NEW INSIGHT IN CORONARY VULNERABLE PLAQUE MECHANICAL PROPERTIES

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Invited Speaker Abstracts

NEW INSIGHTS IN ULTRASOUND IMAGING FOR CARDIOVASCULAR DISEASES AND LARGE ARTERIES PROPERTIES
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Recent developments of ultrafast ultrasound imaging scanners open very exciting possibilities in the field of cardiovascular imaging. Thanks to the new design of the most recent ultrasound scanners that uses a fully software-based ultrasound platform, frame rates as large as 20,000 frames/s are reached today. Compared to classical ultrasound scanners that delivered some 100 frames/s these new possibilities represent a complete breakthrough. We will describe at least three innovations that leverage ultrafast ultrasound imaging. The first one is a new imaging mode that provides quantitative viscoelastic analysis of arterial wall by following the propagation of both pulse waves and shear waves with a spatial resolution and precision that were never obtained with classical techniques. The second one allows to image in a very quantitative way the cardiac elasticity anisotropy by studying shear wave propagation in different directions. The last innovation is new way to perform Doppler flow analysis, from ultrafast scanners, changing completely the performances and workflow paradigms of Color and PW modes. Various results obtained with these techniques in the field of cardiovascular imaging will be presented.

VASCULAR BIOMECHANICS: CONSTITUTIVE MODELLING AND CHARACTERISATION OF THE ARTERIAL WALL
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Insight into the mechanical properties of the arterial wall can give valuable information concerning the understanding of pulse wave propagation in the arterial tree, the genesis and progress of atherosclerosis, vessel wall adaptation and remodelling, and the prediction of the effects of medical intervention, such as blood-pressure regulating drug admission, balloon angioplasty, and bypass surgery. A widely used approach to characterize the mechanical properties of arteries is based on a mixed experimental–numerical method, in which parameters of mathematical constitutive models are fitted to experimental stress–strain data. For wall remodelling studies (Machchyn et al., 2010) these parameters preferably are based on micro-structural information such as collagen content and morphology (Rezakhaniha et al., 2011). A generic set of parameters can be obtained from ex-vivo experiments where stress-strain relations can be obtained for transmural pressures ranging from a non-physiological unloaded to physiological fully loaded configuration (van den Broek et al., 2011). If only clinical data at physiological loading are available, extra constraints on the parameter set can be used to obtain a unique characterization (van der Horst et al., 2011). Several aspects regarding the above mentioned micro-structural based models will be discussed during the presentation. For predictive models of pulse wave propagation, micro-structural based constitutive models must be casted into pressure-area relations, whereas, for prediction of adaptation and arterial wall remodeling, the dynamics of smooth muscle cell behavior must be taken into account. Both facets will be shed light upon and illustrated by results recently obtained.


NEW INSIGHT IN CORONARY VULNERABLE PLAQUE MECHANICAL PROPERTIES
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Vulnerable coronary atherosclerotic plaque rupture is a recognized major cause of acute coronary syndrome. Such vulnerable plaques can be detected clinically by various techniques, including intravascular ultrasound (IVUS) and optical coherence tomography. Detecting lesions vulnerable to rupture is a major issue, as it could lead to the development of specific treatment strategies for the prevention of acute thrombotic events. Clinical and biomechanical studies performed recently by our group have originally identified new morphological factors as the key predictors of vulnerability to rupture. Moreover, it is now recognized that prediction of the vulnerable coronary plaque rupture requires not only an accurate quantification of fibrous cap thickness and necrotic core morphology but also a precise knowledge of the mechanical properties of plaque components (IVUS Modulography of Atheroma Plaque). We demonstrated why, in clinical practice, biomechanical plaque instability is not a consequence of CAPI alone, but rather of a subtle combination of CAPI, CorEchoc and Remodindex. Moreover, Residual Stress/ Strain (RS/S) present in a vulnerable coronary plaque dramatically influences the spatial stress distribution and spotlights some new sites of stress concentration. RS/S could play a major role in the biomechanical stability of vulnerable coronary plaque and in the growth process of the lipid core. Additionally, we showed that plaque rupture is to be viewed as a consequence not of external pressure alone but rather of a subtle combination of external loading and intraplaque RS/S.

Recent publications of our group in this field

Abstracts


MRI IN CAROTID PLAQUE
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The emergence of high-resolution imaging methods has enabled MRI to noninvasively image the fine internal structure of cervical arterial walls. This presentation will provide a comprehensive guide to perform high resolution MRI (HR-MRI) of cervical arteries, including the choice of coils, sequences, imaging parameters, and tips for optimal image quality. HR-MRI of carotid atherosclerosis has the potential to be used in treatment decisions or to monitor the effects treatment options. We will explain and illustrate how to quantify plaque volume, determine atherosclerotic plaque burden, detect plaque composition, and ultimately identify unstable plaque before it leads to a clinical event using HR-MRI. Finally, the role of HR-MRI in the diagnosis of cervical dissection and inflammatory disease of the arterial wall will be emphasized.

WHAT IS THE FUTURE FOR RESEARCH IN ARTERIAL STIFFNESS AND CENTRAL BLOOD PRESSURE?
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MOLECULAR MECHANISMS OF THE VASCULAR REPSONSES TO HAEMODYNAMIC FORCES
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Numerous studies in man and in animals support the relation between low or turbulent shear stress and atherosclerotic plaque location. However, little is known regarding the role of shear stress on the progression and composition of pre-established plaques. A recent prospective study in patients revealed that atherosclerosis regression is a realistic goal in patients, and it can be achieved through increased shear stress. We have used a model of arteriovenous fistula (AVF) developed in the lab, connecting the right common carotid artery with the jugular vein, to increase blood flow over established plaques in the brachiocephalic artery of LDL receptor knockout mice. Animals are placed on a high-fat diet for 12 weeks (wk0-wk12), then divided in three groups: control, sham, or AVF. Sham and AVF animals are maintained on high-fat for 4 weeks post-surgery. Atherosclerotic plaque size in the brachiocephalic artery averages 100,100±13,900μm² at wk12 (control animals) and progresses to 134,200±15,100μm² in sham by wk16, whereas it actually regresses by 53% in AVF in the same timeline (63,500±15,100μm²; p<0.02). Relative smooth muscle cell, macrophage, and collagen content are equivalent between groups, but matrix metalloproteinase (MMP) activity is enhanced in the AVF mice, suggesting that these enzymes might participate in the remodeling process. Indeed, in mice treated with MMP inhibitors and TIMP plasmids, MMP expression and activity diminish, and AVF fails to reduce plaque size. Hence, a favorable local shear stress may reverse the atherosclerotic process through a process involving metalloproteinases.

VASCULAR REMODELLING OF THE RETINAL MICROCIRCULATION IN HYPERTENSION AND DIABETES
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In addition to the classical signs of hypertensive nephropathy (e.g. arterial narrowing, arterial venous nicking, retinal haemorrhages or microaneurysms) new technologies have emerged to characterize hypertensive retinopathy more precisely: Scanning Laser Doppler Flowmetry (SLDF) which allows the precise characterization of the remodelling processes in retinal arterioles, and techniques analyzing the retinal microvascular architecture. For example, in patients with essential hypertension and malignant hypertension the length to diameter ratio (indicating generalized narrowing) has been found to be increased and the number of terminal branches (a parameter of capillary density) reduced. By applying SLDF with automatic full field perfusion imaging analysis, (AFFFIA) our data suggest that retinal arterioles and subcutaneous small arteries undergo the same type of remodelling in hypertension, and also the pattern in quantity of vascular changes are comparable. Most recently, a close correlation between the changes of the subcutaneous small arteries and retinal arterioles have been found. Hypertensive patients with a history of cerebrovascular events showed a greater wall to lumen ratio of retinal arterioles than hypertensive and normotensive controls. Of note, treated hypertensive patients with poor blood pressure control had a greater wall to lumen ratio than those with a better blood pressure control. In diabetic hypertensive patients hypertrophic outward remodeling occurs characterized by increased wall crosssectional area and enlarged outer diameter. This pattern has been observed in subcutaneous and retinal vessels.

REGULATION OF ARTERIAL STIFFNESS: CELLULAR, MOLECULAR AND NEUROGENIC MECHANISMS
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