



## Artery Research

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### **P2.04: ASSESSMENT OF BRACHIAL ARTERY REACTIVITY USING THE ENDOCHECK: REPEATABILITY, REPRODUCIBILITY AND PRELIMINARY COMPARISON WITH ULTRASOUND**

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Aix for the junction ( $p=0.001$ ), tube ( $p=0.011$ ) and aortic arch ( $p=0.016$ ) after adjustment to age sex and BSA. No independent relationship other functional parameters except for Pi and SCBP at the level of the descending aorta ( $p<0.05$ ). **Conclusion:** Aortic diameters were found to be related strongly to age, BSA, sex, and weakly to Zci, Aix and DCBP.

## P2 Methods 1

### P2.01

#### HIGH RESOLUTION IMAGING OF SMALL ARTERIES IN THE HUMAN RETINA DURING HYPERTENSIVE RETINOPATHY

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**Objective:** Morphological changes affecting small arteries are recognized surrogates of end-organ damage due to aging and/or hypertension. However, the corresponding structural modifications of the wall of microvessels are poorly known. Here, using adaptive optics (AO) infrared imaging, we analyzed the vascular microstructures in subjects with various degree of hypertensive retinopathy.

**Methods:** The wall-to-lumen ratio (WLR) of the superotemporal artery was measured in 40 normotensive or treatment-naïve hypertensive subjects using a semi-automated procedure. Areas of focal vascular damage were also analyzed.

**Results:** Intra- and interobserver reproducibility was high (ICC over 0.8 for all parameters measured). In treatment-naïve subjects, the WLR of the superotemporal artery (mean  $\pm$  SD  $0.31 \pm 0.08$ ) was independently correlated with diastolic blood pressure ( $p<0.01$ ), and lumen diameter ( $p<0.01$ ). Neither focal arteriolar narrowing (FANs; ( $n=10$ ) or arteriovenous nicking (AVNs;  $n=12$ ) showed parietal thickening. Instead, at sites of FANs, a reduction of the outer diameter was consistently found, while at sites of AVNs venous narrowing and retinal opacification were observed distal to the arteriovenous interface. In addition, in four cases of AVNs the absence of arteriovenous contact could be unequivocally demonstrated.

**Interpretation:** AO imaging allows a reproducible analysis of the lumen diameter and parietal thickness of retinal vessels. Parietal thickness of retinal arterioles was correlated to blood pressure, but not focal lesions which appeared to involve either focal vasoconstriction and/or periarteriolar changes. AO imaging may thus contribute to a better understanding of end-organ damage linked to microvasculopathy.

### P2.02

#### IN VIVO VISUALISATION AND RECONSTRUCTION OF THE MOUSE CEREBRAL VASCULATURE USING CONTRAST ENHANCED MICRO-CT

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**Introduction:** Recently, a mouse model was developed showing spontaneous plaque rupture leading to stroke (ApoE<sup>-/-</sup>Fbn1<sup>C1039G+/-</sup> mouse). However, a longitudinal follow-up of these mice was hampered by the lack of an accurate in vivo method to visualize the cerebral vasculature.

**Methods:** In this feasibility study, a female ApoE<sup>-/-</sup>Fbn1<sup>C1039G+/-</sup> and an ApoE<sup>-/-</sup> (control) mouse (stable plaques) were fed a western-type diet for up to 20 weeks. At week 10, 15 and 20 after the start of the diet CT-scans were performed before and after injection of a gold-nanoparticle contrast agent (Aurovist<sup>®</sup>, Nanoprobes, New York, USA). Image reconstruction was based on the iterative maximum-likelihood polychromatic algorithm, to reconstruct high quality images at 50- $\mu$ m. Post- and pre- contrast injection images were co-registered and subtracted, using 3D slicer, resulting in angiographic images. These images were segmented by executing a Frangi vesselness filtering, an isosurface extraction and a geodesic evolution step in VMTK.

**Results:** It was feasible to obtain a 3D-visualisation of the mouse cerebral vasculature (see figures for the ApoE<sup>-/-</sup>Fbn1<sup>C1039G+/-</sup> mouse) up to vessels of 0.15 mm diameter. Interestingly, at week 15 and 20 contrast agent from previous injections was still present in plaques (presumably taken up by macrophages), allowing us to determine plaque position and progression over time. More severe stenosis was observed in the ApoE<sup>-/-</sup>Fbn1<sup>C1039G+/-</sup> mouse compared to the control mouse.

**Conclusions:** The described in vivo method enabled us to generate detailed 3D reconstructions of the mouse cerebral vasculature, including presence of atherosclerotic plaques. Future work will include numerical models of the blood flow.

### P2.03

#### AORTIC, BUT NOT RADIAL PRESSURE GIVES A MODEL INDEPENDENT ESTIMATE OF CEREBRAL ARTERY CRITICAL CLOSING PRESSURE

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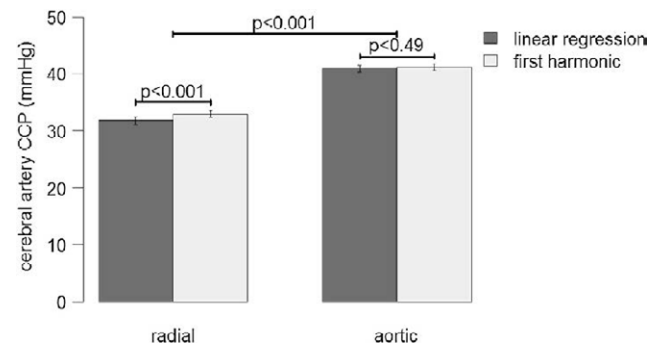
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**Objectives:** Cerebral artery critical closing pressure (CCP) is an estimated parameter with no single accepted method of calculation. Variation between methods could be significant. This study investigates two models to estimate CCP using arterial blood pressure (BP) and middle cerebral artery flow velocity (FV) waveforms, quantifying the difference between radial and aortic BP as the BP input signal.

**Methods:** Suspected and untreated hypertensive subjects ( $n=445$ , 203 female,  $50\pm 10$  years, range 21 to 73 years old), referred to Ruijin Hospital in Shanghai, China, for 24-hours BP monitoring, were recruited. Radial BP and FV waveforms were acquired by applanation tonometry and transcranial Doppler respectively. Aortic BP waveforms were synthesised from the radial waveform using a validated transfer function (SphygmoCor<sup>®</sup>). CCP was estimated using the relationship between BP and FV waveforms by both linear regression (LR), and the first harmonic (H1) in Fourier decomposition. The difference between the two models was quantified if the BP waveform input signal was radial or aortic and compared by Student's paired t-test.

**Results:** Use of aortic instead of radial BP resulted in a 29% increase in estimated CCP using the LR model, and 25% increase using the H1 model (Figure,  $p<0.001$ ). Radial BP resulted in variation between the models (4%,  $p<0.001$ ). Aortic BP did not cause this variation (0.6%,  $p=0.49$ ).

**Conclusions:** Aortic, but not radial pressure gave a model independent estimate of CCP. However, estimated CCP within a model was significantly different depending on whether radial or aortic pressure was used.



### P2.04

#### ASSESSMENT OF BRACHIAL ARTERY REACTIVITY USING THE ENDOCHECK: REPEATABILITY, REPRODUCIBILITY AND PRELIMINARY COMPARISON WITH ULTRASOUND

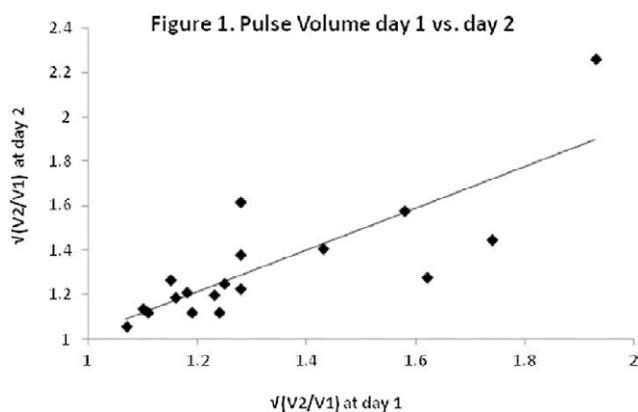
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**Objective:** The Endocheck, embedded within the Vicorder device, uses cuff-based, pulse volume (PV) displacement to record brachial PV waveforms at baseline, and during reactive hyperaemia. The aim of this study was to assess the utility of the Endocheck method.

**Methods:** The study consisted of two parts. Part 1: Healthy volunteers ( $n=9$ ) were studied twice, separated by 24hours. Each visit consisted of two studies, 30min apart, where, after 10min supine rest, brachial BP was assessed and PV waveforms recorded for 10sec (baseline). A cuff placed distally around the forearm was then inflated to 200mmHg for 5min. Following cuff-release, PV waveforms were recorded for 3min. The square root of the ratio of peak:baseline PV during hyperaemia ( $\sqrt{V2/V1}$ ) was calculated. Part 2: Healthy volunteers ( $n=16$ ) were studied once. Brachial artery responses were assessed simultaneously in both arms, using ultrasound (right arm) and Endocheck (left arm), following a similar protocol as above.

**Results:** Part 1: An average change in PV of  $74\pm 82\%$  was detected in response to forearm ischaemia ( $P=0.003$ ). Within-visit repeatability was acceptable, with a mean ( $\pm$ SD) difference in  $\sqrt{V2/V1}$  of  $0.03\pm 0.25$  ( $P=0.6$ ), and a high correlation between studies ( $r=0.64$ ;  $P=0.004$ ). Between-visit reproducibility was high, with a mean difference of  $0.004\pm 0.17$  ( $P=0.9$ ) and a strong correlation between readings ( $r=0.81$ ;  $P<0.0001$ ; Figure 1). Part 2: There was a modest association ( $r=0.14$ ,  $P=NS$ ) between hyperaemic responses assessed using the different methods.

**Conclusion:** The Endocheck can reliably assess changes in brachial PV during hyperaemia. Further studies are required to determine whether the observed changes reflect endothelial function.



#### P2.05

##### CAROTID PULSE WAVE VELOCITY CAN BE MEASURED USING MAGNETIC RESONANCE IMAGING IN PATIENTS WITH CAROTID ARTERY DISEASE

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**Objectives:** Carotid artery stiffness has been suggested to alter local haemodynamic and arterial remodelling. It has also been shown to be associated with ischaemic stroke. The aim of this pilot study is to assess the feasibility of measuring carotid pulse wave velocity (cPWV) using magnetic resonance imaging (MRI) in patients with carotid stenosis.

**Methods:** Patients with stenosis (30-99%) at the carotid bifurcation on duplex ultrasonography were recruited. Non-segmented through-plane velocity was acquired perpendicular to the internal and common carotid arteries to maximise velocity acquisition. Flow images were analysed to convert signal intensity to velocity. The time delay between the pulse waves was determined by plotting the velocity-time curve. The distance travel by the pulse waves was measured on carotid artery time-of-flight images.

**Results:** 22 patients (14 men, mean age  $73\pm 8$ ) with at least one carotid stenosis between 30% and 99% were assessed. Both the intra-class correlation for image acquisition reproducibility and flow data analysis were 0.99 ( $p<0.001$ ). The median (range) cPWV was highest in 30-49% ( $7.56$  m/s (range 4.49-10.64)) and 50-59% ( $6.47$  m/s (range 4.71-19.74)) stenosis with mean path length of 46mm.

**Conclusion:** Carotid pulse wave velocity in patients with carotid artery stenosis is feasible to be measured using MRI. This method is highly reproducible with good intra-observer consistency. Further work is needed to explain the pathophysiology of cPWV in patients with mild and moderate carotid stenosis.

#### P2.06

##### A NOVEL INFLATION TEST TECHNIQUE AND OPTICAL FLOW ESTIMATION FOR IN VITRO DETERMINATION OF THE CROSS-SECTIONAL DEFORMATION OF ARTERY

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**Objectives:** Determination of the cross-sectional mechanical properties of artery is crucial for correlating regional arterial stiffness with the biological components such as collagen, elastin, and deposited calcium. While

ultrasound imaging has been used to determine these properties from the arterial deformation, the accuracy of the measurements is limited due to non-direct imaging on the arterial cross-section. Therefore, we designed a novel inflation test technique allowing this direct imaging.

**Methods:** The test system provides internal pressures to an artery ring using a pump connected to a pressure transducer and a balloon tube (Figure 1). The cross-sectional deformation of the artery is captured using a camera. The images are then analysed using optical flow estimation which determines the deformations from pixel motions. This optical flow technique has been validated with images of a ring structure undergoing known deformations.

**Results:** This test system has been tested with pig aortas. The regional strains of an aortic ring sample are shown in Figure 2.

**Conclusions:** This inflation test design and the optical flow estimation allow *in vitro* determination of arterial regional strains at physiological pressures. A finite element model will be developed to correlate the deformations between the experiments and models to determine the regional mechanical properties of the artery. This approach will be used to investigate the associations of ageing-induced arterial stiffening with regional structural changes such as calcium deposition and elastin fragmentation, promoting the determination of target biological components for drugs.

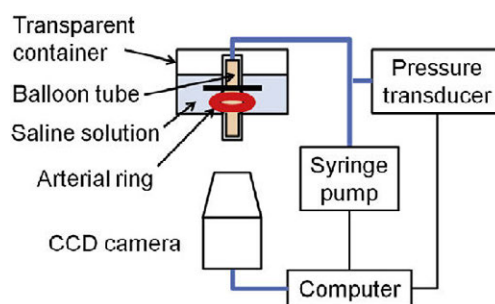


Figure 1 Inflation test system.

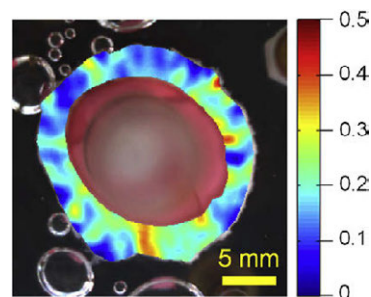


Figure 2 Calculated arterial strains.

#### P2.07

##### VALIDATION OF A NOVEL METHOD TO ASSESS ENDOTHELIAL FUNCTION

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**Objectives:** Assessment of pulse wave velocity (PWV) is normally used as a measure of arterial stiffness. However, measurement of change in PWV before and after a period of reactive hyperaemia may enable the technique to be harnessed as a measure of endothelial function as flow-mediated slowing (FMS). The aim of this study was to validate this approach as a novel method of endothelial function assessment.

**Methods:** FMS and flow-mediated dilatation (FMD) of the brachio-radial arterial tract was assessed in 25 young healthy subjects on two separate occasions to assess reproducibility. To assess the ability of the technique to investigate acute vascular dysfunction FMS and FMD was assessed before and after a 20-minute period of ischaemia-reperfusion (IR) in 15 healthy subjects. Finally, 12 Familial Hypercholesterolaemia patients undergoing lipoprotein apheresis had FMS assessed pre and post treatment.