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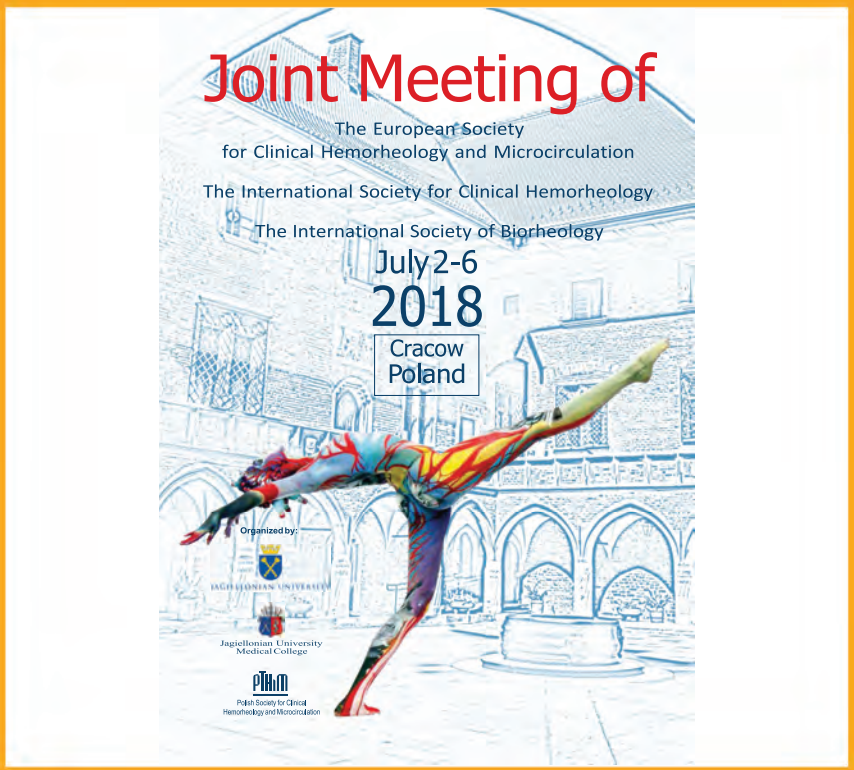
BIORHEOLOGY

THE OFFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF BIORHEOLOGY



Abstracts

Joint Meeting of The European Society for Clinical Hemorheology and Microcirculation, The International Society for Clinical Hemorheology and The International Society of Biorheology
Krakow, Poland
2–6 July 2018

IOS Press

BIORHEOLOGY

Aims and Scope

Biorheology is an international interdisciplinary journal that publishes research on the deformation and flow properties of biological systems or materials. It is the aim of the editors and publishers of *Biorheology* to bring together contributions from those working in various fields of biorheological research from all over the world. A diverse editorial board with broad international representation provides guidance and expertise in wide-ranging applications of rheological methods to biological systems and materials.

The aim of biorheological research is to determine and characterize the dynamics of physiological processes at all levels of organization. Manuscripts should report original theoretical and/or experimental research promoting the scientific and technological advances in a broad field that ranges from the rheology of macromolecules and macromolecular arrays to cell, tissue and organ rheology. In all these areas, the interrelationships of rheological properties of the systems or materials investigated and their structural and functional aspects are stressed.

The scope of papers solicited by *Biorheology* extends to systems at different levels of organization that have never been studied before, or, if studied previously, have either never been analyzed in terms of their rheological properties or have not been studied from the point of view of the rheological matching between their structural and functional properties. This biorheological approach applies in particular to molecular studies where changes of physical properties and conformation are investigated without reference to how the process actually takes place, how the forces generated are matched to the properties of the structures and environment concerned, proper time scales, or what structures or strength of structures are required.

Biorheology invites papers in which such 'molecular biorheological' aspects, whether in animal or plant systems, are examined and discussed. While we emphasize the biorheology of physiological function in organs and systems, the biorheology of disease is of equal interest. Biorheological analyses of pathological processes and their clinical implications are encouraged, including basic clinical research on hemodynamics and hemorheology.

In keeping with the rapidly developing fields of mechanobiology and regenerative medicine, *Biorheology* aims to include studies of the rheological aspects of these fields by focusing on the dynamics of mechanical stress formation and the response of biological materials at the molecular and cellular level resulting from fluid-solid interactions. With increasing focus on new applications of nanotechnology to biological systems, rheological studies of the behavior of biological materials in therapeutic or diagnostic medical devices operating at the micro and nano scales are most welcome.

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Cover figure taken from: Cover page of the program for the Joint Biorheology Meeting, Krakow, Poland.

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Preface

On July 2–6, 2018 it was our great pleasure to organize this joint conference of the three major societies that focus on the rheology of blood, cells and tissues: The European Society for Clinical Hemorheology and Microcirculation (ESCHM), The International Society for Clinical Hemorheology (ISCH) and The International Society of Biorheology (ISB). The venue for this milestone meeting was the Jagiellonian University Conference Center, "Auditorium Maximum," a modern conference and teaching facility in Krakow, Poland. Founded in 1364 the Jagiellonian University is the oldest university in Poland, the second oldest university in Central Europe, and one of the oldest surviving universities in the world. Notable alumni include, among others, mathematician and astronomer Nicolaus Copernicus. Our local host was the Polish Society of Hemorheology and Microcirculation (PTHiM), Chaired by Dr. hab Maria Fornal of the Medical College.

This Conference covered a broad spectrum of topics in bio- and hemo-rheology, from both basic science and clinical investigations points of view. The organizers sought to provide scientific and social parts of the Conference that complemented each other by stressing "the importance of science not only as a system of knowledge but also as a school of criticism, creativity and tolerance." The conference program provided a unique blend of scientific sessions (symposia, free communications and posters) and social activities to support participant interactions and networking. Social activities included an opening reception, a banquet (in the Wieliczka Salt Mine) and a conference tour of the Jagellonian University Museum and Old Town Krakow.

The site of the Conference, the City of Krakow, is one of the most important historical, cultural and tourist centers of Poland and Central Europe. Krakow, with its alluring attractions mixed in the right proportions, has it all to attract millions of tourists a year.

We, the local and society chairs, were pleased to organize this meeting and hope that it serves as a model for future joint meetings of the three principal societies.

Maria Fornal
PTHiM

Jagiellonian University
Medical College, Poland

Jean-Frédéric Brun
ESCHM

French Institute of
Health and Medical
Research, France

Peter Butler
ISB

Penn State University
USA

Sehyun Shin
ISCH

Korea University
Korea

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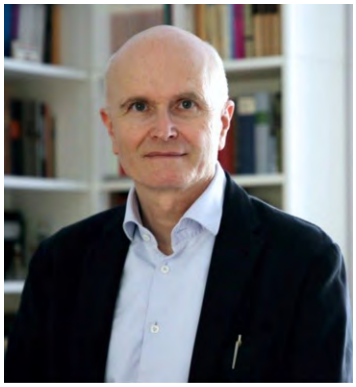
MEDAL RECIPIENTS



Poiseuille Medal

Axel R. Pries
Professor and Dean,
Charité
Universitätsmedizin Berlin

For contributions to hemorheology and remodeling of the microcirculation

Fåhraeus Medal

Carlota Saldanha
Professor Jubilated,
Faculdade de Medicina,
Universidade de Lisboa

For studies of rheology of the red blood cell

ISCH Medal

Brian M. Cooke
Professor of Microbiology,
Monash University

In recognition of outstanding contributions to hemorheology

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Joint Meeting
The European Society for Clinical Hemorheology and Microcirculation
The International Society for Clinical Hemorheology
The International Society of Biorheology
Krakow, Poland
July 2-6, 2018

Scientific Program

*Monday, July 2*nd

12.00–18.00 **Registration**

18.00–19.30 **Opening Ceremony**

20.00–21.30 **Welcome Reception**

*Tuesday, July 3*rd

9.00–10.00 **ESCHM Plenary Lecture (L1)**
Chair: Jean-Frédéric Brun
Lecture: Philippe Connes
Blood rheology: From exercise responses to sickle cell disease pathophysiology

10.00–10.30 **Coffee Break**

10.30–12.00 **Symposia S1–S3/Free Communications O1–O2**

S1: VESSELS AND HEMORHEOLOGY
Chairs: Kalman Toth and Norbert Nemeth

S1-1 Hemorheological parameters and mortality in critically ill patients
Beata Csiszar, Kinga Totsimon, Peter Kenyeres, Kalman Toth, Zsolt Marton

S1-2 Leukocyte antisedimentation rate (LAR) and pituitary adenylate cyclase-activated polypeptid (PACAP) in polytrauma and burn victims. A preliminary study
Csaba Loibl, Csaba Csontos, Livia Szelig, Lajos Bogar, Patricia Kovacs, Andrea Pankaczi, Szilard Rendeki, Martin Rozanovic, Marianna Matancic, Timea Nemeth, Beata Lelesz, Jozsef Nemeth, Attila Miseta, Dora Reglodi, Andrea Tamas

S1-3 Do AB0 and Rh blood groups influence hemorheological parameters in vascular patients?

Katalin Koltai, Dóra Endrei, Gábor Késmárky, Katalin Biró, Zsolt Márton Pécs, Gergely Fehér, Dávid Kovács, Imre Boncz, Antal Tibold, Kálmán Tóth

S1-4 Applications of finite element analysis in clinical hemorheology
Peter Varga, Sz. Javor, G. Jancso, A. Gedei, P Maroti, G. Balazs University of Debrecen Hungary

S1-5 Effects of ischemia-reperfusion and various surgical preconditioning maneuvers on micro-rheological and microcirculatory parameters
Norbert Nemeth, Gabor Varga, Balazs Szabo, Csaba Korei, Bela Turchanyi, Katalin Peto

S1-6 Renal ischemia-reperfusion-induced micro-rheological and microcirculatory alterations and their influenceability by remote organ ischemic preconditioning
Gabor Varga, Kitti Nagy, Noemi Pal, Gabor Nadubinszky, Balazs Szabo, Bence Tanczos, Viktoria Somogyi, Adam Deak, Katalin Peto, Norbert Nemeth

S2: PLATELET ADHESION
Chairs: Shinya Goto and Terumitsu Hasebe

S2-1 Biologically validated model of platelet adhesion under blood flow conditions
Shinya Goto

S2-2 Glycoprotein distribution of surface-induced platelet activation on medical materials by electron microscopy technology
Masamitsu Nakayama, Terumitsu Hasebe, Shunto Maegawa, Kenta Bito, Tomohiro Matsumoto, Tetsuya Suzuki

S2-3 Hemorheological effects of mechanical stress on whole blood of patients with prosthetic heart valve failure
Toru Maruyama, Chiharu Yoshida, Kei Irie, Shohei Moriyama, Taku Yokoyama, Mitsuhiro Fukata, Takeshi Arita, Keita Odashiro, Koichi Akashi

S2-4 Platelet adhesion studies of implantable long-term use Fontan pump biomaterials
Bryan Good, Clare McHugh, Keefe Manning, William Weiss, Chris Siedlecki

S2-5: Development of hemocompatible materials for blood contacting devices by physical and chemical surface modification
Terumitsu Hasebe, Masamitsu Nakayama, Shunto Maegawa, Kenta Bito, Tomihiro Matsumoto, Tetsuya Suzuki

S3: ADVANCES IN HEMORHEOLOGICAL MEASUREMENTS-1
Chairs: Sehyun Shin and Sung Yang

S3-1 Holotomography techniques for imaging 3D label-free imaging of cells and tissues
Yong Keun Park

S3-2 A microfluidic device for simultaneous measurement of blood viscosity, hematocrit, and deformability
Byung Jun Kim, Sung Yang

S3-3 Deformability measurement of continuous soft particles by lattice Boltzmann method and its applications to rheological flow characteristics
Joon-Sang Lee

S3-4 A microfluidic platelet assaying device for function test and antiplatelet response test
Sehyun Shin

O1: CELLULAR RHEOLOGY AND BIOPHYSICS
Chair: Peter Butler

O1-1 Albumin solder covalently bound to a biodegradable polymer membrane: New approach to improve binding strength in laser tissue soldering
Andrea Nies, Bernhard Hiebl

O1-2 Circumferential alignment of smooth muscle cells in micro-tube environment
Yang Jin, Linhong Deng

O1-3 Subhaemolytic mechanical trauma increases RBC aggregation by altering cell electrochemistry
Antony McNamee, Geoff Tansley, Michael Simmonds

O1-4 Subhaemolytic mechanical damage alters erythrocyte behavior in subsequent low-shear flows
Antony McNamee, Geoff Tansley, Michael Simmonds

O1-5 Ultrafast imaging of cell elasticity with optical microelastography
Guy Cloutier, Grasland-Mongrain, Ali Zorgani, Shoma Nakagawa, Simon Bernard, Lia Gomes Paim, Greg FitzHarris, Stefan Catheline

O1-6 The effects of substrate stiffness on HUVEC adhesion with THP-1 cells and molecules associated with adhesion
Yan Wenhua Zhang Tian, Zhang Kang, Qiu Juhui, Wang Guixue

O2: CLINICAL HEMORHEOLOGY
Chair: Jean-Frédéric Brun

O2-1 Pilot clinical study of quantitative ultrasound spectroscopy measurements of erythrocyte aggregation within superficial veins of 50 volunteers
Guy Cloutier, Boris Chayer, Louise Allard, Julian Garcia-Duitama

O2-2 Rapid clinical assessment of the sublingual microcirculation – Visual scoring using microVAS in comparison to standard semi-automated analysis
Joel Sardinha, Christian Lehmann

O2-3 L-cysteine improves blood fluidity that has been impaired by acetaldehyde
Ippo Otoyama, Tatsushi Kimura, Hironobu Hamada, Kiyokazu Sekikawa, Michinori Kamikawa, Teruki Kajiwara, Fumiya Aizawa, Yoshinobu Sato, Haruchi Namba

O2-4 Hemorheological studies in a group of patients with Waldenström's macroglobulinemia
Anna Marcinkowska-Gapińska, Piotr Kowal, Włodzimierz Liebert

O2-5 Adora2b receptor activation mediates flap protection from ischemia/reperfusion injury
Pinar Ulker, Ozlenen Ozkan, Matteo Amoroso, Mutay Aslan, Filiz Ozcan, Ibrahim Bassorgun, Omer Ozkan

O2-6 Purinergic regulation of erythrocyte enzyme activity

Pinar Ulker, Nur Özen, Günel Abdullayeva, Sadi Köksoy, Nazmi Yaraş, Filiz Basrali

13.00–14.00 **Poiseuille Gold Medal Award (L2)**
Ceremony and Lecture
Laudatio: Herbert H Lipowsky
Lecture: Axel R Pries
Microvascular hemodynamics: System properties

14.15–15.45 **Symposia S4-S7/Free Communications O3**

S4: GLYCOCALYX – ITS STRUCTURE AND FUNCTION
Chairs: John Tarbell and Hans Vink

S4-1 Multilayer structures of the endothelial glycocalyx: barrier functions versus red cell hemodynamics
FitzRoy Curry

S4-2 Endothelial Surface Glycocalyx (ESG) components and ultra-structures revealed by Stochastic Optical Reconstruction Microscopy (STORM)
Jie Fan, Yi Sun, Yifan Xia, John Tarbell, Bingmei Fu

S4-3 *In vivo* studies of the enzymatic degradation and structure of the endothelial glycocalyx
Herbert Lipowsky

S4-4 The endothelial glycocalyx and control of microvascular flow and perfused capillary density
Hans Vink

S5: NOVEL MECHANISMS REGULATING BLOOD CELL RHEOLOGY
Chairs: Brian Cooke and Tamas Alexy

S5-1 Interaction of mesenchymal stem cells with platelets: Aid to targeting to tissue or thrombotic risk?
Lozan Sheriff, Asma Alanazi, Lewis Ward, Julie Rayes, Mohammed Alassiri, Steve Watson, Gerard Nash

S5-2 Malaria and babesiosis: Same rheopathobiology but different molecular mechanisms
Brian Cooke

S5-3 Form and function: erythrocyte responses to supra-physiological shears and circulatory support
Michael Simmonds

S5-4 Blood rheology, arterial stiffness, and clinical complications in diabetic patients with and without sickle-cell trait
Sarah Skinner, Mor Diaw, Maïmouna Ndour Mbaye, Brigitte Ranque, Philomène Lopez, Malick Ndour, Fatou Gueye, Demba Diedhiou, Djiby Sow, Saliou Diop, Abdoulaye Samb, Vincent Pialoux, Philippe Connes

S5-5 The importance of hemorheology in the design of continuous flow left ventricular assist devices
Tamas Alexy

S6: ADVANCES IN HEMORHEOLOGICAL MEASUREMENTS-2
Chairs: Sehyun Shin and Sung Yang

S6–1 Optical study of red blood cells interactions in vitro mediated by different plasma components
Alexander Priezzhev, Alexey Semenov, Andrei Lugovtsov, Kisung Lee, Christian Wagner

S6-2 Effect of integrin glycoproteins inhibition on specific adsorption of cells adhesion macromolecules on red blood cell membrane: A microrheologic study
Alexey Semenov, Andrei Lugovtsov, Kisung Lee, Alexei Myravyev, Sehyu Shin, Evgeny Shirshin, Alexander Priezzhev

S6-3 Electrochemical impedance spectroscopy of blood for blood aggregation, sedimentation, and hematocrit
Alexander Zhbanov, Sung Yang

S6-4 Comparison of critical shear stress in RheoScan and adhesion force between RBCs measured in optical tweezer
Sehyun Shin, Hoyoon Lee, Kisung Lee, Alexander Priezzhev

S7: HEMORHEOLOGY AND BLOOD COAGULATION
Chairs: Ursula Windberger and Resia Pretorius

S7-1 Stress sweep tests on whole blood clots
Ursula Windberger

S7-2 The novel discovery of amyloid formation in fibrin(open) and how it affects hemorheology and blood coagulation
Etheresia Pretorius

S7-3 Multiscale mechanics of fibrin networks
Cristina Martinez-Torres

S7-4 Study of blood clotting mechanism by rheological and electrorheological methods
Nadia Antonova, Ivan Ivanov

S7-5 Influence of polymeric nanoparticles on the kinetics of coagulation of conserved blood
Nadya Todorova, Nadia Antonova

S7-6 What are conditions defining blood clot properties in some disorders
Eugene Roitman, Alla Shabalina, Marine Tanashyan, Irina Kolesnikova

O3: ENDOTHELIAL FUNCTION AND SHEAR STRESS
Chairs: Markos Klonizakis and Guixue Wang

O3-1 Arrangement and morphology of endothelial cells under the mechanical microenvironment changes after vascular stent implantation
Tieying Yin, Yuzhen Ren, Ruolin Du, Yuhua Huang, Yazhou Wang, Guixue Wang

O3-2 Blood Flow Regulates Zebrafish CVP Angiogenesis by Inducing ERK5 Signaling
Guixue Wang

O3-3 The role of Id1 in oscillatory shear stress-mediated endothelial lipid uptake
Kang Zhang, Yidan Chen, Guixue Wang

O3-4 Effect of DNA methyltransferase 1 in oscillatory shear stress-induced atherosclerotic vulnerable plaque formation
Lu Huang, Desha Luo, Yuanhang Zhou, Kang Zhang, Juhui Qiu, Guixue Wang

O3-5 The influence of hemodynamic changes on proliferation and adhesion of endothelial progenitor cells
Jinxuan Wang, Li Xiao, Daming Sun, Yiming Zheng, Tieying Yin, Guixue Wang

O3-6 Short term effects of the Mediterranean Diet in human microvascular function – comparison between older and younger healthy, sedentary adults
Yingshan Liu, Marianne Milner, Markos Klonizakis

16.15–17.45 **Symposia S8-S12**

S8: GLYCOCALYX – ITS DIVERSITY
Chair: Herbert Lipowsky

S8-1 Surface glycocalyx mediates tumor cell metastasis
Henry Qazi, Heriberto Moran, Limary Cancel, Mariya Mayer, Lance Munn, John Tarbell

S8-2 Visualization of heparan sulfate proteoglycans in the glycocalyx and the perivascular space of 3-dimensional perfusable microvascular networks in microfluidic devices
Sebastian Beyer, Anna Blocki, Roger D. Kamm

S8-3 Integrin-mediated adhesion is lipid bilayer and glycocalyx dependent
Seoyoung Son, Joseph Moroney, Peter Butler

S8-4 Coupled dynamics of blood flow and endothelial glycocalyx: A large-scale molecular dynamics study
Xi Zhuo Jiang, Kai H. Luo, Yiannis Ventikos

S9: MOLECULAR AND MECHANICAL MARKERS OF VARIOUS PATHOLOGIES
Chair: Małgorzata Lekka

S9-1 Early stage of essential hypertension monitoring
Kvetoslava Burda, Magdalena Kaczmarska, Maria Fornal, Franz Messerli, Jozef Korecki, Tomasz Grodzicki

S9-2 Label-free methods in diagnostics and prognostics of malignant melanoma
Tomasz Kobiela

S9-3 Advanced vibrational imaging techniques to aid clinical research
Tomasz P. Wrobel, Paulina Koziol, Natalia Piergies, Ewa Pieta, Czeslawa Paluszkiewicz, Maria Fornal, Tomasz Grodzicki, Wojciech Kwiatek

S9-4 Effect of dietary carotenoids on erythrocytes from diabetic patients: A spectroscopic study

Joanna Fiedor, Mateusz Przetocki, Grzegorz Gajos, Józef Korecki, Kvetoslav Burda

S10: MiDAS MICROCIRCULATION MEETING (3M)
Chairs: Christian Lehmann and Vladimir Cerny

S10-1 Dynamic Contrast Enhanced Ultrasound (CEUS) of tissue transplants
Ernst Michael Jung, Sebastian Geis, Andreas Kehrer, Philipp Edmund Lamby, Lukas Prantl

S10-2 Assessment of glycocalyx
Vladimir Cerny

S10-3 Automated vs. visual video analyses – where is the future?
Christian Lehmann

S10-4 Is sodium a link between endothelial glycocalyx and microcirculation?
David Astapenko, Vladimir Cerny

S11: BEYOND RED CELL STIFFNESS
Chairs: Jean-Frédéric Brun and Carlota Saldanha

S11-1 RBC deformability: An exquisite homeostasis
Jean-Frédéric Brun, Emmanuelle Varlet-Marie

S11-2 Eryptosis or the death of a rigidified erythrocyte
Etheresia Pretorius

S11-3 Erythrocyte deformability under nitric oxide Influence
Carlota Saldanha, Ana Silva-Herdade

S11-4 The sickle cell: Far more than a rigid erythrocyte
Philippe Connes, Elie Nader, Nicolas Guillot, Romain Fort, Berenike Möckesch, Nathalie Lemonne, Sophie Antoine-Jonville, Céline Renoux, Philippe Joly, Vincent Pialoux, Marie-Dominique Hardy-Dessources, Marc Romana

S11-5 Signaling pathways in regulation of RBC microrheological properties by catecholamines
Irina Tikhomirova, Alexei Myravyov, Elena Petrochenko

S11-6 Complete dynamics of erythrocytes in shear flow: The story behind the term of deformability
Simon Mendez, Luca Lanotte, Johannes Mauer, Franck Nicoud, Gerhard Gompper, Dmitry Fedosov, Manouk Abkarian

S12: MACRO AND MICRO HEMORHEOLOGY *IN VITRO* AND *IN VIVO*
Chairs: Michael Simmonds and Jon Detterich

S12-1 The "tipping point" of mechanical stress on erythrocyte biology
Michael Simmonds

S12-2 Testing the sensitivity of red cell fragmentation and deformability measurements for shear-mediated mechanical damage
Özlem Yalcin, Ali Cenk Aksu, Elif Ugurel, Selcuk Surucu

S12-3 Discussion about high shear stress induced erythrocyte's damage and lysis – Interpretation of hemolysis in cardiovascular devices based on our visualized erythrocytes' behaviors
Nobuo Watanabe, Takahiro Shimada, Nao Ikeda, Kousuke Igarashi

S12-4 Mechanical sensitivity of blood in sickle patients on chronic blood transfusion – understanding erythrocyte exposure to chronic physiologic shear vs. chronic supra-physiologic but sub-hemolytic shear stress
Jon Detterich, Silvie Siriany, Derek Ponce, Michael Simmonds

S12-5 Drag-reducing polymer effects on macro- and microcirculation
Marina Kameneva

Wednesday, July 4

9.00–10.00 **ISB Plenary Lecture (L3)**
Chair: Peter Butler
Lecture: Frank J.Gijsen
Biomechanics and atherosclerotic plaques progression

10.30–12.00 **Symposia S13-S15/Free Communications O4-O5**

S13: MICROCIRCULATION OF INNER ORGANS
Chairs: Ernst Michael Jung and Pamela Zengel

S13-1 Critical analysis of CEUS examinations of the liver in an interdisciplinary ultrasound department
Franz Josef Putz, Anna Erlmeier, Niklas Verloh, Bernhard Banas, Christian Stroszczynski, Ernst Michael Jung

S13-2 VTIQ and VTQ in combination with B-mode and color Doppler ultrasound improve classification of salivary gland tumors, especially for inexperienced physician
Pamela Zengel, Florian Notter, Dirk Andre Clevert

S13-3 CEUS perfusion imaging after ablation treatment in patients with prostate cancer: First results
Isabel Wiesinger, Lukas Beyer, Philipp Wiggermann, Christian Stroszczynski, Ernst Michael Jung

S13-4 Contrast-enhanced ultrasound (CEUS) and gallbladder diseases – a retrospective monocenter analysis of imaging findings with histopathological correlation
G. Negrão de Figueiredo, K. Mueller-Peltzer, P. Zengel, E. Gresser, J. Rübenthaler, D.A. Clevert, München

S13-6 New horizons for kidney imaging: Dynamic microvascularization in contrast-enhanced ultrasound (CEUS)
Franz Josef Putz, Anna Erlmeier, Miriam Banas, Bernhard Banas, Ernst Michael Jung

S14: CELL MECHANICS AND CELL MECHANOBIOLOGY - 1
Chairs: Taiji Adachi and Yukiko Matsunaga

S14-1 Effect of physical environment on cell migration using microchannel device
Toshiro Ohashi, Mazlee Bin Mazalan, Ma Ming, Jennifer H. Shin

S14-2 Protein kinase Cα translocation in endothelial cells in response to mechanical stimulus
Susumu Kudo, Toshihiro Sera, Masataka Arai

S14-3 Hydrostatic pressure-induced DNA breaks in chondrocytes and its relationship with chromatin architecture
Koichiro Maki, Katsuko Furukawa, Takashi Ushida

S14-4 In situ, fluorescence lifetime-based measurements of cell membrane micromechanics
Seoyoung Son, Hari Muddana, Changjin Huang, Sulin Zhang, Peter Butler

S15: HEMODYNAMIC FUNCTIONALITY OF RED BLOOD CELLS IN BLOOD MICROCIRCULATION: EXPERIMENTS AND MODELING
Chairs: Saul Yedgar and Ming Dao

S15-1 Biomechanics of red cell diseases
Ming Dao

S15-2 Microvascular blood flow peculiarities in cancer
Irina Tikhomirova, Yulia Malysheva, Nikolay Kislov, Mihail Ryabov

S15-3 Shape and dynamics of red blood cells in microvessels
Johannes Mauer, Felix Reichel, Jochen Guck, Gerhard Gompper, Dmitry Fedosov

S15-4 Hemodynamic functionality of transfused red blood cells in the microcirculation of blood recipients
Gregory Barshtein, Axel Pries, Neta Goldschmidt, Orly Zelig, Dan Arbell, Saul Yedgar

S15-5 Red blood cell aggregate flow characteristics in bifurcating microchannels
Efstathios Kaliviotis, Joseph Sherwood, Stavroula Balabani

O4: RED BLOOD CELL DEFORMABILITY
Chairs: Edgar O'Rear and Philippe Connes

O4-1 Beta-estradiol and ethinylestradiol enhance RBC deformability dependent on their blood concentration
Paulo Farber, Teresa Freitas, Carlota Saldanha, Ana Silva-Herdade

O4-2 Dual mechanical characterization of red blood cells: Role of surface area, internal viscosity and membrane rigidity
Céline Renoux, Magali Faivre, Amel Bessaa, Philippe Joly, Philippe Connes

O4-3 Proteomic analysis of the role of adenylyl cyclase-cAMP pathway in red blood cell mechanical response
Özlem Yalcin, Elif Ugurel

O4-4 The oxygen scan: continuous measurement of red blood cell deformability with oxygen gradient ektacytometry to monitor disease severity and treatment effect in sickle cell disease

Minke Rab, Brigitte van Oirschot, Tesy Merkx, Annet van Wesel, Sisto Hendriks, Jan de Zoeten, Osheiza Abdulmalik, Martin Safo, Birgitta Versluijs, Roger Schutgens, Gerard Pasterkamp, Eduard van Beers, Richard van Wijk

O4-5 Nitric oxide regulates human erythrocyte deformability through adjusting band phosphorylation status in hypoxia
Yajin Zhao, Xiang Wang

O4-6 Hypoxia: The best stimulator that increases shear-induced response of red blood cells
Elif Ugurel, Ali Cenk Aksu, Senol Piskin, Özlem Yalcin

O5: FLOW VISUALIZATION AND MODELING
Chairs: Sung Yang and Efstathios Kaliviotis

O5-1 Velocity and erythrocyte aggregation characteristics for surface tension-driven flow of blood in rectangular microfluidic channels
Dimitris Pasias, Efstathios Kaliviotis

O5-2 A new approach of blood viscosity: Hemodynamic viscosity
Tilly Alexandre

O5-3 Evaluation and comparison of haemodynamic parameters of vascular end-to side anastomoses
Balazs Gasz, Peter Varga, Peter Maroti, Gabor Jancso

O5-4 Similarities in erythrocyte senescence and microfluidic high shear environment
Damage James Buerck, Dimitrios Papavassiliou, Trevor Snyder, David Schmidtke, Edgar O'Rear

O5-5 Investigation of bright collapsing ring by Lattice Boltzmann method
Young Woo Kim, Chan Soo Min, Joon Sang Lee

13.00–14.00 **ISCH Medal Award (L4)**
Ceremony and Lecture
Laudatio: Kalman Toth
Lecture: Brian M. Cooke
The rheopathobiology of malaria and babesiosis

14.15–15.45 **Symposia S16–S18/Free Communications O6**

S16: SPECIAL SYMPOSIUM TO CELEBRATE THE CENTENNIAL OF DISTINGUISHED PROFESSOR YUAN-CHENG B. FUNG (1)
Chairs: Linhong Deng and Li Yang

S16-1 Morphogenesis and mechanobiology of airway smooth muscle cells on 3D tubular micropatterns as mechanism of bronchial airway development
Linhong Deng, Yang Jin, Mingzhi Luo, Lei Liu, Jingjing Li

S16-2 Glycosylation is a strong molecular determinant of MUC5AC rheology in airway mucus at both single protein and bulk solution levels
Lei Liu, Mingzhi Luo, Yan Pan, Jingjing Li, Linhong

S16-3 Dynamics of neutrophil transmigration mediated by beta-2 integrin via P- and E-selectins
Yan Zhang, Mian Long

S16-5 Influence of different rhythms sound wave to serotonin concentration in rats hippocampus
Yang Ren, Zhidan Deng

S17: RHEOLOGY AND MICROCIRCULATION
Chairs: Lucas Prantl and Gerhard Pindur

S17-1 Longitudinal analysis of thrombin generation biomarkers in venous thromboembolism
Gerhard Pindur, Aida Beye, Bernhard Stephan, Harald Helling

S17-2 Comparison of PIRADS 3 lesions with histopathological findings after MRI-ultrasound fusion targeted biopsy of the prostate in a real-world setting
Boris Schlenker, Maria Apfelbeck, Christian G. Stief, Dirk-Andre Clevert

S17-3 Does acoustic radiation force Elastography help to improve the diagnostic value of ultrasound in the preoperative characterization of tumors of the parotid gland?
Pamela Zengel, Florian Notter, Dirk Andre Clevert

S17-4 Technologies for adipose stem cell isolation
L. Prantl, V. Brebant, S. Klein, A. Anker, C Strauss, O. Felthaus

S17-5 Blood rheology in breast and gynecologic cancer patients at primary diagnosis and stage of cancer progression
O. Schelkunov, P. Tsikouras, R. Csorba, W. Rath, G-F. von Tempelhoff

S17-6 First experiences with a clinical work-flow integrated CAM Assay in Patients with oral squamous cell carcinoma
P. Kauffmann, M. Troeltzsch, P. Brockmeyer, H. Bohnenberger, P. Stroebel, M. Manzke, R. Cordesmeyer, H. Schliephake, L. Prantl, T. Aung

S18: NANOSTRUCTURES IN DISEASE AND HEALTH
Chairs: Květoslava Burda and Marek Cyrklaff

S18-1 Malaria parasites, host-erythrocytes and blood circulation
Marek Cyrklaff

S18-2 Polyhedrocytes in type 2 diabetes
Grzegorz Gajos, Aleksander Siniarski, Joanna Natorska, Michał Ząbczyk, Jakub Siudut, Aneta Undas

S18-3 Differentiation between various melanomas based on biophysical characterization of their properties
Justyna Bobrowska, Joanna Pabijan, Kamil Awsiuk, Jakub Rysz, Andrzej Budkowski, Małgorzata Lekka

S18-4 Endothelial nanomechanics in vascular diseases – an ex vivo AFM nanoindentation study
Marta Targosz-Korecka, Magdalena Jaglarz, Katarzyna Małek-Ziętek, Stefan Chłopicki, Marek Szymoński

O6: RED BLOOD CELL AGGREGATION
Chairs: Dong-Guk Paeng and Norbert Nemeth

O6-1 Alterations in RBC aggregation during incubation in glucose solution
Alicja Szołna-Chodór, Paulina Grychtal, Bronisław Grzegorzewski

O6-2 Numerical study of red blood cell aggregation kinetics under sinusoidal pulsatile flow
Cheong-Ah Lee, Soohong Min, Minho Lee, Dong-Guk Paeng

O6-3 Structure and stability of red blood cell aggregates in model flows
Thomas Podgorski, François Yaya, Gwennou Coupier, Daniel Flormann, Christian Wagner

O6-4 Covalent immobilization of biomolecules on stent materials through mussel adhesive protein coating to promote cell adhesion
Yi Wang, Hualin Lan, Tieying Yin, Yazhou Wang, Guixue Wang

O6-5 The changes of vascular mechanical properties of porcine coronary artery after stent implantation
Yinping Zhao, Lili Tan, Xiaojuan Zhang, Juhui Qiu, Guixue Wang

*Thursday, July 5*th

9.00–10.00 **ISCH Plenary Lecture (L5)**
Chair: Gerard Nash
Lecture: Sehyun Shin
Microfluidic platelet function assays

10.30–12.00 **Symposia S19-S23**

S19: INTERACTION OF BLOOD CELLS/TISSUE ENGINEERING
Chairs: Friedrich Jung and Anna Blocki

S19-1 Long-term prognosis of coronary microvascular dysfunction
Remzi Anadol, Tommaso Gori

S19-2 AD-MSCs change their morphology and secretion profile as a response to changes in substrates' elastic properties in combination with inflammatory stimuli
M. Papagrigorakes, N. Chirico, A. Blocki, A. Neffe, F. Jung, N. Ma, A. Lendlein

S19-3 Thrombogenicity testing of polymers: Round-robin study to assess inter-center variability
Steffen Braune, Claudia Sperling, Manfred F. Maitz, Ulrich Steinseifer, Johanna Clauser, Bernhard Hiebl, Stefanie Krajewski, Hans P. Wendel, Friedrich Jung

S19-4 The controversial origin of pericytes – implications for cell-based therapies
Anna Blocki, Sebastian Beyer, Friedrich Jung, Michael Raghunath

S19-5 A facile way to achieve biomimetic laminin networks on substrates
Thanga Bhuvanesh, Rainhard Machatschek, Burkhard Schulz, Yan Nie, Nan Ma, Andreas Lendlein

S19-6 Medical compression stockings reduce hypertension of nailfold capillaries at the toe of patients with chronic venous insufficiency

Michael Jünger, Anja Oelert, Manuela Kittel, Hermann Haase, Martin Hahn

S20: FLOW VISUALIZATION OF CARDIOVASCULAR DEVICES
Chairs: Keefe Manning and Ajit Yoganathan

S20-1 Visualization of cardiac flows: *In vitro*, *in vivo*, and *in silico* studies
Immanuel David Madukauwa-David, Vrishank Raghav, Prem A. Midha, Vahid Sadri, Phillip Trusty, Zhenglun Wei, Ajit Yoganathan

S20-3 Leveraging fluid dynamic measurements to improve cardiac device design
Keefe Manning

S20-4 Hemodynamics assessment of new transcatheter bi-caval valves in the interventional treatment of tricuspid regurgitation
Munirah Binte Ismail, Foad Kabinejadian, Yen Ngoc Nguyen, Hwa Liang Leo

S21: MACRO AND MICRORHEOLOGICAL BLOOD CHARACTERISTICS UNDER PHYSIOLOGICAL AND PATHOLOGICAL CONDITIONS
Chairs: Nadia Antonova and Eugene V. Roitman

S21-1 Analysis of the cutaneous blood flow responses and microvascular tone regulation in patients with type 2 diabetes mellitus. Relationship to rheological properties of blood
Nadia Antonova, Vasilka Paskova, Irena Velcheva, Nino Chaushev, Sergey Podtaev, Kirill Tsiberkin

S21-2 Relationship between rheological properties of blood and leukocyte adhesion under flow conditions in patients with type 2 diabetes mellitus
Anika Aleksandrova, Nadia Antonova, Alexei Muravyov, Ekaterina Uzikova

S21-3 Hemorheological disturbances as the thrombosis-developing factor
Eugene Roitman, Alla Shabalina, Marine Tanashyan, Irina Kolesnikova

S21-5 Local carotid stiffness in patients with cerebral small vessel disease. Relation to blood viscosity
Irena Velcheva, Nadia Antonova, Tsocho Kmetski, Galina Tsonevska, Anika Alexandrova

S22: THE GLYCOCALYX – ITS ROLE IN DISEASE
Chairs: John Tarbell and Hans Vink

S22-1 Role of the glycocalyx in atheroprotective vs. atheropermissive endothelium function
Eno Ebong, Ian Harding, Solomon Mensah, Ming Cheng, Ronodeep Mitra

S22-2 Loss of the retinal endothelial glycocalyx in diabetes
Norman R. Harris, Wendy Leskova, Haley Peace, Patsy R. Carter, Randa Eshaq

S22-3 Endothelial glycocalyx restoration by growth factors in diabetic kidney disease
Karen Onions, Sara Desideri, Nicola Buckner, Monica Gamez, Gavin Welsh, Andrew Salmon, Simon Satchell, Rebecca Foster

S22-4 Modification of renal macrophage signalling via MCP-1 inhibition reduces albuminuria in diabetic nephropathy

Bernard van den Berg, Margien Boels, Angela Koudijs,Cristina Avramut, Wendy Sol, Annemarie van Oeveren-Rietdijk, Hetty de Boer, Cees van Kooten, Dirk Eulberg, Johan Van der Vlag, Daphne IJpelaar, Ton Rabelink

S23: SPECIAL SYMPOSIUM TO CELEBRATE THE CENTENNIAL OF DISTINGUISHED PROFESSOR YUAN-CHENG B. FUNG (2)
Chairs: Linhong Deng and Li Yang

S23-1 Investigation on energy characteristic of red blood cell deformability: A quantitative analysis of extending and retracting curves based on Atomic Force Microscopy
Dong Chen, Xiang Wang

S23-3 Nitric oxide regulates human erythrocyte deformability through regulating band 3 phosphorylation status in hypoxia
Yajin Zhao, Xiang Wang

S23-4 Development history, progress and future prospects of biorheology and biomechanics in Chongqing University
Wang Guixue

S23-5 Zebrafish caudal vein formation is flow shear stress dependent
Lin Wen

13.00–14.00 **Fahraeus Gold Medal Award (L6)**
Ceremony and Lecture
Laudatio: Nadia Antonova
Lecture: Carlota Saldanha
Multifunctional life of the erythrocyte

14.15–15.45 **Symposia S24-S26/Free Communications O7-O8**

S24: CLINICAL STUDIES IN HEMORHEOLOGY
Chairs: Byoung K. Lee and KyuChang Won

S24-1 The role of hemorheologic changes in diabetic microvascular complications
Jun Sung Moon, Kyu Chang

S24-2 RBC abnormalities presented with clinical diagnostic variables in sepsis
Choon Hak Lim, Jung Min Youn, Eun Gi Ko

S24-3 Decrease myocardial perfusion associated with hemorheologic parameters in patients with type 2 Diabetes
Byoung Kwon Lee, Minhee Cho, Sehyun Shin

S24-4 Erythrocyte aggregation and deformability as factors determining capillary blood flow in patients with arterial hypertension
Andrei Lugovtsov, Alexey Semenov, Yuri Gurfinkel, Petr Ermolinskiy, Anastasiya Maslyanitsina, Nikita Povalyaev, Larisa Dyachuk, Elena Pavlikova, Alexander Priezzhev

S25: CLINICAL MICROCIRCULATION
Chairs: Dirk Andre Clevert and Isabel Wiesinger

S25-1 Postoperative control of vascularized lymph node transfer (VLNT) for the treatment of extremity lymphedema: Ultrasound guided lymph node monitoring using contrast enhanced ultrasound (CEUS)
T. Aung, C. Taeger, S. Geis, A. Kehrer, L. Prantl, E.M. Jung

S25-2 The Use of Indocyanine green (ICG) imaging technique in the groin lymphocele microsurgical resection
M. Ranieri, C.D. Taeger, S. Geis, S. Klein, P. Lamby, D. Schiltz, K. Pfister, L. Prantl, V. Hoesl, T. Aung

S25-3 Significance of high-resolution Color-Duplex-Ultrasound (CDU) designing adipocutaneous, fasciocutaneous and chimeric perforator flaps
A. Kehrer, S. Geis, C. Taeger, N. Platz Batista da Silva, E.M. Jung, L. Prantl, V. Mandlik

S25-4 Influence of systemic vasopressor drugs and fluid administration on microcirculation in free tissue transfer
A. M. Anker, L. Prantl, C. Strauss, V. Brébant, S. M. Klein

S25-5 ICG-fluorescence-angiography– a new indication in revascularized digits and toes
C. Strauss, A. Anker, L. Prantl, N. Heine, C. Wenzel, S. Geis, T. Aung, V. Brébant

S25-6 ICG-fluorescence-angiography in revascularized digits – first results of a standardized clinical study
C. Strauss, A. Anker, V. Brébant, L. Prantl, D. Schiltz, R. Kemper, S. Geis, T. Aung Regensburg, Germany

S26: RED BLOOD CELL NITRIC OXIDE/RHEOLOGY
Chairs: Michael Simmonds and Philippe Connes

S26-1 Nitric oxide synthase activity at various levels and durations of shear stress
Michael Simmonds

S26-2 Erythrocyte nitric oxide dependent of acetylcholinesterase receptor
Carlota Saldanha, Ana Silva-Herdade

S26-3 Hydroxyurea therapy modulates sickle cell anemia red blood cell physiology by acting as a nitric oxide donor: Impact on RBC deformability, oxidative stress and nitric oxide synthase activity
Elie Nader, Marijke Grau, Romain Fort, Nicolas Guillot, Cyril Martin, Giovanna Cannas, Solène Poutrel, Arnaud Hot, Alexandra Gauthier, Wilhelm Bloch, Marc Romana, Philippe Connes

S26-4 The multifaceted role of nitrite and the epigenetic nitric oxide donor, RRx-001 on erythrocyte deformability
Selma Cırrık, Özlem Yalcin

O7: DISEASE AND HEMORHEOLOGY
Chairs: Gerard Nash and Sajad Ahmadizad

O7-1 Do changes in bone marrow pressure contribute to the egress of cells (RBC, reticul.) from bone marrow?
Zbigniew Dąbrowski, Anna Marchewka, Aneta Teleghów, Maria Fornal

O7-2 Platelet-derived extracellular vesicles promote the adhesion of flowing neutrophils to endothelial cells
Sahithi Kuravi, Paul Harrison, G.Ed Rainger, Gerard Nash

O7-3 Morphological and metabolic abnormalities of erythrocytes as risk factors for Alzheimer's Disease
Francesco Misiti, Marco Girasole, Simone Dinarelli

O7-4 Effects of two different high intensity interval training protocols on hemorheological variables in hypertensive patients
Sajad Ahmadizad, Mohammad Soltani, Neda Aghaei Bahmanbeglou

O7-5 Sedentarity status as a regulator of the optimal hematocrit: Involvement of red cell deformability?
Jean-Frederic Brun, Emmanuelle Varlet-Marie, Bénédicte Marion, Céline Roques, Marlène Richou, Eric Raynaud de Mauverger

O7-6 The effects of n-6 polyunsaturated free fatty acids dietary intake on hemorheology and endothelium–dependent microvascular function
Ines Drenjančević

O8: BIORHEOLOGY AND BIOTECHNOLOGY-1
Chair: Guixue Wang

O8-1 Fabrication of gradient nanofibrous scaffold for interface tissue engineering
Li Yang, Peixing Chen, Yu Zhang

O8-2 Tanshinone can inhibit inflammation and angiogenesis in several chondrocytic cells
Li Yang, Yu Zhang, Peixing Chen

O8-3 The preliminary research of mechanical compress damage on neurons induced by hematoma
Wei Wang, Yin Yin, Jun Wang, Tieying Yin, Yazhou Wang, Guixue Wang

O8-4 Hemodynamic analysis of cerebral aneurysms: Suggestions for surgical options
Shicheng He

*Friday, July 6*th

9.00–10.00 **Plenary Lectures in Tribute to Prof. Oguz Baskurt (L7)**
Chair: Jean-Frédéric Brun

Özlem Yalçın
Blood rheology as a determinant of blood flow: Physiological and clinical aspects
Jon Detterich
Red blood cell rheology and nitric oxide production: A scientist on the forefront

10.30–12.00 **Symposia S27-S29/Free Communications O9**

S27: CELL MECHANICS AND CELL MECHANOBIOLOGY – 2

Chairs: Toshiro Ohashi and Susumu Kudo

S27-1 Effect of local tensile stress field on bone matrix and cell alignment: An in vitro study
Taiji Adachi, Kei-ichi Ishikawa, Junko Sunaga, and Yoshitaka Kameo

S27-2 Blood vessel on a chip - 3D vs. 2D
Yukiko Matsunaga

S27-3 Mechanotargeting of nanoparticles to atherogenic endothelium
Pouria Fattahi, Sulin Zhang, Justin Brown, Yin-Ting Yeh, Peter Butler

S27-4 The roles of vessel pulsation and dilation in clearing extracellular waste from the brain
Ravi Kedarasetti, Bruce Gluckman, Patrick Drew, Francesco Costanzo

S28: RHEOLOGY AND MICROSTRUCTURE OF CELLULAR BLOOD FLOW

Chairs: Masako Sugihara-Seki and Ken-ichi Tsubota

S28-1 Effect of internal viscosity on suspension rheology of red blood cells
Naoki Takeishi, Marco Rosti, Yohsuke Imai, Shigeo Wada, Luca Brandt

S28-2 Hemolytic behavior of human red blood cells caused by osmotic pressure difference – Visualization of hemoglobin behavior by use of light absorption characteristics
Ryoko Otomo, Akihito Morita, Kiyoshi Bando

S28-3 Effects of red blood cells on blood flow in micro vessel network: *In vitro* experiment and computer simulation
Ken-ichi Tsubota, Yuya Kodama, Ryoma Kanai

S28-4 Capillary flow imaging with genetically-engineered red blood cells in the living animal brain
Yuika Kurihara, Takuma Sugashi, Kazuto Masamoto

S28-5 Fluid dynamical study of preferential distributions of blood cell components in microchannel flows
Masako Sugihara-Seki, Nozomi Takinouchi, Tenki Onozawa, Junji Seki

S29: ROLE OF GASOTRANSMITTERS (NO, CO AND H_2S) IN BLOOD CELL FUNCTIONS AND THE MOLECULAR MECHANISMS OF THEIR MICRORHEOLOGY ALTERATIONS

Chairs: Carlota Saldanha and Eugene Roitman

S29-1 Leukocytes as a link between inflammation and erythrocyte nitric oxide
Ana Silva-Herdade, Carlota Saldanha

S29-2 Contribution of fibrinogen to erythrocyte scavenger nitric oxide
Carlota Saldanha

S29-3 Role of nitrogen oxide and hydrogen sulfide as signaling molecules in the change of red blood cell microrheology in patients with type 2 diabetes mellitus
Svetlana Bulaeva, Alexei Muravyov, Irina Tikhomirova, Pavel Avdonin

S29-4 Change of microrheological characteristics of erythrocytes under the influence of donors of gasotransmitters NO and H S: *In vitro* study

Yulia Malysheva, Alexei Muravyov

O9: BIORHEOLOGY AND BIOTECHNOLOGY-2
Chair: Jinxuan Wang

O9-1 Proteomic analysis of ApoE-/- mice with disturbed flow model
Li Tianhan, Wang Guixue

O9-2 Effects of suspension state on the biological behavior of breast cancer cells
Yonggang Lv, Xiaomei Zhang, Ying Zhang, Ya Wang

O9-3 Preliminary study of endothelial cell tight junction protein in response to different mechanical stimuli
Yazhou Wang, Desha Luo, Tieying Yin, Guixue Wang

O9-4 PI3K-nos2b signaling is crucial for simulated microgravity-mediated angiogenesis in zebrafish CVP network
Daoxi Lei, Guixue Wang

O9-5 Ferric iron, lipopolysaccharide and lipoteichoic acids can induce anomalous fibrin amyloid formation: An assessment with novel Amytracker™ stains and thioflavin T
Martin Page, Douglas Kell, Etheresia Pretorius

13.00–14.30 **Symposia S30-S32**

S30: **FROM RHEOLOGY TO MICROCIRCULATION: NEW INSIGHTS**
Chairs: Gregorio Caimi and Antonio Colantuoni

S30-1 Red blood cell rheology under different pathological conditions
Patrizia Caprari, Carlotta Bozzi, Sara Massimi, Loretta Diana

S30-2 Role of hemorheological alterations in skin ulcers
Rosalia Lo Presti, Patrizia Caprari, Gregorio Caimi

S30-3 Hemorheology in kidney disease
Francesco Fontana

S30-4 Rat pial microvascular changes during brain hypoperfusion and reperfusion injury: Role of antioxidant substances
Martina Di Maro, Martina Chiurazzi, Dominga Lapi, Teresa Mastantuono, Laura Battiloro, Gilda Nasti, Antonio Colantuoni

S30-5 Bridging the gap from basic microcirculation to the clinical world
Romeo Martini, Antonio Colantuoni

S31: CARDIOVASCULAR BIOMECHANICS FROM CELLS TO ORGANS
Chairs: Noriyuki Kataoka and Ryoko Otomo

S31-1 Biorheology of bile
Minh Nguyen Ngoc, Hiromichi Obara, Kenji Shimokasa, Junfang Zhu

S31-2 Electrical impedance spectroscopic technique for cancerous cell sensing by considering the extracellular fluid around cells

Daisuke Kawashima, Songshi Li, Michiko Sugawara, Hiromichi Obara, Masahiro Takei

S31-3 Matrix metalloprotease production of vascular endothelial cells under extremely high wall shear stress condition
Naoya Sakamoto, Yuki Oyama, Yuta Horie, Masanori Nakamura, Naoyuki Kimura

S31-4 Observation of microscopic elastic structure in arterial tissue by use of a scanning haptic microscope (SHM)
Takeshi Moriwaki, Sadao Omata, Yasuhide Nakayama

S31-5 Ultrafast imaging of cell elasticity with optical microelastography
Guy Cloutier, Grasland-Mongrain, Ali Zorgani, Shoma Nakagawa, Simon Bernard, Lia Gomes Paim, Greg FitzHarris, Stefan Catheline

S32: COMPUTATIONAL MODELS OF THROMBOSIS C
Chairs: Keefe Manning and Shawn Shadden

S32-1 The contact activation system in device-related thrombosis modeling
Rodrigo Méndez Rojano, Simon Mendez, Franck Nicoud

S32-2 Development of a device-induced computational thrombosis model
Keefe Manning

S32-3 Reduced-order computational modeling of thrombogenic potential in large arteries
Kirk Hansen, Shawn Shadden

POSTERS (P1-P36)

P1 Effects of hypertrophy and strength weight training on resting levels and responses of hemorheological parameters to a single session of exercise
Fatholah Havil, Afshar Jafaria, Sajad Ahmadizad, Saeed Nikoukheslat

P2 Modulation of erythrocyte mechanical function by calcium-calmodulin-protein kinase C
Ali Cenk AKSU, Yasemin AKSU, Dilan ATAR, Zeynep Busra Kısakurek, Elif Ugurel, Özlem Yalcin

P3 Clinical relevance of hemodynamic viscosity measurement in vascular study
Tilly Alexandre

P4 Analysis of seismocardiographic signals by the discrete Chebyshev transform
Mikhail Basarab, Natalya Konnova

P5 Fetal growth retardation and oxygen delivery hemorheological predictors in hypertensive vs normotensive pregnant women
Jean-Frédéric Brun, Emmanuelle Varlet-Marie, Pierre Boulot, Bénédicte Marion, Céline Roques, Eric Raynaud de Mauverger

P6 Leg electrical resistance predicts venous blood viscosity and hematocrit
Emmanuelle Varlet-Marie, Laurent Vachoud, Bénédicte Marion, Céline Roques, Marlène Richou, Eric Raynaud de Mauverger, Jean-Frédéric Brun

P7 The transient hyperviscosity syndrome of labor and delivery shifts the hemorheological profile toward a lower ability to deliver oxygen to tissues

Jean-Frédéric Brun, Pierre Boulot, Emmanuelle Varlet-Marie, Bénédicte Marion, Céline Roques, Eric Raynaud de Mauverger

P8 Studies of the chemically induced changes of the mechanical properties of murine RBCs with the use of Atomic Force Microscopy (AFM)
Katarzyna Bulat, Jakub Dybas, Aneta Blat, Mateusz Mardyla, Anna Rygula, Stefan Chłopicki, Małgorzata Baranska, Katarzyna M. Marzec

P9 Investigation on energy characteristic of red blood cell deformability: A quantitative analysis of extending and retracting curves based on atomic force microscopy
Dong Chen, Xiang Wang

P10 Measurement of glycocalyx volume: An unreliable biomarker
FitzRoy Curry, Charles Michel

P12 Resonance Raman spectroscopy in detection and differentiation of various hemoglobin derivatives inside packed human red blood cells
Jakub Dybas, Malgorzata Baranska, Stefan Chlopicki, Katarzyna M. Marzec

P13 Effects of different rehabilitation models on the elongation index of erythrocytes, study of activity of chosen erythrocyte enzymes, and the level of glutathione in elderly women
Katarzyna Filar-Mierzwa, Anna Marchewka, Zbigniew Dąbrowski, Paulina Aleksander-Szymanowicz

P14 Effects of whole body vibration training on hemorheological blood indicators in young healthy women
Halina Gattner, Justyna Adamiak, Magdalena Kępińska, Anna Piotrowska, Olga Czerwińska-Ledwig, Sylwia Mętel, Wanda Pilch

P15 Evaluation of vascular effects of photodynamic therapy in skin microcirculation using different photosensitizers
Tatyana Grishacheva, Dinara Faizullina, Nickolay Petrishchev, Irina Mikhailova

P16 Analysis of flow and thrombus development within PDMS channels of varying geometry
Tice Harkins, Jeremey Myslowski, Keefe Manning

P17 Measurement of blood viscosity by measuring flows in microfluidic channel
Hyeonji Hong, Eunseop Yeom

P18 Repeated whole body cryotherapy treatments does not cause changes in hemorheological parameters in healthy people
Magdalena Kępińska, Zbigniew Szyguła, Zbigniew Dąbrowski

P20 Cell volume regulation via the calcium-activated potassium channel KCa3.1 contributes to red blood cell compliance under shear
Jan Lennart Kuck, Michael J. Simmonds

P21 Effects of rowing on rheological properties of blood
Mateusz Mardyła, Aneta Teleg łów, Zbigniew Dąbrowski, Jakub Marchewka, Jacek Głodzik, Bartłomiej Ptaszek

P22 Impaired deformability of erythrocytes in hypertensive rats and patients: Investigation by nickel mesh filtration technique
Toru Maruyama, Keita Odashiro, Takehiko Fujino, Shiro Mawatari

P23 Determinants of sublethal trauma to red blood cells: Effects of shear rate at standardized shear stresses

Jacob Turner, Antony McNamee, Jarod Horobin, Lennart Kuck, Kieran Richardson, Michael Simmonds

P24 Susceptibility to mechanical damage of density-fractionated red blood cells
Antony McNamee, Kieran Richardson, Lennart Kuck, Kai Robertson, Michael Simmonds

P25 Clinical evaluation of laser Doppler flowmetry for diagnosis of microcirculatory disorders
Christof Mrowietz, R.P. Franke, G. Pindur, R. Sternitzky, F. Jung, U. Wolf

P26 Erythrocytes aggregation index correlate with oxidative stress and hydrogen sulfide plasma concentration in diabetes mellitus
Agata Pietrzycka, Katarzyna Krzanowska, Przemysław Miarka, Władysław Sułowicz, Marcin Krzanowski

P27 Effects of carboxylated multiwall carbon nanotubes on erythrocytes stability and functionality
Mateusz Przetocki, Józef Korecki, Grzegorz Gajos, Leszek Stobiński, Krzysztof Matlak, Kvetoslava Burda

P28 Influence of different rhythms sound wave to serotonin concentration in rats hippocampus
Yang Ren, Zhidan Deng, Xiang Wang

P29 Physical properties of erythrocytes improve in hemochromatosis patients with repeated venesection therapy
Kieran Richardson, Antony McNamee, Michael Simmonds

P30 Experimental characterization of the embolus trapping efficiency of the U.S. FDA generic inferior vena cava filter
Joshua Riley, Nicole Price, Brent Craven, Kenneth Aycock, Keefe Manning

P31 Effects of pentoxifylline on hemodynamic and hemorheological parameters in SHRs during arterial hypertension development
Alexander Shamanaev, Oleg Aliev, Anastasia Sidekhmenova, Anna Anischenko, Mark Plotnikov

P32 Effect of cholesterol-rich diet on hematological and hemorheological parameters in rabbits
Bence Tanczos, Viktoria Somogyi, Mariann Bombicz, Bela Juhasz, Norbert Nemeth, Adam Deak

P33 Changes in biochemical properties of the blood in winter swimmers
Aneta Teleghów, Jakub Marchewka, Anna Marchewka, Zbigniew Dąbrowski, Bartłomiej Ptaszek, Mateusz Mardyła

P34 The paraclinical evolution in diabetic hypertensive patients with increased abdominal circumference
Cornel Cezar Tudorica, Ana Maria Vintila, Stefan Dragos Tudorica, Mirela Gherghe

P35 Alterations of red blood cell deformability and mechanical stability by heat-treatment on animal blood samples
Gabor Varga, Adam Attila Matrai, Balazs Szabo, Viktoria Somogyi, Barbara Barath, Bence Tanczos, Norbert Nemeth

P36 Shear-dependency of the predicted ideal hematocrit

Emmanuelle Varlet-Marie, Laurent Vachoud, Bénédicte Marion, Céline Roques, Marlène Richou, Eric Raynaud de Mauverger, Jean-Frédéric Brun

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PLENARY LECTURES

L1 ESCHM Plenary Lecture

Blood rheology: From exercise responses to sickle cell disease pathophysiology

Philippe Connes
Laboratoire LIBM EA7424, Equipe "Biologie Vasculaire et du Globule Rouge", Université Claude Bernard Lyon 1, France

Blood rheological responses to exercise in the sickle cell disease patient are reviewed in light of the exercise response of normal hemoglobin subjects, and those with heterozygous and homozygous forms of the disorder:
(1) Exercise and blood rheology: Blood viscosity increases during exercise. This increase would be the consequences of the rise in hematocrit, plasma viscosity and red blood cell (RBC) aggregation, and the decrease of RBC deformability. The decrease of RBC deformability has been attributed to lactic acidosis and oxidative stress. However, we and others reported that RBC deformability can also increase during exercise in highly trained individuals, and this increase would be the consequence of a greater production of nitric oxide (NO) into the RBC.
(2) Sickle cell trait (SCT): SCT is the heterozygous form of sickle cell disease (SCD) and is usually considered to be a benign condition. However, large epidemiological studies demonstrated a higher risk for SCT individuals to collapse during exercise. At rest, blood viscosity and arterial rigidity are higher in SCT compared to control individuals. During exercise, blood viscosity of SCT carriers reaches very high values but adequate hydration has been demonstrated to offset this increase.
(3) SCD: SCD patients have abnormal hemoglobin (HbS), which polymerizes under de-oxygenation and causes the sickling of RBC. Sickle RBC are fragile and poorly deformable. Patients with the lowest RBC deformability are at higher risk to develop leg ulcers, glomerulopathy and priapism while those with the highest deformability have frequent vaso-occlusive crises (VOC). Any rise in blood viscosity increases the risk for VOC because vascular reactivity is blunted in SCD. Hemolysis, increased oxidative stress and the high amount of circulating microvesicles are involved in the development of vasculopathy in SCD. Enhanced eryptosis caused by oxidative stress would be the cause of RBC-microparticles genesis in SCD.

L2 ISB Poiseuille Medal Award

Microvascular hemodynamics: System properties

Axel R. Pries
Charité Universitätsmedizin Berlin

Rheological properties of newtonian fluids are fixed material properties and don't change with shear rate or shear stress. However, it is well known, that blood being a complex fluid exhibits a deviation from

that behavior with increasing apparent viscosity at decreasing shear rate. This results from a change in the interaction between the different components of the blood, water and small solutes, macromolecules and blood cells. Such a pseudoplastic behavior can still be seen as a material property of the blood, which is not the case for phenomena reported for the perfusion of blood through narrow bore glass tubes, microvessels or microvascular networks. In these conditions, the observed hemodynamic behavior is dictated by the interacting properties of the blood and the structures it is flowing through – i.e. the systems properties.

These properties deviate from those obtained with a newtonian homogenous fluid perfused through the same structures in several aspects which result from the interactions between the flowing components and the external structure. The presence of a confined space with a (cross-sectional) dimension comparable to that of blood cells causes increasing influence of the tube or vessel wall with the cells for decreasing diameter. This leads to an accumulation of cells in the axial flow regions and to a decrease of viscous cell to cell interactions. The former is the basis of the Fahraeus-Effect, the reduction of hematocrit in small tubes or vessels (volume fraction) relative to the hematocrit of the blood perfused to them (flow fraction). The Fahraeus-Effect together with the latter leads to the surprising and strong reduction of effective viscosity during flow in small tubes or vessels, the Fahraeus-Lindquist-Effect. In microvessels the vessel wall is not a rigid surface but rather a gel with complex mechanical and biological properties, the so called endothelial surface layer or glycocalyx which further modifies the hemodynamic properties of the system. The next level of interactions is seen at microvascular bifurcations where red cells and blood plasma usually exhibit unequal distribution to the daughter vessels (phase separation effect). In microvascular networks the different properties of arterio-veneous flow pathways consisting of the increasingly smaller vessels of the arterial trees, the capillaries and venules with increasing diameter in the veneious vessel trees and the successive microvascular bifurcations lead to additional effects on hematocrit and flow (Network-Fahraeus-Effect and Pathway-Effect).

L3 ISB Plenary Lecture

Biomechanics and atherosclerotic plaques progression

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The role of low and oscillating shear stress as a key factor for localizing early atherosclerotic plaques is generally accepted. Once more advanced plaques protrude into the lumen, the shear stress they are exposed to changes. The influence of shear stress on plaque composition in advanced atherosclerosis is not fully understood. In this review, we discuss our recent studies on the relationship between shear stress, plaque composition and the location of plaque rupture in human coronary arteries. We have shown that elevated shear stress levels can be found over plaques that are not subjected to treatment. Regional exposure of certain plaque regions to high shear stress is therefore a condition that will pertain for a prolonged period of time. We have also shown that in more advanced atherosclerosis the necrotic core experiences higher shear stress. Low shear stress plaque regions can be found downstream of the plaque and are stiffer. High shear stress plaque regions can be found either at the upstream, shoulder or cap region of the plaque, and are softer. The plaque regions exposed to the highest shear stress are the softest and are the ones exposed to the highest shear stresses. The high shear stress plaque regions are the only regions that get softer over time. Finally, high shear stress is also associated with the location of plaque rupture in non-culprit lesion in human coronary arteries. Combining our findings with data from literature, we can conclude that

advanced coronary plaques grow in the distal regions. The distal plaque regions are exposed to low shear stress, are stiffer and have a stable plaque phenotype. The regions exposed to high shear stress are softer, and are associated with vulnerable plaque features.

L4 ISCH Medal Award

The rheopathobiology of malaria and babesiosis

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The pathogenesis of falciparum malaria and bovine babesiosis are remarkably similar. In both, parasite-infected red blood cells (RBCs) accumulate in the microvasculature causing vaso-occlusive clinical syndromes. Whilst the cellular and molecular mechanisms underpinning the pathogenesis of malaria have been intensely scrutinised, babesiosis has been relatively ignored; despite the fact that babesia parasites offer considerable experimental advantages to relate the function of specific parasite genes to pathological sequelae. In the Cooke Laboratory, we characterise the rheological properties of bovine RBCs infected by *B. bovis* (BbRBCs) and compare them with human RBCs infected with *P. falciparum* (PfRBCs). Like PfRBCs, flowing BbRBCs adhere to vascular endothelial cells and form stable interactions that correlate with microvascular sequestration. Intriguingly however, high resolution imaging of BbRBCs reveals structures on their surface (that mediate adhesion) that were morphologically very different to the knob-like structures on the surface of PfRBCs that mediate their adhesion. Using multiple experimental approaches, we have now identified numerous novel proteins at the membrane skeleton of BbRBCs which we believe will be directly involved in the formation of these unique 'ridge-like' structures and hence in pathogenesis and virulence. Linking these novel proteins with physiologically-relevant functions in BbRBCs will also identify future therapeutic strategies to combat both babesia and malaria infections.

L5 ISCH Plenary Lecture

Microfluidic platelet function assays

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There have been many quantitative studies of platelet aggregation and thrombosis, but clinical applications have been poor due to various reasons. For the unmet clinical needs, it is desirable to develop an innovative technology with understanding the basic biology of platelet and utilizing microfluidic technology. Thus, this presentation provides an overview of commercial point of care devices for platelet testing and recent microfluidic studies with a description of their innovative techniques. Furthermore, we have demonstrated the characteristics of our microfluidic device to test platelet function as well as antiplatelet response. In this presentation, major advantages of microfluidics for testing platelets are assessed via mimicking the pathophysiological environment of blood vessels, including hemodynamics as well as injured blood vessels. An analysis is presented of unsolved issues in platelet function tests using microfluidics.

L6 ESCHM Fåhraeus Award

Multifunctional life of the erythrocyte

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Anucleated, erythrocytes or red blood cells (RBCs) may be considered a simple and easily obtained "ex vivo" experimental model that could provide a means to study what occurs in nucleated cells, in terms of metabolism, ion transport, membrane fluidity and exovesicles among other properties. However RBCs are unique in their oxygen transport function in addition to their role in nitric oxide (NO) availability. The biochemical and the biophysical properties of RBCs allow them to be sensors and active partners in hemorheology and in inflammatory conditions. RBCs are more than a hemoglobin container; they are an indispensable player. The aim of this Fahraeus lecture is to summarize the key points obtained from studies centered on the erythrocyte and its multiple functions. The characterization of the RBC's biophysical and rheological properties and its association with inflammatory biomarkers, both in macro and microcirculation, and interactions with white blood cells are highlighted. The RBC's biomolecular behavior, as therapeutic targets and as biomarkers are identified.

Numerous features of RBC function relevant to microvascular function are reviewed, such as: the ability to release exovesicles; receptor function of the erythrocyte membrane enzyme acetylcholinesterase; the identification of the signal transduction for the scavenging and delivery of NO and internal mobilization of NO derivatives; the identification of CD47 as the RBC membrane receptor for soluble fibrinogen (Fib); the influence of Fib on RBC NO efflux; the association between RBC NO efflux and several parameters of inflammatory vascular disease; the interrelationship between erythrocyte deformability and NO and its dependence on internal and external biomolecules; and the role of erythrocyte deformability in affecting microvascular leukocyte margination in inflammatory diseases.

L7 Plenary lectures in tribute to Prof. Oguz Baskurt

Blood rheology as a determinant of blood flow: Physiological and clinical aspects

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It has been previously demonstrated that the effects of blood rheological alterations are less pronounced in vivo compared to in vitro. The first big group of the determinants of the results of experiments on in vivo flow dynamics is the experimental model and the methods used. The properties of the organ or tissue under investigation significantly affects the influence of hemorheological alterations on pressure-flow relationship in vivo. The methods used in in vivo studies also influence the results of the experiments. Another important factor that determines the results of in vivo hemorheology studies is the nature of hemorheological alterations. The results of the experiments investigating the influence of hemorheological alterations on pressure-flow relationship in vivo are also determined by the methods used to modify hemorheological properties of blood. The results of in vivo experiments are also affected by interfering physiological factors directly related to the living organism, organ or tissue. An alteration in hemorheology may result in a decreased blood flow in a vascular segment. This will be followed by decreased oxygen

supply to the tissue, which will trigger a vasodilatory response, or metabolic autoregulation, restoring normal blood flow and tissue oxygen supply. Hemorheological extra load can easily be compensated by decreased vascular hindrance, resulting from metabolic autoregulation. However, this can only work if there is enough autoregulatory reserve. In conclusion, the relation between the hemodynamics and hemorheological alteration is extremely complex but with the systematic analysis of the related data, it is possible to provide better clinical explanations for the pathophysiological processes in which hemorheological factors are involved.

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SYMPOSIA

S1-1 Hemorheological parameters and mortality in critically ill patients

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Purpose: Prognostic scores for mortality of intensive care patients estimate clinical outcome using several anamnestic, physiological and biochemical parameters. In altered hemodynamic conditions of critically ill patients, hemorheological variables may play a significant role in appropriate tissue perfusion. We investigated if hemorheological parameters are altered in critical status and if they could be markers of mortality. Methods: 112 patients (67.8 ± 12 years, 58 males) treated in an intensive care unit with different non-surgical diseases were investigated. Routine laboratory parameters and prognostic scores were determined and hemorheological variables (hematocrit, plasma and whole blood viscosity, red blood cell aggregation and deformability) were measured on the 1st and the 2nd day after admission. Results: ICU prognostic scores predicted 35.2–41.3% mortality rate. Real mortality in intensive care unit was 37.5%, while 30-day mortality was 46.6%. Whole blood viscosity (WBV) and red blood cell (RBC) deformability were lower, red blood cell aggregation was higher in septic than in nonseptic patients ($p < 0.05$). In septic patients calcium was increased, osmolality was decreased, while in nonseptic patients WBV and RBC aggregation were higher in non-survivors compared to survivors ($p < 0.05$). Worsening of RBC deformability from day 1 to day 2 predicted higher mortality ($p < 0.05$). Conclusion: Calcium and osmolality level were associated with outcome in sepsis. Whole blood viscosity, red blood cell aggregation and change in red blood cell deformability could predict mortality in nonseptic patients and they may add prognostic information over the ICU scores. Further investigations are needed to evaluate the benefit of our findings in clinical practice.

S1-2 Leukocyte antisedimentation rate (LAR) and pituitary adenylate cyclase-activated polypeptid (PACAP) in polytrauma and burn victims. A preliminary study

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Introduction: Polytrauma and severe burn injury result in cellular necrosis that leads to immediate immunoreactions. Secondary infectious complications further increase leukocyte activation and consequent leukocyte swelling. It can be monitored with leukocyte anti-sedimentation rate (LAR). Pituitary adenylate cyclase-activated polypeptid (PACAP) has several functions, including anti-apoptotic, antioxidant and anti-inflammatory effects. Objective: Our aim was to evaluate the role and the comparison of conventional (serum C-reactive protein: CRP, procalcitonin: PCT) and non-conventional (LAR, PACAP-38) markers in polytrauma and burn victims. Methods: In our preliminary study patients were followed for 5 days (T1-T5) after admission to a critical care unit immediately with severe polytrauma or burn injury. Serum PACAP-38 concentration was measured with RIA and sandwich-type ELISA, while LAR, CRP and PCT levels were determined with conventional laboratory methods. Results: 13 patients with polytrauma and 5 with burn injury were involved. LAR and CRP kinetics showed elevating tendency at T3 ($p < 0.05$) in both groups, and LAR from T4 ($p < 0.001$) in both groups, respectively. PACAP-38 levels showed significantly higher levels at T4 ($p < 0.01$) in polytrauma patients only. PCT failed to indicate any consistent kinetics. Positive correlations were found between LAR and CRP ($p < 0.05$) as well as CRP and PCT ($p < 0.05$) in both groups. Conclusions: LAR was proved to reliably reflect acute phase reaction. PACAP demonstrated a neuroprotective role in survivors of serious brain injury. The role of elevated PACAP levels could provide its protective function to restore the physiological functions of the body in patients with critical conditions.

S1-3 Do AB0 and Rh blood groups influence hemorheological parameters in vascular patients?

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Background: The ABO blood group system influences the risk of thrombotic cardiovascular adverse events, and exerts a profound effect on hemostasis. Non-O blood type has been associated with a higher risk of developing cardiovascular adverse events. We aimed to clear whether the differences in thrombotic risk between blood groups may be associated with hemorheological differences. Methods: Between 2001 and 2005, we performed hemorheological examinations on subgroups of ASA treated vascular patients. Hungarian National Blood Transfusion Service databases were searched for ABO and Rh blood groups of those patients who had their blood types tested until September, 2017. Blood type data was available for 510 patients who had hematocrit, and for 541 patients who had plasma fibrinogen measured. We found 514 patients who had both blood group analysis and plasma- and whole blood viscosity measurement, and 268 patients who had both red blood cell aggregation and blood type test performed. Plasma-and whole blood viscosity were measured by Hevimet 40 capillary viscometer. Red blood cell aggregation was measured by Myrenne aggregometer.

S1-4 Applications of finite element analysis in clinical hemorheology

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Finite element analysis (FEA) is a well-known, widely used method in the engineering studies. Yet in medical care it is still a novel technique. In a case of the surgical care of a left ventricle (LV) aneurysm, residual LV function and volume are the most crucial factors of the outcome. Planning of these interventions are challenging with conventional methods. Using computational fluid dynamics - a branch of FEA- can provide an effective alternative for these practices. Materials and Methods: We used high resolution CT images to create a virtual model that is capable of computational planning of different patch scenarios for surgical ventricle restoration (SVR). During the simulation, we took into consideration that the left ventricle is a dynamically moving region, and the hemorheological properties of blood. Results: Using virtual planning, operative time decreased, good LV function was achieved and mitral function improved significantly.

S1-5 Effects of ischemia-reperfusion and various surgical preconditioning maneuvers on micro-rheological and microcirculatory parameters

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Ischemia-reperfusion is known to alter hemorheological parameters and also having significant impact on the microcirculation. However, numerous questions have not been completely answered yet concerning the time factor, the border of reversibility-irreversibility, preventive and therapeutic possibilities among others. Ischemic preconditioning, being local or performed on remote organs (e.g., extremities), is one of the maneuvers for reducing ischemia-reperfusion damage. Micro-rheological parameters can be altered by several pathways including metabolic, free-radical-related and inflammatory processes. Depending on the affected organ function, the extension and scheduling of the maneuvers these changes can further vary. Experimental models focusing on renal or hepatic ischemia-reperfusion also revealed that optimization of the remote organ ischemic preconditioning protocols still needs further clarification.

S1-6 Renal ischemia-reperfusion-induced micro-rheological and microcirculatory alterations and their influenceability by remote organ ischemic preconditioning

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The pathological mechanisms and the optimal protocol for remote ischemic preconditioning (rIPC) and its effect on hemorheological and microcirculatory parameters have not yet been clarified. We aimed

to investigate this issue in a rat model. On male CrI:WI rats the left femoral artery was cannulated, via median laparotomy the left kidney was exposed, and a 165-minute period was monitored in the sham-operated group ($n = 7$). In the ischemia-reperfusion (I/R) group ($n = 7$) we used a microvascular clip to induce a 45-minute period of renal ischemia followed by a 120-minute reperfusion period. In the rIPC groups a tourniquet was applied around the right hind-limb for 3 × 10 minutes with 10-minute intermittent reperfusion periods 1 hour (rIPC-1, $n = 7$) or 24 hours (rIPC-24, $n = 6$) prior to the I/R. Blood samples were taken before the renal ischemia phase and during the reperfusion for testing hematological, hemorheological and acid-base parameters. Arterial mean pressure, heart rate, respiratory rate, rectal temperature, organ surface temperature and microcirculation were also recorded. In rIPC-1 group we measured the highest blood pressure and lactate values with the lowest pH. In I/R group microcirculation of the liver increased during reperfusion ($p < 0.05$ vs. base) and the highest leukocyte count ($p < 0.01$ vs. all) was found. Erythrocyte deformability worsened in all ischemic groups ($p < 0.05$ vs. all) with the smallest manner in rIPC-24. However, erythrocyte aggregation markedly increased ($p < 0.001$ vs. rIPC-1). The histology showed better results in the rIPC-24 group ($p < 0.01$ vs. all). Renal I/R caused significant changes in the investigated parameters. However, according to the results it could not be decided which rIPC protocol was more effective for reducing I/R injury in rats.

S2 -1 Biologically validated model of platelet adhesion under blood flow conditions

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Medical implants have been growing in importance. They are widely used in a variety of clinical fields (such as cardiovascular and orthopedic medicine, as well as dentistry) as key applications for the treatment of diseases and restoration of missing and defective organ functions. Almost all implants come into contact with blood in the human body. However, the insufficient hemocompatibility of implant surfaces still remains a major problem that causes life-threatening device failure. In order to reduce the risk, the hemocompatibility of biomaterials must be improved. On the other hand, adhesive capacity is a fundamental factor in clot formation on artificial surfaces after implantation. Therefore, the prevention of platelet adhesion to material surfaces is directly related to the improvement of surface hemocompatibility. There are two approaches: chemical and physical. In chemical, for example changing surface components control surface characteristics. Physical modification is a unique technique to control the cell adhesion by making the micro order shape to the surface. We previously reported that fluorine incorporated diamond-like carbon (F-DLC) film with patterned markedly inhibits platelet adhesion and activation compared to polycarbonate. In this symposium we will introduce our development of new materials through chemical and physical approaches to improve biocompatibility. An appropriate understanding of these technologies will make it possible to develop future medical materials for blood-contacting devices.

S2-2 Glycoprotein distribution of surface-induced platelet activation on medical materials by electron microscopy technology

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Thrombogenic complications remain one of the main problems for blood-contacting medical devices and can trigger life-threatening device failure. To reduce the risk of thromboembolism, we need to understand of thrombus formation mechanism between platelet and protein on material because platelets play a key role in blood coagulation. Platelets attach to an artificial material surface in the earliest stage of cell-material contact and they change in shape by developing pseudopodia (small leg from the platelet) and release granule contents, finally becoming flat. The plasma membrane of human platelets is rich in glycoproteins (GP) that play an important role in its interactions with cell adhesion proteins. On the material surface, Glycoprotein Ibα and IIb/IIIa binds to von Willebrand factor and fibrinogen respectively, which delivers platelet activation signals internally. A complete understanding of the distribution GP and its signaling could lead to new approaches to development of materials. However, these interactions are complicated; the behavior of glycoproteins have not been fully elucidated or visualized. In this study, we attempted to observe the glycoprotein distribution on the membrane surface, platelet internal structures and adhesion interfaces of human platelets attached to medical-material surfaces using electron microscopy technology during the platelet activation process. In addition, we evaluated platelet reactions under flow conditions, using a fabricated blood flow chamber with changing shear stress.

S2-3 Hemorheological effects of mechanical stress on whole blood of patients with prosthetic heart valve failure

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Background: Human blood cells are subjected continuously to mechanical stress in valvular heart diseases and therapeutic interventions using prosthetic heart valves. However, effects of mechanical stress on circulating blood cells remain unclear. Methods: Venous blood was sampled from patients undergoing heart valve replacement surgery after obtaining written informed consent. Erythrocyte deformability was investigated by our specified filtration technique using nickel mesh filter with its pore size of 4.55 micrometer, and platelet activation was quantified by serum beta-thromboglobulin (BTG) and platelet factor IV (PF4). Results: Erythrocyte deformability was significantly impaired and platelet activation was marginal in cases of prosthetic valve failure showing perivalvular leakage. However, these findings were not observed in cases showing normal prosthetic valve functions. Microscopic findings of blood smear demonstrated elliptic, segmented or fusiform deformations of erythrocytes and no remarkable findings in platelet morphology in cases of prosthetic valve failure, but not in cases without perivalvular leakage. Conclusions: Mechanical stresses caused by prosthetic valve failure results in severe damage to circulating blood cells. Erythrocyte deformability was profoundly impaired leading to hemolysis requiring transfusion, and platelets were mechanically activated, leading to adhesion and prosthetic valve failure unless antiplatelet agents were administered.

S2-4 Platelet adhesion studies of implantable long-term use fontan pump biomaterials

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Penn State University is developing a small implantable pump for long-term mechanical support of patients with a failing Fontan circulation. An increasing number of patients who undergo the Fontan operation are surviving to adulthood and require a device to provide sustained support. Many blood contacting components of this pump are manufactured from polyether ether ketone (PEEK), which has not been thoroughly characterized with regards to its biocompatibility. This study will analyze the surface characteristics of PEEK and compare them to previously characterized pediatric pump polyurethane materials to analyze their thrombosis potential. PEEK and polyurethane samples were first analyzed using Optical Profilometry to compare surface roughness from their respective manufacturing protocols. A developed rotating disk system (RDS) protocol was then used to test platelet adhesion to the material surfaces at varying shear rates. The material surfaces were immuno-fluorescently labeled and imaged to quantify the number of adhered platelets. Additionally, x-ray photoelectron spectroscopy (XPS) studies of the PEEK material were performed to determine any surface contamination resulting from the component manufacturing and polishing processes. PEEK samples were found to be smoother than poly urethane samples with surface roughness's of 20 μm and 70 μm, respectively. From RDS experiments, at a radial location of 6 mm (shear rate of 401.86 s^{-1}), a 71% decrease in platelet adhesion was observed with PEEK compared to polyurethane. However, XPS investigation revealed some contamination of the PEEK with PDMS (approximately 7%) resulting from surface polishing and is being further investigated as to its effect on platelet adhesion.

S2-5: Development of hemocompatible materials for blood contacting devices by physical and chemical surface modification

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Medical implants have been growing in importance, and they are widely used in a variety of clinical fields (such as cardiovascular and orthopedic medicine, as well as dentistry) as key applications for the treatment of diseases and the restoration of missing and defective organ functions. Almost all implants come into contact with blood in the human body; however, the insufficient hemocompatibility of implant surfaces still remains a major problem that causes life-threatening device failure. In order to reduce the risk, the hemocompatibility of biomaterials must be improved. On the other hand, adhesive capacity is a fundamental factor in clot formation on artificial surfaces after implantation. Therefore, the prevention of platelet adhesion to material surfaces is directly related to the improvement of surface hemocompatibility. There are two approaches, chemical and physical approaches. In chemical, for example changing surface components control surface characteristics. Physical modification is a unique technique to control the cell adhesion by making the micro order shape to the surface. We previously reported that fluorine incorporated diamond-like carbon (F-DLC) film with patterned markedly inhibits platelet adhesion and activation compared to polycarbonate. In this symposium we will introduce our development of newly material through chemical and physical approaches to improve biocompatibility. Appropriate understanding of these technologies will make it possible to develop future medical materials for blood contacting devices.

S3-1 Holotomography techniques for imaging 3D label-free imaging of cells and tissues

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Quantitative phase imaging (QPI) has emerged as an invaluable tool for imaging small transparent objects, such as biological cells and tissues. QPI employs various interferometric microscopy techniques to quantitatively measure the optical phase delay of samples. In particular, the measured optical phase delay provides information about the morphological and biochemical properties of biological samples at the single-cell level. Recently, QPI techniques have been widely applied to study the pathophysiology of various biological cells and tissues, including red blood cells (RBCs), white blood cells, bacteria, neurons, and cancer cells. In this talk, we will present the recently developed 3-D holotomography setup using a dynamic mirror device, which is an optical analogous to X-ray computed tomography. In particular, we will discuss the visualization of 3D refractive index distributions of biological cells and tissues measured with the 3-D holotomography using the transfer function method, which has been widely used in the visualization field [1–4]. In particular, we will present recent updates on the application of holotomography techniques for the study of various blood-cell-related diseases, including general hematology, malaria, babesia infection, blood cells of diabetes patients, and immune cell diseases. In addition, we will also present the optical manipulation of eukaryotic cells on demand by exploiting 3-D refractive index tomography [5,6].

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S3-2 A microfluidic device for simultaneous measurement of blood viscosity, hematocrit, and deformability

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Elevated whole blood viscosity is related to cardiovascular diseases including diabetes, hypertension, stroke and so on. There are many reasons for elevated viscosity of blood. In particular, whole blood viscosity is strongly dependent on the physical properties of red blood cells e.g., hematocrit and deformability. In this study, a microfluidic device enabling the measurement of whole blood viscosity, hematocrit and red blood cell deformability is proposed for multimodal analysis of the physical characteristics of whole blood. The proposed device is composed of hydrodynamic and electronic parts. In a hydrodynamic part, it has ten microchannel arrays that can generate the multiple sets of shear rates. Once the whole blood is infused with PBS as a reference fluid, viscosity of whole blood can be estimated by comparing the number of channels filled with blood and PBS. In an electronic part, there is a PCB device having a pair of electrodes on the opposite sidewalls for acquiring impedance spectrum of blood. Hematocrit is estimated by comparing the resistances of cytoplasm and plasma. And, deformability is evaluated by changing membrane capacitance. From experimental results for ten sets of blood viscosity measured for

shear rates from 100 to 1,000 /s, a 3.7% relative error was found compared to a rotational rheometer. Multiple hematocrit levels were accurately measured within 1.5% relative error, with good linearity (slope = 1.02) compared to values from centrifugation. For evaluating cell deformability, glutaraldehyde solution was added to the blood sample to harden red blood cells. Changes in constant phase element (CPE) of normal samples at 100 and 500 /s were 1195.6. In contrast, hardened samples yielded 247.9, which was 4.8 times smaller than for normal samples.

S3-3 Deformability measurement of continuous soft particles by lattice Boltzmann method and its applications to rheological flow characteristics

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Technologies that use optical force to actively control particles in microchannels are a significant area of research interest in various fields. An optical force is generated by the momentum change caused by the refraction and reflection of light and changes the particle surface as a function of the angle of incidence of light, which in turn feeds back and modifies the force on the particle. Simulating this phenomenon is a complex task. The deformation of a particle, the interaction between the surrounding fluid and the particle, and the reflection and refection of light should be analyzed simultaneously. Herein, a deformable particle in a microchannel subjected to optical interactions is simulated using the three-dimensional (3D) lattice Boltzmann immersed-boundary method. The laser beam from the optical source is analyzed by dividing it into individual rays. To calculate the optical forces exerted on the particle, the intensity, momentum, and ray direction are calculated. The optical-separator problem with one optical source is analyzed by measuring the traveled distance because of the optical force. The optical-stretcher problem with two optical sources is then studied by analyzing the relation between the intensity of the optical source and particle deformation. This simulation will help the design of sorting and measuring by optical force.

S3-4 A microfluidic platelet assaying device for function test and antiplatelet response test

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Aggregation and adhesion of platelets to the vascular wall play critical roles in hemostasis and thrombosis. The present study introduced a microfluidic device and method to test platelet functions corresponding to various agonists and shear rates. A shearing activation of platelets was induced by a rotating flat bar in a sample chamber and the shearing-magnitude and -time were accurately controlled in the system. When activated blood (by either shear or agonists) in a sample chamber were released to the closure area activated platelets were adhered and aggregated on the closure area, which was eventually blocked. The characteristic of platelet function is to represent with the migration distance (MD) of blood through microscale circular tube. Comparing with similar devices such as PFA-200 and VerifyNow, the present method and device showed an excellent agreement.

S4-1 Multilayer structures of the endothelial glycocalyx: barrier functions versus red cell hemodynamics

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Loss of glycocalyx components is an early indicator of vascular dysfunction. Loss results in increased penetration of red cells into a wall boundary region and increased leakage of water and plasma proteins. A common assumption is that the same glycocalyx structures determine both outcomes. An accumulating body of evidence does not support this assumption. Fluid and plasma protein exchange across the endothelial barrier is accounted for in terms of a quasi-periodic inner endothelial glycocalyx layer (about 300 nm thick) with hydraulic resistivity of the order of 10^{11} dynes sec/cm^4 (Darcy coefficient 10^{-13} cm^2). Glycocalyx layers that extend beyond 300 nm must be more porous to be consistent with measured vascular permeability properties. Red cell flows over layers more than 1 micron thick are accounted by a hydraulic resistivity 10- to 100-fold less than that of the inner layer. These observations, and independent evidence from tracer penetration and enzyme degradation, conform to a multi-layer model of glycocalyx structure. A prediction of the model is that changes in red cell hemodynamics within the boundary region 1 micron or more from the endothelial cell membrane may provide only limited data about the inner glycocalyx layers. Clinical strategies to evaluate loss of glycocalyx components that focus only on imaging red cell flows must be validated by better understanding of the interaction of red cells with a multilayer glycocalyx and the effect of changes in outer glycocalyx layers on transvascular exchange.

S4-2 Endothelial surface glycocalyx (ESG) components and ultra-structures revealed by stochastic optical reconstruction microscopy (STORM)

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The major glycosaminoglycans (GAGs) in the ESG are heparan sulfate (HS), hyaluronic acid (HA), and chondroitin sulfate (CS). In order to play important roles in vascular functions, e.g., as a mechanosensor for the endothelial cells (ECs) to sense the blood flow, a molecular sieve to maintain normal microvessel permeability and a barrier between the circulating cells and ECs forming the vessel wall, the ESG should have an organized structure at the molecular level. Due to the limitations of optical and electrical microscopy, the ultra-structure of ESG has not been revealed until recent development of a super high resolution fluorescence optical microscope, STORM. We used newly acquired STORM to observe the ESG on bEnd3 (mouse brain microvascular endothelial cells) monolayers. The ESG was immunolabeled with anti-HS, followed by an ATTO488 conjugated goat anti-mouse IgG, and with biotinylated HA binding protein, followed by an AF647 conjugated anti-biotin. The ESG was then imaged by the STORM with a 100x/1.49 oil immersed lens. Multiple Reporters of ATTO488 and AF647 with alternating illumination were used to acquire the 3D images of HS and HA. The field of 256 × 256 (40 × 40 μm^2) of HS and HA at the surface of ECs was obtained based on totally 40,000 of EM-CCD captured images for each reporter at a capturing speed of 19 ms/frame. We found that HA is a long molecule weaving into a network, which is horizontal to the EC cell surface. In contrast, HS is a shorter molecule, which is

perpendicular to the cell surface. The height of the HS is ~600 nm. HA and HS seem to overlap with each other at the EC surface. The revealed ultra-structure of ESG by STORM suggests that HS plays a major role in mechanosensing and HA plays a major role in forming the molecular sieve.

S4-3 *In vivo* studies of the enzymatic degradation and structure of the endothelial glycocalyx

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The endothelial cell (EC) glycocalyx serves as a barrier to trans-vascular exchange of solutes and adhesion of leukocytes during the inflammatory process. Observations in post-capillary venules (rat mesentery) revealed that prolonged exposure to high shear results in a matting down of the glycocalyx and reduced thickness of the layer. Rapid reductions in shear resulted in an unfurling of its molecular structure and a significant increase in thickness. The surface of the glycocalyx was found to undergo large deformations in the direction of flow. Observations of lectin coated beads adhered to the EC under pure oscillatory flow revealed excursions of about 400 nm during changes in flow direction. Structural alterations arise from two principal enzymes that cleave glycans from the EC surface: matrix-metalloproteases that cleave core proteoglycans, and heparanase that cleaves heparan sulfate chains from the core protein. Shedding of glycans from the EC in post-capillary venules was observed by EC stimulation with the chemoattractant fMLP. Inhibition of MMP activity by topical application of the inhibitor doxycycline, or scavenging of heparanase by infusion of low molecular weight heparin (LMWH), significantly inhibited glycan shedding due to fMLP. LMWH also resulted in a dose-dependent clustering of glycans on the EC surface. The magnitude of WBC-EC adhesion in response to fMLP varied inversely with clustering of glycans. Although LMWH initially reduced the rate of WBC adhesion in response to fMLP, prolonged stimulation with fMLP resulted in a continued rise in adhesion, thus suggesting that other factors may have played a role in the adhesion response. Nonetheless, the therapeutic value of stabilization of the EC glycocalyx with LMWH appears promising.

S4-4 The endothelial glycocalyx and control of microvascular flow and perfused capillary density

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The endothelial glycocalyx extends up to more than 1 micron into the lumen of microvessels and is expected to affect microvascular blood volume and red cell hemodynamics in capillary blood vessels. In the current study, we determined the level of penetration of red cells in the vascular wall boundary region as a measure of glycocalyx damage in healthy controls and in individuals with type 2 diabetes. In addition, we measured red cell velocities in feed vessels and capillaries to determine the relation between microvascular blood flow and red cell perfused capillary density. Our findings demonstrate increased penetration of red cells into the glycocalyx boundary layer in type 2 diabetes and analysis of intra-individual variability of red cell hemodynamics revealed that glycocalyx damage is associated with impaired flow dependent control of capillary density. It is concluded that uncoupling of microvascular blood flow and capillary exchange capacity may contribute to microscopic areas of tissue injury and loss of organ function at early stages of glycocalyx damage.

S5-1 Interaction of mesenchymal stem cells with platelets: Aid to targeting to tissue or thrombotic risk?

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Mesenchymal stem cells (MSC) may be used therapeutically via injection into the blood, where their adhesive properties and interactions with other blood cells will influence ability to target disease. For therapy, MSC are most commonly derived from human bone marrow (BMMSC) or umbilical cord (UCMSC). When we mixed MSC with human or mouse blood *in vitro*, UCMSC caused a marked drop in platelet count, but BMMSC did not. When mixed with platelet-rich plasma, UCMSC caused platelet aggregation, but BMMSC did not. We next injected UCMSC into the tail veins of mice and found that platelet count decreased in the period 4-24h, and then recovered. Injection of BMMSC had no effect on circulating count. Comparing the surfaces of the MSC, we found podoplanin (a ligand which can activate platelets through its receptor CLEC-2) expressed highly on most isolates of UCMSC but not on BMMSC. Soluble CLEC-2 could inhibit platelet aggregation induced by UCMSC, while those isolates of UCMSC that lacked podoplanin failed to aggregate platelets. Platelets from mice lacking expression of CLEC-2 were not aggregated by podoplanin-positive UCMSC. When UCMSC were infused into these CLEC-2 deficient mice, there were variable responses with some mice experiencing reduction in platelet count and others not. This may reflect imperfect reduction of platelet CLEC2 in the Cre-Lox strains crossed to obtain conditional knockout, or existence of additional pathways for podoplanin to exert effects. Thus, the origins of MSC and their expression of PDPN may have impact on their behaviour in the blood. During therapy, interactions with platelets could be thrombotic, but there is also evidence that interaction with platelets can assist targeting to damaged tissue.

S5-2 Malaria and babesiosis: same rheopathobiology but different molecular mechanisms

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The pathogenesis of falciparum malaria and bovine babesiosis are remarkably similar. In both, parasite-infected red blood cells (RBCs) accumulate in the microvasculature causing vaso-occlusive clinical syndromes. Whilst the cellular and molecular mechanisms underpinning the pathogenesis of malaria have been intensely scrutinised, babesiosis has been relatively ignored; despite the fact that babesia parasites offer considerable experimental advantages to relate the function of specific parasite genes to pathological sequelae. We characterised the rheological properties of bovine RBCs infected by B. bovis (BbRBCs) and compared them with human RBCs infected with P. falciparum (PfRBCs). Like PfRBCs, flowing BbRBCs adhere to vascular endothelial cells and form stable interactions that correlate with microvascular sequestration. Intriguingly however, high resolution imaging of BbRBCs revealed structures on their surface (that mediate adhesion) that were morphologically very different to the knob-like structures on the surface of PfRBCs that mediate their adhesion. Using multiple approaches, we have now identified numerous novel proteins at the membrane skeleton of BbRBCs which we believe will be directly involved in the formation of these unique 'ridge-like' structures and hence in pathogenesis

and virulence. Linking these novel proteins with physiologically-relevant functions in BbRBCs may also identify future therapeutic strategies to combat both babesia and malaria infections.

S5-3 Form and function: Erythrocyte responses to supra-physiological shears and circulatory support

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Mechanical circulatory support is essential for advanced cardiothoracic interventions; these circuits effectively perform the work of the heart and lungs during surgery. Previous generations of these circuits induced haemolysis and platelet damage, although "blood trauma" is now less common in well-functioning mechanical circulatory support. Nevertheless, close inspection of the secondary complications following chronic exposure to mechanical circulatory support indicates that microcirculatory dysfunction may be common and causal. Haemorheological assessment is now providing accumulating evidence that blood trauma should not be simply defined as overt cell destruction, but rather, include "sublethal" changes to the cells' properties and function. At the macro-level, for example, blood viscosity may decrease during surgeries that require rotary blood pumps – a potential indication of haemolysis. On the other hand, high-shear blood viscosity may increase in the absence of haemolysis, highlighting that structural changes to the erythrocyte are likely. Micro-rheological assessments may thus prove to extend our understanding of blood responses to mechanical circulatory support, and several teams have now confirmed that cellular deformability and aggregability of erythrocytes may be negatively impacted by shears previously thought to not induce blood trauma. Whether the altered function and physical properties of erythrocytes is permanent, or simply transient, following exposure to high shears is an important topic of current investigation. Moreover, how blood cells behave under physiological flow conditions following sublethal trauma is topical for exploring clinical outcomes. It appears that sublethal trauma may still be common in mechanical circulatory support, and likely involves both physical and biochemical mediation.

S5-4 Blood rheology, arterial stiffness, and clinical complications in diabetic patients with and without sickle-cell trait.

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Rates of Type 2 diabetes (T2D) are rapidly increasing in sub-Saharan Africa, a region where sickle-cell trait (SCT) is prevalent. T2D is characterized by vascular dysfunction and an increased risk of vascular complications. Although SCT has historically been considered to be a benign condition, recent research has revealed that vascular function is more severely impaired in patients with both T2D and SCT than in those with T2D only. However, the consequences of this exaggerated vascular dysfunction have yet to be fully elucidated. Therefore, the primary objective of this study was to determine whether patients with both SCT and T2D are more likely to suffer from vascular complications than those with T2D only. The present study, conducted in 176 Senegalese individuals, compared blood viscosity, Advanced Glycation End-products (AGEs), arterial stiffness and rates of vascular complications in control subjects (CONT), subjects with T2D or SCT and subjects with both T2D and SCT (T2D-SCT). Blood viscosity was higher in the SCT, T2D and SCT-T2D groups compared to the CONT group, and was higher in the SCT-T2D group than in all of the other groups. AGEs were elevated in the T2D and T2D-SCT groups compared to the CONT group. Carotid-femoral pulse wave velocity measurements revealed increased arterial stiffness in the SCT-T2D group compared to all other groups. Rates of hypertension, retinopathy and renal insufficiency were higher in the SCT-T2D group than in the other three groups. We observed a higher prevalence of vascular complications, increased blood viscosity and elevated arterial stiffness in individuals with both T2D and SCT, compared to those with T2D only. Our results suggest that SCT could increase the risk of developing vascular complications in individuals with T2D.

S5-5 The importance of hemorheology in the design of continuous flow left ventricular assist devices

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Heart failure remains an epidemic of the 21st century; more than 38 million individuals are affected Worldwide and 500,000 new cases are diagnosed annually. An increasing number of patients with end stage disease (Stage D) are supported with a continuous flow left ventricular assist device (LVAD) as the number of hearts available for transplantation is limited. Better understanding and computer modeling of fluid dynamics over the past decades revolutionized axial flow and centrifugal LVAD design, including the development of smaller and increasingly hemocompatible pumps capable of providing circulatory support up to 10 liters per minute. The mechanically suspended or magnetically levitated impeller rotates at high speeds (2,300 RPM–12,000 RPM) exposing the blood to extreme shear forces often leading to hemolysis, pump thrombosis and embolic complications. The importance of various hemorheological factors in the design of contemporary LVAD devices and their clinical relevance will be reviewed in this presentation.

S6-1 Optical study of red blood cells interactions *in vitro* mediated by different plasma components

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Red blood cell interaction resulting in their reversible spontaneous aggregation and shear induced disaggregation is one of the major processes that affect hemorheology and blood microcirculation. It is commonly known to be dependent on the concentration of plasma proteins. The exact role of each plasma protein in RBC aggregation is not well understood so far. Sometimes the experiments conducted using different techniques with whole blood samples or RBC suspensions containing mixtures of different plasma proteins yield somewhat controversial results. We assumed that there might be an unaccounted synergetic effect of proteins (e.g. interference between proteins) on RBC aggregation. The aim of this work was to assess the kinetics of RBC interaction *in-vitro* in samples with varying plasma proteins and their concentrations by direct measurement of cell interaction forces using optical tweezers. We found that albumin in plasma changes its role from agonist to inhibitor of RBC aggregation with increasing the concentration of fibrinogen. When the concentration of fibrinogen is relatively high, an increase in albumin concentration does not increase the aggregation force but weakens the binding force between the RBCs. Furthermore, a model solution including five major aggregation-inducing proteins yields a weak aggregation force that can hardly be measured. These results indicate that there is an apparent interference among various plasma proteins involved in RBC aggregation and that the synergetic effect of plasma proteins determines the degree of RBC aggregation as well as the aggregation and disaggregation forces. The work was supported by the grant of the Russian Foundation for Basic Research #17-02-01200.

S6-2 Effect of integrin glycoproteins inhibition on specific adsorption of cells adhesion macromolecules on red blood cell membrane: A microrheologic study

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Fibrinogen-induced red blood cell (RBC) aggregation was assumed to be caused by nonspecific binding of fibrinogen molecules to cell membranes and further leading to molecular bridging between interacting cells. In contrast, platelets are known to have membrane integrin IIb/IIIa glycoproteins highly specific to fibrinogen. In this work, we present the results of a microrheological study conducted by means of laser aggregometer RheoScan AnD-300 (RheoMedTech, Korea) of the effect of integrin IIb/IIIa glycoproteins inhibition on fibrinogen adsorption on RBC membrane. We measured the hydrodynamic strength of RBC aggregates in the flow of whole blood suspension samples in terms of critical shear stress (CSS). CSS represents the minimal shear stress required to disperse RBCs aggregates in blood sample flow. We studied the effect of several commonly used inhibitors: RGDS, eptifibatide, tirofiban. After incubating RBC in buffer solution, containing fibrinogen (3 mg/ml) and any of these inhibitors, after resuspension in platelet poor plasma at 40% HCT, the CSS significantly decreased by 23 ± 4% for RGDS in concentration 2.6 mg/ml, by 24 ± 3% for eptifibatide (3.3 μg/ml), by 30 ± 5% for tirofiban (4.8 μg/ml) in comparison with control. Similar results were obtained after resuspension in serum. All experiments were performed

on the blood of healthy male donor using EDTA as anti-coagulant. We conclude that there is an inhibition effect which may serve as an evidence of the existence of fibrinogen specific binding sites with IIb/IIIa glycoprotein related structure on RBC membrane. The observed effect of CSS decrease was not strongly dose-dependent which points on more complicated molecular structure of such binding sites. This study was supported by RFBR grants No. 17-02-01200 and No. 18-32-00756.

S6-3 Electrochemical impedance spectroscopy of blood for blood aggregation, sedimentation, and hematocrit

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The study of blood hematocrit, erythrocyte aggregation and erythrocyte sedimentation rate (ESR) is very important both for basic research and medical applications. Electrochemical impedance spectroscopy (EIS) is a highly promising tool for the analysis of blood. The electrical properties of plasma and blood cells provide fundamental insights into the health status of patients. A small chamber with two planar electrodes placed at the bottom was designed for sensitive detection of blood aggregation, sedimentation, hematocrit, and dielectric properties of plasma and erythrocytes. A method for correcting the polarization effect was employed. Changes in the blood impedance spectrum was measured at frequencies between 40 Hz and 110 MHz. A digital camera was used to verify the blood sedimentation curve and to determine the hematocrit profile. Analytical and numerical models were developed for calculating the effective permittivity and conductivity of whole blood in the case of randomly distributed and aligned erythrocytes. An algorithm was proposed to extract the electrical properties of erythrocyte cytoplasm and membranes from the impedance spectrum. Various models of erythrocyte shapes such as spherical, disk-shaped, spheroidal, and biconcave shapes were investigated. The EIS of blood samples reveals β- and δ-dispersions. It was found that the electrical properties of membranes have a significant influence on the blood impedance at frequencies between 100 kHz and 10 MHz (β-dispersion), while the cytoplasm has an effect at frequencies between 10 MHz and 1 GHz (δ-dispersion). Based on the proposed model, the ESR, blood sedimentation curve and hematocrit profiles can be numerically restored using only the first 400 seconds of the recorded changes in blood conductivity.

S6-4 Comparison of critical shear stress in RheoScan and adhesion force between RBCs measured in optical tweezer

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The aggregation of red blood cells (RBC) is a reversible dynamic phenomenon that has a strong effect on blood microcirculation. For past decades, RBC aggregation had been measured with various devices and methods but the results were quantified in a relative values such as AI and M, which are relative or arbitrary units. Our previous study introduced a critical shear stress measured by RheoScan, which is defined as a minimum stress to disaggregate RBCs and is known as hematocrit-independent index.

Another study with optical tweezers confirmed that the CSS is the minimum shear stress to aggregate between RBCs. Therefore, the CSS was proved to be an index to represent RBC aggregation having an absolute dimensional unit such as stress. According to clinical data, CSS for healthy people was 150–300 mPa and that for cardiovascular patients was greater than 350 mPa. Therefore, it is strongly suggested that application of CSS as a diagnostic index of hemorheology can provide a useful clinical tool.

S7-1 Stress sweep tests on whole blood clots

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Not only the time required gaining certain stiffness, but also the response of a clot to deformation or shear stress, or its time-dependent response following certain pre-stresses provides information about clot performance and stability. Such quantitative measures can be tested *in-vitro* by oscillatory rheometry, where the clot can be stressed until it breaks. The elastic limit (yielding), the breakup stress, and the kind of plastic deformation the clot undergoes between these two limits can be analyzed. Clots prepared from plasma show higher elasticity and stress hardening if platelets are depleted. Addition of platelets stiffens the clot, but also reduces its elastic limit. Such clots appear brittle and break at a lower shear stress, possibly because their dense fiber network cannot withstand large deformation. Addition of erythrocytes decreases the strain-stiffening behavior. In contrast, addition of fibrinogen to whole blood clots increases both, strain softening, and strain hardening. By the fractal dimension of the fiber network, SEM images provide important information on the morphology of clots in order to understand the rheological behavior.

S7-2 The novel discovery of amyloid formation in fibrin(ogen) and how it affects hemorheology and blood coagulation

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Most chronic diseases are accompanied by long-term inflammation. Although typically mediated by 'inflammatory' cytokines, the origin of this inflammation is mostly unclear. Our group recently presented a novel explanation for the origin of this inflammation, and suggested that it is due to a (dormant) blood microbiome; and that this can shed highly inflammatory lipopolysaccharides (LPSs) and lipoteichoic acids (LTAs). It is also known that (most) inflammatory conditions are associated with gut dysbioses, and that these may be the site of constant replenishment of this (blood) microbiome and the resulting presence of LPS/LTA. Such inflammatory diseases are also accompanied by a hypercoagulable phenotype. We have also shown directly (using 6 different methods) that very low concentrations of LPS can affect the terminal stages of the coagulation properties of blood and plasma significantly, and that this may be mediated via a direct binding of LPS/LTA to a very small fraction (1 in 10^8) of fibrinogen monomers as assessed biophysically. In particular, we have shown, that during inflammation, fibrin adopts a ß-amyloid form, and thus that fibrin(ogen) is actually an amyloidogenic protein. LPS is also known to compromise the blood brain barrier (BBB), and is frequently used to induce Parkinson's disease (PD) and Alzheimer's disease (AD) symptoms in animal models. It has also been found inside the amyloid plagues in AD brains and there is evidence that it plays important roles in Type 2 diabetes (T2D). In this symposium talk, I will

focus on the amyloid nature of fibrin(ogen) in various inflammatory conditions, its origins, and how it affects hemorheology and pathological clotting.

S7-3 Multiscale mechanics of fibrin networks

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Fibrin networks, the main structural component of blood clots, form a mechanical backbone that is highly extensible and that stiffens by several orders of magnitude when deformed. This remarkable behaviour appears to be crucial for the biological function of blood clots, which need to withstand the forces exerted by blood flow and the embedded cells. Due to the complex supramolecular structure of fibrin, the molecular origin of this mechanical behaviour remains elusive. There are different molecular mechanisms that may contribute to fibrin's extensibility. For example, the fibrin monomers constituting the fibers have specific domains susceptible to unfold upon stretching, leading to an increase of the monomer length. Another possibility involves the unstructured alpha-C regions that act as flexible chains, linking adjacent protofibrils within each fibrin fiber. I will present our recent efforts in understanding how the strain-stiffening behaviour of fibrin is linked to its molecular scale, based on small angle X-ray scattering (SAXS) and optical tweezer measurements. SAXS is an ideal method to quantify changes in the molecular packing order of fibrin fibers, and thus, the monomer length. We performed in situ SAXS measurements on fibrin networks under macroscopic shear, observing the load-induced changes in the internal structure of the fibrin fibers. To further elucidate the molecular mechanisms involved, we stretch isolated fibrin networks.

S7-4 Study of blood clotting mechanisms by rheological and electrorheological methods

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Blood clotting mechanisms were investigated using rheological and electrorheological methods at different flow conditions and under varied electric fields. This study aimed to evaluate the rate of coagulation of the formed clot by means of its rheological and electrical blood properties. Whole human normal blood preserved with CPD-A_1 solution was used for experiments. The process of clotting was initiated *in vitro* and the kinetics of clot formation, viscous properties of blood clot were evaluated at a steady flow conditions. The experiments were carried out by the rotational viscometer Low Shear 30 (LS30) Contraves as a base unit, connected with a specially developed conductivity measurement device. Blood viscosity and conductivity changes with the evolution of the coagulation process and under shear were measured simultaneously. We found that the complete coagulation process until clot formation could be divided into a stage of an initial coagulation process, following by an intensive coagulation. During the initial period a gradual increase of the apparent viscosity and a decrease of conductivity in parallel were observed. During the intensive coagulation the viscosity growth function (viscosity vs. time) at a constant shear rate has been determined and an exponential growth to 16 000 mPa · s ± 60 000 mPa · s was established at shear rates from 0.0175 s^{-1} to 1,25 s^{-1} after recalcification solution addition. Both stages were characterized by a decrease in the conductivity in parallel. The kinetics of clot formation is

dependent on the intensity of flow too. It was found that the apparent viscosity of the stored blood has been elevated during conservation. Hemocoagulation kinetics research demonstrated a decrease of the blood clotting time during storage period.

S7-5 Influence of polymeric nanoparticles on the kinetics of coagulation of conserved blood

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Interactions of nanoparticles with the blood coagulation system can be beneficial or adverse depending on the intended use of the nanomaterial. Nanoparticles can be engineered to be procoagulant or anticoagulant, or to carry drugs to intervene in other pathological conditions in which coagulation is a concern. The underlying basis of the coagulation process is plasma fibrinogen transformation to structural fibrin. As a result of the coagulation process the blood structure has been changed in complicated net formation and from here its rheological and electrical properties vary too. This study aims to provide an overview of the role of polymeric nanoparticle solutions in determining interactions with components of the coagulation system and on the kinetics of coagulation of whole human preserved blood induced *in vitro* with 2% aqueous solutions. Poly(acrylic acid) macromolecules of different architecture and molecular weight were used: (i) a new core-shell type star polymer whose interior forms hyper-branched polystyrene bearing arms of poly(acrylic acid) with molecular weight M_n = 56 920 Da and (ii) linear polyacrylic chains with average molecular weights M_n = 6000, 20000, and 225000 Da. The polymers dissolved in physiological solution with weight concentrations 1 mg/ml and 0.2 mg/ml were used for the experiments. Blood samples in the presence and absence (the control) of nanoparticles were measured using a rotational viscometer Contraves Low Shear 30 (LS 30) at a steady flow at shear rate from 0.0237 to 94.5 s^{-1} and temperature 37°C. A method, based on the measurement of dielectric properties of dispersed systems in Couette viscometric blood flow was applied and blood conductivity under the same flow conditions.

S7-6 What are conditions defining blood clot properties in some disorders?

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Background: Routinely, blood clot properties can be assayed by thromboelastography (TEG) with calculation of shear modulus (G, d/sc) as one of elastic constants. Patients and Methods: Clot firmness (CF, normal values of 3,6-8,5) was assayed in 59 patient with atrial fibrillation (AF), in 115 patients with myeloproliferative neoplasms (MPN), in 96 patients with chronic cerebrovascular diseases comorbid with Ph-negative MPNs (CCVD+MPN), in 174 patients with acute ischemic stroke (AIS), and in 96 patients followed up within 12 months after acute ischemic stroke (After AIS). Additional testing was performed for blood rheology, and with 98 biomarkers reflecting coagulation, anticoagulation, platelets, vascular wall, angiogenesis, fibrinolysis, inflammation, etc. Non-parametric statistics and multivariate analysis has performed for obtained data. Results: Gender differences in CF were not found. CF has correlated with hematocrit, WBC and blood viscosity at the range of 50 to 300 1/s. CF was the highest in AF and above the norm, the smallest in MPN, and additionally showed significant differences between groups CCVD+MPN, and AIS, and after the AIS. The influencing parameters pattern proved to be specific: blood

cells for AF, blood cells, platelets aggregation and angiogenesis factors for CCVD+MPN, clotting factors, inflammation and fibrinolysis for AIS, fibrinolysis, renal function and inflammation for 'after AIS'. These factors have jointed in CF pattern for MPN. Conclusions: We conclude that blood clot properties have differences depending on disorder. Smaller CF was typical of more severe morbidity which had a greater resistance to therapy and caused generally worse outcomes.

S8-1 Surface glycocalyx mediates tumor cell metastasis

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The glycocalyx layer on tumor cells has been associated with cellular functions that enable invasion and metastasis. In addition, aggressive renal carcinoma cells (SN12L1) with high metastatic potential have enhanced invasion rates compared to low metastatic (SN12C) cells in response to interstitial flow stimuli *in vitro*. Our previous studies suggest that heparan sulfate (HS) and hyaluronic acid (HA) in the glycocalyx play an important role in this flow mediated mechanotransduction and upregulation of invasive and metastatic potential. In our recent study, SN12L1 cells were modified to suppress HS production by knocking down its synthetic enzyme NDST1. Using modified Boyden chambers with defined interstitial flow, we showed that flow-enhanced invasion is suppressed in HS deficient cells. We also examined two prominent HSPGs on renal carcinoma cells – glypican-1 and syndecan-1 and one prominent HA receptor – CD44. We observed higher glypican-1 levels in flow dependent SN12L1 cells when compared to SN12C cells, but not syndecan-1 or CD44. Our data suggest that glypican-1 is the core protein responsible for interstitial flow sensing in metastatic cancer cells, consistent with observations in endothelial cells. To assess the ability of tumor cells to metastasize *in vivo*, parental or HS knockdown SN12L1 cells were injected into kidney capsules in SCID mice. Histological analysis confirmed that there was a large reduction (95%) in metastasis to distant organs by tumors formed from knockdown cells compared to control cells. The ability of these knockdown cells to invade surrounding tissue was also impaired. The substantial inhibition of metastasis and invasion upon reduction of HS suggests an active role for the tumor cell glycocalyx and glypican-1 in tumor progression.

S8-2 Visualization of heparansulfate proteoglycans in the glycocalyx and the perivascular space of 3-dimensional perfusable microvascular networks in microfluidic devices

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The endothelial glycocalyx is known as polysaccharide coating located at the luminal interface of the endothelium. It is indispensable from normal blood vessel function. Nonetheless its role in many biological processes is still elusive. Classical approaches to study the glycocalyx *in vitro* employ 2-dimensional cell cultures of e.g. Human Umbilical Vein Endothelial Cells (HUVECs) under fluid motion to promote glycocalyx formation. However, these approaches do not allow to study the role of the

glycocalyx in complex biological processes such as cancer cell extravasation. Here we employed an advanced methodology that allowed growing HUVEC based 3-dimensional microvascular networks with hollow lumens in hydrogel matrices. By confining the cell culture within a microfluidic device, microvessel openings formed that allowed perfusion of the microvascular network, thus mimicking physiological conditions. Perfusion of microvascular networks with specific lectins enabled staining of the glycocalyx in live and fixed samples. Co-staining with antibodies further allowed to distinguish the endothelial glycocalyx from heparansulfate proteoglycans in the perivascular space. The combination of this advanced 3-dimensional cell culture and the developed staining protocols allowed observing complex biological processes with time-lapse live confocal microscopy. Noteworthy, the trans-endothelial migration (luminal to perivascular space) of GFP-labelled breast cancer cells at sites of local glycocalyx defects was observed. Hence, we conclude that the here proposed methodology will allow to shed light on the complex role of the glycocalyx in many biological processes.

S8-3 Integrin-mediated adhesion is lipid bilayer and glycocalyx dependent

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Integrins are heterodimeric transmembrane proteins that facilitate that initial adhesion of cells to surfaces, nucleate the assembly of complex force-sensing focal adhesions, and are the principle ways cells communicate mechanically with the extracellular matrix. To test for bilayer sensitivity of integrin adhesion, we manipulated human aortic endothelial cell membrane properties using benzyl alcohol, which we had shown previously using idealized membranes and molecular dynamics simulations, thins liquid ordered lipid domains and subsequently measured RGD-beta1 integrin affinity using optical trap force spectroscopy and diffusion coefficients using fluorescence correlation spectroscopy (FCS). BA caused an increase of nearly 20% of RGD-integrin affinity and transitioned from single to double valency when contact time of optically trapped bead with cell was 1.5 seconds. These results coincided with dimerization of integrins determined using FCS. This increase in valency was abolished when cells were treated with heparinase, an enzyme that digests away surface glycocalyx. These results are consistent with a new concept of integrin-mediated adhesion in which the glycocalyx creates opportunity for nascent focal contact formation that is abolished when glycocalyx is uniformly stripped from the cell. BA caused an increase in focal-adhesion-kinase/paxillin-positive peripheral adhesions and a subsequent reduction in migration speeds. We conclude that the glycocalyx and the membrane participate cooperatively in the initial adhesion of integrins to extracellular matrix and, thus, play a synergistic role in the earliest events of mechanotransduction.

S8-4 Coupled dynamics of blood flow and endothelial glycocalyx: A large-scale molecular dynamics study

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The atomic events inside the endothelial glycocalyx layers are intimately bounded with the glycocalyx-related diseases, like in some cardiovascular or renal conditions. To reveal the dynamics of both flow

and glycocalyx, an all-atom flow/glycocalyx system including 5.8 million atoms is constructed with the bulk flow velocity in the physiologically relevant ranges for the first time. The flow/glycocalyx system is simulated using a large-scale molecular dynamics method. Flow dynamics, including velocity and shear stress distributions, and corresponding statistics in the presence of the glycocalyx are presented and discussed. Meanwhile, comprehensive dynamic behaviour of the glycocalyx, particularly the dynamics of the sugar chains, is observed in response to blood flow. Based on the conformational changes of the glycocalyx constituents, potential force transmission pathways are discussed, which provides new insight into the mechanism of mechanotransduction of the glycocalyx. The molecular dynamics method used in this research provides a new angle to understand the behaviour of the glycocalyx at an atom-scale, which contributes to our knowledge of pathologies of cardiovascular and renal diseases.

S9-1 Early stage of essential hypertension monitoring

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We searched for differences in the RBC membrane skeleton structure and O_2 membrane permeability between RBCs from patients with both essential arterial hypertension and hypercholesterolemia, from patients having only hypercholesterolemia and from healthy donors. The topography of RBCs and the content of various hemoglobin forms (Hb) were detected using atomic force microscopy and Moessbauer spectroscopy, respectively.
We found that the membrane skeleton of RBCs from healthy donors displays a well-known honeycomb pattern, whereas in patients with essential hypertension and/or hypercholesterolemia, who had never received anti-hypertensive therapy, it displays a corncob pattern. Moessbauer results indicate an impaired oxygen release by Hb in RBCs of patients with hypertension under low oxygen pressure which if present *in vivo* may cause hypoxemia and, in turn, further increases of blood pressure.
[1] M. Kaczmarska, M. Fornal, F. H. Messerli, J. Korecki, T. Grodzicki, K. Burda Cell Biochem Biophys DOI 10.1007/s12013-013-9613-9.
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S9-2 Label-free methods in diagnostics and prognostics of malignant melanoma

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Malignant melanoma is one of the most aggressive type of the skin cancer, which can metastasize to every organ in the human body. Thus, an early and proper melanoma diagnosis influences significantly

the therapy efficiency. The melanoma recognition is still difficult, and generally, relies on subjective assessments. The technological development of label-free methods such as atomic force microscopy (AFM) or quartz crystal microbalance (QCM) has opened new perspectives for melanoma and its biomarker detection. We have compared the recognition of mannose type glycans in melanocytes (HEMa-LP) and melanoma cells originating from the radial growth phase (WM35) and from lung metastasis (A375-P). The glycosylation level on their surfaces was probed using lectin concanavalin A (Con A). The interactions of Con A with surface glycans were quantified with both AFM and QCM techniques that revealed the presence of various glycan structural groups in a cell-dependent manner. The glycans present on WM35 cell surface are rather short and less ramified while in A375-P cells, Con A binds to long, branched mannose and glucose types of oligosaccharides. The results might be further used in the development of a biosensor for the sensitive screening of malignant melanoma cells. This methodology may also allow the study of the effects of new substances on the inhibition of epithelial-mesenchymal transition to develop the procedure that allows the characterization of new therapeutic agents for primary and advanced melanoma.

S9-3 Advanced vibrational imaging techniques to aid clinical research

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Modern molecular imaging modalities based on chemical contrast provide a unique set of tools available to a clinical researcher. These include infrared and Raman spectroscopy techniques also coupled to Atomic Force Microscopes allowing to probe the samples on scales ranging from a few nanometers to centimeters. A short presentation of IFJ PAN Equipment capabilities and a description of a few relevant examples will be made, starting with a most recent work on erythrocyte oxygenation status in human blood. Here, Raman spectroscopy was applied to obtain unique information about the heme-oxygenation levels in red blood cells in the context of early hypertensive status, also called prehypertension. The next example covers the opportunities of FT-IR imaging in aiding histopathology of pancreatic cancer. This research was performed using equipment purchased in the frame of the project co-funded by the Malopolska Regional Operational Program Measure 5.1 Krakow Metropolitan Area as an important hub of the European Research Area for 2007–2013, project No. MRPO.05.01.00-12-013/15. TPW is supported from the "Pancreatic cancer comprehensive histopathology based on IR chemical imaging" project, which is carried out within the Homing program of the Foundation for Polish Science co-financed by the European Union under the European Regional Development Fund. It was also supported by the Collegium Medicum of the Jagiellonian University project K/ZDS/007195.

S9-4 Effect of dietary carotenoids on erythrocytes from diabetic patients: A spectroscopic study

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Carotenoids (Crts) are structurally and functionally a very diverse group of natural pigments of isoprenoid type. They are synthesized by all organisms capable of conducting photosynthesis. To date, ~700 Crts have been described, of which only ~50 become constituents of the human diet, and ~20 is found in human blood and tissues [1]. Crts are known to be efficient physical quenchers of $^1O_2$ and scavengers of other reactive oxygen species (ROS). They also act as chemical quenchers undergoing irreversible modifications [2]. Their antioxidant activity is of special significance to human health [3]. Uncontrolled overproduction of ROS may lead to losing antioxidant-ROS balance resulting in "oxidative stress", a critical factor of the number of pathogenic processes of chronic diseases. Diabetes is recognized as the world's fastest growing chronic condition related to elevated blood glucose level. It considerably increases the risk of cardiovascular disorders, eye and foot failure, affects urinary tract and mental health. On the cellular level, it was shown to modify properties of erythrocyte's membranes. Here, we present the results of experiments taken on isolated erythrocytes from healthy and diabetic donors. The cells were subjected to Crt treatment in the presence or absence of exogenous ROS. To monitor cellular response UV-VIS absorption and Mössbauer spectroscopies were applied, delivering information on i.a. the states of hemoglobin and its ability to bind oxygen.

1. J. Nutr. 1989, 119, 101. 2. Biochim. Biophys. Acta 2005, 1709, 1. 3. Nutrients, 2014, 6, 466.

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S10-1 Dynamic contrast enhanced ultrasound (CEUS) of tissue transplants

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Early detection of reduced microvascularization of tissue transplants is the mean diagnostic point for the survival rate of the tissue transplants. CEUS is the only imaging method for evaluation of dynamic changes of microvascularization of soft tissue transplants monitoring during surgery and for the postoperative follow up. Preoperative panning of tissue transplants: Capillary microvascularization of the margins of the free flaps visualized by CEUS is important for early detection of critical microvascularization. Evaluation by perfusion software enables determination of time to peak (TTP), relative blood flow (rBF) and relative blood volume (rBV) and evaluation the critical micro vascularization in the different layers of the free flaps with rBV less than 200 rU. The main limitation for evaluation of flap perfusion is the fact that CEUS does not allow the continuous monitoring of the whole flap after one bolus injection by time intensity curve analysis. But perfusion imaging in the center from early arterial phase (15–45 sec) up to venous phase (1 min) in combination with sweep technology from the center to the margins in the venous and late venous phase (2–5 min) allows the evaluation of particularly necrosis after one bolus injection up to capillary microvascularization. Recommended use for CEUS are the post-operative monitoring with TIC analysis and color coded perfusion imaging for evaluation critical perfusion by evaluation relative blood volume, early detection of partial necrosis and as only dynamic imaging tool for monitoring osteocutaneous flaps with metal reconstructions and planning, monitoring and realization of new kinds of soft tissue reconstructions, tissue transfer for wound healing processes and new kinds of bone tissue transfer.

S10-2 Assessment of the glycocalyx

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The endothelial glycocalyx (EG) lining the endoluminal surface of the capillaries has been proposed as a key component of the microcirculation and a major player in microvascular pathology. Recent advances in the understanding of its physiological role and clinical significance have been made upon the development of methods allowing EG assessment in clinical medicine. Laboratory methods can assess the amount of EG damage by measuring levels of its degradation products (e.g. syndecan-1, heparan sulphate and hyaluronan sulphate), mostly in the plasma, however, their physiological turnover disqualifies them from being the reliable index of EG damage. At the bedside, *in vivo* video microscopy tools technologies (e.g. Side-stream Dark Field imaging technology) allow indirect assessment of EG thickness in sublingual microcirculation by measuring the penetration extent (called Perfused Boundary Region) of flowing red blood cells into the EG.

S10-3 Automated vs. visual video analyses - Where is the future?

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Microcirculatory alterations are a common etiologic factor in many acute and chronic disorders with significant morbidity and mortality. Due to the small dimensions of the microcirculation, it can only be studied by microscopy or similarly sophisticated techniques. At present, monitoring of the microcirculation in patients is not standard practice, even though technology exists that allows clinicians the ability to observe the microvasculature at the bedside in real time. To quantify microvascular changes, the microcirculatory video recordings need to be analyzed manually, automatically with the help of imaging software, or using recently developed visual scores. Initially, there was only complex, time-consuming, and semi-automated software available to analyze the microcirculation. More recently, software has become available for automated analysis of the microcirculation. However, few studies comparing the accuracy of the automated software with the standard, semi-automated software have been conducted. As a result, the automated method of analysis has not gained traction as the new standard of microcirculation video analysis. Therefore, semi-automated analysis using software remains the gold standard of microcirculation analysis. Multiple barriers to clinical use exist with using software analysis (i.e., cost, delayed results, and expertise with using the software). Alternative, more practical approaches to microcirculation video analysis are needed to overcome these barriers. Visual analysis offers a solution to these barriers by providing a fast and inexpensive method to quantify certain microcirculatory parameters.

S10-4 Is sodium a link between endothelial glycocalyx and microcirculation?

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Sodium is closely related to fluid homeostasis of the body that can be divided into body compartments. One of these compartments is newly established and so far, only slightly understood: the endothelial glycocalyx (EG). EG represents intravascular sugar based endothelial lining creating a three-dimensional mesh. Due to its nature it is a fragile structure degrading in critically ill. Beside albumin and many other molecules, the EG binds significant amount of sodium (up to 7g), which is responsible for its correct conformation and optimal rheological properties of blood in the microcirculation. Plasmatic concentration of sodium, dietary intake and binding to the EG determines the correct function of the microcirculation. Between EG and endothelial cells there is a tiny space called the subglycocalyx. This area is occupied by solute free serum and directs the filtration forces across the capillary barrier (revised Starling principle). Hypervolemia and hypernatremia are one of the etiologies of EG damage. By releasing of atrial natriuretic peptide, the EG is degraded and the filtration equilibrium is distracted. Hypernatremia leads to inhomogeneous and stiff EG compromising release of NO and smooth muscle cell relaxation within the vascular wall. This is the reason high dietary intake of sodium has an impact on arterial hypertension. Moreover, the red blood cell glycocalyx is also influenced by natremia and in the case of hypernatremia its glycocalyx gets disrupted as well as leading to a compromised microcirculation. Giving intravenous fluids with high sodium content is inherent to our clinical practice. The impact of our daily clinical practice has yet to be determined. For now, it is more than obvious that sodium is a link between microcirculation and EG.

S11-1 RBC deformability: An exquisite homeostasis

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A large body of literature shows that red cell deformability is under the influence of the surrounding milieu. A comprehensive scheme of all this regulation is still missing. In particular, it will be important to delineate reversible changes in red cell rigidity that may be involved in physiological regulation, from the irreversible evolution toward cell death that occurs during eryptosis. For example, physiological reversible red cell rigidification during exercise has probably a completely different meaning compared to pathologic alterations of red cells observed in diseases such as diabetes or sickle cell disease. The major regulators of red cell deformability are the clearance of rigid red cells by the spleen, and the physicochemical characteristics of the surrounding milieu such as pH, osmolality, oxidant stress and thermal injury. An environment containing proteins (albumin) is required to avoid shape alterations such as echinocytosis. Divalent cations (magnesium, zinc, Fe + +), as well as circulating molecules such as lactate, ketone bodies, and various hormones modify red cell deformability. Among them special attention has been given to purinergic and nitric oxide (NO) signaling, that are probably important regulators of red cell rheology. Blood lipid concentrations, but also meal composition (caloric and carbohydrate intake) are correlated with increased RBC rigidity. All that suggests that red cell deformability is a tightly regulated property sensitive to many factors. It is likely that some of these influences are involved in complex regulatory loops aiming at maintaining homeostasis, while others represent cell damage leading to erythrocyte destruction and removal from blood.

S11-2 Eryptosis or the death of a rigidified erythrocyte

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The hallmark of cardiovascular disease, including type 2 diabetes, is (systemic) inflammation, with an accompanying upregulated pro-inflammatory profile, characterized by circulating pro-inflammatory molecules, hydroxyl radicals and oxidative stress. These molecules and processes are key role players during inflammation, and results in both pathological clotting and biochemical changes to both erythrocytes (RBCs) and platelets. RBCs are extremely vulnerable in the presence of circulating inflammagens. However, notwithstanding this vulnerability, RBCs are exceptionally adaptable and react quickly to stabilize their membranes and structure in the presence of e.g. hydroxyl radical mopping agents (including treatment regimes). In this symposium, I will focus on using structure and function of RBCs and show their importance as health indicators. RBCs have a highly specialized and organized membrane structure, which interacts and reacts to inflammatory molecule insults, and undergo programmed cell death, like apoptosis, known as eryptosis. Eryptosis in various cardiovascular diseases will be discussed, with special reference to membrane changes, aberrant rheology and pathological clot formation. Techniques to study eryptosis like flow cytometry, confocal microscopy and ultrastructural studies will be discussed. In conclusion, I will suggest novel ways how RBCs may be employed in an *in vivo* cell model system, for the early detection of the presence of inflammation and to track disease status, as well as compliance of patients to treatment regimes.

S11-3 Erythrocyte deformability under nitric oxide influence

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It is well evidenced that the degree of erythrocyte deformability changes as a consequence of alterations on either its membrane properties, or shape or internal composition. Erythrocytes are blood components acting as oxygen and nitric oxide (NO) sensor in the microcirculation. The mobilization of NO between its scavenger molecules S-nitrosohemoglobin, nitrosylhemoglobin, S-nitrosoglutathione and the NO efflux from erythrocyte are under dependence of type of several signal molecules and respective receptors and a variety of activators, or inhibitors of biomolecules belonging to the signaling transduction pathways. We will described the influence of NO donors or of internal or external stimuli which changes the red blood cells NO efflux, NO metabolism, and protein phosphorylation degree and redox thiol status on erythrocyte deformability. All data evidence the inclusion of NO as another influent parameter on erythrocyte deformability.

S11-4 The sickle cell: Far more than a rigid erythrocyte

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Sickle cell anemia (SCA) is a genetic disease characterized by the presence of abnormal hemoglobin (HbS) that polymerizes under deoxygenated conditions causing a mechanical distortion of red blood cells (RBC). SCA patients are characterized by a severe reduction in RBC deformability, which contributes to the occurrence of frequent painful vaso-occlusive crises. In addition, this reduction in RBC deformability is at the origin of the increased cell fragility leading to enhanced hemolysis. While the high hemolytic rate explains why patients are anemic, recent studies demonstrated a key role of hemolysis in the development of vascular dysfunction. In addition, we reported that increased oxidative stress in SCA decreases the bioavailability of nitric oxide and promotes the formation of peroxinitrite, which in turn participates to the reduction of microvascular reactivity. Because the vascular reactivity is reduced, patients with the highest blood viscosity may develop frequent vaso-occlusive crises. More recently, we observed a negative correlation between sickle RBC deformability and the level of circulating microparticles (MPs) released by sickle RBCs. MPs are phospholipid microvesicles with a diameter ranging from 100 to 1,000 nm that are derived from the cytoplasmic membrane of cells submitted to various stresses. We found that the increased oxidative stress in SCA could be at the origin of the important release of MPs from sickle RBCs. In turn, these MPs, known to express a high amount of phosphatidylserine and to carry heme, participate to the genesis of vascular dysfunction in SCA. In conclusion, RBC physiology is severely impaired in SCA, which leads to chronic vascular dysfunction.

S11-5 Signaling pathways in regulation of RBC microrheological properties by catecholamines

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In the circulation, RBCs are in contact with biologically active substances dissolved in plasma. Traditionally, RBCs have been considered as simple reservoirs for oxygen transportation, but now it is evident that erythrocytes have a number of signaling molecules and participate in regulatory processes, which integrate body functions. Catecholamines act as stress hormones ensuring an effective adaptation to environmental factors, by regulating oxygen transport and cell metabolism. They may modify blood flow in nutritive capillaries under stress by alteration of red blood cell aggregability and deformability. Red blood cell microrheological properties connected with oxygen transport efficiency may be regulated through activation of cellular molecular signaling pathways. Likely regulatory pathways causing rheological responses in RBC include: extracellular ligands (hormones, prostaglandins), membrane-receptors coupled with G-proteins, adenylyl cyclase, cAMP, protein kinase A and phosphorylation of membrane proteins (band 3, band 4.1). Specificity of catecholamine action is proved by the experimental evidences of the presence of alfa- and beta-adrenoceptors on RBC membrane and dose-dependent changes of erythrocyte aggregation within elevation of adrenalin concentration. Activation of ligand specific receptors induces local increases in cAMP that are regulated by specific phosphodiesterases which are

associated with individual signaling pathways. The subcellular location of PDEs is critical for coupling these enzymes to specific signal transduction pathways. Our experimental data have demonstrated the involvement of ubiquitous second messengers – cAMP and ionized calcium – in the regulation of RBC aggregability and deformability. Work was supported by RFBR grant 18-015-00475.

S11-6 Complete dynamics of erythrocytes in shear flow: The story behind the term of deformability

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Physiological blood flows being shear-dominated, the dynamics of an erythrocyte subjected to an external shear flow constitutes one of the basic configurations for the understanding of hemorheology. In this configuration, the deformability of the red blood cells can be probed by applying an external shear stress and measuring the cell's deformation, which is the principle of ektacytometry, for instance. However, the term of deformability often masks the complexity of the red blood cell mechanics. In particular, both the viscosity of the cytoplasm and the stiffness of the membrane, resist external stresses and prevent red blood cell deformation. Thanks to recent numerical, theoretical and experimental works, we will review the different motions of a red blood cell under shear flow to identify how the properties of the membrane and of the cytosol control its dynamics. We will notably show how the term deformability includes a variety of mechanical properties that need to be unraveled to understand the motion of erythrocytes and blood rheology. In particular, we will show that membrane and cytoplasm properties may have similar effects on the dynamics at low shear stress. However, at high shear stress, two different regimes appear depending on the ratio of viscosity between the internal and the external media. We will discuss the consequence of these recent findings on our understanding of blood shear-thinning at high shear rates, where aggregation effects are negligible.

S12-1 The "tipping point" of mechanical stress on erythrocyte biology

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Mechanical stresses are important stimuli for many biological processes. Such stresses especially impact blood: its classic shear-thinning viscosity profile results, in part, from disaggregation of red bloods cells (RBC), and cellular deformation, that are each induced by mechanical forces. While it is thus well-known that shear is important for governing blood rheological processes, it is becoming increasingly recognized that other active processes – e.g., ion flux, free radical production – are sensitive to shear. Nitric oxide, for example, is produced in RBC in response to shear, with resultant augmentation of cell deformability over that induced by external forces. Increased attention is now being directed to exploring the interactions between the level and duration of shear exposure on RBC physiology. In general, it appears that the

physiological shear stress range (0–10 Pa) induces beneficial responses in RBC. Once shear exposure is supraphysiological there appears to be three primary domains that characterize blood responses: i. supraphysiological, but below the "sub-hemolytic threshold" tends to have no obvious permanent and detrimental impact on RBC function; ii. above the sub-hemolytic threshold, but less than the "hemolytic threshold" tends to result in impaired RBC deformability, and alterations to cell biochemistry, and; iii. above the hemolytic threshold, which induces RBC rupture. Accumulating evidence indicates that shear exposure within the second domain of supraphysiological shear exposure induces RBC dysfunction that likely contributes to widespread impairments in the microcirculation. Understanding these effects are increasingly important given increased dependence on mechanical circulatory support that operate above the sub-hemolytic threshold.

S12-2 Testing the sensitivity of red cell fragmentation and deformability measurements for shear-mediated mechanical damage

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Under physiological conditions red blood cells (RBCs) can withstand shear stresses (SS) up to 150 Pa, without hemolysis, and have the ability to fully recover back to its original shape. However, alterations in membrane stability may significantly reduce this hemolytic threshold and decreased stability can lead to cell fragmentation. In this study; we focused on: a) evaluating the distribution and the magnitude of the force applied in the ektacytometer via computational fluid dynamics (CFD), b) how supraphysiological SS affects RBC fragmentation and deformability parameters in two damage models (oxidative damage and metabolic depletion). Subsequently, various levels of shear stress (0-100 Pa) were applied to the RBC in a Couette-type shearing system for 300 seconds. RBC deformability was measured immediately following shear stress exposure via ektacytometry. RBC fragmentation was determined using a cell counter system (Beckman Coulter, USA). In each sample, the number of cells in the range of 20–60 fL was divided by the total number of cells and multiplied by 100 to determine the percentage of fragmented cells. The CFD simulations showed that 29% volume percent of the suspension undergoes non-uniform shear stress at the bottom part of the ektacytometer. While the percentage of fragmented cells increased at all shear stresses applied in the group of oxidative damage, it was elevated at 80–100 Pa shear stress in the metabolic depletion group. RBC deformability changes were somewhat similar to the fragmentation rates in these groups. In summary, the subhemolytic threshold and fragmentation measurements are useful tools for close monitoring of shear-mediated mechanical damage and sufficiently sensitive to the damage models employed in the present study.

S12-3 Discussion about high shear stress induced erythrocyte's damage and lysis -Interpretation of hemolysis in cardiovascular devices based on our visualized erythrocytes' behaviors

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It is well known that high shear stress would be the main cause of hemolysis in cardiovascular devices. However, the exact process of erythrocyte damage leading to lysis is still under discussion. In order

to elucidate such high shear stress induced hemolysis, we have successfully prototyped a microscopic observation test setup that incorporates a counter-rotational flow field mechanism between top cone and bottom plate following the previous test setup developed by Dr. Fischer at al. Our originality is its availability to generate extremely high shear stress over 200 Pa. Erythrocytes were diluted in high viscosity polyvinylpyrrolidone phosphate buffered saline solution. This suspension was exposed to extremely high shear stress using our shear device. We observed in such flow visualization tests that even though all the intact erythrocytes showed excellent ellipsoidal shapes at the beginning, as time progressed a portion of them started to exhibit a cyclically waving shape that further transformed into abnormal dissymmetric shapes. Furthermore, they tumbled and fragmented. Additionally, cell destruction through cell-cell collisions was also observed. Taking these aspects into consideration, we speculate that high shear stress had induced localized membrane damage and less deformability of erythrocytes that resulted in their abnormal asymmetric shape and the occurrence of their tumbling behavior. Under such abnormal cellular behavior, maintenance of the Couette flow became quite difficult and it induced disturbances in the extra-cellular flow field. Under such conditions, cell-cell collisions may occur more easily, leading to accelerated hemolysis. Similar phenomena discussed here may happen within clinical cardiovascular devices.

S12-4 Mechanical sensitivity of blood in sickle patients on chronic blood transfusion – Understanding erythrocyte exposure to chronic physiologic shear vs. chronic supra-physiologic but sub-hemolytic shear stress

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Background: Sickle cell disease (SCD) is a hemoglobinopathy where deoxygenated hemoglobin S polymerizes, leading to rigid red blood cells (RBC), and thus increased sensitivity to mechanical stress. Survival is improving in SCD but chronic cardiovascular disease is increasing, potentially necessitating procedures requiring cardiopulmonary bypass. Transfusion therapy acts as primary and secondary prevention of ischemic stroke in SCD. Whether blood transfusion alters the mechanical sensitivity of RBC to sub-hemolytic shears is unknown. Aims: We hypothesized individuals with SCD undergoing chronic blood transfusion would have improved sensitivity to shear, compared with patients not on transfusion therapy. Methods: RBC from individuals with SCD not receiving and receiving chronic simple-transfusion were conditioned to shear for various duration. Deformability of RBC was immediately measured after each. Comparisons were made with healthy controls. A surface-mesh was interpolated to determine the effect of blood transfusion on RBC mechanical sensitivity. Results: Impaired mechanical sensitivity to prolonged supra-physiologic shear was observed in SCD RBC compared to control. Longer shear exposure over the supra-physiologic shear range was required to impair RBC in the transfused group compared with non-transfused. When exposed to prolonged shear stress in the physiologic range, mechanical sensitivity improved in the transfused group. There was no improvement in the non-transfused group. Conclusion: Simple transfusion may be an effective method to improve the mechanical sensitivity of RBC in SCD. Given SCD is listed on the current exclusion criteria for popular ventricular assist devices, these findings may affect strategies for cardiovascular therapies; surgical and otherwise.

S12-5 Drag-reducing polymer effects on macro- and microcirculation

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Drag-reducing polymers (DRPs) are long-chain soluble polymers with fairly linear molecular structure that have been discovered to significantly reduce flow resistance in a developed turbulent flow in pipes, thus increasing flow rate at a constant pressure gradient or decreasing pressure at a constant flow rate when added to the flowing fluid at minute concentrations (Toms effect). The flow conditions associated with the Toms effect do not occur in blood circulation through the vascular system. However, many studies have shown that IV or IP administration of DRPs to experimental animals produce significant beneficial effects on blood circulation increasing tissue perfusion, tissue oxygenation and other hemodynamic phenomena. This paper will review major results obtained over the last decade *in vivo* in various animal models and *in vitro* experiments which employed DRPs as blood additives. Furthermore, the potential mechanisms behind the DRP phenomena in blood circulation including their effects on the traffic of RBCs and other blood cells will be discussed.

S13-1 Critical analysis of CEUS examinations of the liver in an interdisciplinary ultrasound department

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Objective: The examination of unclear liver lesions with contrast enhanced ultrasound (CEUS) has already found widespread use in daily practice. The aim of this study was to assess the diagnostic certainty of CEUS in comparison to other modalities (CT/MRI) in an interdisciplinary ultrasound department. Methods: Between January 2013 and August 2018 in total 138 CEUS examinations of of the liver were analysed. CEUS was performed by one experienced sonographer after bolus injection of 1.0 up to 2.4 ml sulphur hexafluoride microbubbles having used a high-end ultrasound device (LOGIQ E9, GE, USA) and multifrequency probes with Contrast Harmonic imaging. The data collection took place retrospectively on the basis of the patient files with the permission of the Ethical Committee of the University of Regensburg. In 79% of cases findings of CT or MRI were available for the comparison with CEUS. A histological examination as gold standard was available at 39% and was included in the evaluation. The final diagnosis was determined by the synopsis of all examinations, the conducted therapy according to the medical letters and follow-up examinations. Results: The median age of all patients was 62 years, with a known malignant disease in 78% of cases and a known liver cirrhosis in 29%. CEUS described solid lesions in 112 cases (97 malignant lesions, 15 benign lesions), in 26 cases no tumor was detectable. The existence of a tumour was diagnosed by CEUS correctly in 95% of cases (Sensitivity 97,9%, Specificity 87,8%, PPV 95%, NPV 94,7%). Restricted ultrasound conditions (e.g. obesity, meteorism) were present in 38% of cases with a slight decrease of the diagnostic accuracy from 95,6% to 92,0%. The combination with one or two modalities raises the diagnostic accuracy (94,8% vs. 92,4% vs. 100%). Conclusions: CEUS is a safe and indispensable diagnostic in tumour evaluation of the liver. Due to its favourable side-effects, CEUS should be used early in the diagnostic process.

S13-2 VTIQ and VTQ in combination with B-mode and color Doppler ultrasound improve classification of salivary gland tumors, especially for inexperienced physician

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While ultrasound is the method of choice for preoperative evaluation of masses of the parotid glands, existing methods do not allow for definite differentiation between the most common benign and malignant tumors. The aim of our study was to evaluate if acoustic radiation force elastography, Virtual touch quantification (VTQ) and imaging quantification (VTIQ) are beneficial in preoperative evaluation of parotid tumors. We investigated the parenchyma of 82 parotid glands, eight lymph nodes of healthy volunteers and 41 tumors of the parotid gland via ultrasound, color Doppler ultrasound, VTIQ and VTQ elastography. Each examination was documented with pictures and videos, which were viewed by twelve independent examiners with various levels of experience. After viewing the B-mode and Doppler images, each examiner predicted whether the mass was benign or malignant. For benign tumors, each examiner also made a forecast for the tumor type. Subsequently, each examiner also viewed the VTIQ and VTQ elastography images and reevaluated the initial predictions of malignancy and tumor type. In benign tumors, the sensitivity was 76% with only B-mode and color Doppler sonography and increased to 83% with the addition of VTIQ and VTQ, where the specificity also increased from 34% to 40%. Similarly, in malignant tumors elastography improved sensitivity from 34% to 40% and specificity from 76% to 83%. VTQ and VTIQ in combination with classical ultrasound examination provides additional data that improves the capability to distinguish between benign and malignant tumors by increasing both the sensitivity and specificity of the ultrasound examination.

S13-3 CEUS perfusion imaging after ablation treatment in patients with prostate cancer: First results

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With the rising number of percutaneous ablation therapies in prostate cancer there is a need of reliable diagnostics after the intervention to differentiate between reactive changes and tumor.
To assess the success of percutaneous ablation therapies for prostate cancer using transabdominal CEUS with parametric imaging. Retrospective reading of perfusion analysis for 50 patients who were treated with IRE for prostate cancer. CEUS was performed after bolus injection of 1.5-2.4 ml of sulfur-hexafluoride microbubbles. DICOM loops were continuously acquired for 1 minute and were stored digitally in PACS. 8 mm regions of interest were placed clockwise at the margins of the ablation defect and in the center. Additionally parametric images were calculated. For the evaluation of the success after percutaneous treatment the perfusion results were compared to the follow-up control after 6 months with CT and MRI and CEUS. 37 patients were successfully treated, meaning there was no local recurrence after 6 months. 13 patients still showed remaining tumor. In cases of remaining tumor there was a dynamic early nodular hypervascularisation with a fast and high wash in. The corresponding parametric images showed nodular red and yellow pseudo-color shades. Using transabdominal CEUS, parametric imaging and TIC analysis, a critical analysis of post-ablation defects in prostate cancer is possible. With the help of pseudo-colors, remaining tumor-vascularization can be detected.

S13-6 New horizons for kidney imaging: Dynamic microvascularization in contrast-enhanced ultrasound (CEUS)

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Objective: In nephrology, ultrasound diagnostics plays an important role as the method of further investigation following an initial examination. The aim of this study was to identify the indications for CEUS in renal imaging in an interdisciplinary ultrasound department. Methods: Between September 2014 and July 2016, 102 CEUS examinations of the kidney in 82 patients were analysed regarding the indication for ultrasound. CEUS was performed by one experienced sonographer and a nephrologist after bolus injection of 1.0 up to 2.4 ml sulphur hexafluoride microbubbles having used multifrequency probes with Contrast Harmonic imaging. Results: CEUS of the kidney was performed in patients between 20 and 87 years. 44% of the patients had a stage 3 of chronic kidney disease and higher, 38% of the patients had undergone a renal transplantation. No adverse events were observed. 54% of the examinations were requested by nephrologists, the remaining by surgeons, oncologists or gastroenterologists. In 47% of the cases the objectives were the evaluation of complex renal cysts, in 31% the analysis of kidney perfusion, in 19% the assessment of solid renal masses. The remaining were perirenal tumours (2%) and infection (1%). Conclusions: CEUS is a good diagnostic alternative for patients with impaired renal function, complicated cysts, infections, solid renal lesions and after renal transplantation. The visualization of the microcirculation on a capillary level is crucial in the assessment of kidney diseases.

S14-1 Effect of physical environment on cell migration using microchannel device

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Cell migration plays an important role in many physiological and pathological processes such as morphogenesis, wound healing, and tumor metastasis. Although the majority of such events occur with cells moving as a group, called collective cell migration, the mechanism of collective cell migration has not been well understood. Since it is known that mechanical environment may affect cell behavior the aim of this study is to focus on the effect of substrate rigidity and anisotropy on cell migration behavior. A PDMS-based microfluidic device was fabricated, which consists of microchannels with micropillars of circular cross-section to serve different substrate stiffness and micropillars of ellipsoidal cross-section to serve anisotropic substrate stiffness. Cell migration was initiated when the microchannels were backfilled with the medium. A set of microscopic images of the top of micropillars including cells and the bottom of the same micropillars was obtained every 10 min up to 24 h. Cellular traction forces were calculated from the deflection of micropillars and the spring constant of micropillars through an image analysis. After the onset of cell migration experiment, the cells migrated into microchannels with micropillar substrates throughout a 24 h experimental period. It was demonstrated that cells consisting of collective cell migration generated traction forces with different magnitudes and directions depending on their relative positions, possibly reflecting positional differences in mechanical roles within a moving cell group.

It was also found that the cells migrated faster with increasing stiffness of the substrate and that the cells migrated faster in the direction of increased substrate stiffness.

S14-2 Protein kinase Cα translocation in endothelial cells in response to mechanical stimulus

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Mechanical wounding of an endothelial monolayer induces an immediate Ca^{2+} wave. Several hours after mechanical wounding, the denuded area is covered by endothelial cells (ECs) that migrate to the wound. This migration process is closely related to protein kinase Cα (PKCα), a Ca^{2+}-dependent protein that translocates from the cytosol to the cell membrane. Because the cells adjacent to the wounded area are the first to migrate into the wound, we investigated whether mechanical wound induces PKCα translocation in cells adjacent to mechanically wounded ECs. We monitored Ca^{2+} dynamics and PKCα translocation simultaneously using fluorescent microscopy. For this simultaneous observation, we used Fura-2–acetoxymethyl ester to visualize Ca^{2+} and constructed a Green fluorescent protein-tagged fusion protein to visualize PKCα. Mechanical wounding induced an immediate Ca^{2+} wave in the endothelial monolayer that emanated from the mechanically wounded cells to neighboring cells. Almost concurrently, PKCα in cells adjacent to the wounded cells translocates to the cell membrane then accumulates at the periphery of cells near the mechanically wounded cells. We hypothesize that this PKCα translocation is induced (1) by intercellular communication, such as paracrine signaling and gap junction, or (2) by mechanical stress, such as unloading of cell-cell tension. When intercellular communication was inhibited, the directional translocation occurs. On the other hand, it did not occur when the mechanosensitive channel was inhibited. Our results indicated that the implication of PKCα translocation in the Ca^{2+} signaling pathway in response to mechanical stress in ECs.

S14-3 Hydrostatic pressure-induced DNA breaks in chondrocytes and its relationship with chromatin architecture

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Introduction: Hydrostatic pressure (HP) promotes chondrogenesis in development by accelerating differentiation from stem cells to chondrocytes [1]. On the other hand, HP is suggested to induce harmful responses such as DNA breaks and apoptosis [2]. In this study, we hypothesized that HP-induced DNA break/repair plays as a critical biomechanical process to screen specific genes related to chondrocytic differentiation. Specifically, we focused on chromatin dynamics under mechanical force that characterizes gene stabilities [3].
Methods: Mice-derived cell line for chondrocyte progenitor cells (ATDC5), were seeded on glass bottom dishes, which were packed in plastic bags and were loaded under cyclic HP with a peak value of 1 MPa and with a frequency of 0.3 Hz. After pressurization, immunostaining for gamma-H2AX, a histone H2AX phosphorylated near double-strand DNA breaks, was performed. Images for DAPI were binarized and the intensity for gamma-H2AX in the corresponding area was analyzed. Results:We observed significant DNA breaks in more than 20% of ATDC5 cells. Remarkably, we found that cyclic HP (Peak value: 1 MPa)

induced more DNA breaks than constant HP (10 MPa). By employing confocal microscopy, we also found that regions of compacted DNAs with high intensity for DAPI, avoided from DNA breaks under cyclic HP. Discussion: Here we showed that cyclic HP induced DNA breaks in ATDC5 cells. Chromatin dynamics would determine which genes are damaged and conserved under HP. We are going to analyze chromatin dynamics by employing chromatin conformation capture method and gene expression.

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S14-4 In situ, fluorescence lifetime-based measurements of cell membrane micromechanics

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The mechanical moduli of lipid bilayers govern cell adhesion, endocytosis, ion channel conductivity, and organization of signaling complexes. We have developed a new technique to measure bilayer moduli using area per lipid and its variance from the stretched exponential distribution of fluorescence lifetimes of 1'-dioctadecyl-3,3,3'3'-tetramethylindocarbocyanine perchlorate (DiI). The mean and variance of lifetime and corresponding areal distributions were calculated and related to bilayer compressibility (K_A) and bending (K_C) moduli according to $K_A = k_B T * < A > / \mathrm{Var}(A)$ and $K_C = K_A * h^2/24$, where h is membrane thickness. For saturated lipids, area-per-lipid was on the order of 60 nm^2, nearly equivalent to literature values obtained using NMR or x-ray scattering, and were shown to be inversely proportional to the chain length of the lipid. Further, area-per-lipid increased with increasing temperature and swelling of the nanoliposomes in ways related to chain length and saturation state, further validating the technique. Compressibility and bending moduli decreased with increasing temperature, and increased with increasing chain length. Unsaturated lipids had lower moduli than their saturated counterparts. Finally, we provide the first in situ measurements of area-per-lipid and bilayer moduli for intact cells. For human red blood cells, the area-per-lipid was 68 $Å^2$ and compressibility and bending moduli of the lipid bilayer were 6.9 mN/m and 4.4 k_BT, respectively. For human aortic endothelial cells plated onto fibronectin-coated glass dishes K_A and K_C were 165.4 mN/m and 105.7 k_BT, respectively, highlighting differences between red blood cell and endothelial cell moduli that are important for their respective mechanobiological functions.

S15-1 Biomechanics of red cell diseases

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How are biological cells' mechanical/physical properties related to disease states? Recent progress in nanomechanics tools in experiments and computer simulations enable unprecedented opportunities to explore this question in depth. Red blood cells (RBCs) are critical for human health as they transport oxygen as well as carbon dioxide in and out of every part of human body. A discocyte RBC has a diameter of about 8 micrometers, while it has to go through the smallest capillaries as small as 3–4 micrometers in diameter, or thin spleen interendothelial slits with a height of 1.2 micrometers or less. Due to the

large distortion involved in passing through these tiny openings, a RBC has to maintain appreciable deformability throughout its lifespan. Red blood cell diseases, such as Plasmodium falciparum malaria and sickle cell disease, are known to alter the deformability and adhesion of the diseased RBCs, causing various complications in microcirculation. The talk will first focus on malaria biomechanics, RBC spleen clearance, and related pathology. Recent results on sickle cell biomechanics under transient hypoxia will also be presented for better understanding of the vaso-occlusive crisis, a major complication in sickle cell disease.

S15-2 Microvascular blood flow peculiarities in cancer

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One of the oldest theories of the pathophysiology of thrombosis is that of Virchow, which has three overlapping parts: the contents of the blood, the blood vessel wall, and blood flow. There seems too little firm experimental data directly implicating the third aspect of Virchow's triad (abnormalities of blood flow) in the pathogenesis of cancer. The aim of this study was to investigate microvascular blood flow peculiarities in cancer. Cutaneous blood flow, blood clotting process, platelet hemostasis and hemorheological properties were evaluated in patients with solid tumors before and after surgery and in healthy controls. Ensuring of normal values of tissue perfusion in cancer patients was realized by means of hard efforts of microcirculation regulatory mechanisms; in preoperative period passive mechanisms were activated, after surgery passive as well as active regulatory mechanisms were intensified. Blood viscosity in patients was lowered because of dramatic fall of Hct, in spite of the rise of plasma viscosity and substantially worsened RBC microrheological properties (increased aggregability and reduced deformability). The main features of blood clotting process in cancer patients were elevated intensity and shortened period of contact phase of blood clotting and inhibited fibrinolysis stage. Platelets depletion within the high level of spontaneous and ADP-induced platelet aggregation was registered in patients. Combination of a high aggregation activity of platelets, reduced number of erythrocytes (Hct), an increase of RBC aggregation and plasma viscosity caused impairment of blood oxygen transportation efficacy in cancer that provoke hypoxia in the microcirculation favoring thrombosis, settlement of tumor and metastasis.

S15-3 Shape and dynamics of red blood cells in microvessels

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The motion of red blood cells (RBCs) in microcirculation plays an important role in blood flow resistance and in the cell partitioning within a microvascular network. Different shapes and dynamics of RBCs in microchannels have been observed experimentally and in simulations. In particular, a phase diagram mapped by simulations shows a rich dynamical behavior, with snaking and tumbling discocytes, slippers performing a swinging motion, and stationary parachutes. However, the performed simulations

have used a viscosity contrast (the ratio between RBC cytosol viscosity and that of suspending medium) of unity, while under physiological conditions the viscosity contrast is equal to about five. In this study, the combination of mesoscopic hydrodynamics simulations and microchannel experiments is employed to investigate the behavior of RBCs in microchannel flow under physiological conditions. As expected, shape and dynamics of RBCs in microchannels can be associated with the flow conditions and cell properties. Quantitative comparison between simulations and experiments have been made and the differences in RBC behavior due to the viscosity contrast will be discussed.

S15-4 Hemodynamic functionality of transfused red blood cells in the microcirculation of blood recipients

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Background: The primary goal of the red blood cell (RBC) is to supply oxygen to tissues and organs. However, RBCs have unique flow-affecting properties, mainly their deformability, adherence to vascular endothelial cells, and self-aggregability, which play key roles in blood circulation, thereby defining their hemodynamic functionality (HF). In recent years there is growing concern regarding the risks in the transfusion of packed red blood cells (PRBC), as numerous studies have reported negative transfusion outcomes, including reduced blood perfusion. Objectives: In search of this phenomenon's mechanism, we explored the effect of the transfused PRBC HF on the transfusion outcome, particularly the recipients' blood flow. Methods: The effect of PRBC HF was examined by the transfusion-induced change in recipients' skin blood flow (ΔSBF), and hemoglobin increment (ΔHb) in β-Thalassemia-Major patients, who are routinely treated with life-long frequent transfusions. RBC deformability and adherence were determined by image analysis. SBF was determined using a laser-Doppler-imager. Results: Both ΔSBF and ΔHb were clearly elevated with increasing PRBC HF, showing a highly significant dependence on the HF of the transfused RBC. Conclusions: This study provides, for the first time in humans, direct evidence that the HF of transfused PRBC is a potent effector of blood circulation in blood transfusion recipients, and further supports the important role of RBC flow-affecting properties in vasculature function.

S15-5 Red blood cell aggregate flow characteristics in bifurcating microchannels

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The complex mechanical nature of blood is due to red blood cell (RBC) deformability and the aggregation phenomenon, with both found altered in a number of pathological conditions. The time and flow-dependent characteristics of the aggregated structures developed in blood affect its mechanical properties, and can be examined by various techniques. The influence of the RBC aggregation phenomenon on the flow characteristics at the microscale can be examined by employing microfluidics, resembling the microvasculature. In this work it will be illustrated that the aggregation phenomenon, apart from the velocity characteristics (i.e. velocity profile bluntness and skewness, velocity variation, etc.), affects the

aggregate distribution in the bifurcation in a counterintuitive manner, i.e. the smaller aggregates appear in regions of lower shear. Such behaviour is explained when considering the spatial distribution of aggregates in conjunction to the velocity field developed in the parent channel branches. Local viscosity in the microchannels was estimated based on existing constitutive equations for blood, and showed that aggregate formation introduces a local variation in viscosity and a shift in the location of maximum viscosity in the microchannel.

S16-1 Morphogenesis and mechanobiology of airway smooth muscle cells on 3D tubular micropatterns as mechanism of bronchial airway development

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During early development of the lung, airway smooth muscle cells (ASMCs) emerge and form bundles at the terminal airways, and eventually organize as helical structures that surround the airway walls with certain axial orientations. However, it remains unclear how such ASM structures form on the tubular wall. Here we cultured ASMCs on tubular micropatterns fabricated with PDMS coated with collagen, and subsequently assessed in real time the ASMCs' adhesion, migration and self-assembly into stable morphology together with cell stiffness and cytoskeleton remodelling. The tubular micropattern had a diameter ranging from 50 to 150 μm. ASMCs were inoculated on the micropattern for up to 72 h while being imaged by live cell imaging system, fluorescence microscopy, and probed with optical magnetic twisting cytometry (OMTC) and atomic force microscopy (AFM), respectively. We found that ASMCs cultured on the tubular micropatterns seemed to be agile to adjust their shape and orientation to probe and cope with the uneven microenvironment. Ultimately the cells oriented on the curved surface with the cell's long axis in angle conducive to their survival. The cells also change their stiffness. most likely through active remodeling of the cytoskeleton to correlate the changing tubular curvature. Interestingly, the cells rarely oriented to be parallel to the axial direction of the tube, demonstrating that plane surface was not optimal for cell growth based on mechanical equilibrium and energy minimization. In conclusion, our results show that 3D tubular curvature is indeed a factor to affect the structural arrangement and mechanical properties of ASMCs (at least *in vitro*) that may contribute to the morphogenesis and functionalization of the bronchial airways during lung development.

S16-2 Glycosylation is a strong molecular determinant of MUC5AC rheology in airway mucus at both single protein and bulk solution levels

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Airway mucus is an important physical barrier that traps exogenous hazardous matter and expels it out of body via cilia beating and coughing. This defense function largely relies on the appropriate rheological properties of the airway mucus. As airway mucus contains abundant proteins known as mucins (primarily the subtype MUC5AC), it has been shown that airway mucus rheology is closely related to the glycosylation of MUC5AC, but the mechanism remains unclear. Therefore, we modified

MUC5AC's O-glycosylation to various extents by using O-glycosidase. Subsequently, we characterized the rheological behavior of the O-glycosylation modified MUC5AC at either molecular level using atomic force microscopy (AFM) or bulk volume level using advanced rotational rheometry (Kinexus II, Malvern). We demonstrate that at the molecular level, O-glycosylation had a strong effect on the mechanical properties of MUC5AC. At the bulk volume level, the MUC5AC solution in all cases exhibited a gel-like rheological behavior that fitted well to classical Burgers model with a typical shear-thickening at shear rate $\leq 0.02\ s^{-1}$ and nonlinearly shear-thinning afterwards. However, both the storage and loss moduli of the MUC5AC solution were highly dependent on the level of O-glycosylation. We also found that the network structure of MUC5AC polymer filaments was determined at least in part by the extent of O-glycosylation. Taken together, this study provides rheological characteristics of MUC5AC with variable O-glycosylation from micro- to macro scale, which may further an understanding of mucus physiology and associated pathologies. These findings may aid the development of drug delivery systems as well as ideas and methods for treating chronic respiratory diseases such as asthma or COPD with MUC5AC as a target.

S16-3 Dynamics of neutrophil transmigration mediated by beta-2 integrin via P- and E-selectins

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Leukocyte transendothelial migration is a key step in their recruitment to the sites of inflammation. However, the synergic regulation of endothelium-expressed selectins on leukocyte transmigration remains unclear. Here, an *in vitro* model was developed to investigate the dynamic contributions of P- and E-selectin to PMN transmigration under static condition. PMN transmigration is significantly increased on LPS stimulation, which is higher on 4 h LPS-treated HUVECs than on 12 h LPS-treated HUVECs. Blocking and competitive tests indicate that P-selectin engages PSGL-1 to activate β_2-integrin and initiate PMN transmigration within the first 15 minutes, while E-selectin engages CD44 to influence PMN transmigration after 15 minutes. All these P- and E-selectin-induced β_2-integrin activation is likely transduced via Syk signaling pathway. And complicated complementary and competitive mechanisms are involved in the interactions of P-/E-selectin and their ligands to promote PMN transmigration.

S16-5 Influence of different rhythms sound wave to serotonin concentration in rat hippocampus

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Background: In our study, we focused on the influence of music to variations in serotonin concentration on the hippocampus. The effect of rhythm was also studied. We aimed to determine what kind of music was able to improve the mental state of different people. Method: (1) Average heart rates of Sprague Dawley rats were measured, with and without anesthesia for set rhythms (300 beats/min, 350 beats/min, 400 beats/min); (2) Sound waves were made by setting rhythms with Finale 2011 software; (3) Rats were grouped randomly. Some were received different sound waves under anesthesia or normal situations;

some received no sound waves as control. (4) Left and right hippocampus were isolated from brains into tubes filled with 0.9% NaCl solution and weighed. Tissues were then ultrasonicated and centrifuged. Serotonin was measured in the supernatant using an ELISA. Conclusion: (1) Right and left hippocampus had different responses to the same sound wave; (2) Under anesthesia situation, the right hippocampus from the group that received 300 beats/min sound waves secreted the most serotonin concentration, 0.202 ng/(ml·mg); (3) Under normal situation, the right hippocampus from the group that received 400 beats/min sound waves secreted the most serotonin concentration, 0.128 ng/(ml·mg); (4) The group subjected to sound waves at a rhythm closest to their average heart rate secreted the most serotonin.

S17-1 Longitudinal analysis of thrombin generation biomarkers in venous thromboembolism

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Increased thrombin generation (TG) is a key mechanism in the pathogenesis of deep venous thrombosis and pulmonary embolism. In order to evaluate whether monitoring of TG could also be useful to assess the clinical course of venous thromboembolism (VTE), a prospective longitudinal analysis was performed in 354 patients (237 females, 117 males, age: 18–65 y, mean: 45.3 y) with VTE over a period of 12 months. VTE included deep venous thrombosis of the legs, pelvis, pulmonary embolism and visceral venous thrombosis. Thrombin-antithrombin-complex (TAT) and prothrombin fragment 1+2 (PTF) were assayed as biomarkers to characterize TG. Furthermore, the fibrinolytic response to thrombus formation was studied by analyzing D-dimers and plasmin-antiplasmin-complex (PAP). It could be shown that TAT was maximally elevated during the acute stage, decreasing significantly after 4 weeks, reaching lowest levels equivalent to controls not before 3–4 months, and increasing slightly after 4–12 months. This period of time was associated with the cessation of oral anticoagulation. TAT was significantly higher in recurrent thrombosis and pulmonary embolism compared to single thrombosis. The changes in PTF were analogous, but less accentuated. D-dimers showed a similar time course as TAT. This also applied, however at a lesser extent to PAP. Plasmatic viscosity and erythrocyte aggregation as hemorheologic parameters only weakly paralleled the course of TG, but were closely related to changes in fibrinogen. In conclusion, thrombin generation biomarkers, in particular TAT, are useful for monitoring the course and extent of VTE and to evaluate succesful anticoagulation. The fibrinolytic response, especially monitored by D-dimers shows a parallel time course and is therefore closely related to TG due to fibrin formation as a result. Being a highly sensitive marker, D-dimers appear even more suitable than TAT to characterize the course, extent and risk of recurrence in VTE.

S17-2 Comparison of PIRADS 3 lesions with histopathological findings after MRI-ultrasound fusion targeted biopsy of the prostate in a real-world setting

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Objectives: We aimed to evaluate whether PIRADS 3 lesions in multiparametric MRI (mpMRI) represent a significant risk of prostate cancer (PCa) in a real-world setting of different referring radiologic institutes. Materials and methods: Between May 2015 and October 2017, a total of 408 patients were referred to our clinic for MRI-ultrasound fusion targeted biopsy of the prostate (FusPbx) due to suspected prostate cancer. In all patients, preoperatively mpMRI of the prostate was performed by altogether 62 different radiologic institutes. Prostate lesions were classified according to the PIRADS system. A PIRADS 3 lesion was diagnosed in 41 patients. FusPbx was performed transrectally using a Philips EPIQ 7 scanner with plane wise fusion of ultrasound and MRI image data. In addition to FusPbx in each patient a randomized 12-core transrectal ultrasound guided biopsy (USPbx) was performed. Results: Mean PSA Level was 9.5 ng/ml (range: 1–26 ng/ml), mean patients age 66.1 years (48.6–80.4). In 12/41 patients (29.3%) prostate cancer was diagnosed by FusPbx of the PIRADS 3 lesion. In the target lesion PCa was classified as Gleason Score 3+3 in 5 patients, as 3+4 in 3, 4+3 in 1, 4+4 in 1 and 4+5 in 1 patient. In patients with negative FusPbx USPbx revealed PCa in another 7 patients (17.1%). In 5 of these GS 3+3 PCa was found, in another 2 patients GS 3+4 PCa. Conclusions: PIRADS 3 lesions indicate an equivocal likelihood of significant prostate cancer by definition. In our series with a large number of referring radiologic institutes, PCa detection rate was 29.3% in PIRADS 3 lesions. This might indicate that the definition of a PIRADS 3 lesion varies among different radiologic institutes. Quality and reproducibility of mpMRI prostate imaging might be improvable by training.

S17-3 Does acoustic radiation force elastography help to improve the diagnostic value of ultrasound in the preoperative characterization of tumors of the parotid gland?

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Objectives: While ultrasound is the preferred method of preoperative evaluation of masses of the parotid glands, existing methods do not allow for definite differentiation between the most common benign and malignant tumors. The aim of our study was to evaluate if acoustic radiation force with Virtual Touch Quantification (VTQ) elastography improves preoperative evaluation of parotid tumors. Methods: We investigated the parenchyma of 102 parotid glands, fourteen lymph nodes of healthy volunteers and 51 tumors of the parotid gland via ultrasound, color Doppler ultrasound and VTQ. Subsequently, we analyzed the results and compared with histopathology. Results: Perfusion was significantly lower in comparison to malignant tumors in pleomorphic adenoma, the most frequent benign tumor of the parotid gland. Furthermore, all tumors showed statistically significant higher perfusion in comparison to the parenchyma or the lymph nodes of the gland. By a statistically significant amount, the shear wave velocity of the user-defined region of interest was more frequently an overflow value higher than 8.5 m/s in total tumors in comparison to parenchyma or lymph nodes. In comparison, the different tumor types presented no significant difference in the shear wave velocity. Conclusions: VTQ in combination with classical ultrasound examination provides additional data that improves the ability to distinguish between benign and malignant tumors. Thus, VTQ shows promise for integration into preexisting ultrasound protocols. However, despite the improvement, even with VTQ complete differentiation of tumors is still not possible, and further investigation is recommended.

S17-4 Technologies for adipose stem cell isolation

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Background: Fat grafting has become one of the most frequent procedures in plastic surgery. High absorption rates caused by insufficient vascularization and impaired adipocyte vitality lead to unpredictable graft take rates. The proliferative and angiogenic properties of adipose tissue-derived stem cells hold great promise to overcome this problem. Therefore, strenuous efforts have been made to enrich lipoaspirate with stem cells. A comparison of these studies is difficult as many parameters influence the results. Objective: This study summarizes the abundance of factors that influence the stem cell yield, which include harvesting, isolation and quantification. Methods: Stem cells were isolated from lipoaspirates and quantified using flow cytometry, colony forming unit assays and conventional cell counting. However, only one parameter was changed for every comparison evaluated. Results: Isolation of cells from the lipoaspirate of the same patient and harvesting site can show huge differences depending on isolation protocol details and quantification method. Discussion and Conclusion: Stem cell yield is influenced by so many factors that the comparison of different studies should be handled with care.

S17-5 Blood rheology in breast and gynecologic cancer patients at primary diagnosis and stage of cancer progression

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Background: Patients with gynecological malignancies often show increased plasma viscosity and red blood cell aggregation and a tendency of anemia at the time of primary diagnosis, resulting in an hematocrit-independent hyperviscosity syndrome. This is commonly accompanied by coagulation activation characterized by elevated platelet count and increased blood clotting factor turnover. Similar changes in the blood rheological properties were shown in patients with breast cancer that refer to a higher risk for deep vein thrombosis. An association between blood rheological properties including red blood cell deformability and RBC indices in the gynecologic cancer patents has not yet been proofed. Methods: Measurement of the rheological properties including plasma viscosity (PV), red blood cell (RBC) aggregation during stasis (E0) and low shear conditions (E1), red blood cell deformability during exposure to low (RBC 1.2, 3.0), moderate (RBC 6.0, 12.0) and high shear forces (RBC 30.0, 60.0) were performed before primary surgery and at the time of disease progression. Results were compared to those of healthy patients, prior to elective gynecological surgeries. The rheological parameters were correlated to red blood cell indices (RBC-I: MCH, MCV and MCHC). Results: In total 44 patients with gynecological malignancies, here 12 patients with ovarian carcinoma, 13 patients with endometrium carcinoma, 13 patients with cervical carcinoma and 6 patients with vulvar cancer, 8 patients with gynecological cancer progression, 28 women with breast cancer and 19 women with progression or contralateral breast cancer participated in this study. These data were compared to those of 286 healthy women. The plasma viscosity tended to be higher in the patients with carcinoma. RBC aggregation in stasis was moderately higher in breast cancer and highest in stage of gynecological cancer progression, while RBC aggregability during exposure to low shear conditions tended to be higher in all the patients with malignancies,

highest in stage of progression, in comparison to healthy women. Compared to healthy patients RBC deformability in primary breast cancer including metastatic stages and gynecological malignancies was higher. RBC deformability in vulvar carcinoma was highest compared to the other malignancies and lowest in the patients with disease progression. There was a strong inverse correlation between MCV and RBC deformability in all cancer types and stages, being most pronounced under high shear forces. Discussion: We confirm the typical constellation of blood rheological properties in the gynecologic cancer patients in the sense of a hyperviscosity syndrome. Interestingly, compared to healthy individuals, RBC deformability at primary cancer diagnosis was higher – particularly in breast cancer patients – but decreased in the presence of cancer progression.

S17-6 First experiences with a clinical work-flow integrated CAM Assay in Patients with oral squamous cell carcinoma

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Introduction: The oral squamous cell carcinoma (OSCC) is a leading cause of death in human malignancies. The aim of this study is to integrate the CAM Assay as a reliable and good working *in vivo* model for the evaluation of OSCC tumor samples and its growth into the clinical work flow. Material and Methods: Fresh human Tumor samples (OSCCs) 1x1mm in size were cut into 350 μm thick slices by a Vibratome and put on the prepared CAM model. After growth of the tumor tissue on the CAM we started with topical induction of proinflammatory cytokines (TNFα) and growth factors (TGFβ). After further growth of the tumor on the assay we explanted the tumor tissue and first performed microscopic and then immunohistochemical examinations. E-cadherin and vimentin were used as EMT-makers and the histologic preparations were evaluated histomorphometrically. The results were correlated with clinical parameters of the patients. Results: Under TNFα, the small tumors (T1/T2) show higher E-cadherin expression than larger tumors (T3/T4). The vimentin expression under TNFα behaved in the opposite direction, at T1/T2 the expression decreased in T3/T4 increased. Furthermore, an increased E-cadherin expression in N0 and diminished E-cadherin expression in N1/N2b patients could be detected depending on the N-stage of the patients. Vimentin, on the other hand, was reduced in the N0 group and expressed more frequently in the N1/N2b group. TGFβ induction also led to increased expression of vimentin in the T3/T4 tumors and N1/N2b stages. Conclusion: By integrating a CAM assay into the clinical workflow, tumors with preserved tumor architecture can be cultured and subjected to histological and molecular biology studies. Effects on biological behavior are recognizable and demonstrable in this model. The key markers E-cadherin and vimentin alone are not sufficient to represent the complexity of the EMT in this model. Further molecular biology and signaling pathway analyzes are necessary.

S18-1 Malaria parasites, host-erythrocytes and blood circulation

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Malaria deadly threats ensue when Plasmodium parasites massively infect erythrocytes, instigating their massive adhesion in capillaries and obstructing blood circulation to vital organs, such as brain and placenta. However, not everybody will die on the infection; sickle cell patients carry a mutation to hemoglobin that prevents the fatal cytoadhesion. By using cryo-electron tomography, Mössbauer spectroscopy and related techniques we unraveled the molecular basis of sickle cell protection. We showed that irreversibly oxidized sickle hemoglobin interferes with actin dynamics and hinders the transport of adhesins to the host-cell surface, thus thwarting the severe outcomes of malaria. We further propose a novel strategy for antimalarial intervention by which the protective trait would be drug-induced also in the erythrocytes of malaria vulnerable patients.

S18-2 Polyhedrocytes in type 2 diabetes

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Little is known about the composition and structure of contracted blood clots, particularly polyhedral erythrocytes (polyhedrocytes). We investigated the content of polyhedrocytes formed in blood clots and its determinants in type 2 diabetes (T2D) patients. In 97 patients with T2D and cardiovascular disease (aged 41–85 years, median HbA1c of 6.4% [interquartile range, 5.9-7.8]), we measured *in vitro* the composition of blood clots, including a clot area covered by polyhedrocytes using scanning electron microscopy. Additionally, we measured plasma fibrin clot permeability (Ks), clot lysis time (CLT), thrombin generation, oxidative stress (Total Protein Carbonyl and Thiobarbituric Acid Reactive Substances), P-selectin (CD62P) and platelet factor-4 (PF4) were also determined. Patients who generated >5% polyhedrocytes within clots ($n = 83$, 85.6%; high polyhedrocytes group) had higher glucose (+15.7%, $P = 0.018$), fibrinogen (+16.6%, $P = 0.004$), lower red blood cell distribution width (RDW) (−8.8%, $p = 0.034$), reduced plasma clot density (−21.8% Ks, $p = 0.011$) and impaired fibrinolysis (+6.5% CLT, $p = 0.037$) compared to the low polyhedrocytes group. Glucose ≥ 6 mmol/L increased odds for the high polyhedrocytes formation (OR = 4.81, 95% CI 1.49-16.40, $P = 0.009$) when compared with lower glycaemia. The content of polyhedrocytes positively correlated with fibrinogen, glucose, HbA1c and total cholesterol. In the *in vitro* experiment, increase of glucose concentration by 10 mmol/L was associated with 97% increased polyhedrocytes content ($p = 0.031$). Moreover, in the linear regression analysis of T2D patients, an increase in TBARS, total PC, P-selectin, PF4, was associated with the increased content of polyhedrocytes in the blood clots of T2D patients. The content of polyhedrocytes reflected as percent of clot area covered by polyhedrocytes in blood clots generated in T2D patients is determined by glucose level, platelet activation, and oxidative stress.

S18-3 Differentiation between various melanomas based on biophysical characterization of their properties

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Cancer remains the second leading cause of death worldwide. That is why, there is still an urgent need for the development of various scientific methods that increase the chance to detect cancers of different organs and tissues. One of the emerging directions is to correlate cellular biomechanics with biochemical properties of single cancer cells. It can be achieved by the combination of two methods, Atomic Force Microscopy (AFM) and Time-of-Flight Secondary Ion Mass Spectrometry (ToF SIMS). By means of AFM, the nanomechanical properties of cancerous cells were investigated [1]. To study biochemical alterations at the single cell level, ToF SIMS was employed [2,3]. High resolution mass spectra were analyzed by means of Principal Component Analysis (PCA) [4]. The combination of AFM and ToF SIMS gives the information about the alterations between different cancer cells and it may be applied to monitor the effectivity of anticancer drugs. In this way, these two techniques are excellent tools for a complex analysis of cancerous cells.

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S18-4 Endothelial nanomechanics in vascular diseases - An *ex vivo* AFM nanoindentation study

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The progressive dysfunction of the endothelium in diabetes leads to vascular injury and to the development of the cardiovascular disease. Recent studies have reported endothelium stiffening as an important symptom of the endothelium dysfunction in hyperglycemia. Other studies have shown that the degradation of the glycocalyx, which is a brush-like layer on the endothelium, coincide with the endothelial dysfunction in hyperglycemia. In this talk, we will demonstrate that atomic force microscope (AFM) is a valuable tool for studying nanomechanical properties of the endothelium. By means of this method we were able to evaluate the nanomechanical changes of endothelium in both *in vitro* [1] end *ex vivo* experiments [2]. In particular, *ex vivo* study of endothelium from mouse aorta enabled to quantitatively evaluate the changes in glycocalyx degradation and mechanical properties of the endothelium in progression of diabetes. We observed a local spatial redistribution of the glycocalyx and its progressive global degradation in the studied period of diabetes. The measured apparent elastic modulus of the

endothelial layer increased for regions covered by glycocalyx and, in the same age-dependent way, for the whole endothelium layer. These results may indicate that the degradation of the glycocalyx is tightly related to endothelium stiffening and is a consequence of the endothelial dysfunction caused by the long lasting hyperglycemia.

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S19-1 Long-term prognosis of coronary microvascular dysfunction

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Exertional angina with possible signs of ischemia in stress testing and with exclusion of relevant coronary disease or complete lack of it is one of the main clinical presentations of patients with coronary microvascular dysfunction. Though the etiology of this disease, which is not necessarily associated with a cardiac disease - not even with coexisting cardiovascular risk factors - is not fully understood. There have been several approaches to categorizing this entity. The lack of a systematic and uniform diagnostic approach and the lack of monitored follow-up visits in the setting of controlled trials leads to difficulties in the determination of the prevalence of the disease, and thus, the impact and prognosis for it. However, there have been promising new tools, e.g. CMR- or PET-using approaches, to diagnose the coronary microvascular dysfunction, to complement the contemporary gold-standard of invasive coronary angiography and measurement of, e.g. mediator-induced coronary flow reserve. Long-term data of patients with suspected or diagnosed coronary microvascular dysfunction show a higher rate of adverse cardiovascular events and a worse outcome.

S19-2 AD-MSCs change their morphology and secretion profile as a response to changes in substrate elastic properties in combination with inflammatory stimuli

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Background: Mesenchymal stem cells (MSCs) are often deployed to augment wound healing and regeneration and are delivered *in vivo* utilizing various types of biomaterials. As a result, within their delivery vehicle, there are exposed to an inflammatory environment. However, the effect of different mechanical properties on MSC's response is still unclear. Objective: Evaluating the effect of different

mechanical properties of cell culture substrates during inflammatory conditions on adipose derived (AD)-MSCs. Methods: A glycidylmethacrylate (GMA)-gelatin based hydrogel system with adjustable mechanical properties was utilized. This system allowed use of GMA-gelatin with identical degrees of functionalization, while mechanical properties were adjusted by shortening the biopolymer chain length. AD-MSCs were cultured on gelatin-based films (3 mm) with different G' moduli (approx. ranging 400 to 1400 Pa) and subjected to different concentrations of interferon γ (IFN-γ). Results: Hydrogels with various elastic moduli were synthesized and analyzed using rheology and AFM. All hydrogel substrates supported cell viability and spreading, while the mechanical properties affected F-actin rearrangement. For stiffer gels, a higher degree of cell stretching and formation of F-actin stress fibers was observed in the absence of inflammatory stimuli. In contrast, AD-MSCs growing on softer substrates without an inflammatory stimulus exhibited a looser network of F- actin. Only in the presence of IFN-γ AD-MSCs were stimulated to form denser stress fibers. Moreover, VEGF secretion in response to different concentrations of IFN-γ was increased by substrate stiffness. Conclusion: The potential of an innovative *in vitro* platform for simulating an inflammatory ECM-mimetic environment was established with adjustable mechanical properties. Substrate elasticity was shown to influence cell expansion and attachment but also the secretion of VEGF under inflammatory condition. Current findings indicate that the mechanical microenvironment affects AD-MSC response to inflammatory stimuli. This should be taken into account when designing biomaterials to deliver stem cells for tissue healing and regeneration.

S19-3 Thrombogenicity testing of polymers: round-robin study to assess inter-center variability

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Clinical use of cardiovascular devices is continuously increasing along with concerns on the thrombogenicity of such implants. The lack of standardization in the *in vitro* testing of implant materials has led to a situation, where definite specifications about test panels and protocols are lacking and inter-study comparisons are rather impossible. Here, we report about a prospective, randomized and double-blind multicenter trial demonstrating that standardization of *in vitro* test protocols allows a reproducible assessment of platelet adhesion and activation from platelet rich plasma as indicators of the thrombogenicity of cardiovascular implant materials. The stringent standardization of a static platelet adhesion test resulted in a laboratory independent scoring of the polymers; the materials were evaluated in all laboratories in the same order for their thrombogenicity. While poly(dimethyl siloxane) showed very reduced platelet adhesion and activation, the density of cells and the degree of activation were highest on poly(tetrafluoro ethylene). Polyethylene terephthalate showed intermediate values. The results of this

study reveal that inter-laboratory and inter-study comparisons of the thrombogenicity testing of blood-contacting biomaterials can be achieved by a stringent standardization of the test protocol [1]. Future perspectives for the standardization/harmonization in the *in vitro* testing of implant materials will be discussed.

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S19-4 The controversial origin of pericytes - implications for cell-based therapies

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Pericytes isolated from quiescent tissue were demonstrated to be a specialized subpopulation of mesenchymal stem cells and promising candidates for therapeutic angiogenesis applications. However, cell-based therapies of ischemic diseases have not resulted in significant long-term improvement. Just recently pericytes from a hematopoietic origin were observed in embryonic skin. Additionally, a pericyte sub-population expressing leukocyte and monocyte markers was described during adult angiogenesis *in vivo*. Since mesenchymal stem cells do not express hematopoietic markers by definition, the latter cell type might represent an alternative hematopoietic pericyte population relevant to angiogenesis. We therefore sourced blood-derived angiogenic cells (BDACs) from monocytes that closely resembled hematopoietic pericytes *in vitro*, which had only been observed *in vivo* thus far. BDACs displayed many pericytic features (PDGFRb and NG2), while expressing leukocyte markers CD45, CD11b. They enhanced angiogenesis *in vitro* and *in vivo* and accelerated revascularization and functional tissue regeneration in a pre-clinical model of critical limb ischemia. Comparison between BDACs and mesenchymal pericytes in functional *in vitro* assays revealed that in direct co-culture BDACs enhanced, while mesenchymal pericytes impaired endothelial sprouting. We therefore concluded that BDACs (while resembling hematopoietic pericytes) enhanced early stages of angiogenesis, while mesenchymal pericytes were responsible for blood vessel maturation and homeostasis. Since the formation of new blood vessels is crucial during therapeutic angiogenesis, hematopoietic pericytes (and therefore BDACs) might offer an advantageous addition or alternative for cell-based therapies.

S19-5 A facile way to achieve biomimetic laminin networks on substrates

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Background: Laminin (LAM), a major glycoprotein of the basement membrane, has the tendency to form networks *in vitro* and *in vivo* by self-assembly, and plays crucial biological roles such as cellular adhesion, polarization and apoptosis. (1) LAM coatings are used widely for induced pluripotent stem cell (iPSC) maintenance and differentiation. (2) Substantial efforts have focused on the selection of the right type of LAM subtype for iPSC culture. However, only limited attention has been given to controlling the

formation of LAM layers and enhancing their presentation to cells at the material interface. Purpose: Here, we employ Langmuir–Schaefer (LS) method, where LAM forms networks by self-assembly at the air–water (A-W) interface. This layer is subsequently transferred by horizontal touching onto a planar substrate. This approach is scalable to coat large areas of substrates by suitable choice of vessel and substrate dimensions and multilayer coatings can be produced. Materials and methods: LAM-1 (Sigma) was obtained from mouse tumor and the LAM layer was produced in a circular trough (KSV-NIMA) or in the wells of standard six-well culture plate (Corning). Polarization-modulation infrared reflection-absorption spectroscopy (PM-IRRAS; KSV-NIMA) and Atomic force microscope (AFM; JPK instruments) were used to characterize the LS films. Results: LAM forms networks on a subphase with pH 4 and 100 mM NaCl in any vessel, even in wells of six well plate. AFM micrographs showed that controlled LAM networks were transferred on Si-wafers by LS method. Finally, the stepwise increase of LAM amount with multilayer LS deposition on gold was confirmed by PM-IRRAS. Conclusion: LS technique is a facile tool to equip substrates with defined LAM layers for applications such as iPSC culture.

S19-6 Medical compression stockings reduce hypertension of nailfold capillaries at the toe of patients with chronic venous insufficiency

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In five patients who suffered from chronic venous insufficiency clinical stage C4 ($n = 3$) and C6 ($n = 2$) the capillary blood pressure was measured twice by means of invasive direct cannulation of nailfold capillaries of the toe. During one measurement course the patients wore below knee medical compression stockings (40 mmHg) during the other they did not have compression therapy. With the patient in supine position, the CP was investigated by the servo-nulling technique under resting conditions and under dynamic conditions: the calf-muscle/ankle joint venous pump was simulated by means of inflating a blood pressure cuff, which surrounded the mid lower leg, to 60 mmHg for 60 s. Results: The simulated calf-muscle contraction induced a steep increase of CP with 5.65 mmHg/s (Q1 5.27 mmHg/s, Q3 5.92 mmHg/s), which was significantly ($p = 0.013$) reduced by MCS to 2.47 mmHg/s (Q1 1.65 mmHg/s, Q3 3.0 mmHg/s). Time needed to reach the maximum CP was 11.35 s, which was lengthened by MCS to 23.4 s ($p = 0.134$). Conclusion: Compression therapy prevents capillary hypertension, the major hemodynamic reason for the development of advanced stages of chronic venous insufficiency which are defined by skin diseases like hyperpigmentation, lipodermatosclerosis and ulcers.

S20-1 Visualization of cardiac flows: *In vitro*, *in vivo*, and *in silico* studies

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Cardiac fluid mechanics dictate much of how we understand the cardiovascular system, from diagnosis of valvular disease states to surgical strategy for complex congenital heart defects. In addition, fluid mechanics influence pathophysiological processes that could result in stroke, heart failure, malformations in the lungs and liver, or other complications. Hence, a comprehensive understanding of cardiac flow field characteristics is essential to effective patient care. Flow visualization techniques are a critical step in the right direction as they enable the identification of regions of flow stasis, pathological shear, and other key flow characteristics. Over the past four decades, our group has dedicated resources towards a rigorous investigation of valvular and ventricular performance, as well as hemodynamics of congenital single ventricle circulation, using a wide range of techniques. Particle flow visualization, laser Doppler velocimetry, and particle image velocimetry were applied to characterize prosthetic heart valves, the left ventricle, and the total cavopulmonary connection formed to palliate congenital single ventricle defects. Our *in vivo* work included the visualization of flows through heart valves and ventricles in patients and animal models using ultrasound and magnetic resonance imaging. We have also applied computational fluid dynamics methods to visualize prosthetic heart valve flow characteristics and hemodynamics through the total cavopulmonary connection, generating higher-resolution data than *in vitro* methods provide. Taken together, these studies have yielded a better understanding of how design characteristics of valvular prostheses can interact with cardiac flows and how surgical design for congenital heart defects can impact patient outcomes.

S20-3 Leveraging fluid dynamic measurements to improve cardiac device design

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Experimental fluid mechanics is an art form and can impact our understanding of how flow negatively affects biological phenomena. While computational fluid dynamics has been able to extend our knowledge and challenge many paradigms related to cardiovascular fluid mechanics and design, we still need to validate computational simulations as we investigate more cellular behavior and systems. Newer experimental techniques are being developed but is the technology experiencing its swan song? At Penn State, we have been able to successfully use particle image velocimetry (PIV) to improve and influence the design of adult and pediatric pulsatile blood pumps. We will describe our approach to calculate the wall shear rates based on PIV and how to correlate these data to thrombus deposition from animal explants and then leverage into computational simulations and prediction.

S20-4 Hemodynamics assessment of new transcatheter bi-caval valves in the interventional treatment of tricuspid regurgitation

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Elderly patients with co-morbidities are usually denied the replacement tricuspid valve surgery, which may predispose them to a higher risk of surgical complications associated with open heart surgery. The advent of transcatheter technology provides these patients a new treatment alternative. Our team at the National University of Singapore has recently developed two percutaneous caval heart valves that are

designed to deploy at the vena cava and atrium junction. Our previous studies showed that the Reynolds shear stress (RSS) values measured in the proximity of the percutaneous caval heart valves are higher than the threshold of platelet activation. In the present study, we have incorporated new design features in these percutaneous caval heart valves. The study objective is to provide insight on how these two new stented valves with compliant ends affects the surrounding blood flow patterns. To accomplish this, a physiological flow loop was built and the two valves were deployed at the cavo-atrial junction. 3-D PIV measurements were conducted in the vena cava and right atrium in multiple planes. These caval stented valves comprise of nitinol stents, glutaraldehyde-treated porcine pericardial sleeve on the stent and glutaraldehyde-treated porcine pericardial tri-leaflets. Our findings revealed superior performance regarding the reduction of hemodynamic disturbances, particularly in the vicinity of the valves. Lower RSS values were recorded downstream of these valves when compared with previous valve designs. The maximum Reynolds shear stress values in the vicinity of the two valves were approximately 10 dynes/cm^2. Our study demonstrated that the new bi-caval valves could be potentially considered as a minimally invasive option to treat tricuspid regurgitation.

S21-1 Analysis of the cutaneous blood flow responses and microvascular tone regulation in patients with type 2 diabetes mellitus. Relationship to rheological properties of blood

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The aim of the study is to analyse the changes of the cutaneous blood flow responses to cold stress and thermally induced stimulation of microvascular reactivity in patients with diabetes mellitus type 2 through wavelet analysis of the skin temperature oscillations and to estimate their relationship with the blood viscosity values. The amplitudes of the skin temperature pulsations (ASTP) were monitored by "Microtest" device ("FM-Diagnostics", Russia); the whole blood viscosity and the shear stresses were measured by Contraves LS30 viscometer, (Switzerland) at a steady flow in a group of healthy subjects and in the patients with type 2 diabetes mellitus. Different constitutive equations were applied to describe the blood rheological properties. Correlations between the parameters of these equations and the ASTP in the frequency ranges, corresponding to the myogenic, neurogenic and endothelial mechanisms of the microcirculation tone regulation were calculated and analyzed during the cold stress and thermal stimulation. The results prompt manifestation of endothelial dysfunction in patients with type 2 diabetes.

S21-2 Relationship between rheological properties of blood and leukocyte adhesion under flow conditions in patients with type 2 diabetes mellitus

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The work aimed to evaluate the influence of aggregation and deformability of erythrocytes (RBCs) on leukocyte adhesion in patients with type 2 diabetes mellitus (T2DM) using a flow microchamber. Whole blood from patients with T2DM was used to prepare samples of diluted suspensions from erythrocytes in isotonic buffer solution and Dextran 200. These samples were used to determine the erythrocyte aggregation index (EAI) and erythrocyte deformability index (EDI). Diluted suspensions from leukocytes in isotonic buffer solution were prepared for measurement of leukocyte adhesion index (LAI) and diluted suspensions in isotonic buffer solution and Dextran 200 containing both erythrocytes and leukocytes were used for measurement of EAI, EDI and LAI. The suspensions were placed into a flow microchamber and the cells were attached to the bottom part of the chamber. The experiments were carried out at the State Pedagogical University, Yaroslavl, Russia. The results obtained show that with increasing shear rate from 0 s^{-1} to 1480 s^{-1} the number of adhering leukocytes to the bottom part of the chamber model of the vascular wall was decreased. The number of adherent leukocytes at different shear rate and the number of erythrocyte aggregates at rest (13,125 ± 1,705) were determined. There was no statistically significant difference between EDI at constant shear rate of the examined samples of erythrocytes (0,223 ± 0,014) and samples of erythrocytes and leukocytes (0,247 ± 0,007) from the T2DM patients. The flow microchamber method allowed investigation of the influence of RBC aggregation and deformability on leukocyte adhesion in patients with T2DM. These factors are a primary causes of vascular complications in diabetes.

S21-3 Hemorheological disturbances as the thrombosis-developing factor

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This study compared features of blood rheological behavior in 115 patients with myeloproliferative neoplasms (MPNs), 118 patients with chronic cerebrovascular diseases (CCVD), 96 patients with CCVD comorbid with Ph-negative MPNs, 174 patients with acute ischemic stroke, and 96 patients followed up within 12 months after acute ischemic stroke. Hemorheological analyses used rotational viscometry (AKR-2, Russia), for measurements performed with decreasing shear rates (from 300 to 5 s-1) followed by increasing of shear rates (from 5 to 300 s-1). The analysis was performed while samples remained in the device. RBC aggregation/disaggregation and erythrocyte deformability were assayed with laser-assisted optical rotational cell analysis (LORCA, Netherlands). Additionally we measured 98 biomarkers reflecting coagulation, anticoagulation, platelets, vascular wall, angiogenesis, fibrinolysis, inflammation, etc. Non-parametric statistics and multivariate analysis was performed on the acquired data. All patients showed abnormal blood viscosity values after the adjustment to Hct = 40%. Gender-linked features were found within each group of patients. Other hemorheological differences between patient groups appeared for erythrocyte aggregation/disaggregation, and for the composition as well hydrodynamic resistance of cell conglomerates under high shear rates. The magnitude of the difference in viscosity values obtained at the same shear rates correlated with thrombogenicity. Most of hemorheological parameters proved to be middle-forced predictors of the thrombogenic pattern. Comparison of patients with and without thrombotic events showed that hemorheological disorders served as a trigger for shifting the thrombogenicity to thrombosis.

S21-5 Local carotid stiffness in patients with cerebral small vessel disease. Relation to blood viscosity

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Carotid stiffness is an important factor in the pathogenesis of the cerebrovascular diseases and especially of cerebral small vessel disease (SVD). Its major determinants are the vessel wall structure and function and blood pressure values. However the role of blood viscosity has not been sufficiently studied. The aim of our study was to evaluate the local arterial stiffness of the common carotid artery (CCA) and its relation to blood viscosity in patients with SVD. Thirty patients with SVD aged 63 to 84 years and 20 age-matched controls were examined. The inclusion criteria of SVD patients were consistent with the neuroimaging diagnosis standards. An ultrasound examination with a real-time automatic measurement of the CCA intima-media thickness (IMT), the parameters of local CCA stiffness: distensibility (DC) and compliance coefficients (CC), alpha and beta stiffness indices and pulse wave velocity (PWV) was performed by using radio frequency (RF) - data technology (MyLabSeven, Esaote, Italy). Whole blood (WBV) and plasma viscosity (PV) at shear rates of 0.0237 s^{-1} to 128.5 s^{-1} were also examined in patients and controls. The results revealed higher values of IMT, significant decrease of DC and CC and increase of α and β stiffness indices and PWV in the patients with SVD as compared to the control group. Parallel significant increase of WBV was found within the range of shear rates 0.0237 s^{-1} to 128.5 s^{-1}. In the patients with SVD the increased CCA stiffness was associated with increased WBV.

S22-1 Role of the glycocalyx in atheroprotective vs. atheropermissive endothelium function

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Atherosclerosis occurs at vessel sites exposed to complex flow patterns, which damage endothelium. Proper endothelium function relies on the protective glycocalyx (GCX), which is shed in disease. Replacing it may heal ECs and slow disease progression. We studied cultured ECs and performed mice experiments, to examine endothelium in healthy and disruptive flow conditions. Immunocytochemical studies verified spatial variations in EC GCX composition. We correlated GCX composition to EC functions including vasoregulation, communication, barrier function, and vessel wall remodeling, by immunofluorescence microscopy, dye transfer and nanoparticle permeability experiments, and histology. To identify the role played by specific GCX components in EC function, some assays were performed on ECs with intact GCX and others were performed on ECs with experimentally degraded GCX. We also replaced degraded GCX components and assessed subsequent restoration of EC functions. Results demonstrated that the sialic acid (SA) component of cultured EC GCX in healthy flow is 2.66 mm thick and covers ~60% of the endothelial surface. SA thickness decreases in complex flow conditions by a significant 15%. In complex flow conditions, there is significant 58% drop in SA coverage. Heparan sulfate (HS) and hyaluronic acid GCX components were modulated differently in correlation to flow conditions. Vasoregulation, communication, barrier function, and blood vessel wall remodeling were all found to correlate to GCX composition. GCX repair by treating the cells with exogenous HS (and a co-factor) restored barrier function and recovered communication, suggesting that targeting the GCX may be a promising approach to reversing EC dysfunction and vascular disease progression.

S22-2 Loss of the retinal endothelial glycocalyx in diabetes

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The endothelial glycocalyx serves many purposes, one of which is a contribution to barrier function, with molecules greater than 40 kD in size having restricted access to the endothelial cell surface and junction. In the current experiments, we sought to investigate the effects of diabetes and hyaluronidase (HAase) on the thickness of the endothelial glycocalyx layer in the mouse retina. Two different fluorescent dextrans (4 kD-FITC & 155 kD-TRITC) were injected into control nondiabetic mice, diabetic Ins2Akita mice, and also into nondiabetic mice given an intravascular injection of HAase, which can degrade hyaluronic acid (HA) in the glycocalyx. Glycocalyx thickness was measured as one-half the difference in the lumen diameter filled by the 4 kD dye minus that of the 155 kD dye (the latter having limited transport into the glycocalyx). Additionally, a vascular leakage index was calculated from the tissue fluorescence intensity of each dye relative to the vascular intensity (tissue/vessel). We found that diabetes reduced the retinal endothelial glycocalyx layer significantly in the arterioles ($p < 0.01$), but not in the venules, with the same pattern also found in the experiments in which HAase was infused into control mice. Furthermore, wheat germ agglutinin staining of the vessel wall, in which the lectin nonspecifically binds HA residues, was found to be greater in arterioles than in venules, which could explain the greater effect of HAase on the arterioles. HAase increased vascular leakage of both sized dextrans into the surrounding tissue. In summary, our findings indicate that diabetes reduces the thickness of the retinal endothelial glycocalyx, containing HA, which may play a significant role in blood retinal barrier function. Supported by NIH R01EY025632.

S22-3 Endothelial glycocalyx restoration by growth factors in diabetic kidney disease

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The endothelial glycocalyx (eGlx) constitutes the first barrier to protein in all blood vessels. This is particularly noteworthy in the renal glomerulus, the ultrafiltration barrier. Any leakage of protein, such as albumin, across glomerular capillaries results in albumin in the urine (albuminuria), a hall mark of kidney disease. We demonstrate that targeted damage to the glomerular eGlx, using enzymes, results in a direct increase in glomerular albumin permeability using an *ex vivo* isolated glomerulus assay. This was confirmed by a reduction in eGlx coverage and/or depth using quantitative electron microscopy. In rodent models of diabetes, we also demonstrated a loss of glomerular eGlx which was associated with increased albumin permeability. Treatment with paracrine growth factors such as vascular endothelial growth factor (VEGF) C and angiopoietin-1 could rescue albumin permeability and restore glomerular eGlx. In cultured glomerular endothelial cells, these growth factors promoted the synthesis of the eGlx component, hyaluronic acid, and upregulated its biosynthesis enzyme, hyaluronic acid synthase 2 (HAS2). Further, inhibition of HAS2 increased glomerular albumin permeability *ex vivo*. HAS2 appears to have potential as a therapeutic target in diabetic kidney disease and this will be the focus of future work.

S22-4 Modification of renal macrophage signaling via MCP-1 inhibition reduces albuminuria in diabetic nephropathy

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Recently it was shown that interception of MCP-1 with the Spiegelmer emapticap pegol (NOX-E36) resulted in reduced albuminuria in type 2 diabetic nephropathy patients. Pro-inflammatory macrophages express cathepsin L, which activates heparanase, thereby degrading heparan sulfate (HS), one of the major endothelial glycocalyx components. Here we hypothesize that MCP-1 inhibition reduces albuminuria via influencing macrophage function, resulting in reduced heparanase activity and restoration of endothelial glycocalyx dimensions. ApoE KO mice were made diabetic and received a high cholesterol diet (0.15%) for 10 weeks, resulting in proteinuria and diabetic glomerular lesions. Mice were then treated for 4 weeks with mNOX-E36 or control. Cationic ferritin (CF) binding to the negatively charged HS was imaged using TEM and F4/80, cathepsin L and heparanase expression using IHC. Cytokine production upon LPS was measured in isolated kidney macrophages. mNOX-E36 treatment (4wk) reduced albuminuria and was accompanied with reduced glomerular cathepsin L and heparanase expression and increased CF. With equal numbers of glomerular macrophages their functionality was remarkable changed (decreased release of IL6 versus IL10), demonstrating an anti-inflammatory phenotype. In conclusion, MCP-1 inhibition by mNOX-E36 decreases albuminuria in diabetic nephropathy mice. The accompanied induction of anti-inflammatory macrophages resulted in reduced local heparanase presence and glycocalyx restoration. Supported by the Dutch Kidney Foundation Kolff grant 14OKG06 and GLYCOREN consortium grant CP09.03.

S23-1 Investigation on energy characteristic of red blood cell deformability: A quantitative analysis of extending and retracting curves based on Atomic Force Microscopy

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Deformability is a fundamental property of the cells and tissues of living organisms, which is commonly detected to indicate the state of the cells. And the cell deformability usually depends on the methods that we used, which is easy to be confused. The present research is designed to explore the energy characteristic of red blood cell deformability, based on a quantitative analysis of extending-retracting curves acquired from atomic force microscopy. ATP-depleted red blood cell are prepared by treatment with free-glucose Ringer solution. Our results clearly show that the Young's modulus of the erythrocyte is closely dependent on the concentration of intracellular ATP. Using the software Matlab, we obtained the area between the extending and retracting curves. Analysis of the control and ATP-depleted RBC demonstrated that the area could clearly differentiate between normal and ATP-depleted, which implies that ATP-depletion causes a decrease in RBC deformability. Our measures reveal that cell deformability is closely related to the state of intracellular energy, which can be characterized by cell passive and active deformation. This research

also provides a theoretical basis for studies of erythrocyte senescence, enables evaluation of red blood cell apoptosis, and provides a quantitative index of the state of blood storage for clinical blood transfusion.

S23-3 Nitric oxide regulates human erythrocyte deformability through regulating band 3 phosphorylation status in hypoxia

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Aim: To increase the local blood flow in proportion to metabolic demand, NO regulates membrane mechanical properties thereby modulating RBC deformability and oxygen carrying-releasing function. But the clear mechanisms of NO regulation of RBC membrane mechanical properties remain unknown. Methods: We have carried out a systematic study to find the mechanisms of NO regulation of RBC deformability under hypoxia. NO levels, RBCs membrane elongation index (EI), band 3 and membrane bound haemachrome were determined with an NO donor (sodium nitroprusside) or an NO synthase inhibitor (l-nitro-arginine methylester) under hypoxia. Results: Hypoxia increased NO metabolites from 25.65 ± 1.95 μmol L−1 to 35.26 ± 2.01 μmol L−1 compared with control. The elongation index decreased after hypoxia for 60 min from 0.567 ± 0.019 to 0.409 ± 0.042, H+SNP group 0.59 ± 0.031, H+L-NAME group 0.422 ± 0.035 at a shear stress of 30 Pa. Hypoxia-stress induced band 3 clustering and tyrosine phosphorylation increased, and both decreased after hypoxia with SNP (Figs 1 and 2). The elongation index increased in the hypoxia group with SNP compared with the hypoxia group and L-NAME group after hypoxia. NO improved SHP-2 tyrosine phosphatase activity, and also inhibited the activity of Syk-induced by hypoxia stress (Fig. 3). Conclusion: In the present article, it is determined that NO plays a potential role in maintaining RBC deformability in hypoxia through altering band 3 tyrosine phosphorylation by maintaining the activity of SH-PTP2 and reducing band 3 crosslinking, which may occur during hypoxic ischemia diseases, and at high altitudes. This study may provide insights into the molecular mechanisms of RBC adaptation to hypoxia.

S23-4 Development history, progress and future prospects of biorheology and biomechanics in Chongqing University

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The study of biorheology and biomechanics at Chongqing University (CQU) began in the 1970s, which has always been guided and helped by Prof. YC Fung. With his help, Prof. YP Wu founded the first Biomechanics Research Lab in China in the 1970s. Biomechanics of CQU was approved to set up the first program for a master's degree in 1980, and one of the two doctoral programs in 1986, the first National Key Discipline, and received the first State Award for Inventions (1984) and Natural Science Award (1988) in the field of biomechanics and biorheology. The Open Lab on Biomechanics and Biorheology under the National Education Commission was set up in 1994. The College of Bioengineering of CQU was founded in 1998, which developed from the Biomedical Electronics Teaching Lab and the Biomechanics Lab

that were built in 1979. Since then over ten research bases were approved for establishment, such as the National "111 project" Base on Biomechanics and Tissue Repair (2006); Key Lab for Biomechanics and Tissue Engineering of MOE(2008), the Chongqing Public Experiment Center of State Bioindustrial Base (2008), Key Lab for Biorheological Science and Technology of MOE (2011), and the State and Local Joint Engineering Lab for Vascular Implants (2015). Biomedical engineering based on biomechanics and biorheology was approved to be a first-level national key discipline and was also were supported by the National "211" and "985" projects. Currently the College has developed into one of the largest research teams and the most influential high-level talent training bases for biomechanics and biorheology in China. This review summarizes the history, progress and future prospects of biomechanics and biorheology in CQU to celebrate the Centennial of Prof. Y C Fung and encourage later generations to go forward.

S23-5 Zebrafish caudal vein formation is flow shear stress dependent

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Hemodynamic factors play a very important role in the process of blood vessel development and remodeling through the regulation of mechanosensory proteins. The different mechanosensory proteins on endothelial cells that transmit mechanical signals to the cytoplasm through their respective mechanical mechanoreceptive effects, and activated downstream chemical signals, ultimately allow the endothelial cells to line up in the direction of fluid shear forces. Unlike mammals, zebrafish can be observed *in vivo*. Thus, we are interested in investigating functional roles of hemodynamics on zebrafish blood vessel development. We utilized the zebrafish as a model system to investigate the cellular and molecular mechanisms that contribute to zebrafish caudal vein formation. We have successfully utilized the transgenic fish Tg (flk1: GFP) to gain new insights that the zebrafish caudal vein is formed at 60hpf under physiologic blood flow. However, the caudal vein formation was blocked at 60hpf at low flow sheer stress. We used the transgenic fish Tg (Bre: GFP; kdrl: Mchrry) to find strong expression of bmp signal in the zebrafish caudal vein.

S24-1 The role of hemorheologic changes in diabetic microvascular complications

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The prevalence of type 2 diabetes mellitus (T2DM) is increasing worldwide. In Korea, the prevalence of diabetes in those aged 30 years and over is estimated as 13.7% (4.8 million) and in those over 65 years of age as 30%. Diabetic micro- and macro-vascular complications are a major cause of mortality in T2DM patients. Micro-vascular complications, especially DKD, can be a risk factor for macro-vascular complications such as atherosclerosis, myocardial infarction, stroke, and heart failure. Therefore, the effort to screen for micro-vascular complications, including DKD, is essential to prevent the progression to macro-vascular complications and deterioration in the quality of life. Critical shear stress (CSS, mPa) is

an index of red blood cell (RBC) aggregability, defined as the minimal shear stress required to disperse RBC aggregates. This study aimed to investigate the association between CSS and the risk of diabetic kidney disease (DKD). A total of 421 (mean age, 58.1 ± 11.5 years; male, 250) individuals with T2DM were enrolled and divided into three groups according to CSS level. CSS was measured using a transient microfluidic technique. DKD was defined as a glomerular filtration rate (GFR) <60 ml/min/1.73 m2 or a urine albumin-to-creatinine ratio (uACR) ≥30 mg/g. CSS was significantly higher in patients with DKD than in those without (317.43 ± 125.11 vs 385.22 ± 182.89, $p < 0.001$). Compared to the lowest CSS tertile, the highest CSS tertile was independently associated with the risk of DKD after adjusting for age, sex, duration of diabetes, presence of hypertension and hemoglobin. The cut-off value of CSS for DKD was approximately 310 mPa. These results suggest that hemorheological changes may contribute to DKD, and that further prospective studies are warranted to determine the role of CSS as a DKD screening tool.

S24-2 RBC abnormalities presented with clinical diagnostic variables in sepsis

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Sepsis and septic shock are medical emergencies and early detection, antibiotics administration and hemodynamic managements are closely associated with mortality. In clinical and experimental sepsis, red blood cell (RBC) abnormalities have been reported. However, it is not known how early RBC abnormalities are expressed compared to the various clinical manifestations used in the sepsis related organ failure assessment (SOFA). Therefore, we investigated whether RBC abnormalities have any clinical significance as an early indicator for detecting septic induced injury comparing with various clinical variables used on SOFA in endotoxin induced sepsis model. Six-week-old male Sprague-Dawley rats received LPS (20 mg/kg) intraperitoneally. Aggregation indices (AIs) and aggregation half time (T1/2), elongation indices (EI max) were measured for assessing RBC aggregation and deformability. Clinical data related SOFA and lactate, venous-to-arterial carbon dioxide difference/arterial- venous oxygen difference ratio [P(v-a)CO_2/C(a-v)O_2] were measured 2 hr, 4 hr, 8 hr and 12 hr after LPS injection. AIs increased significantly 4 hr, 8 hr, and 12 hr after LPS injection and T1/2 decreased significantly in LPS 2 hr, 8 hr, and 12 hr after LPS injection. Platelets significantly decreased 4 hr, 8 hr, and 12 hr after LPS injection. Lactate significantly increased 2 hr, 4 hr, and 8 hr after LPS injection. AIs has statistically significant correlations with T1/2, platelet, bilirubin, creatinine, and P(v-a)CO_2/C(a-v)O_2. EI max increased significantly 2 hr, 4 hr, and 8 hr after LPS injection, however, EI max had no significant correlation with any other variables. RBC aggregation seems to be presented early with clinical data deterioration in sepsis and may be a helpful diagnostic indicator of septic injury.

S24-3 Decrease myocardial perfusion associated with hemorheologic parameters in patients with type 2 Diabetes

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Myocardial ischemia may be present even when there is no significant stenosis of the epicardial coronary artery, or after coronary angioplasty for significant coronary artery disease. This phenomenon is related to disturbance of the coronary microcirculation or vasomotor tone. The aim of this study was to determine the influence of clinical and RBC hemorheological factors on myocardial perfusion in patients with type 2 diabetes mellitus (DM) when compared to patients without DM, presenting with stable angina or acute coronary syndrome. Myocardial perfusion was graded using the myocardial blush grade (MBG) which describes the relative "blush" or intensity of the radio-opacity of myocardial tissue during coronary angiography. MBG was counted before any medical or mechanical intervention, and in the myocardial territory without anatomical flow limitation (<50% of luminal narrowing on coronary angiogram). Myocardial perfusion in this region was associated with DM, renal function, LV diastolic function, inflammatory biomarkers, but not with the clinical presentation. Among the hemorheological parameters, reduced myocardial perfusion was linked to increased RBC aggregation, but not to variations in RBC deformability. In conclusion, myocardial perfusion was affected by DM, LV diastolic function, and inflammatory activity indicated by clinical parameters, and by the hemorheological factor RBC aggregation.

S24-4 Erythrocyte aggregation and deformability as factors determining capillary blood flow in patients with arterial hypertension

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Erythrocyte reversible aggregation and deformability are the major properties that affect blood microcirculation. Alterations in these properties lead to changing blood viscosity and, as a consequence, to changes in blood flow through capillaries. This can lead to significant impairment of blood function, which increases a risk of occurrence of concomitant vascular diseases, and even the mortality especially in the case of cardiovascular pathologies. In this work, complex studies of the factors determining capillary blood flow in patients suffering from such a clinically significant disease as arterial hypertension were conducted by optical methods. Light scattering laser aggregometer and diffractometer RheoScan AnD-300 (Rheomeditech, Korea) was used to conduct *in vitro* measurements of aggregation and deformability characteristics of the cells on ensembles of erythrocytes. Double-channeled optical tweezers were used for measuring the aggregation speed as well as interaction forces during erythrocyte doublet formation on cellular level. To quantitatively evaluate the capillary blood flow *in vivo* non-invasive capillaroscopy measurements in the nailfold vessels were conducted. *In vitro* measurements were performed with EDTA-stabilized human blood samples drawn from patients with arterial hypertension (AH) (70 people) and practically healthy volunteers – control (18 people). It was shown that in AH-patients, the ability of erythrocytes to deform is slightly reduced while the aggregation speed and forces of the cells interaction are significantly increased relative to the control group. In the case of AH, the blood microcirculation in nailfold capillaries is impaired as well.

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S25-1 Postoperative control of vascularized lymph node transfer (VLNT) for the treatment of extremity lymphedema: Ultrasound guided lymph node monitoring using contrast enhanced ultrasound (CEUS)

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Background and objectives: Most plastic surgeons have been facing lymphedema as a clinical challenge over past few years. However, lymphatic surgery using new technical innovations such as micro and super microsurgery techniques is a rapidly advancing field to manage fractious cases. Vascularized lymph node transfer for treatment of lymphedema is a promising operative technique showing beneficial results in early but also in advanced lymphedema stages. To evaluate lymph node perfusion in various cases, postoperative lymph node monitoring with Contrast-enhanced Ultrasound (CEUS) could be considered a superior method. In this paper, the role for vascularized lymph node flaps positioned at the subcutaneous level in lymphedema patients was evaluated. Methods: Ten patients underwent vascularized lymph node transplantation from 2016 to 2017. By using CEUS, postoperative lymph node vitality and blood flow were evaluated. Lymph node perfusion was assessed by an experienced senior radiologist using linear probes (6–9, 6–15 MHz) and bolus injections of Sulphur-hexafluoride microbubbles. Measurements were recorded for TTP (time to peak) and AUC (Area under curve) by using the time intensity curve (TIC) analysis. Results: All vascular lymph node flaps were successful and showed no major complications. CEUS proved lymph node vitality and blood flow in a minimally-invasive and propagative manner. Conclusions: Contrast-enhanced Ultrasound (CEUS) can perform superiorly for the postoperative monitoring of vascularized lymph node flaps positioned at a subcutaneous level in a quick, propagative and safe fashion.

S25-2 The Use of Indocyanine green (ICG) imaging technique in the groin lymphocele microsurgical resection

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The postoperative occurrence of lymph fistulas and lymphoceles in the groin is a complication that should be taken seriously. These fistulas or lymphocele cause an increase in morbidity and can support local and ascending infections. Furthermore a conservative treatment is not always successful. We recently described the microsurgical resection of peripheral lymphoceles. In the following study we investigated the efficacy of a pre-operative and intraoperative diagnostic and therapeutic protocol to manage inguinal lymphoceles using indocyanine green (ICG) and microsurgical procedures. All fifteen patients completely recovered without the need of any compression garment, after the surgery.

S25-3 Significance of high-resolution Color-Duplex-Ultrasound (CDU) designing adipocutaneous, fasciocutaneous and chimeric perforator flaps

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Background: Perforator flaps have become a popular solution for reconstructive tissue transfer. The "hot/cold zone" allows rapid dissection and thin flap harvest at the same time. However, a dependable preoperative perforator mapping is compulsory. Identifying perforating vessels, Color Duplex ultrasonography (CDU) has demonstrated to have the highest pooled sensitivity and positive predictive value in the literature. The following study presents the technology addressing advantages as well as limitations of ultrasound-guided flap design. Methods: Experience with sonography-guided flap design gained from 80 perforator flap free tissue transfers performed at the department of plastic, hand and reconstructive surgery, University of Regensburg without using any other technology, was the basis of our study. Our standardized approach includes regular markings, patient positioning, and easy ergonomics. CDU device settings, program selection, and conventional maneuvering of probe are outlined. Scanning directions through thigh tissues and identification of micro vessels in color duplex mode are outlined. Results: Multifrequency 6–15 MHz linear transducers were utilized for micro vessel localization. Recommendable device settings are depth focused to 3–5 cm, sufficient color gain, wall filter (WF) low and a pulse repetition frequency (PRF) at 0.5–20 Mhz. A 100% correlation rate was found comparing CDU-guided pre-operative micro vessel mapping with surgical exploration of perforators. Perforator mapping with CDU was easy to learn for microsurgeons. It proved to be highly accurate, inexpensive and convenient. Respective video and picture material is demonstrated. Conclusion: Color Duplex ultrasonography (CDU) is a powerful instrument for preoperative perforator mapping in reconstructive surgery using perforator flaps.

S25-4 Influence of systemic vasopressor drugs and fluid administration on microcirculation in free tissue transfer[1]

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Background: Perioperatively, patients' hemodynamics are modulated predominantly by intravenous fluid administration and vasoactive pharmacological support. Vasopressor agents are suspected to be detrimental on free flap survival by the cause of vasoconstriction of the pedicle with consecutive reduced overall flap perfusion and by aggravation of flap dissection. Objective: A novel, standardized fluid restrictive perioperative hemodynamic management was assessed for its feasibility in clinical practice in free flap patients undergoing breast reconstruction. Methods: Patients were randomized to two perioperative regimens with different fluid and vasopressor limits. The primary endpoint regarded flap survival. Secondary endpoints included surgery times, time of patient ambulation and length of hospital stay. Results: There was one total flap failure with liberal fluid administration (LFA). No total or partial flap failure was noted in the fluid restrictive regime with norepinephrine administration up to 0.04 μg/kg/min (FRV). No delay regarding operation time ($p = 0.217$), patient mobilization ($p = 0.550$) or hospital discharge ($p = 0.662$) was registered in the FRV study subpopulation compared to LFA. Conclusions: The results of this prospective interventional trial could not detect any negative impact of vasopressors, neither for the primary endpoint of flap survival nor for the overall patient outcome. The fear of vasopressor associated flap complications has led to a traditional liberal fluid administration,

which failed to demonstrate any benefits when compared to a fluid restrictive vasopressor strategy. [1]Anker AM, Prantl L, Strauss C, et al. Vasopressor support vs. liberal fluid administration in deep inferior epigastric perforator (DIEP) free flap breast reconstruction - a randomized controlled trial. Clin Hemorheol Microcirc 2018: 69: 37–44.

S25-5 ICG-fluorescence-angiography – a new indication in revascularized digits and toes

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Background: Intra- and post-operative assessment of flap perfusion with near-infrared fluorescence imaging is frequently used among plastic surgeons. As clinical evaluation of perfusion in revascularized digits can be difficult, near-infrared fluorescence may offer a new evaluation tool. Objective: As microsurgical anastomosis can be monitored with near-infrared fluorescence imaging there is potential concerning revascularized digits and toes with soft tissue depths not exceeding 7 mm above anastomosis. In a case of a severe crush injury of the hand and in a case of two reattached toes more information about the perfusion was necessary as clinical assessment suspected loss of perfusion. Methods: After intravenous application of ICG the near-infrared imaging showed a delayed but sufficient perfusion in both cases so that a salvage surgery was not necessary. Conclusion: In scenarios of critical perfusion in revascularized fingers and hands, the perfusion control via application of ICG and near-infrared fluorescence imaging can be a helpful tool.

S25-6 ICG-fluorescence-angiography in revascularized digits – First results of a standarized clinical study

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Background: Intra- and post-operative assessment of perfusion with near-infrared fluorescence imaging is commonly used among plastic surgeons to evaluate the quality of a microsurgical anastomosis in free flaps. As microsurgical anastomosis can be monitored there is also potential concerning revascularized fingers and hands. Objective: A novel standardized study evaluating the perfusion of revascularized digits with near-infrared fluorescence imaging was assessed for its reliance compared to clinical assessment and predictive value. Methods: The primary endpoint regarded the survival of revascularized digits. Secondary endpoints included the need of salvage surgery, follow-up surgeries and evaluation of DASH-score. Conclusion: Preliminary results suggest that fluorescence imaging with indocyanine green is a reliable and helpful tool to evaluate the perfusion of revascularized digits. The detection of critical perfusion seems to be even more accurate than clinical evaluation.

S26-1 Nitric oxide synthase activity at various levels and durations of shear stress

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Background: Nitric oxide (NO) is an important free radical that is produced within red blood cells (RBC) by a local NO-synthase (RBC-NOS). The level of shear required for RBC-NOS activation is poorly described, thus we have been exploring the magnitude-duration interactions of RBC-NOS activity, and the resultant levels of intracellular NO produced. Moreover, interactions with other oxygen free radicals have been of interest. Methods: In a series of studies, we examined RBC-NOS activation via immunohistochemistry, and the level of NO produced via a fluorescent tag, following exposure to discrete shear stress levels (up to 100 Pa) over varying durations (1–45 min). Effects of intracellular superoxide have been explored using phenazine methosulfate incubation. Results: Physiological levels of shear appear to result in monotonic activation of RBC-NOS. The amount of NO produced within RBC appears to be sensitive to the level and duration of shear exposure. A particularly interesting change in NO concentration within RBC is observed when shear exposure is 5 Pa below an individuals sub-haemolytic threshold (increased NO), when compared with shear exposure above the sub-haemolytic threshold (decreased NO). We have also observed that high levels of intracellular superoxide impairs RBC-NOS activation. Conclusion: Accumulating evidence indicates that the level and duration of shear exposure regulates RBC-NOS activity, and intracellular NO concentration. Oxygen free radicals appear to negatively impact RBC-NOS activity. The collective findings of our studies highlight special consideration of blood exposure to high shear and oxygen environments, including mechanical circulatory support.

S26-2 Erythrocyte nitric oxide dependent of acetylcholinesterase receptor

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The erythrocyte membrane enzyme acetylcholinesterase (AChE) activity is a biomarker of membrane integrity, aging and inflammation. AChE has the particularity to be inhibited by high concentrations of acetylcholine (ACh), meaning its own natural substrate. Nitric oxide (NO) was observed inside erythrocytes in presence of ACh, by fluorescence microscopy. From studies to date, evidence has been obtained that erythrocyte AChE functions, beyond its enzyme activity, as a receptor for signaling molecules that induce rescue or NO efflux from human erythrocytes and its mobilization from or to reservoir molecules such as S- nitrosohemoglobin or nitrosoglutathione (GSNO). Here we describe the dependency of the signal transduction pathway on the active, less active or inactive complexes that result from the hydrophilic binding of ACh, timolol, indomethacin and velnacrine to the AChE receptor. Also examined is the effect of entry into the erythrocyte of lipophilic molecules such as adenylyl cyclase, guanylyl cyclase, protein tyrosine kinase, protein phosphatase and phosphatidylinositol 3 kinase inhibitors. Within this framework, the relationships between NO efflux, GSNO and its derivative molecules nitrite, nitrate and peroxynitrite, are also described.

S26-3 Hydroxyurea therapy modulates sickle cell anemia red blood cell physiology by acting as a nitric oxide donor: Impact on RBC deformability, oxidative stress and nitric oxide synthase activity

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Sickle Cell Anemia (SCA) is a hereditary hemoglobinopathy and the first genetic disorder in the world. It is characterized by the production of an abnormal hemoglobin (HbS), which polymerizes under deoxygenation. SCA patients suffer from hemolytic anemia, repeated vaso-occlusive crises and chronic vascular complications. Hydroxyurea (HU) is the only approved drug and is known to improve the clinical course of patients by raising foetal hemoglobin levels. However, this mechanism cannot explain alone the beneficial effects of HU in SCA. 16 healthy subjects (AA) and 37 SCA patients treated (HU+, $n = 24$) or not (HU−, $n = 13$) with HU were included. Red blood cell (RBC) deformability was measured by ektacytometry. RBC nitric oxide synthase (RBC-NOS) activation was assessed by immunostaining and RBC and plasma nitrite levels were measured by chemiluminescence. Reactive Oxygen Species (ROS) level within RBC were analysed by flow cytometry. Besides, RBC from SCA patients were incubated with Sodium Nitroprusside (SNP) and the same parameters mentioned above were measured. RBC deformability was decreased in the SCA compared to AA group. HU+ patients had higher RBC deformability, RBC and plasma nitrite levels than HU- patients. RBC-NOS activation was lower in the HU+ compared to both AA and HU- groups. SCA had higher RBC ROS levels than AA individuals and HU+ patients showed decreased RBC ROS content in comparison with HU-patients. *In-vitro*, SNP improved RBC deformability and decreased RBC-NOS activation and ROS levels in SCA patients. HU improves RBC deformability and reduces oxidative stress in SCA. These effects could be attributed to the NO donor effect of HU. The decrease of RBC-NOS activation in SCA under HU suggests a negative retro-control effect of HU on the RBC NO production.

S26-4 The multifaceted role of nitrite and the epigenetic nitric oxide donor, RRx-001 on erythrocyte deformability

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RRx-001 is an anti-cancer immunotherapeutic that increases the sensitivity of drug resistant tumors via multiple mechanisms including covalent binding to hemoglobin. This binding stimulates the nitrite reductase activity of deoxyhemoglobin, resulting in enhanced nitric oxide (NO) production from nitrite in hypoxia. In the present study, the effect of clinically used doses of RRx-001 on erythrocyte deformability was examined. A dose dependent effect of RRx-001 (0.001–1 mM) on erythrocyte deformability was measured by ektacytometry under hypoxia ($n = 8$). The effects of low dose RRx-001 (0.02 mM) on deformability in the presence of ODQ, L-NAME or nitrite were examined both in normoxia and hypoxia. NO release from erythrocytes was measured fluorometrically using a fluorescent probe. During hypoxia, higher doses of RRx-001 (0.1 and 1 mM) significantly increased SS1/2:EImax ($p < 0.01$; $p < 0.05$, respectively). Lower dose of RRx-001 (0.02 mM), alone or combination with ODQ or L-NAME, did not affect deformability. However, in the presence of nitrite, RRx-001 (0.02 mM) caused an increase in

erythrocyte deformability ($p < 0.01$) under hypoxia. NO release was significantly higher during RRx-001 incubation ($p < 0.05$) and a further increment was observed after the co-administration of RRx-001 and nitrite ($p < 0.05$). This study shows that under hypoxic conditions, clinically used dose of RRx-001 caused a significant increase in erythrocyte deformability in the presence of nitrite. This effect of RRx-001 might be attributed to increased NO production. In conclusion serum nitrite level is an important factor for RRx-001 effectiveness and should be considered during RRx-001 treatment in cancer patients.

S27-1 Effect of local tensile stress field on bone matrix and cell alignment: An *in vitro* study

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Osteocytes are mechano-sensory cells embedded within the bone matrix that align their bodies along the major principal stress direction in the bone and play an important role in regulating functional bone adaptation by remodeling. These osteocytic processes are believed to act as mechanosensors detecting the interstitial fluid flow generated in the pericellular canaliculae and are perpendicularly extended to the trabecular and osteonal micro-surfaces. To investigate the role of the local mechanical environment on osteocytes during their differentiation from osteoblasts, we developed a novel, *in vitro* experimental system to control the local mechanical (tensile) stress field produced by cellular contraction and observed the self-organizing, cellular alignment generated via mechano-feedback. Primary osteoblasts were isolated from mouse calvariae and were seeded onto square, type I collagen gels with different mechanical boundary conditions as follows: (A) all four boundaries fixed and (B) two opposite boundaries fixed along one axis and left freely perpendicular to the axis. After culturing the osteoblasts for 24 h, the cell body alignment was determined by measuring the angle from the fixed axis. Cells cultured on the gel with the (A) boundary condition were observed to be randomly aligned, whereas those grown under the (B) boundary condition aligned along the fixed axis. This specific alignment resulted from the uniaxial tensile stress field generated by cellular self-contraction in the gel, which further enhanced the alignment of the cells with higher contraction. These results suggest that positive mechano-feedback may cause osteoblasts to align along tensile stress fields. Considering that this initial alignment will affect the alignment of the osteocytes following their differentiation, further experiments on osteocytes stimulated by differentiation factors will be conducted to investigate the mechanism of osteocytic alignment within the bone matrix.

S27-2 Blood vessel on a chip - 3D vs. 2D

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Inhibiting or normalizing pathological angiogenesis is a therapeutic strategy that has been extensively studied and already brought up clinically with approved drugs. However, most experimental assays for drug development rely on 2D-cell culture models, which fail to mimic sprouting from a parent vessel. We have developed a microvessel-on-a- chip which enables the study of drugs targeting a specific pathway of angiogenesis. Microvessels were prepared using human umbilical vein endothelial cells (HUVEC) within a collagen gel scaffold. Sprouting angiogenesis was induced by VEGF-A, and it was shown to depend on

the Notch signaling. The 3D structure of the microvessel model was non-invasively well characterized by optical coherence tomography. To examine the efficacy of angiogenic inhibitors, two types of inhibitors, sorafenib and sunitinib, which target the VEGF-A/VEGFR-2 pathway were used. A dose dependency of the angiogenesis inhibition could be observed using both inhibitors. Furthermore, the design of the chip enables the study of microvessel permeability by introducing a fluorescent molecule (FITC-dextran; 70 kDa) in the lumen of the parent vessel. It revealed that sorafenib impaired the endothelial barrier function whereas sunitinib did not. Overall this technology should contribute to improve the discovery of promising anti-angiogenic molecules and provide a convenient tool to assess fundamental questions about mechanisms at work at an endothelial-level during VEGF-A-induced angiogenesis.

S27-3 Mechanotargeting of nanoparticles to atherogenic endothelium

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Nanoparticles (NPs) facilitate drug internalization to cells in diseased tissues, which often are characterized by altered mechanical properties (e.g. atherosclerosis). We recently developed a thermodynamic model for nanoparticle uptake that predicted that N(total NP uptake) $= M\varphi \exp[A_0(\mu - \sigma) - 8\kappa\pi]$ where M is cell surface area, φ is NP bulk density, A_0 = NP surface area, μ is NP adhesion energy, σ is tension energy, and κ is membrane bending energy. Using patterning of extracellular matrix proteins, we show that NP endocytosis is suppressed when cells convert from a low stress (low aspect ratio) to a high stress (high aspect ratio) state independent of cellular area and time. Human aortic endothelial cells (HAECs) spread to fill the desired patterns that varied in area and aspect ratio. Larger cells exhibited higher total cellular uptake, due to higher available cell surface area for NP internalization. Cellular uptake was highest on aspect ratios of 1.5 and 2 which is the resting states for cells when they are cultured in 2D culture dishes and decreased as aspect ratio increased. A mechanical model that predicted the internal stress state of cells from focal adhesion location, cell shape, and size, demonstrated that changes in NP uptake from changes in cellular morphology are explained by alteration in internal stress and actin cytoskeletal organization, which was validated using imaging by structured illumination microscopy. Our findings illustrate the role of cellular mechanics on overall NP uptake in HAECs. Understanding the relationship between changes in cellular mechanical properties and NP endocytosis is essential for designing more effective delivery strategies in tissues affected by mechanobiology-related diseases.

S27-4 The roles of vessel pulsation and dilation in clearing extracellular waste from the brain

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Neuron activity causes the release of metabolites in their extracellular environment. Often these metabolites are neurotoxic and/or detrimental to brain health. For example, increases of extracellular potassium ion concentration in brain can cause spreading depolarization, while buildup of amyloid-β is linked to Alzheimer's disease. The brain lacks a lymphatic vasculature for metabolite clearance, and the clearance pathways remain a major standing question in brain physiology. Recently, it has been hypothesized that the brain has a circulation system, dubbed the glymphatic system [1], by which clearance

has a major convective component in promoting metabolite exchange between interstitial fluid and cerebrospinal fluid along the fluid-filled paravascular spaces around cerebral blood vessels. Understanding the mechanics of said flow would have major implications in all aspects of brain pathophysiology. From a fluid dynamics viewpoint, convective flow needs a pumping mechanism. We consider various convective flows as generated by arterial wall movement induced by cardiac driven pulsations and functional hyperemia. We model fluid flow through the paravascular space, the latter modeled as a poroelastic matrix. Boundary conditions are deduced from two photon-imaging in awake, head-fixed mice as well as from hypotheses formulated in the literature. The equations of motion for the fluid are solved using an arbitrary Lagrangian-Eulerian mixed finite element method [2]. The predicted flow rates are critically reviewed to establish whether or not they are consistent with known physiological conditions.

References

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S28-1 Effect of internal viscosity on suspension rheology of red blood cells

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We present a numerical analysis of the rheology of a suspension of red blood cells (RBCs) in a wall-bounded shear flow in the Stokes flow regime for a wide range of viscosity ratio (from 0.1 to 10) between the cytoplasm and plasma. An RBC is modeled as a biconcave capsule, or a Newtonian fluid enclosed by a thin elastic membrane, which follows the Skalak constitutive law. The problem is solved by GPU computing, coupling the lattice-Boltzmann method for the fluid dynamics with the finite element method for the membrane dynamics. The volume-of-fluid method and front-tracking method are employed to update the viscosity on the fluid mesh. Since our numerical model successfully demonstrates the behavior of single RBC and also multi-cellular interaction, we apply it for the problem of hemorheology. Our numerical results show that the deformation mode of RBCs continuously changes from rolling to swinging motion as increasing volume fraction of RBCs. The deformation of RBCs is evaluated by the Taylor parameter, and the contribution of individual deformed RBCs to the bulk suspension rheology is quantified by using the stresslet tensor. We also investigate the effects of shear rate and volume fraction of RBCs on those values, and reveal the relationship between the deformation mode of individual RBCs and bulk suspension of rheology.

S28-2 Hemolytic behavior of human red blood cells caused by osmotic pressure difference - Visualization of hemoglobin behavior by use of light absorption characteristics

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The hypotonic swelling and hemolysis of red blood cells (RBCs) has been studied in terms of the changes in shape and volume of RBCs as well as the time required for hemolysis. For a detailed investigation of the process leading from swelling to hemolysis of single RBC, we applied a visualization

method of the hemoglobin by use of the light absorption characteristics to the experiment of the hypotonic hemolysis. Human RBCs from healthy volunteers were washed with PBS and diluted by mannitol-adenine-phosphate solution. After a hypotonic solution (0.1wt% NaCl aq.) was added to the RBC solution, the swelling behavior was observed and recorded by a microscope with EMCCD camera. A bandpass filter was installed at the lamination in order to irradiate the light of the wavelength close to the hemoglobin maximum absorption. Based on the Lambert-Beer law, the light absorbance is proportional to the medium concentration and thickness. The hemoglobin molarity contained in single RBC was calculated from the absorbance measured by use of the brightness values in the experimental results. Before adding the hypotonic solution, the light absorption of a RBC is weaker at the center than that around the edge. The local difference in thickness of biconcave shape was visualized. The hemoglobin mass results in 128pg, which is slightly larger than the MCH (30–35pg) but roughly on the same order. After adding the hypotonic solution, the concave shape disappears and strong absorption arises at the center, indicating the change of RBC shape into spherical due to the swelling. As the hemolysis occurs, the gradual decrease of hemoglobin in the RBC is obtained. From the time variation of the hemoglobin mass, the shape, and the volume of RBC, the onset of the hemolysis is suggested.

S28-3 Effects of red blood cells on blood flow in micro vessel network: *In vitro* experiment and computer simulation

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A blood flow behavior with multiple red blood cells was examined by using *in vitro* experimental measurements for Polydimethylsiloxane (PDMS) channel constructed for micro vessel network. Blood flow velocity was determined by tracing individual red blood cells as markers in the blood, while flow velocity of the purified water was determined by using fluorescent particles as the markers. In the measurement, flow rate distribution was different between blood and purified water. Red blood cells tended to increase blood flow resistance, affecting the flow rate distribution in the vessel network. Experimental results could be mechanically explained by computer simulations based on a phenomenological hematocrit-apparent viscosity relationship, as well as by those based on coupled analysis of blood plasma flow and motions of deformable red blood cells.

S28-4 Capillary flow imaging with genetically-engineered red blood cells in the living animal brains

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Cellular function in our body relies on continuous supply of blood. Understanding interplays between information processing in the cells and flow states consisting of blood plasma and blood cells is therefore crucial to prevent and treat any diseases related to blood flow disturbances. Here, we developed a fluorescence-based novel imaging technique for capillary blood flow using genetically-engineered rat models in which red blood cells (RBCs) express fluorescent proteins. The fluorescent RBCs and blood plasma labeled with sulforhodamine 101 were simultaneously captured with two-photon laser scanning microscopy in the animal brains under anesthesia conditions. Automatic segmentation by means of

machine learning software were applied to assign the pixels into RBC or plasma for the vessels imaged. Then, a width of the plasma and RBC flow was calculated at the cross-section of the vessels. Apparent dwell time of the fluorescent RBCs were also quantified in each pixel along a centerline of the vessels to map spatiotemporal features of the capillary RBC flow. As expected, a larger width of the plasma flow than RBC's were successfully visualized in the parenchyma arteioles and venules. According to pulsation, a thickness of the plasma layer largely fluctuates in the arterioles, but less in the venules. For capillaries (<8 μm in diameter), intermittent distribution of the plasma and RBCs along the vessels was characterized. The results demonstrated that the distribution of capillary flow varies among the multiple networks as well as within single vessels over time, independent of changes in diameters of the capillaries. In conclusion, the present imaging techniques will allow for fluorescently capturing RBC flow and cellular activity simultaneously in the capillary beds.

S28-5 Fluid dynamical study of preferential distributions of blood cell components in microchannel flows

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It has long been known that red blood cells (RBCs) in blood flow through microvessels are depleted near the vessel wall, whereas platelets have enhanced concentrations in this RBC-depleted marginal layer. In order to elucidate the mechanism of these preferential distributions, we performed two types of *in vitro* experiments, investigating effects of RBC deformability on the axial migration of RBCs and the margination of platelets, respectively. In the first type experiment, we measured the cross-sectional distributions of normal or hardened RBCs flowing through capillary tubes with high spatial resolution by a newly devised observation system. In the second type experiment, we adopted platelet-sized fluorescent particles for platelet substitutes to measure the particle distribution in the cross section of circular or rectangular tubes in the presence of RBCs, using a confocal laser scanning microscope system. The first type experiments demonstrated that normal RBCs showed significant axial accumulation, but hardened RBCs were dispersed widely over the tube cross section dependent on the degree of hardness. The second type experiments indicated that, in rectangular tubes, platelet-sized particles mixed in normal RBC suspensions were concentrated near four corners in the cross section, although in circular tubes they were concentrated near the entire circumference of the tube wall. For particles mixed in highly hardened RBC suspensions, their margination was scarcely observed in both tube flows. These results suggest that preferential distributions of RBCs and platelets can be attributed to high deformability of RBCs, which induces axial accumulation of RBCs and platelets are expelled into the marginal layer where RBCs are depleted, due to the interaction with RBCs.

S29-1 Leukocytes as a link between inflammation and erythrocyte nitric oxide

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Vascular endothelial cells change their phenotypes to participate in the acute inflammatory response, which involves a fast and a slow response as white blood cells approach them. Also, release of chemical

signals like histamine, prostaglandins and nitric oxide (NO) by endothelial cells occurs. NO generation into the vessel lumen is scavenged by erythrocytes through its membrane band 3 protein. The availability of erythrocytes to deliver or scavenger NO is in accordance with the extent of inflammation. For instance in non-survivor sepsis patients the amount of NO efflux was higher, than in survivor ones. The homeostatic human body mechanisms try, through NO liberated by erythrocytes, to compensate for the vasoconstriction observed due to unequal blood flow and decreased microvascular blood flow index, as observed in the case of the sub-lingual microcirculation. Intravital microscopy coupled with fluorescence detectors and confocal microscopy allowed us to visualize, *in vivo*, the development of acute inflammation. Using specially designed software, video images were captured and analyzed to obtain hemodynamic data, leukocyte rolling velocity, number of leukocytes rolling on, and adherent to, the endothelial wall. The efflux of NO from erythrocytes decreased during the acute phase of inflammation as verified in an animal model of acute inflammation with labeled neutrophils, where increased number of neutrophil rolling and adhesion were observed. Erythrocyte deformability was observed to decrease, thus favoring an increase of whole blood viscosity and consequently pouching the neutrophil from the endothelium of post capillary venules.

S29-2 Contribution of fibrinogen to erythrocyte scavenging of nitric oxide

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Fibrinogen (Fib) is a plasma protein participant in the hemostatic and the hemorheological process known also as one of the acute phase inflammation factors when at high concentrations. Nitric oxide (NO) liberated by endothelium cells or lymphocytes enters into erythrocytes and binds to hemoglobin and to glutathione originating reservoirs of NO molecules. Fib binding to CD47 erythrocyte membrane protein decreases nitric oxide (NO) efflux from erythrocyte and increases the NO derivatives (NOx) molecules. Mimicking an hyperfibrinogenemia condition NO efflux and NOx levels change according a signal transduction mechanism under dependence of cAMP concentration and erythrocyte membrane band 3 protein, protein kinase C, phosphodiesterase -3, phosphorylation status and also adenylyl cyclase enzyme activity and acetylcholinesterase enzyme conformation and active state degree. Some of the above biomolecules are already therapeutic targets which the mechanism of action is used in glaucoma and obesity can be explained by the erythrocyte availability in NO.

S29-3 Role of nitrogen oxide and hydrogen sulfide as signaling molecules in the change of the red blood cell microrheology in patients with type 2 diabetes mellitus

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Introduction. It is known that type 2 diabetes mellitus (DM-2T) is associated with impaired blood rheology and red blood cells (RBCs) too. There are some reports that RBC microrheology (RBCM) varies under the influence of nitric oxide (NO). The aim of this study was to estimate the effect of gasotransmitters (GT) donor: sodium nitroprusside (SNP) and sodium hydrosulfide (NaHS - hydrogen

sulphide donor) on RBCM in normal conditions and under DM-2T. Methods. Erythrocytes were incubated with: (1) SNP (100 μM); (2) NaHS (100 μM); (3) methylene blue (MB, 20 μM) and (4) glibenclamide (GkL, 10 μM). The RBC deformability (RBCD) and their aggregation (RBCA) after incubation with each of the GT donor was recorded. Results. Incubation of cells with SNP has led to an increase in RBCD by 12% ($p < 0.01$), and RBCA was decreased by 34% ($p < 0.01$). The H_2S donor had a similar effect on RBCM – RBCD which was significantly increased by 8%, and RBCA decreased by 17% ($p < 0.05$). MB - inhibitor of soluble guanylate cyclase (s-GC) reduced the positive effect of SNP on red cell microrheology. Blocking K^+_{ATP} channels with GkL did not eliminate the positive effect of NaHS on RBCM. It was found that after combined action of "GkL + NaHS" RBCD was higher than in the control ($p < 0.01$), and RBCA by 30% less ($p < 0.01$). Conclusion. Taken together, GT donors have a positive effect on red cell microrheology. The molecular target for NO in erythrocytes is p-GC, which was confirmed in experiments with its inhibition, whereas for the role of K^+_{ATP} channels, as a target for hydrogen sulphide, under these conditions was not revealed. This study was funded by RFBR according to the research project No. 18-015-00475.

S29-4 Change of microrheological characteristics of erythrocytes under the influence of donors of gasotransmitters NO and H_2S: An *in vitro* study

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Background. The signal role in cellular reactions of gaseous transmitters (NO and H_2S) is known. However there are only a few studies on the effect of NO on red blood cell aggregation and deformability (RBCD). Role of H_2S as a signaling molecule in the RBC microrheology changes remains unexplored. The aim of this study was to investigate the effect of NO and H_2S donors on microrheological parameters of RBCs. Methods. RBC microrheology was recorded after cell incubation with: (1) NO donors – spermine NONOate (10–5 M) and sodium nitroprusside (SNP, 10–4 M); (2) hydrogen sulphide donor – (NaHS, 10–4 M); (3) a blocker of K+(ATP) channels – glibenclamide (10–5 M). RBC suspension prepared in drug-free solution was used as a control sample. Results. RBCs under the influence of both types of the gasotransmitter (GT) donors was reduced by an average of 25% ($p < 0.01$). Under these conditions, a moderate increase of RBCD (by 7–14%, $p < 0.01$) was also found. We incubated RBCs with glibenclamide, a blocker of K+(ATP) channels and observed a decrease in aggregation of 27% ($p < 0.01$) and an increase in cell deformability by 8% ($p < 0.01$). It is important to note that blocking the potassium channels with glibenclamide did not eliminate the noticeable microrheological effect of the hydrogen sulphide donor (NaHS). Conclusion. Obtained data allow us to conclude that both types of gasotransmitters may positively affect RBC microrheology: significantly reduce their aggregation and moderately but statistically significant increase the RBCD. It is likely that with changes in RBC microrheology, both gasotransmitters acted on the same key intracellular molecular target. This is probably gaunilate cyclase. The reported study was funded by RFBR 18-015-00475.

S30-1 Red blood cell rheology under different pathological conditions

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Blood viscosity and erythrocyte deformability play a key role in maintaining and regulating the microcirculation. Hemorheological changes due to alterations of blood cells and plasma components lead to hyperviscosity, which may slow blood flow and facilitate occlusive events through erythrocyte rouleaux formation and platelet aggregation. Hemorheological alterations have been described in Sickle Cell Anemia (SCA) and Thalassemia. SCA is characterized by sickle red blood cells which do not easily flow through the microcirculation, causing frequent vaso-occlusive episodes, with resulting red cell rigidity, poor microvascular blood flow, tissue ischemia and infarction. In Thalassemia a high incidence of thromboembolic events, a hypercoagulable state and an increased risk of thrombosis have been demonstrated which can result in significant morbidity and mortality. The molecular and cellular mechanisms contributing to hypercoagulability are diverse and include chronic platelet activation, alteration of red blood cell membranes, abnormal expression of adhesion molecules on vascular endothelial cells, and dysregulation of hemostasis. In this study the hemorheological profiles of patients with SCA and Thalassemia have been characterized in order to point out new indices of vascular impairment.

S30-2 Role of hemorheological alterations in skin ulcers

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Several diseases are associated with both hemorheological alterations and skin ulcers. The most important conditions include hematological diseases such as plasma cell disorders (multiple myeloma and Waldenstrom's macroglobulinemia), cryoglobulinemia, fibrinogen alterations (cryofibrinogenemia, dysfibrinogenemia) and hereditary anemias (spherocytosis, thalassemia, sickle cell disease). Also connective tissue diseases can be complicated by hyperviscosity and skin lesions. Morevover, a hemorheological impairment can contribute to the skin lesions observed in diabetes mellitus (diabetic foot syndrome), critical limb ischemia, arterial hypertension (Martorell's ulcer) and venous insufficiency. The mechanisms of the rheological alteration vary in different clinical conditions, being related to an altered behaviour of circulating cells or a variation in quantity or quality of plasma proteins. The circulating cells involved in the pathophysiology of skin lesions are primarily erythrocytes but in some instances, and particularly in chronic venous diseases, leukocytes can play a major role. As regards plasma factors, the main point is the prominent influence of fibrinogen on plasma viscosity, much larger than what expected on the basis of its concentration. This effect, resulting from the molecular characteristics in physiological conditions, is amplified when circulating fibrinogen is abnormal. The most relevant site of intervention of rheological factors is microcirculation, where rheology interacts with hemodynamics and vessel wall function. Hemorheological impairment, besides having a pathophysiological role in skin ulcers, may have implications for their treatment.

S30-3 Hemorheology in kidney disease

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Patients in renal replacement therapy (RRT), namely dialysis and renal transplantation, present a cardiovascular risk substantially higher than the general population, due to both traditional and non-traditional risk factors. Hemorheological alterations have been extensively described in hemodialysis patients (HD), while little data exist about peritoneal dialysis patients (PD) and kidney transplant recipients (KT). We characterized the hemorheological profile of 49 PD and 108 KT patients, and compared these data with hemodialysis patients (HD). PD showed lower plasma viscosity, whole blood viscosity at 1-Hz, erythrocyte aggregation index and yield stress (parameters related to macro-circulation) when compared to HD, while microcirculatory function resulted severely impaired, as expressed by high values for whole blood viscosity 200-Hz shear rate and lower erythrocyte deformability (ED). KT, when compared to HD, showed lower plasma viscosity, whole blood viscosity at 1-Hz and 200-Hz shear rate, erythrocyte aggregation index and yield stress. Nevertheless, KT show a markedly reduced ED. Low ED in PD patients may be due to exposure to high-glucose dialysis fluids in PD; although we suspect a role for immunosuppressive treatment for ED reduction in KT, we found no differences among hemorheological parameters between the different classes of immunosuppressive drugs used. In conclusion, we found several hemorheological alterations in patients in RRT, which may contribute as a non-traditional risk factor to the high burden of cardiovascular disease in this population. More specifically, we confirm profound hemorheological dysfunction in HD patients; KT and, in part, PD patients showed a lower plasma viscosity and whole blood viscosity, but had an important defect in ED.

S30-4 Rat pial microvascular changes during brain hypoperfusion and reperfusion injury: Role of antioxidant substances

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Our studies were aimed to evaluate the *in vivo* polyphenol protective effects on damage induced by 30 min cerebral blood flow decrease (CBFD) and subsequent 60 min cerebral blood flow recovery (CBFR) in rat pial microcirculation. In particular, we tried to detect changes in ROS production after different polyphenol administration. Rat pial microcirculation was observed using fluorescence microscopy through a closed cranial window. In all animals, pial arterioles were classified in five orders of branching according to Strahler's method. Furthermore, neuronal damage and radical oxygen species (ROS) formation were detected by 2,3,5-triphenyltetrazolium chloride staining and 2'-7'-dichlorofluorescein-diacetate assay, respectively. After 30 min of CBFD, induced by bilateral common carotid artery occlusion, and 60 min of CBFR, hypoperfused rats showed a decrease in arteriolar diameter, an increase in microvascular leakage and leukocyte adhesion, accompanied by decreased capillary perfusion. Moreover, marked neuronal damage and evident ROS generation were detected. Conversely, rats treated with different polyphenols, such as oleuropein, malvidin and apigenin, showed a dose-related arteriolar dilation, a reduction in microvascular permeability as well as leukocyte adhesion compared to hypoperfused rats; moreover, capillary perfusion was protected. Finally, ROS generation and neuronal damage were reduced in animals treated with these antioxidant substances. Polyphenols, intravenously infused, showed dose-related protective effects on rat pial microcirculation during CBFD and subsequent CBFR, preventing blood-brain impairment and neuronal loss. Furthermore, a significant reduction in ROS generation was observed.

S30-5 Bridging the gap from basic microcirculation to the clinical world

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In recent years research on the microcirculation has received significantly increased interest. Numerous clinical studies have emphasized the role of microcirculation in the pathophysiology of several diseases. At the same time basic research has produced a huge number of observations that have broadened the knowledge of microcirculatory function (MF), providing clinicians with additional elements to be used for diagnostic and therapeutic purposes. However, basic and clinical research do not still succeed in dialogue. The assessment of the cutaneous hemodynamic by laser Doppler flow meter (LDF) with Wavelet Analysis (WA) may be considered an example. Between 1998 and 2003 the WA has been applied to calculating the frequency spectrum of the human cutaneous LDF flow-motion waves. Although application of WA to the LDF signal would allow a detailed evaluation of MF, by selecting each individual component the use of this methodology does not seem to be yet widespread, resulting in a gap between basic research and the clinical world. In a systematic review of the literature on WA, it appears that its application to the LDF cutaneous signal analysis over the last 20 years, seems to be scarce. Between 1998 and 2017, in 98 publications, 45 with 45,9% (95%CI 36.3–55.7%) pooled rate, reported data on 1679 patients (PTS) and 53, with 54.0% (95%CI 44.2–63.6) pooled rate, have been performed on 892 healthy subjects (HS). No significant difference between the two group's pooled rates have been found ($p = 0.84$). The reasons of the poor application of WA to the LDF are not easy to find. But the construction of a common language between basic and real clinical worlds could bridge the gap. Scientific societies may play a significant role.

S31-1 Biorheology of bile

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Bile is an important secretion from a liver for our life and one of the most important rheological characteristics is extensional rheology. Due to the extensional viscosity of bile is much greater than shear viscosity. Bile flow in biliary is also influenced by extensional viscosity. In this study, a shear thinning capillary device was used to measure the stretching properties of bile. The liquid bridge was set up between upper and lower endplates. The endplates with diameter $D_0 = 1$ mm initially separated by $h_0 = 0.5$ mm (aspect ratio $= 0.5$) were used for the measurements of the filament. In the experiment, the top plate moves up rapidly to a set distance $h_{max} = 4$ mm. The mid-point diameter of a liquid bridge was recorded by laser micrometer (Keyence corp.) and plotted against time. The zero point of the time ($t_0 = 0$ s) measurement was defined as the timing of the end of the moving process of the plate. The filament self-thinning dynamics were captured by a high-resolution digital video using a high-speed camera. The results showed the stretching phenomenon of bile. Additionally, the shear viscosity of bile was examined by a rheometer (HAAKE RS600, Thermo Fisher Scientific, USA). All samples showed a shear thinning behavior. At the low shear rate, the viscosity of bile behaved as a non-Newtonian fluid and at the high shear rate the viscosity of bile attained a low constant value.

S31-2 Electrical impedance spectroscopic technique for cancerous cell sensing by considering the extracellular fluid around cells

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This study proposes a novel method of cancer cell detection by using microchannels with multi-layer electrodes based on electrical impedance spectroscopy (EIS) technique. This cancer cell detection method is based on the ion production of biological cells through their ion channel. By using EIS the ion production rate can be measured from the impedance change in extracellular fluid. We apply the ion production rate to the detection of cancer cell because the ion channel can be different in between normal cells and cancer cells and it causes the different ion production rate. In the experiment, we measured the electrical impedance spectroscopy in order to estimate the ion production rate. In a microchannel with five sensing sections, and with 16 layer electrodes in each section, different kinds of cells were allowed to flow into the channel. The results show the difference of ion flux among the different kinds of cells.

S31-3 Matrix metalloprotease production of vascular endothelial cells under extremely high wall shear stress condition

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Dilatation, dissection, and rupture of the ascending aorta are frequently associated with bicuspid aortic valves. It has been reported that the aortic wall is exposed to eccentric flow jets due to the abnormal valve anatomy and wall shear stress more than 10 Pa exerts on endothelial cells lining the lumen of the wall, whereas physiological shear stress in arteries on average is 2 Pa. Hence, such extremely high wall shear stress may induce imbalance between proteases and their inhibitors through changes in matrix metalloprotease (MMP) expression, leading to the aneurysm formation. However, the detailed mechanism is still unknown. In this study, we evaluated the effect of extremely high wall shear stress on the expression of MMP-2/-9, known to degrade elastic fibers and associated with the early stage of aneurysm formation. Bovine aortic endothelial cells were exposed to fluid shear stress up to 40 Pa for 24 h using a parallel-plate flow chamber. After the flow-exposure experiment, endothelial cells were cultured with serum-free medium for 8 h, and MMP-2/-9 activities of the conditioned medium were then detected by gelatin zymography. After being exposed to shear stress of up to 40 Pa, cells aligned to the direction of wall shear stress and maintained an intact monolayer. The level of the MMP-2 activity showed a tendency to decrease according to the increase in shear stress. The MMP-9 activity was also lower at 10 Pa compared to the static, and we could not detect the MMP-9 activity at 20 and 40 Pa conditions. To reveal the effect of high shear stress conditions on the aneurysm formation, we will further investigate the regulators for MMPs activities such as their inhibitors and nitric oxide, and the roles of smooth muscle cells in the tunica media.

S31-4 Observation of microscopic elastic structure in arterial tissue by use of a scanning haptic microscope (SHM)

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We developed a scanning haptic microscope (SHM) for precise observation of the distribution of the elastic modulus over a slice sample of biological tissues. We have mainly measured vascular tissues, and have revealed variations of the microscopic elastic structure along the entire length and strain condition. In this study, to evaluate mechanical compatibility and regeneration degree, an autologous collagen vascular graft called a Biotube was measured by SHM. The SHM measurements were performed on circumferential slice samples of the canine carotid artery and Biotubes before and after implantation. Embedded and implantation period of Biotubes were 2 weeks and 3 months, respectively. After the SHM measurements, the slice samples ware stained with elastic-van Gieson stain for elastin or Masson's trichrome stain for collagen. In the SHM measurement of the carotid artery, hard/soft laminated structures corresponding to elastin and collagen layers were observed. SHM images of a Biotube before implantation had a relatively soft elastic structure with its main component being collagen fibrils. After 3months implantation, the main component of the Biotube remained as collagen fibrils, although invasion of elastin fibers was observed near the luminal surface of the Biotube. In the SHM measurement, however, the Biotube after implantation had hard/soft laminated structures, and its average elastic modulus was almost the same as that of the carotid artery. It is thought that collagen fibrils in the Biotube reorganized by cyclic mechanical loading due to the heart beat after implantation, and its elastic structure also changed. SHM can be expected to be useful for evaluating compatibility and the degree of regeneration of implanted tissues by measuring differences between native tissues and following changes after implantation.

S31-5 Ultrafast imaging of cell elasticity with optical microelastography

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Elasticity is a fundamental cellular property that is related to the anatomy, functionality and pathological state of cells and tissues. However, current techniques based on cell deformation, atomic force microscopy or Brillouin scattering are rather slow and do not always accurately represent cell elasticity. Here, we have developed an alternative technique by applying shear wave elastography to the micrometer scale. Elastic waves were mechanically induced in live mammalian oocytes using a vibrating micropipette. These audible frequency waves were observed optically at 205,000 frames per second and tracked with an optical flow algorithm. Whole cell elasticity was then mapped using an elastography method inspired by the seismology field. Using this approach, we showed that the elasticity of mouse oocyte is decreased when the oocyte cytoskeleton is disrupted with cytochalasin B. The technique is fast (less than 1 ms for data acquisition), precise (spatial resolution of a few micrometers), able to map internal cell structures, robust, and thus represents a tractable novel option for interrogating biomechanical properties of diverse cell types.

This new technique is opening the possibility of studying dynamic cellular processes and elucidating new mechanocellular properties. We call this technique "cell quake elastography."

S32-1 The contact activation system in device-related thrombosis modeling

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Biomaterial surfaces used in blood-coated medical devices initiate blood coagulation that may lead to device malfunction or thromboembolism. To reduce thrombosis risk in this type of devices computational fluid dynamics (CFD) is often used to predict the formation of thrombus. The current work consists in the coupling of a CFD solver with a biochemical scheme that generates thrombin considering the contact activation system (CAS). A strategy is proposed to initiate the coagulation reactions by contact activation of factor XII with the device wall. In this view, a boundary condition is introduced which relates the species diffusive wall flux to the surface reaction rate of factor XII activation. This new predictive method contrasts with conventional in-vivo models in which the reactions are initialized at user-defined and arbitrary injury sites. The model of Chatterjee et al. 2010 was applied to a backward facing step geometry (BFS) inspired from the experimental setup of Taylor et al. 2014. The results show a significant amount of thrombin generated in the recirculation region formed behind the BFS. Interestingly, this result was obtained without a priori knowledge of the regions prone to thrombosis. Qualitatively results align well with the experimental data which showed that the thrombus forms behind the BFS, in the recirculation zone area. Our results thus show that accounting for the CAS provides a novel strategy to initiate thrombus formation. The current strategy coupled to existing models that consider platelet activity and thrombus growth may lead to a predictive pipeline for device-related thrombosis. References: Chatterjee MS et al. (2010) PLoS Comp Biol 6(9), Taylor JO et al. (2014) J Biomech Eng 136:071012, Mendez et al. (2018) Biomech Model Mechanobiol (2018).

S32-2 Development of a device-induced computational thrombosis model

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Thrombosis remains an obstacle in current blood-contacting devices, primarily due to regions of disturbed flow. Specifically, regions of high shear stress activate platelets and regions of low wall shear rate allow for platelet adhesion and thrombus growth. Both of these phenomena occur in regions of flow separation. A computational model capable of predicting device-induced thrombosis on a macroscopic scale and relatively quickly, compared to existing models, would be useful in the device development process. A single-scale thrombosis model was modified to predict device-induced thrombosis. Bulk concentrations of platelets (non-activated and activated) and a chemical activator are considered. A power law model is used to predict platelet activation based on the local shear stress, and a non-linear weighting function is used to quantify thrombus deposition based on the local wall shear rate. A modified Brinkman term is added to the Navier–Stokes equations to account for a growing thrombus by modeling it as a porous material. In summary, a model that predicts macroscopic thrombus is presented to achieve the goal of expediting the cardiovascular device design process.

S32-3 Reduced-order computational modeling of thrombogenic potential in large arteries

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Computational modeling of large artery thrombosis is challenging for several reasons. First, it involves a wide range of spatial and temporal scales. Blood flow dynamics span up to centimeters, while platelet interaction and near-wall chemical concentration boundary layers are on the order of microns. Second, the underlying processes are highly complex and in some cases not fully understood. Simulation of the coagulation cascade alone, for example, requires the knowledge of dozens of reaction rates and initial conditions, many of which are not well known. The goal of this work is the development of reduced-order techniques for the modeling of thrombogenic potential in large arteries. We will first discuss a method for bridging the gap between length scales in the mass transport problems associated with thrombotic processes. Due to the high Peclet and Schmidt numbers associated with these types of problems, coagulation enzymes are expected to be concentrated in micron-scale boundary layers near the vessel wall. Based on these physics, we develop a model that converts the three-dimensional micron-scale transport problem to one that can be solved as a two-dimensional problem on the vessel wall surface, greatly reducing computational cost. Second, we will discuss a framework for developing reduced-order models of the coagulation cascade. This framework utilizes nested genetic algorithm optimizations to both reduce the number of model species and optimize the rate constants of the resulting reactive network. These reduced-order models have lower model complexity and computational cost, while potentially reproducing essential dynamics of the full reactive system.

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O1-1 Albumin solder covalently bound to a biodegradable polymer membrane: New approach to improve binding strength in laser tissue soldering

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As the gold standard of small blood vessel anastomosis, micro-suturing shows drawbacks such as increasing risks of hypoxia as well as tissue damage. Laser tissue soldering (LTS) might be a promising alternative. However the achieved shear strength is too weak in many cases. It has been shown that the cohesive strength of the liquid solder can be enhanced by using carrier materials. In the present study a poly(ether imide) (PEI) membrane served as carrier material and indocyanine green (ICG)-supplemented albumin as solder substrate. In order to further strengthen the obtained solder weld, albumin was covalently coupled to the carrier membrane. The coating was performed under physiological conditions to prevent structural protein changes. The albumin functionalized carrier membrane was placed onto the tunica media of explanted pig thoracic aortae forming an overlapping area. Using a diode continuous-wave laser an ICG-mediated heat-denaturation of the albumin could be achieved. The LTS could generate a membrane-blood vessel connection corresponding to 15% of the tensile strength of the native blood vessel. According to these results the shear strength of a native blood vessel can be achieved by applying this method at an overlapping zone of appropriate size. Further studies in animal models should be conducted to confirm the beneficial effects of the results obtained in vitro.

O1-2 Circumferential alignment of smooth muscle cells in micro-tube environment

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Ordered arranged smooth muscle is an important component of tubular tissues (such as trachea and blood vessels) in vivo, which is responsible for maintaining morphology and mechanical properties. Growing evidence reveals that tubular environment could affect the movement and alignment of cells, but it is unknown whether this is sufficient to form a stable arrangement of cells. Thus, we fabricated micro-patterned cylindrical concave and convex surfaces with different curvature diameters (cell scale) with PDMS and inoculated with different types of cells in the tubular tissues. Results showed that different degrees of morphology and biology differentiation occurred in all kinds of cells compared with the planar environment. Significantly, both of the two kinds of smooth muscle cells (ASMCs, VSMCs) could form a highly ordered pattern perpendicular to the tube axis in a given curvature environment. In our models, these behaviors of cells might be related to the architecture on curved surface and change with cell tension

and adhesion ability. Altogether, our findings help to better understand the tissue development and provide new idea for tissue engineering.

O1-3 Subhaemolytic mechanical trauma increases RBC aggregation by altering cell electrochemistry

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The ability of red blood cells (RBC) to aggregate, disaggregate, and deform greatly influences systemic blood fluidity and oxygen delivery. The major intrinsic disaggregating force of RBC is determined by their electronegative charge, created by sialic acids (SA) located within the glycocalyx. Given subhaemolytic shear environments within mechanical circulatory support (MCS) have been reported to alter cell morphology, we hypothesised that similar shear exposure would also cleave membrane bound SA, altering the electrochemical and physical properties of RBC. RBC from 20 healthy donors were isolated and resuspended in an isotonic viscous suspending medium at 0.15 L/L. A Poiseuille shearing system was constructed and used to expose RBC suspensions to 125 Pa for 1.5 s. RBC were examined for: aggregation in autologous plasma, disaggregation shear rate threshold, ability to aggregate extrinsic to plasma factors (i.e. aggregability), SA concentration (utilising periodate-resorcinol method), and electrophoretic mobility. Shear exposure increased RBC aggregation, disaggregation shear rate threshold, and RBC aggregability. The concentration of SA significantly increased in the shearing supernatant, and decreased in isolated RBC membrane ghosts. The electrophoretic mobility significantly decreased following shear exposure, confirming RBC had become less negatively charged. Acute subhaemolytic shear exposure may remodel the RBC membrane, removing SA, thereby altering electrochemical and physical properties of RBC. As RBC aggregation/disaggregation is a primary determinant of blood fluidity (and oxygen delivery), the present observation may partly explain the increased incidence of microvascular dysfunction and ischaemic complications in patients receiving MCS.

O1-5 Ultrafast imaging of cell elasticity with optical microelastography

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Elasticity is a fundamental cellular property that is related to the anatomy, functionality and pathological state of cells and tissues. However, current techniques based on cell deformation, atomic force microscopy or Brillouin scattering are rather slow and do not always accurately represent cell elasticity. Here, we have developed an alternative technique by applying shear wave elastography to the micrometer scale. Elastic waves were mechanically induced in live mammalian oocytes using a vibrating micropipette. These audible frequency waves were observed optically at 205,000 frames per second and tracked with an optical flow algorithm. Whole cell elasticity was then mapped using an elastography method inspired by the

seismology field. Using this approach, we showed that the elasticity of mouse oocyte is decreased when the oocyte cytoskeleton is disrupted with cytochalasin B. The technique is fast (less than 1 ms for data acquisition), precise (spatial resolution of a few micrometers), able to map internal cell structures, robust, and thus represents a tractable novel option for interrogating biomechanical properties of diverse cell types. This new technique is opening the possibility of studying dynamic cellular processes and elucidating new mechanocellular properties. We call this technique "cell quake elastography".

O1-6 The effects of substrate stiffness on HUVEC adhesion with THP-1 cells and molecules associated with adhesion

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Vascular stiffness makes the conditions favorable for various cardiovascular disease. Apart from collagen and elastin, adhesion between endothelial cells and immune cells is mediated by molecules associated with adhesion and chemokines. Substrate stiffness can influence molecules associated with adhesion. The relationship between vascular stiffness and endothelial cell adhesion may provide a new target for the treatment of cardiovascular diseases. We sought to simulate the stiffness of normal and abnormal vessel, and assess the influence of substrate stiffness on molecules associated with adhesion in endothelial cell. Arcylamide and bis-arcylamide were reacted in various proportions for each polyacrylamide gel. The Young's modulus of gels were 11.15 ± 0.1 kPa, 32.51 ± 1.91 kPa and 80.64 ± 2.11 kPa. The influence of stiffness on adhesion molecules (ICAM-1,VCAM-1 and MCP-1) was tested by IF, WB and q-PCR technology. The relation of inhibitors of differentiation-1 (Id1) with adhesion molecules was studied by Id1 overexpression in HUVEC. Protein and mRNA expression levels of adhesion molecules associated with HUVEC on physiological stiffness (30 kPa) were lower than on the pathological stiffnesses (80 kPa and 10 kPA). We found that both mRNA and protein levels of Id1 in HUVEC cultured on gel with different stiffness had the same trend as adhesion molecules, namely the lowest on 30 kPa. Likewise, Id1 is also highly expressed in pathological stiffness and molecules associated with adhesion will be highly expressed in transfected HUVEC, which may provide a new sophisticated way for prevention of cardiovascular disease by controlling vessel stiffness. [Supported by the NSFC (11572064, 11332003, 31701275), the NKTR&DPC (2016YFC1102305).]

O2-1 Pilot clinical study of quantitative ultrasound spectroscopy measurements of erythrocyte aggregation within superficial veins of 50 volunteers

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An enhanced inflammatory response is a trigger to the production of blood macromolecules involved in abnormally high levels of red blood cell (RBC) aggregation. This study aimed to demonstrate the clinical feasibility of a non-invasive ultrasound-based erythrocyte aggregation measurement method for potential application in critical care medicine. RBC aggregation was evaluated using modeling of the ultrasound

backscatter coefficient with the structure factor size and attenuation estimator (SFSAE). SFSAE spectral parameters W (packing factor describing spatial organization of RBCs) and D (fractal dimension of RBC aggregates) were measured within the antebrachial vein of the forearm and tibial vein of the leg in 50 healthy participants at two flow shear rates. Recordings were performed under natural flow or reduced flow controlled by a pressurized bracelet applied on the skin. Blood samples were also collected to measure RBC aggregation ex-vivo with a laser erythroaggregometer (parameter S_{10}). W and D measured in-vivo were positively correlated with ex-vivo S_{10} index for both measurement sites and shear rates (correlations between 0.35–0.81, $p < 0.05$). SFSAE W and D measurements on the forearm were correlated with values over the leg for similar shear rates ($p < 0.05$). For both venous sites and shear rates (natural flow at 37 s-1 on average, and reduced flow at 0.8 s-1 on average), intra-observer variability for 5 repeated measures of D varied between 26.3–28.2%, whereas it was higher (34.1–48.9%) for W. Repeatability might be improved by readjusting the bracelet applied pressure at each measure. In conclusion, designed bracelet, ultrasound system, and SFSAE software may have application for continuous patient monitoring in critical care unit to predict sepsis events.

O2-2 Rapid clinical assessment of the sublingual microcirculation - Visual scoring using microVAS in comparison to standard semi-automated analysis

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Rationale: Alterations in human microcirculation occur in many disease states leading to morbidity and mortality, however assessing the microcirculation is not standard clinical practice. Standard microcirculation analysis using semi-automated analysis is expensive, time consuming, and expertise dependent making it unfeasible. We proposed a novel visual scoring system (microVAS) for the analysis of microcirculation videos that can be performed at the patient bedside in real time. Objective: Validate our microVAS score by training health professionals unfamiliar with the microcirculation field to use our microVAS score and compare their scores to the standard method of semi-automated analysis using AVA3 software. Methods: Using a prospective double-blind study design, we recruited and trained 20 participants to use our microVAS score. Participants scored 40 videos (from 22 healthy and 18 septic patients) for MFI and PPV. The same 40 videos were analyzed by an expert using the gold standard semi-automated method of analysis. Results: Overall correlation of MFI was $r = 0.3283$ (95% CI 0.27–0.39), $p < 0.05$; overall correlation of PPV was $r = -0.1123$ (95% CI −0.18 to −0.04), $p < 0.05$. The Krippendorff's alpha for MFI was 0.56 (healthy videos: $\alpha = 0.34$, sepsis videos: $\alpha = 0.31$). For PPV Krippendorff's alpha was 0.43 (healthy videos: $\alpha = 0.56$, sepsis videos: $\alpha = 0.17$). Conclusions: Overall for both MFI and PPV, there was a small correlation between our microVAS score and AVA 3 scores. Regarding inter-rater reliability both MFI and PPV showed fair agreement between raters. Going forward multiple improvements to the microVAS scoring system as well as the training program are suggested to improve reliability and consistency.

O2-3 L-cysteine improves blood fluidity that has been impaired by acetaldehyde

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Regular heavy consumption of alcohol increases the risk of stroke and ischemic cerebrovascular diseases. Acute heavy alcohol consumption leads to increased whole-blood viscosity, decreased erythrocyte deformability, and impaired fibrinolytic potential. Acetaldehyde (ACD) causes abnormal erythrocyte morphology due to cross-linking of erythrocyte ghost proteins, and decreased erythrocyte deformability. It was reported that blood ACD levels are reduced in mice pretreated with L-cysteine (L-cys). However, there is no study on the effect of ACD and/or L-cys on blood fluidity. In this study, we evaluated whether ACD impaired whole-blood fluidity. In addition, the effect of L-cys on blood fluidity that had been impaired by ACD was examined. Methods: Blood samples were obtained from 10 healthy, non-smoking, male volunteers (age: 23.3 ± 1.3 years, body mass index: 21.6 ± 2.6 kg/m^2). ACD or ACD and L-cys were added the blood samples before each experiment. We measured blood passage time (100 μL and consecutive 20-μL volumes) using Kikuchi's microchannel method (MC-FAN: Hitachi Haramachi Electronics Co., Ltd., Japan). The blood passage time increased after adding ACD in a dose-dependent manner. The blood passage time that increased after adding ACD, decreased after adding L-cys in a concentration-dependent manner. The sequential blood passage time at 20-μL intervals after adding ACD gradually increased, but this was not observed after adding ACD and L-cys. Conclusion: Blood fluidity is impaired by adding ACD in a dose-dependent manner. Adding L-cys improves blood fluidity that has been impaired by adding ACD.

O2-4 Hemorheological studies in a group of patients with Waldenström's macroglobulinemia

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Waldenström macroglobulinemia (WM) is defined by the World Health Organization as lymphoplasmacytic lymphoma (LPL). Increased concentration of IgM is one of the factors that lead to increase of blood viscosity. Blood hyperviscosity in patients with Waldenström's macroglobulinemia is serious clinical problem. The aim of this work was to observe the rheological parameters in a group of Waldenström's macroglobulinemia patients in a two year period. During this time the blood samples from each patient were collected five times. The evaluation included such factors as whole blood viscosity, plasma viscosity, hematocrit value and the tendency to aggregation and deformation of erythrocytes. The latter features were quantified using the mathematical rheological model of Quemada. Compared to the hemorheological parameters obtained for healthy objects, elevated value of plasma viscosity and an increased tendency to aggregation were observed in the studied group. Other rheological parameters values did not differ significantly form the values in healthy objects. All patients were under constant medical control.

O2-5 Adora2b receptor activation mediates flap protection from ischemia/reperfusion injury

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Background: Ischemic preconditioning (IPC) is defined as increasing tolerance to subsequent ischemic stress by exposing tissues to sub-lethal ischemia. Although many candidates have been suggested, recent studies have clearly demonstrated that adenosine-mediated ADORA2B receptor (ADORA2BR) activation is the main mechanism involved in IPC. While the tissue-protective role of this mechanism has been demonstrated in different ischemia/reperfusion (I/R) models, its role in flap surgery-derived I/R damage has not been investigated to date. The aim of this study was to investigate the role of adenosine and ADORA2BR activation in IPC-mediated tissue protection in an epigastric flap model. Methods: 80 female Wistar rats were divided into five groups, which were all exposed to epigastric flap surgery comprising 6 hours of ischemia and 6 days of reperfusion in the presence or absence of IPC. No drugs were administered to Group 1. In Group2, animals were pretreated with specific CD73-inhibitor in order to inhibit adenosine generation. In Group3, animals were pretreated with adenosine. In Group4, animals were pretreated with a specific ADORA2BR antagonist, and in Group5, animals were pretreated with ADORA2BR agonist before ischemia induction. After 6 days of reperfusion, tissue survival was evaluated via histological and macroscopic analysis. Results: IPC application significantly enhanced tissue CD73 expressions and adenosine concentrations ($p < 0.01$). Flap survivals were increased by IPC application in Group1 ($p < 0.05$). However, CD73 inhibition blocked this increase (Group2). In Group3, adenosine therapy improved flap survival even in the absence of IPC ($p < 0.01$). Similarly, while an ADORA2BR antagonist attenuated the tissue-protective effect of IPC ($p < 0.01$), an ADORA2BR agonist improved flap survival by mimicking IPC in groups 4 and 5. Conclusion: These results provide pharmacological evidence for a contribution of CD73 enzyme-dependent adenosine generation and its signaling through ADORA2BR to IPC-mediated tissue protection. They also suggest for the first time ADORA2BR agonists may be used as a potential preventive therapy against I/R injury in flap surgeries.

O2-6 Purinergic regulation of erythrocyte enzyme activity

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Background: eNOS activity in several cell types including endothelial cells, has been shown to be induced by purinergic receptors. Although erythrocytes have an active eNOS enzyme, its regulation with purinergic reseptors remains unknown. The aim of the present study was to evaluate purinergic receptor P2X mediated eNOS activation and NO production in erythrocytes. Methods: Erythrocytes

were isolated from healthy volunteers and re-suspended in HEPES solution at a hematocrit of 0.01 l/l. Intracellular NO and Ca^{+2} levels and eNOS activation were measured by flow cytometry in response to P2X receptor agonist, in the absence and presence of eNOS, P2X receptors and PI3K inhibitors. Results: Activation of purinergic P2X receptors was found to induce intracellular NO generation, Ca^{+2} influx and phosphorylation of eNOS enzyme in erythrocytes. These responses were blunted in response to incubation of erythrocytes with P2X receptor agonist in the presence of NOS enzyme, P2 receptors and PI3K inhibitors. Conclusions: The results of the study clearly demonstrated purinergic activation of eNOS enzyme in erythrocytes through Ca^{+2} dependent and independent mechanisms. Considering erythrocytes are continuously exposed to purinergic receptor ligands, such as ATP, in the plasma, our results may help to understand basal in-vivo activation mechanisms of erythrocyte eNOS enzyme activity.

O3-1 Arrangement and morphology of endothelial cells under the mechanical microenvironment changes after vascular stent implantation

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Vascular stent implantation will cause intravascular hemodynamic changes and vascular endothelial cells (VECs) will be damaged during the process of stent expansion. The purpose of this study was to investigate changes in morphology and function of VECs after vascular stent implantation which can effect shear stress on the surface of stents. The stents were implanted to the coronary arteries of pigs and removed after 1 month, 3 months, 6 months, 12 months and 24 months. Then, the morphology of neointima with stents was observed by scanning electron microscopy. According to the results of the simulation, the VECs were cultured under different mechanical conditions to observe the morphology and arrangement of the cells. To verify the changes of intercellular junctions after stent implantation the expression of F-actin, VE-cadherin and Rac1 were investigated. We found 4 weeks after implantation, neonatal VECs had completely covered the surface of the scaffolds, and the cells were rounded. As the time prolonged, the cell morphology gradually changed to the spindle shape. Studies have shown that round-like VECs were unhealthy, and long spindle-shaped VECs could play a normal function to maintain the stability of the blood vessel environment. In the strut and V-shaped of the stent, the VECs were paving along the strut. The connecting rod ("S" position) was structurally complex, and the arrangement of the VECs in these parts was also complicated. The phenomena in animal experiments were basically consistent with the computer simulation. In vitro, cell experiments found the cytokines related to arrangement and intercellular connection, and obtained similar results.

O3-2 Blood flow regulates zebrafish CVP angiogenesis by inducing ERK5 signaling

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Vascular network formation induced by angiogenesis plays important roles in physiological and pathological processes. Much is known about the role of blood flow in regulating angiogenesis for

the straight or curving vessels in zebrafish. However, the contribution of blood flow and underlying mechanisms in vascular network formation such as caudal vein plexus (CVP) development is poorly understood. Here, our data from tnnt2a-MO injection and treatment with chemical blood flow modulators showed that decreased blood flow disrupted CVP formation in zebrafish and the hemodynamic force was quantitatively analyzed. Furthermore, CVP angiogenesis in zebrafish embryos was inhibited by disruption of blood flow downstream effector ERK5, klf2a and nos2b by treatment with ERK5 specific inhibitor or injecting klf2a-MO, nos2b-MO. Meanwhile, overexpression of klf2a mRNA or nos2b mRNA could rescue vascular defects in tnnt2a or klf2a morphants. These data suggested that flow-induced ERK5-klf2a-nos2b signaling is involved in CVP angiogenesis in zebrafish embryos. Finally, we found the mechanical signal transduction pathway in which mechano-sensitive F-actin polymerization induced cell contractility to activate klf2 and nos3 signaling. Taken together, we have demonstrated that blood flow is essential for vascular network termed CVP angiogenesis in zebrafish. A novel genetic and mechanical mechanism was discovered in which the F-actin contractility facilitates integration of blood flow with the downstream ERK5-klf2a-nos2b signaling axis to guide CVP angiogenesis.

O3-3 The role of Id1 in oscillatory shear stress-mediated endothelial lipid uptake

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Inhibitor of DNA binding 1 (Id1) has been shown to be involved in lipid metabolism, which is pivotal for atherosclerotic progression. However, it remains unclear whether Id1 regulates endothelial cell functions and atherosclerosis in response to oscillatory shear stress. The current study aimed to evaluate the effects of oscillatory shear stress on LDL uptake by endothelial cells and to delineate the roles of Id1 in this process. Using an in vivo ligation model of $ApoE^{-/-}$ mice and applying low and oscillatory shear stress (OSS) in vitro, we found that OSS can effectively promote lipid uptake. The results from in vivo en face staining showed that OSS exposure decreased Id1 expression. In vitro, OSS transiently promoted Id1 expression at early time, but eventually OSS resulted in a reduced expression of Id1 with the passage of time. Furthermore, we found that overexpression of Id1 can abolish OSS-mediated lipid uptake in ECs. Mechanically, we demonstrated that Id1 interacted with srebp1 to regulate LDLR expression, therefore influencing lipid uptake in endothelial cells. Our study shows a biomechanical role of endothelial Id1 in lipid uptake by down-regulating LDLR, which could help us understand oscillatory flow how to affect atherosclerotic development.

O3-4 Effect of DNA methyltransferase 1 in oscillatory shear stress-induced atherosclerotic vulnerable plaque formation

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Oscillatory shear stress (OSS) is one of the important hemodynamics factors that contribute to atherosclerosis progression. Epigenetic mechanisms such as DNA methylation have been reported to play roles in regulating endothelial functions in this pathological process associated with flow characteristics. Here, we aim to explore the mechanism of action of OSS on vulnerable plaque formation. We established a carotid partial ligation model combined with high-fat diet, and found aggravated intima thickening and eventually vulnerable plaque formation accompanied with abundant new immature vessels. Matrix metalloproteinase 9(MMP9) and vascular endothelial growth factor (VEGF) immunohistochemical staining also marked the neovascular location in the vulnerable area. Furthermore, Masson and Sirius red staining confirmed the degradation of collagen which indicated the reduced stability of the plaque. In vitro, we applied a parallel flow chamber system to study how the OSS affected endothelial cell function. We found that OSS upregulated both DNA methyltransferase 1 (DNMT1) and MMP9 expression. Pharmacological inhibition of DNMT1 by 5-Aza-2'-deosycytidine diminished the OSS induced DNMT1 and MMP9 upregulation, and also inhibited the migration and angiogenic capacity of endothelial cells. In conclusion, our data demonstrated that OSS accelerated the vulnerable plaque formation likely through DNMT. [Supported by the NSFC (11572064, 11332003, 31701275), the NKTR&DPC (2016YFC1102305), the FRFCU (CDJZRPY0021, CDJZRPY0202).]

O3-5 The influence of hemodynamic changes on human umbilical vein endothelial progenitor cells

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It has been well documented that biomechanical factors have impact on the physiological function of vascular cells. Vascular endothelial cells are important components of the vascular wall, which directly or indirectly are responsive to hemodynamic changes. Here, we studied the dynamic changes in the orientation and morphology of human umbilical vein endothelial progenitor cells upon exposure to flow shear force for different times. We found that appropriate shear stress promoted proliferation of human umbilical vein progenitor endothelial cells. The proliferation rate was decreased when the shear stress was too high or too low. Furthermore, we found that cells rarely dropped off in central zone, but a few did in the edge, entrance and exit of flow chamber. The results indicate that the adhesion phenomenon of human umbilical vein endothelial progenitor cells was taken off. We suggest that the effect of shear stress on physiological function still need to be further explored.

O3-6 Short term effects of the Mediterranean Diet in human microvascular function - Comparison between older and younger healthy, sedentary adults

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Objective: To determine whether short-term adherence to the Mediterranean Diet (MD) is associated with improved microvascular function. Methods: We conducted a single-centre, cohort pilot study in

Sheffield, UK. Twenty-four healthy, sedentary younger (18–35 years) and older (55–75 years) adults were instructed and supported to adapt their current diet to meet the Mediterranean Diet adherence criteria for 4 weeks. We conducted baseline and post-intervention measurements of microvascular function using laser Doppler fluximetry, Transcutaneous oxygen pressure. Results: We identified statistically significant improvements in axon-mediated microvascular vasodilation (2.24 (± 0.56) to 3.14 (± 0.84), $P = 0.03$) and endothelial-mediated NO synthesis (2.59 (± 0.67) to 3.32 (± 0.87), $P = 0.022$) in the younger group. No statistical significance was reached within the older participants' group, although Raw CVC increased following the intervention. Conclusion: Improvements in physiological function were observed following a short-term dietary intervention based on the MD in a younger population. These were not matched in an older group. Our findings suggest that different durations should be applied when designing dietary interventions in different age-groups, with expectations in physiological improvements differing between groups.

O4-1 Beta-estradiol and ethinylestradiol enhance RBC deformability dependent on their blood concentration

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Background: Natural and synthetic estrogens seems to have opposite effects on thrombosis and the female cardiovascular system, since natural estrogen was supposed to be protective against cardiovascular diseases and synthetic estrogen has been related to thrombosis and cardiovascular diseases. In this work we have investigated if these differences could be related to the effects on those hormones on some hemorheological parameters. Objective: The objective of this work was to investigate the hemorheological changes of different concentrations of beta-estradiol and ethinylestradiol, on RBC aggregation and RBC deformability. Methods: Samples of blood of healthy donors were added with different concentrations of natural beta-estradiol or synthetic ethinylestradiol and were analyzed for red blood cell (RBC) aggregation and RBC deformability. Results: There were no significant changes in RBC aggregation. Both beta-estradiol and ethinylestradiol increase the RBC deformability in shear stresses above 3.0 Pa accordingly with the hormone's concentration. Conclusions: Beta-estradiol and ethinylestradiol enhance RBC deformability dependent on their concentration. These findings may explain the different patterns of thrombotic and cardiovascular effects in different phases of the menstrual cycle or different dosages of oral contraceptive or hormonal replacement therapy.

O4-2 Dual mechanical characterization of red blood cells: Role of surface area, internal viscosity and membrane rigidity

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Osmotic gradient ektacytometry is the gold standard to assess red blood cell (RBC) deformability. It has been proposed that, when measured in iso-osmolar condition, RBC deformability under 3 Pa would depend on membrane elasticity while it would be influenced by internal viscosity above 3 Pa, but this hypothesis remains to be tested. Healthy RBCs were treated by (i) lysolecithine (LPC), (ii) diamide or (iii) nystatine associated with hyperosmolar solutions, which reduces membrane surface area, decreases membrane elasticity or promotes cell dehydration, respectively. In iso-osmolar condition, LPC reduced RBC deformability at 30 Pa only, diamide decreased RBC deformability at all shear stresses and nystatine decreased RBC deformability above 3 Pa. The modification of the surface area to volume ratio and cell dehydration affected RBC deformability mainly at high shear stresses whereas a reduction in membrane elasticity affected RBC deformability at both low and high shear stresses. The consequences of these rheological modifications on the dynamic behavior of RBCs were then evaluated by perfusing them in a microfluidic channel implementing a series of restrictions and enlargements, which dimensions were chosen to deform significantly the cells. Mechanical response was measured through RBCs amplitude of deformation DeltaD, their elongation at the exit of the last constriction D_{out} and their relaxation time (t, i.e. the time necessary to recover a stationary shape). Diminution of membrane elasticity and surface area reduced DeltaD, D_{out} and t. However, the dynamic response of RBC was insensitive to internal viscosity. Combining results from both techniques allowed discrimination between the effects of different RBC rheological properties on the flow dynamics of RBCs.

O4-3 Proteomic analysis of the role of adenylyl cyclase-cAMP pathway in red blood cell mechanical response

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Red blood cell (RBC) cytoskeleton plays a key role in the modulation of cell deformability which is structured by several membrane proteins. The goal of this study was to investigate the regulation of RBC deformability in response to shear forces and the molecular changes in RBC membrane proteins via cAMP/Protein kinase A (PKA) mediated signaling pathway. Blood from healthy donors were treated either with or without SQ22536, Pentoxifylline or H89 which are known to inhibit adenylyl cyclase, phosphodiesterase and PKA, respectively. Shear stress (SS) at 5 Pa level was applied by (I) a capillary tube system (0.05 cm radius, 1 m length) connected to a syringe pump and (II) an ektacytometer with a shearing system (LORRCA) at 37°C. RBC deformability were measured by LORRCA and matched results were included in the study. Phosphorylative changes in serine and tyrosine residues of membrane proteins and expression profiles were studied by immunoblotting and two dimensional gel electrophoresis, respectively. Differentially expressed proteins were identified by mass spectrometry (LC MS/MS). Inhibitors act on cAMP/PKA pathway significantly decreased SS-induced improvements of deformability upon 5 Pa SS compared to controls ($p < 0.05$). Inhibitors increased both serine and tyrosine phosphorylation. Mass spectrometric analysis revealed that differentially expressed proteins are mostly belong to cytoskeletal and proteasomal protein families. SS-induced improvements of deformability were diminished by the inhibitors of signaling molecules in cAMP/PKA pathway. The manipulation of this pathway may be responsible for altered expression and phosphorylation status of membrane proteins that determines the associations within the cytoskeleton and further regulates SS-induced RBC deformability.

O4-4 The oxygenscan: continuous measurement of red blood cell deformability with oxygen gradient ektacytometry to monitor disease severity and treatment effect in sickle cell disease

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In Sickle Cell Disease (SCD) hemoglobin S (HbS) polymerizes upon deoxygenation, resulting in sickling of red blood cells (RBCs). In this study we validated the Oxygenscan: a method to measure RBC deformability as a function of oxygen tension. RBC deformability (Elongation Index – EI) was measured as a function of oxygen tension using the Laser Optical Rotational Red Cell Analyzer (Lorrca, Zwaag, The Netherlands) during deoxygenation (using nitrogen) and reoxygenation, under fixed shear stress. Read out parameters are: EImax: maximum EI, EImin: minimum EI, ΔEI: difference between EImax and EImin, Point of Sickling (POS): pO2 (mmHg) at which >5% decrease in EI is observed during deoxygenation. Oxygenscan curves were highly reproducible (CV < 5%). POS likely reflects an individual patient's hemoglobin dissociation curve. Upon ex vivo exposure to anti-sickling agents, currently in clinical development, that alter the oxygen affinity of hemoglobin, a left-shift of the POS was observed, indicating improved deformability at lower oxygen tensions. In addition, a substantial decrease in ΔEI was observed, suggesting less cells are able to sickle. When RBCs from 19 SCD patients with different genotypes and treatment regimens were analyzed the POS was highest in untreated HbSS patients. Treatment with either Hydroxyurea or transfusion caused a decrease in the POS, and an increase in EImax and EImin. Notably, RBCs from healthy control blood samples show no change in EI during the assay. The Oxygenscan brings the sickling assay to a new level with unparalleled repeatability, and with multiple parameters that quantify different aspects of sickling biology. We suggest that the Oxygenscan can be used to assess an individual patient's disease severity and monitor treatment effect.

O4-5 Nitric oxide regulates human erythrocyte deformability through adjusting band 3 phosphorylation status in hypoxia

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Hypoxia is a problem in diverse conditions; systemic adaptations to hypoxia permit people to adjust to the hypoxic environment at high altitudes and to disease processes. In addition to the cardiopulmonary and hematologic adaptations that support systemic oxygen delivery in hypoxia, RBCs assist through newly described NO-based mechanisms, in line with their vital role in oxygen transport and delivery. Furthermore, to increase the local blood flow in proportion to metabolic demand, NO regulates membrane mechanical properties thereby modulating RBC deformability and oxygen carrying-releasing function. But the clear mechanisms of NO regulation of RBC deformability remain unknown. Here, we have carried out a systematic study to find the mechanisms by which NO regulates RBC deformability under hypoxia. NO levels, RBCs membrane elongation index (EI), band 3 and membrane bound haemachrome

were determined with an NO donor (sodium nitroprusside) or an NO synthase inhibitor (l-nitro-arginine methylester) under hypoxia. In the present article, it is determined that NO plays a potential role in maintaining RBC deformability in hypoxia through altering band 3 tyrosine phosphorylation by maintaining the activity of SH-PTP2 and reducing band 3 crosslinking, which may occur during hypoxic ischaemia diseases, and at high altitudes. This study may provide insights into the molecular mechanisms of RBC adaptation to hypoxia.

O4-6 Hypoxia: The best stimulator that increases shear-induced response of red blood cells

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Red blood cells (RBC) carry and deliver oxygen (O2) to peripheral tissues through different microcirculatory regions where they are exposed to various levels of shear stress (SS). O2 affinity of hemoglobin (Hb) decreases as the blood enters to the microcirculation. This phenomenon determines Hb interactions with RBC membrane proteins that can further regulate the structure of cytoskeleton and affect mechanical properties of cells. The goal of this study was to evaluate shear-induced RBC deformability and simulate RBC dynamics in blood flow under oxygenated and deoxygenated conditions. Venous blood samples from healthy donors were oxygenated with ambient air or deoxygenated with 100% nitrogen gas for 15 minutes and immediately applied into an ektacytometer (LORRCA). RBC deformability was measured before and after the application of continuous 5 Pa SS by LORRCA and recorded as elongation index (EI) values. RBC deformability significantly increased in deoxygenated blood compared to oxygenated samples both before and after 5 Pa SS implementation ($p < 0.01$). A computational model was generated for the simulation of blood flow in an artery section. Distribution of EI was calculated during oxygenation/deoxygenation which is 5–10 times higher around the vessel wall compared to the center of the lumen for sections of the pulsatile flow profile. Deoxygenation substantially improved RBC deformability andt these improvements were also significant with shear exposure. Oxygenation status of RBC may modulate its membrane properties in the microcirculation. Although the extent of RBC deformability increases as RBCs approach to the vessel wall for both oxygenated/deoxygenated conditions, this increase is higher for deoxygenated condition compared to oxygenated condition.

O5-1 Velocity and erythrocyte aggregation characteristics for surface tension-driven flow of blood in rectangular microfluidic channels

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Surface tension as a flow-drive mechanism is used in various microfluidic applications due to its simplicity and low construction cost. Microfluidic blood flows based on such mechanism have been examined in the literature, however, the majority of the studies have not investigated in detail the influence of the red blood cell aggregation phenomenon on the flow characteristics. In the present study, we examined the flow of aggregating and non-aggregating blood, for surface tension driven flows in rectangular microchannels. The flow characteristics of the samples in the micro channel were analysed

utilising micro-PIV based techniques, and aggregation was assessed via image processing methods. Preliminary analysis shows that RBC aggregation was suppressed during the initial stages of the flow, and had a small impact in the velocity profile compared to the non-aggregating case. This is mainly due to the elevated shearing conditions developing in the flow. The shear strength is higher at the onset of the flow, where the meniscus front is found accelerated, and persists at relatively high levels for all observation times. The results indicate that the surface tension mechanism may be a promising alternative for blood manipulation in microfluidic devices.

O5-2 A new approach of blood viscosity: Hemodynamic viscosity

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The aim of this talk bears on viscosity of blood as a complex flowing liquid. The liquid layers inside the vessels flows are not homogeneous. Blood composition in vascular flow is organized as a sheath and a plug flow, from Thurston works. Blood viscosity is the number one parameter for biomechanical studies of the blood flow behavior in cardiovascular net. Various techniques for blood viscosity estimation do not give a true viscosity: instead, they give an apparent or effective viscosity. But being able to measure a true and unique viscosity parameter is challenging for physicians, researchers, etc. In a first part, basing our work on high speed visualizations of blood flow, we will define hemodynamic viscosity, by its equation, and how it is usable and which protocol to be used to have a consistent value. Hemodynamic viscosity is adequate to a unique estimation of viscosity, which value refers exactly to the friction coefficient between blood layers in vessel flows. In the second part, we will develop this method, the applications to routine measurements, a database of blood numeration related to viscosity, and comparable results for diagnostics. In the last part, we compare blood and plasma viscosity, either estimated by several approaches of fluids mechanics based on perfect fluids (Poiseuille, Couette, plan-cone) either qualified by several indirect techniques like hematocrit which are influencing onto viscosity. We show here joint protocols such as creep, flow curves at under controlled shear rate or shear stress, We show how the organization of the compounds modify the flow behavior and viscosity. We will present viscosity data on both blood and plasma. Application to sepsis case shows that “hemodynamic viscosity” is a specific indicator.

O5-3 Evaluation and comparison of haemodynamic parameters of vascular end-to side anastomoses

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0.1% of inhabitants receive vascular sutures or anastomosis (artificial connection between vessels). 20–60% of these vascular sutures lost their function in 10 years. Since the beginning of coronary surgery, it has been a problem in every-day practice that surgeons are not able to control the quality of vascular sutures. Apart from some indirect assessment tool, there is no objective method for analysing the vascular suture’s quality even during the education of medical students and trainees. We have developed a detailed and easy to understand method for anastomosis analysis. The method can be used in surgical education, clearly presenting the technical aspects of surgical technique. A novel educational tool has been introduced for graduate students and trainees. The method applies a reconstruction of high-resolution 3D morphological

assessment of vascular anastomosis. Based on the data of the detailed 3D model of vascular anastomosis, computational simulations (computational fluid dynamics, CFD) of blood flow properties were performed. The attendees used a realistic replica of different surgical situations during the training. Attendees were informed about the results of the morphological and functional assessment and a gamified scoring system was used to inspire them for better performance. The novel training system was proven to be more effective for surgical skill training compared to the conventional method. The attendees of courses and workshop gave more satisfied feedback. The detailed, feedback-based education method can be used as an effective tool in surgical skill training.

O5-4 Similarities in erythrocyte senescence and microfluidic high shear environment damage

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Medical devices can impose supra-physiological flow on the cellular components of blood as it passes through the unit. Increased shear stresses and pressures may alter blood cell biology in a way that is detrimental to their routine function. We hypothesized that membrane alterations and other changes after exposure to high stress might be similar to that seen in senescent cells. As red blood cells (RBCs) age, certain changes in their cellular properties begin to be evident. Senescent RBCs have reduced deformability as do mechanically traumatized cells. Using microfluidic channels and a set flow rate, washed RBCs were subjected to a known shear stress for varied exposure times between 1 to 15 ms. The collected effluent was then tagged using fluorescent antibodies towards known senescent markers and the samples analyzed using flow cytometric techniques. Flow cytometry enabled detection of subtle changes to RBCs below the threshold for complete hemolysis of the cell. Trends similar to those seen with senescent RBCs were found for exposure to high shear stresses in the explored time range, including formation of 0.5–1.0 μm microparticles, a presence of externalized phosphatidylserine on microparticles shed from the RBCs and the aggregation of Band 3 transmembrane protein with subsequent binding of IgG. According to the literature, aggregation of Band 3 with increased IgG binding to the RBC promotes clearance of the cell by means of macrophages. The changes found in senescent RBCs, as well as the cells exposed to shear stresses, affect their flow properties and can ultimately result in their removal from the circulatory system by the spleen.

O5-5 Investigation of bright collapsing ring by Lattice Boltzmann method

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Bright collapsing ring is a characteristic phenomenon of RBCs exposed in pulsatile flow. Paeng DG et al. (2009) used a Doppler flowmeter to measure blood flow in microchannels and found that RBCs frequently aggregated in a ring shape. By controlling the bright ring phenomenon, it might be able to passively control the cell migration inside cell chips. However, the cause of bright ring is unclear and needs to be studied by computational methods. Two main factors that affect bright ring are analyzed:

the flow deceleration and shear stress. When flow velocity reduces as it is shifted from systolic phase to diastolic phase, plasma and RBCs experience the flow acceleration force which is the opposite direction of main flow. However, velocity itself is lower near wall and faster at center of the channel. Due to this velocity gradient, the flow acceleration force also shows a gradient, which is high at center and low near wall. This causes RBCs to move away from the center toward the wall. However, flow deceleration does not explain the cause for RBC aggregation near the wall. The cause of aggregation is mainly due to low shear stress of flow. Shear stress becomes lower when flow velocity decreases, which becomes enough for RBCs to aggregate at diastolic flow. Therefore, at diastolic phase, RBCs which already migrated away from the center of channel aggregates with each other and form a ring-shaped formation. The purpose of this paper is to analyze the bright ring phenomenon by a computational method in terms of flow deceleration and shear stress. A Lattice–Boltzmann method along with immersed boundary method was used for the simulation. Flow characteristics related to RBC migration are analyzed along with cell-to-fluid and cell-to-cell interaction.

O6-1 Alterations in RBC aggregation during incubation in glucose solution

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An abnormally elevated blood glucose level may result in cardiovascular disease, as occurs in patients with diabetes. Thus, precise determination of changes in hemorheology can be helpful in the diagnosis of the disease and monitoring its course. Alterations in RBC aggregation cause changes in blood rheology. The change of the RBC aggregation in the presence of elevated glucose can be observed both in vivo and in vitro. To show the alterations, we have determined the effect of different concentration of glucose on the process of RBC aggregation during in vitro incubation. For this purpose, RBC suspensions with hematocrit 40% were investigated in autologous plasma with the addition of glucose at a concentration of 1 to 3 g/dl. The direct effect of the incubation of erythrocytes on the aggregation process was observed in a Couette system during one or two hours, starting immediately after preparation of the sample. The rotation of the inner cylinder of Couette system causes disaggregation of the cells. After cessation of the rotation, RBC aggregation develops which is manifested by a decrease in the intensity of the backscattered light. The following sequence of rotations was used: two minutes rotation is followed by two minutes stop, and in this way we have obtained a time series of back scattered intensity. From the time series we have obtained individual syllectograms responsible for a given time of incubation. From the syllectograms we have obtained the time T_{slow} and T_{fast} describing RBC aggregation. We found that both T_{slow} and T_{fast} changed with the time of incubation and glucose concentration. As a result, alterations in the process of RBCs aggregation during incubation in glucose solutions were described.

O6-2 Numerical study of red blood cell aggregation kinetics under sinusoidal pulsatile flow

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Previous numerical modelling studies of red blood cell (RBC) aggregation elucidated the inverse relationship between shear rate and RBC aggregation under steady flow. However, information on

RBC aggregation under pulsatile flow remains lacking. In this study, RBC aggregation was numerically simulated to investigate the complex interactions among RBCs under pulsatile flow. RBCs were driven by hydrodynamic force, aggregation force, and elastic force under sinusoidal pulsatile flow in a two-dimensional particle model. The RBC aggregation kinetics were simulated based on the depletion model, and analyzed by averaged values from five cycles. We calculated the number of aggregated RBCs in the different regions with similar acceleration levels to observe aggregated RBC variation in the pulsatile flow. The simulation results were in agreement with the previous experimental results for the formation and destruction of RBC aggregates with a parabolic radial distribution during a pulsatile cycle. In addition, the results demonstrated that the cyclic variation in the mean aggregate size of RBCs increased as velocity amplitude increased from 1 cm/s to 3 cm/s, as mean steady flow velocity decreased from 6 cm/s to 2 cm/s, and as stroke rate decreased from 180 beats per minute (bpm) to 60 bpm. As anticipated, the computational results demonstrated that the number of aggregated RBC decreased exponentially with shear rate under sinusoidal pulsatile flow. The maximum RBC aggregation occurred at the acceleration region of about 2 cm/s^2. The simulation results verified the previous experimental results of parabolic radial distribution and improved the current understanding of the complex spatiotemporal changes of RBC aggregates during a sinusoidal pulsatile cycle.

O6-3 Structure and stability of red blood cell aggregates in model flows

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RBC aggregation is a strong determinant of blood rheology at low to moderate shear rates and influences the structure of blood flow in capillary networks. The stability of RBC aggregates or rouleaux is governed by many parameters which include fibrinogen concentration (or other aggregation promoter) and red blood cell properties which can vary with the age of RBCs or pathological situations. Through experimental and numerical approaches, we investigated the shape of RBC aggregates, revealing a large variety of shapes of contact zones between cells, which involve a buckling instability of membranes resulting from a competition between adhesion energy and membrane elasticity. The attractive interaction between cells also leads to clustering (rouleau formation) in flow, with a cluster size that is governed by a competition between hydrodynamic stresses and aggregation forces. We show that hydrodynamic stresses in the bifurcations of a capillary network can lead to rupture of clusters at a critical speed which is in the range of physiological values, and increases with interaction energy. Overall, the clustering phenomenon tends to increase phase separation and hematocrit heterogeneities in the microcirculation.

O6-4 Covalent immobilization of biomolecules on stent materials through mussel adhesive protein coating to promote cell adhesion

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It is widely accepted that surface biofunctional modification may be an effective approach to improve biocompatibility and confer new bioactive properties on biomaterials, especially to promote cell adhesion and viability. In this work, mussel adhesive protein (MAP) was applied as a coating on 316L stainless steel substrates (316L SS) and stents, and then either immobilized VEGF or CD34 antibody were added to create a promoting cell adhesion and viability films. The properties of the MAP coating were characterized by scanning electron microscope (SEM), atomic force microscope (AFM) and water contact angle test. Universal tensile testing showed that the MAP coating has adequate adhesion strength on a 316L stainless steel material surface. Subsequent cytotoxicity and hemolysis rate tests showed that the MAP coatings had good biocompatibility. Moreover, using N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride and N-hydroxysulfosussinimide (EDC/NHS) chemistry, VEGF and CD34 antibody were immobilized on the MAP coatings. The amount and immobilized yield of VEGF on the MAP coatings were analyzed by enzyme-linked immuno-assays (ELISA). Finally, an endothelial cells culture showed that the VEGF biofunctional film could promote the adhesion, viability and proliferation of endothelial cells. An in vitro $CD34^+$ cells capturing test also verified that the film could capture $CD34^+$ cells and promote cell adhesion. These results showed that the MAP coatings allowed effective biomolecules immobilization. After biomolecules immobilization, the biofunctional film can promote cell adhesion and viability, providing a promising platform for vascular device modification.

O6-5 The changes of vascular mechanical properties of porcine coronary artery after stent implantation

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Background and Aims: In-stent restenosis seriously affects the postoperative efficacy of percutaneous coronary intervention. The vascular cells could receive the stimuli of vascular mechanical environment changes during restenosis. At present, numerical simulation is often used to study the changes in mechanical properties of coronary arteries after stent implantation which still had disparity with actual data. This study aimed to reveal the mechanical properties of coronary artery after stent implantation. Methods: Bose mechanical tensile test system was used to test the uniaxial tensile stress and strain, relaxation mechanics of artery samples. Balloon dilation was used instead of stent implantation to detect the changes in the opening angle of the stent after implantation. Results: The stress strain curves were plotted through the results of the vascular multirate uniaxial tensile test, and the stent implantation could lead to the decrease of the viscoelasticity of the blood vessels. According to the results of relaxation experiments, the stress relaxation of stent implantation segment decreased sharply with the increase of time, unlike the normal vascular being stable after decreasing. The opening angle of the vessel without balloon dilation was changed with vessel position, farther away from the heart, the smaller was the opening angle. While the opening angle of the vessel with balloon dilatation was larger and had no difference between the proximal and distal segments. Conclusions: The viscoelasticity, shear stress and opening angle of coronary arteries were significantly changed after stent implantation. [Supported by the NSFC (11332003, 11572064, 31701275), the NKTR&DPC (2016YFC1102305), the FRFCU (CDJXY230001, CDJXY230002).]

O7-1 Do changes in bone marrow pressure contribute to the egress of cells (RBC, reticulocytes) from bone marrow?

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Pressure was measured in the femoral medullary cavity of rabbits whose femoral muscles were subjected to electrostimulation. After electrostimulation the pressure in the medullary cavity increased five-fold. In groups of experimental animals, the number of reticulocytes leaving the bone marrow and the number of reticulocytes in the peripheral blood were determined and it was observed the electrostimulation was followed by a several-fold rise in the amount of reticulocytes in both the bone marrow and the peripheral blood. The authors found that a great role in the egress of reticulocytes from the bone marrow into the circulation is played by regulation of the pressure in medullary cavity effected by changes in blood flow through the bone marrow.

O7-2 Platelet-derived extracellular vesicles promote the adhesion of flowing neutrophils to endothelial cells

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Activation of platelets causes them to shed numerous extracellular vesicles (PEV) which may have inflammatory effects. We tested the ability of PEV to promote adhesion of flowing neutrophils to endothelial cells (EC), and the separate contributions of PEV subpopulations, platelet membrane microvesicles (PMV) and exosomes (Pexo). PEV were collected from platelets stimulated with collagen-related peptide, and PMV and Pexo were separated by differential centrifugation. Vesicle binding and resultant activation of neutrophils and EC were assessed by flow cytometry. Flow-based adhesion assays assessed binding of neutrophils directly to deposited vesicles or to EC, after neutrophils or EC had been treated with vesicles. In suspension, PEV bound efficiently to neutrophils or EC, with resultant upregulation of activation markers on both types of cell. Binding was Ca^{++}-dependent, and dominantly mediated by CD62P for neutrophils, or by integrins for EC. When PEV were deposited on surfaces of flow chambers, they supported mainly short-lived attachments of flowing neutrophils through CD62P, and some stable adhesion induced by CXC-chemokines. Neutrophil adhesion to EC was promoted when either cell was pre-treated with PEV, although the effect was less prominent when EC were pre-activated with tumor necrosis factor-α. The pro-adhesive effects on neutrophils could largely be attributed to PMV rather than Pexo. Thus, surface-bound PEV can capture flowing neutrophils, while PEV also activate neutrophils and EC to promote interactions. PEV may potentiate inflammatory responses (thromboinflammation) after platelets are activated in tissue injury.

O7-3 Morphological and metabolic abnormalities of erythrocytes as risk factors for Alzheimer's disease

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Alzheimer's disease (AD) is the most common form of dementia, that affects about 30 million people worldwide. A step towards this whole-scale problem is to study a new model based on red blood cells (RBC) interaction with amyloid beta 1-42 peptide (Aβ). RBC are highly deformable to assist blood flow in the microcirculation and for this reason morphological and functional abnormalities in RBC could contribute to AD by obstructing oxygen delivery to brain causing hypoxia. We show that treatment with Aβ accelerates the occurrence of morphological and biochemical aging markers in human RBC and influences the cell metabolism. The morphological pattern was monitored using AFM imaging. We found that Aβ boosts the development of crenatures and proto-spicules simultaneously to acceleration in the weakening of the cell-cytoskeleton contacts and to the induction of peculiar nanoscale features on the cell membrane. Incubation in the presence of glucose can remove all but the latter Ab-induced effects. Biochemical data demonstrate that contemporaneously to morphological and structural alterations, Aβ triggers: (i) metabolic and antioxidant defense alterations and (ii) a complex signaling pathway involving membrane acetylcholinesterase, caspase 3, protein kinase C and nitric oxide derived metabolites. Our study provides a comprehensive picture in which Aβ treatment of RBC induces changes in specific cell signalling events and/or metabolic pathways, in turns affecting the membrane–cytoskeleton interaction and the membrane integrity. Understanding these processes is highly relevant for the comprehension of the biochemical events which predispose to AD.

O7-4 Effects of two different high intensity interval training protocols on hemorheological variables in hypertensive patients

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Purpose: The present study examined and compared the effects of two different HIIT protocols on markers of blood fluidity in hypertensive patients. Methods: Thirty hypertensive (stage 1, systolic BP > 140 and diastolic BP > 90 mmHg) patients (age, 47.96 ± 3.20 yrs), were randomly allocated to short duration HIIT (SDHIIT, $n = 10$), long duration HIIT (LDHIIT, $n = 10$), and control ($n = 10$) groups. After two weeks of continuous mild training, patients in SDHIIT group performed 8 weeks of HIIT included 27 min HIIT that encompassed 27 repetitions of 30s activity at 80%–100% of VO_{2peak} interspersed by 30s passive/active (10%–20% of VO2peak) recovery, while, patients in LDHIIT group performed 8 weeks of HIIT (32min per session) included 4 repetitions of 4 min activity at 75%–90% of VO_{2peak} interspersed by 4min passive/active (15%–30% of VO_{2peak}) recovery. Two blood samples were taken before and after training and were analyzed for hemorheological variables. Results: Significant ($P < 0.05$) reductions in systolic blood pressure (SBP), blood and plasma viscosity, fibrinogen concentration, and red blood cell (RBC) aggregation were found following the two training protocols, though, the differences between the two training protocols were not statistically significant. Conclusions: It is concluded that HIIT training

reduces SBP and markers of blood fluidity in patients with stage 1 hypertension irrespective of the HIIT intensity and duration.

O7-5 Sedentarity status as a regulator of the optimal hematocrit: Involvement of red cell deformability?

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We recently proposed to calculate a "theoretical optimal hematocrit" as the value associated with the higher value of hematocrit/viscosity (h/η) on the bell-shaped curve predicted with Quemada's equation (viscometry at 1000 s^{-1}). We reported that this approach provides values of optimal hematocrit and h/η well correlated with the actual values, but closer to them in well trained athletes and higher than them in sedentary and obese individuals. Applying this model to several databases used in our previous studies we confirm that obese subjects with or without metabolic disturbances exhibit a higher discrepancy between actual and "predicted ideal" values of hematocrit and h/η, and that this discrepancy is not related to the level of insulin sensitivity. By contrast this discrepancy is well correlated with red cell rigidity. In sedentary patients with the metabolic syndrome 3 months of regular low intensity exercise training shifted the bell-shaped curve of predicted h/η toward higher values ($p < 0.01$). Therefore, sedentarity seems to shift hematocrit and h/η toward values lower than the theoretical optimal ones while exercise training decreases this discrepancy. This mechanism is not related to insulin resistance but correlated with red cell rigidity. It may reflect an adaptive mechanism allowing to maintain an optimal oxygen supply during exercise in sedentary individuals whose hemorheological profile is impaired.

O7-6 The effects of n-6 polyunsaturated free fatty acids dietary intake on hemorheology and endothelium-dependent microvascular function

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Potential beneficiary effects of dietary or supplementary daily intake of n-3 polyunsaturated fatty acids (n-3 PUFAs), such as α-linolenic fatty acid, eicosapentaenoic acid, and docosahexaenoic acid on hemorheology and vascular function are currently intensively investigated. Depending on the source of n-3 PUFAs and the study subjects (i.e. healthy individuals or cardiovascular patients) n-3 PUFA supplementation has been shown to have antithrombotic effects (by decreasing blood viscosity, decreasing FIIc, FIXc, FXc, FVIIc, FVIIa, FXIIa, PAI-1 levels and platelet aggregation/reactivity, enhancing fibrinolysis, but without effects on erythrocyte deformability). They decrease inflammation by decreasing IL-6, MCP-1, TNF-alpha and hsCRP levels, expression of endothelial cell adhesion molecules and significantly

affect blood composition of fatty acids. It is well accepted that the metabolites of n-6 PUFA, such as the metabolites of arachidonic acid have very important role in many physiological processes in cardiovascular system. On the other hand, there are controversies in the beneficial effects of n-3 PUFAs consumption on macrovascular function, and studies on microvascular function are rare. Recently we have shown significantly enhanced endothelium-dependent microvascular reactivity to reactive hyperemia in a young healthy population. Plasma hsCRP and lipid peroxidation products were decreased and antioxidative enzymes function was enhanced (i.e. increased glutathione peroxidase activity). The possible underlying protective mechanisms of n-3 PUFA intake may be a change in balance of n-6 PUFA metabolites (e.g. prostaglandins and leukotrienes) and n-6 PUFA metabolites (such as resolvins, maresins and protectins), reduced inflammation and decreased vascular oxidative stress.

08-1 Fabrication of gradient nanofibrous scaffold for interface tissue engineering

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For the special biomolecular composition, microstructure and micromechanics in the interfacial region, surgical reconstruction of ruptured ligament/tendon with soft tissue grafts creates bone-graft interfaces within bone tunnels, where mismatched properties can result in poor osteointegration and increased rate of graft failure. Therefore, improvements in bone-graft integration are critical to allow for earlier and more aggressive rehabilitation with the hope of promoting a speedier return to normal daily activities. In the current study, we developed a nanofibrous scaffold based on silk fibroin to mimic the native interfacial region, which had a gradually increase of mineral content demonstrated with scanning electron microscope, energy-dispersive X-ray spectroscopy and fourier transform infrared spectroscopy analysis. Furthermore, human mesenchymal stem cells were cultured on different areas of the scaffold with gradual mineralization and the effects of scaffold structure and topography on cell morphology, proliferation, viability and differentiation were also investigated. The fabricated scaffold showed a high proliferative capacity, viability and biocompatibility and could direct osteogenic or tenogenic differentiation. In summary, the fabrication of gradient scaffold based on silk fibroin can improve the integration and has the potential application in the interfacial tissue engineering. [This work was supported by the National Natural Science Foundation of China (Nos. 11532004, 31270990), and Innovation and Attracting Talents Program for College and University (“111” Project) (No. B06023).]

08-2 Tanshinone can inhibit inflammation and angiogenesis in several chondrocytic cells

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Objective: To investigate the potential effects of tanshinone on oxidation, inflammation and angiogenesis in various kinds of chondrocytic cells.

Methods: Various kinds of chondrocytic cells were used in this project such as human primary articular chondrocyte (PHC), SW1353 human chondrosarcoma cell line, C-28/I2 and T/C-28a2 human immortalized chondrocyte lines. Treatment of human TNF and IL1B was used to stimulate inflammatory reaction. After the inflammatory response was activated, we evaluated the anti-inflammatory and anti-angiogenesis effects of 10 mmol/L tanshinone treatment using qRT-PCR and western blot which tested VEGF, PAK1, IL6 and IL10. We also tested the potential anti-oxidant effect of tanshinone on chondrocytic cells by BES-H_2O_2-Ac and AlamarBlue staining and flow cytometry. Results: After treatment of either TNF or IL1B, PHC and other chondrocytic cell lines exhibited an upregulated inflammatory response based on the expression of IL6 and IL10. The expression of interleukins was suppressed after the subsequent treatment with 10 mmol/l tanshinone. Tanshinone treatment also downregulated the expression of VEGF and PAK1 in TNF-treated and IL1B-treated PHC and other chondrocytic cells. After fluorescence analysis of BES-H_2O_2-Ac and AlamarBlue treated cells, we found tanshinone could also play an antioxidant role. Conclusion: In human primary articular chondrocytes and other chondrocytic cell lines, tanshinone can inhibit angiogenesis, inflammation and oxidation after stimulation with TNF or IL1B. It gives an opportunity for tanshinone to take part in OA treatment. [Grants: Natural Science Foundation of China (11532004, 31270990); "111" project (B06023)].

08-3 The preliminary research of mechanical compress damage on neurons induced by hematoma

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Hemorrhagic stroke is the most lethal and crippling cerebrovascular disease, with serious dysneuria among the survivors. Besides biochemical damages, there are various mechanical factors in the process of cerebral hemorrhage. However, whether these mechanical factors play key roles in the occurrence and development of cerebral hemorrhage is rarely studied. In our studies, the primary process of neuron and tissue injury induced by hematoma is researched through brain slices and with the auxiliary proof of neuron culture. Brain slices were obtained through vibratome and cultured with Transwell, and then compressed by the mechanical compress system constructed by ourselves. The primary process of neuron damage was investigated by detecting lactate dehydrogenase, fluorescent quantitative PCR, immunofluorescence and western-blot. The activity of neurons and glial cells declined rapidly after being compressed. The genes of ion channel proteins PIEZO and TRPV4 raised rapidly after being compressed, and continued to increase significantly and reach a peak value after 12 hours culture following stress removal. However, the PIEZO and TRPV4 protein expression increased after being compressed, but did not continue to rise. After being compressed, the intracellular Ca^{2+} concentration and the apoptosis promoting gene BAX increased rapidly while apoptosis restraining gene Bcl-2 decreased significantly, and the tendency continued after mechanical stress was removed. The high concentration of intracellular Ca^{2+} activates the expression of apoptosis promoting gene BAX and prevent Bcl-2, and ultimately accelerates cell apoptosis.

08-4 Hemodynamic analysis of cerebral aneurysms: Suggestions for surgical options

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Hemodynamic factors play a significant role in the development of cerebral aneurysms. Factors such as wall shear stress (WSS), blood velocity or pressure can change over time and may contribute to aneurysm growth and rupture. Computational fluid dynamics has become a popular tool for studying intracranial aneurysm hemodynamics and discriminating rupture status. In this study, we observed a rare case of a middle cerebral artery aneurysm in which a small aneurysm attaches to the main aneurysm. We obtained the computed tomography angiography (CTA) data when the patient was admitted to the hospital, and calculated hemodynamic factors in this aneurysm. We found that there was an obvious vortex within the aneurysm, and the WSS in the small aneurysm was significantly lower, and high pressure occurred on the neck of the small aneurysm. Based on the calculation results, we recommend clamping the lateral aneurysm while the main aneurysm will not be treated for the time being. The patient's CTA data for three days after the surgery were further analyzed. And we found that the volume of the aneurysm after clipping significantly reduced, the blood flow within the aneurysm was more stable, the WSS distribution of the aneurysm uniform, and the area of low shear stress significantly reduced, which indicated the surgical effect was good. Patient's CTA data for one-year post the surgery showed that the main swelling gradually shrank and the patient was in good condition. Overall, our study successfully assessed the hemodynamic environment of patients with cerebral aneurysms, and put forward a better surgery plan, which may be useful for clinical application. [Supported by the NKTR&DPC (2016YFC1102305), the NNSFC (11332003), the FRFCU (CDJXY230002, CDJZRPY0202, CDJQJ238814).]

09-1 Proteomic analysis of ApoE-/- mice with disturbed flow model

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The formation of atherosclerotic plaque induces human cardiovascular disease and disturbed flow can accelerate the process. However the mechanism of atherogenesis in the disturbed flow region is still not clear. We used apoE-/- mice to establish the disturbed flow model as previously reported, which was verified through a small animal ultrasound instrument. We extracted total protein of left carotid artery at 48 h after surgery, then made proteomics analysis. In total 168 significant differential expressed proteins were found between the left carotid of disturbed flow group and sham group, including 18 down-regulated and 150 up-regulated proteins. Further gene ontology analysis showed that these proteins were related with single-organism process, macromolecule metabolic process, cellular component organization or biogenesis, response to stimulus, localization and so on. KEGG pathway results indicated that they were enriched in complement and coagulation cascades, hematopoietic cell lineage, phagosome, fat digestion and absorption, phagocytosis, cell adhesion molecules signal pathways, such asItgb2, CD9, CD36, VACM, which were consistent with the previous reports and closely related to atherogenesis. We also found

some proteins that were less concerned in atherogenesis in disturbed flow regions. The function and mechanisms of these proteins need to be studied. Through the construction of a disturbed flow model and proteomics, we showed the differential proteins involved in biological process classification and signal pathways, which provides the foundation for further understanding the mechanism of disturbed flow influencing the progression of atherosclerosis. [Supported by the NSFC (11572064, 11332003, 31701275), the NKTR&DP (2016YFC110230 5).]

09-2 Effects of suspension state on the biological behavior of breast cancer cells

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The mechanical microenvironment can strongly affect the metastatic efficiency of circulating tumor cells. However, the effect of suspension state on their biological behavior and its mechanism are still unclear. The objective of this study was to investigate the effect of suspension state on the metastasis, extravasation and drug resistance of breast tumor cells. MDA-MB-231 cells were suspension cultured in complete medium, while the adherent cells were used as control. Our study demonstrated that (1) The suspension state significantly increased the metastatic potential of breast cancer cells, but slightly suppressed their tumor growth. The cytoskeleton state and activation of Ca^{2+}/CaN/NFAT are responsible for the up-regulation of cyclooxygenase-2 (COX-2), which plays an important role in suspension-promoted metastasis. (2) The increasing expression of integrin β1 induced by suspension culture promoted the adhesion and transendothelial migration of MDA-MB-231 cells, but had no significant influence on their spreading. (3) Suspension state plays a vital role in promoting methotrexate (MTX) resistance of MDA-MB-231 cells by inducing adenosine triphosphate binding cassette subfamily C member 3 (ABCC3) overexpression. These findings highlight the important role of suspension state for tumor cells in tumor metastasis. This work was supported by the National Natural Science Foundation of China (11672051).

09-3 Preliminary study of endothelial cell tight junction protein in response to different mechanical stimuli

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It is generally accepted that the damage of the structure and function of endothelial cells (EC) is the first step in the development of atherosclerosis (AS) and plays an important role in the development of AS. Subendothelial lipoprotein deposition is one of the foundations of AS plaque formation, indicating that the permeability of EC has changed. It has been found that paracellular pathway opening is the main reason for increased vascular permeability. Tight junctions mainly determine the strength of intercellular junctions and play an integral role in maintaining endothelial barrier. Among the physiological stimuli that impact on the endothelium, mechanical or hemodynamic forces associated with blood flow are of central importance. These include cyclic circumferential strain, caused by a transmural force acting perpendicularly to the vessel wall, and shear stress, the frictional force of blood dragging against cells.

As such, one can hypothesize a dynamic regulatory association between endothelial permeability and hemodynamic stimuli. To study the effect of different mechanical models on the tight junctions of human umbilical vein endothelial cells (HUVECs), HUVECs were subjected to flow shear stress, static pressure and cyclic strain. To detect tight junction protein changes, PCR analysis was made including claudin-5, occludin, ZO-1 and tricellulin. The results showed that under the action of flow shear stress and cyclic strain, the morphology of the cells changed from fusiform to polygonal shape. After withdrawal of mechanical stimulation, the cells tended to recover from the initial morphology. Fluorescence quantitative PCR results showed that the tight junction protein response was different under different mechanical models.

09-4 PI3K-nos2b signaling is crucial for simulated microgravity-mediated angiogenesis in zebrafish CVP network

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Microgravity was reported to regulate angiogenesis and vascular remodeling. However, the mechanism by which microgravity affects the vascular development remains unclear. Our study aimed to evaluate the effects of microgravity on vascular development by the caudal vein plexus (CVP) network of zebrafish and to delineate the roles of PI3K-nos2bsignaling in this process. Using a ground-based simulation microgravity bioreactor, we found that the simulated microgravity (SM) could significantly promote the angiogenesis in CVP of zebrafish larvae. Then we also found that injection with nos2b-Morpholino or treatment with PI3K inhibitors LY294002 could partially rescue the CVP network abnormality caused by SM, indicating that nos2b was involved in SM mediated CVP development. Furthermore, overexpression of nos2b could partly rescue LY294002-caused CVP network failure. Taken together, our results indicate that SM can affect zebrafish CVP angiogenesis by promoting PI3K-nos2b signaling. [Supported by the NSFC (11572064, 31771599), the NKTR&DPC (2016YFC110230, 2016YFC1101101), the FRFCU (CDJXY230002, CDJZRPY0021).]

O9-5 Ferric iron, lipopolysaccharide and lipoteichoic acids can induce anomalous fibrin amyloid formation: an assessment with novel Amytracker™ stains and thioflavin T

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Most chronic diseases include an inflammatory component. This inflammatory component is closely linked to a procoagulant phenotype of some kind, appending thrombotic conditions as comorbidities of inflammatory diseases. A potential trigger of this state may be highly inflammatory bacterial wall components; and these components may have a prominent role in hypercoagulability. In recent work, we discovered that the presence of a tiny amount of lipopolysaccharide (LPS) from Gram-negative bacteria caused fibrinogen clotting to lead to the formation of an amyloid form of fibrin. Here, we show that the broadly equivalent lipoteichoic acids (LTAs) from two species of Gram-positive bacteria, as well as ferric iron, have similarly potent effects. The ability of these inflammagens to divert fibrin formation to

an amyloid form was confirmed with the fluorescent markers thioflavin T, as well as the novel amyloid-selective AmyTracker dyes, where the products were added to human plasma, clotted via thrombin and detected by confocal microscopy. We show that all three bacterial wall inflammagens and iron give very large fluorescence enhancements. The staining patterns differed significantly as a function of both the amyloidogens and the dyes used to assess them, indicating the altered nature of the clots formed. These results highlight the amyloid-forming potential of fibrin(ogen) in the presence of various inflammagens. Thus, the data provide further evidence for an important role of bacterial cell wall products and also increased iron, in the various coagulopathies that are observable in inflammatory diseases. Finally, these assays may have an application in diagnostics and these findings may offer novel therapeutic targets in the treatment of anomalous clot formation.

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POSTERS

P1 Effects of hypertrophy and strength weight training on resting levels and responses of hemorheological parameters to a single session of exercise

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Introduction: The present study was carried out to determine the effects of 12 weeks of two different resistance training programs on resting levels and responses of hemorheological factors to a single session of resistance exercise. Methods: Thirty nine male students were randomly divided into three groups of hypertrophy (n = 14), maximal strength (n = 13) and control (n = 12). Hypertrophy resistance training program included 12 weeks of training, three times per week, 3–4 sets of 10–12 repetitions at 65–70% of one repetition of maximum (1-RM). The strength training program included 12 weeks of training, three times per week, 3–4 sets of 4–7 repetitions at 80–85% of 1-RM. Before and 48 hours after training, all subjects performed a single session of resistance exercise at 80% of 1-RM. Hemorheological variables were measured before and after the two acute exercise trials in the three groups. Results: Resting levels of blood and plasma viscosity reduced in hypertrophy group compared to both strength and control groups ($P < 0.05$), while, red blood cell aggregation decreased and deformability increased significantly ($P < 0.05$) in both training groups compared to the control group. Changes in resting levels of hematocrit, fibrinogen, total protein and albumin in training groups were not significantly different than control group ($P > 0.05$). Except for RBC deformability, 12 weeks of resistance training did not induce any significant changes in responses of all other variables to acute resistance exercise ($P > 0.05$). Conclusion: It is concluded that except for blood viscosity, hypertrophy and strength weight training improve all other hemorheological variables similarly, and that different types of weight training have no effect on acute hemorheological responses.

P2 Modulation of erythrocyte mechanical function by calcium-calmodulin-protein kinase C

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Red blood cell (RBC) deformability is of vital importance for the microcirculation as RBCs traverse narrow capillaries under shear stress. RBC deformability could be regulated with the protein kinase

C (PKC) cascade by phosphorylative changes in membrane proteins. The aim of this study was to investigate the role of the Ca^{2+}-Calmodulin-PKC signaling pathway on RBC mechanical responses with Ca^{2+}. Fresh venous blood samples were collected from healthy donors ($n = 7$). Verapamil, Chelerythrine and Calpeptin drugs were used to inhibit Ca^{2+} channels, PKC and tyrosine phosphatase, respectively. The final concentration of drugs in blood was 10^{-5} M. Ca^{2+} was added in blood (3 mM) alone or with the drugs. RBC deformability was measured as the change in the elongation index (EI) at different shear stresses (SS) (0.3–50 Pa) by a laser-assisted optical rotational cell analyzer (LORRCA). Shear stress at 5 Pa level was applied with the same device for 300 seconds and immediately deformability was measured again. Maximum RBC elongation at infinite stress (EI_{max}) and the shear stress required to achieve one-half of this maximal value ($SS_{1/2}$) were calculated from EI-SS curves by using Lineweaver-Burke (LB) model. RBC deformability significantly increased by Verapamil ($p < 0.05$), decreased by Calpeptin ($p < 0.05$) and was not significantly changed by Chelerythrine before 5 Pa SS. Shear-induced RBC deformability was not significantly changed with drugs after SS application. Ca^{2+} deteriorated RBC deformability in all conditions with or without the effect of drugs. Ca^{2+}-Calmodulin-PKC cascade might have a role on the regulation of RBC mechanical properties through phosphorylative changes in RBC membrane proteins and alterations in Ca^{2+} influx.

P3 Clinical relevance of hemodynamic viscosity measurement in vascular study

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The rheological behavior of whole blood has been of basic science and clinical interest, notably beginning with the work of Jean-Louis-Marie Poiseuille (1799–1869). But most reports have focused on testing blood as a homogenous fluid, ignoring the presence of formed elements. Usually, RBCs are the most important formed elements that cause changes in blood viscosity but we show that Igs have a greater effect on flow in septic shock. We show experimental results of both normal and sepsis blood, and with plasma, not ignoring RBCs role. The formation of a cell-poor or cell-free layer near the tube wall and modulation of this layer by RBC aggregation is the most important determinant of hemodynamic viscosity. RBC aggregation far from the wall layer reduces resistance to flow but Igs increase the problem. The conclusion is that hemodynamic viscosity is operational to study blood viscosity and flow and substitute old techniques that are too much approximative like sedimentation, hematocrit, aggregation rate or Couette model. Hemodynamic viscosity appears thus as a unique parameter that completes the whole blood equation pressure and flow rate. According to the Poiseuille Law, blood viscosity is viewed as a key component of vascular resistance. Hemodynamic viscosity causes a rise in wall shear stress, in flow pressure, which may stimulate endothelial cells to produce nitric oxide and cause vasodilation. The role of vascular function is correlated to blood flow and hemodynamic viscosity. In diseases where vascular function is impaired (hypertension, coronary disease, etc.), any increase in hemodynamic viscosity is of poor prognosis even if it increases the risks for vaso-occlusive crises. The lack of oxygenation is the first consequence in viscosity increase.

P4 Analysis of seismocardiographic signals by the discrete Chebyshev transform

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Since seismiocardiographic (SCG) signals have complex time-frequency characteristics, one of the popular methods of their investigation is the wavelet analysis [1]. However, this powerful technique is computationally expensive, especially in real-time processing. That is why it is interesting to apply traditional polynomial approximations which are successfully used, for example, for analysis of electrocardiographic (ECG) signals [2]. The aim of this work is the develop a new scheme of SCG signal approximation using the Discrete Chebyshev Transform (DChT) [3]. It does not require a segmentation of the signal into blocks coinciding with the cardiac cycle and it is possible to use long portions of SCG signals made of multiple cardiac cycles. The SCG filtration is based on the thresholding of significant coefficients. The performance of the proposed method was evaluated with the compression ratio (CR) and Percent Root square Difference (PRD). Chebyshev polynomials of up to the 256th order were used for high quality approximation. The proposed method is very fast that makes it useful in the data communication in telemedicine. The results obtained are optimistic in terms of SCG signal reconstruction error at given compression rates.

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P5 Fetal growth retardation and oxygen delivery hemorheological predictors in hypertensive vs normotensive pregnant women

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Physiological modifications of blood rheology during pregnancy and their alterations in pregnant hypertensive women have been extensively studied in the 1980's. Since vascular resistance is higher in hypertensive pregnant women whose newborns are small for gestational age, we investigated in a personal

database if growth retardation of newborns is related to the oxygen delivery index (ratio hematocrit/blood viscosity) and to the difference between hematocrit and the prediction of its optimal valued based on Quemada's equation. A sample of 38 hypertensive pregnant women (age 29 yr±1) was compared with 64 controls matched for age and gestational age, studied at 35 ± 1 weeks gestation, extracted from a larger series of 162 pregnant women. On the whole the hypertensive group gave birth to smaller children (p = 0,014). Plasma viscosity correlated with blood pressure only in hypertensive women (r = 0.403 p < 0.05). The bell shaped curve of predicted optimal hematocrit of nonhypertensive pregnant women was similar to that of nononpregnant women, but in hypertensive women it was shifted toward higher values (p = 0.07), and the predicted optimal hematocrit (but not the actual one) was correlated with systolic (r = 0.349 p < 0.001) and diastolic (r = 0.218 p < 0.05) blood pressure. The predicted optimal h/h was higher in hypertensive women whose newborns exhibited a low birth weight (p = 0,03), resulting in a higher discrepancy between actual and model-predicted "ideal" values of h/h (p = 0.03) and hematocrit (p = 0.02) compared with the subgroup with no growth retardation. Therefore in hypertensive women whose newborns exhibited a low birth weight, hemorheological parameters predicting oxygen supply are shifted to lower values than predicted by the model.

P6 Leg electrical resistance predicts venous blood viscosity and hematocrit

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We previously reported that whole body bioelectrical impedance analysis (BIA) measurements are correlated to some hemorheologic factors, suggesting a relationship between viscosity factors and electric properties of flowing blood not only in vitro but also in vivo. Recently we reported that with segmental BIA (analyzing the body considered as composed of 5 cylinders) predictive equations for various determinants of blood viscosity were closer than for the wole body. Another widely used BIA technique uses leg-to-leg impedance measurements so that two cylinders (the two legs) are analyzed. We investigated whether impedance measured with this technique (Tanita TBF-300) is also a predictor of blood viscosity factors. From viscometric measurements performed on venous blood drawn in recreative athletes over the range of shear rates 1 to 6000 s^{-1} (RHEOMETRE Anton Paar CP 50-1), we found a correlation between leg-leg resistance at 50 kHz (Rx[50 kHz]) and blood viscosity at 1000 s^{-1} (h_{1000} = 0.0051 Rx[50 kHz] + 1.3265; r = 0,521 p = 0,028 yielding a prediction of h_{1000} (Bland Altman plot: bias 0,05 [RANGE −0,24; 0,34]. Neither plasma viscosity nor the red cell rheology index "k" of Quemada's model are correlated with Rx[50 kHz], but hematocrit (Hct) does (Hct (%) = 0,0217 Rx[50 kHz] + 33.783 r = 0.480 p = 0.044) yielding a prediction of Hct (Bland Altman plot : bias −0,11, [range −1,67; 1,45]. The discrepancy between actual and predicted Hct is also correlated with resistance at 50 kHz (r = 0.575; p = 0.031) as does the discrepancy between actual and predicted Hct/viscosity ratio (r = −0.651; p = 0.006). Therefore,

as other previously studied methods, leg to leg BIA predicts viscosity, suggesting that blood rheology may influence the passage of an electric current in the legs.

P7 The transient hyperviscosity syndrome of labor and delivery shifts the hemorheological profile toward a lower ability to deliver oxygen to tissues

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Labor and delivery induce a transient hyperviscosity syndrome which is mainly due to a decrease in RBC flexibility, with no change in either hematocrit or plasma viscosity, and a decrease in red cell aggregation. We investigated whether these alterations modify the hemorheologic determinants of oxygen transfer modelized with the prediction of the 'optimal' hematocrit' (hct). In 80 pregnant women we measured blood viscosity, plasma viscosity and red blood cell (RBC) aggregation during labor (before and after 4 cm dilatation), during delivery, and during delivery of the placenta. Blood viscosity increases ($p < 0.001$) with a peak during delivery, explained by an increase in RBC rigidity. The 'optimal' hematocrit' (hct) was assessed as previously reported with the reconstruction of bell-shaped curve of the "oxygen delivery index" hematocrit/viscosity ratio h/η according to the equation of Quemada. The hct resulting in the highest value of h/η on this curve was considered as the "theoretical optimal hematocrit". Hematocrit was unchanged during labor and during delivery, and then decreased during delivery of the placenta. By contrast theoretical hematocrit increased during labor and decreased during delivery, and then increased again during delivery of the placenta, so that the discrepancy between actual and theoretical hematocrit (as well as the discrepancy between predicted and actual h/η) became minimal during delivery. Both actual and theoretical h/η were as usual closely related and exhibited a decrease during delivery. These results show that during delivery the hemorheological determinants of oxygen transfer predict a trend toward lower oxygen supply which is not fully compensated and may contribute to the increased risk of tissue anoxia in mother and newborn.

P8 Studies of the chemically induced changes of the mechanical properties of murine RBCs with the use of Atomic Force Microscopy (AFM)

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Atomic force microscopy (AFM) provides a real-space, three-dimensional (3D) image of a surface through the detection of an interaction between a sharp mechanical tip and the surface features. This technique allows researchers to view high resolution topographies of materials at the atomic or molecular scale. AFM is also the source of information about local mechanical properties such as stiffness, viscoelasticity, hardness and adhesion. Such technique can be very useful for analysis of biological materials such as cells and tissues[1,2]. In this work, we have focused on studies of mechanical properties of murine red blood cells (RBCs) obtained from the healthy control and mice model of the advanced atherosclerosis. We present the results of the AFM investigations of RBCs stiffness, topography and adhesion changes characteristic for alteration and due to interaction of RBCs with fixative. Isolated mice RBCs were fixed with various concentrations of glutaraldehyde and the monolayer of the RBCs was prepared on CaF_2 windows and measured with the application of the DPFM and AC modes. All mechanical properties were measured for both RBCs in buffer solution as well as for dried smears. Our preliminary results prove that AFM is a sensitive technique to study the alternations of murine RBCs membrane on the single cell level.

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P9 Investigation on energy characteristic of red blood cell deformability: A quantitative analysis of extending and retracting curves based on atomic force microscopy

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Deformability is a fundamental property of the cells and tissues of living organisms, which is commonly detected to indicate the state of the cells. And the cell deformability usually depends on the methods that we used, which is easy to be confused. The present research is designed to explore the energy characteristic of red blood cell deformability, based on a quantitative analysis of extending-retracting curves acquired from atomic force microscopy. ATP-depleted red blood cell are prepared by treatment with free-glucose Ringer solution. Our results clearly show that the Young's modulus of the erythrocyte is closely dependent on the concentration of intracellular ATP. Using the software Matlab, we obtained the area between the extending and retracting curves. Analysis of control and ATP-depleted RBCs demonstrated that the area could clearly differentiate between normal and ATP-depleted, which imply that ATP-depletion caused the decrease of RBC deformability. Our measures reveal that cell deformability is closely related to the state of intracellular energy, which can be characterized by cell passive deformation and active deformation. This research also provides a theoretical basis for studies of erythrocyte senescence, and offers a means of quantitating red blood cells apoptosis, as well as to provide an indicator of the state of blood stored for clinical transfusion.

P10 Measurement of glycocalyx volume: An unreliable biomarker

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One approach to evaluate changes in glycocalyx function in human subjects is measurement of a glycocalyx volume as a biomarker. The glycocalyx volume is the difference between the combined volume of plasma and glycocalyx measured using a tracer dilution principle and a plasma volume estimated from the red cell volume and large vessel hematocrit. The assumptions in the dilution method are: (1) tracer concentration within the glycocalyx equals plasma concentration; (2) a first order decay curve accounts for any early loss of vascular tracer; (3) no preferential binding of tracer to the glycocalyx. Errors arise from the use of large vessel hematocrit as a measure of whole body hematocrit, and the use of tracers that do not conform to the assumptions of the dilution principle. For example, the plasma volume Vp, derived from red cell volume (Vc) and large vessel hematocrit (H_{LV}) is given by the relation: $Vp = Vc\ (Tp/Tc)[(100/H_{LV})\text{-}1]$ where Tp and Tc are transit times for plasma and red cells respectively. The relation predicts that an increase in plasma volume (3 to 3.5 L) would be underestimated by 40% if red cell velocity relative to plasma was also increased by the volume expansion and Tp/Tc decreased from 0.9 to 0.85. Such errors in plasma volume are misinterpreted as variation in glycocalyx volume. Michel and Curry (Microcirculation16, 213:2009; also Chapters 2 and 3 of "Perioperative Fluid Management" edited by Farag and Kunz, Springer, 2016) have described additional errors in tracer dilution methods resulting from tracer heterogeneity, steric exclusion of tracer in the glycocalyx, and tracer binding. To date, estimates of whole body glycocalyx volume are confounded by other vascular changes and are unreliable biomarkers.

P12 Resonance Raman spectroscopy in detection and differentiation of various hemoglobin derivatives inside packed human red blood cells

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Red blood cells (RBCs) are stored for transfusion inside polyvinyl chloride blood-bags up to 42 days. During this time numerous biochemical changes may occur, thus lowering effectiveness of transfusion. Resonance Raman Spectroscopy (RRS) is a technique of molecular spectroscopy, which is a convenient tool to study biological samples, as the measurements can be done in water environment in a nondestructive and label-free manner.[1,2] This technique is especially unique in studies of hemoporphyrin, because of resonance Raman effect which causes the enhancement of the signal when proper excitation wavelength is used. Here we present that RRS combined with UV-Vis absorption spectroscopy allows us to quickly obtain information about Hb forms inside the whole volume of the human RBC sample, as well as to estimate the oxidation and the spin state of the centrally coordinated iron ion and the presence of ligands in axial positions. We have shown that RRS is able to differentiate and characterize not only typical forms of functional Hb, like oxyhemoglobin and deoxyhaemoglobin, but also various types of dysfunctional Hb such as different types of methemoglobins (metHb-H_2O, metHb-NO_2^-, metHb-CN), as well as hemichrome (bihistidine complex of Hb).

P13 Effects of different rehabilitation models on the elongation index of erythrocytes, study of activity of chosen erythrocyte enzymes, and the level of glutathione in elderly women

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Introduction: Ageing has a considerable effect on the rheological properties of human blood. The aim of this study was to analyze the effects of two various rehabilitation protocols – dance movement therapy exercises (DMT) and general rehabilitation exercises (GRE) – on the elongation index of erythrocytes, study of activity of chosen erythrocyte enzymes, and the level of glutathione in elderly women. Material and method: The study encompassed two groups of women (mean aged: 67 years), who were subjected to three-month rehabilitation programmes: DMT (n = 20) or GRE (n = 19). Blood samples from all the women were examined for their rheological and biochemical parameters both prior to the study and three months thereafter. Deformability of erythrocytes was determined using a laser rheometer SSD Rheometer-Rheodyne. Activity of acethylcholinesterase (AChE), gluco-6-phosphate dehydrogenase (G6PD) and level of reduced glutathione was determined in washed erythrocytes according to spectrophotometric method Beutler. Results: DMT affected the rheological parameters of the blood in elderly women, improving the erythrocyte deformability at the lowest shear stress value. GRE reduced the erythrocyte deformability at shear stress values equalling 4.24 and 8.23. AChE and level of reduced glutathione are not affected by DMT and GRE. G6PD activity increased (1.642 ± 0.286 vs. 1.797 ± 0.285; p = 0.0358) and reticulocytes count also (7.650 ± 3.543 vs. 12.95 ± 4.796; $p < 0.0001$) after DMT. Conclusions: DMT and GRE modulates erythrocyte deformability in elderly women. Some indicators are not affected by DMT and GRE in older women, suggesting the maintenance of homeostasis.

P14 Effects of whole body vibration training on hemorheological blood indicators in young healthy women

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Introduction: Vibrations have a stimulating effect on the cardiovascular system. The vibrations transmitted to the human body dilate the blood vessels, increase the blood perfusion through the tissues, so that the muscles are better provided with oxygen and nutrients. However, the changes in the rheological properties of blood under the influence of training on the vibrating platform have not been clearly described in the literature. Aim of the study: The aim of the study was to assess the impact of whole body vibration training on hemorheological blood indicators in healthy, young and non-training women. Material and methods: The study was attended by 10 female students of the University of Physical Education in Krakow aged 19 to 23. All women took part in 36 individual training sessions on the vibrating platform (3 times a week for 3 months). In the subjects, venous blood was collected twice - immediately before and after the last training.

Using the LORCA device, the erythrocyte elongation index (EI) and erythrocyte aggregation indexes were determined, i.e. AMP - total aggregation, T1/2 - half time of total aggregation, AI - aggregation index. The haematological indicators such as RBC (red blood cell), haemoglobin, haematocrit, MCV (mean corpuscular volume), MCH (mean corpuscular hemoglobin) and MCHC (mean corpuscular hemoglobin concentration) were also determined. Results: After completing the training in the studied women, there was a statistically significant increase in the AMP and EI indexes measured at shear stresses: 0.3; 0.58; 1.13 (Pa). Conclusions: A three-month training on the vibrating platform causes favourable changes in the rheological properties of the blood. The increase in the elongation index results in better blood flow through the capillaries.

P15 Evaluation of vascular effects of photodynamic therapy in skin microcirculation using different photosensitizers

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The effect of photodynamic therapy (PDT) is largely related to the effect on the microvasculature (MV). The peculiarities of changes in tissue perfusion when using various photosensitizers (PS), differing in their physicochemical properties have not been studied sufficiently. The goal of this research was to study the effect of PDT with PS on different chemical structures in the MV in the skin. The study was carried out on 96 male rats. Used PS: chlorin e6 derivative - Radachlorin (RH) 5 mg/kg; Coproporphyrin (CP) 10 mg/kg; Bengal pink (BR) 17 mg/kg. We used semiconductor laser devices with wavelengths of 662, 635 and 530 nm. Irradiation modes: (1) power density-0.38 W/cm^2, light dose-300 J/cm^2; (2) power density-0.1 W/cm^2, light dose-50 J/cm^2. Blood flow was evaluated before, immediately and 1 hour after irradiation with a laser flowmeter. The administration of PS to rats did not lead to significant changes in blood flow. An increase of perfusion of 13 and 15%, respectively ($p < 0.05$) was observed in the red region (635 and 662 nm, 300 J/cm^2) an hour after irradiation, and when irradiated in the green region (530 nm, 300 J/cm^2) there was a decrease in perfusion of 23% ($p < 0.05$). Photoactivation of CP and BR by laser radiation (635 and 530 nm, respectively) at 300 J/cm^2 resulted in an improvement in the perfusion of 32 and 66% respectively ($p < 0.05$). The experiments with RH and irradiation of 662 nm, the decrease in perfusion of 63 and 71% ($p < 0.01$) occurred immediately after irradiation at both 50 and 300 J/cm^2. The physicochemical properties of PS used differed in a number of characteristics: the quantum yield of singlet oxygen in RH is 0.96; BR-0.76; CP-0.37. This can explain a more significant disturbance of the MV in the photodynamic action on the skin in experiments with RH.

P16 Analysis of flow and thrombus development within PDMS channels of varying geometry

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Cardiovascular disease is the number one cause of death in the United States, affecting over 600,000 people annually. Many cardiovascular diseases are thought to be caused by a microcirculatory dysfunction. The blood flow pathway, through an implant (e.g. ventricular assist device) and in microcirculation, is one of the known factors that contribute to clot formation. Understanding the micro-scale factors that cause thrombosis is of paramount importance. Few studies have examined flow patterns around geometric irregularities and their effect on coagulation. The goal of this study was to quantify the flow pathway

and subsequent thrombus development in two PDMS channels. Each channel has a geometric irregularity (crevice or sudden expansion) to serve as a nidus of thrombus formation. In order to quantitatively measure flow at the micro scale, a particle image velocimetry system was coupled with an inverted epi-fluorescent microscope. Due to the nature of PIV, whole blood cannot be used as the fluid medium. A solution to this problem is the use of tracer-particle seeded ghost erythrocyte cells in which the hemoglobin and cellular components are removed preceding tracer particle impregnation. Preliminary data support the micro-particle image velocimetry system's (μPIV) ability to quantitatively measure flow. Results were compared to a computer COMSOL model under the same flow conditions. The experimental data validated the computational model. The data demonstrate the technique's ability to generate stable flows within each PDMS channel. Thrombus formation was confirmed using time-lapse, fluorescent images.

P17 Measurement of blood viscosity by measuring flows in microfluidic channel

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Blood contains plasma, red blood cell (RBC), white blood cell, platelet and various proteins. RBCs have a substantial role in the hemorheological characteristics. Increased blood viscosity significantly changes the flow resistance and wall shear stress (WSS) related with cardiovascular diseases. The relation between the blood viscosity and circulatory diseases has been studied in many previous studies. The general viscometers require a relatively large amount of samples and repetitive experiment for the accuracy. To measure viscosity with a smaller amount, the microfluidic method using micro channel was proposed. It is conducted by monitoring pressure between sample and reference fluids at the downstream of a microchannel with two inlets. However, it is difficult to apply this method to unknown inlet flow conditions. This microfluidic measurement was conducted under the known inlet flow rate condition. Therefore, the present study measures flow rate by micro particle image velocimetry (PIV) and then obtain viscosity from the measured data. Flow rate in the microchannel was estimated by assuming velocity profiles represent mean value along its channel depth. To demonstrate the measurement accuracy of flow rate, injected flow rate was compared with the flow rates measured at both upstream and downstream of a T-shaped microchannel. Blood viscosity could be reasonably estimated according to shear rate by measuring the interfacial width and flow rate of blood flows. As a result, it can be used for the case of unknown flow rate such as ex vivo condition. This method would be useful for understanding the effects of hemorheological features on cardiovascular diseases.

P18 Repeated whole body cryotherapy treatments does not cause changes in hemorheological parameters in healthy people

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Study aim: The aim of the study was to examine the influence of systemic cryotherapy on the rheological properties of the blood. Study material: The study groups consisted of 18 healthy men, aged 19–26, 10 students engaged in high-intensity physical activity and 8 students who engage in moderate-intensity physical activity participated in the research experiment. All subjects participated in 24 whole body cryotherapy (WBC) treatments (3 min treatment time, −120°C chamber temperature). In order to analyze the rheological parameters of the blood, venous blood samples were drawn from the participants of the study nine times (before 1, 12, 24 and after 1, 12, 24 WBC and after 24 hrs after 1, 12, 24 WBC). Blood samples were also collected four times after the completed treatments of WBC (after 1, 2, 3, 4 week break from the last treatment). RBC aggregation and deformability were measured at 37°C using a Laser assisted Optical Rotational Cell Analyzer (LORCA, RR Mechatronics, Hoorn, The Netherlands). Morphological blood test was obtained in a medical laboratory in Krakow.
Results: There were no significant changes after a single and after a series of WBC treatments in the elongation index (EI) in both study groups and in the aggregation of RBC also in both groups. A single WBC did not cause changes in the morphological properties of the blood in both groups. The biggest differences between the examined indicators were noticed after the series of WBC. The reduction of HGB, RBC levels and increase in MCV was the most noticeable. All obtained results were in the reference values.
Conclusions: WBC treatment does not increase the aggregation and deformability of red blood cells and thus does not increase the viscosity of the blood in healthy young, active males.

P20 Cell volume regulation via the Calcium-activated Potassium channel KCa3.1 contributes to red blood cell compliance under shear

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Background: Red blood cells (RBC) are exposed to varying magnitudes of shear stress (SS), resultant from varying vessel diameters of 2.5 μm–25 mm, whilst traversing the cardiovascular system. Upon shear exposure, calcium enters the cell, most likely via the mechano-sensitive piezo1 channel. Intracellular calcium activates KCa3.1-mediated K^+-efflux and augments H_2O extrusion, thus reducing cell volume. It is thought that micro-volume regulation of cell hydration facilitates perfusion through the microcirculation and impacts RBC deformability. Aim: The current study explored the effect of shear-induced calcium influx and subsequent Gardos-channel activation in RBC; corresponding changes in cellular deformability were also examined. Method: Whole blood from healthy, male volunteers (age: 22.5 ± 0.7 yr) was separated by centrifugation (1500×g, 5 min). Packed RBC were incubated with Senicapoc, a selective Gardos-channel blocker, at a final concentration of 10 nM, or phosphate buffered saline as Control at 37°C for 20 min. RBC deformability was quantified in an ektacytometer, before and after, conditioning shear exposure, with cells suspended in isotonic polyvinylpyrrolidone solution containing distinct concentrations of $CaCl_2$ (0, 25 μM, 2 mM). Results: Shear-conditioning with 10 Pa increased cell deformability; this effect was amplified with blockade of the Gardos-channel. Exposure to 64 Pa SS significantly impaired cell deformability regardless of channel blockade. High extracellular calcium impaired cell deformability, although blockade of the Gardos-channel reduced this impairment. Conclusion: The Gardos-channel plays a significant role in the regulation of RBC deformability, which is dependent upon presence of extracellular Ca^{2+} and the magnitude of SS exposure.

P21 - Effects of rowing on rheological properties of blood

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Rowing is one of the most challenging disciplines where the best athletes are characterized by excellent performance and factor that affect it such as power, force, technique and aerobic capacity. Rowing is a strength-endurance sport where most energy produce to muscle work is obtain from aerobic transformation of carbohydrates and lipids. The aim of the study was to assess the changes in morphological-rheological properties of blood in female elite rowers at the beginning and after full competition season. In order to examine these changes, blood was collected twice, in January and in November. The study group consisted of 11 female rowers and 10 non-trained women. A qualified nurse collected blood from athletes in the Laboratory of Blood Physiology at the University School of Physical Education in Krakow. Calculation were performed using the Statistica 12 (StatSoft®, USA) software. Our research found that regular endurance training cause decrease in red blood cell count. However, the other properties such as mean corpuscular volume (MCV) and average mass of corpuscular hemoglobin (MCHC) was significant higher at athletes in comparison with non-trained subjects. Result of control group accord to norm determine by ICSH. The biggest change occurred in the plasma viscosity compered to untrained woman. This could be due to an increase in plasma volume and relocation of the intracellular water. The lesser elongation index on different shear stress in athletes indicate smaller deformability of red blood cell. This could be due to the larger concentration of lactate in blood at rest compare to that in untrained subjects. It could also suggest an important role of free radical production in exercise and its influence on red blood cell stiffness.

P22 Impaired deformability of erythrocytes in hypertensive rats and patients: Investigation by nickel mesh filtration technique

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Background: Hypertension is associated with microcirculatory disturbance, and erythrocyte deformability is a major determinant of the microcirculation. Aim: The present study aimed to investigate the impairment of erythrocyte deformability in spontaneously hypertensive rats (SHR) and hypertensive patients under medication. Methods: Erythrocyte suspension was prepared after adjustment of hematocrit. Erythrocyte deformability was quantified as filterability by highly sensitive and quantitative filtration technique using nickel mesh. Wister-Kyoto rats (WKY) and normotensive subjects were served as controls. Results: In rats, erythrocyte filterability of SHR was significantly impaired than that of age-matched WKY. The impairment was marked in young (7 week) SHR and sustained in mature (18 week) SHR. In human, erythrocyte filterability in hypertensive group was significantly lower than that of the normotensive group. The filterability of hypertensive group was inversely proportional to the mean blood pressure ($r = -0.303$, $p = 0.002$). This impairment could not be explained by erythrocytes features

(mean corpuscular volume and hemoglobin concentration). Conclusions: Filterability of hypertensive erythrocytes is impaired, which is presumably caused by the mechanical membrane damage of circulating erythrocytes under the high shear stress and high blood pressure in the resistance vessels. Perspectives: Linkage of impaired deformability in hypertensive erythrocytes to target organ damage and hypertensive complications is a matter of future study.

P23 - Determinants of sublethal trauma to red blood cells: Effects of shear rate at standardised shear stresses

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Background: Red blood cell (RBC) deformation in shear is dependent upon the magnitude of shear stress exposure, and when levels become excessive, sublethal trauma is observed. Whether the corresponding shear rate contributes to sublethal trauma remains unresolved. Aim: The present study explored the effect of exposing RBC to supraphysiological shear stress (64 Pa) in three different suspending media of specific viscosities, in an attempt to discern whether shear rate, independently, is a major determinant of sublethal trauma. Method: RBC were suspended at 0.5 L/L in media of known viscosity (12.2, 20, or 29.6 cP). RBC deformability was assessed via ektacytometry at 37°C for all suspensions: i. without prior shear exposure (i.e., baseline), and ii. Following 64 Pa shear exposure for 300 s. Fresh samples were used for each measurement. Given diffraction patterns and maximal elongation of RBC are sensitive to viscosity, each diffraction pattern was standardised to a 10 cm ellipse, and deformability measurements was expressed relative to the respective maximal elongation index (EI). Results: Exposure to 64 Pa for 300 s decreased RBC deformability in all suspending media, with the most effect initially appearing in the highest shear rate suspension (i.e., 12.2 cP). Once deformability was standardised relative to maximal EI, however, it was found that the relative change in the 20 and 29.6 cP solutions (i.e., medium and low shear rate, respectively) displayed no significant differences following exposure to 64 Pa. Excessive artefact in the 12.2 cP sample precluded analyses of this data. Conclusion: The present study demonstrated that sublethal trauma is primarily determined by the shear stress magnitude, independent of the corresponding shear rate.

P24 - Susceptibility to mechanical damage of density-fractionated red blood cells

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Background: Cytoskeletal and cytosolic properties of red blood cells (RBC) undergo changes throughout the physiological ageing process. Given these physical properties determine the ability of RBC to deform in response to shear stress (SS), cellular ageing likely alters this process. Aim: The present study investigated how physiological ageing of RBC altered the responses to mechanical stresses within the physiological and supraphysiological ranges. Methods: RBC were density fractionated to provide 'young' and 'old' fractions, through centrifugation at 1500g × 300 s. Assessments of the fractionated cells included: i. osmotic gradient ektacytometry; and, ii. laser diffractometry to assess RBC deformability across a discrete range of SS (0.3–50.0 Pa). Specifically, RBC deformability was determined for fractionated

populations without previous shear conditioning, and also immediately after 300 s of shear exposure to: i. 10 Pa ("physiological"), and ii. 64 Pa ("supraphysiological"). Results: Old RBC (i.e., most dense) exhibited significantly decreased deformability under all osmotic conditions compared to young cells (i.e., least dense). Both young and old RBC fractions displayed typical increases in cell deformability following 10 Pa shear conditioning, and decreased deformability following 64 Pa shear conditioning; however, the magnitude of decreased cell deformability in old RBC was disproportionate to that of young RBC. Conclusion: Older RBC subpopulations exhibit decreased deformability and increased susceptibility to sublethal mechanical damage. These data may be of value in blood storage and transfusion processes.

P25- Clinical evaluation of laser Doppler flowmetry for diagnosis of microcirculatory disorders

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Background: Laser Doppler flowmetry (LDF) is a noninvasive method used to study skin blood perfusion by measuring the flow of blood cells inside a volume without harming the tissue. The results of LDF measurements for the diagnosis of circulatory disorders of the skin are generally evaluated by comparisons between a reference population of apparently healthy and "pathological" subjects. Methods: This study investigates the value of LDF in the diagnosis of microcirculation disorders in patients with coronary heart disease ($n = 20$) and in patients diagnosed with microcirculation disorders by capillary microscopy ($n = 46$). Results: The average LD amplitudes for patients with coronary heart disease were in the reference range. Some patients however showed decreased LD values. In eleven of the twenty patients the average LD values were below the reference range. Four of the eleven patients showed pathologically decreased capillary erythrocyte velocities of very = 0.09–0.21 [mm/s], while the other seven patients exhibited normal blood circulation at rest. All patients with a microcirculatory disorder had one significant pathologically reduced LD amplitude in one or more frequency window FF2 to FF4. Conclusion: The DOP method is a noninvasive diagnosis technique for the reliable detection of microcirculatory disorders of the skin.

P26 Erythrocytes aggregation index correlate with oxidative stress and hydrogen sulfide plasma concentration in diabetes mellitus

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Protein glycation of cellular membranes may result in rheological changes of erythrocytes and vascular complications during diabetes mellitus (DM). High glucose produced a significant increase in oxidative stress and reduction in the levels of small antioxidants (reduced glutathione - GSH, ascorbate - FRASC)

and enzyme activities (superoxide dismutase - SOD and ascorbate radical reductase – AFR). Hydrogen sulphide (H2S) has been found to counteract changes via regulation interference with adhesion molecules or antioxidant properties. The aim of this study was to examine possible link between erythrocytes aggregation, advanced oxidation protein products (AOPPs), H2S level and antioxidants (GSH, FRASC, SOD, AFR), in patients with diagnosed diabetes mellitus. Red blood cell aggregation was measured as microscopic aggregation index (MAI) proposed by the International Commission for Standardization in Hematology. Results: It has been proven that chronically occurring hyperglycemia in diabetes affects negatively the rheological properties of RBCs, leading to the increase in the MAI. A correlation of the increase in MAI values with the increase in AOPPs and H2S concentrations were demonstrated. It was found marked and negative link between MAI and GSH, FRASC levels.

P27 - Effects of carboxylated multiwall carbon nanotubes on erythrocytes stability and functionality

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Carbon nanotubes due to their unique properties are interesting materials for electronics, nanotechnology, material science etc. In medicine they could be applied as drug containers and carriers. The aim of the study was to examine a potential toxicity of multiwall carbon nanotubes functionalized with carboxyl groups (MWCNTs-COOH) on red blood cells. Using optical microscopy, spectrophotometry and Mössbauer spectroscopy we investigated size and shape changes of erythrocytes, their stability and functionality resulting from MWCNTs-COOH action, respectively. We observed, that erythrocytes swelled and their shape became irregular in the presence of MWCNT-COOH. Osmotic resistance curves showed variable behavior and they strongly depended on the applied concentrations of MWCNTs-COOH. This suggests complex interaction of these carbon nanotubes with the membrane structures of red blood cells. Moreover, we found that MWCNTs-COOH could modify the affinity of hemoglobin to bind. O_2.

P28 Influence of different rhythms sound wave to serotonin concentration in rats hippocampus

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Background: In our study, we focused on the influence of music and rhythm on the variation of serotonin concentration variation in the hippocampus. We aimed to determine what kind of music was able to improve the mental status of different people. Method: (1) Heart rates of SD rats were detected under anaesthesia and normal situation, averages were calculated for set rhythms of 300 beats/min, 350 beats/min, and 400 beats/min; (2) Sound waves were made according to setting rhythms with Finale 2011 software; (3) Rats were grouped randomly. Some rats received different sound waves under anaesthesia or normal situations whereas some received nothing as a control. (4) The left and right hippocampus were isolated from brains into tubes filled with 0.9% NaCl solution, weighed. These tissues were then ultrasonicated and centrifuged. Serotonin in the supernatant was obtained by ELISA. Conclusions:

(1) Right and left hippocampus have different responses to the same sound wave; (2) Under anaesthesia situation, the right hippocampus from the group that received 300 beats/min sound wave secreted the most serotonin concentration, 0.202 ng/(ml·mg); (3) Under normal situation, the right hippocampus from the group that received 400 beats/min sound wave secreted the most serotonin concentration, 0.128 ng/(ml·mg); (4) The closer to the resting current heart rate that the sound wave rhythm was set, the greater the amount of serotonin secreted.

P29 Physical properties of erythrocytes improve in hemochromatosis patients with repeated venesection therapy

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Background: Physical properties of red blood cells (RBC), including cell aggregation and deformability, are significantly impaired in individuals with hemochromatosis (HH). Although many of the complications associated with HH (e.g., endothelial dysfunction) may be attributed to impaired blood rheology, it remains unknown whether common therapies have an effect on the physical properties of RBC. Aims: The current study investigated whether venesection therapy, a common therapy in HH for normalising iron levels, alters hemorheological parameters. Methods: Blood samples (~450 mL) were collected from recently diagnosed HH patients who, at the time of recruitment, were receiving their first venesection treatment (n = 18; age = 60 yr; female = 11%). Additional blood samples (~450 mL each) were collected ~10.5 wk later following initial treatment, and ~6.3 wk after each individual's second treatment. RBC aggregation was measured via an aggregometer after 10-s at stasis (M_0) and after 10-s at low shear (i.e., 3 s^{-1}; M_1). RBC aggregation was measured for two conditions: i. at native haematocrit; and, ii. after haematocrit was standardised to 0.4 L/L. RBC aggregability was also measured in 3% dextran-70 at 0.4 L/L haematocrit. RBC deformability was measured using an ektacytometer. Results: Venesection significantly improved M_0 for both native (12.3 ± 24.3) and adjusted haematocrit (13.9 ± 27.4%) conditions. Additionally, M_1 improved in plasma at 0.4 L/L haematocrit (10.6 ± 27.0%), and also for RBC in dextran (18.0 ± 14.8%). Venesection treatment was also found to significantly improve RBC deformability. Conclusion: The findings of the present study indicate that routine venesection therapy is an effective method for improving the hemorheological impairments associated with HH.

P30 Experimental characterization of the embolus trapping efficiency of the U.S. FDA generic inferior vena cava filter

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Inferior vena cava (IVC) filters are placed to prevent pulmonary embolism in at-risk patients who cannot tolerate anticoagulation therapies. The objective of this study is to characterize the embolus trapping efficiency of the U.S. FDA generic IVC filter. The filter is made of nitinol and consists of 16 identical struts equally spaced in a conical fashion around the hub. Experiments were performed in an optically

accessible anatomical model of the IVC with the filter placed in the infrarenal region. Nylon spheres (n = 110, ρ = 1.14 g/cm^3) of diameters 3.2 mm, 4.8 mm, and 6.4 mm and bovine whole blood spherical clots (n = 100, ρ = 1.10 g/cm^3) of diameters 3.5 mm, 4.8 mm, and 6.0 mm were injected into either the left or right iliac entrances for each trial. The Reynolds number was 1470 and the clot-to-fluid density ratio was approximately 1.02 for each trial. The trapping efficiency for the 3.2 mm diameter nylon spheres and 3.5 mm diameter blood emboli was approximately the same: ≈75% for emboli from the left iliac vein (45 total trials) and ≈10% for emboli from the right iliac vein (45 total trials). All of the larger 4.8 mm and 6.4 mm nylon spheres were captured (15 of 15 for each side), whereas the trapping efficiency of the 4.8 mm blood clots was 93% (14 of 15) from the left iliac vein and 66% (10 of 15) from the right iliac vein. The 6.0 mm blood clots were also captured with 100% efficiency (14 of 14 for each side). These results suggest that the trapping efficiency depends on embolus size, the iliac vein from which the embolus originates, and, in some cases, the embolus material. In future work, these results will be leveraged to validate a physics-based computational model of embolus transport and capture.

P31 Effects of pentoxifylline on hemodynamic and hemorheological parameters in SHRs during arterial hypertension development

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Blood viscosity is the one of the principal determinant of total peripheral resistance (TPR), and its increase contributes to some extent to developing of arterial hypertension. This means that there is a potential opportunity to reduce TPR and blood pressure (BP) by agents which directly improve the rheological properties of blood. Previously, it was shown that pentoxifylline (PTX) exerts a positive influence on hemorheological parameters, but it had no effect on hemodynamic parameters in spontaneously hypertensive rats (SHRs) with stable hypertension. The present study was aimed to investigate the effect of this agent administration on BP, TPR, and rheological parameters of blood in SHRs during the development of arterial hypertension. SHRs were treated intragastrically with PTX at a dose of 100 mg/kg for 6 weeks (from 5th to 11th week of life). In control SHRs BP increased steeply during this period with the progressive growth of TPR. In addition, an evident manifestation of hyperviscosity syndrome in SHRs aged 11 weeks was observed. By the end of the experiment, PTX-treated rats had lower BP (by 19%) and TPR (by 31%) compared with the control group ($p < 0.05$), while cardiac output was unchanged. Hemorheological measurements showed that blood viscosity at shear rates from 60 to 450 s^{-1} was significantly lower (by 4–6%) in PTX-treated animals. There was no effect on hematocrit, plasma viscosity and half-time of RBC aggregation, but RBC deformability was higher significantly (by 1.5–1.7%) compared to control SHRs. These results show that administration of PTX to young SHRs can attenuate the severity of hyperviscosity syndrome, which is probably why this agent managed to decrease TPR and, therefore, limit the BP increasing during the development of arterial hypertension.

P32 Effect of cholesterol-rich diet on hematological and hemorheological parameters in rabbits

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Introduction: Little is known about the effect of cholesterol-rich diet on hemorheological factors. We aimed to investigate this issue on rabbits, as one of the best animal models in atherosclerosis research. Materials and methods: California-New Zealand hybrid rabbits were subjected to two experimental groups: the control group animals (RCC, $n = 6$) were fed with normal rabbit chow, while the rabbits in cholesterol-rich diet group (RHC, $n = 6$) were fed with chow supplemented by 1% cholesterol and 1% triglyceride for 16 weeks ad libitum (permission Nr.: 25/2013/UDCAW). Blood samples were taken from the marginal ear vein into Vacutainer tubes containing K3-EDTA for determining hematological parameters, red blood cell deformability, membrane stability and aggregation. Results: In the RHC group the white blood cell count ($p < 0.001$) and mean corpuscular volume ($p = 0.009$) increased, while the red blood cell count ($p < 0.001$), hemoglobin ($p < 0.001$) and hematocrit ($p < 0.001$) decreased, with lowered blood viscosity. Erythrocyte deformability and membrane stability values were lower than the control data (EI at 3 Pa: $p < 0.001$; EImax/SS1/2: $p = 0.035$). Red blood cell aggregation parameters reflected lower aggregation (AI%: $p = 0.021$, Amp: $p = 0.002$, t1/2: $p < 0.001$). Conclusions: The 16-week cholesterol-rich diet resulted in significant changes in several hematological and hemorheological parameters. Red blood cell deformability impairment was significant, and probably due to the decreased hematocrit, erythrocyte aggregation markedly lowered. These micro-rheological changes may contribute to the development of microcirculatory alterations.

P33 Changes in biochemical properties of the blood in winter swimmers

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The aim of this study was to assess the influence of regular immersions and swimming in cold water on blood biochemical properties of individuals voluntarily involved in such activities.
Winter swimmers are persons taking winter baths when the water temperature ranges from 1°C to 4°C. The participants belonged to the Cracow Society of Winter Swimmers “Kaloryfer” - “The Heaters”. In order to investigate changes in the biochemical blood properties of people participating in the study, venous blood was collected and tested twice. The study took place at the Bagry lagoon, at the beginning of the season in November 2015 and at the end of the season, in March 2016. The study group consisted of 11 men aged 30–50 years, ‘walrusing’ throughout the season from November to March. The blood was collected by a qualified nurse under medical supervision. After collection, the blood was transported to the Maria Sklodowska-Curie Memorial Institute - Center of Oncology in Krakow and to the Department of Laboratory Diagnostics - “Diagnostyka” in Krakow. All calculations were performed using the Statistica 12 (StatSoft®, USA) software. We found that systematic winter swimming has impact on several biochemical and immune system parameters. Electrolytes. Observed substantial

decrease in sodium and chloride levels is possibly caused by several mechanisms. The most possible explanation of this phenomenon is diuretic-urine sodium loss. Increased diuresis after swimming leads to greater electrolytes loss with the urine. Renal function tests of Winter swimming was associated with a downward tendency in urea levels which is consistent with previous findings. Liver function tests revealed no significant changes in plasma enzymes such as AST, ALT, GGT and LDH after regular winter swimming.

P34 The paraclinical evolution in diabetic hypertensive patients with increased abdominal circumference

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Objective: to assess paraclinical evolution in patients with essential systemic hypertension, DM2 ± IHD and increased abdominal circumference. Method: 220 patients >40 yrs, with SH+DM2 (<5 years), treated with OADs examined in the last 3 yrs. It was a retrospective study. All the patients with heart failure NYHA II–IV and coronary major events were excluded. In all patients were recorded retrospective data: clinic, blood tests (lipids, HbA1c, hs CRP), ECG, US. The patients were divided into two groups: the control group (n = 106) with abdominal circumference <100 in men, 90 in women– and the study group (n = 89): patients with abdominal circumference >100 in men, 90 in women. In all patients were assessed LV function and rest heart rate. In both groups were included only pts with HR < 90b/min, in sinus rhythm and EF > 55%. Results: The mean age was 58.7, 51.9% women. The patients from the two groups had the same profile of risk factors and associated comorbidities (except obesity) In control group – medium abdominal circumference: 97.8 cm in men, 88.2 cm in women; average hs-CRP was 2.3 mg/L, and average rest HR was 71beats/min. In study group - medium abdominal circumference: 116.3 cm in men, 101.2 cm in women; average hs-CRP was 3.6 mg/L, and average rest HR was 79b/min. Conclusion: Increased abdominal circumference seems to influence the evolution of hypertensive diabetic patients ± ischemic heart disease and decreases the possibility of control of paraclinical parameters even if the clinical evolution of the subjects seems to be similar. Maybe it is important to check more often these parameters in people with increased abdominal circumference because could be an additional marker for impaired evolution of cardiovascular diseases. Further studies are needed to confirm these findings.

P35 Alterations of red blood cell deformability and mechanical stability by heat-treatment on animal blood samples

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The long-lastingly elevated body temperature caused by different reasons may alter hemodynamics and hemorheological parameters. However, literary data is scarcely available in this topic. Therefore, we

investigate the effect of heat-treatment at normal or fever-ranged temperature on the micro-rheological parameters of erythrocytes in animal models. Blood samples were obtained from 7 Sprague-Dawley rats and 6 Beagle dogs. The K3-EDTA anticoagulated samples were centrifuged (1000g, 10 minutes), and red blood cell - normal phosphate buffered saline suspensions (10%) were prepared. Every sample was subdivided into 3 aliquots and heat-treated for 10 minutes at 37, 40 or 43°C. Conventional and osmotic gradient deformability as well as mechanical stability of erythrocytes were determined by ektacytometry. Elongation index (EI) values were significantly lowered in the samples treated at 43°C than the 37°C group ($p < 0.01$), accompanied by altered ratio of maximal EI and the corresponding shear-stress values ($p < 0.01$) in both species. Moreover, values at 43°C were significantly lower than those of 40°C ($p < 0.01$) in rats. Changes in mechanical stability and osmotic gradient deformability parameters were also similar, but most markedly between the minimal and maximal elongation index values ($p < 0.01$ 43°C vs. 37°C), and in the area under the curve ($p < 0.001$ 43°C vs. 37°C) parameter. Deformability of red blood cells was significantly impaired by the applied heating in both species, showing slight inter-species differences as well. The deterioration was larger in magnitude when the temperature increased, however, the relation was non-linear. These data suggest that high fever may have an impact on the micro-rheological properties of erythrocytes that may further influence microcirculation.

P36 Shear-dependency of the predicted ideal hematocrit

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The ideal hematocrit is the hematocrit (hct) value resulting in the highest value of hct/viscosity (h/η) ratio and can thus be predicted from viscometric measurements with the use of equations such as Quemada's one which yield the determination of the bell-shaped curve of h/η as a function of hct. In a series of recent papers we applied this approach to various populations, using viscopetry at high shear rate (1000 s^{-1}). However the shape of this curve is dependent on the shear rate, resulting in a right-shift in this top value when hct increase, as previously described by Nemeth et al. [Biorheology. 2009;46(2):155–65]. We present here in 11 young recreative athletes the evolution of the predicted top of the h/η curve and optimal theoretical hct and the discrepancy between theoretical and optimal values over the range of shear rates 1 to 6000 s-1 (RHEOMETRE Anton Paar CP 50-1). Results show that the predicted optimal value of both h/η and Hct increases when shear rate increases when shear rate increases and that the discrepancy between predicted "optimal" and actual values decreases and becomes almost asymptotic at very high shear (500 s^{-1}). It is minimal at 2720 s^{-1}. The correlation between predicted "optimal" and actual values of both parameters describes the same evolution. Therefore, it is better for assessing h/η and its agreement with theoretical values, and for determining the theoretical ideal hematocrit, to measure blood viscosity at shear rates equal or superior to 500 s^{-1}.

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