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# ARTERIAL STIFFENING ACROSS MULTIPLE LENGTH SCALES

Riaz Akhtar

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## Invited Speaker Abstracts

### Opening Lecture

#### IMAGING OF THE CARDIOVASCULAR SYSTEM

Rene Botnar

*Chair of Cardiovascular Imaging, Imaging Sciences Division, King's College London, UK*

MR and PET vessel wall imaging have progressed substantially in the past decade and considerable technical improvements have been made in image acquisition and the development of cell and protein specific contrast agents that allow plaque characterization both on a morphological and molecular/cellular level. Studies in animal models of experimental atherosclerosis and small single center pilot clinical studies have demonstrated the feasibility of molecular MR and PET vessel wall imaging in the carotid artery, the aorta and the coronary arteries. These studies demonstrate the potential of those techniques for the non-invasive quantification of plaque burden and molecular composition, which could lead to improved risk stratification in patients with cardiovascular disease. With the advent of PET/MRI and continued development of target specific contrast agents, these novel techniques have potential to be useful for the non-invasive assessment of atherosclerosis and for monitoring response to treatment in clinical practice.

### Career Development Lecture

#### ARTERIAL STIFFENING ACROSS MULTIPLE LENGTH SCALES

Riaz Akhtar

*Lecturer in Biomedical Engineering, School of Engineering (Centre, for Materials and Structures), University of Liverpool, UK*

It is well established that aortic stiffness increases with age, and as a result of a number of risk factors including diabetes. Most quantitative measurements of arterial stiffness involve the use of *in vivo* techniques such as pulse wave velocity or *ex vivo* techniques such as tensile testing. However, the aorta has a complicated and intricate structure, governed by the properties and composition of the microstructural components of the vessel wall. Hence, these methods provide an average macroscopic response of the material properties and little is known about the effects of ageing and disease on individual components of the aorta.

We present data obtained with novel materials science techniques that allow us to localise mechanical property changes at the microstructural and molecular scale. The scanning acoustic microscope (SAM), when operated at frequencies close to 1 GHz, can provide quantitative measurements of acoustic wave speed (related to tissue stiffness) with a spatial resolution around 1  $\mu\text{m}$ . We have employed SAM to examine changes in the aorta due to ageing, diabetes and Cardiotrophin-1 treatment using animal models. In each case, the inter-lamellar regions of the media have been found to be a key determinant of the overall mechanical and structural properties of the aorta. At the molecular level, we examine the role of fibrillin microfibrils on aorta properties using atomic force microscopy (AFM). These data are compared with the *in vivo* and macroscopic response of the vessel.

### Career Development Lecture – ARTERY 13

#### CARDIOVASCULAR AGING: INSIGHTS FROM MAGNETIC RESONANCE IMAGING

Alban Redheuil

*Head, Imaging Core Lab ICAN, Cardiovascular Imaging Pitie Salpetriere Hospital, Cardiology Institute, INSERM U678, Paris, France*

Aortic stiffness is now established as an independent marker of cardiovascular aging and cardiovascular risk. However, the specific role of the proximal aorta, specifically the ascending aorta, remains understudied. Magnetic resonance imaging (MRI), a non invasive technique has recently been proposed to measure new local and regional stiffness indices in the thoracic aorta. We will here review the available data on aortic stiffness assessed by MRI. We will discuss the methodological advantages and challenges of MRI, combined with applanation tonometry, to evaluate local aortic distensibility and pulse wave velocity (PWV) and summarize available results concerning the distribution of such parameters in both the general population and disease and their prognostic value.

Aortic distensibility has been shown to be an early subclinical marker of vascular target organ damage in the general population and expected ranges for ascending aortic distensibility and aortic arch pulse wave velocity assessed in MRI have been described in the general population and in disease. Changes in aortic distensibility and arch PWV have been related to age-related geometric changes, specifically lengthening, enlargement and unfolding of the thoracic aorta. Increased proximal aortic stiffness measured by MRI has also been related to decreased systolic and diastolic function and concentric remodeling of the left ventricle in healthy individuals. Data are now available for proximal aortic stiffness in diabetes, hypertension and aortic diseases such as bicuspid aortic valve or Marfan syndrome. We will review data on aortic distensibility as an independent predictor of mortality and incident cardiovascular disease in the general population.

### Special Guest Lecture

#### PROTEOMICS OF THE VESSEL WALL

Manual Mayr, Professor

*Senior Fellow of the British Heart Foundation and Professor of Cardiovascular Proteomics, King's College London, UK*

Proteomics has made tremendous progress over the recent years. Initiatives, such as the Human Protein Atlas project, provide a great resource by capturing the *in vivo* location of proteins in different tissues and by making these data publicly available ([www.proteinatlas.org](http://www.proteinatlas.org)). Apart from the inherent limitations of antibody-based detection (antibody specificity, epitope masking, etc.), the only cardiovascular relevant tissue in the Human Protein Atlas is the heart. No large blood vessels are included in the tissue bank. At present, functional analysis tools do not capture some of the vascular proteins because these proteins are either only expressed during disease and/or not annotated as vascular proteins in the public databases.

Our group introduced new methods for the use of proteomics to study the vascular extracellular matrix and applied them to uncover extracellular