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### **P137: ESTIMATING LEFT VENTRICULAR ELASTANCE FROM NONINVASIVE AORTIC FLOW AND BRACHIAL PRESSURE MEASUREMENTS**

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Nowadays employment world is increasingly shifting towards service-related labour, changing focus from physiological to psychological loads for workers. Thus, a deeper psychological stress understanding arises, not only for jobs within extreme conditions (as astronauts or pilots) but also for regular jobs with high emphasis on mental stressors. With the intend of developing a method and technology able to detect psychological stress we perform this pilot laboratory study in 14 male volunteers under stress and relax situations. As a stressor and the relaxer were used a standardized cognitive Paced Auditory Serial Addition Test (PASAT) and a relaxing video, respectively. Galvanic Skin Response (GSR) and Heart Rate (HR) were continuously measured as golden standard techniques to indicate physiological stress levels. Before each stimulus intervention a Braquial Blood Pressure were measured by standard Omron M6 apparatus. A continuous monitoring of Central Aortic Pressure (CAP) were assessed by non-invasive small WiFi sensors and equipment, developed by NMT, S.A., which allowed on-line detection and long-term effect of stress evaluation. HR and GSR measurements showed high variations under stressor application, proving physiological stress among volunteers and validating PASAT suitability. From analysis of obtained CAP data were found the good correlation with HR and GSR measurements in both, stress and relax sections. In addition of being a highly innovative study on mental stress detection, it is obvious the necessity of increase study population in future similar studies in lab and/or in the field condition.

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#### A COMPUTATIONAL INVESTIGATION OF CONFOUNDING FACTORS AFFECTING FLOW MEDIATED DILATION: TOWARDS IMPROVED ENDOTHELIAL FUNCTION ASSESSMENT

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**Objective and motivation:** Endothelial dysfunction is associated with cardiovascular diseases. Flow mediated dilation (FMD), assesses the endothelial function by measuring the brachial artery vasodilation following deflation of a sphygmomanometer cuff around the forearm. Vasodilation is assumed to be due to an increase in wall shear stress (WSS) only. However, there is evidence that the vasodilation may be affected by other confounding factors<sup>1</sup>. We aim to investigate the effects of confounding factors on the results of FMD. **Methods:** A dynamic simulation of FMD was carried out using a one-dimensional haemodynamic solver of blood flow in the arm arterial vasculature (Fig. 1a) <sup>2</sup>. Haemodynamics during cuff deflation was simulated by prescribing a decrease in peripheral resistance (Fig. 1b) in a novel mathematical model which dynamically couples increasing WSS (Fig. 1c) to decreasing arterial wall Young's modulus (Fig. 1d), taking into account endothelial function. **Results:** Our results show that the initial increase in flow velocity (Fig. 1e) is caused by the prescribed decrease in peripheral resistance and leads to an initial pressure drop affecting the FMD value. WSS induces a drop in Young's modulus leading to vasodilation (Fig. 1f). In addition, for the same prescribed endothelial function (relating WSS to Young's modulus variation) and decreased peripheral resistance, FMD increases with decreasing arterial stiffness (3.17% vs 5.31% vs 8.56% (Fig. 1f)). **Conclusion** Our numerical model successfully described FMD haemodynamics and highlighted one of the important confounding factors of FMD values: arterial stiffness. We are currently investigating other factors and ways of correcting those factors.

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#### SYSTEMIC CARDIOVASCULAR INPUTS IN MODELS ESTIMATING INTRACRANIAL PRESSURE MAGNITUDE AND WAVEFORM

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**Background:** Monitoring Intracranial Pressure (ICP) is key for appropriate clinical treatment of patients with conditions potentially causing raised ICP. The adequacy of using Heart Rate (HR), aortic Blood Pressure (aBP) and carotid Blood Flow (cBF) to estimate ICP magnitude (pulse and mean)

and waveform is investigated as an alternative means to invasive ICP measurement.

**Methods:** ICP (sequentially raised from resting ICP to 30–40 mmHg with infusions of artificial intracranial fluid), aBP (lowered with sodium nitropruside and raised with phenylephrine, 30 µg/kg/min, across a physiological range), HR (paced at 400 and 500 bpm), and cBF were measured in 11 anaesthetised Sprague Dawley rats. Potential cardiovascular predictors of ICP magnitude were assessed by stepwise mixed-model regression. Two transfer function models were constructed to estimate the ICP waveform from aBP or cBF waveforms.

**Results:** Systolic, mean and diastolic aBP as well as peak and minimum cBF had significant predictive value for mean ICP ( $p < 0.001$ ,  $R^2 = 0.25$ ). HR ( $p < 0.05$ ), systolic and mean aBP ( $p < 0.001$ ), peak ( $p < 0.001$ ), mean ( $p < 0.05$ ) and minimum ( $p < 0.01$ ) cBF had significant value for pulse ICP ( $R^2 = 0.35$ ). The transfer function models showed potential to reproduce the ICP waveform (Root Mean Square Error (RMSE)  $\leq 4$  mmHg), being more accurate for mean aBP above 100 mmHg and mean ICP below 20 mmHg (RMSE  $\leq 0.5$  mmHg).

**Conclusions:** The models developed from the comprehensive rat experiment demonstrated that systemic cardiovascular measures have predictive value in estimating the ICP magnitude and waveform, but other inputs may be necessary to improve accuracy in estimating ICP across the full physiological range.

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#### SIMULATING MYOCARDIAL OXYGEN BALANCE CHANGES DUE TO ANTI-HYPERTENSIVE DRUGS

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**Background:** Hypertension clinical treatment largely relies on different drugs. Some of these drugs are thought to exhibit specific protective functions in addition to those resulting from blood pressure reduction per se. Through a validated multiscale mathematical model of the cardiovascular system, we studied the impact of commonly-used antihypertensive drugs on myocardial oxygen supply–consumption balance, which plays a crucial role in type 2 myocardial infarction.

**Methods:** Forty-two wash-out hypertensive patients were included in this study. Patients' demographics, heart rate, brachial pressure, Left Ventricular (LV) volumes and carotid-femoral pulse wave velocity were used to set to patient specific condition a largely accepted benchmark data set describing generic healthy subjects. Starting from literature data, drugs effects were modeled by means of six coefficients, describing LV function, heart rate, peripheral resistances and arterial stiffness. These drug-specific sextuplets were used to multiply some parameters of each patient model to simulate drugs impact.

**Results:** Our results ascribed the well-known major cardioprotective efficiency of  $\beta$  blockers to a positive change of myocardial oxygen balance. This was due to the concomitant reduction in LV work and increase in coronary flow. Similarly, RAAS blockers induced several positive changes, but to a reduced extent. In contrast, calcium channel blockers seem to induce some potentially negative effects on myocardial oxygen balance.

**Conclusions:** Patient specific multiscale mathematical model is able to reproduce clinically-relevant changes in coronary hemodynamics and ventricular function driven by anti-hypertensive drugs. Further studies are needed to evaluate eventual clinical usefulness of in-silico modeling of anti-hypertensive drugs.

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#### ESTIMATING LEFT VENTRICULAR ELASTANCE FROM NONINVASIVE AORTIC FLOW AND BRACHIAL PRESSURE MEASUREMENTS

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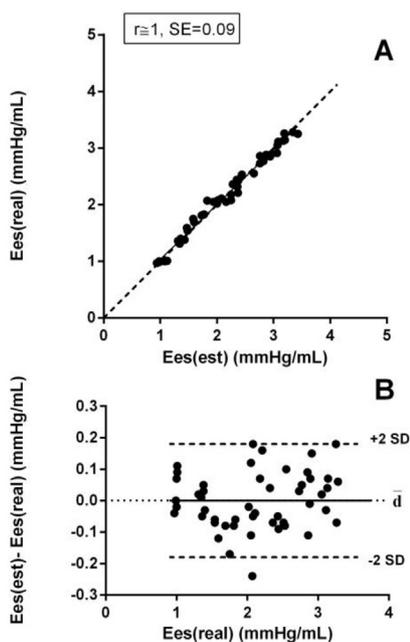
**Background and Aim:** Left Ventricular (LV) End-systolic elastance (Ees) serves as a major determinant of cardiac systolic contractility. Traditional Methods: to evaluate the ventricular mechanics directly from measurements require intraventricular pressure and volume recordings during an acute preload

alteration. The noninvasive derivation of Ees remains thus challenging. Here, we present a novel method to estimate the LV pressure-volume loop and elastance in humans from given aortic flow waveforms, LV ejection fraction and brachial pressure using a 1-D model of the cardiovascular system (1).

**Methods:** Initially, the measured aortic flow waveform is used as the input to the default 1-D model and the output brachial systolic and diastolic pressure are compared with the 'real' values. Subsequently, arterial compliance and peripheral resistance are modified accordingly until peripheral pressure is accurately predicted. In a second step, this person-specific model is used to estimate the elastance parameters that produce the 'real' aortic flow waveform. Additional knowledge of the LV ejection fraction can allow us to derive the entire pressure-volume loop, including end-diastolic elastance. The method was tested on a database of 50 different in silico hemodynamic cases generated after varying cardiac and arterial model parameters.

**Results:** Implementation of the method yielded good agreement ( $r = 0.99$ ) and accuracy ( $n\text{-RMSE} = 4\%$ ) between 'real' and estimated values of Ees (Figure 1). Furthermore, a sensitivity analysis revealed that errors due to poor arterial adjustment and measurements are small ( $\leq 8\%$  for Ees).

**Conclusion:** The insilico validation of the proposed method gave promising results and we are currently planning its testing against in vivo data.



**Figure 1.** A. Scatter plot of the method-derived Ees (Ees(est)) vs the 'real' values (Ees(real)) for the 50 simulated cases. B. the respective Bland-Altman plot

#### References

1. Reymond P, Merenda F, Perren F, Rufenacht D, Stergiopoulos N. Validation of a one-dimensional model of the systemic arterial tree. *Am J Physiol - Heart Circ Physiol.* 2009 Jul 1;297(1):H208–22.

#### P138

##### INFLUENCE OF ULTRASOUND SETTINGS ON CAROTID BIOMARKER ASSESSMENT BY B-MODE IMAGE PROCESSING

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**Purpose/Background/Objectives:** This study aims to investigate how image settings affect carotid Intima-Media-Thickness (IMT) and diameter estimation performed with CarotidStudio (Quipu Srl).

**Methods:** 14 healthy volunteers ( $24.4 \pm 4.4$  years; 8 men) were recruited. Longitudinal scans 3cm deep of common-carotid-arteries with the same region-of-interest were obtained by expert operator, starting from a "default" setup (central Time Gain Compensation-TGC; gain:50 dB; no persistence filter) and adjusting one parameter at a time (oblique TGC; gain:10 dB increments from 30 to 70 dB; persistence filter). The acquisition was performed twice and repeatability was expressed for each setup as coefficient of variation (CV). Significant changes ( $p < 0.05$ ) with respect to the "default" setup were analysed by paired Student-t-test.

**Results:** A 70 dB gain results in overestimating IMT (from  $0.46 \text{ mm} \pm 0.01 \text{ mm}$  to  $0.54 \text{ mm} \pm 0.01 \text{ mm}$ ), underestimating diameter (from  $6.04 \text{ mm} \pm 0.04 \text{ mm}$  to  $5.70 \text{ mm} \pm 0.23 \text{ mm}$ ), increasing their CVs (from  $2.14\% \pm 1.92\%$  to  $6.85\% \pm 5.23\%$  for IMT, from  $1.79\% \pm 1.22\%$  to  $4.77\% \pm 4.71\%$  for diameter) and in 4/14 cases the estimation wasn't possible. Distension CV increases also with 60 dB (from  $5.71\% \pm 4.31\%$  to  $10.84\% \pm 5.91\%$  and to  $12.59\% \pm 7.97\%$ ). Persistence and TGC do not affect repeatability, whereas diameter ( $5.96 \text{ mm} \pm 0.03 \text{ mm}$ ) and distension (from  $0.82 \text{ mm} \pm 0.02 \text{ mm}$  to  $0.66 \text{ mm} \pm 0.02 \text{ mm}$ ) values are influenced by persistence.

**Conclusions:** CarotidStudio precision does not show significant alterations except from 70 dB gain, which, due to the image grey-level saturation, results in poor image quality and modified values. Persistence does not affect precision but leads to reduced diameter and distension, possibly for the intrinsic behaviour of mathematical operator and image temporal filtering. Gain and persistence influence ultrasound biomarker estimation; the chosen setup should be documented and replicated in follow-up scans.

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##### AUTOMATIC CLASSIFICATION OF ARTERIAL AND VENULAR TREES IN COLOUR FUNDUS IMAGES

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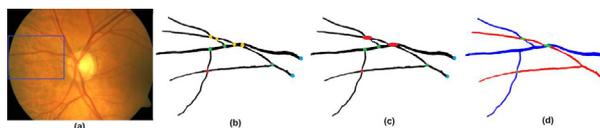
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**Background:** Quantitative imaging of retinal arterioles and venules offers unique insights into cardiovascular and microvascular diseases but is laborious. We developed and tested a method to automatically identify Arterial/Venular (A/V) vessels in digital retinal images in conjunction with a semi-automatic segmentation technique.

**Methods:** Segmentation of blood vessels and the Optic Disc (OD) was performed as previously described [1] using a dataset of X colour fundus images. Using the OD as a reference point a graph representation was constructed using the vessel skeletons. Vessel bifurcations and crossings were identified based on direction and local geometry, and A/V classification was carried out by fuzzy logic classification using colour information. Results were compared with expert classification.

**Results:** 157 arterial and 150 venular segments were classified. Preliminary Results showed sensitivity, specificity and accuracy of 42.20%, 99.21% and 97.73% for arteries and 50.89%, 98.70% and 97.54% for veins. An example is shown in Figure 1.

**Conclusions:** Computer-based systems can assess local and global aspects of the retinal microvascular architecture, geometry and topology. Automated A/V classification will facilitate efficient cost-effective assessment of clinical images at scale.



**Figure 1** (a) Colour image, rectangle crop area in (b)-(d), (b) segmented blood vessels, red crossing, green bifurcations, blue root and yellow ambiguous points, (c) ambiguous points corrected, and (d) classified vessels, red artery and blue vein.

#### Reference

1. Martinez-Perez et al. *Med Image Anal* 2007; 11(1):47-61.