVAD (BH EXCOR) from 2011 to 2016 were retrospectively reviewed before and after implantation at 1, 3 and 6-months follow-up.
Results: Eighteen consecutive pts were enrolled in the study. Fourteen pts were affected by dilative cardiomyopathy, 2 by restrictive cardiomyopathy and 2 by left ventricular noncompaction. Mean age at implantation was 18.3 ± 27.4 months, with mean weight of 7.6 ± 4.2 kg. Mean LVAD support was 203.7 ± 117.8 days. Thirteen pts (73%) were transplanted, 5 pts (27%) died (4 for major neurological complication, while 1 showed temporary recovery of heart function). At follow-up in all we observed: 1) LVEF increase at 1-month ($p = 0.001$) and at 3-months ($p = 0.01$), 2) A significant decrease of mitral regurgitation at 1-month ($p = 0.00008$), 3) GLS improvement at 1-month ($p = 0.0008$), 3-months ($p = 0.02$) and 6-months ($p = 0.002$), 4) RVFW-LS increase at 1-month ($p = 0.01$), 5) RVFAC followed the trend of RVFW-LS, but not reaching significance. RVFW-LS remained stable at 3-months and then slightly worsened at 6-months follow-up.
Conclusions: At short term follow-up after LVAD implantation, both LV and RV ECHO functional parameters improved. The temporary benefit provided by LVAD implantation decreased over time. A subsequent worsening of LV function has been followed also by a worsening of RV function probably due to the ventricular interdependence mechanism.

P14
DO ADULTS WITH A DURABLE CONTINUOUS-FLOW LEFT VENTRICULAR ASSIST DEVICE (LVAD) REQUIRE AN ASSIGNED CAREGIVER ON DISCHARGE?
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Background: The use of LVADs has increase dramatically due to increased safety and efficacy of continuous flow devices. However, the lack of a caregiver is a relative contraindication to durable LVAD implantation.
Aim: To compare outcomes in adult LVAD patients discharge home with or without caregiver support.
Methods: We retrospectively reviewed the caregiver status of all adult patients implanted with durable continuous-flow LVAD (24 Ventrassist, 126 HeartWare HVAD) as a bridge to transplantation from October 2004 to March 2017. Patients were divided into two groups: those with an assigned caregiver (CG group), and those with no assigned caregiver (No-CG group) and living independently on discharge home. Median distance from implanting facility in the No-CG group was 53.7 km (range 8.4 km-1373 km). Support for No- CG patients included 24 hour phone contact support, and medical review once per month. All patients were required to demonstrate competency of controller awareness and drive-line care prior to discharge. Post implant-outcomes were compared.
Results: A total of 152 LVAD patients were included, 136 (89.5%) in the CG group and 16 (10.5%) in the No-CG group. The No-CG group included 2 BiVAD patients. The mean ages were similar (56.2 ± 11.2 vs 50.2 ± 14.1 years) in the No-CG and CG group respectively. No-CG patients tended to be more likely to be male (93.7% vs 76.5%, $p = 0.11$). Duration of support was comparable between two groups (359 ± 283 days vs 353 ± 256, No-CG vs CG). Successful support to transplantation rates was similar between the two groups (No-CG 56.2% vs CG 61%). Mortality was also similar (25% vs 28%). Three of the four No-CG patients who died, passed away in hospital, with one dying at home. No device failures were reported.
Conclusions: Patients implanted with a LVAD with no assigned caregiver had comparable outcomes to those who with an assigned caregiver. In appropriate competent patients, social isolation should not be an absolute contraindication to chronic mechanical circulatory support.

P15
INTERNATIONAL VAD COORDINATOR PRACTICES: CLINICAL UTILITY AND APPLICATION OF HEARTWARE HVAD SYSTEM WAVEFORMS AND LOGFILES
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Background: This joint ICCAC and HeartWare survey was performed to investigate how HVAD system waveforms and logfiles are globally used within the field.

Aim: Our aim was to gain an understanding of the benefits, possible difficulties, and areas of improvement that could be made to enhance this assessment tool.
Methods: A web-based SurveyMonkey questionnaire (12 questions) was sent to all ICCAC members were n = 48 (43% of invited participants) responded. The majority of responses came from centers located in the U.S. (n = 34), Europe (n = 10) and Asia/Pacific (n = 4). The professional background of most VAD Coordinators was nursing (53%), ANPs (19%) and engineering (12%).
Results: Nearly 50% indicated that their center has over 60 patients on long-term LVAD support and 65% implant between 21-60 durable VADs per year. 72% of the participants feel very comfortable utilizing HVAD waveforms as a diagnostic tool to assist in treating conditions or complications. 91% of the VAD Coordinators use waveforms to assess the patient´s status, also cardiologists (78%) and surgeons (70%) commonly use this tool for patient management, but only 40% of ICU nurses. 49% download HVAD logfiles during every follow-up, 36% only for emergency issues and 5% never download them. 56% evaluated the alarm and event history of the log file reports, provided by HeartWare, very useful. The 30-day historical graphical view as well as equipment performance of these reports was weighed as at least useful by over 75%. 90% of VAD Coordinators desire to receive the HVAD logfile report back immediately, while assessing routine patients in clinic and n = 18 VAD Coordinators stated that clinical explanations and waveform interpretation should be included.
Conclusions: This HeartWare/ICCAC survey represents how the HVAD waveform and log files are used in a global assessment. The results may help to understand benefits as well as areas of difficulty and desires for improvements to future products.

P16
DEVELOPMENT OF A SUCTION DETECTION ALGORITHM FROM PATIENT PUMP DATA
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Background: Currently available Left Ventricular Assist Devices (LVADs) may provoke ventricular wall collapse into the inflow cannula, so-called suction, possibly causing tricuspid regurgitation or rhythmological problems. There are currently no accurate methods to detect these events and allow prompt intervention and pump speed adaptation.
Aim: To develop a suction detection algorithm was developed that does not require any additional sensors.
Methods: 500 pump data snapshots of 38 individual patients, containing 10 seconds of continuous recording each were annotated by 6 experts on a beat to beat basis, according to a 5-grade scale of ventricular suction severity. Expert agreement was determined by Krippendorffs' Alpha for ordinal scales, while beats that were contradictorily labelled were excluded. The labelled beats were used to train a support vector machine- (SVM), decision tree-(TREE) and a quadratic discriminant-(QDIS), classifier. 16 beat-wise features were engineered from raw pump data. Leave-one-patient-out cross-validation was used to assess generalizability of the classifiers.
Results: Expert agreement was acceptable with a Krippendorffs' Alpha of 0.76 before exclusion of contradictorily annotated beats (perfect agreement = 1). The classifiers achieved an accuracy of 97.7%, 96.8% and 95.2% respectively for the SVM, TREE, and QDIS. Specificities were 98.7%, 97.8%, 97.5% and sensitivities 96%, 95.2% and 91.3%. Leave-one-patient-out crossvalidation additionally revealed, that the beats of 3 out of the 38 patients could only be classified with accuracies of 80-90%, with all 3 classifiers.
Conclusions: Three beat-wise suction detection algorithms were developed based on expert opinion. Increased complexity and computational cost correlated with increased predictive accuracy. These algorithms could be used to determine adequate pump speed in LVAD patients.

Cardiac Assist Devices: Blood Trauma and Various Topics

P17
THE EVALUATION OF HEMOLYSIS IN A VENTRICULAR ASSIST DEVICE-PRELIMINARY STUDY
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Background: The plasma free hemoglobin (PFH) has been widely employed as an index for the evaluation of hemolytic properties of VADs. Even so, it was believed that PFH is not enough sensitive to meet the demands of the accurate exams.
Aim: The aim of this research work is to test whether lactic dehydrogenase (LDH) can be used as an additional indicator, in order to make a better evaluation of hemolysis in a VAD.
Methods: In this work, an experimental study was performed for the evaluation of the injuries and damages of erythrocytes in a VAD. PFH and LDH were used as two indicators. Through 24 hours in vitro hemolysis test, the changes of LDH and PFH concentrations in blood samples were evaluated in combination with the microscopic histological test and ultrastructural test of erythrocytes morphology.
Results: The results revealed that the modifications of the concentration of LDH were more sensitive than that of PFH in the test under different shear stress and exposure time. In the 24 hours in vitro hemolysis assay, the PFH concentration in the blood samples showed no significant changes in the first 8 hours, in contrast, the LDH concentration increased significantly in the first 3 hours, which was consistent with the morphological changes of erythrocytes, observed by microscopes. Compared with the adjustments of the PFH concentration, the LDH concentration are sensitive to the damages of erythrocytes caused by VADs
Conclusions: It was concluded that LDH could be an additional indicator in the evaluation of erythrocyte damages and hemolytic properties of VADs.

P18
BLOOD DAMAGE BY HANDLING: THE CRUX OF THE MATTER
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Background: The ability to characterize red blood cell (RBC) mechanical properties is important in clinical and research contexts: To diagnose and monitor hematological disorders and to optimize the design of blood circulating devices towards minimal blood damage. However, investigation of RBC properties generally involves preparatory and processing steps, e.g. centrifuging. Even though these impose mechanical stresses on cells, little is known about their impact on the final measurement results. Beyond lysis, subtle changes in RBC membrane properties also deserve attention.
Aim: Here we aim to address this knowledge gap by investigating the effect of centrifuging, vortexing, pipetting and high pressures on several markers of mechanical blood damage and RBC membrane properties.
Methods: We used venous blood of 22 healthy volunteers. Blood was exposed to one of the following procedures: 1) Centrifuging: 1-4 steps for 5/10 min each @900 g. 2) Vortexing: for 20 s or 40 s. 3) Pipetting: Normal tip vs. cut pipette tip. 4) Pressure: 1, 3, 5, 7 bar for 1 s/30 s. We analyzed blood damage using the following measures: 1) Free hemoglobin (Hb). 2) Flow cytometry. 3) Ektacytometry. 4) Complete Blood Count.

Results: We observed increased levels of free Hb for all tested procedures. The release of Hb to plasma depended significantly on the level of stress. Elevated pressures and centrifuging also altered mean cellular volume, mean corpuscular Hb and maximal deformability.
Conclusions: While the effects of blood handling involved in standard laboratory workflows or in vitro experiments are generally not considered, our results show that centrifuging, vortexing, pipetting and pressure clearly influence human RBCs, leading to significant release of Hb. Careful quantification of their influence as well as other unwanted secondary effects should be included in experimental protocols and accounted for in clinical laboratories.

P19
INFLUENCE OF THE THROMBUS FORMATION ON THE HEAT GENERATION IN THE SPUTNIK RBP: IN VITRO STUDIES
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Background: Researches around the world try to improve design of ventricular assist devices by reducing weight and dimensions, increasing reliability and independence of operation. Despite the widespread usage of VADs as a treatment of various heart failure conditions, the problem of thrombus formation and recognition is not completely solved. Our research team carried out in vitro tests of Sputnik rotary blood pump (RBP) using testing bench for analysis the influence of the thrombus formation on electrical power and temperature change in the pump.
Aim: Impact study of thrombus formation on the heat generation of Sputnik RBP.
Methods: The experiments were conducted on a testing bench that allows receiving heat distribution characteristics of pump. Sputnik RBP was embedded into a silicone which properties are the same as properties of soft tissue. Simulation of different cardiovascular conditions was performed by changing the referenced pump speed (5000, 7000 or 9000 rpm), varying the test fluid (distilled water or aqueous glycerol solution of various viscosity) and thrombus clamping of the pump components.
Results: At initial fluid temperature of 24°C and rotational speed of 5000 and 7000 rpm the pump surface temperature equalized within 60 minutes of testing. For 9000 rpm the temperature increased and equalized after 120 minutes, the maximum temperature growth was 8°C. Temperature distribution plots showed that temperature of the thrombus area exceeds temperature of the stator area. For diffuser thrombus clamping temperature distributed evenly across the pump body, but dropped sharply and increased to its maximum value in the thrombus area. This result is typical for 8 of 10 measurements within trial using aqueous glycerol solution with blood viscosity at pump rotational speed of 5000 rpm.
Conclusions: The result obtained during heat generation analysis of Sputnik VAD allows determining the presence and location of thrombus formation with high probability.

P20
REGURGITANT FLOW IN MECHANICAL HEART VALVES: FLUID STRESSES AND SPATIAL CORRELATION
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Background: Regurgitant flow in mechanical heart valves (MHVs) is known to be a possible cause of blood trauma (hemolysis, platelet activation). This in turn may cause a series of pathological states, especially in presence of comorbidities. One of the principal guidelines in the design of MHVs is the minimization of device-related turbulence, due to its detrimental effects, in terms of thrombus formation as well as hemolysis. More generally, disturbed flow is to be avoided, as a design requirement.
Aim: To characterize the regurgitant flow in MHVs with Particle Image Velocimetry (PIV), addressing fluid stresses and self-similarity of the velocity field.
Methods: A prism-shaped physical model of the regurgitant flow was used for the measurements, with optimized optical access to the coaxially-seated MHV, enabling easy positioning of the video camera used with the PIV system. This model was inserted in a closed flow loop, with regurgitant steady flow, representative of diastolic phase, at 75 mmHg transvalvular pressure. Average velocities and maximum turbulence shear stresses (TSSmax) were calculated with PIV, by ensemble averaging 1000 instantaneous flow fields. The normalized autocorrelation functions (AF) of the velocity fluctuation, parallel and perpendicular to the jet direction, were also calculated.
Results: The distribution of the jets exiting the valve was observed. Low peak TSSmax and viscous stress values were found, confirming the low impact profile of the valve design. Different self-similarity properties of the flow field were found, with regard to the particular type of AF considered. Moreover, the distance from the jet origin was also found to be important: at increasing distance, a slower convergence of the AF to low plateau values was observed, suggesting a higher coherence of the velocity fluctuations at increasing distance from the valve.
Conclusions: MHVs' flow field in leakage phase was accurately characterized, thanks to a set-up optimized for PIV measurements. Self-similarity properties of the valve jets could be reliably quantified.

P21
OXIDATIVE STRESS INCREASES SUSCEPTIBILITY OF RED BLOOD CELLS TO SHEAR-MEDIATED DAMAGE
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Background: Patients receiving mechanical circulatory support tend to present with heightened inflammation and free radical production associated with pre-existing conditions, in addition to blood interactions with non-biological surfaces.
Aim: The aim of the present study was to assess changes in red blood cell (RBC) deformability and the susceptibility of these cells to mechanical forces for RBC previously exposed to free radicals.
Methods: RBC from 15 healthy donors were washed and incubated for 60 min at 37°C with 10 μM phenazine methosulphate (PMS; an agent that generates superoxide within RBC). Incubated RBC (and negative controls) were assessed for their deformability and susceptibility to mechanical damage (using ektacytometry) prior to the application of shear stress, and also following exposure to 25 different shear conditions of varied magnitudes (shear stress 1-64 Pa) and durations (1-64 s).
Results: Incubation with PMS impaired important indices of RBC deformability indicating decreased blood cell function by ~20% in all conditions (pre and post exposure to shear stress). The typical trends in RBC susceptibility to mechanical damage following conditioning shear were maintained for experimental and control conditions.
Conclusions: Free radicals hinder the function of RBC to deform; however, RBC retained their typical mechanical response to shear stress, albeit at a decreased level compared with Control. Patients receiving mechanical circulatory support are at elevated exposure to free radicals which limits RBC deformability, thus concomitant exposure to high shear environments needs to be further evaluated, as the effects of oxidative and mechanical stress compound the deleterious effects to important parameters that regulate microcirculatory blood flow.

P22
HAEMODILUTION INCREASES THE FRAGILITY OF RED BLOOD CELLS IN RESPONSE TO MECHANICAL STRESS
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Background: Haemodilution with phosphate buffered saline (PBS) is routinely carried out during in vitro haemolysis testing to adjust haematocrit values (30 ± 2%) as per ASTM (American Society for Testing and Materials) standards. However, research suggests that haemodilution with PBS increases haemolysis and reduces total protein concentration in the blood. This may provide unfavourable effects following exposure to mechanical stress such as increased red blood cell fragility, which may occur during clinical settings such as cardiopulmonary bypass.

Aim: To evaluate whether bovine serum albumin (BSA) ought to be included in the ASTM standards for haemodilution, to maintain physiological protein concentrations. Thereby, reducing haemolysis in response to mechanical stress.
Methods: The CentriMag (Thoratec Corp) was tested in vitro (n = 3) using bovine blood (ongoing). Whole blood with a haematocrit ≥36 was diluted to 30% PBS to 70% blood, ± 6% BSA. Total protein concentration was measured and plasma free haemoglobin levels were obtained to calculate the normalised index of haemolysis (NIH).
Results: The haematocrit was diluted from 39.2 to 27.1. Total protein concentration decreased from 6.62 g/dL to 4.16 g/dL following haemodilution with PBS only, however with 6% BSA, protein concentrations remained at physiological levels (6.76 g/dL). Preliminary results show that blood diluted with PBS only, showed higher haemolysis compared to blood diluted with PBS + 6% BSA (5.5 ± 1.7 mg/100 L and 2.0 ± 0.6 mg/100 L, respectively).
Conclusions: Whole blood diluted with PBS alone is more susceptible to haemolysis than blood diluted with PBS + 6% BSA, using the CentriMag. This suggests that plasma proteins may exert protective effects on red blood cells and therefore reduce the degree of haemolysis. These results may have implications for modifications to the ASTM standards of in vitro haemolysis testing, by removing the bias caused by haemodilution to gain true NIH readings for each pump design.

P23
ERYTHROCYTE TOLERANCE TO SUPRA-PHYSIOLOGICAL SHEAR STRESS WITH EXPOSURE TIMES REFLECTIVE OF CLINICAL BLOOD PUMPS
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Background: Mechanical circulatory support (MCS) devices are designed to minimise exposure to supra- physiological shear stress (SS) and thus minimise hemolysis (i.e., the absolute tolerance of red blood cells - RBC - to SS). While absolute tolerance of RBC to SS is clearly defined, and the threshold of RBC functional tolerance to SS has recently been elucidated, the functional tolerance of RBC to SS and exposure durations typical of MCS devices, however, remains unclear.
Aim: The current study aimed to investigate the tolerance of RBC to supra-physiological SS by defining the relation between the magnitude and duration of SS exposure at the upper limits expected to be observed within MCS devices.
Methods: RBC suspensions were exposed to discrete magnitudes of SS (5-100 Pa) for specific durations (1-16 s), immediately prior to RBC deformability being measured. Analyses included exploring the maximal RBC deformation (EImax) and SS required for half EImax (SS1/2). A surface-mesh was interpolated onto the raw data to predict impaired RBC deformability. To identify whether hemolysis occurred during exposure to SS, plasma-free hemoglobin was quantified via spectrophotometry.
Results: The current study indicates that when SS is applied at 5 Pa for 1-16 s, limited changes in RBC deformability are observed. When RBC are exposed to 25-50 Pa, small improvements in EImax and SS1/2 were observed after only 1 s, while prior exposure to 75-100 Pa for 8-16 s impaired RBC deformability as indicated by the increase in EImax and SS1/2. For all shear conditions, there was no significant increase in plasma-free hemoglobin.
Conclusions: The current study has identified the upper limits of functional tolerance to supra-physiological shear stress observed in MCS devices. Use of this method to determine functional capacity of RBC may be useful for hemocompatibility testing of MCS devices and provide insight for the design of future devices.

P24
INDUCTIVE ENERGY TRANSFER FOR PERSONALIZED ARTIFICIAL ORGANS
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Background: Inductive powering has become a popular technique in the design of artificial organs (AO). Now it is desirable to have a tool for providing personalized inductive powering units (IPU) for AOs.
Aim: The purpose was to investigate the relationship between human body size and coils form in terms of their influence on the IPU output characteristics. Providing the design optimization method was also within the scope.
Methods: We have developed numerical modeling tool for the relatively fast calculation of mutual inductance for a coils couple in arbitrary orientation. We have proposed a design approach based on a link geometry optimization. We have developed flexible experimental rig for verification of the results.
Results: Extensive numerical modeling was performed. We have investigated link geometry which is specific for biomedical applications (coil diameters in the range of 30...70 mm, distance between coils in the range of 5...30 mm). We have performed the geometry optimization procedure for an inductive link and have shown that careful adjustment of a controlled geometrical parameter (a number of turns, for example) may provide relatively stable output characteristics for various distances between coils (which greatly depends on a human body size). The characteristics of the proposed IPU design were verified experimentally.
Conclusions: Link geometry optimization ensures the most rigid design of a displacement tolerant inductive powering system and thus may be considered as a preferable design technique in terms of safety which is of special interest in biomedical applications of inductive powering. It is clear that human body size greatly affects IPU performance by imposing restrictions on the implanted coil size (especially for neural stimulators which is placed on the skull) and the distance between coils (due to the thickness of the skin and subcutaneous tissue). Link geometry optimization may be used to deal with it and to solve the problem by providing the person specific coils couple design which can be manufactured using 3D-printing.

P25
EFFICIENCY MEASUREMENT OF AIR-CORE TRANSCUTANEOUS ENERGY TRANSMISSION SYSTEMS FOR VENTRICULAR ASSIST DEVICES CONSIDERING COMMON-MODE CURRENTS FOR A TRANSFORMER IMMERSED IN A NACL SOLUTION AT A TRANSMISSION FREQUENCY OF 500 KHZ
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Background: Air-core transcutaneous energy transmission systems (TETS) use magnetic fields to transfer energy to a ventricular assist device (VAD) from a coil on the surface of the body (primary coil) to one inside the body (secondary coil), without direct electrical connectivity. Measuring the energy transmission efficiency of air-core TETS accurately was difficult previously because of a common-mode (CM) current, which flowed into the ground through an AC source and the measuring equipment.
Aim: We compare with the measured value of the efficiency in air, and in a NaCl solution which imitates human biological tissue by suppressing the CM current at a frequency of 500 kHz.
Methods: Air-core coils covered by a polyethylene terephthalate insulation sheet were immersed in a NaCl solution (0.22 S/m) to imitate wet skin. To reduce the CM current, a CM filter (Daishinmusen, DCF-RF37-BCL) was inserted between the AC source and the primary coil. The oscilloscope (Agilent, DSO- X2002A, 2 GSa/s) measuring a load resistance imitating VAD was floated on the ground by using an uninterruptible power supply battery. For the theoretical calculation, the load resistance, inductance, winding resistance, etc., were measured precisely using an LCR meter (HIOKI, IM3536) that measures impedance and phase difference as a function of frequency. The efficiency and CM current were measured by using two oscilloscopes.
Results: The measured value of the efficiency ± SD was 98.68 ± 0.03% in air and 94.82 ± 0.01% in a NaCl solution, respectively, whereas theoretical estimate ± SD was 95.36 ± 0.30% in air. Moreover, the CM current ± SD were 62.81 ± 0.03 μA in air and 103.1 ± 0.1 μA in a NaCl solution.
Conclusions: We succeeded in suppressing the CM current both in air and in a NaCl solution because the CM current was 0.2% below the primary current. Moreover, the efficiency in a NaCl solution decreased by 3.86% compared to that in air because of an eddy current loss and the increase of the winding resistance.

P26

TRANSCUTANEOUS ENERGY TRANSMISSION BY CAPACITIVE COUPLING

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Background: Nowadays, ventricular assist devices (VADs) are being used for longer and longer periods, some of which are recommended as destination therapy. Transcutaneous Energy Transmission (TET) technology can greatly contribute to the quality of life of implanted patients, because it reduces infections due drive line crossing the skin and mobility problems. Generally the TETs use the variant magnetic field coupling between coils; one external and other subcutaneous. But this technology has two major limitations: the need for a good alignment (both axial and angular) between the coils and the overheating of metallic parts in the vicinity of the coils, by inducing parasitic currents (Foucaut currents). This paper presents a model for the transmission of energy through the electric field coupling between the external circuit and the implanted circuit, in an attempt to mitigate those problems.
Aim: This work has the objective of discussing the viability of the transmission of energy through the skin, to feed implantable devices, through a capacitive coupling (electric field).
Methods: Initially, low power energy transfer tests were performed between circuits through a capacitor formed by conductive surfaces, interposing between them an arbitrary dielectric, whose characteristics were not well defined. The receiver circuit has a high quality factor (Q), i.e. narrow band. Once the capacitive coupling transfer ability was demonstrated, a concentrated parameters modeling of electric circuit was proposed for the coupling by means of a multilayer capacitor, whose dielectric was constituted of skin and subcutaneous tissues.
Results: The initial tests demonstrated the advantage of the system over axial alignment and the electric circuit model allowed verify a region of lower dissipation of Energy (Joule effect) from a few hundred MHz.
Conclusions: The technique discussed may be interesting for feeding implantable devices, but a refinement of model, at high frequency, is necessary.

P27

TRANSCUTANEOUS ENERGY TRANSMISSION USING CAPACITIVE COUPLING FOR CARDIAC PACEMAKER: CALCULATION OF AC-AC ENERGY TRANSMISSION EFFICIENCY

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Background: A cardiac pacemaker is battery-operated and has to be replanted approximately every seven years, which is the life of the battery. This paper proposes a transcutaneous wireless energy transmission system using capacitive coupling for a rechargeable cardiac pacemaker.
Aim: This study was performed to estimate the optimized transmission frequency and size of receiving electrodes by calculating the AC-AC energy transmission efficiency.
Methods: Two parallel transmitting electrodes and two parallel receiving electrodes are prepared. The receiving electrodes are assumed to be attached on the pacemaker embedded in the body, while the transmitting electrodes are placed on the human body surface. The pacemaker is assumed to be embedded at 10 mm from the surface of the skin. We measured the S-parameter using a network analyzer and calculated the AC-AC energy transmission efficiency while the transmitting frequency was increased from 2 to 2000 MHz. For tissues including skin and fat, 0.2 S/m NaClaq was applied between the transmitting and receiving electrodes. Three types of receiving electrodes of sizes 5 × 30 mm (model 1), 10 × 30 mm (model 2), and 15 × 30 mm (model 3) and one type of transmitting electrode, whose size was 10 × 50 mm, were used. Additionally, to estimate the parasitic short-circuit current between the two receiving electrodes, electromagnetic field analysis was conducted.
Results: The maximum energy transmission efficiency was determined to be 25.2% at 122 MHz in the case of the model 1. In the case of model 2, it was determined to be 28.6% at 122 MHz. However, in the case of model 3, it was determined to be significantly lower, 18.0% at 102 MHz. Analysis results indicated that the short-circuit current of model 3 increased to approximately 2.7 times that of model 2.
Conclusions: The maximum energy transmission efficiency was determined to be 28.6% at 122 MHz. As a cardiac pacemaker requires approximately 20 mW for operation, in future, we propose to analyze the specific absorption rate of each organ by electromagnetic simulation.

P28

EXPERIMENTAL AND NUMERICAL ANALYSIS OF DYE WASHOUT IN VENTRICULAR ASSIST DEVICES

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Background: Ventricular Assist Devices (VADs) are associated with complications due to the damage done to the blood, which relates to shear stress and exposure time. Designing VADs to minimise both should then reduce damage.
Aim: The aim of this work was to use washout of a dye to investigate local and overall residence times in VADs.
Methods: A flow rig was developed such that initially dyed glycerol circulated and a three-way tap was used to switch to a transparent solution. A camera was focused on the transparent VAD outlet tube, and the colour change in the images calibrated to dye concentration. The concentration change at the outlet, dye washout curve, was used as an indicator of the residence times in the VAD. Computational Fluid Dynamics was used to calculate dye washout curves. An established flow field was first obtained with a transient simulation. A scalar variable was introduced to represent the dye, and a transport equation was used to model its convection. Simulated dye washout curves were compared with experiment, and simulations were used to understand fluid dynamic factors determining the different curves.
Results: The time taken for the outlet concentration to drop from 100 to 5%, T05, was an initial indicator of residence time. At 5 l/min experimental and numerical T05 were 1.11 and 1.14 s respectively in the CentriMag (magnetic suspension). In contrast T05 was just 0.26 s in the HeartMateII (axial & contact bearings). This difference may be explained by the larger volume of the CentriMag. Despite a similar internal volume to the HeartMateII, the HVAD (centrifugal & hydrodynamic suspension) had T05 0.42 s. The difference is likely due to the secondary flow in the HVAD, required for suspension; from simulation results, an additional 0.08 s is required for the concentration in the secondary flow to reach 5%.
Conclusions: The secondary flow path plays a critical role in determining blood residence time in the VADs. Ongoing work is focused on investigating the importance of secondary flow path parameters.

Dialysis/Apheresis - Experimental Approaches

P29

MATHEMATIC MODEL OF BLOOD GLUCOSE DYNAMICS

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Background: Diabetes mellitus is one of the most widespread and serious diseases. The aim of modern science in diabetes therapy is to develop a closed-loop system, which can compensate diabetes. Modern systems for blood glucose (BG) monitoring and subcutaneous insulin injection systems give opportunity to enhance the quality of diabetes mellitus therapy. However, any errors in such systems can cause dangerous consequences for the patient's health: hypo- or hyperglycemia.
Aim: Closed-loop systems need a reliable algorithm that would detect errors in its operation. A part of this algorithm is mathematic model of BG regulation. Mathematic model can be used to predict BG for short and long periods of time in order to give reference data for invasive or what is more important – for non-invasive glucometer.
Methods: Developed "sigma-model" of BG regulation assumes that accents and descents of BG are strongly connected to food intakes and insulin injections corresponsive. Form of accent depends on three parameters: weight

of intaken food, its relative carbohydrate coefficient and its glycemic index. Form of descent depends on the amount of injected insulin and its action time. The pattern of accents and descents is logistic or sigma-function. For experimental evaluation of developed mathematic model we used DirecNet protocols that contain information about insulin injections, food intake of patients with diabetes mellitus type 1, and data from glucose monitors. Besides sigma-model, also Sturis's, Engelborghs', and Bennett-Gourley's models were approbated.
Results: RMSE of Bennett-Gourley', Sturis', Engelborghs' model was 18.2 mg/dl, 64.5 mg/dl and 45.3 mg/dl corresponsive. In spite of its simplicity, Sigma-model had the lowest RMSE among all tested models -15.7 mg/dl.
Conclusions: Sigma-model rather accurately describes BG dynamics in patients with diabetes mellitus type 1. It can be used as a part of blood glucose prediction algorithm. This work was financed by the Ministry of Education and Science of Russian Federation: agreement No 14.578.21.0186, RFMEFI57816X0186.

P30
STUDY OF THE EFFECT OF MODULE GEOMETRY ON FORWARD FILTRATION IN HOLLOW FIBER DIALYZERS WITH A TWO-DIMENSIONAL MOMENTUM TRANSPORT MODEL
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Background: The enhancement of convective transport by increasing the extent of forward filtration at blood inflow is crucial to remove middle molecular weight solutes in high-flux dialyzers for the treatment of chronic renal failure. Mathematical models of momentum transport in dialyzers may help to optimize module geometry and membrane transport properties to control forward filtration to maximize solute clearance while avoiding undesired effects at fixed operating conditions and blood properties.
Aim: Since a systematic analysis of all the dialyzer-related parameters affecting momentum transport has not been reported yet, the effect of geometrical and membrane-related dimensionless groups on forward filtration was investigated with a two-dimensional axisymmetric momentum transport model in the hollow fiber of a dialyzer.
Methods: Steady-state momentum transport in the compartments of a dialyzer (i.e. blood, membrane, dialysate) was described with motion, Darcy-Brinkman and Navier-Stokes equations, respectively. The effect of non-newtonian blood behavior was also taken into account. The complete set of dimensionless groups determining momentum transport in the dialyzer was obtained with dimensional analysis of model equations. Their effect on forward filtration was investigated by solving model equations for values typical in clinical practice.
Results: Good agreement was found between model-predicted and experimental values of forward filtration flow rates at increasing blood flow rates. At given operating conditions, forward filtration increases for increasing membrane pressure moduli and module packing density. At given membrane pressure moduli and module geometry, forward filtration increases with Reynolds number at blood inlet and dialysate-to- blood flow rate ratio.
Conclusions: Model predictions may be helpful to optimize dialyzer geometry to control forward filtration and allow for the removal of middle molecular weight solutes at given operating conditions.

P31
MODELING WATER TRANSPORT ACROSS THE CELL MEMBRANE IN HD PATIENTS
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Background: Mathematical models are useful tools to predict fluid shifts between body compartments in the organism of hemodialysis (HD) patients. A correct description of the flow of water between cells and interstitium (Jv-cell) is important to accurately represent the fluid status. Jvcell is often calculated as proportional to the total osmotic gradient across the cell membrane, but this approach is limited in its accuracy by the number of osmotically active species whose kinetics is described by the model.
Aim: We evaluated the effect on the model parameters of changing the number of substances appearing in the equation describing Jvcell.
Methods: A mathematical model was applied to data from 20 patients who underwent a standard HD session. The substances described in the baseline version were: water, proteins, Na, K, and urea. In the expanded version it was added Cl. Small solutes moved only between intracellular and extracellular compartments. Solute transport across the cell membrane took place via passive diffusion and, for Na and K, through the ATPase pump, characterized by the maximum transport rate, JpMAX. The optimal values of JpMAX, and two transcapillary transport parameters, the capillary filtration coefficient Lp and its large pores fraction αLP, were estimated.
Results: The median value of the estimated parameters in the baseline model was: Lp = 11.63 [7.9, 14.2] mL/min/mmHg, αLP = 0.056 [0.050, 0.058], JpMAX = 5.52 [3.75, 7.54] mmol/min. In the expanded model all parameters were significantly different: Lp = 8.14 [6.29, 10.01] mL/min/mmHg, αLP = 0.046 [0.038, 0.052], JpMAX = 16.7 [11.9, 25.2] mmol/min.
Conclusions: The biggest change in the estimated parameters was a 300% increase in the value of JpMAX. This can be explained as a need for a faster turnover of solute molecules between intra- and extracellular space when more contributors to total osmolarity is kinetically modeled, and thus available for removal by HD. The parameter JpMAX is highly sensitive to the number of solutes modeled, and its value should be interpreted only in relation to this factor.

P32
MODIFIED P(HEMA) CRYOGELS AS POTENTIAL CELL CARRIERS FOR LIVER TISSUE ENGINEERING
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Background: Macroporous polymers synthesised by cryogelation have properties which make them suitable for liver tissue engineering. We have previously shown that antibody bound cryogels may be used to remove biotoxins related to life threatening anthrax infection. It may also be possible to manipulate the properties of these materials for bioartificial liver.
Aim: To investigate the effect of changes in cross-linker, freezing temperature and short- peptide RGD covalent binding on the mechanical and cell supporting properties of p(HEMA) cryogels.
Methods: Cryogels were synthesized using variable gelation temperature (-12C,-20C); cross-linker (PEGDA and N,N'-MBA); and RGD-PEGDA incorporation. Porosity, elastic modulus and swelling were examined by SEM, textural analysis and equilibrium drying. HepG2 cell studies were carried out using MTT, fluorescent labelling and confocal microscopy.
Results: Cryogels were synthesised with an open porosity of up to 100 um and variable porous and mechanical structure depending on cross-linker and cryogelation temperature. Metabolising HepG2 spheroid formation was evident after 72 h particularly in the RGD bound cryogels.
Conclusions: Modified p(HEMA) cryogels made using variable synthesis parameters have physicochemical properties promoting HepG2 adhesion and growth. Further studies are required to further optimise parameters and model functional cell growth over time.

P33
SIEVING COEFFICIENTS OF HEMODIALYSIS MEMBRANES
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Background: It is common to refer to ISO8637 to describe the sieving coefficient (SC) test, which requires to adjust the ultrafiltration (UF) rate to cover the manufacturer's specified range. The specified UF range is lower for devices not intended for convective therapies (if specified at all) compared to devices which include convective therapies in the intended use. Strict interpretation of ISO8637 would lead to the situation that SC for devices not intended for convective therapies, (e.g. Theranova®), are based on low UF conditions, whereas SC for devices intended for both non-convective and convective therapies, (e.g. Polyflux® H or Revaclear®), are based on high UF conditions. SC values can only be compared in a meaningful way when data are obtained under identical conditions.

Aim: SC are often used to compare permeability of membranes in dialyzers used in different modes of renal replacement therapy. This work describes SC data obtained under identical, and therefore comparable, conditions.
Methods: SC of dialyzers were tested according to ISO8637 with a recirculating fluid setup with human plasma (total protein content 60 ± 5 g/L). Blood side flow rate (QB) was set 300 ml/min and UF was set 60 ml/min and both were kept constant until stable pressure, temperature and flow rates were attained and samples were drawn. SC was calculated as solute concentration on filtrate side divided by average solute concentration of blood inlet and blood outlet side. Beta-2-microglobulin (b2M), myoglobin (myo) or albumin (alb) were analyzed with turbidometric assays.
Results: The results are shown as mean SC value [%] of 6-8 replicates ± standard deviation. Baxter Revaclear® 400 SC were b2M 95 ± 4.2, myo 68 ± 1.5, and alb 0.27 ± 0.04. Baxter Polyflux® 170 H SC were b2M 82 ± 6.0, myo 37 ± 6.6, and alb 0.22 ± 0.10. Baxter Theranova® SC were b2M 99 ± 5.4, myo 89 ± 5.7, and alb 0.8 ± 0.16.
Conclusions: Care must be taken when SC of dialyzers are compared when the intended use is only partly the same but not identical. This study thus offers SC obtained under identical conditions. Critical view of SC tests should become common practice.

P34
POSSIBLE INFLUENCE OF HEMODIALYSIS ON OXIDATIVE STRESS
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Background: Inflammation, oxidative stress (OS) and atherosclerosis are closely related and have much in common in hemodialysis (HD) patients.
Aim: The aim of the study was to determine the level of OS in patients undergoing HD.
Methods: A number of 67 patients (mean age 53 ± 12 years) undergoing (45 male and 20 female). Polysulphone type of membrane was used for a period of 2-5 years (n = 25); 6-10 years (n = 30); more than 11 years (n = 12). The control group had 30 healthy subjects (15 male and 16 female) mean age of 50 ± 7 years. Lipid peroxidation (fluorimetric method, Yagi et al, 1967), using the end product of malonyldialdehyde - MDA and anti-LDL antibodies (Biomedica gruppe, Vienna, Austria) were used as markers of OS. TAS (total antioxidative capacity, Randox, Crumlin, G. Britain) was used as an antioxidative defence marker as well as antioxidative enzymes such as SOD – superoxide dismutase and Gpx – gluthation peroxidase.
Results: LP showed higher value of 4.82 ± 0.22 µmol/L ($p<0.01$) and so did anti-LDL antibodies (251 ± 73 mU/ml) ($p<0.05$). TAS value increased to 1.65 ± 0.3 mmol/L compared to controls (1.25 ± 0.2 mmol/L) ($p<0.05$). Antioxidative enzymes did not show any statistical difference.
Conclusions: Due to the results, it can be concluded that there is evident OS in HD patients which may lead to other system impairment such endothelial dysfunction and other cardiovascular morbidity. OS may be caused by the activation of polymorphonuclear cells, activated by HD membrane. The use of antioxidant therapy might be a matter of choice to diminish OS in these patients.

P35
TREATMENT OF THROMBOTIC MICROANGIOPATHY WITH THERAPEUTIC PLASMA EXCHANGE USING CITRATE ANTICOAGULATION
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Background: Therapeutic plasma exchange (TPE) with fresh frozen plasma is initiated emergently in patients after diagnostic suspicion of thrombotic microangiopathy (TMA). We use regional citrate anticoagulation for membrane TPE to reduce the bleeding risk in these patients with thrombocytopenia and bleeding diathesis, and to decrease the adherence of blood constituents to the plasmafilter.
Aim: The aim of our study was to assess the safety and response to the citrate TPE and recovery from TMA in patients, treated in University Medical Center Ljubljana between January 2009 and January 2017.
Methods: We included 23 patients, 15 females and 8 males, with a mean age of 44 ± 20 years. Idiopatic TTP was confirmed in 21, aHUS in 1 and HUS in 1 patient. Membrane TPE with fresh frozen plasma of 3444 ± 809 ml per procedure was performed daily. Regional anticoagulation was achieved with 4% or 8% trisodium citrate. Calcium was supplemented as 1 mol/L calcium chloride infusion to maintain serum ionized calcium stable throughout the treatment. All complications were noted. Data were obtained from the hospital's laboratory database and the patients' plasmapheresis charts.
Results: 561 TPEs were performed in 31 treatments. The average duration of treatment was 27 ± 29 days and the average number of 18 ± 13 TPEs per patient was needed. Anticoagulation was excellent. Mild metabolic alkalosis and hypokalemia were noted in 21 patients but correction with heparin-free hemodialysis was not needed. We did not observe any citrate reactions. The average platelet count was 41 ± 38 × 109/L before treatment and reached 204 ± 96 × 109/L after treatment. 84% of treatments had complete response, 2 patients had partial remission. Three patients died. Two of them responded partially, but died due to sepsis. The third was nonresponder and death was not procedure-related.
Conclusions: 90% of patients had an excellent response. We believe that citrate TPE is safe and effective treatment for patients with TMA and thrombocytopenia.

P36
CITRATE ANTICOAGULATION: INFLUENCE OF HAEMATOCRIT ON THE EXTRACTION RATIO OF CITRATE AND UREA
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Background: As citrate is not able to penetrate the erythrocyte membrane, it is only distributed in plasma, whereas urea readily diffuses into erythrocytes potentially resulting in differences of the extraction ratio.
Aim: The aim of this study was to examine whether the haematocrit has an impact on the extraction ratio of citrate and urea during dialysis.
Methods: We compared the in vitro extraction ratio of citrate and urea in blood with different haematocrit (20% versus 40%) as well as in plasma. For anticoagulation, blood/plasma (1.2 l) was citrated (18 mM) and heparinised (2 IU/mL). Urea was added to a concentration of 100 mM. Blood flow rates of 200 mL/min and dialysate flow rates of 67 mL/min or 500 mL/min were applied. Samples were drawn at the start and after 2.5, 5, 7.5, 10, 12.5, 15, 17.5 and 20 minutes pre and post filter to analyse citrate and urea concentrations. The extraction ratio was calculated as the difference of the pre minus post filter concentration divided by the pre filter concentration.
Results: We found increasing extraction ratios for citrate with increasing haematocrit at low dialysate flow, whereas the extraction ratios were not influenced by haematocrit at higher dialysate flow. Extraction ratios for urea were independent of haematocrit. This suggests that at lower dialysate flow, the dialysate is saturated and, due to the lower distribution volume of citrate in blood with higher haematocrit, the concentration gradient can be maintained. In case of higher dialysate flow, the removal of citrate is fast enough to maintain the concentration gradient. Due to the fast penetration of the erythrocyte membrane by urea, its extraction ratio does not depend on haematocrit.
Conclusions: We could show a haematocrit dependent extraction ratio at low dialysate flow compared to standard dialysate flow in chronic dialysis. Whether this finding is relevant for the clinical setting in acute dialysis, where a low dialysate flow is applied, remains to be further evaluated.

P37
INFLUENCE OF DIFFERENT ANTIKOAGULANTS ON ENDOTOXIN ACTIVITY IN HUMAN SERUM
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Background: Endotoxins are the major components of the outer membrane of most Gram-negative bacteria and are one of the main targets in pathogen-induced inflammation. The presence of endotoxins in blood can provoke septic shock in case of pronounced immune response.
Aim: In recent years, endotoxins have gained increasing of interest as targets in extracorporeal blood purification. Aim of this study was to test if the anticoagulant has an influence on endotoxin activity and inflammatory response

in extracorporeal therapies. The anticoagulants which were tested are unfractionated heparin, low molecular heparin, fondaparinux, and citrate.
Methods: Human serum from freshly drawn blood was spiked with increasing concentrations of anticoagulants. After adding 1 ng of endotoxin from E. coli, the samples were incubated for 30 min at 37°C and the endotoxin activity was measured using the kinetic chromogenic Limulus amoebocyte lysate (LAL) test. The inflammatory effect of endotoxins in differently anticoagulated blood samples was evaluated by measuring pro-inflammatory cytokines after 4 h incubation of fresh blood with 1 ng/ml LPS. All experiments were conducted at least in triplicates.
Results: The endotoxin activity increased with the heparin dose. Serum with 2.5 IU/ml heparin showed a 60% higher endotoxin activity in the LAL test compared to serum without heparin. A dose-dependent increase was also observed with low molecular weight heparin. Fondaparinux did not show an influence on the endotoxin activity, whereas citrate caused a reduction of endotoxins in the LAL assay. The cytokine levels in blood after LPS stimulation show the same trend.
Conclusions: As endotoxins induce a strong host immune response, there is an urgent need to reduce their activity. Based on our in vitro experiments, the results suggest that patients who suffer from endotoxemia could benefit from citrate anticoagulation during extracorporeal treatments.

P38
LIPOPROTEIN-ASSOCIATED PHOSPHOLIPASE A2 PREDICTS CARDIOVASCULAR OUTCOMES IN PERITONEAL DIALYSIS PATIENTS
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Background: Cardiovascular disease is the primary cause of mortality in Uremia patients; Moreover, CVD is not associated with the classical blipoprotein abnormalities, new biomarkers for predicting Cardiovascular events is essential to be explored. Lipoprotein-associated phospholipase A2 (Lp-PLA2) is a lipoprotein-bound enzyme involved in inflammation and atherosclerosis contrast to the general population, which has been shown to predict future cardiovascular events in normal population.
Aim: In this research we aimed to evaluate Lp-PLA2 in peritoneal dialysis patients in order to evaluate the potential relationship with the cardiovascular accidents.
Methods: This single-center retrospective study included 849 peritoneal dialysis patients enrolled between July 1, 2009 and December 31, 2013 and followed to June 30, 2016. We detect baseline Lp-PLA2 level of all the patents, as well as patents' demographic characteristics, clinical and laboratory measurements were also collected.
Results: This single-center retrospective study included 849 peritoneal dialysis patients enrolled between July 1, 2009 and December 31, 2013 and followed to June 30, 2016. We detect baseline Lp-PLA2 level of all the patents, as well as patents' demographic characteristics, clinical and laboratory measurements were also collected.
Conclusions: Lp-PLA2 level is predictive for cardiovascular events in peritoneal patients. However, Lp- PLA2 was not independently associated with all-cause mortality.

P39
CHALLENGE TO A PORTABLE HEMOFILTRATION SYSTEM IN GOAT
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Background: Commercially available blood purification system is too big and complicated to be provided in disaster areas and developing countries for blood purification. We have developed a portable hemofiltration system that can be safely enforced by anyone in disaster areas and developing countries of hemodialysis.
Aim: We made a portable hemofiltration system (size 300 × 160 × 95 mm) with the tiny hemofilter (size 75 × 99 × 21 mm, membrane area 0.3-0.5 m^2 with Ø100 µm hollow fibers) and the small centrifugal blood pump (impeller diameter Ø34 mm). In this study, we examined whether this system can be safely used for blood purification in a goat.
Methods: A double lumen vascular access catheter ((10.8 Fr, BloodMax HC, Nipro®, Japan) and (12Fr,BA/UK UB-1220-WHO, Nipro®, Japan)) was placed into the carotid vein of a healthy 30 kg goat under general anesthesia. After awakening, the portable hemofiltration system was put on the back of the goat. The blood flow rate was set at 50-100 mL/min with 2000-3000 rpm. The filtration flow rate was set at 150-180 mL/hr using a conventional infusion pump (FP-N11, Nipro®, Japan). As the anticoagulant, heparin was used for the first goat, and citric acid was used for the second goat.
Results: Continuous hemofiltration with the portable hemofiltration system could be performed for 6 days and 10 hrs with the first goat, and for 5 days and 12 hrs with the second goad without the change of a tiny hemofilter and the small centrifugal blood pump.
Conclusions: By developing this portable hemofiltration system, long-term blood filtration becomes possible in disaster areas and developing countries. Further development of this system, we would like to make a wearable and/or implantable artificial kidney possible.

P40
MODELING OF BIOTECHNICAL SYSTEM OF ARTIFICIAL BLOOD PURIFICATION WITH WEARABLE ARTIFICIAL KIDNEY
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Background: The problem of extrarenal removal of metabolites from the human body is one of the most urgent in modern medicine. Wider use of hemodialysis is hindered by the high cost of the procedure. A system for dialysate regeneration (SDR) would considerably reduce the resource consumption. Wearable artificial kidney SDR-01 on the basis of peritoneal dialysis was assembled.
Aim: The aim of this work is to suggest a mathematic model of biotechnical system of artificial blood purification with SDR-01.
Methods: The biotechnical system includes patient with dialysate in peritoneum cavity, wearable artificial kidney and tubing lines that connect extracorporeal hydraulic circuit to patient's peritoneum cavity. Patient is assumed as a reservoir with equivalent fluid volume that is separated from dialysate by peritoneal membrane. Dialysate is continuously recirculated through regeneration unit that reduces concentration of metabolites in it. Regeneration unit contain sorption elements and electrolyzer. Mathematic model includes diffusive and convective mass transfer across peritoneal membrane, kinetics of sorption by activated carbons and urea elimination via electrolysis. Ion transfer is also taken into consideration. The model was approbated in the following way: mass transfer across peritoneal membrane was tested on the data from three patients that undergone peritoneal dialysis; dialysis regeneration processes were approbated on the data received during in vitro testing of SDR-01.
Results: RMSD for glucose concentration in dialysis fluid were 3.9, 9.7 and 2.6 mmol/l for three patients. RMSD for volume of fluid in peritoneal cavity were 39.1, 149.6 and 68.2 ml. RMSD for urea elimination with electrolysis were 0.3, 0.5 and 0.8 mmol/l for three different materials of electrodes. RMSD of creatinine elimination by sorption elements were 174.5, 121.9 and 124.5 umol/l for three different activated carbons.
Conclusions: The developed model imitates processes of blood purification biotechnical system with a wearable artificial kidney based on peritoneal dialysis.

P41
TRIALS OF WEARABLE ARTIFICIAL KIDNEY SDR-01
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Background: Patients with chronic renal failure need artificial blood purification in order to maintain living organism. Contemporary clinical techniques for that are quite useful but for recent several decades research groups were focused on developing a wearable artificial kidney, because such a device

has a potential to possess the following advantages: unrestricted patient's mobility, enhancement of physiologic impact, reduce of water consumption and costs of procedure.
Aim: Wearable artificial kidney SDR-01 (System for Dialysis with Regeneration unit) is a device for carrying out continuous peritoneal dialysis with dialysate regeneration. Dialysate regeneration unit allows maintaining maximal flows of metabolites during more than 24 hours. In 2016 there were laboratory and animal trials of this system.
Methods: For in vitro trials a mock of biotechnical system of peritoneal dialysis was assembled. The mock included a three-neck bulb in a thermostat (to imitate peritoneal cavity), syringe dispenser that added to the bulb solution of metabolites (to imitate their transfer from blood across peritoneal membrane), and biochemical analyzers to measure metabolites and ions concentration. For the animal model a dog with weight of 15 kg was chosen. Two Tenkhoff catheters were implanted into peritoneum. Acute renal failure was imitated via infusion of 200 g of x-ray contrast.
Results: Laboratory trials showed that SDR-01 can eliminate metabolites from dialysis fluid with the following rates: up to 1.2 g/h (urea), 0.3 g/h (creatinine, uric acid). pH of dialysis fluid tended to and was about 7.0 (for fluids with starting pH 5.2 and 7.0) during the whole procedure. Animal trials showed that SDR-01 eliminate urea, creatinine and uric acid with rates of 0.2 g/h, 0.3 g/h and 0.3 g/h respectively. Na, Ca, Cl ions in dialysate were in diapason of 10% from the initial concentration, pH tended to 7.4. By the end of day 2 blood biochemical characteristics were stabilized.
Conclusions: Wearable artificial kidney SDR-01 can be used to carry out continuous peritoneal dialysis and ultrafiltration.

P42
RISK FACTORS AND OUTCOMES OF EARLY PERITONITIS IN CHINESE PERITONEAL DIALYSIS PATIENTS
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Background: Peritoneal dialysis (PD) is one of the main renal replacement treatments. Study concerning risk factors and outcomes of peritonitis within first 6 months in peritoneal patients is sparse.
Aim: This study aims to investigate risk factors associated with early-onset peritonitis (EOP) and its influence on patients'technique survival and mortality.
Methods: This is a retrospective observational cohort study. A total of 483 patients who having at least one episode of peritonitis were the study subjects, followed up from March 1st, 2002 to August 31, 2016, in our center. According to the time to first peritonitis, we divided patients into two groups: EOP (≤6 months, n = 167) and late-onset peritonitis (LOP, >6 months, n = 316). Logistic regression was used to analyze the factors associated with EOP. Cox proportional hazard model was conducted to examine the influence of EOP on clinical outcomes.
Results: Of 483 patients, 167 (34.6%) patients developed the first episode of peritonitis within first 6 months. The multivariate logistic analysis showed that factors associated with EOP include male gender (odds ratio(OR) 1.920, p = 0.002), and a low serum albumin level at the start of PD (OR 0.950, p = 0.007). In the Cox proportional hazard model, EOP was a significant predictor of all-cause mortality (hazard ratio (HR) 2.766, p<0.001). There were no differences between EOP and LOP for technique failure. However, in continuous analyses, a negative correlation was observed between time to first peritonitis and technique failure (HR 0.988, p = 0.006). In the Spearman analysis, time to first peritonitis was negatively correlated with peritonitis rate (r = -0.573, p<0.001).
Conclusions: Male gender and a low serum albumin level before PD were strongly associated with an EOP. Also, an EOP patient had a higher risk of poor clinical outcomes. More importantly, an early peritonitis onset was associated with a high peritonitis rate.

P43
LONG-TERM OUTCOME OF PATIENTS WITH RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS REQUIRING DIALYSIS TREATED WITH PLASMAPHERESIS: A RETROSPECTIVE, SINGLE-CENTRE STUDY
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Background: Plasma exchange (PE) has been used routinely for treatment of rapidly progressive glomerulonephritis (RPGN), but the long-term benefit of PE in severe RPGN requiring dialysis remains unclear.
Aim: We aimed to describe the longterm outcomes of severe RPGN patients treated with PE in our centre and share our experience.
Methods: Patients diagnosed with RPGN and required dialysis at entry between June 2004 and August 2016 in our centre were included. Renal biopsy was performed if the patient had no contraindication.
Clinical and biological data were collected from the initial evaluation throughout follow-up at months 1, 3, 6, 12, 24, 36 after PE onset, and at last visit.
Results: A total of 37 RPGN patients required immediate dialysis at entry were identified. Among them, 15 patients were diagnosed with anti-GBM disease, 16 patients were diagnosed with ANCA-Associated Vasculitis (AAV), and 6 patient were diagnosed with Systemic lupus erythematosus (SLE). A total of 109 PE sessions were performed. The total volume of the plasma per patient was 8.8 ± 4.2 L (range 2-18 L). 31 AAV and anti-GBM disease patients received treatment with a combination of glucocorticoids and cyclophosphamide. All 6 SLE patients received only glucocorticoids. The renal survival rates at 1 year and 5 years were 64.86% and 50.00%, respectively. 7 (46.67%) patients with anti-GBM disease and 6 (25%) patients with AAV developed ESRD and dialysis dependent. The patient survival rates at 1 year and 5 years were 97.30% and 91.89%, respectively. Three AAV patients died during follow-up time, and all of them were directly attributed to infection. A total of 9 adverse events were reported in 5 patients (13.51%).
Conclusions: In this retrospective study, we found RPGN patients required dialysis at entry could also benefit from PE and had a relatively high rate of dialysis independence and low mortality after PE. This effect was sustained to 5 years from diagnosis. Infections after immunosuppression initiation were the leading cause of death.

Biomaterials: Hydrogels - Scaffolds I

P44
MODIFICATION AND OPTIMIZATION OF POLYSACCHARIDES FOR HYDROGEL FORMATION
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Background: An important goal of tissue engineering is to mimic the extracellular environment and to control cell functions through cell–material interactions. Recently, injectable hydrogels have attracted considerable attention as cell carriers and bioactive agents in regenerative medicine due to their ability to fill complex 3D tissue gaps with relative ease of administration in-vivo. Therefore, hydrogels should exhibit specific morphological, biophysical and biomechanical characteristics.
Aim: The main goal of this study was to use different approaches to modify and optimize the synthesis of succinylated chitosan (S-Chi) and oxidized glycosaminoglycans (GAGs) to act as hydrogel precursors for preparing stable polysaccharide-based hydrogel systems that favour tissue regeneration.
Methods: The hydrogel formation is driven by Schiff base cross-linking between the amino groups of chitosan and the aldehyde groups of Ox-GAGs resulting in imine bond formation. Different oxidation degrees of the Ox-GAGs together with different mixing ratio for both of the hydrogel components and different final volumes of the hydrogel systems were prepared and compared, aiming to improve the mechanical properties. Characterization of functional groups for both hydrogel components together with gel content measurements were used to study and evaluate physical properties of composite hydrogels.

Results: The gel content measurements were dependent on cross-linking and structure of the composite hydrogels. All the hydrogels possess relatively low stiffness due to low aldehyde content present in the different Ox-GAGs, indicating potential use for cartilage tissue engineering. The best hydrogel system was S-Chi/Ox-hyaluronic acid due to its higher gel content. This formulation does not require the use of any chemical initiator and thus may be a biocompatible alternative to other formulations.
Conclusions: The dual utility of using S-Chi and Ox-GAGs as both structural and bioactive component is promising for cell adhesion and proliferation, which can enable mesenchymal stem cell encapsulation.

P45
PEGYLATED HYDROGELS AS A NOVEL DRUG DELIVERY SYSTEM AGAINST PROSTATE CANCER
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Background: Prostate cancer is one of the leading types of cancer for the male population and several therapeutic strategies are currently used, including anti-cancer agents. However, systemic side effects and other treatment disadvantages led to the use of alternative medicine products. Amygdalin (B17) is a vitamin that can be found in the kernels of some fruits and nuts, such as apricots and bitter almonds. It has been studied for a long time against several forms of cancer, including bladder and prostate cancer. Nevertheless, the results so far are inconclusive, with questionable drug efficiency and potential systemic HCN poisoning.
Aim: Our main goal was to create a drug delivery system (DDS) in the form of a pegylated hydrogel that can encapsulate B17 and used locally for targeted delivery.
Methods: In our preliminary studies we used human LNCap cancer cells that were cultivated in complete culture medium (RPMI 1640 & 10% FBS, 1% P/S), with and without the presence of B17 and polyethylene glycol (PEG). The cell number and metabolic activity were measured at predetermined time points, using an automatic cell counter (Vicell) and an MTS assay, respectively.
Results: The presence of B17 had a significant effect on the number of viable cells after 3 days of cultivation. The addition of PEG in combination with B17 led to a similar effect in the number of viable cells. The MTS assay revealed a significant decrease in cell metabolic activity which was further enhanced by the addition of PEG. Taking into account that the number of viable cells remained the same, we concluded that the combination of PEG and B17 was the most effective against LNCap in vitro.
Conclusions: In the future we will focus on creating pegylated hydrogels from polysaccharides for the encapsulation of B17 and local infusion.

P46
REVERSIBLE GELATIN HYDROGELS BASED ON SEMI-COVALENT INTERACTIONS
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Background: Hydrogels synthesized using semi-covalent interactions, exhibit shear thinning property as a major feature that makes them ideal for a variety of applications.
Aim: The aim of this study was to synthesis a novel gelatin hydrogel employing semi-covalent interactions. To this end, telechelic polyethylene glycol was functionalized with aldehyde end groups and used as a biocompatible crosslinking agent for gelatin to form a three-dimensional (3D) hydrogel network.
Methods: Bi-functionalized polyethylene glycol was synthesized by esterification reaction between hydroxyl- terminated-PEG and 4-formylbenzoic acid. FTIR analysis was used for verification of the product. The hydrogel fabrication was carried out by simply mixing of gelatin and the bi-functionalized PEG, both in aqueous solutions.
Results: Synthesis of the bi-functionalized PEG was proven by FTIR spectroscopy by appearance of various peaks at v (cm-1) = 3490, 2882, 1976, 1717, 1466, 1345, 1280, 1104, 961, 842. Hydrogel preparation was performed by mixing the solutions containing the gel making components (namely gelatin and the PEG dialdehyde). It was observed that the hydrogel formation was took place in less than 60 seconds.
Conclusions: In this study, a gelatin-based hydrogel was prepared by induction of semi-covalent interactions between gelatin and a bi-functionalized PEG dialdehyde. The resulted hydrogels showed shear- thinning properties that are useful for applications as injectable and/or printable materials for bio- applications. The obtained hydrogel can be used as drug delivery system, cell culture scaffolds and other applications where materials with shear thinning are required.

P47
MECHANICAL AND IN-VITRO PERFORMANCE OF POROUS HYDROXYAPATITE/POLY(LACTIC ACID)/POLYCAPROLACTONE COMPOSITE SCAFFOLDS
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Background: The successful engineering of such scaffold with particular mechanical properties, surface chemistries, and porous morphology for cell invasion and angiogenesis is a long-lasting challenge in bone tissue engineering.
Aim: The aim of this research is to produce a three-component system with suitable microstructure, bioactivity and mechanical properties for bone tissue defect repair combining mechanical performances of polycaprolactone (PCL) and poly(lactic acid) (PLA), in terms of high elasticity and stiffness, with bioactive and osteoinductive ability and highly porous microstructure of hydroxyapatite (HAp) derived from cuttlefish bone.
Methods: Hydrothermal transformation of cuttlefish bone into hydroxyapatite (HAp) was performed while retaining the cuttlebone architecture. Composite structures were obtained using vacuum impregnation technique with different PCL/PLA ratios. Final systems were characterized by XRD, FTIR spectroscopy, TGA and SEM. Mechanical properties were investigated by compressive test, while cytotoxicity of materials was evaluated by MTS assay.
Results: Compressive test showed that the PCL/PLA-coated HAp scaffold resulted in a material with improved mechanical properties with interconnected porous structure indispensable for tissue growth and vascularization. Variation of PCL-PLA ratio has resulted in alteration of scaffolds elasticity. Additionally, prepared PCL/PLA-HAp systems are non-cytotoxic.
Conclusions: The results show that PCL/PLA-coated hydroxyapatite scaffold derived from cuttlefish bone, processed by a hydrothermal synthesis and a vacuum impregnation technique, might be an alternative to the current biomaterials and processing techniques used in bone tissue engineering.

P48
OXYGEN PERMEABILITY MEASUREMENT OF CONTACT LENSES: CRITICAL POINTS
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Background: Contact lens (CL) are medical devices of ubiquitous use. Soft CL have marked a great advancement with respect to traditional lenses, due to the higher comfort experienced by the user. CL are still a subject of research, particularly in terms of new materials, due to the importance of assuring a high permeability to oxygen and preserving the cornea from hypoxia-associated pathologies.

Aim: Taking into account the limitations of the methods for testing soft CL, as presented in the relevant international standards, this contribution reviews critically the polarographic method and, in particular, the approach of measuring oxygen permeability of same-type, stacked CL. This method is often used to circumvent the difficulty of obtaining material specimens of appropriate thickness.
Methods: The polarographic method measures the number of oxygen molecules diffusing through a test material by electrochemically removing the molecules from solution as soon as they pass through the material. As an O_2 molecule emerges from the sample material, it contacts the electrode of the oxygen sensor, placed against the back surface of the sample, and is instantaneously converted to four hydroxyl ions, i.e., the electric current which is quantified by the apparatus, and is proportional to the number of molecules removed. Then, the oxygen permeability (Dk) can be calculated. In the modified polarographic method, measurements on lens stacks are used to extract a robust value of Dk. The effect of the interspersed saline solution layers on the measurable permeability of the CL stack was considered, using Fick's law of diffusive flux.
Results: The relationship between the measurable and corrected value of Dk was derived analytically, taking into account the presence of the saline solution layers. Without the proposed correction, a remarkable underestimation of Dk may be expected, especially for hyperpermeable lenses (Dk>80).
Conclusions: The presented model was found to improve the accuracy of lens permeability measurements, which are essential in the assessment of the performance of such devices.

P49
VIBRATIONAL SPECTROSCOPY OF ALBUMIN AND COLLAGEN AS MATERIALS FOR CREATION OF BIOSTRUCTURES
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Background: Currently, proteins, such as bovine serum albumin (BSA) and bovine collagen (BC), is widely used in tissue engineering. Using BSA and BC, it is possible to create biocompatible nanocomposites with a laser, implant coverings, and solders for laser welding of biological tissues. BSA and BC are susceptible to denaturation, which is characterized by the change of a native biological conformation of a protein molecule. This occurs due to various destabilizing factors of biostructures creation process such as heat, ultrasonic mechanical waves and laser radiation.
Aim: Determination of structural changes of a native biological conformation of bovine serum BSA and BC during the biostructures creation.
Methods: BSA and BC aqueous solution were obtained by mechanical mixing 2.5 g protein and 7.5 g water. After that solutions were processed by ultrasonic mechanical waves using homogenizer, heated to 100 °C and irradiated by laser radiation with 810 nm diode laser. Next samples were dehydrated for study by vibrational spectroscopy.
Results: The following bands are observed in the Raman spectra of protein molecules: Amide I, Amide II and Amide III. In the spectra of the treated samples, the peaks at 1450 cm-1, 1608 cm-1 and 1660 cm-1 have a different intensity compared with the original samples. These differences in the spectra indicate structural changes due to denaturation after treatment. In the FTIR spectra there are absorption bands typical for proteins,: Amide I (1650 cm-1), Amide II (1540 cm-1), Amide III (1240 cm-1). As the absorption peak position and shape of the Amide I band differ according to the secondary structure, peak analysis have yielded information on the secondary structure.
Conclusions: Using vibrational spectroscopy, we investigated the structural changes of BSA and BC that occur due to denaturation caused by the thermal heating, ultrasonic processing and laser irradiation of the protein. These changes of protein structure are result of biostructures creation process.

P50
THE STUDY OF ZETA POTENTIAL OF GOLD NANORODS BASED ON THE ELECTROPHORETIC LIGHT SCATTERING METHOD
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Background: Nowadays, liquid dispersions of nanoparticles are widely used in medicine. Among other particles, gold nanorods are of particular interest because their optical properties can be tuned in the visible and near-IR range, they do not photobleach or blink, and they are chemically inert and biocompatible.
The zeta potential determines the nature and the extent of the interaction between particles and liquid medium. The zeta potential is an important indicator of the colloidal stability of liquid dispersions.
Aim: The electrophoretic light scattering method is used to measure the zeta potential. However, in existing devices, the data on the zeta potential of particles is obtained under the assumption of particle sphericity that can lead to erroneous conclusions about colloidal stability of liquid dispersions of nanorods. This fact must be considered in the measurement of the zeta potential for nanorods in liquid dispersions by existing devices.
Methods: In the electrophoretic light scattering method the velocity of particles that move under the influence of electric field is measured. The zeta potential for a particle of arbitrary shape depends on the capacitance and the diffusion coefficient of the particle. Analytical expressions of the zeta potential for cylindrical and spheroidal particles are obtained that more accurate than formula for spherical particles in the case of nanorods.
Results: It is shown that the zeta potential of nanorods is determined by the functions, which depends only on the aspect ratio, not on the particle size. Dependence of the zeta potential for nanorods on the aspect ratio is calculated. This dependence can be useful for analysis of liquid dispersions of nanorods with different aspect ratio.
Conclusions: The obtained results can be used for analysis of colloidal systems of nanorods with different aspect ratios.

P51
INVESTIGATION OF THE LONG-TERM VISCO-ELASTIC MECHANICAL PROPERTIES OF HERNIA MESHES
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Background: In recent years a variety of mesh brands are available in the surgical practice. The different characteristics of the meshes allow the surgeon to choose the most appropriate one. The suitable choice of hernia meshes however depends on many factors including visco-elastic properties of the meshes.
Aim: The aim of this study is to present results about the long-term visco-elastic mechanical properties of hernia meshes and to compare them with visco-elastic properties of human fascia.
Methods: Uniaxial stress relaxation tests on mesh and fascia samples with dimensions (10 × 70) mm were performed using testing device FU1000/E. Three heavy meshes (Surgimesh (SM), Surgipro (SP), Technomesh (TM)) and two light meshes (VyproII (VP), Ultrapro (UP)) were investigated. The initial deformation was between 4% and 6% at 1.26 mm/sec rate of elongation. From the obtained relaxation curves the following parameters were calculated: initial stress and elastic modulus, equilibrium stress and modulus at the end of the relaxation process as well as the reduction of the stress during the relaxation. The parameters were determined before and after expiration date(ED) of meshes.
Results: The initial stress for fascia samples was in range 0.11-0.76 MPa and for meshes was 0. 12-0.59 MPa. Stress reduction for fascia samples varies between 37-55%, while for meshes was 35-65% (for heavy meshes) and 55-70% (for light meshes). The visco-elastic properties of both type of meshes were close to the visco-elastic proper¬ties of fascia only in one direction. The level of orthotropy of meshes (determined from the ratio of initial stress in transversal and longitudinal direction) was between three and six time higher than those of fascia. Investigation of the long-term changes in visco-elastic properties of hernia meshes (up to three years after ED) showed that their initial stress increased about 30% while stress relaxation decreased.

Conclusions: This investigation can be used to access the mechanical compatibility of hernia meshes and to improve their design.

P52
TWO SCIENTIST, THREE RESULTS - WHAT IS THE CHALLENGE IN MEASURING MAGNESIUM DEGRADATION?
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Background: Magnesium based degradable materials are highly biocompatible and have favorably mechanical properties that contrast with polymeric materials. Mechanical properties and degradation can be tailored to the required application by using a wide range of modifications e.g. coatings and alloys.
Aim: This study is focused on finding an explanation for the large disparity in results from similar experiments in literature. The hypothesis is that many different measurement protocols are used to quantify degradation and this leads to inconsistent results.
Methods: Cylindrical, pure magnesium samples were used for this study. The degradation took place in r- SBF immersion solution at 37°C. Hydrogen evolution and weight loss were measured for 3-7 days to quantify the degradation. Two commonly used experimental protocols were examined: static conditions and a fluid changing method. The fluid volume to sample surface area ratio (481 mm) was the same under static and under fluid changing condition. The fluid was changed after 24 h of immersion. Additionally, a new method with continuous fluid flow was established.
Results: All degradation protocols show an initial phase where the degradation is fast. After this phase the results confirm that for all three methods the degradation behavior differs strongly. The static condition results in a very slow degradation rate after the initial fast degradation. The fluid change method leads to a similar behavior like the static condition except that the degradation was speeded up after the fluid change. The continuous degradation is linear for a long time period after the initial phase. In comparison with in vivo degradation behavior degradation process in continuous flow shows the best fitting.
Conclusions: The degradation behavior strongly depends on the measurement method. The accumulation of degradation products especially the increasing pH-value, have a strong inhibiting effect. This cannot be observed in vivo a constant experimental environment realizable by continuous flow is more suitable for magnesium based implant material testing.

P53
HAEMOCOMPATIBILITY ASSESSMENT OF A-C:N:H NITROGEN MODIFIED, AMORPHOUS HYDROGENATED CARBON SURFACE LAYERS ON POLYETHER ETHER KETONE
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Background: Surface engineering was used to improve biocompatibility of blood contacting surfaces in medical devices related with heart support, in order to reduce platelet activation and avoid blood clothing.
Aim: a-C:N:H layers on polyether ether ketone (PEEK) haemocompatibility evaluation in terms of haemolysis and thrombogenicity.
Methods: a-C:N:H nitrogen modified, amorphous hydrogenated carbon surface layers were developed on PEEK in RF CVD surface treatment. The comparative study was performed for unmodified PEEK and PEEK a-C:N:H coated. Haemolytic properties of a-C:N:H surface were evaluated in static conditions. Investigation was performed utilizing CPDA-1 preserved human blood. Blood was diluted with PBS to a haemoglobin concentration of 10 g/L. Investigated material was incubated with blood in temperature of 37 C for 3 h. Free haemoglobin factor was assessed and haemolytic index was calculated for blood, after incubation. Thrombogenic properties of a-C:N:H surface were assessed. Investigation was performed utilizing platelet rich plasma obtained by centrifugal separation of CPDA-1 preserved whole human blood. The material was incubated in temperature of 37 C for 1 h. Presence of adhered blood elements was investigated using SEM.
Results: Haemolysis index of blood after contact with a-C:N:H surface was below 2% (classification of non- haemolytic material according to ASTM F756-00 standard). Microscopic analysis of a-C:N:H layers showed a lower thrombocytes adhesion and activation on investigated surface. Mean value of adhered thrombocytes was 97, 16 for the a-C:N:H surface and 187 for the native surface (p = 0,008).
Conclusions: The a-C:N:H layers improved the haemocompatibility of PEEK especially in terms of thrombogenicity. Acknowledgements: Project no. RH-ROT/266798/STRATEGMED-II supported by NCBiR.

P54
PREPARATION OF ATORVASTATIN CALCIUM LOADED PLGA MICROSPHERES USING SOLID-IN-OIL-IN-WATER EMULSION METHOD
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Background: Poly lactic-co-glycolic acid (PLGA) microspheres have attracted much attention in tissue engineering as drug delivery system. PLGA microspheres loaded with atorvastatin calcium (ATC), which increase bone mass, can be considered as a drug delivery system bone-repairing therapeutics.
Aim: This study aimed at fabrication and characterization of ATC loaded PLGA microspheres for bone tissue regeneration. To achieve such a goal, biodegradable drug loaded microspheres was prepared using solid-in-oil-in-water emulsion solvent evaporation method.
Methods: Briefly, appropriate amount of ATC powder was distributed homogenously in 10% PLGA/DCM solution with ultrasoncation. The organic phase then added dropwise into 1% polyvinyl alcohol aqueous solution under homogenization followed by stirring at room temperature until complete evaporation of the organic solvent. Drug loaded efficiency was determined by an extraction method.
Results: Determination of drug loading suggested a drug encapsulation efficacy >50%. FTIR spectra of ATC loaded PLGA microspheres exhibited a broad peak in the region of 3500 to 3400 cm-1 corresponding to OH stretching vibration of ATC. This broad peak compared with the sharp one of pure ATC showed a possibility of a change in crystal structure of ATC during the emulsion process. DSC thermographs corroborated the FTIR results and confirmed the conversion of crystalline ATC into an amorphous form due to its polymorphic nature of atorvastatin.
Conclusions: We showed that PLGA microspheres can effectively loaded with atorvastatin calcium by solid- in-oil-in-water emulsion method for bone tissue engineering applications.

P55
SUSTAINED DRUG DELIVERY OF CYCLOSPORINE A (CYA) FOR EXTENDED TREATMENT OF DRY EYE SYNDROME
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Background: Current methods in respect with dry eye syndrome treatment, considered eye drops as a basis for topical drug delivery system. The major drawbacks of using eye drops are difficulties of prolonged continues administration, and fluctuations of the concentration of daily drug released.
Aim: Our proposed idea is to use the subconjunctival root of ocular drug delivery and a polymeric substrate specifically designed to be inserted there straightforwardly. The drug (here CyA) can be loaded on the polymeric substrate and subsequently release in a sustain manner for more than one month.
Methods: A medical grade silicone substrate has been used and the CyA loading and releasing methods have been optimized through large number of in-vitro experiments. The substrate was placed in a solution containing CyA in shaking incubator. Then the loaded substrate was soaked in 1.75 ml of PBS solution to measure the daily release dosage.

Results: The substrate could be loaded up to 350 µg of CyA on a 13.49 cubic millimeter of specifically designed silicone. CyA could be released in a sustained manner between 2-4.5 µg/day for 45 days. In addition the specific design make the substrate well tolerated during the intended period of treatment subconjunctivally.
Conclusions: One of the advantages of using this method as a drug delivery system is that patients suffering from dry eye syndrome are not forced to use eye drops every day and dealt with the challenges of such a treatment since dry eye syndrome is a long-term disease. Another advantage of this method is the elimination of the high fluctuations of other drug delivery methods such as eye drops that may prolong the treatment period.

P56
INFLUENCE OF THE DEGRADATION PROCESS ON THE RELEASE PROFILE OF IDARUBICIN FOR THE TREATMENT OF GLIOBLASTOMA MULTIFORME
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Background: Idarubicin (IDA) is widely used for the treatment of various types of leukemia or metastatic breast cancer. IDA also has an effect on glioblastoma cells, which allows for its use in the treatment of glioblastoma multiforme (GBM). However, the blood brain barrier and side effects of intravenous and oral administration limit the application of IDA in glioma therapy. An novel approach such as biodegradable, implantable wafers with IDA locally administrated may solve therapeutic problems connected with GBM.
Aim: The main aim of the study was to investigate the influence of degradation on the release of IDA from polymer wafers.
Methods: Poly(L-lactide-co-glycolide) (L-PLGA) and poly(glycolide-co-ε-caprolactone) (PGACL) were synthetized in mass with the use of zirconium (IV) acetylacetonate as an initiator. Wafers with IDA (5% w/w and 10% w/w) were obtained by solution casting. Degradation of the wafers was performed in artificial cerebrospinal fluid (37°C, 240 rpm). The concentration of released IDA was measured by UV-VIS spectroscopy (485 nm) and the properties of the wafers were analyzed by AFM and FTIR.
Results: IDA was released from the matrices for 587 days. The release profile indicated two stages of IDA release ensured bolus dose with maintenance dose. The greatest intensity of release ratio in the first stage was achieved for the L-PLGA wafer with 5% content of IDA. This wafer was characterized by a relatively least differentiated morphologically surface. The FTIR analysis indicated the lack of IDA-polymer interactions.
Conclusions: The proposed new approach of IDA administration may be an interesting solution in the therapy of GBM.

Biomaterials: Hydrogels - Scaffolds II

P57
A CONCEPTUAL KNOWLEDGE-BASED APPROACH TO SUPPORT DENTAL IMPLANTS PLANNING
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Background: The oral rehabilitation has a directly impact of the patient life quality. Dental Implant treatment is complex and multivariable once diverse information must be proper shared and interpreted. The efficient and effective can be reached by enabling suitable decision-making in a shortest period of time, based on completed and updated information about the diagnostics.
Aim: This paper proposes a conceptual knowledge-based approach to define the most proper dental implants in order to support the dentistry decision-making during the dental implant planning process.
Methods: The knowledge-based has rules to extract the information from medical images in DICOM, patient physiology and dental implant features and computational reasoning engines to identify the dental implants sets more suitable to the patient. The rules were defined based on the tacit knowledge modelling intrinsic to the dental implant process. The rules share, convert and translate information in a rigorously structure in order to precisely define in a computational form the dental arch geometry, nerves position, bone density, implant thread model, implant diameter and length, and so on.
Results: Three different oral rehabilitation cases were performed based on the proposal approach. The test cases were a mandible rehabilitation process and one test case was maxillary rehabilitation process. The accuracy of the process for the cases was 0,2 mm and the dental implant sets available for the analysis and application were 250 different types.
Conclusions: In this way the surgical procedure becomes faster, more reliable and the time of the post- surgery is reduced. The results presented that it is possible see the approach potential due to the autonomy that the systems showed in the decision-making of the surgical planning. Therefore several themes for future researches can be proposed, for example: (i) The use of the artificial intelligence for the reconstruction of the bone area in the dental arch region to the implant insertion; (ii) Development of new tools and accessories; (iii) Development of real time monitoring systems for the implant insertion.

P58
REQUIREMENTS TO ELABORATE NEW DESIGN OF DEVICES AND ACCESSORIES OF OSTOMY POUCHING SYSTEM
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Background: The ostomized person receives multiprofessional assistance (from physicians, nurses, stomatherapists, psychologists, social assistants and others) and becomes user of ostomy pouching system according to the type of ostomy, which involves hygiene conditions, quality of life (QoL) and user- friendliness aspects.
Aim: The objective of this research is to investigate the requirements of the ostomized patients and multidisciplinary professionals involved, who influence on the design of new devices and accessories.
Methods: This study has qualitative approach and the scientific objective is explanatory. Data collection includes bibliographic research of 136 pre-selected articles in Capes Periodics, which belongs to the Brazilian government and has access to the main scientific production databases, and also in published and available materials from 20 institutions related to ostomized patients.
Results: Types of ostomy are classified in colostomy, urostomy and ileostomy. Ostomy devices present pieces of one or two elements, closed or drainable pouches, and by irrigation system used only in cases of terminal colostomy on the left side. Among the accessories there are: paste, belts, adhesives, elastic barrier strips, support plates, gelling, filter and others. In bibliographic research and in the Institution's materials related to ostomized patients were found different forms of using devices and accessories.
Conclusions: In spite of having many alternatives of products and accessories available on the market, isolation due to embarrassing situations (leakage, odor and sound of excretion) still occur. The considered requirements for the design of new devices and accessories are: type of ostomy, stoma shape, stoma length (long or retracted), patient's abdomen size, and user's type of skin (flaccidity, wrinkled or smooth). This study considers the user's life style and contributes to the person's mobility, self-care, hygiene, autonomy and promotes QoL and security.

P59
DEVELOPMENT FOR THE DRIVING MECHANISM OF IMPLANTABLE ARTIFICIAL TONGUE
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Background: After the surgical resection of the carcinoma of the tongue, swallowing and peristaltic motion must be disturbed, unfortunately, in some cases. If the swallowing motion will be able to be added to the artifiical tongue after the surgical resection, the cause of the aspiration pneumonia may be able to be reduced. Implantable artificiel tongue had been developed in our university and the implantable actuator has evaluated in this study.
Aim: The aim of this study is the development of an artificial tongue for the patients after the resection of the tongue carcinoma. For this purpose, hydrodynamic actuator implantable in the chin is proposed.

Methods: Implantable artificial actuator for the embodiment of the artificial tongue had been studied and developed in this study by the use of the shape memory alloy mechanism. Implantable artificial organ must be developed for the small small space. For the smaller size, the Origami technology may be useful in some cases. Implantable Origami actuator had been developed in this study.
Results: Implantable artificial actuator by the use of the Origami Triangle shape had been embodied. Shape memory alloy actuator by the use of the BIOMETAL had been successfully embodied the actuation of the fluid hydrouslic mechanism for the implantable artificial tongue.
Conclusions: An implantable artificial tongue may be able to become good news for the patients in future.

P60
MAGNETICALLY-CONTROLLED ARTIFICIAL URINARY SPHINCTERS
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Background: Urinary incontinence (UI) is a dysfunction that implies an involuntary leakage of urine due to a deficient action of the urethral sphincter muscles. When UI is particularly severe, it must be managed in an invasive way via surgical procedures. Currently available artificial sphincter (AS) are surgically placed around the urethra tissues (extra-urethral AS) and squeeze them, thus restoring continence. Current solutions do not show a unisex design and are constituted of several components, which must be installed in a rather invasive way.
Aim: The aim of this work is the design of novel AS prototypes, magnetically controlled and focusing on two main features: i) a unisex design suitable for both female and male anatomies; ii) compact dimensions to minimize the invasiveness.
Methods: We propose two different solutions. The first one is an extra-urethral AS based on a single component, installable through a short surgical procedure around the urethra. The second one is an endo- urethral AS that is delivered into the urethra with an endoluminal (minimally invasive) procedure. Both solutions are based on a wireless magnetic activation system used as a trigger to easily allow the bladder emptying, when desired.
Results: The extra-urethral AS was based on a clamp managed by a wireless magnetic control, which allowed to compress the urethra by exerting a force perpendicular to its axis. The system was developed and underwent bench tests. The endo-urethral AS embedded a check polymeric valve and a magnetically activated safety system, able to modulate its opening pressure. The system was developed and underwent both bench tests and ex vivo tests on a human anatomy.
Conclusions: This study demonstrates the feasibility of novel unisex wireless magnetically controlled AS solutions to address UI with low invasiveness. They are promising in view of a future clinical translation not only on incontinent patients but also in other contexts in which an easy minction management is desirable, such as in the case of paraplegic and tetraplegic patients.

P61
RESEARCH OF INDUCTIVE POWERING UNIT OPERATION MODES
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Background: Wireless inductive powering can be used for energy supplying of numerous different implantable medical devices (IMDs).
Aim: The main aim of the work was a comprehensive analysis of inductive powering unit (IPU) output characteristics in order to account for specific IMD requirements.
Methods: The energy transfer efficiency and voltage gain of IPU were calculated for series-series and series-parallel compensation of the system. Three IPU operational modes were considered: operation at the point of critical coupling, operation in the overcoupling area and stagger tuning of the IPU. Dependencies of the efficiency and gain from operating frequency, coupling coefficient and load resistance for all three modes were found. The results of the calculations were verified experimentally.
Results: Operation at the point of critical coupling provides maximum output power for the given parameters of the IPU. Moreover, high stability for a given range of misalignments can be achieved using proper geometric optimization of the transmitting and receiving coil. However, the efficiency of the system is limited by 50%. Operation in the overcoupling area ensures perfect stability. The efficiency can go up to 100% for this mode. However, maximum output power in overcoupling area is lower than at the point of critical coupling. Moreover, coils with high quality factors are necessary for IPU operating in overcoupling. Due to this reasons range of applications for implementation of this mode is restricted. Stagger tuning provides high stability of voltage in a wide range of frequencies. It enables easy combining of data and energy transfer in one channel. Drawbacks of stagger tuning are similar to the ones for overcoupling mode.
Conclusions: There is no single best operational mode of IPU. Benefits and drawbacks of different operational modes must be taken into account in regards to specific IMD. Achievable quality factors and critical coupling point are important parameters in the IPU design procedure. However, both these parameters are defined by the geometry of the system mostly.

P62
LASER FABRICATION OF NANOCARBONE SCAFFOLDS IN PROTEIN MATRIX FOR RECONSTRUCTION CARTILAGE AND BONE TISSUE
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Background: Of particular importance is the research in tissue engineering of ways of developing new synthetic implantation materials, whose purpose is to stimulate cell proliferation during tissue formation. Much existing research describes how to obtain tissue scaffolds using laser methods.
Aim: This work presents theoretical and experimental studies of the fabrication of nanocarbone scaffolds (NS) by laser structuring of carbon nanotubes in the water matrix of proteins (albumin/collagen).
Methods: Fabrication NS was carried out using the 3 D laser setup. The diode laser (2 W, 970 nm) was the main element of the setup optical part. The laser light introduced into the optical fiber, which was fixed on the 3-axis system of movement (step 10 nm). Laser radiation interacted with a layer of water-protein solution of single-walled carbon nanotubes (SWCNTs). The concentration of SWCNTs was minimal -0.1 wt.%. The thickness of the layer was 10-100 µm. The laser radiation is focused to a spot diameter of 10-500 nm. By the method of molecular dynamic simulation was proved the formation of a frame of SWCNTs. The Raman spectra of the NS for the description of the binding of proteins with SWCNTs were used.
Results: Under the exposure of laser radiation, the proteins solution with SWCNTs is heated, causing water to evaporate. This creates a solid composite which is either 3D or in film types. Simulation showed how SWCNTs frames are formed, for example, through the use of laser heating (80-100 C) to splice the open end of one nanotube to a defective area of another nanotube. The energy of the interaction between the oxygen atoms of amino acid residues of proteins and the carbon atoms of SWCNTs was to range up to 580 kJ/mol. Cell proliferation of chondroblasts and osteoblasts on the NS for 72 h of incubation was demonstrated. Tissues regeneration of laboratory animals in the field of implantation of NS was shown.
Conclusions: NS can be used to fill 3D defects of tissues. NS films can be used to fabricate coatings for implants, such as for joint ligaments.

P63
A NEW STRONTIUM AND ZINC DOPED BIOGLASSES FOR TISSUE ENGINEERING
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Background: Bioglasses are materials known for the ability to create a strong bond with tissues. Numerous studies revealed beneficial effects of Sr on bone tissue such as increasing osteoblasts proliferation or stimulating bone remodeling, whereas Zn is reported to have antibacterial performance.
Aim: The aim of the study was to describe influence of the glass modifiers (Sr and Zn) on the glass structure and in vitro bioactivity. What is more, their

influence on the growth and differentiation of bone and cartilage tissue cells have been investigated.
Methods: Glasses from the SiO_2-CaO-P_2O_5-SrO and the SiO_2-CaO-P_2O_5-ZnO systems have been obtained by the sol-gel route. They were differing in CaO/SiO_2 ratios and the concentration of modifier oxides (SrO and ZnO). Materials were subjected to the structural analyses (XRD diffraction, FTIR spectroscopy, NMR spectroscopy). In vitro bioactivity tests in simulated body fluid solution were performed. For the biological test purposes glass powders were incorporated into PLGA polymer matrix. The series of in vitro biological tests was made in order to evaluate the influence of the additives concentration on the bone and cartilage cells phenotype and the behavior. Cultures were analyzed for cytotoxicity, level of ALP, Col II and aggrecan.
Results: Bioactivity in vitro tests indicated that all of obtained materials were bioactive, but the intensity of the process depended on the glass composition. Biological tests indicated that incorporation of Sr and Zn to glasses significantly affects cell behavior and phenotype. Strontium containing glasses favored osteoblast cells differentiation and increased ALP activity, whereas both Zn or Sr-containing glasses significantly increased level of Col II and aggrecan production by the chondrocytes.
Conclusions: Our study has confirmed that addition of Sr and Zn to glasses can improve their biological response in vitro in contact with various cell lines. This work was supported by the National Science Centre Poland Grant nos. 2014/13/B/ST8/02973.

P64
INCREASING OF MECHANICAL PROPERTIES OF ARTIFICIAL JOINT LIGAMENT BY THE BIONANOMATERIALS LASER APPLICATION METHOD
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Background: The method of artificial ligament fixation in bone canal is traumatic, especially right after operation time. The laser welding using solders based on the bionanomaterials let connect areas of artificial and living tissues.
Aim: The aim of this work is to study the mechanical properties of artificial ligaments based on polyethylene terephthalate (PET) and coated with bionanomaterial.
Methods: The bionanomaterial was aqueous dispersion of 25 wt.% bovine serum albumin (BSA) and 0,2 wt.% single-walled carbon nanotubes (SWCNTs). The bionanomaterial was applicated on PET fibers using ultrasonic homogenizer. At next it was irradiated by laser radiation until fibers drying. The artificial ligament sample had dimension 100 × 5 × 0.5 mm. As the control samples were chose artificial ligaments without coating and artificial ligaments sodden with BSA-SWCNTs dispersion, but not irradiated by laser radiation. The samples deformation ratio at elastic strain range was studied with tensile machine.
Results: As the experimental result was obtained that the artificial ligaments with BSA-SWCNTs coating had 20% more deformation ratio and 1.5 times wider elastic strain range than the control samples.
Conclusions: In this way the artificial ligaments with BSA-SWCNTs bionanomaterial coating applied by the ultrasound and laser methods has got positive properties: increased modulus of elasticity and range of linear tensile-strain dependence. The increasing of artificial ligament fixation strength to bone canal will be reached using the laser welding method.

P65
SMALL, SMALLER, SMALLEST - A METHOD TO PRODUCE VERY SMALL POLYMERIC BEADS
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Background: Contrary to conventional methods of polymeric bead fabrication like electrospraying or pressurised air flow methods, microfluidic devices offer high process control and produce beads with very small diameters. Polymeric beads created this way can be made in a large variation of sizes (from a few to hundreds of microns).
Aim: Small polymeric beads are beneficial especially for encapsulation of cells or for use as controlled drug eluting particles. The only disadvantage is the extremely high cost of using microfluidics. We propose a novel and cost-effective microfluidic device.
Methods: A microfluidic system was created by using easy available laboratory equipment. Silicone was used as the base bulk material and microchannels were introduced with the help of thin metallic wires (Ø = 0.3 mm). Bifurcation was realised with docking stations made from Poly(ethylene oxide) which was used as a water soluble glue. Alginate was the chosen polymer for this study. Laboratory syringe pumps were used to transport the alginate and the separating fluid (vegetable oil) in the microfluidic system. Cross linking was achieved by dropping the fabricated beads into $CaCl^2$ solution. The sizes of the alginate beads were measured to evaluate the viability and efficiency of the microfluidic device. Additionally, the results were compared with the currently used electrospraying method to produce small alginate beads.
Results: The results show that it is possible to create a working, low-cost microfluidic device. The lowest diameter of the beads was at 33 ± 17 µm with a regular spherical shape. The diameter can be modified by changing the flow parameters (flow rate of the oil or the alginate, concentration of alginate, etc) and the channel diameter. The production rate of the micro fluidic system was around 120 beads per minute.
Conclusions: It was possible to produce much smaller beads than the currently used method of electrospraying. The method is easy to realise with laboratory standard equipment and provides a good alternative for producing beads for different applications.

P66
NUMERICAL ANALYSIS OF THE PMMA-BASED CEMENT FLOW IN A TRABECULAR STRUCTURE OF A VERTEBRAL
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Background: Constant improvements in healthcare, achieved due to physician's commitment with engineers cooperation, allowed mankind to elongate significantly life expectancy. This in a result caused a more frequent appearance of aging-associated diseases, including osteoporosis. Although not commonly used nowadays, vertebroplasty and kyphoplasty can be a preventive remedy in case of osteoporosis in vertebra, when used prior bone fracture. Such treatments can become more common practices only when surgeon will be convinced that a positive effect for patient can be achieved. This is strictly connected with prediction of cement filling inside a vertebra during an injection.
Aim: The main aim of this study is to predict the flow of the cement in the patient-specific osteoporotic vertebra. A development of a model of PMMA-based cement used during vertebroplasty and kyphoplasty, which can be used in numerical simulations, is the secondary aim.
Methods: Numerical simulations of PMMA-based cement flow within the vertebra were performed with a use of Navier-Stokes solvers. The patient-specific trabecular bone was recovered from micro-CT images. Multiphase transient flow predictions were performed. Time-dependent apparent viscosity model developed within the project was used.
Results: Authors performed a transient analysis of the flow in a part of a trabecular bone structure during the injection of the cement. The process of the cement hardening – apparent viscosity increase was monitored. The cement flow inside the vertebra was predicted by different solvers and then the obtained paths of fluid propagation were compared.
Conclusions: It was shown that the time-dependent cement viscosity model allows one to mimic PMMA- based cement flow in the trabecular structure of a vertebra.
Acknowledgements: This project was financially supported by The National Center for Research and Development in Poland (PBS3/B9/45/2015).

P67

ELECTROACTIVE POLY(VINYLIDENE FLUORIDE) MEMBRANES WITH HYDROPHILIC DOMAINS FOR OSTEOGENIC DIFFERENTIATION

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Background: Bone is a piezoelectric tissue in which electrical charges generated in the extracellular matrix by deformation are considered fundamental for bone growth and remodelling [1]. Poly(vinylidene fluoride)(PVDF)is a piezoelectric polymer very attractive for bone tissue engineering to direct osteogenesis [2].

Aim: We aim to produce new electroactive PVDF membranes with different porosities, topographies and hydrophilicity to evaluate the effect of these parameters on mesenchymal stem cell adhesion and proliferation.

Methods: PVDF membranes were prepared by freeze-extraction. Their micropores were filled with a poly(vinyl alcohol) solution to obtain electroactive hydrophilic-hydrophobic surfaces. Morphology, porosity, equilibrium water sorption, piezoelectricity and mechanical properties were determined. Human mesenchymal stem cells (hMSCs) were cultured on the surface of the materials and proliferation, cell adhesion and cell shape were analyzed.

Results: Solvent content allowed regulating membranes porosity from 85% to 65%, with pores size ranging from 0.5 µm to 5 µm. The membranes were piezoelectric and porosity and hydrophilicity regulated the mechanical properties of the materials. Hydrophilic domains of the electroactive surfaces were smaller than the cell size and modulated cell adhesion and morphology. All materials allowed cell proliferation.

Conclusions: The new PVDF-PVA membranes are good candidates to induce osteogenesis of MSCs as they are piezoelectric and promote cell adhesion and proliferation.

Acknowledgments: MINECO MAT2016-76039-C4-R project.

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P68

CONDUCTING BIOCOMPATIBLE NANOMATERIAL LAYERS

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Background: Novel biocompatible nanomaterials should have characteristics no worse than those of the natural intercellular matrix facilitating the cell formation, adhesion, proliferation, and differentiation. These materials should be applicable to the electric stimulation of cell growth [1].

Aim: The aim of this study was to investigate the conductivity of flexible nanomaterial layers consisting of a bovine serum albumin (BSA) matrix filled with single-walled carbon nanotubes (SWCNTs).

Methods: The aqueous suspension contained 20 wt.% of BSA and 5 wt.% of SWCNTs. The BSA/SWCNT layers were deposited onto flexible (cotton and polyethyleneterephthalate) and solid (silicon wafers and specimen glass) substrates by silk screening. The samples were rectangular strips 5-20 mm in size with a thickness of 0.1 ÷ 10 ?m. Half the sample area (5-10 mm) coated with the investigated suspension was exposed to continuous laser irradiation (LI) with a power of 0.1 MW/m2 and a generation wavelength of 970 nm. The exposure lasted until drying this half-sample. The other half-sample served as a reference.

Results: The obtained specific conductivities were s~0.001-0.1 S/m for group I (reference samples) and s~1-10 S/m for group II (irradiated samples). The conductivity of the layers dried by LI increased from 250 to 2000%.

Conclusions: It was established that LI did not change the conductivity of the dried samples of both groups. The growth of the conductivity of the BSA/SWCNT layers under LI can be explained as follows: the LI electric field arranges SWCNTs in one preferred direction and highly conducting contacts form in the places of nanotube contacts due to the plasma currents induced by LI. Thus, the investigated BSA/SWCNT biocompatible nanomaterial layers are characterized by the high (1-10 S/m) conductivity. They are promising for biomedical applications, including study and stimulation of the cell culture growth and fabrication of electrodes and conducting implants.

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Varia

P69

SUPERCONDUCTING FILM CONCENTRATOR IN ULTRAWEAK MAGNETIC FIELD SENSORS

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Background: The ultraweak (10 pT ÷ 1 fT) magnetic field sensors (MFSs) are the main instruments of magnetic systems for noninvasive medical diagnostics. The magnetic-field sensitive elements used in such sensors are superconducting quantum interference devices (SQUIDs). To reduce the threshold sensitivity of the MFSs and SQUIDs, the superconducting film-based magnetic field concentrators (MFCs) are widely used.

Aim: The aim of this work was to clarify the possibility of optimal nanostructuring of the superconducting films used in the MFCs to enhance their concentration factor.

Methods: We calculated and mathematically simulated the MFC construction and optimized the parameters of the superconducting film MFCs with nanostructured active strips. The typical parameters of two MFC constructions (sandwich and planar) were determined. In the sandwich construction, the MFC active strip and MSE are separated by an insulating film. In the planar construction, the MSE is placed between two MFC active strips and all the elements are located in one plane and do not intersect.

Results: The active strips are nanostructured by fragmenting in alternating parallel 20 ÷ 1000 nm wide superconducting branches and slots. This allowed us to enhance the concentration factor by two orders of magnitude and reduce multiply the MFC dimensions. The main parameter of the nanostructured MFC is its small size (≤1 mm), which is smaller than the size of the SQUID MFC without nanostructuring in several times.

Conclusions: Modern medicine needs in noninvasive diagnostics of implants based on biocompatible materials (nanomaterials with ferro- or superparamagnetic particles, carbon nanotubes, etc.) and controlling the operation of implanted apparatus (artificial heart, stimulators, etc.). The urgent problems of medicine can be solved using the MFSs containing the superconducting film MFCs with nanostructured active strips.

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P70

CAPACITIVE-COUPLING-BASED INFORMATION TRANSMISSION SYSTEM FOR IMPLANTABLE ESOPHAGEAL PH MONITORING SENSOR AND STIMULATOR: ANALYSIS OF RECEIVING VOLTAGE FOR ELECTRODE POSITION MODIFICATION IN HUMAN ANATOMICAL MODEL

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Background: Recently, medical electronic devices implanted deep inside the body are being required to transmit information to the outside. Therefore, this study focused on capacitive coupling based information transmission system wherein two transmitting electrodes embedded inside the body transmit information to two receiving electrodes on the surface of the body. However, it is necessary to consider the electrode position because transmission efficiency is affected by the distribution of organs. The electrical properties of organs are not uniform. In this study, we investigate the optimum position of the electrodes of the information transmission system of an implantable esophageal pH monitoring sensor and stimulator (IEPS), using a human anatomical simulation model.

Aim: We observed the receiving voltage when the receiving electrodes were attached to the abdominal and back surfaces of the body, for analyzing the information transmission system.
Methods: A CT based human anatomical model was used for this simulation. The electrodes were made of Ti. The transmitting electrodes (7.5 mm^2) of the IEPS were attached to the bottom of the esophagus. The receiving electrodes (4500 mm^2) were attached to the abdominal or back surface of the body. The distance between the esophagus and abdominal or back surface was set to 105 mm. The voltage and frequency of the AC power supply were set to 2 V and 2.5 MHz, respectively. The load resistance was 200 Ω. The receiving voltage was analyzed by the Transmission Line Matrix method.
Results: The receiving voltages obtained with the receiving electrodes attached to the abdominal and back surfaces were 92.8 μV and 293.3 μV, respectively.
Conclusions: According to the results obtained, it was more effective to attach the receiving electrodes to the abdominal surface than to the back surface. In future, we intend to investigate other positions, shapes, and sizes of receiving electrodes to increase the receiveing voltage.

P71
POSSIBILITIES OF USING COMBINED MAGNETIC FIELD SENSORS IN MAGNETOCARDIOGRAPHY
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Background: Magnetocardiography (MCG) allows to register cardiac diseases. High MCG indices are achieved by using numerous magnetic field sensors with a threshold sensitivity of B ≤1 pT in them.
Aim: The purpose of this paper is to compare the parameters of superconducting quantum interference devices (SQUID) and combined magnetic field sensors (CMFS) aiming at a possible decrease of their overall dimensions.
Methods: The MCG includes tens or hundreds of SQUIDs with B ≤1 pT, and their dimensions are determined by the sizes of the receiving ring with a diameter of D~5-10 mm. CMFS contains a magnetic field concentrator (MFC) and a structure based on the giant magnetoresistance (GMR) effect as a magnetosensitive element (MSE). CMFS based on MFCs from a superconducting film (niobium, critical current density ≥1010 A/m2, London penetration depth 50 nm, thickness 100 nm) and MSE from a GMR resistor with a relative magnetosensitivity of ~10%/mT were analyzed. The MFC had a nanostructured active band consisting of alternating parallel superconducting branches and slits with widths of 20-500 nm.
Results: The following parameters are obtained. SQUID based on a high-temperature superconductor (HTSC): energy equivalent to noise En~10-27 J/Hz, magnetic field equivalent to noise Bn~0.03 pT/Hz1/2, D~1 cm; CMFS having the above parameters: En~10-27 J/Hz, Bn~0.1 pT/Hz1/2, D~0.2 cm. These values are an order of magnitude better than those obtained in the CMFS as part of MFC with a non- nanostructured active band [1].
Conclusions: Thus, in the CMFS with nanostructured MFC the parameters close to HTSC SQUIDs are reached, while the dimensions are several times smaller. The use of multiple CMFS along with SQUIDs will significantly improve the MCG capabilities in recording the signs of the onset of cardiac diseases.
Acknowledgments: This work was provided by agreement No. 14.581.21.0014 (Project ID RFMEFI58115X0014).[1] M. Pannetier- Lecoeur [et al.]. Review of Scientific Instruments, 84, 095116 (2013).

P72
FLEXIBLE AND IMPLANTABLE ENCAPSULATED ELECTRODE FOR MEASUREMENT OF ELECTROCARDIOGRAM
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Background: Monitoring of biosignals is apparently required to detect diseases such as arrhythmia, and epilepsy, etc. Currently, metal-based wet electrodes such as Ag/AgCl electrodes are widely used to acquire biosignals from body. However, Ag/AgCl electrodes that meet with unstable condition of skin form conformal contact to skin. To overcome limitation of metal-based electrode, the flexible and implantable electrode is needed to adapt highly adaptive to the curves of body.
Aim: The electrode should be adhered onto the body continously and stably under the motion, and be implanted safely in the tissue with accurate signal acquisition. Also, they should be shielded from tissues to prevent suface delamination from the device itself and side effect such as irritation, allergy, or inflammation. Here, we introduce flexible and implantable encapsulated electrode for the measurement of electrocardiogram using a lithograpy process.
Methods: The fabricated electrode consists of polyimide and metal layer was fully encapsulated in polydimethylsiloxane which shows high biocompatibility and transparency. The fabricated electrode was empolyed to obtain electrocardiogram with enhanced strength over the observation period. Here, PDMS layer performed as a protection layer that resulted in no damages on metal layer after implantation.
Results: ECG was obtained without distortions or attenuation of signal over 4 weeks. We demonstrated a method to measure the electrocardiogram by using PDMS-encapsulated electrodes. The electrode showed stable adhesion properties enough to be implanted into a rat without additional sutures. The suggested electrode shows non-toxic, non-flammable, even flexible on an irregular surface and highly biocompatible.
Conclusions: The electrode was fully encapsulated by polydimethylsiloxane (PDMS), Not only the biocompatibility issues, but encapsulated PDMS also protected the Au metal patterns on the PI layer from harsh environments. A tightly adhered and flexible electrode contact non the irregular surface with stable and accurate electrocardiogram.

Valves

P73
METHODS OF TILTING DISC VALVES EVALUATION
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Background: Due to the lack of specific standards for examination of tilting disk valves used as part of pulsatile VADs and need for assessment of its appropriable parameters, evaluation methods were designed and implemented as part of pump development, production and qualification routines.
Aim: Presented evaluation methods were used in development and production of Moll type tilting disc valves.
Methods: Main test procedure consists of static and dynamic flow measurements. Static test is based on ASTM F1841-97 (2005) standard. Valve is placed inside a tube (L > = 10Φ), and subjected to constant laminar flow. Depending on test, back or forward flow through valve and pressure drop is measured.
Dynamic test is conducted on Windkessel model, which simulates resistance and compliance of human body. Valve is mounted inside test pump (properties same as clinical model) and powered by pneumatic unit. Test duration varies from 2 h to over one week on different types of fluid. Parameters (flows and pressures) are acquired in real time. In addition to main procedure visual validation was used. Valve movement was recorded through transparent mount using high-speed camera (700 fps). Acquired video provided detailed data about valve disc movement trajectory, impossible to observe with unaided eye.
Acquired data was used in automatic image analyses. For the purpose of data analysis, dedicated software was developed, which allowed long-term data analysis and calculation of parameters (avg. flow, SV per cycle, statistical distribution), used in clinical product qualification.
Results: Since 2015 over 60 tests were conducted on various valve models (Moll, Medtronic Hall, Sorin Carbocast) and constructions (PEEK and DLC leaflet, PUR valve). In a process of Moll valve development over 40 models were evaluated in more than 100 tests, leading to discovery and elimination of various technical problems like disc blocking.
Conclusions: Presented methods were performed in process of development and production of clinical Moll type valves used in Religa Heart VADs, proving their usability for purposes of design, testing and clinical product qualification.

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POLYURETHANE FLEXIBLE VALVE FOR PULSATILE VENTRICULAR ASSIST DEVICES

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Background: Extracorporeal pulsatile ventricle assist devices (PVAD) are a well-known method for prolonged heart support in end-stage heart insufficiency, especially for children as the only common applicable method. It has been designated for use in patients during high-dose radiotherapy in cancer treatment and in future, may assist gene therapy to treat myocardial infarction. However, major problem of PVADs is thrombus formation due to inadequate blood flow dynamics of mechanical valves.
Aim: Re-design of the flexible mechanical heart valves in ReligaHeart (RH) PVADs.
Methods: Using Solid-Edge CAD the new polyurethane (PU) valves were designed for RH PVADs: single- leaflet inflow valve and two-leaflet outflow valve, consisting of flexible leaflets and valve house, equipped with titanium cores. Numerical analysis were performed to simulate the optimal injection process for valves prototype manufacturing by IB Steiner. The first technological trials were carried out for titanium cores manufacturing by Chirmed. Technological equipment was developed for valves assembling in RH PVADs.
Results: Inflow valve leaflet shape ensures wall surface continuity of inflow pump connector and open leaflet surface. To strengthen the moving leaflet, exposed to long-term work, the titanium mesh was designed (thickness 0,06 mm). The valve ring was equipped also with titanium core, to fix the ring inside the pump.
The open-work core design allows the visual control inside the valve. Similar titanium core was developed for both outflow valve leaflets. Small channels were designed in leaflets for proper valve wash.
Conclusions: Flexible valve design guarantees: athrombogenic construction, by reduction of turbulence and sufficient valve wall washing. The work will be continued by manufacturing RH PDAVs equipped with flexible valves and testing the pumps in acute thrombogenicity test.
Acknowledgements: Project bioVALVE (M-Era.Net programme) supported by NCBiR.

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IN VITRO EVALUATION OF A STYRENE-BASED POLYMERIC TRANSCATHETER AORTIC VALVE: THE EFFECT OF LEAFLET THICKNESS ON HYDRODYNAMIC FUNCTION

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Background: Few polymeric valves have advanced beyond preclinical investigation despite different polymers, leaflet geometries and manufacturing techniques being adopted. Recently, styrenic block copolymers (BCPs) consisting of a plurality of polymer chains have been proposed.
Aim: To optimize the hydrodynamic performance of a styrene-based polymeric transcatheter valve.
Methods: Nitinol-based 23 mm transcatheter valves were fabricated with varying thicknesses (range: 80-513 µm, n = 16) using poly(styrene-block-ethylene-propylene-block-styrene). Hydrodynamic performance was evaluated across 4 pulsatile flow rates (3.9 L/min, 5.0 L/min, 6.1 L/min and 7.1 L/min), reported as effective orifice area (EOA), mean pressure gradient and total regurgitant fraction. Minimum performance was defined as EOA ≥1.25 cm^2, total regurgitant fraction ≤20% and a transvalvular pressure gradient ≤15 mmHg, measured under the following conditions: frequency of 70 cycles/min, simulated cardiac output of 5.0 L/min, mean aortic pressure of 100 mmHg and systolic duration of 35%, in accordance with ISO 5840:2013.
Results: Leaflet thickness was significantly correlated with hydrodynamic function across all cardiac outputs. At 5.0 L/min, thickness was inversely correlated with EOA ($y = -1.86x + 2.23$; $\tau b = -0.597$, $p<0.001$) and total regurgitant fraction ($y = -27.16x + 5.08$, $\tau b = 0.724$; $p<0.001$), and positively correlated with mean pressure gradient ($y = -19.97x + 19.84$, $\tau b = -0.469$; $p<0.001$). Estimated maximum leaflet thickness to achieve the minimum performance requirement was 360 µm.
Conclusions: This study quantifies the effect of leaflet thickness on hydrodynamic performance for a styrene-based transcatheter valve. Further study evaluating long-term in vitro fatigue is required to determine long-term durability.

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IN VITRO MODELLING OF CALCIFIC PARTICLES UNDER PHYSIOLOGICAL CONDITIONS: A TESTBED FOR CEREBRAL PROTECTION DEVICES (CPDS)

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Background: Different CPDs are available or being developed to reduce stroke risk as a major cause of mortality after transcatheter aortic valve implantation (TAVI), because of the high risk of calcification detachment. These particles can be washed into the branches of the aortic arch causing a stroke which can be prevented using CPDs. Due to missing standards, CPDs are tested under different conditions and test results are not comparable.
Aim: Therefore, this study presents an in vitro calcification model and a testbed designed to investigate the behavior of detached calcifications during TAVI. The evaluation of the test conditions was performed without CPDs.
Methods: A left heart pulse duplicator serves as basis for the testbed. It consists mainly of an electrohydraulic drive unit, a flexible silicon ventricle in a compression housing, a rigid aortic root model and adjustable compliances and resistances. Different anatomies of the aortic arch including the branches were reproduced as silicon models. Quartz sand particles were used as detached calcifications due to their similar density and geometry. The particles were injected into the anatomical models under physiological pulsatile flow and pressure conditions (5 ± 0.2 l/min cardiac output, 95 ± 5 mmHg mean aortic pressure). Filters were positioned behind the branches and the descending aorta to collect the particles. To determine the number of particles washed into the branches the filters were weighed before and after the test after drying in a vacuum oven. Furthermore, high speed recording was used to evaluate the experiments.
Results: About 8-10% of injected particles were washed into the branches, while about 98% of all particles were recovered. Thus a specific number of particles which has to be filtered by CPDs can be adjusted.
Conclusions: Reproducible results were achieved under physiological test conditions. Therefore, both calcification model and testbed are feasible to test available CPDs under identical conditions for a better comparability.

P77

INFLUENCE OF THE BULGING SINUS SIZE AND SHAPE OF THE SIMULATED LIVESIZE EPTFE VALVE ON THE LEAFLET MOVEMENT OF THE VALVE CONDUIT

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Background: Contegra and Expanded polytetrafluoroethylene (ePTFE) valved conduits may be a good choice for treating right ventricular outflow tract (RVOT) reconstruction in congenital heart defects. ePTFE valve with bulging sinus seem to show good valve opening characteristic, however, fluid mechanical research proving the effect of bulging sinus has been limited. Our study showed that bulging sinus size and leaflet shape affect on flow inside the conduit and vortex center location relative to the leaflet tip. It also showed valve opening area reduced when bulging sinus size was reduced.
Aim: This paper further investigates the effect of the bulging sinus size and shape of the simulated live-size ePTFE valve on the leaflet movement inside the conduit.
Methods: Five simulated live-size ePTFE valves of different bulging sinus sizes and three different bulging sinus shapes were used. Effect of the bulging sinus size and shape on flow field inside the simulated ePTFE valve and vortex center location were analyzed using Dynamic PIV system running at 1000 frames/s. Valve opening and closing phenomenon were directly observed and compared using high speed digital camera running at 240 frames/s.
Results: Vortex was generated inside the bulging sinus. Number of vortex generated and strength seem to be affected by size of bulging sinus. Normal bulging sinus generate stronger vortex more frequently than reduced bulging sinus. Bulging sinus shape also influence on this trend. Direct observation of

the opening area of the valve showed that wider opening area was observed with larger bulging sinus including normal size similar to the result of enlarged model of preceding research.
Conclusions: As in the preceding experimental studies, live-sized valve opened and closed quick with normal bulging sinus even though conduit size changed almost half of the preceding studies using enlarged model. Existence of vortex inside the bulging sinus seems to play key role on valve opening behavior. Bulging sinus size greatly affect on flow inside the conduit.

Poster Session II

Pump Development

P78
LONG-TERM USE ASSESSMENT OF THE APICO-AORTIC BLOOD PUMP: DURABILITY AND WEAR ASSESSMENT
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Background: Apico-Aortic Blood Pump (AABP) is a centrifugal intrathoracic LVAD in development in our laboratories. At this project phase, we conducted studies to observe AABP's bearing system long-term behavior and implemented modifications to improve its performance.
Methods: A durability test was performed in a mock-loop system to analyze AABP's failure modes and bearing wear. Mock-loop operates with head pressure of 100 mmHg and 5 L/min of flow. A computer simulation of AABP's bearing shaft mechanical strain analysis was performed to elucidate possible causes for a fracture occurred during the durability tests. Wear tests were performed to evaluate load effect at the bearing shaft. For this test, a system that simulates bearing shaft rotation, load and corrosive proprieties of blood was constructed. In this system, a weighting-machine was used to the measure load. Three sets of AABP's bearing system were tested, wear was determined through system weight loss in each set.
Results: 3200 hours of durability test were performed, without none significant change in AAPB's temperature or electric current consumption. After this period, two failure modes were registered: decoupling of the bearing system due to wear at the bottom pivot and a fracture in the bearing shaft. Computer simulation showed a region with concentrated mechanical tension in the bearing shaft. These results are consistent with the fracture observed in the durability test.
Conclusions: Bearing shaft geometry was adjusted to reduce the mechanical tension concentration, thus reducing fracture probability. A motor topology modification was implemented to reduce bottom pivot wear, this modification was designed to reduce the load in the bearing system. Overall, this study contributed to AABP's improvement for long-term application.

P79
TRANSVENTRICULAR ASSIST DEVICE (TVAD) – IN VITRO EVALUATION OF A NEW AXIAL BLOOD PUMP USING POLYMERIC VALVE FOR ROTATIONAL SPEED REDUCTION
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Background: A new model of ventricular assist device has been developed and evaluated in our laboratories to be used as bridge to decision, bridge to recovery or bridge to transplantation, called "Transventricular Assist Device (TVAD). TVAD is to be implanted inside the left ventricle, introduced from the apex and throughout aortic valve. TVAD consists of a miniaturized brushless direct current motor to be located inside the myocardium at the left ventricle apex, connected to the motor rotating shaft is an axial impeller inside a tube to be trespassing the left ventricle and the aortic valve. At the tube outlet port is a bileaflet polymeric valve that will stay inside aorta, after the aortic natural valve.
Aim: To evaluate the hydrodynamic performance of a new miniaturized transventricular axial pump with and without bloob valve.
Methods: A cardiovascular simulator system was used simulating different heart failure conditions by varying stroke volume and cardiac contractibility. TVAD was connected to simulator from left ventricle chamber to aortic chamber. Pump rotational speed was fixed and flow and total pressure head were registered, by varying peripheral resistance. TVAD hydrodynamic performance was analyzed with and without the polymeric valve for behavior comparison.
Results: TVAD was able maintain physiological flow and pressure in different heart failure conditions (5 L/min of mean flow against 100 mm Hg of average arterial pressure). The usage of polymeric valve allows TVAD to operate in lower rotational speed without appearance of reverse flow.
Conclusions: Minimally invasive surgery is very important for physician´s decision, aiming patient´s safety and easier recovery. Ventricle assist devices need to present low level of hemolysis. A device that have valve can operate in lower rotational speed since it does not need to generate high total pressure head during diastolic phase to avoid reverse flow throughout the pump. Hemolysis tests will be made.

P80
PRECISION MATCHING PULSATILE BLOOD PUMP
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Background: Otary blood pumps are increasingly used as a standard therapy for patients with end stage heart failure as bridge to heart transplantation, or life time support as destination therapy. But the low pulsatility of aortic pressure results in a negative effect on the structures and functions of blood vessels, and the high shear stress in the rotary pump induces some blood damages. To increase the pulsatility of the continuous-flow blood pumps, the rotary blood pump rotation speed is modulated. However the aortic valve remains staying closed during some heart cycles.
Aim: To realize pulsatile pump with small size and low blood damage.
Methods: A precision matching pulsatile blood pump is developed, in which a small, precision and fast ultrasonic motor is used as an actuator and the pulsatile motion is produced by a cam.
Results: The pump with a diameter of 86 mm and a thickness of 47 mm is tested in a mocked circulation loop. It is found that a flow of 5 L/min in a mocked circulation loop is achieved when the average afterload is 100 mmHg, and the pump could synchronize with natural heart beat with a dynamic response less than 70 ms.
Conclusions: Precision matching pulsatile blood pump could potentially enhance the possibility of heart failure recovery.

P81
TOTAL ARTIFICIAL HEART (TAH): PRELIMINARY RESULTS IN VITRO
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Background: Number of heart transplants (HTX) has remained relatively unchanged since its peak in the 1990s, while increasing number of patients on waiting list. At the same time, ventricular assist devices (VADs) are not a feasible alternative for other large numbers of patients.
Aim: Develop a mechanical circulatory support system by means of two centrifugal pumps replacing the left and right ventricles, which works as TAH.
Methods: The technique used in the preparation of the pumps was micromachining, performed in a CNC (Computer Numerical Command) machine, able to obtain parts with the necessary quality for manufacture of the device. Numerical computational simulation was performed by creating several

scenarios of rotation, flow velocity and flow, for simulation with the main turbulence models. Tests in hydrodynamic performance bench showed flow rates of up to 10 lpm at 1,800 rpm, capable of supplying flow under physiological conditions of pressure and flow (VQ). Practical tests allowed to compare the results of the numerical computational simulation; Thus, it was possible to verify critical zones of each scenario and to propose changes in the mechanical design of the pump.
Results: Initial results indicate critical turbulence zones in the outflow. Changes made for correction and other improvements are under bench test with water, 66% and bi-distilled glycerin, 34%. For all the VQ gradients (right atrium-pulmonary artery and left atrium-aorta) simulating physiological conditions (eg. intense physical exercise) and pathological (sepsis, hypovolemia, hypervolemia, pulmonary hypertension, systemic arterial hypertension), there was good flow generation.
Conclusions: TAH allows treatment of patients who do not find HTX or LVADs good options: Fontan failure; Chronic rejection, including those highly sensitized; Chronic RV failure after VAD; Biventricular failure; Heart tumors; Intractable ventricular arrhythmias; Active malignancy; Restrictive cardiomyopathy; Congenital cardiomyopathies in pediatric and adult patients. However, much remains to be learned about the long-term effects of pulseless perfusion.

P82
METHODOLOGY FOR THE APPLICATION OF RISK ANALYSIS TO IMPROVE THE RELIABILITY OF VENTRICULAR ASSIT DEVICE
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Background: Within this context, failures due to malfunctioning of the DAV (12.32%) it becomes important to search for methodologies that can identify and treat the causes of adverse events related to equipment malfunction, with controls within inherent safety concepts for continuous improvement of the reliability of these devices. In this sense, the research group carried out a hazard survey for a continuous flow type DAV with a magnetic drive.
Aim: To propose that methodology with reference to the ISO 14971 Medical Device Risk Management standard.
Methods: The methodology proposed for this work was the use of the Preliminary Analysis of Risks (PHA) in view of the limitation of project data, but which provides a broad view of the elements, at this stage, according to ISO 31010. The matrix chosen was a 3 × 3 model, with 3 severity criteria and 3 frequency criteria. The final event without frequency originated from an initial event summarized malfunction of the device.
Results: After the application of the PHA, the main adverse events identified were: friction between motor and housing; engine heating; slow motor actuation response time; fixed rotation without suitability to the demands of body movement. The event tree indicate the heading event malfunction of the device (MOD) and show us success or failure of the control barriers in the device, first regenerate the device to normal condition, second degenerate to a minimal functional state. The final events, originated from the success or failure of the control barriers is: malaise, sudden illness with hospitalization and death of the patient.
Conclusions: The methodology of risk analysis to increase the reliability of the DAV has proven to be quite practical and usual, allowing the manufacturer a previous analysis, still in the design phase, of the necessary controls with inherent safety concept. Frequencies can be obtained for each manufacturer from its database.

P83
REMOTE MONITORING OF RUSSIAN VAD SYSTEM AVK-N
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Background: The modern VAD systems provide long-term MSC in the out-of-hospital conditions with high quality of life of patients. Nevertheless, further implementation of this technology is constrained by the lack of continuous RM of the key technical and biological parameters which are necessary for early recognition of technical defects and violation of physiological functions. Owing to remoteness of a patient from the specialized medical center RM leads absence to decrease in efficiency of rendering a medical and technical assistance (MTA) to the patient.
Aim: The aim of this work is development of the principles and methods of realization of system of RM of operation of the Russian implanted axial pump ABK-N undergoing successful clinical approbation since 2012.
Methods: The RM realizes technology of data transmission in two formats: operational and expanded. The operational format supports on-line broadcast over the GSM channel to the specialist of the AVK-N status and emergency messages for abnormal operation mode. The expanded format the transfer of parameters of the AVK-N is a condition of physiology of the patient synchronized with parameters on channels of wireless Internet during the out-patient researches. Thus, simultaneous support of two formats within one technology allows to increase efficiency of remote inspections of patients with wearable systems of VAD.
Results: There is a GSM-module in control unit, which implemented for transmission of data on the status of AVK-N and which sends technical data to a RM expert (the rotor speed, the voltage and current drain, battery level etc.) in on-line mode. The data is sending to a Web server, where it is recording and initially processing in the required data storage format. After receiving the ready-made information dates analysis for the purpose of detecting the state of the system AVK-N and alerting the operator. The developed algorithms visualize critical situations and help the RM specialist to make a prompt decision to fix the possible malfunctions. Synchronously with the registration of technical parameters the patient's cardiovascular system is monitored through the channels of the wireless Internet on the basis of the information computational module included in the AVK-N package with channels for recording physiological parameters (arterial pressure, saturation, respiration, ECG, heartbeat).
Conclusions: In course of the project implementation, a highly functional telemedicine complex was created that supports a wireless connection between VAD measuring equipment and a virtual database. This ensures continuous monitoring of cardiovascular system's parameters and technical characteristics of AVK- N modules for a long time. Prospects for further development of complex with the improvement and automation of algorithms for support and decision making that provide access to reliable information.

P84
TELE-CARE AND TELE-REHABILITATION MODEL FOR VAD PATIENT'S TREATMENT
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Background: VAD therapy offers patients with advanced HF improved survival and quality of life. Development of dedicated cardiovascular monitoring and rehabilitation programs might help to raise awareness about the benefits of VAD therapy.
Aim: IT platform for tele-care of VAD patients and their heart assist devices was developed, in order to perform continuous remote monitoring during everyday life and rehabilitation training carried out in patient home or rehabilitation centre.
Methods: Central Patient Monitoring System (CPMS), as IT platform for VAD technology was developed together with dedicated application, in line with the guidelines for signal interpretation algorithms, including: testing scenarios, software functional and performance testing, integration testing of the software and external devices, assessment of system's user interface, emergency event detection and support algorithms.
Results: CPMS covers: patient's environment peripheral devices, offering wireless pump data transfer to the system, wireless transfer of chosen patient medical parameters (weight, ECG signal, INR, capillary blood oxygen saturation, body movements), communication between patient and CPMS through wireless communicator; mobile device for direct access to remote monitoring system within Internet or GSM network; IT platform equipped with tools for secure data collection and analysis, providing ongoing monitoring of adverse events, acquiring medical and technical data for building of treatment's trends, safe management of patient's home rehabilitation session supervised by constant maintenance of available transmission channel with patient in order to overcome the emergency.

Conclusions: CPMS safety, functionality and interoperability with other systems used in the patient care process (e.g. the Hospital Information System or patient tele rehabilitation support system) will be continued in clinical trials.
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P85
INTEGRATION OF ULTRASONIC FLOW MEASUREMENT IN CARDIAC SUPPORT SYSTEMS
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Background: Cardiac support systems with an impeller pump often calculate liquid flow indirectly, based on the hydraulic load resulting in a force on the impeller which can be measured electrically. Yet, such an indirect flow measurement does not satisfy all needs regarding patient safety and pump management and additionally requires a running pump.
Aim: Integration of non-invasive transit time ultrasonic flow measurement in existing cardiac support pumps.
Methods: The pump design is analysed in detail to identify the optimal position for a stable and reliable flow measurement and ultrasonic sensor element placement. Regulatory conditions for medical device development and relevant technical standards for circulatory support devices have to be considered to ensure compliance with market approval requirements for the device. Technical challenges are addressed to hydrodynamic and electrical distortions in ultrasonic signals, which is well-known from available cardiac assist device systems. Therefore, a special signal correlation analysis of the entire signal with a high sample rate is used to measure flow even under compromised conditions.
Results: First experience with integration of flow measurement in the pump head of "Rotaflow" (Maquet, Getinge Group) was gained more than 15 years ago and is still manufactured by em-tec. Since 2005 the transit time flow measurement was integrated in extracorporeal and implantable impeller pumps made of titanium alloys, e.g. "Circulite Synergy System". In-vivo trials demonstrated long-term reliability of the flow measurement in implanted systems.
Conclusions: The integration of transit time flow measurement in existing implantable and extracorporeal pump systems is possible. Preclinical trials demonstrated the reliability of the technique in-vivo. Yet, an experienced team familiar with the relevant standards as well as state-of-the art risk and development management are necessary to integrate the sensor and establish a safe and stable manufacturing process for successful device approval.

P86
DESIGN OF A SMART SYSTEM FOR A VENTRICULAR ASSIST DEVICE
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Background: The VAD is mainly a blood pumps, like a centrifugal one. A physiologic controller that shares a live body control with an operating heart is a very big challenge. The patient profile, clinical states, and even the daily behavior can change parameters like cardiac demand, heart rate, and blood pressure. Several control technics might be used and each one has advantages for a specific patient. Actually the VAD controllers have just the motor speed and the motor current as direct inputs. Blood flow, heart rate and the blood pressures are indirect inputs, and the motor speed is the controlled output. In the future, that parameters will be direct and other parameters like movements and vibrations could be used.
Aim: This work's goal is designing a Smart System with a Central Processing (CP) and a Basic Control System (BCS) that learn with its own results, as it is important to create a method that avoids consecutive new designs when some new parameter appears.
Methods: The CP works offline and it analyzes the data of many patients to estimates optimal controller parameters for each one, using the data collected by the BCS and the simulator. From time to time each optimal parameter is loaded in the BCS. The BCS collects the patient data in real time, recognizing patterns and adapts controller parameters according to the CP previews. The simulator is a part of CP and must be developed with artificial intelligence technics as it should learn with data received from the BCS and simulate the body, so it can try different controller parameters and choose the best ones. The proposed routine was implemented in Matlab with CP and one BCS.
Results: Results of simulation of estimated speed curve changes proportionally to the change in heart rate, showing an appropriate behavior.
Conclusions: Future works should implement the SS in software simulation and during In Vitro tests.

P87
PRELIMINARY RESULTS OF IN VITRO ENDOTHELIALIZATION ON PLASMA MODIFIED TITANIUM SURFACE
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Background: The tribological characteristics of the implant, roughness, allows to anchor and adherence of circulating cells under conditions of circulatory assistance
Aim: After the titanium be subjected to oxidation by eletrolytic plasma process presents rough surface appearance with pores and scaffolds of 5 to 20 microns.
Methods: An in vitro pilot endothelialization experiment was performed to compare the number of cells adhered to the different surfaces, polished titanium and textured titanium. An in vitro pilot endothelialization experiment was performed to compare the number of cells adhered to the different surfaces, polished titanium and textured titanium. Using HUVEC as a model of human aortic endothelial cells; as usual, these cells were cultured in DMEM. After defining the number of cells using Neubauer's Camera, the medium was distributed on a Culture Plate, containing 3 reference materials and 3 test samples, one in each well. The culture conditions were at 37°C in a greenhouse and pH control to 48 hours. The cell counting was carried out at the end of the period proposed to determine the number of cells viable; the samples were isolated on a new plate prior of trypsinization to ensure that the number of counted cells matched those adhered only to the samples and not to the culture plate.
Results: The number of viable cells in the surface in rough titanium was 3 times higher than in polished titanium.
Conclusions: The increase of Ra actually provides better geometric condition of interactive contact with cells. From this in vitro evaluation with the HUVECs it was possible to predict how such a process will be in in vivo conditions.

P88
DESIGN OPTIMIZATION AND IN VITRO AND IN VIVO VERIFICATION OF CORWAVE DISK MEMBRANE LVAD
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Background: While LVAD technology has improved significantly over earlier generation devices, the use of a highspeed rotary pump fundamentally exposes the blood to relatively high levels of stress and the potential for red blood cell damage. Moreover, the momentum of inertia of the rotor limits the acceleration of the pump speed constraining the possibility of re-creating a natural pulsation to a non-energetic efficient option. CorWave is developing an LVAD that offers significant advantages over the currently available devices. A completely novel approach to pumping blood is used: an undulating discoidal polymer membrane gently pushes the blood. A magnetic actuator drives the membrane oscillation up to a rate of 120 cycles per second, permitting precise adjustment of the pressure profile during a typical cardiac cycle.
Aim: In this work, we present the results of design optimization that have been verified in vitro and in vivo testing.
Methods: Starting with custom FSI algorithm where time-dependant Navier-Stokes equations and a hyperelastic model are used for solving the membrane interaction with blood, the design improvements were verified with hundreds of hydraulic tests. Hemocompatibility, including haemolysis,

thrombus formation and Von Willebrand factor, was optimized on the basis of hundreds of blood tests and few animal trials.
Results: The results verify excellent hemodynamic performances, especially in pulsatile mode. Hemocompatibility results were strongly improved and still we believe not to have reached yet the limits of this technology.
Conclusions: The disk oscillating membrane is a very promising alternative technology to rotary actuators. Future work will validate design and technology in chronic animal trials.

Experimental and Numerical Modelling

P89
IN-VITRO MEASUREMENT OF CENTERING FORCES ON A TRANSVALVULAR VENTRICULAR ASSIST DEVICE CANNULA

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Background: In transvalvular positioned cardiac support devices the cannula-leaflet interaction is of special interest and importance. Valve damage, backflow and thrombus formation might be improved if the cannula is kept in a central position within the valve orifice.
Aim: In a pulsatile in-vitro setup, forces acting on transvalvular cannulas were identified and the influence of cannula diameter and transvalvular pressure were investigated.
Methods: Radial and tangential forces acting on transvalvular cannulas were measured in a pulsatile setup. Fresh native porcine, bioprosthetic and artificial pericardial tissue valves were mounted in a test rig. The cannula position was deflected from a central position to the wall in 10° rotational steps for the whole circular range. Further the cannula diameter (4, 6, 8 mm) and transvalvular pressure (40 - 100 mmHg) were varied.
Results: Centering forces of the aortic cusps in the direction of the coaptation point were identified. At the mid of the leaflets and at the largest deflection the forces were highest (up to 0.8 N). In the commissures lower forces (up to 0.2 N) were measured. In symmetric valves with equal cusp sizes (pericardial tissue valve) the position of the commissures and cusps were clearly pronounced by the force distribution. Natural variations in the valve leaflets affected these distributions but lowest forces were always found in the commissures. A change in cannula diameter had only a minor influence. However rising transvalvular pressure linearly increased the forces, but did not alter the distribution patterns.
Conclusions: Centering forces that act on transvalvular cannulas were identified in an in-vitro setup for several valves and valve types. Lowest centering forces were found in the commissures and highest forces were found directly at the cusps. At low pressures low centering forces and an increased cannula movement can be expected.

P90
BLOOD VISCOSITY INVESTIGATION TO DEFINE BEST NUMERICAL AND IN VITRO TEST VALUES TO BENCHMARK VAD PERFORMANCE

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Background: The hydraulic performance of Ventricular Assist Devices (VADs) can be measured using a fluid with an equivalent viscosity to blood, such as an aqueous glycerol solution. This solution is more manageable and cost-effective than blood. Despite this there is no agreed industry standard, with various groups using different solution concentrations of glycerol and test temperatures.
Aim: This work aims to establish representative ranges of viscosity for bovine(μB) and human blood(μH) by performing a set of measurements while considering haematocrit (HctB, HctH). In addition to this, a quantification of the effects that changes in viscosity have on the hydraulic performance of VADs is provided to facilitate the benchmarking of the MiniVAD and to build on the current literature.
Methods: Measurement of viscosity involved shearing whole blood at 37°C using a range of shear rates (1-6000s-1), measuring both bovine and human blood. A spreadsheet was developed to calculate the glycerol solution to mimic blood viscosities at the desired temperatures. Aqueous glycerol solutions were mixed by mass to achieve the measured blood viscosities and these solutions tested using current radial flow VADs, specifically the CentriMag.
Results: This study is still on going, more test data is required to establish the representative ranges of viscosity for bovine and human blood. Once this has been concluded the pump performance testing will be conducted. Preliminary results for the measured blood parameters:-μB = 1.9 ± 0.15 mPa·s; HctB = 29.3 ± 1.25%; n = 9. μH = 2.2 ± 0.25 mPa·s; HctH = 37.4 ± 2.31%; n = 10. Preliminary results for pump performance: variations in viscosity have a direct impact on the hydraulic characteristic of a pump, specifically in the case of the HQ curve, an increase in viscosity will steepen the curve.
Conclusions: Testing is still underway but based on the current test results it can be concluded that changes in viscosity will affect the hydraulic performance of VADs. The measured blood viscosity could be used as standard to numerically and experimentally test VADs.

P91
QUANTITATIVE ASSESSMENT OF HEART-PUMP INTERACTION FOR AN AXIAL- FLOW ROTARY BLOOD PUMP SPUTNIK: IN VITRO STUDY

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Background: At this time debates are under way about the importance of pulsation in rotary blood pumps, especially about the influence of pulsations on ventricular unloading.
Aim: The aim of this study is to quantitative assessment of heart-pump interaction by analysis of pulsations in the rotary blood pump using data of pump flow, pressure head on the pump, motor electric current and pump speed. This experimental data were collected on a mock circulatory loop under dynamic conditions.
Methods: The rotary blood pump Sputnik investigated on the mock circulatory loop in two different states of heart failure. Using experimental data a pulsation and pulsatility index of the signals were calculated. Data processing made with the Python language and Butterworth filter.
Results: The pump speed increase diminishes pulsations of pump flow and pump outlet pressure regardless of ventricular function. At the same time pump speed increase augments pulsation of motor electric current in the speed range corresponded to partial assist of the ventricle with open aortic valve and pump outlet pressure pulsations within 9-17 mmHg. In contrast, this pulsation diminishes at full assist of the ventricle. The pulsations of the electric current during partial assist without backflow augmented by a mean of 29% and this value is higher by 55% in relation to the pulsations at full assist with negative diastolic pressure in the ventricle. The pump speed pulsation mainly depends on design properties of the pump.
Increase of ventricular contractility leads to the pulsations decrease up to 0.5% at speed with near zero aortic valve flow or up to 4.5% under the negative diastolic pressure of the ventricle.
Conclusions: The study suggests several observations about heart-pump interaction in vitro. The pump motor electric current is considered a feedback signal inherently reflecting heart-pump interaction.

P92
DEVELOPMENT OF FRANK-STARLING MECHANICAL MOCK CIRCULATORY LOOP FOR ROTARY BLOOD PUMP TESTING

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Background: The mock circulatory loop (MCL) is a hydraulic model used for simulating the human circulatory system and is commonly introduced into the in vitro evaluation of the cardiac assist device.
Aim: In this study, the MCL was developed to mimic the Frank-Starling response for investigating the interaction between the left ventricle and the rotary blood pump (RBP).
Methods: A linear drive system in combination with a rubber bellow, called as bellow pump, was newly designed as a ventricular simulator to implement the behavior of left ventricle during systole and diastole. The control

system of MCL simulated the Frank-Starling response (FSR) was developed based on the volume and elastance control loop. This system was validated by varying the preload and afterload during maintain the maximal elastance (Emax). In addition, the value of Emax was varied from 1.1 to 1.9 mmHg/ml, covered range of normal and abnormal heart. RBP was inserted into MCL and was altered pump speed from 1000 to 3000 rpm with steps of 200 rpm. Pressure-Volume loop (PV) was created both with and without RBP.
Results: For reduced preload at the same Emax, the end diastolic volume (EDV) decreased from 131 ± 1.8 to 104 ± 1.8 ml whereas the stroke volume (SV) calculated from PV loop reduced by 8%. For increased afterload at the same Emax, PV loop showed the end systolic pressure increased from 120 ± 4.8 to 188 ± 1.25 mmHg in contrast to the SV reduced from 72 ± 0.85 to 63 ± 0.33 ml. For increment of contractility, the resulting of PV loop and the regression line at the setting of Emax was closely mimicking those cardiac conditions (R2 = 0.98). In addition, PV loops from MCL during different levels of RBP support revealed changes similar to in vivo test. The increment of RBP speed effected on the reduction of EDV from 107 ± 1.48 to 55 ± 1.39 ml and thus leaded to reduce SV in responses to FSR.
Conclusions: This study demonstrated the capability of MCL that can represent the Frank-Starling mechanism in similar to physiological cardiac response both with and without cardiac circulatory support.

P93
MODELLING THE IMPACT OF HYPERTENSION ON CONTINUOUS FLOW LEFT VENTRICULAR ASSIST DEVICE FUNCTION
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Background: Hypertension is a major determinant of poor long term outcomes post left ventricular assist device (LVAD), including thromboembolic, cerebrovascular, and suction events.
Aim: This study examined the differences in the impact of hypertension on pump function in a pulsatile mock loop.
Methods: A pneumatically driven pulsatile mock loop was used to generate a range of physiological range mean arterial pressure (MAP, range 70-110 mmHg). The mock loop recreated physiological viscosity, and outputs. Hypertension was induced using two techniques. In the first, the effective systemic vascular resistance (SVR) was gradually increased and titrated to increased MAP in 10 mmHg increments. The second techniques increased the effective contractility by increasing the pneumatic pumping pressure applied to the mock left ventricle to increase MAP.
Results: With increased MAP as a result of increasing SVR, mean pump flow (Qmean) consistently fell. Qmean decreased from 4.81 down to 3.79 L/min for MAP 70 to 110 mmHg respectively. Minimum flow (Qmin) decreased from 3.42 to 2.60 L/min. Flow pulsatility did not change. With increasing contractility Qmean increased slightly (4.72 to 5.15 L/min for MAP 77 to 94 mmHg). There was a similar decrease in Qmin (3.42 to 2.44 L/min), but a very significant increase in flow pulsatility from 3.20 to 6.36 L/min at maximum contractility. Increased SVR was associated with an increase in pump preload, whereas with increased contractility, pump preload decreased.
Conclusions: There are significant differences in the impact on LVAD pump function according to the driving forces for hypertension. While there are often mixed contributions to increasing MAP, these studies suggest changes in anti-hypertensive medications (negative inotropes compared to vasodilators), may impact LVAD function differently. Both scenarios are associated with a decrease in Qmin, consistent with an increase in risk of suction in the setting of continuous flow LVAD support with hypertension.

P94
COMPUTERIZED CLOSED-LOOP PROPOFOL ANAESTHESIA IN CARDIAC SURGERY
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Background: Computerized closed-loop propofol system (CLPS) with arterial pressure (AP) controller to manage the depth of anesthesia was developed and is already 10 years used in our research center.
Aim: The purpose of study was to design and investigate the closed-loop propofol system (CLPS) with a mean arterial pressure(MAP) controller in cardiac surgery.
Methods: CLPS consists of a computer (PC), invasive AP sensor and Graseby 3400 infusion pump. AP is used in the CLPS as input parameter and indicator of anesthesia depth. Computer program determines the rate of intravenous propofol infusion so as to maintain the measured mean AP (MAP) as close as possible to the target MAP (85% of the patient normal MAP). The propofol concentrations are calculated by Runge- Kutta´s method PK/PD model differential equations solving with Marsh´s microconstants and Kazama´s BIS effect site microconstant and age-dependent AP effect site microconstants every 30 s. We use a combined empirical control algorithm with a proportional component of the dependence of the propofol infusion rate on the difference between the measured and the target MAP, with thresholds breaking the feedback given by the maximum and minimum concentrations of propofol in the blood (7 and 1.2 mcg/ml). It starts working after an automatic infusion of propofol induction dose (1 mg/kg for 1 min). Fentanyl was administered fractionally on the clinical indications or by program STANPUMP to ensure the effect site concentration 1.2-4.4 ng/ml needed for analgesia. Relaxation was maintained by rocuronium in standard dosages.
Results: With the help of the CLPS was conducted over 1000 surgeries. The data of 214 NYHA I-IV patients (16-74 years old) undergoing cardiopulmonary bypass operations have been processed to present here.
Now the system is still routinely used in the operating room. Monitoring depth of anesthesia was carried out by BIS (BIS module of monitor Agilent M1167A). The difference between the measured and the target MAP during operations did not exceed 22%. Depending on the stage of anesthesia a blood concentration of propofol was 1.2-6.5 mcg/ml, BIS effect site 1.2-5.3 mcg/ml, AP effect site-1.1-4.6 mcg/ml. BIS was 8-75%.
Cortisol in plasma in some very traumatic stages did not exceed 550 nmol/l. Following the end of propofol infusion, recovery time was 17.4 ± 0.5 min. 95,5% of patients was extubated in the operating room. Cases slow awakening occurred in patients with cardiac index less 3 l/m2, the elderly and patients undergoing significant blood loss. Based on detailed analysis of objective indices and clinical criteria of narcosis quality.
Conclusions: The CLPS ensures satisfactory anesthesia, taking into account patient individual peculiarities. The system is very efficient and helpful, especially for early extubation. It greatly facilitates the work of an anesthesiologist. We believe that the system can be used with slightly modified parameters for sedation in intensive care. We are now working with the new version of control algorithm- adaptive.

P95
VIRTUAL PATIENT IN STUDIES OF VENTILATION CAPACITY IMPROVEMENT BY LVAD SUPPORT IN CONGESTIVE HEART FAILURE
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Background: Dyspnea is one of the most important symptoms in congestive heart failure (CHF). In particular, the ventilation required at each level of physical activity is significantly higher in CHF than in healthy subjects, which causes poor tolerance to physical exertion.
Aim: To analyze whether, when and how the mechanical support by means of the left ventricular assist device (LVAD) can improve the tolerance to physical exertion.
Methods: The virtual patient (ViP) previously elaborated, i.e. a system of cooperating models of the respiratory system, pulmonary and systemic circulation, and gas exchange and transport, was used in the analysis. CHF was simulated by means of a left ventricular maximal elastance decrease. A rotary blood pomp model was added to ViP to simulate the LVAD support. Physical activity was expressed by the rate of CO_2 production (pCO_2). The slope of the linear dependence of the required ventilation on pCO_2 (V-P) was treated as an index of the tolerance, where the required ventilation means the ventilation that enables to keep the arterial CO_2 tension at the physiological level.
Results: CHF caused pulmonary edema and hyperemia affecting ventilation, and thus increasing the V-P slope, in four ways: (a) it made lungs heavier, which led to collapse of dependent lungs regions and thus to the shunt, (b) it

impaired gas diffusion, (c) it took place in the thoracic cavity decreasing FRC without changes in the closing capacity, (d) it increased airway resistance (decreased FEV1). Despite established opinions, an increase in the alveolar dead space had no significant influence on the slope. If LVAD decreased the pulmonary pressure (edema) and/or blood amount in the pulmonary circulation (hyperemia), the slope decreased.
Conclusions: Dyspnea in CHF is a complex but understandable phenomenon. ViP is a very useful tool in analyses of sophisticated interactions between the respiratory and cardiovascular systems in health and diseases.

P96
FLUID DYNAMICAL STUDY OF THE UNIVENTRICULAR PATIENT: THE CASE OF HLHS
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Background: Hypoplastic Left Heart Syndrome (HLHS) is a congenital condition which can severely impair the subject's health. The surgical treatment of HLHS requires careful planning in order to optimize the mechanical power exerted by the functional ventricle, avoiding power dissipations as much as possible, along the surgically created connections.
Aim: The objective of this study is to model the central venous and pulmonary compartments, starting from diagnostic MRI data taken during the follow-up of a HLHS subject, previously operated on at the Bambino Gesù Pediatric Hospital (Rome), and to calculate the flow field associated to the obtained numerical model.
Methods: MRI volume sets were analyzed using open-source image processing software. A two-level thresholding was imposed, to isolate as much as possible the blood compartment from the rest of the anatomy. A manual pruning of the resulting volume was required, since two constant thresholds are generally insufficient to perfectly segment vessels. The blood compartment volume was then discretized, using an unstructured mesh (1.036.000 tetrahedral cells). Suitable boundary conditions (BC) were set, using clinical data obtained in the follow-up. A computational fluid dynamics (CFD) study was then carried out, using the subject's model and the BCs.
Results: The morphology of the calculated flow field was highly dependent on vascular remodelling, due to the growth of the subject, after the operation. Another evident effect was given by the closeness of the IVC and SVC anastomoses to the right pulmonary bifurcation: this entailed a complex flow field, with a marked deviation of the pathlines' direction, especially along the path from the inferior vena cava to the inferior right pulmonary artery.
Conclusions: Patient-specific studies of HLHS or other relevant congenital pathologies can help in assessing the subject's health status during follow-up, possibly suggesting further interventions (e.g., vessel stenting).

P97
MINIMAL MODEL OF CARDIOVASCULAR SYSTEM ASSISTED BY A VENO- ARTERIAL EXTRACORPOREAL MEMBRANE OXYGENATION
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Background: Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) is often used for patients with cardiogenic shock. A mathematical model of the cardiovascular system assisted by a VA-ECMO could be helpful to provide a better understanding of the dynamics of the system. Broomé et al (J. Tranl Med, vol. 14, no. 1, pp. 4, 2016) have already built such a mathematical description but their model is very complex (32 compartments for the cardiovascular system and 1 ECMO compartment) and its many parameters cannot be identified with the data available in intensive care unit (ICU). Their model is thus very hard to be made patient-specific. On the other hand, a minimal model of the cardiovascular system was proposed in Pironet et al. (Computer Methods and Programs in Biomedicine, vol. 21, pp. 1-13, 2017) and shown identifiable in ICU.
Aim: The purpose of our work is to complement the cardiovascular model of Pironet et al. by an additional compartment describing the VA-ECMO and to build a tool that could help clinicians in their therapeutic approach.
Methods: The mathematical model is based on the model by Pironet et al., to which an additional pump is connected, which takes a fraction of blood in the vena cava, oxygenates it and rejects it in the aorta. This model can be identified by using data available in the ICU. Experimental data obtained from the experiments of Ostadal et al. (J. Tranl Med, vol. 13, no. 1, pp. 266, 2015) are used to determine the values of 5 parameters of the model.
Results: The results show an excellent agreement between the simulations and the experimental data. The minimal model, which is identifiable in ICU, is able to reproduce the experimental data and can thus be considered as validated.
Conclusions: A mathematical model of the cardiovascular system assisted by a VA-ECMO has been built and validated with experimental data. This model is identifiable in ICU and could thus be used at the patient bedside, in order to improve the therapeutic approach.

P98
EVALUATION OF A HYBRID CARDIOVASCULAR SIMULATOR
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Background: HCS has two sections: a physical model which includes: a reservoir, mimicking a passive left atrium; a pumping chamber with two bileaflet valves, used as left ventricle; an air tight compliance chamber; a proportional valve for systemic vascular resistance generation; and a set of tygon tubes. The electromagnetic actuator of the pumping chamber, the air volume at the compliance chamber and a proportional valve are controlled by a real time platform, located in the second section, a numeric model which is composed by: vena cava; right heart; pulmonary artery; lungs and pulmonary vein. All systems of numeric section have been programmed in LabVIEW® RT. Both sections interact with each other through pressure and flow signals that are acquired by sensors located at the physical section.
Aim: A Hybrid (numeric and physical) Cardiovascular Simulator (HCS) was constructed in order to evaluate Left Ventricle Assist Devices (LVAD). However, before to be used as LVAD assessment, HCS tool must be validated.
Methods: According to literature, validation of cardiovascular simulators is made verifying system's ability to follow Frank-Starling law when left ventricle pre-load, afterload and elastance changes are imposed.
Results: Through Pressure × Volume loop analysis was possible observe changes in left-ventricle pre-load, afterload and elastance.
Conclusions: Evaluation tests with HCS showed that its behavior under preload, afterload and elastance are according to literature results using computational cardiovascular simulators. Therefore, we conclude that as HCS is validated it can be used as tool in LVAD studies.

P99
MEASUREMENTS OF PRESSURE DROP IN ARTERIOVENOUS FISTULA MODELS - IN VITRO INVESTIGATIONS
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Background: A pressure drop and its oscillations occurring in the arteriovenous fistula due to sudden changes in the velocity vector direction or the transitional or turbulent flow, related to its complicated geometry, can have a significant impact on the blood vessel wall behaviour. On the other hand, the pressure drop cannot be precisely measured in vivo if one wants to conduct non-invasive measurements.
Aim: The aim of this study is to assess the pressure drop with experimental methods in patient-specific fistula models taking into account a pulsating nature of the flow and the elasticity of blood vessel walls.
Methods: In vitro simulations of the blood flow were performed for a patient-specific models of fistulas. Basic geometrical data of the correctly

functioning mature fistulas were obtained with angio-computed tomography. These data were applied to develop a spatial CAD model of the fistula, which allowed for creating in vitro model made with rapid prototyping techniques. The material used to build the in vitro model is characterised by similar mechanical properties to the arterial tissue. The experiments were performed at the test stand, where the blood mimicking fluid was a water solution of glycerine. During the experiments, the static pressure was measured downstream and upstream of the anastomosis with precise pressure piezoresistive transducers.
Results: The obtained results show that the pressure drop within the fistula is not so high as reported in literature, which is correlated with the precision of measurement methods and the fact that a large portion of the fluid energy is accumulated by the elastic vessel walls.
Conclusions: The pressure drop was determined with experimental methods, which take into account the elasticity of blood vessels. This is a novel approach, since most of similar studies were conducted on the assumption of rigid blood vessel walls.
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P100
NUMERICAL SIMULATION OF THE HEARTMATE 3
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Background: Patients with ventricular assist devices (VADs) for a short term or a destination therapy suffer from adverse events, such as stroke, bleeding or infection. Most severe are strokes, because they severely disable patients. There is a general consent, that complications such as thromboembolic events, due to activated or damaged platelets, are caused by an insuffient hemocompatibility of the blood pumps. The new Thoratec © HeartMate 3 is intended to provide an improved hemocompatibility by the means of reduced blood shearing due to larger flow gaps, a contact-free design realized by a magnetically levitated rotor and pulsed rotational speed.
Aim: Objective of the research is the investigation of critical flow areas to gain a better understanding of the flow inside the pump and the calculation of different operating points of the HeartMate 3 in order to compare these results with a performance curve that is derived by experimental measurements.
Methods: With the help of reverse engineering a CAD model is generated from an explanted HeartMate 3. The rotor has been cut up to assess the exact geometry of the blades. A grid of 4 mio. cells is derived from this. An advanced simulation is performed using the flow solver StarCCM+. A sliding mesh is used for the rotor.
Results: Different operating points are calculated and can be compared with experimental data of the HeartMate 3. Critical flow patterns and areas can be depicted and qualitatively evaluated.
Conclusions: Numerical Simulation is a useful method and enables detailed investigations of the flow inside the pump and can be used for comparison with experimental data of the HeartMate 3.

P101
CAN SIMULATION BECOME A PREOPERATIVE PLANNING APPROACH IN PATIENTS REQUIRING MECHANICAL CIRCULATORY SUPPORT?
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Background: Modelling and simulation may become clinically applicable tools for detailed evaluation of the cardiovascular system and clinical decision-making to guide therapeutic intervention. Models based on pressure-volume relationship and zero-dimensional representation of the cardiovascular system seem a suitable choice because of their simplicity and versatility. They show great flexibility in haemodynamic simulation and maintain the ability to be run in real time on desktop, laptop or mobile devices. This approach has a great potential for application in heart failure and mechanical circulatory support.
Aim: We sought to investigate the value of simulation in the context of three heart failure patients already discussed at a multi-disciplinary team meeting with a view to predict or guide further management and compare the outcome with the clinical decision.
Methods: Simulations were run with CARDIOSIM©, a software package developed by the Institute of Clinical Physiology, CNR, Rome, Italy. The software is interactive and based on lumped parameter models and on a modular approach with an updatable library of numerical models of different sections of the cardiovascular system, which can be assembled according to the need of the simulation.
Results: The outcome of the simulations either agreed or challenged the clinical decision. Remarkable agreement between measured and simulated data was observed.
Conclusions: Patient-specific modelling may become a daily approach for the selection and optimisation of device-based treatment for heart failure patients. A simulation setting may add a more quantitative approach and help the decision process.

Artificial Lung and Respiratory Support

P102
EFFECTS OF HOLLOW FIBER OSCILLATION ON ARTIFICIAL LUNGS
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Background: Previous studies have shown that gas transfer through hollow fibers can be increased via fiber oscillation through disruption of the diffusional boundary layer. However, prior work was performed in settings that do not directly translate to present-day, full-scale artificial lungs.
Aim: This in vitro study characterized the effects of fiber oscillatory motion parameters on oxygenation and hemolysis for a clinically relevant hollow fiber membrane (HFM) bundle. A lumped parameter model for prediction of oscillation-induced blood flow was also developed to further elucidate device performance. Our goal was to establish design criteria for an artificial lung that uses fiber oscillation to enhance gas exchange.
Methods: The effects of varying stroke length (2-10 mm) and frequency (1-25 Hz) of fiber oscillations in line with blood flow were investigated using a HFM bundle (0.25 m^2). Oxygen exchange rates were evaluated in accordance with ISO standard 7199. Normalized index of hemolysis values were measured over a 3-hour period for select conditions. All measurements were performed at a blood flow rate of 2.5 L/min.
Results: Oxygen exchange rate at a constant stroke length increased with oscillation frequency until plateauing at frequencies of 13-25 Hz. Trends in oxygen exchange rate matched well with those for oscillation-induced blood flow through the bundle predicted by the model. Based on initial findings, the system was optimized through reduction of device housing compliance. A maximum oxygenation efficiency of 510 mL/min/m^2 (97% enhancement relative to no oscillation) was achieved at a stroke length of 6 mm and frequency of 20 Hz. At a constant level of oxygenation enhancement, hemolysis increased with oscillation frequency.
Conclusions: Fiber oscillation may represent an approach to increasing gas exchange efficiency of artificial lungs. The optimal design for maximizing efficiency at small fiber displacements should maximize oscillation- induced blood flow through the bundle by minimizing both bundle resistance and housing compliance.

P103

MULTIOBJECTIVE DESIGN OPTIMIZATION OF ENDOTHELIALIZABLE OXYGENATOR MEMBRANES USING COMPUTATIONAL FLUID DYNAMICS

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Background: Seeding oxygenator membranes with native endothelial cells promises an increased hemocompatibility and, thus, offers great potential for the long-term use as implantable lung. The endothelial cell layer represents an additional diffusive resistance to gas transfer which only can be compensated by passive laminar mixing while retaining a functional cell layer under defined shear stress.
Aim: In this study, laminar vortex mixing through pulsatile flow over a structured membrane was evaluated and optimized numerically regarding maximum oxygen uptake while wall shear stress (WSS) not exceeds a physiological range.
Methods: A dimpled membrane surface was parameterized by 4 geometric variables. Pulsatile blood flow was described by Strouhal, and peak and mean Reynolds number. A validated numerical model was used to solve gas transfer and flow simultaneously. Design of Experiments and multi-objective optimization with 280 design points were applied to maximize the oxygen uptake for a constrained WSS.
Results: The sensitivity analysis shows high impact of the peak Reynolds number and an opposed influence of the membrane distance on the maximum WSS. The normalized gas transfer is mainly affected by the spere distance. The optimized design shows a slight improvement in oxygen uptake at the expense of elevated WSS by 28%.
Conclusions: Current research promises improved shear resistance of the cellular layer and, therefore, a comprehensive study for increased WSS thresholds will provide valuable information about the achievable gas transfer performances of laminar vortex mixing.

P104

EXPERIMENTAL FLOW VISUALIZATION AND WALL SHEAR STRESS MEASUREMENTS IN AN ENDOTHELIALIZABLE MEMBRANE OXYGENATOR USING PARTICLE TRACKING VELOCIMETRY

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Background: In biohybrid artificial lungs functionality and adhesion of the cellular layer are predominantly influenced by flow-induced wall shear stress (WSS). Computational Fluid Dynamics allow insight into flow conditions and deriving WSS. However, flow ans WSS are in need of validation. In contrast to other flow visualization methods, Particle Tracking Velocimetry (PTV) promises an adequate resolution of wall near flow for the determination of WSS.
Aim: In this validation study, flow visualization and determination of WSS on a structured oxygenator membrane suitable for endothelialization was performed using PTV.
Methods: A transparent and upscaled (M = 27.4) model of the structured membrane was fabricated. A test circuit was developed that allows a controlled sinusoidal flow profile with a positive net flow. Model, inflow and fluid properties were adjusted under consideration of similitude theory. 3D-PTV and 2D-PTV was performed for different operational points.
Results: PTV was successfully applied on a membrane oxygenator. A high resolution of the wall near flow was achieved with a dimensionless wall distance of y+ = 1.4. The measured WSS peak value (220 mPa) retransformed matches the simulation (0.41 mmHg). The resulting WSS distribution agrees with the simulations. Regarding the validation of the transient flow field, the same vortex formations can be confirmed.
Conclusions: PTV allows a quantitative validation of WSS in endothelializable membrane oxygenators and shows high potential for the application in hollow fiber modules.

P105

OXYGEN MASS TRANSFER IN A SURROGATE SYSTEM OF MEMBRANE BLOOD OXYGENATORS

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Background: The design of extracorporeal membrane blood oxygenators (MBO's) requires the assessment of mass transfer that very often is only estimated through correlations of the type Sh = Sh(Re,Sc) to yield the partial mass transfer coefficients in the blood chamber.
Aim: This work addresses the quantification of oxygen mass transfer in a MBO surrogate system, oxygen/membrane/water flow, to yield an experimental global mass transfer coefficient incorporating three resistances in series and serves as a design tool of MBO's for different conditions of fluid dynamics and membrane surface area arrangement.
Methods: The set up consists of an oxygen chamber at constant pressure and a slit for water circulation (2X × 2B × Z where 2B<<Z,2X) as a surrogate of the blood chamber, separated by integral asymmetric poly(ester urethane urea) PEUU membrane. The bi-soft segment membranes designated by PEUU 100, PEUU 95, PEUU 90 and PEUU 85 have 0, 5, 10 and 15% of polycaprolactone respectively [1]. They display increasing degrees of hemocompatibility and decreasing oxygen permeation flow rates. The oxygen concentration, $C(O_2)$, was measured as a function of time, t, by a sensor at oxygen pressures of 22.5 and 45 cmHg and water flow rates of 2.0, 2.5 and 3.0 L/min.
Results: An experimental global mass transfer coefficient, $K(O_2)$, was determined by $K(O_2) = (dC(O_2)/dt).V/(A \cdot C(O_2^*))$, where V is the reservoir volume, A is the membrane permeation area, $C(O_2^*)$ is the equilibrium oxygen concentration at the liquid/membrane interface and $(dC(O_2))/dt$ is the slope of the straight line $C(O_2)$ vs t, for the short times range. The resistances to oxygen transfer in the liquid stream and in the membrane were predicted respectively by convection/diffusion and solution/diffusion models. Neglecting the resistance in the oxygen chamber, a three resistances in series model was used to predict the global mass transfer coefficient.
Conclusions: The good agreement of predictions with experimental values of global mass transfer coefficients was observed mainly for PEUU 90 and PEUU 95 membranes, with approximate average values of 4.5 × 10-5 m/s.

P106

INTRACORPOREAL MEMBRANE CATHETER FOR CO_2 REDUCTION IN THE BLOOD – DRIVE UNIT AND CONTROL SYSTEM

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Background: Patients with respiratory insufficiency may, in the worst cases, develop the so called acute respiratory distress syndrome (ARDS), which is commonly treated using external mechanical respiration. However using such therapeutic approach may potentially damage the alveoli of the

patients' lungs. A different approach is to reduce CO_2 in blood by an intracorporeal membrane catheter already before the gas exchange in the lung takes place.
Aim: The aim of this study was to develop a system consisting of a drive unit and a corresponding controller that together provide the means for a rapid CO_2 removal from venous blood. The system ensures optimal functionality of the membrane by separately regulating the flow rate of blood and sweep fluid.
Methods: The drive unit is an assembly of a blood pump and power unit generating the torque, which is transmitted to the pump by a patented magnetic coupling. The blood pump is designed to overcome the pressure difference in the membrane of the catheter and to provide an optimal blood flow in the membrane area. An external controller regulates torque generation in the power unit and adjusts the working point of the blood pump based on the sensory outputs measured in the system. The central control unit is a microcontroller based on the ARM Cortex M3 architecture.
Results: The characteristic of the blood pump describing the flow against the pressure difference was recorded. The working point of the pump depends on the operating mode of the membrane catheter and the controlled CO_2 reduction and can be set on a stable part of the pump's characteristic curve.
Conclusions: In the blood pump sufficient specific work is done to overcome the pressure difference in the membrane prototype. The current state of the system provides a firm basis for further refinement of the intracorporeal membrane catheter device. Further work will investigate blood hemolysis caused by the pump.

P107
THE USE OF AN ARTIFICIAL PATIENT IN ANALYSIS OF POSSIBLE CAUSES OF CHANGES IN ARTERIAL BLOOD GASES DURING THERAPEUTIC THORACENTESIS
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Background: Ambiguous data on changes in the arterial oxygen (PaO_2) and carbon dioxide ($PaCO_2$) tensions during therapeutic thoracentesis have been published. In particular, factors affecting the changes are not clearly determined.
Aim: The aim of this study was to analyze possible causes of the changes during the procedure by means of simulations on a universal artificial cardio-respiratory patient (AP) elaborated previously. The analysis was based on and supported by own clinical data.
Methods: PaO_2, $PaCO_2$, tidal volume and pleural pressure (Pp) were measured during thoracentesis in 45 patients with pleural effusion. Then, the procedure was simulated on AP being a system of cooperating models of the respiratory system, pulmonary and systemic circulation, and gas exchange and transport. Influence of particular factors on PaO_2 and $PaCO_2$ were estimated analyzing effects of deviations of models parameters from the standard values.
Results: Despite pleural fluid withdrawal, persistence of lung collapse in dependent regions were observed. The collapse and an increase in perfusion resulted in a considerable shunt. Nevertheless, both simulations and clinical data showed that $PaCO_2$ did not change significantly. However, according to the clinical data, PaO_2 may vary and, in general, it increases when Pp increases if previously it has decreased with Pp decrease. Simulations suggested that not the shunt but a degree of lung edema affecting O_2 diffusion could be responsible for PaO_2 variations.
Conclusions: Simulations suggest that PaO_2 may decrease during thoracentesis if lung edema appears as a consequence of a decrease in perivascular pressure due to pleural fluid withdrawal associated with lack of reexpansion of collapsed lung regions.
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P108
IN-VIVO STUDY OF A NOVEL LUNG SUPPORT DEVICE FOR PAH AND BRIDGE-TO- TRANSPLANT/CANDIDACY
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Background: RAS-Q is a novel device for pulmonary arterial hypertension (PAH) and bridge-to-lung- transplant/candidacy. It is composed of a PMP fiber bundle with integrated compliance to provide a pulmonary-mimetic flow environment and low pressure loss at high performance. RAS-Q is connected between pulmonary artery (PA) and left atrium (LA). Due to its minimal pressure loss of <10 mmHg, it does not require an additional blood pump.
Aim: RAS-Q was validated in 6 acute in vivo trials (sheep, 53 ± 7 kg). One trial was designed to benchmark against the Quadrox Pediatric in a paracorporeal setting. Pediatric device sizes were used to accommodate the sheep's lower CO.
Methods: RAS-Q was connected using 20 Fr cannulas. PAH was induced by constricting the PA to analyze failing lung and right heart conditions. Flow rates and pressures were measured in the PA, RAS-Q and aorta.
Results: Results show oxygenation of >60 mlO_2/lBlood and CO_2 removal of >50 $mlCO_2$/lBlood. Compared to Quadrox, RAS-Q provides a 3 times higher paracorporeal flow rate and a 10 times higher pressure relief inside PA. For induced PAH, RAS-Q is able to reduce pulmonary pressure from 38 mmHg back to baseline (26 mmHg), while it remained at 37 mmHg with Quadrox. Right heart failure after induced severe PAH results in decreasing systemic pressure and system failure (baseline: CO = 3.1 ± 0.5 l/min, MAP/PAP = 3.9 ± 0.02; induced PAH: CO 1.3 ± 0.9 l/min, MAP/PAP = 1.2 ± 0.01). Using RAS-Q, the relation between MAP and PAP is restored to 1.7 ± 0.2, whereas the HMV reaches baseline level (CO = 3.03 ± 0.6 l/min).
Conclusions: Results demonstrate RAS-Q's capability to treat patients with severe lung diseases. Its unique low pressure loss and integrated compliance allow RAS-Q to react and adapt to patient needs. It lowers RV afterload and restores CO in the otherwise failing circulation.

Dialysis/Apheresis - Clinical

P109
THERAPEUTIC APHERESIS IN SEVERE GUILLAIN-BARRE SYNDROME – OUR EXPERIENCE FROM 2009 TO 2017
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Background: In patients with acute severe Guillain-Barre syndrome (GBS) a combination of therapeutic plasma exchange (TPE) and iv immunoglobulin have proved effective but the optimum number of TPE has not been established.
Aim: Aim of our study was to evaluate the treatment strategies in our patients between January 2009 and January 2017, treated at the University Medical Center Ljubljana.
Methods: We retrospectively studied 32 GBS patients, 15 women and 17 males, with a mean age of 55 ± 17 years. All patients were tetraplegic, 14 of them needed mechanical ventilation. They received at least five apheresis treatments. During TPE therapy one plasma volume was exchanged and replaced with a mixture of 20% human albumin and hemofiltration solution. In immunoadsorption 2-3 plasma volumes were run over two cartridges containing protein A in an Immunosorba column. A decision regarding the duration of apheresis therapy was based on the clinical improvement of the patient.

Results: We performed 351 apheresis treatments, including 311 plasma exchanges and 40 immunoadsorption procedures. The average duration of apheresis therapy was 19.7 ± 10.0 days and 5-29 sessions were needed. The average number of treatments per patient was 10.0 ± 5.6 and the exchange volume was 3401 ± 686 mL. Among 14 patients requiring respiratory support, 6 recovered from disability almost completely, but 1 died later due to pulmonary embolism. Two patients cannot walk unaided, one remains severely disabled, one still requires assisted ventilation, 2 were lost to follow-up. Two patients died after being weaned from mechanical ventilation, both deaths were not procedure-related. The rest of 17 tetraparetic patients survived. Five patients recovered completely, 6 need assistance for walking and 6 cannot walk.
Conclusions: Our retrospective analysis shows that the number of apheresis treatments should be adjusted to disease severity and that patients with moderate symptoms did also benefit from apheresis therapy.

P110
IMMUNOLOGY ABSORPTION INDUCES REMISSION IN ANCA-ASSOCIATED VASCULITIS
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Background: Immunology Absorption (IA) has been used in the treatment of several autoimmuno diseases as IA can eliminate pathological immunoglobulin. However, its effect on ANCA-associate vasclulitis has not been illuminated.
Aim: IA was evaluated as additional therapy in petient suffering from ANCA-associated vasculitis.
Methods: Three patients underwent immunoadsorption onto protein A sepharose with concomitant immunosuppressants.
Results: Remission of disease was achieved in two patients. The first patient discharged without dialysis, and the second patient underwent hemodialysis regularly. Therapy had to be stopped in the third patient due to side-effect and this patient died of severe infection in the end. The average reduction of the titer of MPO per treatment was 60.7 ± 14.9% with a reduction of fibrinogen for 14.8 ± 12.7% in meanwhile.
Conclusions: Immunoadsorption onto protein A might be used as an extracorporeal treatment option in ANCA-associated vasculitis.

P111
CHANGES OF SUBJECTIVE GLOBAL ASSESSMENT IS ASSOCIATED WITH CLINICAL OUTCOMES OF PERITONEAL DIALYSIS PATIENTS
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Background: Subjective global assessment (SGA) is generally considered as a classic nutritional marker and has been reported previously to be associated with the mortality of peritoneal dialysis patients.
However, little is known whether changes of SGA after peritoneal dialysis affect the clinical outcomes.
Aim: This study aim to elucidate the association between changes in nutrit ional status determined by SGA during the first year of peritoneal dialysis and clinical outcomes of these patients.
Methods: The study included all incident patients receiving peritoneal dialysis at The First Affiliated Hospital of Zhejiang University between January 1, 2005 and December 31, 2015 with available SGA data at both baseline and 12 months after dialysis commencement. Nutritional status was defined as well nourished (WN, SGA A) or malnourished (MN, SGA B or C). The patients were divided into 4 groups according to the change in nutritional status: group 1, WN to WN; group 2, MN to WN; group 3, WN to MN; and group 4, MN to MN. Statistical method used in this study included Kaplan-Meier survival analysis and multivariate Cox regression model analysis.
Results: There was a significant difference in the all-cause mortality among the groups (P<0.01). Multivariate Cox regression analysis revealed that the all-cause mortality was significantly higher in group 4 than in group 1 and group 3 (P<0.01) whereas the cardiovascular mortality was significantly lower in group 1 and 3 compared with group 4 (P<0.01). Moreover, the hospitalization time of group 4 was significantly higher than in group 1 and 3 (P<0.05); There was no significant difference between groups 1 and 2.
Conclusions: The changes in nutritional status assessed by SGA during the first year of peritoneal dialysis are associated with clinical outcomes.

P112
RELATIONSHIP BETWEEN SERUM URIC ACID AND ALL-CAUSE MORTALITY IN MAINTENANCE HEMODIALYSIS PATIENTS
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Background: The relationship between serum uric acid (SUA) levels and prognosis in maintenance hemodialysis (MHD) patients has not been fully elucidated. Hyperuricemia in ESRD patients is very common. It is generally believed that hyperuricemia is associated with hypertension, peripheral arterial disease, diabetes, chronic kidney disease, cardiovascular disease. While MHD patients with high uric acid are considered to be well nutritious and may indicate a good prognosis. However, most of the current research conclusions were drawn from only for a dialysis time point during the MHD period and were not the same. Therefore, this study will analyze the relationship between SUA level and prognosis in MHD patients from multiple dialysis time points.
Aim: To investigate the association between serum uric acid (SUA) and survival in maintenance hemodialysis patients(MHD).
Methods: All included patients were from Zhejiang Dialysis Quality and Management Center (ZDQM), initiating MHD between Jan 1, 2010 and Dec 31, 2014, whose dialysis time were more than 3 months. Cox proportional hazards regression was used to analyze the association between SUA and survival in three time points respectively, including the first dialysis, 3 months after first dialysis and 12 months after first dialysis.
Results: 13270 patients were included in the retrospective study. The median follow-up was 868 (interquartile range, 502-1375) days. 2560 patients were dead and the mortality was 19.3%. SUA was negatively correlated to age and positively correlated to serum creatinine, blood urea nitrogen, albumin and phosphorus at all the three time points (P<0.05). When adjusted by COX multivariate regression model, an increase in SUA predicted lower mortality only appeared at 3 months after first dialysis (HR = 0.99, P = 0.03).
Conclusions: Hyperuricemia may be a protective factor for MHD patients at 3 months after first dialysis, but still need to be proved by prospective study further more.

P113
ASSOCIATION BETWEEN MEDICAL INSURANCE TYPE AND SURVIVAL IN HEMODIALYSIS PATIENTS IN CHINA
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Background: There are two major medical insurances in China: the New Cooperative Medical Scheme (NCMS), mainly for rural residents, and the Urban Employees' Medical Insurance (UEMI) for urban patients. These medical insurances may have influence on the outcomes of patients treated with hemodialysis (HD), and there is no study about the association between disparities in medical insurance and HD outcomes in China.
Aim: This study aimed to assess the association between medical insurance type and survival of patient undergoing HD.
Methods: The data were from the Zhejiang Dialysis Quality and Management Center Database, between 2010 and 2014, which including 225 blood purification centers and 93 peritoneal dialysis centers in Zhejiang Province of China. All patients were followed up until death or the end of 2015. Patients with malignancy, dialysis vintage less than 90 days and under 18 years old were excluded. Patients were divided into two groups according to their medical insurance. Demographic data, biochemical parameters and primary clinical outcomes including all-cause mortality, switch to peritoneal dialysis and kidney transplantation were analyzed. Survival analysis was performed using the Kaplan–Meier method, Log-Rank test and Cox proportional hazard regression model.
Results: There were 6779 patients with UEMI and 7177 with NCMS. Compared with UEMI, patients with NCMS were younger, had a smaller proportion of

diabetic nephropathy and hypertensive nephropathy, and a bigger proportion of chronic glomerulonephritis, and with shorter dialysis vintage, more severe anemia, more frequent hypocalcemia, hyperphosphatemia and hyperuricemia. Urban patients yielded superior overall survival rates compared to rural patients (P<0.001). Multivariate analysis showed that NCMS was independently associated with lower survival (NCMS:UEMI HR = 1.567; 95% CI = 1.443-1.701).
Conclusions: Medical insurance type is independently associated with HD patient survival.

P114
EPIDEMIOLOGICAL SURVEY OF INCIDENT END STAGE RENAL DISEASE PATIENTS FROM 2010 TO 2014 IN ZHEJIANG PROVINCE, CHINA
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Background: Dialysis registration is an important component for standardized management of dialysis patients. Zhejiang Dialysis Quality and Management Center (ZDQM) was built in 2007. It includes basic profile of dialysis patients, clinical data, medical treatment data, laboratory data and so on.
Aim: Our aim was to analyze the epidemiological literature in incident end stage renal disease (ESRD) patients in Zhejiang province, which in turn to provide epidemic data to doctors, researchers, and improvement and formulation of health insurance policy.
Methods: We retrospectively review all incident ESRD patients registered in the ZDQM from 2010~2014. The demographic information, clinical and laboratory data were collected. Their incidence of ESRD patients, primary causes changes in them, structure of sex and gender, and cause of mortablity were investigated.
Results: 31146 incident ESRD patients were included (25153 maintenance hemodialysis patients, and 5993 maintenance peritoneal dialysis patients). The incidence rate of ESRD from 2010 to 2014 was 90.4 to 155.4 pmp. The average age was 58.3 years old in 2010 and 59.4 years old in 2014. The proportion of new ESRD patients over 65 years old was 43.1% in 2010 and 43.7% in 2014 especially. Male to female was 1.43 vs 1.0. The first three primary cause of ESRD were chronic glomerulonephritis (CGN)(51.3%), diabetic nephropathy (DN)(18.9%) and hypertensive nephrosclerosis(HTN)(6.3%). The ratio of DN was growing year by year. In ESRD patients, the cardiovascular mortality was the leading causes of death.
Conclusions: In Zhejiang province from 2010~2014, the incidence of ESRD rises annually. Main dialysis modality is hemodialysis, meanwhile, the proporation of peritoneal dialysis is increasing recent years. The leading cause of ESRD is CGN, DN rises with years. Cardiovascular mortality is the leading causes of mortality.

P115
GENOME-WIDE ANALYSIS OF DNA METHYLATION AND GENE EXPRESSION CHARACTERISTICS OF DIALYSATE-INDUCED PERITONEAL FIBROSIS
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Background: Peritoneal fibrosis is a severe and common complication of long-term peritoneal dialysis. Recent epigenetic studies indicate that alterations in DNA methylation may explain the mechanism by which epithelial cells adopt the mesenchymal phenotype that promotes fibrosis progression. However, genome-wide analysis of the DNA methylome of peritoneal fibrosis is lacking.
Aim: To explored the extend of DNA methylation in the progression of peritoneal fibrosis and ultrafiltration failure, which is vital in the development of specific prediction, prevention, and treatment strategies.
Methods: Infinium HumanMethylation 450 K BeadChip was employed to define the DNA methylome and transcriptome of peritoneal fibrosis from the peritoneum and dialysate of participants (n = 3) with ultrafiltration failure or normal peritoneal function. Sub-networks and genes interactions that included the most differentially methylated genes were examined via GO pathway enrichment analysis in order to identify the most relevant pathophysiological pathways related to fibrotic disease.
Results: A marked thickening of peritoneal interstitial expansion with collagen accumulation and changes in EMT markers were observed in ultrafiltration failure patients. CpG islands in SOS1, RNF39, and RPL13AP3 were hypermethylated to a larger extent in subjects with normal peritoneal function, while CpG islands in SLC7A5, CPLX2 and MAFB were significantly hypomethylated (P-values of 1.05E-08 to 1.64E-06). GO pathway enrichment analysis of the data also identified candidate molecular interactions relevant to fibrosis pathology.
Conclusions: Fibrosis-specific DNA methylome and epigenetic states are important in process of pathological peritoneal fibrosis after long-time dialysis, which can serve as new therapeutic targets.

P116
TAMOXIFEN ATTENUATES PDF-INDUCED PERITONEAL FIBROSIS VIA REDUCING GSK3β/β-CATENIN AXIS ACTIVATION
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Background: Peritoneal fibrosis is a severe complication of long-term peritoneal dialysis, which has been successfully attenuated by Tamoxifen in clinic treatment; however, the definite mechanism remains obscure.
Aim: To explored the role of GSK3β/β-catenin signal in the protective effect of Tamoxifen.
Methods: C57BL/6 mice received daily intraperitoneal injection of saline, 4.25% high glucose PDF or PDF combined with Tamoxifen for 30 days, and mouse peritoneal epithelial cells (mPECs) were cultured in 4.25% glucose or combined with Tamoxifen for 48 h.
Results: Tamoxifen alleviated thickening of peritoneum, and reversed the expression of E-cadherin, Vimentin, MMP9, fibronectin and β-catenin induced by PDF in mice model. Furthemore, Tamoxifen diminished epithelial-to-mesenchymal transition, as well as the phosphorylation of GSK3β, nuclear β- catenin and Snail in mPECs after high glucose exposure.
Conclusions: In conclusion, Tamoxifen significantly attenuates EMT progression of peritoneal epithelial in fibrosis pathology partly via suppressing GSK3β/β -catenin axis activation.

Tissue Engineering and Organ Regeneration I

P117
AN IN VITRO SKIN WOUND INFECTION MODEL AND BIOEVALUATION OF ANTIMICROBIAL WOUND DRESSINGS
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Background: An in vitro wound infection model based on human cells is highly demanded representing a biomimetic system of the in vivo state of chronic wounds for the testing of antimicrobial polymeric biomaterials (AMBs). The bioanalysis of antimicrobial polymers in this system can lead to the understanding of antimicrobial, cytotoxic and wound healing properties at the same time in an in vitro infected skin wound condition. It will also provide the relationship between this interaction and the underlying molecular mechanisms that occur as a result of this interface.
Aim: The main purpose of this 3D wound infection model is to serve as an in vitro tool recapitulating enough biological response for the bioevaluation of antimicrobial and wound healing properties of novel AMBs. This work was aimed at the development of an in vitro skin model able to maintain cell viability over time.
Methods: The 3D skin equivalent was obtained having both a dermal and an epidermal compartment, by embedding human primary fibroblasts in rat

tail tendon collagen type I hydrogel (mimicking skin extracellular matrix) and then seeding human primary keratinocytes on it to generate the epidermal layer. Different fibroblast seeding densities and matrix concentrations were evaluated to determine the cell morphological differences. Culture conditions for keratinocytes were evaluated to determine the a fully differentiated and stratified squamous epithelium. This leaded to the model for wounded skin eventually for the inoculation with clinically challenging bacteria e.g. Staphylococcus aureus at wound site, to generate a 3D wound infection model. The model was characterized by H&E histostaining, immunohistochemical analysis (Anti Cytokeratin 10, Cytokeratin 14, collagen type IV and Laminin 5 antibodies), SEM and fluorescence-microscopy analysis using z-stack imaging (Promokine Live/Dead and Phalloidin/DAPI). The bacterial adherence and localization within epidermal tissue was observed through confocal microscopy.
The wound dressings along with the commercially available controls were evaluated for antibacterial as well as cytotoxic properties in 2D as well as in 3D system.
Results: The Z-stacked imaging revealed the filopodia like morphology and a uniform distribution of fibroblasts at different planes inside the matrix in 3D. However, no morphological differences were found among different collagen I matrix concentrations. H & E results demonstrated the architectural features of dermal and fully differentiated epidermal layers. Immunohistology demonstrated the details of epidermal markers and remodelled intercellular connective soft tissue. The "irregular" fibril formation by rat tail tendon collagen type I constitutes an in vivo like matrix, however in the future we will change it with a biofunctionalized synthetic hydrogel to avoid the use of xenogeneic materials such as collagen from rat origin, that is additionally characterised by batch-to-batch variations. Three-dimensional skin culture is an informative experimental test system for evaluation of antimicrobial wound dressings in an environment that mimic the interface between pathogenic bacteria and skin tissue.
Conclusions: Although a model based on human primary cells is more sensitive but is clinically relevant. The in vitro wound infection model better relates to the in vivo situation for the evaluation of antimicrobial properties as well as cytocompatibility. Next step will be the evaluation of gene expression and cytokine levels by keratinocytes to identify model skin response to bacteria that will also help exploring host- pathogen interaction and thus the antimicrobial strategies.

P118
DEVELOPMENT OF TISSUE-ENGINEERED CARDIAC PATCH BASED ON SILK FIBROIN
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Background: Silk Fibroin (SF) is a biopolymer that has been in demand for tissue engineering materials recently. However, most of SF materials are used for regeneration of hard tissue such as bone, cartilage and tendon rather than soft tissue because it has high physical properties. Moreover, physical properties of processed SF still became poor for surgical operation.
Aim: With these situations as a background, non-woven scaffold composed of SF and thermo- plasticpolyurethane (PU) fabricated and evaluated as tissue-engineered cardiac patches for pediatric patients.
Methods: SF/PU composite scaffolds were fabricated by electrospinning methods with different weight ratio of SF/PU solution. Structural analysis and compatibility of material observed by several solid-state NMR methods. SF/PU composite scaffolds implanted to rat abdominal aorta to evaluate tissue response with comparison of current materials.
Results: The tensile tests of fabricated scaffolds showed that each scaffold was shown the ratio-depended changes of the values of Young's modulus. Moreover, 13C CP/MAS NMR analysis indicated that the primary structures of SF and PU were kept after blending process. Implantation study confirmed early cell infiltration and immigration at one and four weeks after transplantation. SF/PU patch also showed collagen fiber infiltration, endothelial and smooth muscle cell formation with vascularization. In addition, resolving of acute inflammation has been observed in longer implantation period.
Conclusions: SF/PU patch showed excellent adhesive and biocompatible properties in-vivo studies which results supports with NMR structural evaluation. We believe micro-phase separation structure gives high ability to use SF/PU composite for cardiac repairing. These results indicated that the SF/PU composite patch have some good functions supports to use as a cardiac repairing patch.

P119
MICROPARTICLES FROM DECELLULARIZED HUMAN LIVER TISSUE FOR INCREASING THE BIOCOMPATIBILITY OF ARTIFICIAL GRAFTS
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Background: Development of bioengineered constructions for tissues and organs regeneration is the major goal of regenerative medicine. Silk fibroin is biodegradable polymer with suitable mechanical properties and can be used as a material for such grafts. Extracellular matrix of native tissue may be used to improve the biocompatibility of an artificial graft. Decellularization of organs and tissues is a promising technique to obtain such matrix.
Aim: To produce a method for decellularization of human liver and to obtain decellularized liver tissue microparticles for modification of silk fibroin films.
Methods: Donor liver from a healthy patient was used. The liver was milled into 1-10 mm pieces and decellularized by incubation in lysing solution containing detergents. There are two methods of films modification: 1) microparticles suspension was blended with fibroin solution before films preparation; 2) microparticles were covalent crosslinked with silk fibroin film by EDC/NHS solution. Optical and scanning electron microscopy were used for modified films analysis. Human hepatocellular carcinoma cell line Hep- G2 was used to assess the cells adhesion on the films.
Results: Microparticles with a size less than 5 μm were prepared from decellularized human liver tissue and it was the prevailing fraction. Modified silk fibroin films were obtained. The Hep-G2 cells adhesion was significantly higher on films, modified with decellularized liver tissue microparticles in comparison with non- modified films.
Conclusions: The invented protocol allows obtaining microparticles of the extracellular matrix of human liver with size less than 5 microns. Obtained modified silk fibroin films maintain high level of cells adhesion.
Microparticles manufactured from decellularized human liver may be used in tissue engineering and regenerative medicine for increasing the biocompatibility of the artificial grafts.

P120
TISSUE ENGINEERING AS A WAY FOR WORKING OUT A BIOARTIFICIAL LIVER SUPPORT AT THE TREATMENT OF CHRONIC LIVER FAILURE
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Background: Treatment of chronic liver failure (CLF) is an actual problem of regenerative medicine. For this reason, there is great interest in cell-tissue engineering technologies as a method of supporting and stimulating therapy at CLF.
Aim: Is CLF-treatment by using new tissue engineering technology.
Methods: CLF was modeled on Wistar rats by means of CCl4. Isolated liver cells(LC) and mesenchymal stromal cells(MSC) were obtained by standard procedure. Suspension of LC (2,5-4,0 × 106 cells/cm^3) and MMSC (0,5-0,8 × 106 cells/cm^3) was immobilized on tissue specific small-dispersed matrices(TSSDM), obtained from decellularizated liver. Formed cell engineering constructions(CECs) were implanted into damaged rat liver. All animals (n = 80) were divided into 2 groups:control(gr.1) without treatment-injected saline(n = 40); experimental(gr.2) with implanted CECs(n = 40). Dynamics

reduction of CLF; liver and CECs morphology were investigated within 365 days after implantation.
Results: In gr.1 took place the formation of liver cirrhosis. In gr.2 all biochemical indices returned to normal levels within 30 days and the degree of liver damage to this term (dystrophia, saved liver structures, fatty vacuoles et al) was significantly reduced on comparison with gr.1. Moreover, in gr.2 at late terms observation liver morphology practically did not differ from the norm. CECs was fully integrated into structures of the liver. In CECs were detected viable hepatocytes, and newly formed bile ducts. In the liver parenchyma hepatocyte proliferation, neogenic plethoric vessels and neogenic bile ducts were detected.
Conclusions: It is found out that the proposed method of correction and treatment CLF is effective and can be used in clinical practice.

P121
PREPARATION OF DECELLULARIZED PORCINE RENAL SCAFFOLDS FOR POTENTIAL XENOTRANSPLANTATION: TECHNIQUE AND BIOCOMPATIBILITY EVALUATION
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Background: Kidney transplantation remains the therapy of choice for patients with end stage kidney disease. However, the number of patients, waiting for a kidney graft continues to grow constantly and far exceeds the availability of donor grafts. This disparity has fomented the search for therapeutic alternatives using regenerative medicine approaches. One approach combines cells with acellular kidney scaffolds derived from animal tissue especially pigs. The reaction of the host toward these porcine scaffolds depends on the biocompatibility of the construct.
Aim: To prepare decellularized kidneys of a clinically relevant size and evaluate its biocompatibility in terms of immunogenicity, pathogenicity, cytotoxicity, and biodegradability.
Methods: Porcine kidneys were cannulated via the renal artery, then perfused with heparinized PBS, followed by 0.1% sodium dodecyl sulfate solutions.
Results: Hematoxylin and eosin as well as DAPI staining confirmed cellular clearance from pig kidneys, with removal of nuclei and cytoskeletal components in addition to preservation of the microstructure. SEM confirmed the absence of any cellular content within the scaffold, which is maintained in a well-organized 3-D architecture. Decellularized kidneys retained the intact renal vasculature upon examination with contrast radiography. The essential structural extracellular matrix molecules were well-preserved. Decellularization was efficient as the protocol removed approximately 97.7% of DNA from native kidneys in addition to the immunogenic and pathogenic antigens. Scaffolds did not induce the human immune response in vitro. The SDS-treated decellularized scaffolds were non-cytotoxic to PK cells. Decellularized scaffolds were susceptible to enzymatic degradation upon treatment using collagenase. PK cells were able to grow and proliferate within the decellularized renal scaffolds with maintaining a higher function than cells grown as monolayers.
Conclusions: Thus, we have developed a rapid decellularization technique for generating safe biocompatible kidney scaffolds that represents a step toward development of a transplantable organ using tissue engineering techniques.
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P122
EXTRACT OF CRYOPRESERVED PIGLETS HEART FRAGMENTS AS REGULATING AGENT PROCEEDING OF EXPERIMENTAL MYOCARDIAL NECROSIS
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Background: Nowadays in regenerative medicine in particular cardiology much attention is giving for investigations the biological effect of regulators of natural origin.
Aim: To establish the influence of extracts of cryopreserved pigles' heart fragments (EPsH) on electrocardiographical indices of healthy heart and evidence of lipid peroxidation (LP) in blood serum of rats with experimental myocardial necrosis (MN).
Methods: The research was carried out on breedless male rats of 180-250 g. Modeling the MN was done by applicator, which was cooled with liquid nitrogen. For obtaining the EPsH the cryopreserved fragments of heart were incubated in physiological saline solution (PSS) and cleared from thermolabile proteins.
Animals with MN were injected with PSS (28 animals) or with EPsH (28 animals), 9 animals were control (norm). The dose of peptides injected once daily during whole experiment was 50 μg per 100 g to body weight. Electrocardiograms (ECG) were recorded and analyzed with hardware-software "Poly-Spectrum-8/V" (Neurosoft, Russia). The intensity of processes of free-radical oxidation was examined with chemiluminescent method and lipid peroxidation by the level of thiobarbituric acid reactive substances (TBARS) in blood serum. The results were statistically analyzed with MANOVA method.
Results: Injections of EPsH to animals with MN influences on process of heart remodulation, and also contributed to normalization of ECG indices, neurohumoral regulation of heart function and balance of impact of sympathetic and parasympathetic divisions of vegetative nervous system. In the animals with experimental MN, which were injected with EPsH, the intensity of LP and TBARS in blood serum decreased more rapidly if compare with MN.
Conclusions: Injection of the PIHE to animals with MN facilitate to normalization of electrocardiographic indices of healthy heart and also more rapidly normalizing the intensity LP.

P123
CHARACTERIZATION OF THE FUNCTIONALIZED BIODEGRADABLE COLLAGEN SCAFFOLDS FOR IN VIVO DELIVERY OF SDF-1α AND SUBSTANCES WITH BACTERICIDAL ACTIVITY
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Background: Chronic wounds are a consequence of impairment of normal reparative processes caused by imbalance in cytokine regulation network frequently complicated with infections. After injury, a stromal cell derived factor-1a (SDF-1α) attracting the stem cells is expressed by the cells of damaged tissue. However, in chronic wounds the stimulus may be insufficient due to quick degradation of the protein which is increasing additionally in a case of infection.
Aim: Present study focuses on the development and characterization of the functionalized biodegradable collagen scaffolds for in vivo delivery of SDF-1α and polyhexamethylene guanidine hydrochloride (PHMG) as a biocide.
Methods: The scaffolds were prepared by freeze-drying collagen I solution containing polymer based on cross-linked modified heparin or PHMG. The recruitment of MSCs was studied in allogenic transplantation model. In the study, the bone marrow MSCs were isolated from FVB-CgTg(GFPU) 5 Nagy/J mice and administered to ICR mice, implanted with the scaffold loaded with SDF-1α. In xenogeneic transplantation model unmodified human cord MSCs (hMSC) or hMSC with enhanced expression of hSDF-1α were seeded on the scaffold and implanted into ICR mice.
Results: It has been show that the developed functionalized collagen scaffold can be efficiently loaded by recombinant SDF-1α. The data obtained in the model of allogenic transplantation of bone marrow MSCs revealed that

the scaffold loaded with SDF-1α could induce targeted migration of the host stem cells into the place of implantation. Comparable effects have been demonstrated in a xenogeneic transplantation model. The developed scaffold with PHMG reduced microbial growth of E. coli strain DH10B.
Conclusions: The developed delivery systems for SDF-1α and PHMG can be used as vehicles for their in vivo administration.

P124
GENETICALLY MODIFIED HUMAN HEPATOMA AND FEEDER LAYER CELLS FOR BIOARTIFICIAL LIVER DEVICES
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Background: Liver diseases are still a major clinical challenge. The main limitations in the liver treatment based on transplantation are: the shortage of liver donors, low number of available human hepatocytes and their rapid dedifferentiation in vitro. To overcome these drawbacks the efforts have been directed towards the use of xenogenic hepatocytes, obtaining hepatocytes-like cells from stem cells, optimization of hepatocytes culture conditions by supplementation of media with growth factors, use of various growth surface coatings, decellularized organ matrices, 3D printing growth scaffolds, and coculture with other cell types.
Aim: The aim of our research project was to investigate the feasibility of genetic modifications of human hepatoma C3A cell line and isolated human skin fibroblasts (HSF) to sustain and improve their specific functions.
Methods: The genetic modifications were carried out with the use of self-produced lentiviral vectors bearing following human genes: hEGF which encodes epidermal growth factor and two genes engaged in the urea cycle - arginase 1 (hARG1) and ornithine transcarbamylase (hOTC).
Results: This strategy allowed us to generate new stable cell lines: C3A_ARG1_OTC_III and HSF_EGF. Our results showed that C3A_ARG1_OTC_III cells produced more albumin, better tolerated high ammonia concentration and more efficiently synthesized urea than non-modified counterpart. In the experiments with modified fibroblasts, HSF_EGF, used as the feeder layer cells, we observed their long-term positive impact on the specific hepatic functions of the cocultured hepatoma cells. We have also noticed similar positive effects of the new growth surface coatings made by drying confluent culture of the isolated human skin fibroblast.
Conclusions: The new, genetically modified cell lines, have shown their potential in the improvement of the human liver cells coculture parameters and could be used in such applications as cytotoxicity tests and construction of Bioartifical Liver devices.

Tissue Engineering and Organ Regeneration II

P125
DEVELOPMENT OF AN IN-SITU TRANSFECTION SYSTEM FOR REGENERATION OF BONE
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Background: Liposomes made of cationic lipids were previously successful for cell transfection having the advantage of lower toxicity and immunogenicity. Because of their intrinsic charge, they might be useful also as polycations for Layer-by-Layer technique (LbL) to embed vectors that permit localized transfection without the disadvantages of systemic applications of gene therapy.
Aim: Here, a multilayer system (PEM) made of glycosaminoglycans and collagen was prepared by LbL technique for embedding liposomes on terminal layers. First, adsorption and stability of liposomes on multilayers was studied here to develop a system for in situ-transfection.
Methods: Cationic liposomes were prepared by film hydration procedure to obtain multilamellar vesicles. Their size distribution was characterized using dynamic light scattering. Polyelectrolyte multilayers were prepared by alternating adsorption of collagen type I as polycation and chondroitin sulphate (CS) or hyaluronic acid (HA) as polyanions with intermediate washing steps and final adsorption of liposomes. The growth of multilayers was studied by surface plasmon resonance (SPR) while their thickness was measured with ellipsometry.
Results: The SPR results showed a change in angle shift corresponding to an increase in the adsorbed mass indicating that both systems grew exponentially. The increase in angle shifts during the adsorption was higher for the CS system in comparison to HA, due to the higher charge density of CS. In addition, the liposome adsorption caused a steep increase in angle shift indicating their successful adsorption.
Ellipsometry results showed corresponding results with an increase in the thickness after embedding the liposomes onto the terminal layers.
Conclusions: Collagen I and CS or HA are convenient for multilayer formation and final adsorption of liposomes. Collagen I and CS demonstrated higher thickness and stability during the adsorption process of the liposomes in comparison to HA. Use of labelled liposomes showed stable incorporation into the PEM after changing the pH value to physiological conditions.

P126
STUDIES ON OSTEOGENIC DIFFERENTIATION OF CELLS ON MULTILAYERS LOADED WITH BMP-2
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Background: Layer-by-Layer (LbL) technique permits the formation of nanostructured surface coatings useful for delivery of bioactive molecules, like growth factors (GF). Recombinant human bone morphogenetic protein-2(rhBMP-2) can promote osteogenic differentiation of mesenchymal and other cells and is used in the treatment of non-healing bone fractures. However, bolus injections of BMP-2 are rapidly cleared off and lose their activities upon exposure to blood. Hence, high dosages are needed resulting in inflammation, increased cancer incidence and high costs. Thus, controlled release systems lowering therapeutic concentrations of GF are badly needed in the field of regenerative medicine.
Aim: Loading of BMP-2 to multilayers composed of different GAG was used to control adhesion and osteogenic differentiation of C2C12 myoblasts. Interestingly, the use of oxidized GAG for intrinsic cross- linking to improve multilayer stability and affect GF release.
Methods: Heparin, chondroitin sulfate and their oxidized forms as polyanions were combined with chitosan and collagen I as polycations to form different multilayer coatings. The myoblast cell line C2C12, which can differentiate into osteoblasts was seeded on BMP-2 loaded multilayers. Osteogenic differentiation was studied by activity of alkaline phosphatase (ALP); cell number was measured by BCA and viability by QBlue assay.
Results: BMP-2 loaded multilayers made of heparin provoked the highest ALP activity in C2C12 cells, by diffusive transport, cultured in transwell supports. C2C12 cells cultured on top of multilayers showed that particularly BMP-2 loaded multilayers made of oxidized GAG promoted an osteogenic differentiation of C2C12 cells nearly comparable to the positive control, when 5 µg/mL BMP-2 was added directly to the medium.
Conclusions: Oxidized GAG forming cross-linked mutlilayers are useful as reservoirs for sustained release of BMP-2, which can pave the way for coating implants and scaffolds for repair and regeneration of bone fractures.

P127

EFFECT OF PO2 ON VIABILITY AND STAGING OF BOVINE FOLLICLES CULTURED IN VITRO IN DISHES IN STRIPS OF OVARIAN CORTICAL TISSUE

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Background: Cryopreservation of ovarian tissue followed by thawing, in vitro culture (IVC), fertilization and re-implantation is a regenerative strategy to restore fertility in women with ovarian failure or malignancies. IVC of ovarian strips is limited by difficulties to keep follicles viable and guide their progression. Optimal dissolved oxygen concentration (pO_2) near follicles may favour their viability and maturation.
Aim: To identify IVC conditions inducing optimal pO_2 near follicles, that maintain them viable and promote progression from primordial to secondary stage.
Methods: Ovarian cortical biopsies were harvested from abattoir bovines at 4°C and dissected in 2 h into 1 × 1 × 0.5 mm^3 strips. Ten strips per dish from same ovary were cultured for 9 days in αMEM with 0.1% BSA, 3 mM glutamine, 50 µg/ml ascorbic acid, 1% ITS and 1% pen/strep in conventional (CD) or oxygen- permeable (PD) 5 cm dishes in 5% CO_2/air. Tissue was cultured in 2.5 (LV) or 5 ml (HV) of medium to vary medium height above tissue and resistance to O_2 transport. Fresh and cultured strips at day 3, 6, 9 were fixed for histological analysis and stage grading or labelled with live-dead far red and Hoechst 33342 for viability assessment with confocal microscopy.
Results: An oxygen transport model in an ideal tissue slab at the dish bottom predicts average perifollicular pO_2 increasing in order CDHV<CDLV <PDHV<PDHV. Consistent with predicted pO_2s, ovarian tissue culture in CDLV and PDHV best preserved activation and viability of bovine follicles and promoted progression to secondary stage. Low pO_2 in CDHV caused formation of necrotic core and worse follicle parameters. Too high pO_2 in PDLV undermined follicle viability and quality, possibly being cytotoxic.
Conclusions: An optimal range of perifollicular pO_2 exist ensuring better viability and progression of follicles cultured in ovarian cortical tissue strips.

P128

MATHEMATICAL MODELING AND EXPERIMENTAL PROCEDURES FOR TISSUE ENGINEERING OF BLOOD VESSELS BY ELECTROSPINNING

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Background: Coronary and peripheral vascular bypass graft procedures are performed in millions patients annually in the world. Although the use of autogenous vascular substitutes has had a major impact on advancing the field of reconstructive arterial surgery, these tissue sources may be inadequate or unavailable.
Aim: In this study we would like to develop tissue engineered blood vessel by using mathematical modeling for optimization and experimental procedures for developing scaffold.
Methods: We used mathematical modeling for the electrospinning process, as well as modeling of cell migration, diffusion and growth. The mass transfer, diffusion-reaction process is modeled with finite element continuum and discrete modeling techniques. Docking methodology is simulated with Density Functional Theory DFT which is giving answer on many questions of biomechanics of nanofibers before their creation. Scaffolds from natural polysaccharides like alginate, chitosan, pectin and hyaluronic acid are developed. These scaffolds should mimic the native vascular tissue's extracellular matrix mechanical and chemical properties and therefore molding of these polymers has been done by electrospinning.
Results: Statistical analysis of the fiber diameters (nonparametric Mann-Whitney test) showed no significant difference between 4% native alginate vs. 8% alginate modified with 2.5 mol% tyramine for scaffold.
Conclusions: Mathematical modeling for electrospinning technology is of high importance in the fields of regenerative medicine and tissue engineering, as well as for the enzyme immobilization and drug delivery applications. We intend to further expand our evaluations of the electrospun tyramine-alginate nanofibers for their cytotoxicity, as well as for their mechanical properties with the aim of producing scaffolds for tissue engineering.

P129

A DATAMINING APPROACH FOR ANATOMIC SKULL PROSTHESIS MODELLING OPTIMIZATION

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Background: Currently computational modeling tools, processing algorithms and image segmentation and three-dimensional printing devices help doctors to the process of production of customized human body parts. The anatomic prosthesis modeling by geometrical descriptors obtains solutions for prosthesis design using sets of slices of CT scans as basis to create the reconstructed image of bone curvature. In this case, the study problem is in order to evaluate which are the ideal features to build the respective anatomical geometric model.
Aim: The objective is to search patterns from descriptors' features by Data Mining process (clustering and classification) applied to an CT image database in order to reconstruct the 3D model of a skull prosthesis piece.
Methods: The conceptual model of the process is in order to apply descriptors defined by Bezier Cubic Curves in order to create a testing database whose data consists of specific features extracted from CT images which can be applied to evaluate the measure error value in 3D model. In a preprocessing step of data mining, the calculated errors values were grouped in datasets to proceed to the clustering and classification tasks in WEKA software. After classification, the process found the best parameters whose data have a minor error as possible.
Results: It was found that among a set of features, just a unique variable can influence the result in fitting curvature in order to obtain a low error between the original bone image and fitted Bezier curve.
Conclusions: It was found that Data Mining can have key role in the relationship between descriptors and error for the design of anatomic prosthesis. The geometric features automatically selected in pre- processing to the KDD for filtering the collection of data, permit us to work with a lower amount of data without compromising the results. In this way it is possible to find the parametric curve coordinate without human intervention, which permits the automation of anatomic prosthesis building process.

P130

EFFECT OF NON-UNIFORM CONSTRUCT PERMEABILITY ON MATTER DISTRIBUTION IN RADIAL FLOW PACKED BED BIOREACTORS (RPBBS) FOR BONE TISSUE ENGINEERING (BTE)

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Background: Perfusion of osteogenic cells seeded in porous hollow scaffolds cultured in rPBBs should supply cells with even oxygen and nutrients to ensure uniform tissue maturation of bone substitutes. Operating conditions not matching this requirement cause uneven cell proliferation and ECM deposition, and non-uniform construct permeability as tissue matures. This may affect matter distribution hindering construct maturation.
Aim: To investigate the effect of non-uniform construct permeability on matter distribution in rPBBs for BTE with tracer experiments.
Methods: A rPBB with clear PMMA walls and hollow porous β-TCP scaffolds custom-made by lithography- based ceramic manufacturing were used. In visualization and tracer experiments the rPBB was challenged with a step inlet concentration of trypan blue at flows typical of BTE. Non-uniform construct permeability was simulated by obstructing with wax 25% of the scaffold and positioning the obstructed part at the bottom or the top of the rPBB. Tracer concentration leaving the rPBB was measured on-line spectrophotometrically.
Results: Experiments with patent scaffolds showed that matter is well mixed in the rPBB but for the lag of inlet and outlet sections. Consistent with visualization experiments, low permeability of the scaffold top increased the lag and decreased the time constant of the mixed bioreactor zone. Low permeability of the scaffold bottom trapped tracer in stagnating zones and extended the tailing part of rPBB response. In all cases perfusion occurred at

higher radial fluxes. rPBB response was well described by transport models consisting of pure lag and mixed zone communicating with a stagnating zone.
Conclusions: Non-uniform scaffold permeability causes perfusion at higher radial fluxes and formation of stagnant zones where nutrients are quickly depleted stressing the importance of optimal cell seeding and operation for uniform bone tissue maturation. Study co-funded by MIUR (PRIN 2010/ MIND).

P131
NON-CONTACT MEASUREMENT OF DIELECTRIC PROPERTIES OF BIOLOGICAL TISSUES USING MAGNETIC INDUCTION AT 500 KHZ
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Background: Recently, transcutaneous energy transfer systems have been developed for ventricular assist devices and pacemakers using 100 to 1000 kHz electromagnetic fields. Consequently, the adverse effects of electromagnetic fields on the human body have emerged as a topic of concern. To evaluate these effects, electromagnetic field analysis is performed. When it is performed, the dielectric properties of the human body are required. Dielectric properties measured and described by Gabriel are being widely applied. However, these values may be unreliable between 100 and 1000 kHz because of the contact between the measurement electrodes and the sample.
Aim: Non-contact measurement using magnetic induction is proposed to accurately measure dielectric properties of biological samples between 100 and 1000 kHz.
Methods: A non-contact measurement system with primary and tertiary toroidal coils, and a secondary coil as the measuring case, was been developed. The AC voltage output from the function generator (IWATSU SG-4105) was supplied to the primary coil through an amplifier (NF 4025) and a common mode choke coil (DCF-RF37-BCL). Then, the voltage ratio and phase differences of the primary and tertiary coils were measured using a digital oscilloscope (Agilent 54832D) when the measuring case was filled with pig liver. The lumped parameter elements were used as a secondary coil. The conductivity and relative permittivity of pig liver were obtained by comparing measurement results of the pig liver and lumped parameter elements.
Results: The conductivity and relative permittivity were measured to be 0.142-0.174 S/m and 0-81 at 500 kHz respectively. The corresponding results measured by Gabriel at 500 kHz were 0.148 S/m and 2769.
The relative permittivity obtained at 500 kHz was 3% or less of that reported by Gabriel.
Conclusions: A non-contact measurement system is developed to measure the dielectric properties of biological samples. The relative permittivity obtained at 500 kHz is 3% or less of Gabriel's. The results indicate that the human liver may have lower relative permittivity.

P132
CONTROLLED INFILTRATION OF CELLS INTO ELECTROSPUN SCAFFOLDS FABRICATED FOR APPLICATION IN SMALL DIAMETER VASCULAR GRAFTS
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Background: Owing to the paradoxical nature of electrospinning, it is difficult to produce a nanofibrous structure with large pores, the ideal environment for cell infiltration. The literature shows many attempts to achieve this with varied results. This project proposes a novel twist (alginate-cell printing in multilayers) to traditional sacrificial electrospinning to increase cell infiltration.
Aim: To fabricate a multilayered hybrid polymeric scaffold by electrospinning, characterise it, seed it with appropriate cells using a cell printer, and measure the cell infiltration of the resultant structure.
Methods: PCL-gelatin fiber mats with different concentration ratios were electrospun. Fiber diameter and pore size before and after gelatin leaching were measured and the mats were tested for tensile strength and wettability. 3T3 fibroblasts are printed on an optimised fiber mat with alginate in defined patterns as opposed to direct manual cell seeding (lacking in homogeneity). Multiple layers are stacked according to the native anatomy, incubated and allowed to attach to each other. Cell infiltration depth is then studied by z-axis fluorescence microscopy.
Results: PCL-gelatin produces a wide range of nano- and microfibres (3.5 ± 2.5 µm) as compared to monodisperse fibres in PCL scaffolds (1.8 ± 0.3 µm). It is even possible to fabricate PCL-gelatin mats of thicknesses as low as 10 µm, a clear advantage. Fiber diameters are reduced greatly after 8 hrs of gelatin leaching in acidic water (2.3 ± 1.5 µm) indicating an increase in pore size. Contact angle measurements indicate a drastic increase in hydrophilicity on the addition of gelatin.
Conclusions: The addition of alginate cell printing onto PCL-gelatin electrospun scaffolds is important to protect the cells from shear forces and mechanical stresses during printing and stacking. As both gelatin and alginate slowly dissolve away during cell culture, the cells will be able to infiltrate the multilayered structure to a larger extent and with more ease than before.

Tissue Engineering and Regenerative Medicine

P133
POLY(L-LACTIC ACID) MICROSPHERES INDUCE "IN VIVO" ARTICULAR CARTILAGE REGENERATION IN RABBITS
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Background: Traumatic articular injuries are very common and often affect young people, causing focal lesions. Different treatments are currently applied but most of the time they evolve towards extensive joint destruction (osteoarthritis).
Aim: To prevent the progression of focal lesion towards extensive articular damage through the implant of biodegradable microspheres as mechanical support, along with microfracture of subchondral bone to allow mesenchymal cells migration to the chondral defect, for in vivo regeneration of articular cartilage.
Methods: A 3-mm lesion was carried out in the femoral condyle of rabbits, allowing bleeding from subchondral bone. Defects were filled with poly(L-lactic acid), PLLA, microspheres (5-60 microns) and covered by a PLLA membrane (n = 7); control group received the PLLA membrane but the lesion remained unfilled (n = 4). Three months after surgery samples were histologically evaluated.
Results: Microscopic study revealed that PLLA microspheres induced the formation of a neotissue with a good surface architecture and extensive areas with a chondral matrix with hyaline-like aspect. PLLA microspheres persisted inside and under the neocartilage, but the membrane was observed between neocartilage and subchondral bone. However, control group presented a neotissue with a poor architecture and a fibrous appearance.
Conclusions: PLLA microspheres provide a favorable mechanical support for inducing the differentiation of invading mesenchymal cells into the chondral phenotype, thus achieving articular cartilage regeneration.
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P134

SILK FIBROIN/COLLAGEN FILMS FOR RAT SKIN WOUND REGENERATION

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Background: One of the current interests of tissue engineering problem is the development of biological skin equivalent to promote wound regeneration. Silk fibroin of silkworm Bombyx mori can be applied as a material for the skin equivalent fabrication. The unique properties of silk fibroin expand its application as a substantive material or major component of product or as a cell carrier for cellular transplants.
Aim: Research an effect of silk fibroin films fabricated by casting method on Wistar rat full-thickness skin wound regeneration.
Methods: Two kinds of films with different protein concentration equal to 20 mg/ml were produced by casting method: films from silk fibroin aqueous solution, films from silk fibroin aqueous solution containing 30% collagen by mass. The scanning electron microscopy and atomic force microscopy were used to characterize the surface structure of the films. The tensile strength and elasticity of produced films were measured. The film cytotoxicity was researched by MTT-test on mice fibroblasts 3T3 cell culture. The fabricated films were utilized as wound coatings for Wistar rat full-thickness wound regeneration.
Results: It was shown that micro- and nanorelief presents on film surface. The cytotoxicity experiment revealed that films have no cytotoxicity effect on cells. The obtained films increased Wistar rat full-thickness wound regeneration by an average of 25%. Slice histological analysis evolved structural skin regeneration and no inflammatory.
Conclusions: The derived films are characterized by biocompatibility and optimal surface structure for fibroblasts adhesion and proliferation. Films' application for Wistar rat full-thickness wound regeneration increases its restoration rate, which is confirmed by histological evaluation.

P135

3D POROUS POLYCAPROLACTONE SCAFFOLDS FOR CARTILAGE REGENERATION

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Background: Extrapulmonary airway obstruction, including tracheal stenosis, leads to dyspnoea and can even lead to the death if a correct and timely treatment is not performed. Currently, there is a need to generate artificial tracheas for those patients in whom surgery is not a therapeutic option. The key element responsible for biomechanical properties of the trachea is the hyaline cartilage layer, which is organized in rings throughout the entire organ. For this reason, an ideal substitute for tracheas should incorporate a chondral compatible scaffold.
Aim: To evaluate the utility of a porous PCL scaffold to support cartilage regeneration.
Methods: PCL scaffolds were prepared by a mixed particle leaching/freeze extraction process. Acrylic microspheres (diameter 200 µm) were used as a porogen. Human primary chondrocytes were isolated and cultured in a mix hydrogel consisting in 3% alginate and 1% agarose in chondrocyte differentiation culture medium for up to 6 weeks. Cell differentiation was evaluated by collagen (type I and II) and aggrecan immunofluorescence. Cell morphology was evaluated by fluorescence actin fibbers staining using phycoerythrin labeled phaloidine. To study compatibility of scaffolds with cartilage, chondrocytes were suspended alginate/agarose hydrogels and injected in the scaffolds.
Results: Chondrocytes grown in alginate agarose hydrogels expressed type II collagen as well as aggrecan and non-detectable type I collagen. They grew grouped together forming spheroids of 15-20 cells. They expressed non-polymerized actin contrary to non-differentiated chondrocytes which expressed actin stress fibers. PCL scaffolds showed cell compatibility after 6 weeks culture.
Conclusions: Results presented here enforce the use of PCL scaffolds for cartilage regeneration.

P136

FORCE INDUCED PIEZOELECTRIC EFFECT OF PVDF AND PVDF-TRFE SCAFFOLDS

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Background: Polyvinylidinefluoride (PVDF) and its co-polymer with trifluoroethylene (PVDF-TrFE) are promising biomaterials for supporting nerve regeneration processes because of their proven biocompatibility and piezoelectric properties that could stimulate cell ingrowth due to electrical activity upon mechanical deformation.
Aim: This study reports the piezoelectric effect of electrospun PVDF and PVDF-TrFE scaffolds in response to mechanical loading. An impact test machine was used evaluate the generation of electrical voltage upon application of an impact load.
Methods: Scaffolds were produced via electrospinning from PVDF and PVDF-TrFE with concentrations of 10-20 wt% dissolved in N,N-dimethylformamide and acetone (6:4). In the electrospinning process, a flow rate of 2 ml/h and voltages of 20-30 kV were applied to produce aligned fibers. The electrospinning time of each sample was 2.5 hours. The piezoelectric response of the scaffolds was induced using a custom-made manual impact press machine. Impact forces between 0.4 and 14 N were applied.
Results: Electrospun PVDF and PVDF-TrFE scaffolds with different concentrations exhibited piezoelectric responses in form of voltage by applying impact load. PVDF-TrFE scaffolds showed higher values in the range of 6-30 V as compared to pure PVDF. Here, the mechanically induced electrical impulses measured were between 2.5 and 8 V. Increasing the impact forces did not increase the piezoelectric effect.
Conclusions: The results demonstrate the possibility of producing electrospun PVDF and PVDF-TrFE scaffolds as nerve guidance with piezoelectric response. That can in turn stimulate Schwann cell ingrowth and axonal elongation. Further experiments are being carried out to analyse the piezoelectricity at dynamic conditions using an automatic impact machine. Furthermore, the response of cells on this piezoelectric stimulation will be evaluated in vitro with organotypic cell culture models and in vivo using rat sciatic nerve repair models.

P137

POLY(L-LACTIC ACID) (PLLA) MATS FOR HUMAN AIRWAY MUCOSA REGENERATION

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Background: Tracheal prosthesis represent the only therapeutic alternative for those patients affected of tracheal stenosis for whom surgery is limited because the extension of the defect. One of the disadvantages of tracheal prosthesis is the lack of a mucous layer containing ciliated cells which leads to the accumulation of secretions affecting the pulmonary function of the patients.

Aim: To study if nasal mucosa was a possible source of epithelial stem cells for airway mucosa regeneration and was to evaluate the usefulness of PLLA scaffolds to support airway mucosa growth.
Methods: Mats of PLLA were obtained with a home-made electrospinning equipment. A 10-mL syringe was loaded with PLLA solution. A syringe pump was used to feed the polymer solution at a rate of 4 mL/h. Twenty kilovolts was applied with a high-voltage power supply. The needle being in vertical position and the collector below in horizontal position. Nasal cells were obtained by nasal biopsy while bronchial cells were obtained by bronchoscopy from the same donor. Cells were cultured using ALI culture systems. Cilia activity was evaluated by digital high speed video. Cilia length, morphology and density of goblet cells were estimated by microscopy.
Results: No differences in cilia beat frequency and in the density of goblet cells were observed in nasal cultures compared to bronchial cultures (n = 3). Cultured nasal cells shown longer cilia and generated a thicker epithelium than cultured bronchial cells form the same donor. Nevertheless, greater differences were found between individuals than those related to the origin of the biopsy. PLLA mats showed good adherence properties for human airway epithelial cells
Conclusions: Results suggest the utility of nasal biopsies and PLLA mats for airway epithelium regeneration.

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DOES EXCESS GRAVITY AFFECT CELL DEFORMATION AND ORIENTATION AFTER STIMULATION?
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Background: A biological cell is sensitive to the mechanical stimulation, and shows several responses: deformation, and migration. The response includes passive one and active one. The cell is deformed by the force. The cell deforms, on the other hand, to minimize the intra force. The cell is moved by the force. The cell moves, on the other hand, in response to the force. The muscle tissue might decrease in the micro gravitational field. The previous study, on the other hand, shows that the excess gravitational fields thicken the myotubes in vitro. Control methodology for orientation of cells would be applied to the regenerative medicine.
Aim: The effects of excess gravitational field on orientation and extension of cells have been studied using centrifuge in vitro.
Methods: Two kinds of cells were used in the test: C2C12 (mouse myoblast), and Neuro-2a (mouse neural cell). To apply the continuous mechanical force field for 24 hours to the cells adhered on the glass plate, the plate was set in the tube in a conventional centrifugal machine, which was placed in an incubator (310 K, CO_2 5%). At C2C12, the variation was made on the gravitational environment: 50 G, and 100 G. At Neuro-2a, the variation was made on the direction of the force on the surface of the scaffold: normal, and tangential. The behavior of cells was analyzed at the time lapse images every five minutes for 24 hours after the excess gravitational stimulation. The contour of each cell was traced and approximated to an ellipse to analyze the angle between the longitudinal axis of the cell and the direction of gravity.
Results: The longitudinal axis of C2C12 tends to align to the direction of gravity, and tilt to the perpendicular direction against gravity after stopping of the excess gravitational stimulation. C2C12 tends to proliferate to the direction perpendicular against gravity. The neurite of Neuro-2a extends along the direction of gravity, and tends to extend the direction of the smaller stimulation of gravity.
Conclusions: The excess gravity affects cell deformation and orientation after the stimulation.

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MEASUREMENT OF CONTRACTION OF MYOTUBE ON SCAFFOLD FILM WITH MICRO-MARKERS BY ELECTRIC STIMULATION
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Background: The biological tissue can be made by the cell culture technique in vitro. The tissue should have enough strength for the clinical application in regenerative medicine. Measurement of intra- and inter- cellular forces has been tried by several preparations: the laser technique, the atomic force microscope, and the fluorescence technique.
Aim: The scaffold of the transparent film with micro markers array has been designed to estimate the contractile force of myotube under the electric stimulation in vitro.
Methods: The scaffold consists of a thin film (0.006 mm) of polydimethylsiloxane with arrangement of micro- protrusions (hemisphere shape, 0.004 mm diameter, 0.002 mm height) on the back side. Ten million protrusions were made in the area of 9 mm^2 at equal intervals (0.03 mm) by the photolithography technique. Each protrusion plays a roll of the position marker. The scaffold was exposed to the oxygen gas to be characterized as hydrophilic before the cell culture. C2C12 (mouse myoblast) was seeded on the film at the counter surface to the protrusions at the density of 5000 cells/cm^2. The cells were cultured for 12 days in the medium containing 10% FBS (fetal bovine serum) and 1% penicillin/ streptomycin at 310 K with 5% of CO_2 content. The electric pulses (amplitude of 30 V, 0.06 A; pulse cycle of 1 s; pulse width of 1 ms) were applied between electrodes of platinum wire dipped in the medium.
Results: The micro markers are able to be manufactured on the thin film of polydimethylsiloxane, and observed through the scaffold of the transparent film by the microscope. The myoblasts are able to be cultured on the film to be differentiated into myotubes, which shows contraction synchronized with stimulation of electric pulses. The contractile force of myotube at the electric stimulation estimated by the deformation of the film is 0.01 mN.
Conclusions: The contraction of myotubes is able to be observed through the transparent scaffold film with micro-markers at the microscope.

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EFFECT OF THE CO-APPLICATION OF MATRIDERM AND MESENCHYMAL STEM CELLS ON WOUND HEALING
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Background: Human amnion-derived mesenchymal stem cells (hAMSCs) are a promising tool in regenerative medicine. hAMSCs have anti-inflammatory and immunomodulatory properties and can be obtained in large numbers with low ethical problems, using non-invasive procedures. Intradermal injection of hAMSCs around the wounds resulted in contradictory effects on wound healing. Therefore, alternative application methods are required to improve the healing outcome of mesenchymal stem cells.
Aim: The aim of this study was to evaluate the utility of Matriderm® (a dermal collagen-elastin matrix) as carrier for the topical application of hAMSCs to mice skin wounds.
Methods: Two circular 8 mm punch biopsy full-thickness skin wounds were created on the dorsal side of nude mice and covered with Matriderm®. The Matriderm® was supplied with or without hAMSCs (control) suspended in culture medium. In addition, the effects of hAMSCs were tested under co-application with placental endothelial cells (PLEC). 8 days after surgery, mice were sacrificed and wounds were photographed to evaluate the wound closure. Wound areas were excised, fixed and sectioned up to the maximal wound area to perform H&E staining. Sections of interest were further processed for immunohistochemistry. Analysis of wound closure and vessel quantification was calculated using AxioVision software.
Results: Due to its mechanical properties, Matriderm® enabled easy and durable positioning on the wound. Although hAMSCs did not adhere to Matriderm®, and despite most transplanted cells have vanished, hAMSCs/Matriderm® co-application significantly enhanced wound closure and promoted neovascularization compared to Matriderm®-only and the co-application with PLEC.
Conclusions: The combined administration of Matriderm®/hAMSCs reliable induced wound contraction and shows encouraging results for further clinical application.

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SPHEROID-BASED 3D CULTURE MODEL WITH PC12 CELLS FOR APPLICATION OF NEURONAL STIMULATION ELECTRODES

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Background: When a metal electrode is implanted into the tissue, microglia become activated and migrated to the site of implantation. After that response, the reactive astrocytes encapsulate the implanted electrode. Since the encapsulation response increases impedance, it is hard to stimulate from neuronal region. In addition, the implanted metal electrode increases induced currents so that the tissue damage occurs.
Aim: We propose the technology procedures and concept of development: Spheroid-based 3D culture model with PC12 cells for application of neuronal stimulation electrodes. Compared with the implantable electrodes that mentioned above, the newly developed bio-lead will enable stimulation the neuronal tissues without tissue encapsulation responses.
Methods: Neuronal differentiation were assessed by total neurite length measurement for PC12 cells. Prior to form neuronal-like spheroid structure, we examined using the PC12 cultured in the collagen coated dish and maintained in 1% FBS medium with 200 ng/ml NGF to induce neurite formation for cellular differentiation. To development 3D spheroid structural neuronal tissue with PC12 cells, we used PDMS- based microwells with 400 μm diameters, fabricated using soft-lithography and photo-lithography techniques. This PDMS-based microwells offer substantial advantages for formation and harvesting of 3D micro-tissue.
Results: Upon exposure to NGF, PC12 cells gradually begin to differentiate after 2~3 days. We used immunofluorescence microscopy to investigate the microtubule cytoskeleton protein (MAP-2) during the development of spheroids culture. Also, immunostaining of spheroids for MAP-2 and β3-tubulin to investigate possible neuronal differentiation effects showed that spheroid-based model positively affected growth and neuronal differentiation of PC12 cells.
Conclusions: It appears that spheroid-based 3D culture model with PC12 cells may offer a better technique for future neuronal tissue engineering investigations such as development of neuronal stimulation electrodes.

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MYOBLAST MIGRATES UNDER CONTROLLED WALL SHEAR STRESS FIELD IN VITRO

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Background: Control methodology for orientation of cells would be applied to the regenerative tissue technology. The mechanical stress is one of the interested points in the environment of cells. In many studies, the stress is applied to the scaffold. When fixation between the cell and the scaffold is not enough, the stress is not transmitted to the cell. A flow, on the other hand, can be used to apply a stress field to a specimen. In the previous study, the effect of flow stimulation on cultured cells has been studied in a donut-shaped open channel in vitro.
Aim: An experimental system of the Couette type flow with a rotating disk has been designed to apply the wall shear stress quantitatively on the cell culture at the microscopic observation in vitro.
Methods: The shear stress on the wall is calculated with the estimated Couette type of the velocity profile between parallel disks: the rotating disk and the stationary culture disk. The distance between disks is 0.5 mm. The constant rotational speed (<30 rad/s) produces the shear stress <2 Pa. C2C12 (mouse myoblast cell line) was used in the test. After the cells were incubated in D-MEM (Dulbecco's Modified Eagle Medium) for 24 hours without flow stimulation to adhere to the scaffold of the stationary disk, the cells were exposed to the shear field (310 K, CO 5%). At the time lapse images (every five minutes for 24 hours), the contour of each cell was traced and approximated as the ellipsoid to measure the movement of the center of the cell and the orientation of the major axis of the cell.
Results: Each myoblast migrates independently to every direction includes the counter direction of the flow. The most of myoblasts tend to migrate to the direction of the lower shear stress field. In many myoblasts, the major axes tilt to the perpendicular direction against the flow direction.
Conclusions: Myoblast migrates actively under the controlled stress field in vitro. The designed experimental system of the Couette type flow with the rotating disk is effective to observe the cell migration under the controlled wall shear stress field.