S15: Hemodynamic Functionality of Red Blood Cells in Blood Microcirculation: Experiments and Modeling

S15-1 Biomechanics of Red Cell Diseases

Ming Dao

Massachusetts Institute of Technology, USA

How biological cells' mechanical / physical properties are related to disease states? Recent progresses 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

Irina Tikhomirova[a], Yulia Malysheva[a], Nikolay Kislov[b], Mihail Ryabov[b]

[a]*Yaroslavl State Pedagogical University, Russia*
[b]*Yaroslavl Regional Cancer Hospital*

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 control. 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

Johannes Mauer[a], Felix Reichel[b], Jochen Guck[b], Gerhard Gompper[a], Dmitry Fedosov[a]

[a]*Forschungszentrum Juelich, Germany*
[b]*Technical University of Dresden, Germany*

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 microchannel can be associated with the flow conditions and cell properties. Quantitative comparison between simulations and experiments is 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

Gregory Barshtein[a], Axel Pries [b], Neta Goldschmidt [c], Orly Zelig [c], Dan Arbell [c], Saul Yedgar[a]

[a]*Hebrew University Medical School*
[b]*2Charité-Universitätsmedizin*
[c] *Hadassah University Hospital*

Background: The primary goal of red blood cell (RBC) is to supply oxygen to tissues and organs. However, RBC 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 the vasculature function.

S15-5 Red Blood Cell Aggregate Flow Characteristics in Bifurcating Microchannels.

Efstathios Kaliviotis

Cyprus University of Technology, Cyprus

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.