

**Abstracts**

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Guest Editor

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**Friday, August 29<sup>th</sup>**  
**Flowmotion waves in laser doppler signals: the low frequency components.**  
**Parallel Symposium – S38**

**S38A**

**PRESENCE AND SIGNIFICANCE OF SEVERAL LOW FREQUENCY COMPONENTS IN LASER DOPPLER BLOOD FLOW SIGNALS**

A Stefanovska

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Laser Doppler flowmetry can be used for non-invasive monitoring of blood perfusion in arterioles and the capillary bed. The resultant signal is highly complex and contains several oscillatory components. In addition to the cardiac and respiratory oscillations (also propagating through the small vessels), several lower frequency components have also been identified, ranging from 0.007 to 0.1 Hz. All components vary slightly with time in both frequency and amplitude, thus presenting a very challenging task in terms of signal analysis. We will discuss the importance of time-frequency methods and logarithmic resolution, as well as length of recording and sampling frequency. The aim is for optimal decomposition of the signal into components that can be related to the specific physiological mechanisms involved in blood flow regulation within the microvasculature. Several studies investigating the physiological origins will be reviewed and current understanding will be outlined. Changes in the oscillatory components with ageing will be illustrated. The results of clinical studies of patients with cardiac failure, diabetes, and post-acute myocardial infarction, will be used to emphasize the potential of the approach.

**S38B**

**MICROVASCULAR CORRELATES OF FLOWMOTION WAVES: FROM ARTERIAL DIAMETER CHANGES TO LASER DOPPLER FLOWMOTION. THE LOW FREQUENCY COMPONENTS IN LASER DOPPLER SIGNALS OF HYPERTENSIVE PATIENTS**

D Lapi[1], C Morizzo[2], F Vittone [2], M Varanini [3], C Palombo [2], A Colantuoni [4]

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In experimental microvascular models, such as the hamster skin fold window preparation, the arteriolar rhythmic diameter changes were characterized and several frequency components (FCs) were computed, according to vessel branching orders. These FCs in the range 0.01 – 0.25 Hz were related to several factors, such as myogenic activity, respiratory and heart rates. Many FCs were evidenced in laser Doppler tracings derived from healthy volunteers and patients, corresponding to those detected in experimental animals. We studied the effects of short term therapy with the beta-blocker Nebivolol (5 mg/die for one month) on skin microcirculation in newly-diagnosed hypertension patients (HP). Twenty-eight subjects (20 males, 50.9 ± 9.1 years old) were studied before and after treatment, compared with twenty-four healthy volunteers. Skin blood flow was significantly reduced in HP (6.9 ± 2.1 PU vs 10.7 ± 4.8 PU,  $p < 0.01$ ) as well as the total power (1.18 ± 1.02 PU<sup>2</sup> vs 3.5 ± 2.6 PU<sup>2</sup>,  $p < 0.05$ ). The relative power spectral density (PSD) of low FCs (0.009 - 0.06 Hz) was reduced compared with the heart rate-related component. The endothelium-dependent and independent dilation, reduced in HP, recovered at the end of treatment as well as the total and relative PSD of low FCs.

**S38C**

**LOW FREQUENCY FLOWMOTION WAVES IN POAD PATIENTS**

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Endothelial, myogenic and sympathetic activities on microvessels sustain the skin microcirculation autoregulation. The break down of these mechanisms leads to gangrene in patients with peripheral arterial disease (POAD). With power spectrum analysis it is possible to assess the endothelial (0.009-0.02 Hz) the sympathetic (0.02-0.06 Hz), the myogenic (0.06-0.2 Hz) frequency components, the so called "slow flowmotion waves" (SFW) within the entire spectrum of flowmotion waves (0.009-1.6.Hz)

In a group of 20 Intermittent claudication (IC) and 20 Critical limb ischaemia (CLI) patients matched with a group of 20 healthy subjects (hs), we assessed the medium power spectrum of all flowmotion waves (0.009-1.6 Hz) and the prevalence of SFW (0.009-0.2 Hz)

Our results showed a significant reduction of all medium power spectrum (mps) of flowmotion waves in all the POAD patients vs hs,  $p < 0.001$  (0,097 ± 0,020. 0,40 ± 0,10 vs 1.0 ± 0,5, respectively). The mps of SFW was particularly reduced in CLI.

Moreover, the SFW prevalence was markedly reduced by 70% ± 5% in CLI, while in IC the reduction was only by 20%± 4%. The sympathetic activity mps was not significantly reduced in CLI vs IC ( 0,45 ± 0,20 vs 0,54± 0,60).

In conclusion, our findings show that in POAD patients there is a decreased amplitude of all the flowmotion frequencies (0.009-1.6.Hz) in both IC and CLI patients while the reduction of SFW (0,009-0,02 Hz) seems to be marked only in CLI. These results are in accordance with clinical findings in POAD patients where the claudicant ones have less risk of gangrene because the autoregulative microvascular mechanisms are still present.

**S38D**

**LINEAR AND NONLINEAR ANALYSES OF LASER DOPPLER FLOWMETRY SIGNALS RECORDED DURING ISOFLURANE-INDUCED ANAESTHESIA IN HEALTHY RATS**

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Laser Doppler flowmetry (LDF) signals recorded in healthy rats are studied during anaesthesia induced by isoflurane, an anaesthetic commonly used in clinical practice. For this purpose, isoflurane is administered in thirty two rats. The doses of anaesthetic are chosen to obtain two groups of rats: a first one (sixteen rats) with light anaesthesia, and a second one (sixteen rats) with deep anaesthesia. The LDF probe is positioned on the rat thigh. The mean value of each recording is determined. The complexity of the LDF signals is also analyzed by computing their multifractal spectra. For the latter analysis, the processing method is first calibrated with an *a priori* known synthetic multifractal process. The results show that the average LDF mean value is lower in the group of deep anaesthesia than in the group of light anaesthesia. However,  $P > 0.05$  when these differences are analyzed with the Mann-Whitney test. Moreover, depth of anaesthesia does not modify the weakly multifractal properties of the signals: average multifractal spectra of LDF signals in each group have the same width. These findings infer that isoflurane may change the microvascular tissues properties but these modifications have no influence on LDF signals complexity measured by multifractal spectra. The authors would like to thank the Perimed company for the loan of the blood flow monitor and probes.

**POSTER PRESENTATION ABSTRACTS**  
**Tuesday, August 26<sup>th</sup>**  
**Angiogenesis**  
**Poster Session - PAG**

**PAG1**

**HOW ARTERIES DIRECTLY CONTROL THE VENOUS PATTERN THROUGH MECHANICAL FACTORS DURING VASCULAR MORPHOGENESIS.**

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The vascular network spanning the vertebrates' body is so finely branched that the positions of each vessel cannot be genetically encoded. However, in many cases, mature arteries and veins follow an exactly parallel path, which is often interpreted in favor of a genetic cross-talk between them during embryonic development. We present a detailed study of the spatio-temporal development of yolk-sac and brain arteries and veins in growing chicken embryos: a metamorphosis of the vasculature, from an organization in series to an organization in parallel, spontaneously occurs when the size of the tissue increases. Based on optical and local mechanical measurements, we demonstrate that this metamorphosis is due to the visco-elastic response of the tissue, which induces a local rearrangement of capillaries, leading to an increase of the hydraulic conductivity along paths strictly parallel to the growing arteries. These paths are further selected by blood flow, and subsequently remodeled into veins, when the size of the tissue becomes greater than a threshold, which has been confirmed using numerical simulations (electrical analogy) of idealized vascular configurations. Therefore, the developing arteries directly induce their mated veins by a mechanical, self-organized universal process of hemodynamic and visco-elastic origins.

**PAG2**

**CHANGES IN IMMUNOPHENOTYPE, BEHAVIOUR AND MICROCIRCULATION OF HUMAN TUMORS IMPLANTED ON THE CHICK CHORIOALLANTOIC MEMBRANE**

AM Cimpean [1], M Raica [1], D Oasim [2], R Ceausu [1], P Gaje [1], V Bocan [1], O Ferician [1], DV Poenaru [2], M Iacovliev [1]

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The behaviour of a tumor and its metastasis are different concerning therapy response and prognosis because of an incomplete molecular characterization of the tumors and their microcirculation. Metastasis and their vascularization are not well understood. The chick embryo chorioallantoic membrane represents an experimental model for dynamic study of tumors metastasis and its angiogenesis. Our purpose was to study phenotypic changes of the human tumors and their vascularization at several passages on the chick CAM. Two bone metastasis (breast cancer and lung cancer), one ovarian tumor and one gastric carcinoma were studied. Immunophenotyping included cytokeratins, proliferation markers, vascular markers, VEGF and its receptors, AC 133 and TIE2. Bone metastasis survived for three passages on the chick CAM. Cytokeratin expression was lost at the first implant compared with initial tumor and few or no proliferation was observed in the tumor implant. A high proliferation of host blood vessels and a particular type of vascular anastomoses between host and graft blood vessels were observed. AC133, TIE2 + cells were detected in the wall of the tumor blood vessels. Our findings support a „personalized” immunophenotype for each tumor type and metastasis as a base for targeted therapy.

**PAG3**

**ROLE OF EXTRACELLULAR RNA IN ARTERIOGENESIS**

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Arteriogenesis describes the growth of functional collateral arteries from preexisting arterio-arteriolar anastomoses. Initial triggers are physical forces such as altered shear forces, which activate the endothelium. Inflammatory features of the endothelium are apparent by increased expression of adhesion molecules or the chemoattractant molecule MCP-1 leading to increased adhesion and migration of monocytes to the endothelium. Pretreatment of mice with RNase but not with DNase for 10 min before occlusion of the arteria femoralis significantly reduced the extent of arteriogenesis suggesting that extracellular RNA might play a role in the process of arteriogenesis. Accordingly, *in vitro* studies confirmed that RNA acts as a chemoattractant for monocytes. The migration of monocytes through an endothelial cell monolayer was increased by RNA to nearly the same extent as by MCP-1. Additionally, the adhesion of monocytes to microvascular endothelial cells was increased by extracellular RNA, but not by DNA. Furthermore, RNA increased the expression of ICAM-1 on endothelial cells, which was abolished in the presence of RNase. Extracellular RNA also leads to exocytosis of Weibel-Palade bodies, which