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# VASCULAR REMODELLING OF THE RETINAL MICROCIRCULATION IN HYPERTENSION AND DIABETES

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#### 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 RESPONSES 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  $100,100 \pm 13,900 \mu\text{m}^2$  at wk12 (control animals) and progresses to  $134,200 \pm 15,100 \mu\text{m}^2$  in sham by wk16, whereas it actually regresses by 53% in AVF in the same timeline ( $63,500 \pm 15,100 \mu\text{m}^2$ ;  $p < 0.02$ ). 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, (AFFPIA) 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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